B. Pharmacy

Semester- VII

ABSTRACT BOOK

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2025-26

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Research & Development (R&D) Cell and Internal Quality Assurance Cell (IQAC)

P.R. PATIL INSTITUTE OF PHARMACY

Talegaon (S.P.), Wardha, Maharashtra- 442 202

DECLARATION

This is to declare and certify that, the abstracts compiled in this book are based on the reports of the Practice School (BP706 PS) submitted by the students of the P.R. Patil Institute of Pharmacy, Talegaon (S.P.), Dist-Wardha as a part of the academic curriculum during the Academic Year 2025-26.

It is further certified that the published research papers included in this abstract book are outcomes derived from the Practice School projects carried out by the students during the Academic Year 2025-26 under the guidance of faculty members. These publications are included solely to highlight the academic and research contributions emerging from the Practice School projects.

The contents of this abstract book are intended strictly for academic, educational, and reference purposes only. The material shall not be used for any commercial purpose without prior written permission from the concerned authors and the Institute.

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Place: PRPIOP, Talegaon (S.P.)
Date: 15/12/2025

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FOREWORD

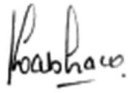
It gives me immense pleasure to present this 'Abstract Book' of Practice School Reports and Related Publications for the Academic Year 2025-26. The Practice School is an integral component of our academic curriculum, designed to bridge the gap between classroom learning and real-world professional practice.

Through this program, students gain valuable exposure to research environments, enabling them to apply theoretical knowledge, develop technical competence, and cultivate professional ethics. The abstracts compiled in this book reflect the diverse areas of study, problem-solving approaches, and research aptitude demonstrated by our students during their Practice School training.

A notable feature of this compilation is the inclusion of published research papers derived from Practice School work, which highlights the quality of training, mentorship, and research culture fostered at the Institute. These outcomes reaffirm our commitment to promoting experiential learning, innovation, and scholarly activity among students.

I sincerely appreciate the efforts of the students, faculty guides, and the Practice School Coordination Team, as well as the Research & Development (R&D) Cell and Internal Quality Assurance Cell (IQAC) for their dedicated contribution in compiling and presenting this academic document.

I am confident that this abstract book will serve as a valuable academic resource and a source of inspiration for students, faculty members, and stakeholders, encouraging continuous improvement and excellence in professional education.



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Abstracts Included in the Submitted Practice School Report

Published Scientific Papers Based on the Practice School Report

S. No.	Paper Title	Journal Name	Volume, Issue, Page No and Year
1.	In process testing for sustained release beads	European Journal of Pharmaceutical and Medical Research	12(12): 99-105, 2025
2.	A review on documentation and record management in the pharmaceutical industry	International Journal of Pharmaceutical Sciences	3(11): 1770-1783, 2025
3.	Calibration and qualification report of equipment used in sustained released bead- UV spectrophotometer	International Journal of Pharmaceutical Sciences	3(11): 3189-3196, 2025
4.	Sustained release beads: A short review	International Journal of Pharmaceutical Research and Development	7(2): 612-616, 2025
5.	Analytical instrument qualification: A comprehensive review on HPLC and UV systems	International Journal of Pharmaceutical Sciences	3(11): 2581-2593, 2025
6.	A review on analytical method validation as per ICH guidelines and protocols	International Journal of Pharmaceutical Sciences	3(11): 2595-2600, 2025
7.	An overview of liposome	International Journal of Pharmaceutical Sciences	3(11): 4191-4206, 2025
8.	Assuring aseptic integrity: Unified strategies for cleaning validation, environmental surveillance	European Journal of Pharmaceutical and Medical Research	12(12): 303-308, 2025
9.	An overview on UV spectroscopy with applications	International Journal of Pharmaceutical Sciences	3(11): 2925-2930, 2025
10.	Exploring documentation in modern pharmaceutical production and marketing	European Journal of Pharmaceutical and Medical Research	12(12): 285-291, 2025
11.	Validation study on reported UV method used for estimation of ibuprofen from marketed tablet preparation	International Journal of Pharmaceutical Sciences	3(11): 3302-3310, 2025

12.	Advances in oral thin films: Modern strategies for patient-centric drug delivery and global regulatory perspectives	Journal of Emerging Technologies and Innovative Research	12(11): e862-e879, 2025
13.	A review on calibration of pharmaceutical instruments	European Journal of Pharmaceutical and Medical Research	12(12): 126-132, 2025
14.	Performulation studies in sustained release development with experimental insights into drug polymer incompatibility	International Journal of Pharmaceutical Sciences	3(11): 2741-2744, 2025
15.	Integrating analytical method development, selection and validation in NDDS	European Journal of Pharmaceutical and Medical Research	12(12): 330-337, 2025
16.	Regulatory, uses and safety aspects of microbeads sustained released system in cosmetics	Journal of Emerging Technologies and Innovative Research	12(12): b667-b671, 2025

Abstracts Included in the Submitted Practice School Report

Abstract-1

In process testing for sustained release beads

D. Rathod, F. Pote, G. Dukare and H. Pandey

Supervisor- Dr. Chetan V. Ghulaxe

Abstract:

Novel Drug Delivery Systems (NDDS) are advanced approaches designed to deliver drugs at the right site, at the right time, and in the right concentration to achieve maximum therapeutic effect with minimal side effects. Unlike conventional dosage forms (tablets, capsules, injections), NDDS aim to overcome limitations such as poor bioavailability, frequent dosing, and fluctuating plasma drug levels. These systems use modern carriers like microspheres, nanoparticles, liposomes, niosomes, transdermal patches, implants, and beads to control the release, target specific sites, or protect drugs from degradation. NDDS can provide sustained, controlled, or targeted release, which improves patient compliance, reduces side effects, and enhances the overall safety and efficacy of therapy. Sodium alginate has been used as a matrix material to achieve controlled-release drug delivery due to its hydrogel forming properties. The ability of alginate sodium salt, to rapidly form viscous solutions and gels on contact with aqueous media has been exploited by the pharmaceutical industry in sodium alginate's wide application as a carrier in hydrophilic matrix controlled-release oral dosage forms. Matrices incorporating alginate salts have been employed to successfully prolong the release of many drugs. Evaluation parameters and in process testing of sodium alginate, Stability studies ensuring the maintenance of product quality, safety and efficacy throughout the shelf life are considered as pre-requisite for the acceptance and approval of any pharmaceutical product. Various parameters like size, friability, drug loading, swelling index, mathematical models of release kinetics.

Keywords: Sodium alginate, microbeads, NDDS, evaluation parameter, release kinetics.

Abstract-2

A review on documentation and record management in the pharmaceutical industry

H. Firdaus, J. Watsar, K. Mekalwar and K. Jepulkar

Supervisor- Dr. Vivek G. Pete

Abstract:

Documentation in the pharmaceutical industry is a critical component of quality assurance, regulatory compliance, and efficient manufacturing practices. It encompasses a wide range of records, including Standard Operating Procedures (SOPs), Master Formula Records (MFR), Batch Manufacturing Records (BMR), and in-process quality control (IPQC), Drug Master File (DMF) data. These documents provide a structured framework for planning, executing, and monitoring manufacturing activities, ensuring consistency and traceability of each batch. Proper documentation not only supports regulatory inspections and audits but also facilitates validation, reduces human errors, and enhances overall data integrity. In addition, it serves as a communication tool between different departments, ensuring that processes are clearly defined and deviations are promptly addressed. This review emphasizes the importance of meticulous documentation in maintaining compliance with Good Manufacturing Practices (GMP), improving operational efficiency, and safeguarding patient safety. It also highlights common challenges, such as documentation errors, incomplete records, and data management issues, and discusses strategies to overcome them, including digitalization and automated record-keeping systems. Overall, robust documentation practices are indispensable for achieving reliable, safe, and high-quality pharmaceutical products.

Keywords: Master formula record, SOP, in-process quality control, drug master file, stability studies.

Abstract-3

Calibration and qualification report of equipment used in sustained released beads by UV Spectrophotometer

S. Bhunte, S. Salunke, S. Shaha and S. Yawale

Supervisor- Ms. Trusha R. Gurnule

Abstract:

Calibration and qualification of analytical instruments are critical steps to ensure the accuracy, precision, and reliability of pharmaceutical analysis. In this study, the calibration and qualification procedures of the UV-1900i spectrophotometer manufactured by Shimadzu Corporation were carried out to evaluate its performance for the analysis of sustained release beads. The UV spectrophotometer was calibrated for wavelength accuracy, absorbance accuracy, stray light, and resolution using standard reference materials. Qualification activities were performed to verify that the instrument operates according to predefined specifications, ensuring compliance with regulatory standards. The study emphasizes that proper calibration and qualification enhance the reliability of analytical results, which is essential for the development and quality control of sustained release dosage forms.

Keywords: Calibration, qualification, uv-spectrophotometer, sustained release beads.

Abstract-4

Overview of sustained release beads

A. Sabane, B. Gandhre, B. Kolse and D. Ramdhan

Supervisor- Dr. Nilesh B. Banarase

Abstract:

Sustained release formulations are currently regarded as one of the most significant novel systems for the formulation of essential drugs. The sustained release system exhibits greater therapeutic activity of a drug in comparison to immediate release. This technique has been utilized in an aqueous outer phase for numerous water-insoluble monomers, both with and without the drug. The bead polymerization technique represents an emerging variant of this system, which has attracted considerable attention in pharmaceutical research due to its capacity to sustain therapeutic drug levels, decrease dosing frequency, and improve patient compliance. This review study encompasses a detailed examination of the preparation and evaluation of sustained release beads utilizing both natural and synthetic polymers, along with their physical properties such as particle size, shape, surface morphology, and drug content.

Keywords: Sustained release, sodium alginate, drug-loaded beads, polymers, cross linking.

Abstract-5

Basic calibration, qualification and SOPs preparation of HPLC and UV visible spectroscopy

S. Charpe, S. Metkar, R. Surjuse and S. Kardikar

Supervisor- Mr. Mohit A. Raut

Abstract:

Analytical instrument qualification (AIQ) is a fundamental requirement in regulated industries to ensure the accuracy, reliability, and consistency of analytical results. It provides documented evidence that instruments are properly designed, installed, operated, and maintained for their intended purpose. This review focuses on High Performance Liquid Chromatography (HPLC) and Ultraviolet-Visible (UV-Vis) spectroscopy, two of the most widely applied analytical techniques in pharmaceutical, clinical, environmental, and food sciences. The qualification process is categorized into four essential stages: Design Qualification (DQ), Installation Qualification (IQ), Operational Qualification (OQ), and Performance Qualification (PQ). Each stage is critical in establishing confidence that the instrument performs according to predefined specifications and regulatory expectations. The review also elaborates on the principles, instrumentation, and method development approaches associated with HPLC and UV-Vis systems. For HPLC, method development emphasizes chromatographic conditions, sample preparation, optimization of parameters, and validation to ensure reproducibility and accuracy. Similarly, UV-Vis spectroscopy, based on Beer– Lambert's law, is highlighted for its simplicity, cost-effectiveness, and versatility in both qualitative and quantitative analysis. Overall, this article integrates qualification protocols with practical insights into HPLC and UV-Vis methodologies, emphasizing their role in maintaining analytical quality assurance, regulatory compliance, and data integrity across research and industrial settings.

Keywords: Analytical instrument qualification, HPLC, UV-Visible spectroscopy, SOP, quality assurance.

Abstract-6

Overview of analytical method validation as per ICH guidelines and protocols

P. Gawande, P. Darange, P. Thakre and P. Ikhar

Supervisor- Mr. Vaibhav D. Dapurkar

Abstract:

Analytical method validation plays a vital role in the pharmaceutical sector, ensuring that test results remain accurate, reliable, and consistent throughout the stages of drug development and production. It establishes documented proof that an analytical technique is appropriate for its intended use and aligns with regulatory requirements. This review discusses the fundamental principles, procedures, and parameters of method validation, focusing on essential characteristics such as accuracy, precision, specificity, linearity, range, detection limit, quantitation limit, robustness, ruggedness, and system suitability. These parameters collectively confirm the dependability of methods applied in drug identification, impurity profiling, active ingredient assay, and formulation quality control. The article further distinguishes between full and partial validations, highlighting their significance in routine analysis, stability assessments, and process monitoring. In addition, the benefits of method validation—including enhanced product quality, prevention of batch rejections, cost savings, and regulatory adherence—are emphasized. By presenting current practices and acceptance criteria, this review offers a clear and comprehensive overview of analytical method validation, serving as a valuable resource for researchers, quality professionals, and students in pharmaceutical sciences.

Keywords: Analytical method validation, ICH guideline, parameters.

Abstract-7

Overview and development of standards operating procedure (SOP)

S. Salve, S. Ghatol, T. Agole, V. Kadu and Y. Talmale

Supervisor- Ms. Vaishnavi G. Bahe

Abstract:

The Standard Operating Procedure (SOP) serves as a documented guideline that outlines the step by-step instructions required to perform specific tasks consistently and effectively. The aim of preparing an SOP is to ensure uniformity, quality, and compliance with regulatory standards in laboratory and operational practices. The objectives include improving efficiency. Maintaining safety, minimizing errors, and ensuring that all personnel follow standardized methods. This document provides an overview of the process involved in developing an SOP from identifying the purpose and scope of the procedure, defining responsibilities, drafting and reviewing the content, to its approval and implementation. The preparation of an SOP involves collecting relevant data, consulting subject matter experts, formatting the document in a clear and concise manner, and validating its applicability through periodic review and updates. SOPs play a crucial role in maintaining operational control, ensuring safety, and enhancing the quality of outcomes in pharmaceutical and laboratory environments. The review further discusses shortcomings related to nonexistence of standard operating procedure including inconsistent quality of service; performance variation; procedural mix-ups; and misinterpretation or miscommunication of information. In conclusion, standard operating procedure, if realized and materialized as a component of an effective management system, helps cultivate transparent functions; implement error prevention measures and facilitate corrective actions and transfer knowledge and skill.

Keywords: SOP, documentation, purpose, preparation, quality.

Abstract-8

Assuring aseptic integrity: Unified strategies for cleaning validation and environmental surveillance

S. Mahure, S. Sable, S. Gawai, S. Doye and S. Raut

Supervisor- Ms. Vaishnavi Ghati

Abstract:

Assuring aseptic integrity is a critical component of sterile pharmaceutical manufacturing and depends on two interrelated programs: cleaning validation and environmental surveillance. Cleaning validation ensures that equipment, surfaces, and systems are free from residues of previous products, cleaning agents, and microbial contaminants. Environmental surveillance monitors the manufacturing environment to detect and control microbial and particulate contamination that could compromise product sterility. Current regulatory guidelines, including FDA (2020) and EU Annex 1 (2022), emphasize an integrated, risk-based approach linking these two systems. Unified strategies involve scientifically justified cleaning procedures, effective disinfectant rotation, monitoring of high-risk areas, trend analysis, and the use of rapid microbiological methods (RMMs) for timely decision-making. Biofilm control in water systems and cleanroom surfaces remains a major challenge requiring continuous improvement. Data-driven environmental monitoring programs help identify contamination sources and ensure consistent compliance with aseptic standards. The harmonization of cleaning validation results and environmental monitoring data supports root-cause investigations, corrective and preventive actions (CAPA), and continuous process improvement. Together, these strategies build a robust contamination control framework that maintains product safety, efficacy, and regulatory compliance.

Keywords: Aseptic integrity, cleaning validation, sterile manufacturing, biofilm control, FDA guidance.

Abstract-9

Fundamentals of UV visible spectroscopy- Preparation of sample and calibration curve

L.Ingole, L. Aglawe, M. Rithe and M. Niwal

Supervisor- Mr. Mahesh Gadge

Abstract:

UV-Visible Spectroscopy is a widely used analytical technique that measures the absorption of ultraviolet and light by chemical substances to determine their concentration and structural properties. It operates by passing light through a sample and recording the absorbance at specific wavelengths. The major components of a UV spectrophotometer include a light source, monochromator, sample cuvette, detector, and display system. The technique is fast, nondestructive, and suitable for routine quantitative and qualitative analysis in pharmaceutical research. The present study focuses on the development and validation of a simple, accurate, and precise UV–Visible spectrophotometric method for the estimation of Samples (Metronidazole). UV spectroscopy is based on the absorption of ultraviolet light (200–400 nm) by molecules, causing electronic transitions from lower to higher energy states. The analysis was carried out using a SHIMADZU UV–Visible double beam spectrophotometer (Model UV– 1900I) with quartz cuvettes. The standard solution of Metronidazole was prepared, and serial dilutions ranging from 0.5 to 2.0 µg/mL were analyzed. The wavelength of maximum absorbance (λmax) was observed at 321 nm. The calibration curve plotted between absorbance and concentration showed a linear relationship in accordance with Beer– Lambert's law, with absorbance increasing proportionally to concentration. The developed method was found to be accurate, reproducible, sensitive, and economical, making it suitable for the routine quality control and quantitative analysis of Metronidazole in bulk and pharmaceutical formulations.

Keywords: UV spectroscopy, Beer-Lambert law, electronic transition, metronidazole.

Abstract-10

Exploring documentation in modern pharmaceutical production and marketing

K. Meshram and K. Burange

Supervisor- Mr. Krunal Takarkhede

Abstract:

In the pharmaceutical industry, documentation is a key element of quality, safety, and compliance, and includes the master formula record (MFR), which is prepared by the research and development department and includes detailed information about the exact ingredients, raw material specifications, and the manufacturing steps required to create a product, the batch manufacturing record (BMR), which is a historical document that contains information about each step of the manufacturing process for an individual batch, including raw materials, equipment, and operators to ensure traceability, and standard operating procedures (SOPs), which provide written, step-by-step instructions for routine operations that help ensure accuracy, productivity, and consistency in pharmaceutical practices. Regulatory authorities at the national and international Level also take a vital role in protecting public health by assessing the safety, efficacy, and quality. Additionally, dossiers serve as official submissions to these authorities, containing comprehensive information on product safety, efficacy, manufacturing, labelling, and compliance, thereby enabling approval for international marketing. Collectively, these documentation practices form the backbone of modern pharmaceutical production marketing, ensuring high-quality medicines and global regulatory compliance.

Keywords: Documentation, marketing, SOP.

Abstract-11

Validation study on reported UV method used for estimation of ibuprofen from marketed tablet preparation

P. Ingale, P. Bargat, P. Bhonde, P. Jadhav and P. Mahajan

Supervisor- Mrs. Farah Khan

Abstract:

Ibuprofen is non-steroidal anti-inflammatory drug (NSAID) drug which used for relief of symptoms of arthritis, primary dysmenorrhea, and fever and as an analgesic. The aim of this study was to develop highly sensitive, selective and rapid quantitative analytical method for estimation of ibuprofen as well as evaluation of marketed tablet of ibuprofen (Brufen400). The drug shows absorption maxima at 226nm. The liner dynamic response was found to be in the concentration of 2-10µg/ml. The slop, intercept and correlation coefficient were found to be 0.0389, -0.0454 and 0.977091 respectively. The estimated amount of ibuprofen in marketed tablets was found to be 99.80±0.12%. The marketed tablets evaluated for weight variation, hardness, friability, and disintegration time and dissolution study. The tablets show acceptable weight variation as per pharmacopeial specification. Friability shows below 1% indicating good mechanical resistance of tablets. The marketed tablet shows average 5.4 kg/cm2 hardness which indicate good strength of tablets. The disintegration time varies from 5.53 min. to 7.34 min. and 97.16% drug release in 50 minutes. The newly developed method and the evaluation of marketed tablets can be used for analysis of ibuprofen of equal significant drug as well as evaluation parameters can be help for quality control and quality assurance of the drug.

Keywords: Ibuprofen, Brufen-400, UV spectrophotometric method, validation.

Abstract-12

Advances in oral thin films: Modern strategies for patient-centric drug delivery and global regulatory perspectives

R. Bhojane, R. Lokhande and R. Shelke

Supervisor- Ms. Samruddhi Khonde

Abstract:

Oral thin films (OTFs) have emerged as a cutting-edge drug delivery platform designed for enhanced patient centric care. These thin, rapidly dissolving films provide a convenient alternative to traditional oral dosage forms, enabling fast drug release and absorption through the oral mucosa, which bypasses first-pass metabolism and improves bioavailability. OTFs are particularly beneficial for paediatric, geriatric, and dysphagic patients who face difficulties swallowing tablets or capsules. Advances in manufacturing techniques, such as solvent casting, hot melt extrusion, and novel printing technologies including inkjet and 3D printing, have enabled precise dosing, personalized therapies, and rapid onset of action. The films can also incorporate taste masking and controlled release features, further improving patient compliance and therapeutic efficacy. On the regulatory front, global agencies are evolving guidelines to ensure safe, effective OTF quality control and manufacturing standards, fostering wider adoption. The OTF market is rapidly growing, reflecting the increasing demand for user-friendly, efficient drug delivery systems. Future directions explore multilayer films and multi-drug combinations, positioning OTFs as transformative solutions in modern pharmacotherapy and nutraceutical applications. This review elucidates these advances and regulatory perspectives underpinning the OTF landscape today and beyond.

Keywords: Oral thin films (OTF), patients-centric drug delivery, fast-dissolving films, regulatory guidelines, global market.

Abstract-13

Equipment calibration and verification report in compliance with good manufacturing practices standard for in house equipments

S. Pokale, S. Adokar, S. Wakilahmad, S.Inkane and S. Kadu

Supervisor- Ms. Tejaswini G. Malge

Abstract:

The present study focuses on the calibration and verification of in-house laboratory equipment, including the pH meter, weighing balance, and UV-visible spectrophotometer, in accordance with Good Manufacturing Practice (GMP) standards and relevant Pharmacopoeial requirements. Accurate and reliable analytical measurements are critical in pharmaceutical and research laboratories, and periodic calibration ensures data integrity, traceability, and compliance with regulatory guidelines. The pH meter was calibrated using standard buffer solutions at pH 4.00, 7.00, and 9.20 under controlled temperature conditions. The weighing balance was verified for accuracy, repeatability, linearity, and eccentricity using certified standard weights, confirming proper performance for routine analytical weighing. The UV-visible spectrophotometer was calibrated. All performance parameters were found to comply with the specified limits. The outcome of this study confirms that all three instruments are fit for routine analytical use, maintain compliance with GMP standards, and provide reliable and reproducible results.

Keywords: Calibration, weighing balance, pH meter, UV spectrophotometer.

Abstract-14

Formulation and kinetic modelling of matrix tablet for controlled drug delivery system

P. Barange and P. Khante

Supervisor- Ms. Samruddhi Khonde

Abstract:

Controlled drug delivery systems have become a vital advancement in pharmaceutical technology, offering clear benefits over conventional dosage forms. These systems are engineered to maintain consistent therapeutic drug concentrations in the bloodstream or target tissues for extended durations, thereby maximizing efficacy and minimizing side effects. Among oral controlled drug delivery methods, matrix tablets are widely recognized due to their simplicity, cost-effectiveness, and reliable provision of sustained and predictable drug release profiles. Matrix tablets consist of an active pharmaceutical ingredient uniformly dispersed within a hydrophilic, hydrophobic, or biodegradable polymer matrix that modulates the drug release rate and duration via diffusion, dissolution, or erosion mechanisms. The drug release behaviour is frequently described using mathematical models such as zero-order, first-order, and Higuchi kinetics. Zero-order models depict a constant release rate, first-order models depend on drug concentration, and the Higuchi model characterizes diffusion-controlled release. Various natural, semi synthetic, and synthetic polymers play crucial roles in modifying drug release characteristics and ensuring matrix stability. Progress in polymer science and kinetic modelling has enabled the development of more robust and patient-compliant formulations. Continued advancements in matrix-based controlled release systems demonstrate their potential to enhance therapeutic outcomes, reduce dosing frequency, and improve patient adherence. Overall, controlled release matrix tablets represent a promising and efficient strategy to achieve predictable, sustained, and targeted drug delivery in contemporary pharmaceutical applications.

Keywords: Sustained release, matrix tablet, zero-order kinetics, Higuchi model, polymer matrix.

Abstract-15

Practical aspects of novel drug delivery system

A. Mhaisgawli, A. Sirsat, A. Watane and A. Dukare

Supervisor- Dr. Vikrant Salode

Abstract:

Preformulation studies are crucial to formulation development because they offer crucial details regarding a drug's physicochemical and compatibility characteristics. In order to create a sustained release bead formulation that would prolong drug release and enhance patient compliance, the current study was conducted on molnupiravir. A controlled release system is necessary for molnupiravir, an antiviral medication with a short half-life, to maintain a constant plasma concentration and minimize frequent dosing. Solubility analysis, partition coefficient determination, melting point, drug stability, and organoleptic evaluation were among the preformulation studies carried out. FTIR spectroscopy techniques were used to evaluate drug-polymer compatibility studies in order to detect any potential interactions. The findings showed no appreciable alterations in the distinctive peaks, demonstrating that molnupiravir is compatible with the chosen polymers, including sodium, ethyl cellulose, and HPMC K4M.

Keywords: Molnupiravir, preformulation studies, incompatibility, FTIR, Sustained release bead.

Abstract-16

Integrating analytical method development, selection and validation In NDDS

L. Fating and L. Wange

Supervisor- Mr. Krunal Takarkhede

Abstract:

UV- Visible Spectroscopy is a widely used analytical technique that measures the absorption of ultraviolet and light by chemical substances to determine their concentration and structural properties. It operates by passing light through a sample and recording the absorbance at specific wavelengths. The major components of a UV spectrophotometer include a light source, monochromator, sample cuvette, detector, and display system. The technique is fast, non-destructive, and suitable for routine quantitative and qualitative analysis in pharmaceutical research. The present study focuses on the development and validation of a simple, accurate, and precise UV– Visible spectrophotometric method for the estimation of Samples (Metronidazole). UV spectroscopy is based on the absorption of ultraviolet light (200– 400 nm) by molecules, causing electronic transitions from lower to higher energy states. The standard solution of Metronidazole was prepared, and serial dilutions ranging from 0.5 to 2.0 µg/mL were analysed. The wavelength of maximum absorbance (λmax) was observed at 321nm. The calibration curve plotted between absorbance and concentration showed a linear relationship in accordance with Beer– Lambert's law, with absorbance increasing proportionally to concentration. The developed method was found to be accurate, reproducible, sensitive, and economical, making it suitable for the routine quality control and quantitative analysis of Metronidazole in bulk and pharmaceutical formulations.

Keywords: UV spectroscopy, Beer- Lambert law, electronic transition, metronidazole.

Abstract-17

Exploring sustained release beads: From theoretical concepts to practical comparative analysis

A. Zade, A. Nandagawali, A. Kokate and A. Bure

Supervisor- Dr. Koshish B. Gabhane

Abstract:

The present study focuses on the comparative evaluation of sustained release bead preparations and conventional tablet preparations highlights significant differences in drug release behaviour, therapeutic efficacy, and patient compliance. Sustained release beads are prepared using ionization technique. Conventional tablets were formulated by direct compression for rapid disintegration and dissolution. Sustained release beads are designed to control and prolong the release of active pharmaceutical ingredients, maintaining a more constant plasma drug concentration and minimizing fluctuations typical of conventional tablets. This steady release profile helps in reducing dosing frequency, thus improving patient compliance and reducing side effects associated with peak drug concentrations observed in conventional tablets. The preparation of sustained release beads often involves advanced techniques such as the use of biopolymer matrices, which allow for gradual drug diffusion and offer superior control over release kinetics compared to traditional tablets, which release their drug content rapidly after administration. Studies comparing these preparations have demonstrated that sustained release beads not only enhance the bioavailability of certain drugs but also contribute to prolonged therapeutic effects, reduced dosing frequency, and minimized risks of overdose, all of which are notable limitations of conventional tablet forms.

Keywords: Sustained release beads, conventional tablet, ionization technique, direct compression method, biopolymer matrices.

Published Scientific Papers Based on the Practice School Report

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IN PROCESS TESTING FOR SUSTAINED RELEASE BEADS

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ABSTRACT

Novel Drug Delivery Systems (NDDS) are advanced approaches designed to deliver drugs at the right site, at the right time, and in the right concentration to achieve maximum therapeutic effect with minimal side effects. Unlike conventional dosage forms (tablets, capsules, injections), NDDS aim to overcome limitations such as poor bioavailability, frequent dosing, and fluctuating plasma drug levels. These systems use modern carriers like microspheres, nanoparticles, liposomes, niosomes, transdermal patches, implants, and beads to control the release, target specific sites, or protect drugs from degradation. NDDS can provide sustained, controlled, or targeted release, which improves patient compliance, reduces side effects, and enhances the overall safety and efficacy of therapy. Sodium alginate has been used as a matrix material to achieve controlled-release drug delivery due to its hydrogel forming properties. The ability of alginate sodium salt, to rapidly form viscous solutions and gels on contact with aqueous media has been exploited by the pharmaceutical industry in sodium alginate's wide application as a carrier in hydrophilic matrix controlled-release oral dosage forms. Matrices incorporating alginate salts have been employed to successfully prolong the release of many drugs. Evaluation parameters and in process testing of sodium alginate, Stability studies ensuring the maintenance of product quality, safety and efficacy throughout the shelf life are considered as pre-requisite for the acceptance and approval of any pharmaceutical product. Various parameters like size, friability, drug loading, swelling index, mathematical models of release kinetics.[1]

KEYWORDS: Sodium alginate, Microbeads, NDDS, In-process Testing, Evaluation Parameter, Release kinetics.

INTRODUCTION

Sustained release beads are a type of drug delivery system designed to release medication gradually over a prolonged period. These beads are tiny particles containing medicine that dissolve or degrade slowly, providing a controlled and steady effect. The goal of sustained release beads is to improve treatment effectiveness and patient convenience by reducing the need for frequent dosing. the basic goal of therapy is to achieve a steady state blood or tissue level that is therapeutically effective and nontoxic for an extended period of time. The design of proper dosage regimen is an important element in accomplishing this goal. A basic objective in dosage form design is to optimize the delivery of medication so as to achieve a measure of control of therapeutic effect in the phase of uncertain fluctuation in the in vivo environment in which the drug release takes place. This is usually accomplished by maximizing drug availability, i.e. by attempting to attain maximum rate and extent of drug absorption however control of drug action through formulation also implies controlling bioavailability to reduce drug absorption rates. Multiple unit dosage forms such as microspheres or micro beads have gained in popularity as oral drug delivery systems because of more uniform distribution of the drug in the gastrointestinal tract, more uniform drug absorption, reduced local irritation and elimination of unwanted intestinal retention of polymeric material, when compared to non-disintegrating single unit dosage form. Microbeads are small, solid and free flowing particulate carriers containing dispersed drug particles either in solution or crystalline form that allow a sustained release or multiple release profiles of treatment with various active agents without major side effects.[2-3]

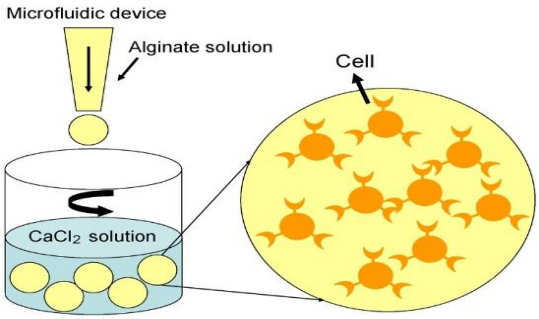

Fig. 1: Sodium Alginate Beads.

Advantages[4]

1. Biocompatibility: Alginate is a naturally derived polymer, making it biocompatible and non-toxic.
2. Mild Gelation Conditions: Alginate beads can be formed under mild conditions, preserving the activity of sensitive compounds.
3. Controlled Release: Alginate beads can provide sustained release of encapsulated compounds.
4. Targeted Delivery: Alginate beads can be designed for targeted delivery to specific sites in the body.

Disadvantages[4]

1. Limited Stability: Alginate beads can be unstable in certain environments, such as high pH or presence of chelating agents.
2. Rapid Release: Alginate beads can exhibit rapid release of encapsulated compounds, which may not be desirable.
3. Limited Mechanical Strength: Alginate beads can be fragile and prone to breakage.
4. Difficulty in Scaling Up: Alginate bead production can be challenging to scale up while maintaining uniformity.

METHODS OF PREPARATION OF ALGINATE BEADS

Alginate beads are made in different ways to get beads of uniform size and good production rate. These beads are usually made by pushing alginate solution (with drug) through a needle into a calcium solution, where they form solid beads. Methods like air-jet, electrical, and vibration systems can help make the process faster and more efficient.

1. Air Atomization

In this method, an extrusion device with a small opening (orifice) is used. The alginate solution containing the drug is pushed out through this small hole using air. Beads formed are between 5 to 200 micrometers in size. The bead size can be changed by adjusting the air pressure, liquid flow, or distance between the orifice and the calcium solution surface.[5]

2. Coaxial Bead Generator

In this method, air is used to pull droplets from the needle tip into a gelling bath (usually calcium solution). The beads formed are spherical and about 400 micrometers in size.

3. Dropping Method

This is the simplest and most common method. A syringe or pipette is used to drop the alginate solution into a calcium solution.[6]

4. Electrostatic Bead Generator

In this method, electrostatic (electric) force pulls small drops of alginate solution from the needle tip into a gelling bath. Beads formed are about 150 to 1000 micrometers in size. The size of beads depends on: The voltage used, The distance between the needle and gelling bath, The thickness (viscosity) and flow rate of the alginate solution, And the diameter of the needle.

5. Emulsification

This method is used only for stable drugs, because it needs strong chemicals to remove oil at the end. It forms small particles ranging from 1 to 150 micrometers. The size of the micro beads depends on: The stirring speed, And the rate of adding the cross-linking (gelling) solution.

6. Laminar Jet Break-up

Uses a device that breaks a liquid stream into beads (300-600 micrometers) by vibrating.

7. Mechanical Cutting

Cuts a liquid stream into small pieces that turn into round beads in a gel bath. Makes beads of 150 micrometers to 3 millimeters.

8. Spinning Disk Atomization

Uses a spinning disk to make beads of 300 to 600 micrometers.

9. Vibrating nozzle technique

This uses a special nozzle that vibrates to make tiny particles (more than 200m particles).[7]

10. Complex coacervation

This method uses stuff like gelatin and gum Arabic. When you mix them under certain conditions (like pH 3.9, ionic strength of 1mM, and polyion concentration of 0.15% w/v), they form microbeads.[8]

Sodium alginate beads are commonly prepared using the following method

1. Ionotropic Gelation Method

Ionotropic gelation (IG) is a phenomenon in which polyelectrolytes (PEs) come in contact with oppositely charged small molecules or macromolecules causing a liquid-gel phase separation, with the formation of a polymer-rich phase (gel) and a polymer-poor phase (liquid) surrounding the former.[9] The process is strictly governed by the experimental variables of the buffer medium, such as pH or ionic strength and the physico-chemical composition of the polyelectrolyte. This

method is usually employed for the synthesis of natural water-soluble polymeric nanoparticles with a high control in the release of bioactive materials by polymer relaxation. The hydrogel beads are synthesized by addition of drug-loaded polymeric solution drops to the aqueous solution containing a cationic polyelectrolyte.[10-12] Polymers usually involved in these processes are natural, hydrophilic and biodegradable ones, such as sodium alginate, gelatin, carboxymethyl cellulose and chitosan. Synthetic polymers can be also used (Table 1)[13-16]

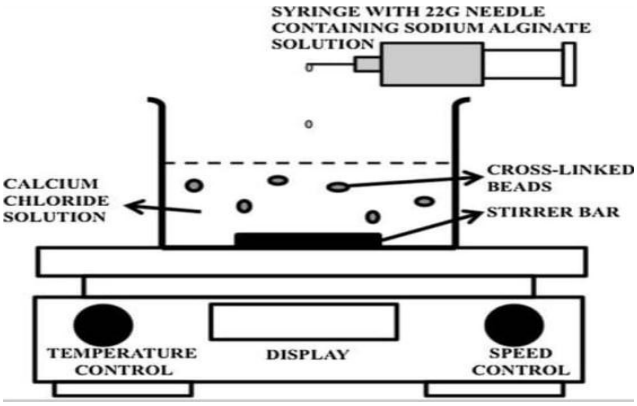

Fig. 2: Ionotropic Gelation Method.

Table 1[17]

Polymers and polyelectrolytes used in ionotropic gelation. Adapted from under open access CC-BY license.

Natural polymer	Synthetic monomers/Polymers	Multivaent Cation/ Anions
Chitosan	Hydroxyethyl methacrylate	Ca^{2+}, $Mo_7O_2^{6-}$,$(PW_{12}O_{40})^{3-}$
Alginate	N- (2-Hydoxypropyl) Methacrylate	K^+
Fibrin	N-Vinyl-2-Pyrrolidone	Fe^{2+}, Ba^{2+}, Na^+, Mg^{2+}
Collagen	N-isopropylacrylamide	Al^{3+}
Gelatin	Vinyl acetate	Zn^{2+}

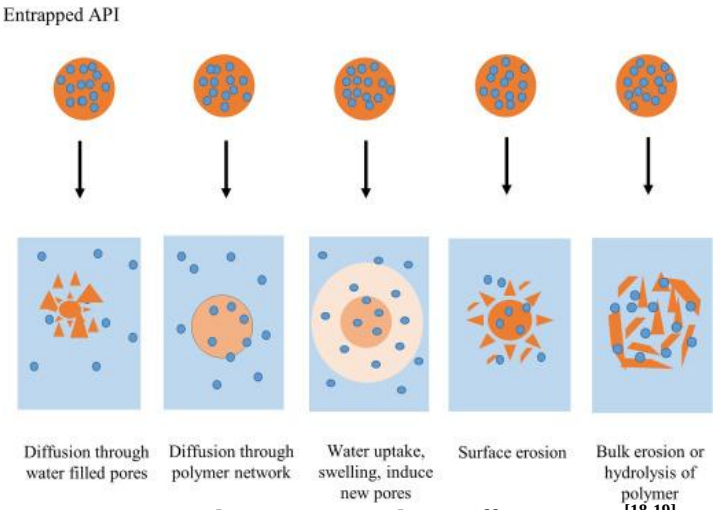

Fig. 3: Drug Release From Beads In Different Way.[18-19]

Advantages[20]

1) Mild conditions — suitable for heat- and solvent-sensitive drugs.
2) No need for harsh organic solvents.
3) Easy, low-cost, and reproducible.
4) Good control over size and drug release profile.

Disadvantages[21]

1) Poor mechanical strength of beads (especially alginate-based).
2) Possible burst release of drug.
3) Swelling or instability in physiological fluids (depending on polymer and cross-linker).

Table 2.

Sr. No	Drug Of Sustained Release Beads	Class of drugs	Methods Of Preparation	Mechanism Of Action	Application
1	Diclofenac Sodium[22]	NSAID	Ionotropic Gelation (Using Sodium Alginate Crosslinked With Cacl2)	It Inhibits Cyclooxygenase Enzymes (COX-1 And COX-2), Leading To Decreased Synthesis Of Prostaglandins, Which Are Responsible For Pain, Inflammation, And Fever.	Sustained Release To Reduce Dosing Frequency And Side Effects In Pain And Inflammation
2	Venlafaxine	Antidepressant	Ionotropic Gelation	1. Inhibiting Serotonin	Sustained Release

	Hydrochloride[23]	(SNRI)	With Sodium Alginate, Gelatin, Pectin	Reuptake: Increasing Serotonin Levels In The Brain. 2. Inhibiting Norepinephrine Reuptake: Increasing Norepinephrine Levels In The Brain.	For Prolonged Antidepressant Effect
3	Propranolol Hcl[24]	Beta-Blocker	Gelatin Bead Formation Method	1. Blocking Beta-1 Receptors: Decreasing Heart Rate, Contractility, And Cardiac Output. 2. Blocking Beta-2 Receptors: Reducing Smooth Muscle Contraction And Vasodilation.	Sustained Release For Hypertension And Cardiac Conditions
4	Metformin[25-26]	Anti-Diabetic Drugs	Ionotropic Gelation. Extrusion-Spheronization	1. Decreasing Hepatic Glucose Production: Reducing Gluconeogenesis. 2. Increasing Insulin Sensitivity: Enhancing Peripheral Glucose Uptake.	- Manage Type 2 Diabetes Mellitus: Improving Glycemic Control. - Reduce Risk Of Complications: Like Cardiovascular Events.
5	Aceclofenac[27]	BCS Class II Drug	Floating Beads Nanosponge-Based Drug Delivery System	Aceclofenac Works By Inhibiting Cyclooxygenase Enzyme (COX), Specifically COX-2, Which Is Involved In The Synthesis Of Prostaglandins. This Leads To Reduced Inflammation, Pain, And Swelling.	Aceclofenac Is Used To Treat Various Conditions, Osteoarthritis Rheumatoid Arthritis
6	Valsartan[25-26]	Angiotensin II Receptor Blocker (ARB)	Ionotropic Gelation Extrusion-Spheronization	- Blocking Angiotensin II Receptors: Reducing Vasoconstriction And Aldosterone-Mediated Volume Expansion. - Lowering Blood Pressure: By Relaxing Blood Vessels And Reducing Peripheral Resistance.	- Treat Hypertension: Managing High Blood Pressure. - Manage Heart Failure: Reducing Morbidity And Mortality.
7	Ceftriaxone Sodium[25-26]	Cephalosporin Antibiotic.	Ionotropic Gelation	Inhibiting Bacterial Cell Wall Synthesis: Binding To Penicillin-Binding Proteins (Pbps) And Disrupting Peptidoglycan Synthesis.	- Bacterial Infections: Such As Meningitis, Pneumonia, And Urinary Tract Infections. - Surgical Prophylaxis: To Prevent Surgical Site Infections.

- **Evaluation parameters and In-process testing of sodium alginate beads**

1. Size
2. Drug Entrapment
3. Swelling Index
4. Dissolution Test
5. In Vitro Drug Release Study

1. Size

An optical microscope fitted with an ocular and stage micrometer, having accuracy of 0.01 mm, was used to determine the particle size of the beads. Analysis of the prepared beads was performed using a resolution of 30× to determine the diameter of 10 randomly selected beads. The instrument was calibrated at 1 unit of eyepiece

micrometer equal to 1/30 mm (33.33 µm), and the average diameter of the beads was calculated using the following equation,[28]

$$X = \frac{\sum(X_i)}{N}$$

2. Drug Loading and Entrapment

Drug loading quantifies the actual amount of drug incorporated in the beads compared to the total bead weight, while entrapment efficiency measures the percentage of the initial drug amount successfully encapsulated inside the beads.[29]

$$\text{Drug Loading} = \frac{\text{Actual drug weight in beads}}{\text{Total weight of beads}} \times 100$$

$$\text{Drug Entrapment} = \frac{\text{Actual drug conent}}{\text{Theoretical drug content}} \times 100$$

3. Swelling Index

This study was conducted to estimate the percentage swelling of the beads that causes leaching or degradation of the drug in the gastric fluid. Only batches with an entrapment efficiency of more than 30 % were selected for further studies. Dried ionically, cross-linked beads increase their volume after few minutes in water or in buffers due to matrix rehydration that is dependent on the degree of cross-linking. 200 mg of beads were suspended in 50 ml of simulated gastric fluid (pH 1.2) and samples were shaken at 60 rpm speed in a mechanical shaker (Thermo Scientific™ Precision reciprocating shaker bath, USA) and allowed to swell for 2 h at 37 ± 0.5 °C, simulating the gastric medium. After 2 h, the beads were carefully removed, blotted dry and weighed. The difference between the initial and final weights of the beads was used to determine water sorption, and the swelling index was calculated using the following formula,[29-31]

$$\text{Swelling index} = \frac{W_f - W_o}{W_O}$$

Where,
W o is the initial weight of beads and
W f is the final weight of the beads after swelling.

4. Dissolution Test

Dissolution testing is a critical quality control and performance evaluation tool for sustained release (SR) dosage forms, including polymeric beads. The test simulates drug release from dosage forms under physiological conditions and helps to predict in vivo performance. The dissolution test plays a crucial role in assessing the release profile and ensuring batch-to-batch uniformity. It provides insight into the mechanism of drug release, which is essential for regulatory approval and formulation optimization. Beads are accurately weighed and introduced into the dissolution medium. Typically 37 ± 0.5°C with stirring speeds of 50–100 rpm. Aliquots are withdrawn at predetermined intervals and replaced with fresh medium. Drugcontent is determined spectrophotometrically or by HPLC.[32-35]

5. In Vitro Drug Release Study

The in vitro drug release studies were performed using Dissolution test apparatus. The dissolution medium was hydrochloric acid buffer (pH 1.2) for first 2 h and 7.4) for subsequent h. The microbeads were efficiency was calculated by the following 1601, Japan)16. Each double-sided carbon adhesive tapze and the scanning electron phosphate buffer (pH allowed to sink in the vessel containing 900 ml of dissolution medium and the release of Diclofenac sodium was investigated at about 50 rpm at temp 37 ± 0.5°C. During dissolution 10 ml aliquot was withdrawn at interval of 1 h and same was replaced with equal volume of fresh medium. The withdrawn samples were filtered through Whatmann filter paper no.42 and diluted with the same buffer to 10 ml. Absorbance was measured at 282 nm using UV-Visible Spectrophotometer.[36-37]

Comparative Study of In-Vitro Release

1. Comparative study of in-vitro release and bioavailability of sustained release diclofenac sodium from certain hydrophilic polymers and commercial tablets in beagle dogs
2. The study made beads of diclofenac sodium using sodium alginate or sodium CMC, crosslinked with aluminum.
3. In vitro, the beads showed no release in 0.1 N HCl for 2 h, then sustained release in pH 6.8 buffer over 24 h.
4. Bead size, polymer type/concentrations, and pH of dissolution medium affected release rate.[38]

➢ In vitro release study:

- Select release media: e.g. 0.1 N HCl for 2 h (simulate stomach), then pH 6.8 phosphate buffer (simulate intestine)
- Temperature: 37 ± 0.5 °C
- Agitation/stirring: e.g. USP dissolution apparatus I or II, rotation speed etc.
- Sampling at time points (e.g. 0.5, 1, 2, 4, 6, 8, 12, 24 h)
- Replace withdrawn volume with fresh medium to maintain sink conditions.[39]

Application of sustained release beads[40]

1. Sustained release beads serve as an effective drug delivery system that releases active pharmaceutical ingredients gradually over an extended period to maintain therapeutic drug levels in the body.
2. These beads improve patient adherence by reducing the frequency of drug administration due to their ability to sustain drug release.
3. Commonly utilized in oral formulations, they enhance the bioavailability of drugs with short half-lives and limited absorption windows.
4. The beads can be engineered using various natural or synthetic polymers, such as sodium alginate,

which control the drug release rate through gelation and diffusion mechanisms.
5. sustained release beads find applications in targeted drug delivery, including passive targeting of tumor sites and localized therapies, thereby improving therapeutic efficacy and minimizing side effects.
6. Their ability to float in gastric fluids further prolongs gastric residence time for drugs that require localized stomach absorption.

CONCLUSION

Sodium alginate beads as drug delivery systems provide several advantages, including greater flexibility and adaptability of dosage forms. alginate beads were easily and successfully formulated by employing the ionotropic gelation technique**.**

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Review Article

A Review on Documentation and Record Management in the Pharmaceutical Industry

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ABSTRACT

Documentation within the pharmaceutical industry plays a vital role in ensuring quality assurance, regulatory adherence, and smooth manufacturing operations. It includes various essential records such as Standard Operating Procedures (SOPs), Master Formula Records (MFR), Batch Manufacturing Records (BMR), In-Process Quality Control (IPQC) reports, and Drug Master File (DMF) data. These documents establish a systematic framework for organizing, executing, and tracking manufacturing processes, ensuring product consistency and complete batch traceability. Effective documentation not only aids in regulatory audits and inspections but also supports process validation, minimizes human error, and upholds data integrity. Moreover, it acts as a communication bridge between departments, providing clear process guidelines and enabling prompt management of deviations. This review underscores the significance of accurate and comprehensive documentation in maintaining Good Manufacturing Practice (GMP) compliance, enhancing operational performance, and protecting patient health. It further addresses common issues such as documentation mistakes, incomplete data, and record management challenges, while suggesting solutions like digital transformation and automated documentation systems. In summary, strong documentation practices are essential for producing safe, effective, and high-quality pharmaceutical products.

INTRODUCTION

Documentation:

A document refers to any written record or proof. the Quality Assurance (QA) and Quality Control (QC) systems and is closely associated with all aspects of Good Manufacturing Practices (GMP).

It primarily outlines the specifications for materials, manufacturing methods, and control

Documentation serves as a vital element of both procedures. Additionally, it ensures that all personnel involved in production have the

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necessary information to determine whether a batch should be released for sale. Documentation also provides an audit trail, enabling the investigation of any potentially defective batch.

Purpose of Documentation:

- Provides written evidence, traceability, and records, creating an audit trail for investigation.
- Ensures the availability of data required for validation, review, and statistical evaluation.
- Establishes clear specifications and procedures for materials, manufacturing, and control methods.
- Ensures that all staff members are aware of their responsibilities and timing of activities.
- Provides authorized personnel with complete and accurate information necessary for product release.

The pharmaceutical industry has shifted from paper-based to digital documentation for marketing authorization dossiers, emphasizing the need for long-term or permanent recordkeeping and the competencies required for managing digital records.

Proper documentation, including the Master Formula Record (MFR), Batch Manufacturing Record (BMR), and Standard Operating Procedures (SOPs), forms the foundation of the pharmaceutical quality management system. These documents are essential for maintaining uniformity in manufacturing, meeting regulatory guidelines, and ensuring complete traceability of each batch. They serve as official records that guide formulation, processing, and quality control, thus supporting compliance with Good Manufacturing Practices (GMP) and facilitating audits, process validation, and continual quality improvement.

Good Documentation Practices (GDP):

In the pharmaceutical industry, Good Documentation Practices (GDP or GDocP) refer to the principles that ensure the accuracy, reliability, and integrity of data recorded throughout the processes of drug development, registration, manufacturing, commercialization, and lifecycle management. Adhering to GDP minimizes errors during manufacturing and analysis, thereby protecting product quality, patient safety, and maintaining proper operational standards within manufacturing facilities. Regulatory authorities such as the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) mandate compliance with GDP through guidelines like the FDA's Code of Federal Regulations (CFR) and the European EudraLex. Additionally, the United States Pharmacopeia (USP) has issued general chapter <1029> on GDP, while other organizations, including the World Health Organization (WHO) and Health Canada, have also provided specific guidance. In the U.S., GDP is a key component of the Current Good Manufacturing Practices (cGMPs) framework.

Definition:

Good Documentation Practice (GDP) refers to the standards governing the preparation, maintenance, and management of documentation within the pharmaceutical sector. While some standards are set by the FDA, others are defined under cGMP regulations. Compliance with GDP is mandatory for pharmaceutical, biotechnology, and healthcare companies—as well as their suppliers—to avoid penalties and regulatory actions.

According to the WHO, the main purposes of GDP are to:

- Provide clear guidelines for creating, reviewing, approving, maintaining, correcting, verifying, and archiving documents.
- Ensure that all personnel involved in production understand their duties and the appropriate timing of actions.
- Guarantee that authorized personnel possess complete information to make decisions on product batch release.
- Maintain documented evidence, traceability, and records that enable effective investigation and audits.
- Ensure the availability of data for validation, evaluation, and statistical review.
- Define specifications and procedures for all manufacturing and control operations.
- Enhance operational efficiency and performance.
- Fulfill international and national regulatory requirements.

Objectives:

- To establish, monitor, and record all activities that directly or indirectly influence the quality of pharmaceutical products.
- To apply appropriate documentation standards depending on the document type.
- To ensure that documents remain accurate, complete, readable, and accessible throughout their lifecycle.
- To maintain error-free records, and in cases where corrections are necessary, ensure they are made with proper justification, signature, and date.
- To define the term "written" as any data recorded in a format that can be read and interpreted by humans.
- To prepare a Site Master File, which outlines the manufacturer's GMP-related operations and activities.

General Requirements:

1. Good documentation is a fundamental component of the quality assurance system.
2. Clearly written procedures help prevent mistakes that can occur through verbal communication, while proper documentation allows for tracking and verification of activities performed.
3. All documents should be carefully designed, prepared, reviewed, and distributed to ensure accuracy and reliability.
4. Each document must be reviewed, approved, signed, and dated by authorized and qualified personnel.
5. Documents should have clear, specific, and unambiguous content. Their title, purpose, and type must be explicitly stated. They should be well-organized, easy to verify, and all copies must be legible and clear.
6. Documents must be reviewed regularly and updated as needed. A proper control system

should ensure that outdated or superseded versions are not used and that only the current, approved versions are available.

7. Documents should not be handwritten; however, when information such as dates or signatures must be entered manually, it should be done clearly in permanent ink (not pencil). Adequate space should be provided for these entries.
8. Any corrections made in a document or record should include the signature or initials and date of the person making the change. The original entry must remain visible, and where applicable, the reason for the correction should also be documented.

Master Formula Record (MFR)

The Master Formula Record (MFR) is one of the most essential documents in the pharmaceutical industry. It serves as the "master recipe" for the

preparation of a drug product and contains detailed instructions on how each batch of medicine should be manufactured. The pharmaceutical industry is highly regulated, and no product can be manufactured without proper documentation. Among the documentation practices, the Master Formula Record plays a critical role in ensuring that every batch produced is consistent, safe, effective, and compliant with regulatory guidelines. The Master Formula Record (MFR) is a comprehensive document that specifies the formulation composition, list of raw materials, quantities, equipment required, and detailed manufacturing instructions. For SR formulations, the MFR also includes details about the polymer system or coating materials responsible for controlling the drug release rate. The MFR is prepared by the formulation development team and approved by the Quality Assurance (QA) department. Once approved, it acts as a reference for the preparation of Batch Manufacturing Records (BMR) and guides operators, supervisors, and quality control personnel during the production process. It acts as the foundation of Good Manufacturing Practices (GMP) because it provides step-by-step details of how a pharmaceutical product should be made, tested, packaged, and labeled.

Objectives of the Master Formula Record

- To provide a standardized set of instructions for manufacturing each dosage form.
- To ensure batch-to-batch consistency and reproducibility of drug products.
- To maintain product quality, safety, and therapeutic efficacy.
- To comply with regulatory requirements such as GMP, ICH, USFDA, and WHO guidelines.
- To provide a permanent reference document for audits, inspections, and regulatory submissions.

Contents of a Master Formula Record

According to international regulatory agencies such as WHO and USFDA, an MFR must contain the following information:

1. Product Information

- Name of the product (brand name and generic name).
- Dosage form (tablet, capsule, injection, etc.).
- Strength of the product (e.g., Diclofenac Sodium 100 mg SR).
- Batch size (e.g., 100,000 tablets).
- Description of the product.

2. List of Ingredients

- Name of active pharmaceutical ingredient (API).
- Names of excipients (binders, fillers, disintegrants, lubricants, etc.).
- Exact quantity of each ingredient per unit dose and per batch.
- Specifications of raw materials (purity, grade, and quality requirements).

3. Instructions

- Step-by-step details of the manufacturing process.
- Sequence of mixing, granulation, drying, blending, compression, coating, or filling.
- Critical process parameters (e.g., temperature, humidity, pressure, speed of equipment).
- Special precautions to be taken during processing.

•

4. Packaging Instructions

as weight variation, hardness, friability, and

Finished Product Specifications

the final product (appearance, colour, size, shape).

chemical specifications (assay, purity, uniformity).

specifications (if applicable). •

7. Signatures and Approvals

• Prepared by: Formulation scientist or

production pharmacist.

• Approved by: Head of Quality Assurance.

- Type of packaging material to be used (blister packs, bottles, strips, etc.).
- Quantity of packaging material required for each batch.
- Printing and labeling instructions.
- Storage conditions (temperature, humidity, protection from light).

5. In-process Controls

- Date of approval.

•

•

Tests to be performed during manufacturing such

and the patients consuming the medicine.

Objectives of Batch Manufacturing Record 6.

- • Description of
- • Physical and
- Microbiological

dissolution.

To provide documentary evidence of each step performed during manufacturing.

To ensure that the product was manufactured strictly according to the

- approved Master Formula Record.

To maintain traceability of raw materials, processing steps, and operators involved. To provide a reference during product recalls, complaints, or investigations.

• To demonstrate compliance with

GMP and

regulatory requirements.

operator signatures, and in-process control data. It ensures traceability of each batch and helps identify the source of errors in case of deviations.Every pharmaceutical company must maintain BMRs for all products and strengths manufactured, as per Good Manufacturing Practices (GMP) and regulatory requirements. It ensures traceability, accountability, and compliance, thereby protecting both the company

Batch Manufacturing Record (BMR)

The Batch Manufacturing Record (BMR) is one of the most important documents in the pharmaceutical manufacturing process. It is a detailed, step-by-step document that records the actual history of the manufacturing of a specific batch of a pharmaceutical product. While the Master Formula Record (MFR) provides the general blueprint or recipe, the BMR is the practical execution document that records how a particular batch was manufactured based on that master formula.The Batch Manufacturing Record (BMR) is prepared for every batch manufactured and contains details such as batch number, lot numbers of raw materials, equipment used,

- To serve as a legal document during audits and inspections.

Contents of a Batch Manufacturing Record

According to regulatory guidelines, a BMR should contain the following information:

1. General Information

- Product name (brand and generic).
- Dosage form (tablet, capsule, syrup, etc.).
- Strength (e.g., Metformin Hydrochloride 500 mg SR).
- Batch number.
- Batch size (e.g., 200,000 tablets).
- Date of manufacture and expiry.

2. List of Raw Materials Used

Names of APIs and excipients.

- Quantities weighed and used.
- Reference to the raw material batch numbers.
- Signatures of personnel who weighed and checked the materials.

3. Manufacturing Instructions and Processing Steps

- Detailed steps as per the MFR.
- Equipment used with equipment ID numbers. Time and date of each operation.
- Signatures of the operator and supervisor.
- In-process checks (e.g., blending uniformity, drying temperature, compression speed).

4. Packaging Details

- Type of packaging material used (blister, bottle, strip).
- Quantity of packaging material issued and used.
- Labeling instructions.
- Balance of unused packaging material and its reconciliation.

5. In-Process Quality Control (IPQC) Results

- Tests performed during manufacturing such as hardness, friability, weight variation, and dissolution.
- Acceptance criteria and actual results obtained.
- Signatures of quality control personnel.

6. Yield Reconciliation

- Expected yield as per MFR.
  Actual yield obtained (both in-process and final yield).
  Percentage yield.
- Any deviations or losses during manufacturing.

7. Signatures and Approvals

- Prepared by (production operator).
- Checked by (production supervisor).
- Verified by (quality assurance officer).
- Approved by (Head of QA).

Drug Master File (DMF)

A Drug Master File (DMF) is a confidential document submitted by manufacturers of Active Pharmaceutical Ingredients (APIs), excipients, or finished drug products to regulatory authorities such as the U.S. FDA. It contains comprehensive information on the chemistry, manufacturing processes, and quality control measures of a drug substance or component. DMFs are primarily used to provide regulatory authorities with detailed technical data while protecting proprietary information.

Role of DMF:

- The Drug Master File (DMF) records the purity, potency, and identification of drugs in the Chemistry, Manufacturing & Controls (CMC) segment.
- It aids in preparing registration or approval paperwork for drugs.
- It safeguards confidential and proprietary information

Fig. Schematic representation of drug master file mechanism

Purpose of a DMF:

- **Regulatory Support**: Assists in the approval process for drugs by providing detailed Chemistry, Manufacturing, and Controls (CMC) information.
- **Confidentiality**: Protects sensitive manufacturing information and trade secrets from being disclosed to third parties.
- **Collaboration**: Enables multiple pharmaceutical companies to use the same API or intermediate without revealing proprietary processes.
- **Internal Reference**: Supports internal documentation, validation, and IND (Investigational New Drug) applications.

Types of DMFs:

DMFs are categorized based on the type of information they provide:

- **Type I**: Manufacturing Site, Facilities, Operating Procedures, and Personnel (rarely used now).

- **Type II**: Drug Substance, Drug Substance Intermediate, and Material Used in Their Preparation.
- **Type III**: Packaging Materials.
- **Type IV**: Excipients, Colorants, Flavorings or Materials Used in Drug Formulation.
- **Type V**: FDA-accepted reference information (any other information supporting CMC)

Contents of a DMF:

- Chemical Information: Structure, properties, and specifications of the drug substance or excipient.
- Manufacturing Process: Detailed description of synthesis, processing, in-process controls, and equipment.
- Quality Control: Analytical methods, specifications, impurity profiles, and stability data
- Packaging and Storage: Container-closure systems, labeling, and storage conditions.
- cGMP Compliance: Evidence of adherence to current Good Manufacturing Practices.

Importance of DMFs:

- Ensures consistency, quality, and safety of drug substances and products.
- Protects intellectual property while facilitating regulatory review.

  Streamlines drug development by avoiding duplication of technical data.
- Serves as a critical tool in global regulatory compliance, especially for multinational companies.

Standard Operating Procedures (SOPs)

SOPs are detailed written instructions to perform specific processes consistently. In SR formulations, SOPs are required for critical steps like granulation, compression, coating, cleaning of equipment, and packaging. They ensure standardization and compliance with GMP. In the pharmaceutical industry, Standard Operating Procedures (SOPs) are one of the most critical elements of documentation and quality management. An SOP is a written, step-by-step instruction that describes how to perform a particular task or operation in a consistent and controlled manner. It ensures that processes are carried out uniformly every time, regardless of who performs them, thereby minimizing errors and variations. Pharmaceutical manufacturing is a highly regulated industry where quality, safety, and compliance with Good Manufacturing Practices (GMP) are non-negotiable. Regulatory agencies such as the World Health Organization (WHO), US Food and Drug Administration (USFDA), European Medicines Agency (EMA), and Central Drugs Standard Control Organization (CDSCO, India) mandate the preparation and use of SOPs in all pharmaceutical operations.SOPs act as the backbone of training, compliance, and quality control, serving as evidence during audits and inspections. Without approved SOPs, no activity in a pharmaceutical plant can be carried out legally or effectively.

Objectives of SOPs

- To ensure consistency and uniformity in all activities.

  To minimize human errors and reduce variability.

  To provide clear instructions for routine operations.
- To train new employees and refresh existing staff on standard practices.
- To comply with GMP and other regulatory requirements.
- To serve as a reference document during internal and external audits.

- To maintain product quality, patient safety, and company reputation.

General Format of an SOP

A typical pharmaceutical SOP includes the following sections:

1. Title Page

- SOP title (e.g., "Cleaning of Fluid Bed Dryer").
- SOP number and version.
- Department name.
- Effective date and review date.
- Prepared by, reviewed by, and approved by signatures.

2. Objective

Clearly states the purpose of the SOP.

3. Scope

Defines the area of application (e.g., applicable in the granulation section of the production department).

4. Responsibilities

Lists the personnel responsible for performing, checking, and approving the activity.

5.Definitions (if required)

Provides meaning of technical terms used in the SOP.

6.Materials/Equipment Required

Specifies tools, raw materials, or instruments needed.

7. Procedure

Step-by-step description of the activity to be performed.

Includes precautions, critical control points, and acceptance criteria.

8. References: Cites related guidelines, regulations, or documents.

9. Annexures/Attachments

Includes forms, checklists, or flowcharts to support the SOP.

10 .Revision History

Records details of any changes made in previous versions.

Types of SOPs in the Pharmaceutical Industry

SOPs are broadly classified into the following categories:

1.General SOPs

2.Production SOPs

3.Quality Control (QC) SOPs

4.Quality Assurance (QA) SOPs

5.Safety and Environmental SOPs

6.Engineering and Maintenance SOPs

7.Warehouse and Distribution SOPs

In-Process Testing Reports

In pharmaceutical manufacturing, quality cannot be tested into a product; must be built into the product. This principle, highlighted by Good Manufacturing Practices (GMP), emphasizes that ensuring product quality is not limited to testing the final drug but also involves monitoring every stage of production. In-Process Quality Control (IPQC) refers to the checks and tests carried out during the manufacturing process, rather than after completion. These controls help to detect and correct errors at an early stage, preventing defective batches and ensuring uniform quality. IPQC is considered a critical component of the pharmaceutical quality system because it ensures that the finished product consistently meets its specifications. IPQC testing is documented in InProcess Testing Reports, which serve as proof that controls were performed and that the batch met required standards before further processing. Inprocess quality control (IPQC) is essential for maintaining batch uniformity.

Typical tests include:

- Weight variation
- Hardness and friability
- Content uniformity
- Dissolution profile over 12–24 hours

Objectives of In-Process Quality Control

- To monitor the production process in real-time and ensure compliance with approved procedures.
- To identify and correct deviations during manufacturing before they affect the final product.
- To minimize batch failures, rework, and wastage.
- To ensure uniformity, safety, and efficacy of pharmaceutical products.
- To provide documentary evidence of compliance for audits and inspections.
- To maintain product quality and patient safety at all times.
- Parameters Checked During In-Process Quality Control
- IPQC varies depending on the dosage form. Below are the common tests:
- **1.For Tablets**
- Weight Variation Test: Ensures uniformity in tablet weight.
- Hardness Test: Determines the mechanical strength of tablets.
- Friability Test: Assesses resistance to breaking or crumbling.
- Disintegration Test: Ensures tablets break down within the specified time.
- Thickness and Diameter: Checked using vernier calipers.
- Appearance: Tablets should be free from cracks, spots, or contamination.

2.For Capsules

- Weight Variation: Ensures uniform filling of capsules.
- Disintegration Time: Should fall within pharmacopeial limits.
- Moisture Content: Measured to prevent microbial growth.

3.For Liquids and Syrups

- pH Measurement: Ensures stability and palatability.
- Viscosity: Checked to ensure proper consistency.
- Appearance: Free from particulate matter.

4.For Injections (Parenteral)

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Clarity Test: Must be free from visible particles.

pH and Osmolarity: Should be within safe physiological limits.

- **Sterility Checks (preliminary):** Ensures aseptic processing.
- **Volume in Container:** Ensures correct filling of vials or ampoules.

5.For Ointments and Creams

- **Consistency:** Smooth and uniform texture.
- **pH Measurement:** Must be skin-compatible.
- **Spreadability:** Checked for patient acceptability.
- **Documentation:** In-Process Testing Reports
- Every in-process check must be documented in an official In-Process Testing Report. This ensures traceability and accountability.

A typical format includes:

1.Product Details

- Product name, dosage form, and strength.
- Batch number and batch size.
- Date and time of testing.

2.Test Parameters and Specifications

- Lists the in-process tests (e.g., hardness, friability, pH).
- Provides reference limits as per pharmacopeia or MFR.
- Records the actual test results obtained.

4.Remarks

Notes any deviations or special observations.

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5.Signatures

- Signed by production personnel performing the test.

- Verified by Quality Control or Quality Assurance staff.

Strategies for Effective IPQC

- Regular training of production and QC staff.
- Use of validated equipment and calibrated instruments.
- Implementation of electronic data management systems (EDMS) for recording results.
- Periodic internal audits to ensure compliance.
- Strict supervision by QA at every stage of production.

Stability Studies

Stability studies are performed to evaluate the shelf life of formulations. Both accelerated stability studies (40°C/75% RH) and long-term stability studies (25°C/60% RH) are conducted. Reports are generated to ensure the release profile remains consistent throughout the product's life cycle. Pharmaceutical products are expected to remain safe, effective, and of acceptable quality throughout their intended shelf life. However, drugs are chemical entities and may degrade over time due to factors such as temperature, humidity, light, and microbial contamination. To ensure that a drug product maintains its intended quality until its expiry date, stability studies are conducted. Stability studies are systematic investigations carried out to determine how the quality of a drug substance or drug product changes over time under the influence of various environmental factors. These studies help establish shelf life, storage conditions, and recommended packaging materials. Regulatory bodies such as the International Council for Harmonisation (ICH), USFDA, WHO, and CDSCO (India) have issued detailed guidelines for conducting stability studies. These guidelines form the backbone of stability testing programs worldwide.

Objectives of Stability Studies

- To determine the shelf life (expiry date) of pharmaceutical products.
- To recommend suitable storage conditions (e.g., "Store below 25 °C, protect from light").
- To select appropriate packaging materials that protect the product from degradation.
- To evaluate the impact of environmental factors such as temperature, humidity, and light.
- To ensure compliance with regulatory guidelines.
- To guarantee patient safety by ensuring product quality throughout its lifecycle.

Types of Stability Studies

Stability studies are classified into several types depending on the conditions and objectives: **1. Real-Time Stability Studies**

- Carried out under recommended storage conditions.
- Provide actual data on product stability over the intended shelf life.
- Time-consuming (can last 12–36 months).

2. Accelerated Stability Studies

- Conducted at higher stress conditions (e.g., higher temperature and humidity).
- Provide quick data on degradation patterns.
- Help predict shelf life within a short period. **3. Intermediate Stability Studies**

- Conducted under conditions between real-time and accelerated studies.

- Useful when accelerated studies show significant degradation.

4. Stress Testing (Forced Degradation Studies)
Subject the drug to extreme conditions (heat, light, oxidation, acidic and basic environments).

- Helps identify degradation products and pathways.
- Provides data for developing stabilityindicating analytical methods.

5. Ongoing Stability Studies

- Conducted after product approval and during commercial manufacturing.
- Ensures that marketed batches remain stable until expiry.

Factors Affecting Stability

Stability of pharmaceutical products is influenced by several factors:

- **Temperature**: Higher temperatures accelerate degradation reactions.
- **Humidity**: Promotes hydrolysis, microbial growth, and physical changes.
- **Light:** Causes photodegradation of lightsensitive drugs (e.g., nifedipine, riboflavin).
- **Oxygen**: Leads to oxidative degradation of drugs like vitamin C.
- **pH of Formulation:** Affects hydrolysis rate; e.g., esters degrade faster in alkaline pH.
  Packaging Material: Poor packaging may allow moisture or oxygen ingress.
  Formulation Excipients: Certain excipients may accelerate or retard degradation.

Parameters Evaluated in Stability Studies

- Stability testing involves monitoring various physical, chemical, and microbiological parameters over time:
- Physical Parameters: Appearance, color, odor, dissolution rate, hardness (for tablets), viscosity (for liquids).
- Chemical Parameters: Assay of active ingredient, degradation products, pH, preservative content.
- Microbiological Parameters: Sterility (for injectables), microbial limits (for nonsterile products), preservative efficacy.
- Functional Parameters: Drug release profile, performance of delivery system (e.g., inhalers).

ICH Guidelines for Stability Studies

The International Council for Harmonisation (ICH) has defined stability testing conditions based on climatic zones:

Table:-Stability testing conditions based on climatic zone

Climatic Zone	Storage Condition	Example Regions
Zone I	21 °C/45% RH	Temperate climate
Zone II	25 °C/60% RH	Subtropical, Mediterranean
Zone III	30 °C/65% RH	Hot and dry countries
Zone Iva	30 °C/65% RH	Hot and humid
Zone IVb	30 °C/75% RH	Hot and very humid(India, Southeast Asia)

Standard Testing Conditions (ICH Q1A):

- Long-term (real-time): 25 °C ± 2 °C / 60% RH RH for 12–24 months.
- Accelerated: 40 °C ± 2 °C / 75% RH ± 5% RH for 6 months.
- Intermediate: 30 °C ± 2 °C / 65% RH ± 5% RH ± 5% for 6–12 months.

CONCLUSION:

Documentation and record management form the foundation of pharmaceutical quality assurance and are indispensable for ensuring that all operations comply with regulatory and Good Manufacturing Practice (GMP) standards. Every document — including the Master Formula Record (MFR), Batch Manufacturing Record (BMR), Standard Operating Procedures (SOPs), Drug Master File (DMF), In-Process Quality Control (IPQC) reports, and Stability Study records — contributes to the overall framework that governs product quality, safety, and efficacy. Together, these documents establish a transparent, traceable, and verifiable system for monitoring manufacturing processes from raw material procurement to the release of the finished product. Effective documentation minimizes the risk of human error, facilitates communication across departments, and serves as a legal and regulatory requirement during audits and inspections. It also provides a comprehensive record of all processes and decisions, ensuring accountability and consistency across batches. Good Documentation Practices (GDP) further enhance the credibility and reliability of data by emphasizing clarity, accuracy, completeness, and timely recording of all information. Regulatory authorities such as WHO, USFDA, and EMA strictly mandate adherence to GDP and cGMP to ensure that pharmaceutical companies maintain high standards of quality and safety. In the modern pharmaceutical landscape, the transition from paper-based to digital documentation systems has brought significant advancements. Electronic Data Management Systems (EDMS) and automation technologies have improved data integrity, accessibility, and long-term record preservation. These systems enable real-time tracking, faster approvals, and efficient document retrieval, thereby reducing manual errors and improving overall productivity. Moreover, digital record management supports sustainability by minimizing paper use and storage requirements. Ultimately, well-maintained documentation and records are not just regulatory necessities but strategic assets that enhance operational efficiency, product reliability, and patient safety. They enable continuous process improvement, foster a culture of quality, and strengthen the global competitiveness of pharmaceutical organizations. As the industry continues to evolve, integrating modern digital tools and fostering a documentation-driven quality culture will be essential for ensuring consistent compliance,

innovation, and the delivery of safe and effective medicines to patients worldwide.

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Review Paper

Calibration and Qualification Report of Equipment Used in Sustained Released Bead- UV Spectrophotometer

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ABSTRACT

To ensure the precision, accuracy, and reliability of pharmaceutical analysis, analytical instrument calibration and qualification are essential processes. The UV-1900i spectrophotometer, which is made by Shimadzu Corporation, was calibrated and qualified in this study in order to assess how well it performed when used to analyze sustained release beads. Standard reference materials were used to calibrate the UV spectrophotometer for resolution, stray light, wavelength accuracy, and absorbance accuracy. In order to ensure compliance with regulatory standards, qualification activities were carried out to confirm that the instrument performs in accordance with predetermined specifications. The study highlights how accurate calibration and qualification improve analytical data' reliability, which is crucial for the development and quality assurance of sustained release dosage forms.

INTRODUCTION

Calibration is essential in pharmaceutical analysis to guarantee that analytical tools like pH meters, balances, UV spectrophotometers, and HPLC produce precise and repeatable results [1,2]. Because faulty instruments can produce incorrect results that impact drug quality, safety, and compliance, it is an essential requirement under Good Laboratory Practices (GLP) and regulatory requirements. In order to preserve the integrity of analytical data, calibration is therefore both a quality assurance process and a legal necessity in the pharmaceutical industry [3].

One of the most common analytical tools for pharmaceutical quality assurance, research, and development is the UV-visible spectrophotometer. It works on the basis of the Beer-Lambert rule, which links absorbance to concentration, and measures how much visible (400–800 nm) and ultraviolet (200–400 nm) light is absorbed by molecules. UV spectrophotometry is frequently used for drug assay, dissolution studies, impurity

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detection, and kinetic investigations due to its sensitivity, ease of use, and accuracy [4].

The UV spectrophotometer must be calibrated in order to guarantee the accuracy of analytical results. The process of checking and adjusting an instrument's accuracy in relation to pharmacopeial or approved standards is known as calibration [5]. It involves studying important performance parameters like resolution, baseline stability, stray light, wavelength accuracy, and absorbance accuracy. Reference standards including potassium dichromate, holmium oxide, and toluene in hexane are frequently used for this purpose.

UV spectrophotometers must be calibrated on a regular basis by regulatory bodies and pharmacopeias (such as USP, IP, BP, and EP) in order to preserve data integrity, verify methods, and adhere to Good Laboratory Practices (GLP). In pharmaceutical analysis, accurate, repeatable, and legally acceptable results are guaranteed by proper calibration [6,7].

In order to guarantee precision as well as reliability of results, calibration is the act of comparing the measurement values provided by an instrument or piece of equipment with a recognized standard under certain conditions and modifying the instrument as needed. It helps in figuring out whether an instrument is operating within reasonable limits.

Advanced pharmaceutical dosage forms known sustained release beads are made to release a medication over an extended period of time at a specific frequency. Maintaining a steady therapeutic medication concentration in the bloodstream, reducing the frequency of dose, and improving patient compliance is the main objective of using sustained release formulations [8].

Usually, polymers that regulate the drug's diffusion or rate of degradation are used to create these beads. They can be added to pills, capsules [9,10]. Depending on the kind of polymer and formulation, the method of drug release from sustained release beads could involve erosion, diffusion, or a combination of both [11].

For drugs with short biological half-lives, when frequent dosage is unfavorable or unpleasant, this method is very helpful. Sustained release beads decrease side effects and variations in plasma doses while increasing therapeutic efficacy by offering controlled and uniform release properties [12].

PRINCIPLE OF UV-VIS SPECTROSCOPY

When radiation causes an electronic transition in a molecule's or ion's structure, the molecule or ion will exhibit absorption in the visible or ultraviolet spectrum. As a result, when a sample absorbs light in the visible or ultraviolet spectrum, the electronic state of the molecules within the sample changes. Electrons will be promoted from their ground state orbital to a higher energy orbital, such as an excited state orbital or an anti-bonding orbital, by the energy provided by the light. Three different kinds of ground state orbitals could be at motion [13, 14].

1. σ (Bonding) molecular
2. π (Bonding) molecular orbital
3. n (non-Bonding) atomic orbital.

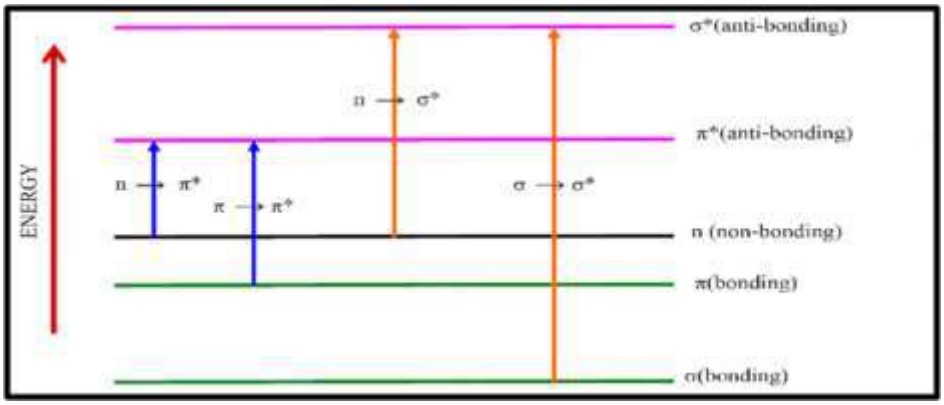

Fig 1:- Electron Transition Graphically Represented

INSTRUMENTATION OF UV SPECTROPHOTOMETER

The instrumentation of a UV spectrophotometer involves several key components that work together to measure the absorbance or transmittance of a sample in the ultraviolet (200–400 nm) region.

COMPONENTS

a. Source
b. Monochromator
c. Sample cell
d. Detector[13].

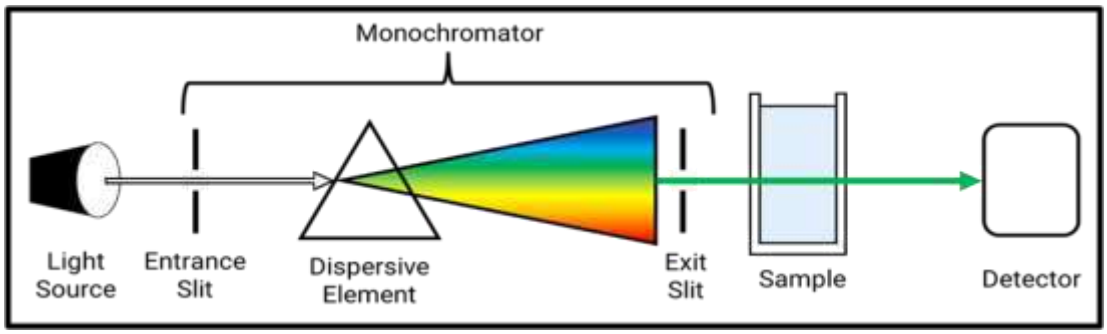

Fig 2:-Instrumentation of UV Spectrophotometer

QUALIFICATION OF UV SPECTROPHOTOMETER

Qualification-The process of ensuring that a particular system, location, or piece of equipment can meet the established acceptance standards in order to validate its claims is known as qualification. There are four components to the qualification procedure in total: The four qualifications are as follows

a. Qualifications for design (DQ)
b. Qualification for Installation (IQ)
c. Qualification for Operational (OQ)
d. Qualifications for Performance (PQ)[15]

QUALIFICATION FOR DESIGN

Fig 3:-Design Qualification

The steps to follow for passing as well as recording design reviews to demonstrate that every area of quality has been taken into account from the beginning of the design phase is known as design qualification or DQ. Making sure that every requirement for the finished systems has been precisely stated from the beginning is the goal. The Design Qualification (DQ) outlines the supplier's deliberate choices as well as the functional and operational requirements for the device. DQ should make sure that instruments fulfill user needs and can be successfully implemented for the intended application by making sure they have all the required functionality and performance standards [16,17].

QUALIFICATION FOR INSTALLATION

Fig 4:-Installation Qualification

The procedure known as installation qualification (IQ) involves examining the installation, to guarantee that the parts adhere to the authorised standard and are appropriately installed, as well as to observe how that Data is kept on file. The goal is to guarantee that every feature (static properties) of the apparatus or facility are installed accurately and in accordance with the original blueprint. Every component of the apparatus is recognised and confirmed with the component listing provided by the manufacturer. The conditions of the workplace are recorded and examined to make sure they are appropriate for the equipment's operation. Installation qualification confirms that the instrument is delivered as intended, That the device has been correctly mounted at the designated location as well as that the place of installation is appropriate for usage and functionality of every measuring device [18].

QUALIFICATION FOR OPERATIONAL

Fig 5:-Operation Qualification

The process of evaluating individual and combined systems to make sure they satisfy predetermined performance standards and to verify how test results are recorded is known as operational qualification, or OQ. Ensuring that every dynamic property adheres to the original design is the goal. Every function of the instrument is examined to make sure it complies with the manufacturer's requirements.

QUALIFICATION OF PERFORMANCE

Fig 6:-Performance Qualification

Practice competence, a different term for perform competence, is the method of analysing a to make sure because are distinct & interconnected structures operate to consistently fulfil predetermined. The goal is guaranteeing given requirements can be met consistently over an extended period of time [19].

MATERIALS AND METHODS

MATERIALS

Instrument :- UV Visible Spectrophotometer

Apparatus:- Volumetric Flasks (100 ml), Beakers

Chemicals:- Potassium dichromate, Sulphuric acid, Potassium chloride, Distilled water

METHODS

1. CONTROL OF ABSORBANCE

1. Dry a quantity of potassium dichromate by heating to constant weight at 130°C.
2. Weigh & transfer accurately a quantity not less than 57.0 mg & not more than 63.0 mg to 1000 ml volumetric flask. Dissolve & dilute in

sufficient 0.005M H2SO4 to produce 1000 ml.

3. Measure the absorbance of potassium dichromate solution at the wavelengths given below.
4. Calculate the value of A (1% 1cm) for each wavelength.

A (1% 1cm) = Absorbance X 10000 / Weight of Potassium dichromate in mg

Sr No.	Wavelength (nm)	Maximum Tolerance
1	235	122.9 to 126.2
2	257	142.8 to 145.7
3	313	47.0 to 50.3
4	350	104.9 to 108.2
5	430	15.7 to 16.1

2. LIMIT OF STRAY LIGHT

1. Dry a quantity of the Potassium chloride by heating to constant weight at 130°C.
2. Weight accurately 1.20 g of dried potassium chloride and dissolve it in 50 ml distilled water. Make upto 100 ml with the same solvent
3. Select the method file of LIMIT OF STRAY LIGHT in the instrument.
4. After selecting the file press Reference button for baseline correction.
5. Check the absorbance of above solution using water as a blank at 198, 199, 200, 201, 202.
6. Absorbance should be greater than 2.0 [20]

RESULT

1. Control of Absorbance

A (1%,1cm)= Absorbance x 10000 / weight of pottassium dichromate (60mg)

Sr. No.	Wavelength (nm)	Absorbance	A (1%,1cm)
1	235	0.735	122.5
2	257	0.873	145.5
3	313	0.280	46.66
4	350	0.642	107.00

All absorptivity values are within the acceptable range

2. Limit of Stray Light

Sr No.	Wavelength(nm)	Absorbance
1	198	2.290
2	200	2.466
3	201	2.573
4	202	2.532

All absorbance value are grreater than 2.0, indicating that the instrument passes the limit of stray light test. The UV visible spectrophotometer is calibrated

DISCUSSION

The calibration results indicate that the UV–Visible spectrophotometer is performing correctly. The specific absorbance values obtained for potassium dichromate at all tested wavelengths fall within acceptable limits, confirming accurate absorbance measurement and proper optical alignment. Additionally, the stray light test shows absorbance values above 2.0 at the critical low-wavelength range, indicating minimal stray radiation and reliable instrument optics. Overall, the instrument meets the required performance criteria and is suitable for routine analytical use and is calibrated.

CONCLUSION

The UV-Visible spectrophotometer is an essential analytical instrument used to determine the absorbance and concentration of substances accurately. It operates based on Beer-Lambert's law, which relates absorbance to concentration and path length. Regular calibration of the UV-Visible spectrophotometer ensures the instrument provides precise and reliable results by

maintaining wavelength and absorbance accuracy. The instrument plays a vital role in pharmaceutical quality control, chemical analysis, and research laboratories, where accurate quantitative and qualitative determinations are required. The UV spectrophotometer used is calibrated.

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Sustained release beads: A short review

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Abstract
Sustained release formulations are currently regarded as one of the most significant novel systems for the formulation of essential drugs. The sustained release system exhibits greater therapeutic activity of a drug in comparison to immediate release. This technique has been utilized in an aqueous outer phase for numerous water-insoluble monomers, both with and without the drug. The bead polymerization technique represents an emerging variant of this system, which has attracted considerable attention in pharmaceutical research due to its capacity to sustain therapeutic drug levels, decrease dosing frequency, and improve patient compliance. This review study encompasses a detailed examination of the preparation and evaluation of sustained release beads utilizing both natural and synthetic polymers, along with their physical properties such as particle size, shape, surface morphology, and drug content. This review of the work will undoubtedly serve as a valuable resource for researchers and academicians in various capacities.

Keywords: Sustained release, advantages, polymers, preparation techniques, physicochemical

Introduction
The release of a drug from a microparticle is determined by a number of factors, including the carrier utilized to make the microparticle and the amount of drug contained within it [1]. Beads are one of the most widely employed strategies in continuous release dosage forms. These are spherical particles with a diameter ranging from 50 nm to 2 mm, and include core constituents. To formulate as SRDF, the drug particle's molecular size must be less than 1000 Dalton [2]. Many APIs demonstrate difficulties like limited biological availability and repeated dosing due to poor solubility and penetration across lipid membranes. Oral API administration is the most common route to take medications [3]. Many are restricted in use due to their short for and loss of absorption through a portion of the small intestine. This has an effect on pharmacokinetic action, requiring periodic doses of multiple APIs to get an effective dosage. This increases pill load and reduces patient compliance [4]. Any medication delivery system's objective is to deliver a therapeutic dosage to the right location in the body in order to quickly and sustain the target concentration. That is, throughout a given treatment time, the drug delivery system should administer the medication at a pace determined by the body's demands [5]. The design of effective drug delivery systems an recently become an integral part of the development of new medicines. Hence, research continuously keeps on searching for ways to deliver drugs over an extended period of time, with a well-controlled release profile Oral drug delivery is the most desirable and preferred method of administering therapeutic agents for their systemic effects [6]. For decades, the majority of therapies for both acute and chronic illnesses have involved administering drugs to patients using a variety of traditional pharmaceutical dosage forms, including as pills, suppositories, creams, ointments, squids, aerosols, and injectable as drug carriers. It is well known that this kind of drug delivery device releases the medication quickly. Therefore, it is frequently necessary to take this kind of drug delivery system multiple times a day in order to reach and maintain the drug concentration within the therapeutically effective range required for treatment, which causes a large fluctuation in drug levels. Conventional immediate release formulations of many pharmacological substances offer clinically effective therapy with an acceptable level of patient safety while preserving the necessary balance of pharmacokinetic and pharmacodynamics characteristics [7].

A prolonged release formulation was designed to maintain medication concentration levels. To maintain the effective concentration in the blood for a longer period, the sustained release dosage form releases the drug at a constant rate, while the controlled release dosage form releases the drug at an equal pace [8]. In sustained release dosage forms, an adequate amount of drug is initially made obtainable to the body to cause a desired pharmacological effect [9]. The residual fraction is released occasionally and is required to maintain the maximum early pharmacological activity for some enviable period of time in surplus of time expected from usual single dose [10, 11]. The prolonged release of medications, vaccinations, antibiotics, and hormones can all be achieved with beads. For instance, by utilizing the properties of beads, in addition to their basic advantages, they may be able to offer a greater vehicle area and make it simpler to estimate the behavior of diffusion and mass transfer. Natural polymers are used in the process that is detailed in this study. The primary benefits of natural polymers are their biocompatibility, biodegradability, and ability to cause systemic toxicity during the administration, manufacture, and testing of propranolol HCL beads. It has been attempted to achieve an appropriate oral sustained drug delivery system using biodegradable natural polymers, such as fish gelatin and gelatin B as carriers, by employing physical cross-linking to prevent the toxicity of chemical crosslinking agents [12, 13].

Multiple unit dosage form includes

1. Microgranules/spheroids: Drug wet granulated alone or incorporated into inert granules, and then coated to controlled the release pattern.
2. Pellets: Pellets are prepared by coating inert drug pellets with film forming polymers. The release depends upon coating composition of polymer and amount of coatings.
3. Microcapsules: Microcapsules are prepared by applying relatively thin coating to small particles of solids, droplet of liquid and dispersion.
4. Beads- Microbeads, as the name suggests they are nearly spherical, small with diameter of 0.5-1000µm in size, solid and free flowing particulate carriers containing dispersed drug particles either in solution or crystalline form that allow a sustained release or multiple release profiles of treatment with various active agents without major side effects. Additionally, the heads maintain functionality under physiological conditions, can incorporate drug to deliver locally at high concentration ensuring that therapeutic levels are reached at the target site while reducing the side effects by keeping systemic concentration low. The microbeads are produced from several polymers such as cationic polymers e.g. chitosan, anionic polymers e.g. sodium alginate, and binding components e.g. gelatin, chondroitin sulfate, avidin in predetermined ratio [14, 15].

Advantage

1. Reduction in frequency of drug administration.
2. Improved patient compliance.
3. Reduction in drug level fluctuation in blood.
4. Reduction in total drug usage when compared with conventional therapy.
5. Reduction in drug accumulation with chronic therapy.
6. Reduction in drug toxicity (local/systemic).
7. Stabilization of medical condition (because of more uniform drug levels).
8. Improvement in bioavailability of some drugs because of spatial control.
9. Economical to the health care providers and the patient [16-19].

Disadvantage

1. Delay in onset of drug action.
2. Possibility of dose dumping in the case of a poor formulation strategy.
3. Increased potential for first pass metabolism.
4. Greater dependence on G1 residence time of dosage form.
5. Possibility of less accurate dose adjustment in some cases.
6. Cost per unit dose is higher when compared with conventional doses.
7. Not all drugs are suitable for formulating into ER dosage form.
8. Decreased systemic availability in comparison to immediate release conventional dosage forms, which may be due to incomplete release, increased first-pass metabolism, increased instability, insufficient residence time for complete release, site specific absorption, pH dependent stability etc.
9. Poor *In vitro In vivo* correlation.
10. Retrieval of drug is difficult in case of toxicity, poisoning or hypersentivity reactions.
11. Reduced potential for dose adjustment of drugs normally administered in varying strength [20-23].

Review of Literature

Polymers used in the preparation of sustained release beads

Sodium alginate

Another popular mucoadhesive polymer for creating different delivery systems is the sodium version of alginic acid. It is a linear anionic polymer derived from brown algae that is both biodegradable and biocompatible. It possesses high mucoadhesive qualities due to the presence of free carboxyl groups, which enable the polymer to interact with mucin in the mucous membrane through electrostatic and hydrogen bonding. It has been employed in the creation of sustained-release formulations as a matrix material. It administers the medication over an extended period of time because of its hydrogel forming qualities. Both sodium alginate and GG have the ability to go through ionotropic gelation in an aqueous solution with Ca2+, Al3, etc. The mucoadhesive nature of sodium alginate and the gel-forming ability of GG are primarily utilized in pharmaceutical drug design for applications involving controlled drug delivery [24].

Hydroxypropyl methylcellulose (HPMC)

Hydroxypropyl methylcellulose (HPMC) is the most often used hydrophilic carrier material in the creation of oral controlled drug delivery systems. Another name for it is hypromellose. HPMC is classified as a cellulose ether because it contains ether linkages formed by the substitution of more than one of the three hydroxyl groups from the cellulose glucopyranose unit. When making sodium alginate beads, the most often used med polymers are carboxymethyl cellulose, hydroxyl propyl methyl cellulose K100m (HPMC

K100m), etc. Formulations using CMC sodium salt as the matrix agent have the highest rate of drug release, while formulations using HPMC K100M as the matrix agent have the lowest rate. This demonstrates that HPMC created the gel. Despite using a highly viscous CMC sodium salt, it is evident [25].

Cross-linking agents

Various investigations have demonstrated that the type of cross-linker has a significant impact on how pharmaceuticals release from the cross-linked matrix. There are many other physical and chemical ways to cross-link alginates, but generally speaking, alginic acid and calcium chloride combine to generate calcium alginate hydrogel beads [26].

Preparation of Techniques

Ionotropic gelation techniques

Microbeads containing Diclofenac sodium were prepared by Ionotropic gelation technique. The sodium alginate solution was prepared by dispersing the weighed quantity of sodium alginate in deionized water. Accurately weighed quantity (1 g) of Diclofenac sodium was added to 100 ml polymeric solution of Sodium alginate and drug were thoroughly mixed with help of homogenizer at 1500 rpm to get a homogenous drug polymeric mixture. The formed mixture allowed to stand for 1 h to make it bubble free. By following the same procedure the alginate beads of different ratios of drug polymer were prepared. The resulted homogenous dispersion was extruded into 100 ml of 6% cross-linker solution ($CaCl_2$) through hypodermic syringe with flat lip needle (18 G) and stirred at 100 rpm. The formed microbeads were allowed to cure for 30 min in the cross-linker solution to complete the gelation. The beads were removed after the gelation period and washed with ethanol to harden the heads surface and finally with distilled water repeatedly to make free from un-reacted ion. The microbeads were then filtered and dried in hot air oven at 400°C for 18 h [27].

Emulsion gelation techniques

Another method of beads preparation is emulsion gelation techniques. The sodium alginate solution was prepared by dispersing the weighed quantity of sodium alginate in deionized water. Accurately weighed quantity of drug was added to polymeric solution of Sodium alginate and drug stirred magnetically with gentle heat to get a homogenous drug-polymeric mixture. Specific volume of cross-linking agent were added to form a viscous dispersion which was then extruded through a syringe with a flat tipped needle of size no 23 in to oil containing span 80 and 0.2% glacial acetic acid being kept under magnetic stirring at 1500 rpm. The beads are retained in the oil for 30 min to produce rigid discrete particles. They were collected by decantation and the products thus separated was washed with chloroform to remove the traces of oil the beads were dried at 400°C for 12 h [28].

Emulsion cross-linking techniques

The medication was dissolved in the gelatin solution in this form, which has previously been heated at 40°C for 1 hr. The solution was added drop by drop to liquid paraffin while in 35°C. resulting in w/o emulsion, this mixture was reused at 1500 rpm for 10 minutes. Optional stirring should at 15°C for 10 min. in 5 ml of aqueous glutaraldehyde saturated toluene solution at 28°C for 3 hours for cross-linking the spherically shaped beads were washed three times with acetone and isopropyl alcohol, respectively, air dried and discrete. Then formed beads with a 100 ml. 10 mm glycine solution containing 0.1 percent w/v between 80 and 370C we preserved for 10 min to lump unreacted glutaraldehyde[29].

Dropping method techniques

It's an easy way. It is necessary to use a pipette or a syringe with a needle. It is the technique most frequently used to prepare particles larger than 500 micrometer. The viscosity of the alginate solution and the size of the needle used determine the size of the beads that are produced [30].

Factors affecting of Sustained Release Beads

-Two types of factors involved:

1. Physicochemical factor
2. Biological Factor

Physicochemical factor

Aqueous Solubility

The drug of good aqueous solubility and pH independent solubility are most desirable candidate for sustained-release beads. Poor aqueous solubility possess oral bioavailability problem and drug which having extreme aqueous solubility are unsuitable for sustained release because it is difficult task to control the release of drug from the dosage form.

Partition coefficient

Also called as distribution coefficient, the bioavailability of a drug is greatly influenced by the partition coefficient, as the biological membrane is lipophilic in nature transport of drug across the membrane is depends upon the partition coefficient of the drug. The having low partition coefficient are considered as poor candidate for the sustained release formulation in the aqueous phase.

Drug stability

Sustained release beads is designed to control release of a drug over the length of the gastrointestinal tract (GIT); hence high stability of drug in GI environment is required.

Protein binding

Proteins binding of drug play a key role in its therapeutic. Pharmacological activity of a drug depends on unbound concentration of a drug rather than total concentration. The drugs which bound to some extent of a plasma and tissue proteins enhances the biological half-life of a drug. Release of such drug extended over a period of time and therefore no need to develop extended release drug delivery for this type of drug.

Drug pKa & ionization at physiological pH

If the unionized drug is absorbed and permeation of ionized drug is negligible, but the rate of absorption is 3 to 4 times is less than that of the unionized drug. Since the drug shall be unionized at the site an extent 0.1 to 5%. Drugs existing largely in ionized form are poor candidates for sustained release beads e.g. Hexamethonium.

Molecular size and diffusivity

Diffusivity depends on size & shape of the cavities of the membrane. The diffusion coefficient of intermediate molecular weight drug is 100 to 400 Dalton. For drugs having molecular weight > 500 Daltons, the diffusion coefficient in many polymers is very less. e.g. Proteins and peptides.

Dose size

For oral administration of drugs in the upper limit of the bulk size of the dose to be administered. In general, a single dose of 0.5 to 1.0g is considered maximal for a conventional dosage form. This also depends on sustained release dosage form. Compounds that require large dosing size can sometimes be given in multiple amounts or formulated into liquid systems.

Biological factors

Absorption

To maintain the constant uniform blood or tissue level of drug, it must be uniformly released from the sustained release system & then uniformly absorbed in the body. Since the purpose of forming a SR product is to place control on the delivery system, it is necessary that the rate of release is much slower than the rate of absorption. If we assume that the transit time of most drugs in the absorptive areas of the Gl tract is about 8-12 hours, the maximum half-life for absorption should be approximately 3-4 hours, otherwise, the device will pass out of the potential absorptive regions before drug release is complete. Thus corresponds to a minimum apparent absorption rate constant of 0.17-0.23 h-1 to give 80-95% over this time period. Hence, it assumes that the absorption of the drug should occur at a relatively uniform rate over the entire length of small intestine. For many compounds this is not true. If a drug is absorbed by active transport or transport is limited to a specific region of intestine, SR preparation may be disadvantageous to absorption. One method to provide sustaining mechanisms of delivery for compounds tries to maintain them within the stomach. This allows slow release of the drug, which then travels to the absorptive site. These methods have been developed as a consequence of the observation that co- administration results in sustaining effect.

Distribution

Drugs with high apparent volume of distribution, which influence the rate of elimination of the drug, are poor for sustained release beads e.g. Chloroquine.

Metabolism

The metabolic conversion of a drug is to be considered before converting into another form. Since as long as the location, rate, and extent of metabolism are known a successful sustain release product can he developed. Drugs those are significantly metabolized before absorption, either in the lumen or the tissue of the intestine, can show decreased bioavailability from slower-releasing dosage form. Even a drug that is poorly water soluble can be formulated in SR dosage form. For the same, the solubility of the drug should be increased by the suitable system and later on that is formulated in the SR dosage form. But during this the crystallization of the drug, that is taking place as the drug is entering in the systemic circulation, should be prevented and one should be cautious for the prevention of the same.

Half-life of drug

The drug having short biological half-life between <5 but drugs is soluble in water. The drugs should have larger therapeutic window absorbed in GIT. The usual goal of an oral SR product is to maintain therapeutic blood levels over an extended period of time. To achieve this, drug must enter the circulation at approximately the same rate at which it is eliminated. The elimination rate is quantitatively described by the half-life (t1/2). Each drug has its own characteristic elimination rate, which is the sum of all elimination processes, including metabolism, urinary excretion and all over processes that permanently remove drug from the bloodstream [31-33].

Summary and Discussion

The basic goal of therapy is to achieve a steady-state blood or tissue level that is therapeutically effective and nontoxic for extended period of time. Modified-release delivery systems may be divided conveniently into four categories:

1. Delayed release
2. Sustain release
3. Site-specific targeting
4. Receptor targeting

Delayed release systems are those that use repetitive, intermittent dosing of a drug from one or more immediate-release units incorporated into a single dose form. Example delayed release system include repeat action tablets, capsules and enteric coated tablet where timed release is achieved by barrier coating. Sustain release system includes any drug delivery systems that achieves slow release of drug over an extended period of time. If the systems can provide some control, whether this is of temporal or spatial nature, or both, of drug release in the body, or in other words, the system is successful at maintaining constant drug levels in the target tissue or cells, it is considered a sustained release beads. Site-specific targeting refers to targeting of drug directly to a certain biological locations. In the case of site-specific release, the target is adjacent to or in the diseased organ or tissue. Receptor targeting refer to the target is particular receptor for a drug within an organ or tissue. Both of these systems satisfy the spatial aspects of drug delivery and are also considered to be sustained release beads.

Conflict of Interest

The authors declare that there is no conflict of interest.

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Review Article

Analytical Instrument Qualification: A Comprehensive Review on HPLC And UV Systems

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ABSTRACT

Analytical instrument qualification (AIQ) is a fundamental requirement in regulated industries to ensure the accuracy, reliability, and consistency of analytical results. It provides documented evidence that instruments are properly designed, installed, operated, and maintained for their intended purpose. This review focuses on High Performance Liquid Chromatography (HPLC) and Ultraviolet-Visible (UV-Vis) spectroscopy, two of the most widely applied analytical techniques in pharmaceutical, clinical, environmental, and food sciences. The qualification process is categorized into four essential stages: Design Qualification (DQ), Installation Qualification (IQ), Operational Qualification (OQ), and Performance Qualification (PQ). Each stage is critical in establishing confidence that the instrument performs according to predefined specifications and regulatory expectations. The review also elaborates on the principles, instrumentation, and method development approaches associated with HPLC and UV-Vis systems. For HPLC, method development emphasizes chromatographic conditions, sample preparation, optimization of parameters, and validation to ensure reproducibility and accuracy. Similarly, UV-Vis spectroscopy, based on Beer–Lambert's law, is highlighted for its simplicity, cost-effectiveness, and versatility in both qualitative and quantitative analysis. The diverse applications of these techniques—from pharmaceutical quality control and impurity profiling to environmental monitoring and clinical diagnostics—underscore their significance in modern analytical science. Overall, this article integrates qualification protocols with practical insights into HPLC and UV-Vis methodologies, emphasizing their role in maintaining analytical quality assurance, regulatory compliance, and data integrity across research and industrial settings.

INTRODUCTION

Instrument qualification is a systematic procedure that generates documented proof showing that an

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instrument is suitable for its intended purpose and is properly maintained and calibrated for consistent use. The qualification process is generally divided into four main stages:

- Design Qualification (DQ)
- Installation Qualification (IQ)
- Operational Qualification (OQ)
- Performance Qualification (PQ)

Design Qualification (DQ) outlines the user's requirements and specifies the functional as well as operational features of the instrument. Its purpose is to confirm that the selected instrument possesses the capabilities and performance characteristics needed for the intended applications. The DQ documentation also serves as a reference point for verification tests carried out during the Operational Qualification (OQ) stage.

Installation Qualification (IQ) confirms that the instrument or equipment has been delivered as per the approved design and specifications. It also ensures that the system is correctly installed in the intended location and that the installation environment is appropriate for its intended operation and use.

Operational Qualification (OQ) is the step where the instrument is tested to confirm that it operates as intended under the chosen conditions. It ensures that the HPLC system meets the essential functional and operational criteria defined during the Design Qualification (DQ).

Performance Qualification (PQ) involves confirming that the instrument delivers results reliably and in line with the specifications required for its routine applications. The emphasis is on verifying that the instrument performs consistently over time.

Documentation

After completing equipment qualification, the following records should be maintained:

- Design Qualification (DQ) report
- Installation Qualification (IQ) report, including details of hardware and software
- Standard procedures for Operational Qualification (OQ) testing
- Test reports generated during OQ
- Performance Qualification (PQ) protocols along with representative test results.

High Performance Liquid Chromatography (HPLC)

High Performance Liquid Chromatography (HPLC) is a highly sophisticated and flexible analytical technique utilized for the separation, identification, and quantitative determination of components in complex mixtures. The process involves the passage of a liquid sample through a column packed with a stationary phase under elevated pressure. Variations in the interactions of analytes with the stationary phase enable their separation according to distinct physicochemical characteristics. Due to its superior sensitivity, resolution, and reliability, HPLC has become an indispensable tool in diverse fields such as pharmaceutical quality control, environmental monitoring, food analysis, and clinical research.

Principle

The fundamental principle of HPLC lies in the differential distribution of analytes between a stationary phase and a mobile phase. The stationary phase generally comprises finely divided, porous particles contained within a column, while the mobile phase consists of one or more solvents propelled at high pressure. The sample is introduced into the mobile phase stream

through an injection valve and sample loop, allowing it to enter the column. Based on their affinity toward the stationary phase, individual components migrate at different rates, resulting in effective separation. Upon elution, the analytes are detected by a suitable detector, and the signals are processed through system software to generate a chromatogram. This chromatogram provides both qualitative and quantitative information regarding the separated constituents.

Types of HPLC

HPLC techniques can be broadly categorized in two ways

According to the scale of operation:

Preparative HPLC – primarily used for the isolation and purification of compounds in larger quantities.

Analytical HPLC – employed for qualitative and quantitative analysis of samples

According to the separation principle:

- Affinity chromatography Adsorption chromatography,
- Size-exclusion chromatography
- Ion-exchange chromatography
- Chiral phase chromatography

Based on the elution technique:

Isocratic separation – employs a mobile phase of constant composition throughout the run. Gradient separation – involves a gradual change in the composition of the mobile phase to improve separation efficiency.

Based on the mode of operation:

Normal phase chromatography – utilizes a polar stationary phase and a non-polar mobile phase.

Reverse-phase chromatography – employs a non-polar stationary phase with a relatively polar mobile phase.

Normal Phase Chromatography:

Normal Phase HPLC (NP-HPLC) separates compounds on the basis of polarity. It uses a polar stationary phase combined with a non-polar mobile phase. Polar analytes interact more strongly with the stationary phase, resulting in greater retention. As the polarity of an analyte increases, adsorption forces strengthen, causing a longer elution time.

Reversed Phase Chromatography:

Reversed Phase HPLC (RP-HPLC or RPC) employs a non-polar stationary phase and a moderately polar or aqueous mobile phase. The separation mechanism relies on hydrophobic interactions, where non-polar analytes are retained due to their affinity toward the hydrophobic stationary phase. The extent of retention is proportional to the size and surface area of the analyte's non-polar groups in contact with the stationary phase.

• **Instrumentation of HPLC:**

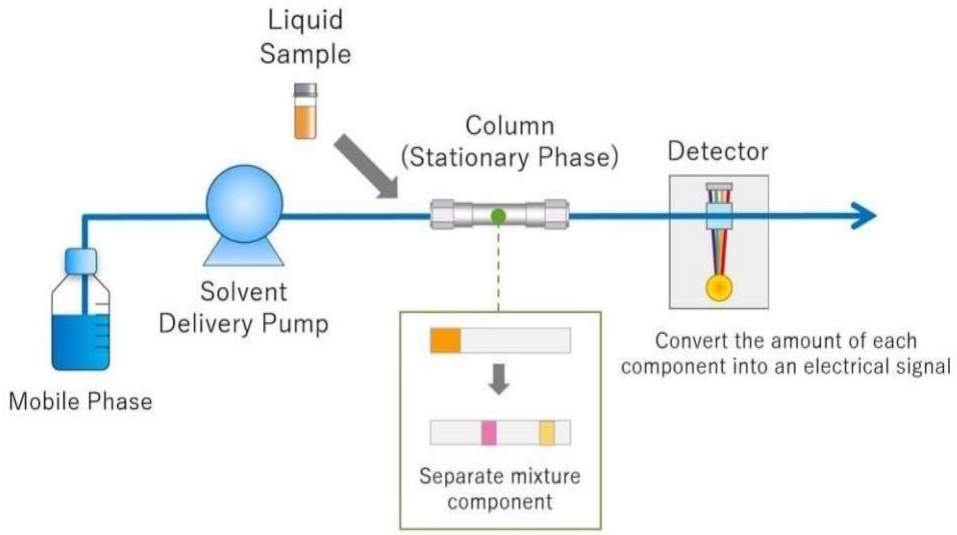

Figure 1. Instrumentation of HPLC

Method Development for HPLC

The development and validation of analytical methods are crucial in the research, formulation, and large-scale production of pharmaceutical dosage forms. These processes ensure the identity, purity, potency, safety, effectiveness, and overall performance of medicines. In cases where no official methods are available, new analytical procedures are established to meet the requirements of novel drug products. For non-pharmacopoeial substances, alternative methods are often created to reduce cost, save time, and enhance accuracy and robustness. Whenever an alternative technique is proposed to replace an existing one, comparative data must be presented to demonstrate its benefits and potential limitations. The primary aim of HPLC method development is to obtain efficient separation and precise quantification of the active pharmaceutical ingredient (API), impurities, intermediates, and degradation products.

Essential Steps in HPLC Method Development

Assessment of Physicochemical Properties

Evaluate solubility, stability, molecular weight, pKa, and other parameters that influence chromatographic performance.

Selection of Chromatographic Conditions

Choose the suitable stationary phase, mobile phase, column type, and detection technique based on the drug's properties.

Defining the Analytical Strategy

Establish clear objectives such as resolution, sensitivity, reproducibility, and acceptable run time.

Sample Preparation

Develop optimized procedures for sample preparation to ensure reproducibility, minimize interferences, and achieve reliable results.

Optimization of Method Parameters

Adjust critical factors including flow rate, column temperature, gradient conditions, and injection volume to improve separation efficiency and overall method performance.

Method Validation:

Establish the reliability of the developed method by systematically evaluating its accuracy, precision, specificity, and robustness through a structured validation process.

Applications of HPLC

Purification:

Purification through HPLC involves isolating a specific compound from a mixture containing structurally similar substances or impurities. Under optimized chromatographic conditions, each compound produces a unique peak. To achieve successful purification, the analyst must carefully choose suitable mobile and stationary phases according to the physicochemical properties of the compounds, ensuring efficient separation and recovery of the desired analyte during elution.

Chemical Separation:

HPLC is widely applied for chemical separation by utilizing differences in compound interactions with the stationary phase and their mobility in the mobile phase. This approach enables the resolution of structurally related molecules, including enantiomers. The effectiveness of separation depends largely on the appropriate choice of chromatographic phases, making HPLC a powerful tool for differentiating compounds within complex mixtures. Identification:

One of the major uses of HPLC is compound identification and assay. Analytical parameters are adjusted to ensure that the chromatographic peak of the test sample corresponds to that of the reference standard. At the detection limits employed, the peak must be well-defined, properly labelled, and distinctly resolved from other signals, allowing reliable identification.

Other Applications:

Beyond pharmaceutical analysis, HPLC has extensive applications across multiple fields. It is employed in clinical diagnostics, forensic investigations, food and environmental monitoring, and various research domains where accurate separation, quantification, and characterization of compounds are essential.

Introduction Of Spectroscopy

Spectroscopy refers to the study of how matter interacts with electromagnetic radiation. During these interactions, matter can either absorb or emit energy in the form of radiation. Broadly, spectroscopy is categorized into two types: absorption and emission spectroscopy. Absorption spectroscopy—such as UV-Visible, Infrared (IR), Nuclear Magnetic Resonance (NMR), microwave, and radiofrequency spectroscopy—focuses on analysing the specific wavelengths of electromagnetic radiation absorbed by a sample.

Ultraviolet (UV) Spectroscopy

Ultraviolet (UV) spectroscopy, commonly referred to as UV-Visible (UV-Vis) spectrophotometry, is based on the measurement of light absorption within the ultraviolet and visible regions of the electromagnetic spectrum. This method is widely adopted across scientific disciplines owing to its simplicity, cost-effectiveness, and versatility. For a compound to be analysed, it must contain a chromophore— a functional group capable of absorbing radiation in the UV-Vis range.

UV-Visible spectrophotometry is extensively applied for both qualitative and quantitative analysis of compounds in diverse samples. The principle involves passing a beam of light through the sample and detecting absorbance at selected

wavelengths. The extent of absorption is proportional to the concentration of the absorbing species, forming the basis for quantitative determinations.

In addition, this technique serves as a complementary tool to fluorescence spectroscopy. Key analytical parameters evaluated include absorbance (A), transmittance (%T), and reflectance (%R), along with monitoring their variations over time.

Terms used in spectroscopy

A. Chromophore

- In Greek word: chromo means colour and phores means bearer
- A Chromophore is the part of molecules responsible for its colour. The colour that is seen by our eyes.
- Define as any isolated covalently bonded group that shows a characteristic absorption of electromagnetic radiation in the UV or visible region.
- A group that gives rise to absorption in visible and near ultra violet is called "chromophore"
- There is a faint absorption band between 200 and 300 nm for compounds with nonconjugated carbonyl groups.

B. **Auxochrome:**

- In Greek: Auxo means increase and chromo means colour
- Auxochrome is defined as the any group of which does not itself act as a chromophore but whose presence brings about the shift of the absorption bands towards the red end of the spectrum, (longer wavelength).
- The effect is due to its ability to extent the conjugation of a chromophore by sharing the non- bonding electrons.
- Take benzene, phenol, and aniline as examples; their Amax values are (255 nm), (270 mm), and (280 nm).

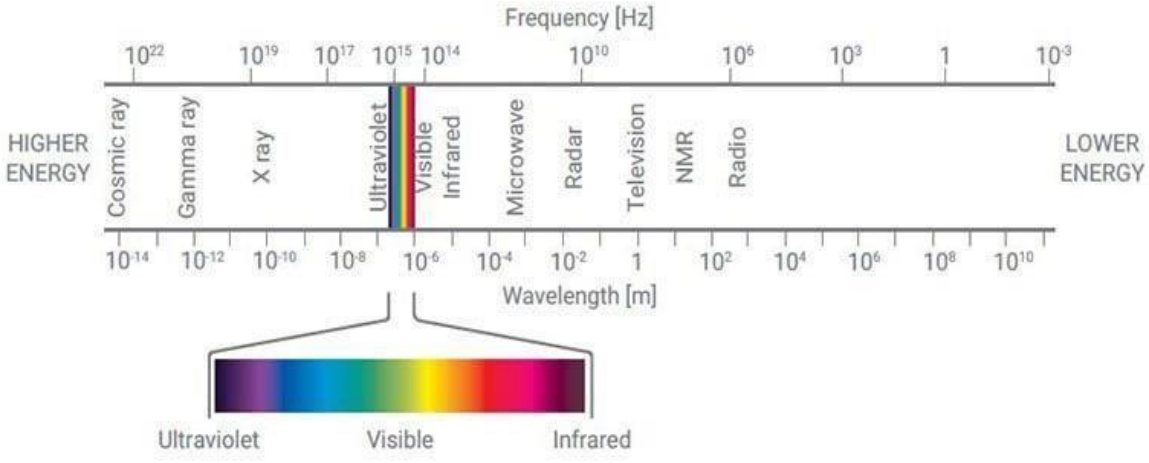

Fig 2. The electromagnetic spectrum with the visible light section expanded

Principle of UV-Visible Spectroscopy:

Beer's Law forms the theoretical basis of UV–Visible spectroscopy. It states that when a beam of electromagnetic radiation passes through an absorbing medium, the transmitted intensity (I) is lower than the incident intensity (I_0). The absorbance (A) is quantitatively related to the concentration (c) of the absorbing species and the path length (b) of the sample cell as: $A = \varepsilon Lc$

where ε represents the molar absorptivity ($L \cdot mol^{-1} \cdot cm^{-1}$). This direct proportionality enables UV–Visible spectroscopy to be a powerful tool for quantitative analysis.

When molecules absorb UV or visible light, electrons are promoted from lower-energy orbitals to higher-energy orbitals. This process involves transitions between bonding, non-bonding, and antibonding orbitals.

Ground state orbitals:

1. σ (bonding orbital)
2. π (bonding orbital)
3. n (non-bonding orbital)

Antibonding orbitals: σ* (sigma antibonding orbital)

1. π* (pi antibonding orbital)

It is noteworthy that non-bonding (n) electrons do not participate in bond formation; hence, no corresponding n antibonding orbital exists. As a result, only specific electronic transitions are possible upon absorption of ultraviolet or visible radiation. These include:

1. σ → σ* (sigma to sigma star)
2. n → σ* (non-bonding to sigma star)
3. n → π* (non-bonding to pi star)
4. π → π* (pi to pi star)

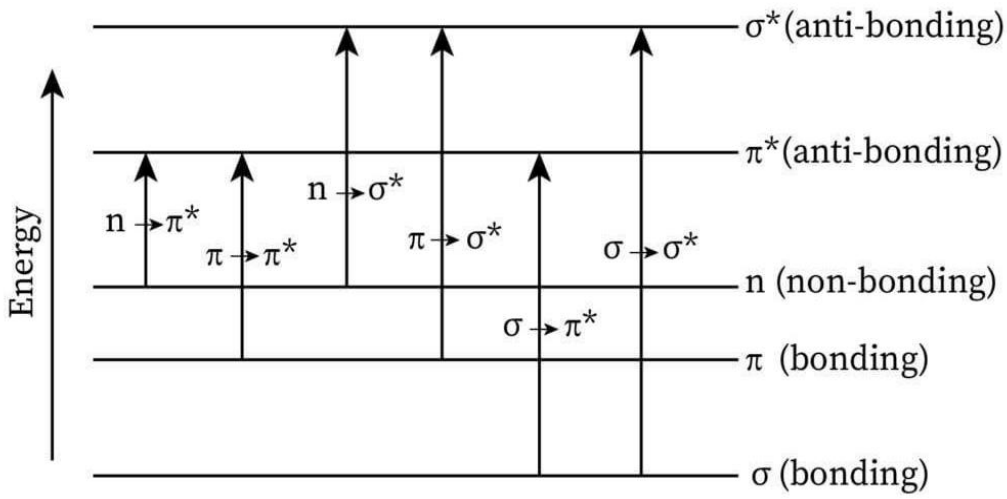

Fig 3. Electronic Transition graphically represented

Instrumentation Of UV-Visible Spectrophotometer:

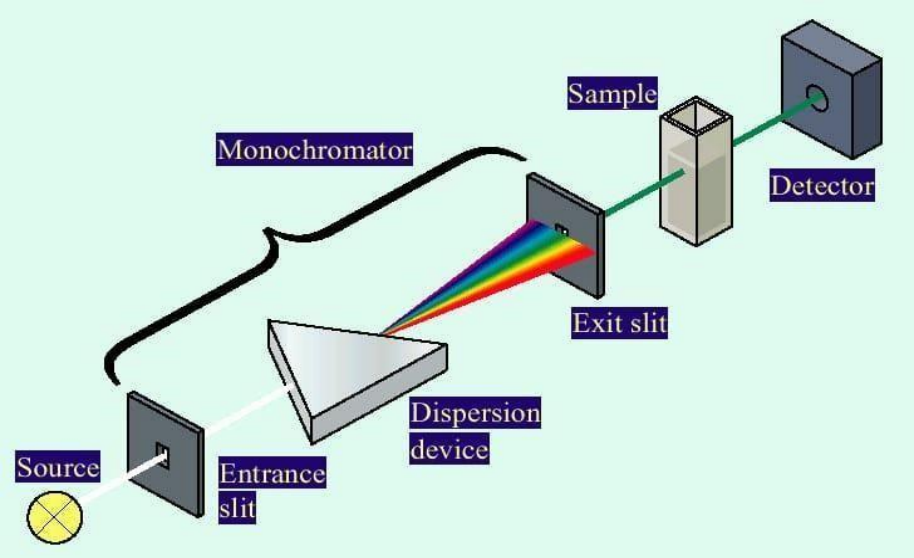

Fig 4. Instrumentation Of UV-Visible Spectrophotometer

1. Source of radiation
2. Filters and Monochromators
3. Sample cell
4. Detectors
5. Recording Devices

1.Sources of Radiation

The ideal light source for spectroscopic applications should provide high stability, strong intensity, and a broad emission range, typically from 180–700 nm.

Hydrogen Discharge Lamp

This lamp contains hydrogen gas maintained under high pressure. When subjected to an electric discharge, the excited hydrogen molecules emit radiation in the ultraviolet region.

Deuterium Lamp

Structurally similar to the hydrogen discharge lamp, this source uses deuterium gas instead of hydrogen. It provides higher intensity, approximately three to five times greater than hydrogen lamps, making it more efficient for UV applications.

Xenon Discharge Lamp

In this type, xenon gas is pressurized between 10–30 atm and placed between two tungsten electrodes. It offers significantly greater intensity compared to hydrogen lamps.

Mercury Arc Lamp

This lamp operates using mercury vapours. However, due to its discontinuous spectrum, it is less favoured and rarely used as a reliable source of radiation.

2. Filters and Monochromators

The main function of these devices is to separate a broad band of polychromatic radiation into a narrower band of nearly monochromatic radiation.

➤ Filters

Filters are employed to isolate a specific, narrow range of radiant energy from the overall spectrum. They selectively transmit radiation within the desired wavelength region while absorbing most of the unwanted wavelengths.

Types of Filters:

Glass filters

Gelatine filters

Interference filters

➤ Prisms

Prisms, generally fabricated from materials such as glass, quartz, or fused silica, serve as dispersing components in spectrophotometers. Among these, glass exhibits approximately three times greater dispersing power than quartz, making it particularly suitable for use in the visible region of the spectrum. The ability of a prism to separate polychromatic radiation into narrow wavelength bands arises from the variation in refractive index with wavelength.

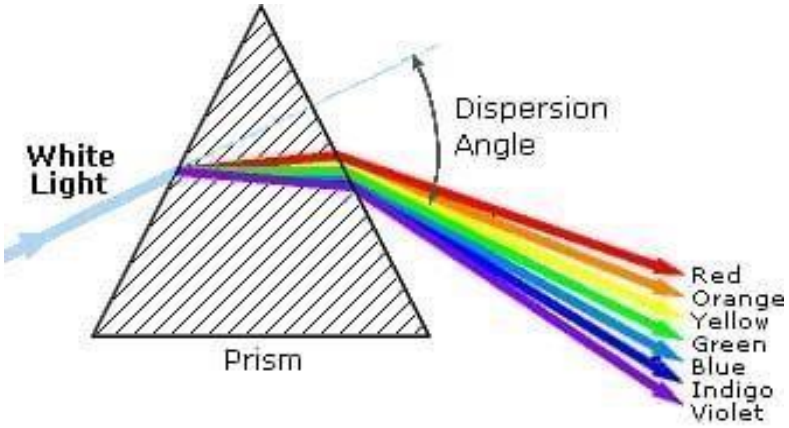

Fig 5. Prism

o Types of Monochromators:

Cornu Type

Littrow Type

□ Diffraction Grating

A higher degree of spectral dispersion can be achieved using diffraction gratings. These consist of a large number of finely ruled, parallel grooves—typically ranging from 15,000 to 30,000 lines per inch—on a highly polished aluminium surface. The grooves act as scattering centers for the incident light beam, producing diffraction. The resolving power of a grating is directly related to the number of lines per unit length, with greater line density resulting in enhanced resolution.

3. Sample Cells

Sample containers, commonly referred to as cells or cuvettes, are designed with optically transparent windows suitable for the spectral range under investigation. Quartz or fused silica cuvettes are essential for ultraviolet measurements (below 350 nm) but can also be used in the visible region. For wavelengths between 375–2000 nm, silicate glass is preferred due to its lower cost compared to quartz. Plastic cuvettes are also employed for measurements in the visible region.

For optimal performance, the cell windows should be oriented perpendicular to the incident light beam to minimize reflection losses. The standard path length for UV-visible spectroscopy is 1 cm, with matched and calibrated cuvettes of this dimension being readily available from commercial suppliers.

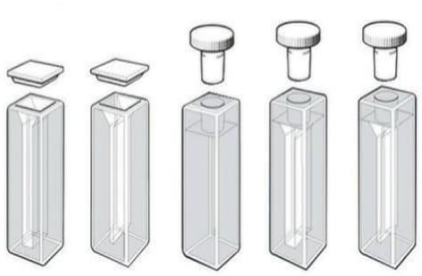

Fig 6. Sample Cells

4. Detectors

Detectors used in UV–visible spectrophotometers are generally referred to as photometric detectors. The most widely employed types include:

1. Barrier layer cell (photovoltaic cell)
2. Phototube (photo-emissive tube)
3. Photomultiplier tube

Barrier Layer Cell (Photovoltaic Cell):

Also called a photonic cell, this detector operates without an external power source. It is composed of a metallic base plate, usually made of iron or aluminium, which serves as one electrode. A thin layer of a semiconductor material such as selenium is coated on this base. The selenium surface is further covered with a very thin film of silver or gold, functioning as the second collector electrode.

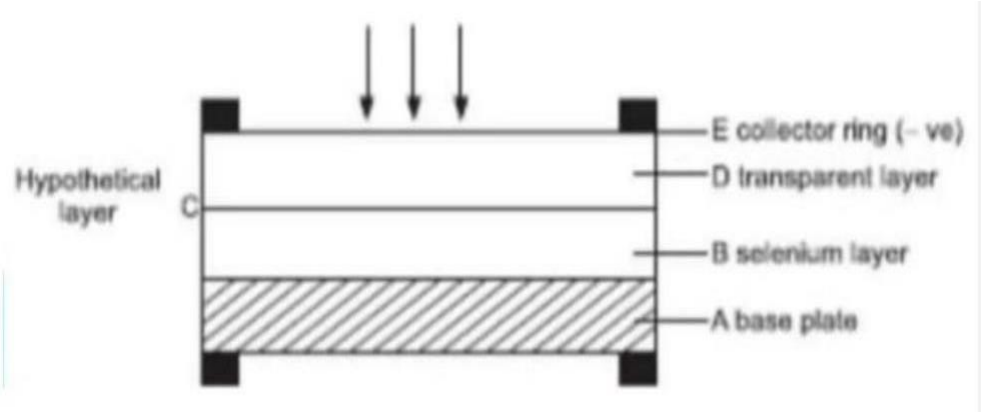

Fig 7. Barrier Layer Cell

Phototubes (Photo-emissive Tubes):

A phototube consists of an evacuated glass tube that houses a photocathode and a collector anode. The photocathode is coated with materials of high atomic weight, such as caesium, potassium, or silver oxide, which emit electrons upon exposure to light. These emitted electrons are attracted to the anode, generating a current directly proportional to the incident light intensity. To enhance performance, composite coatings like caesium/caesium oxide/silver oxide are often employed, extending sensitivity and operational range, particularly in the UV region. Additionally, the output signal can be amplified using external circuits. Compared to photovoltaic cells, phototubes offer greater sensitivity, making them more commonly utilized in spectrophotometric applications.

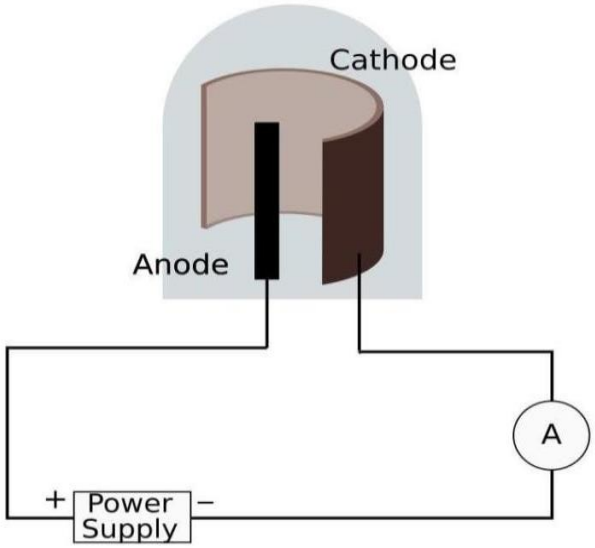

Fig 8. Phototube (Photo-Emissive Tube)

Photomultiplier Tubes (PMTs):

Photomultiplier tubes are highly sensitive detectors, commonly integrated into advanced instruments such as spectrofluorometers, due to their ability to measure extremely low light intensities. Their working principle is based on the multiplication of photoelectrons through secondary electron emission. This is achieved using a photocathode in combination with a cascade of anodes, known as dynodes, typically arranged in a series of up to ten. Each dynode is maintained at a potential difference of about 75–100 V higher than the preceding one, resulting in progressive amplification of the electron signal.

Owing to this mechanism, PMTs are capable of detecting signals up to 200 times weaker than those measurable with photovoltaic cells, making them invaluable in fluorescence-based measurements. However, to ensure accuracy, they must be adequately shielded from stray light interference.

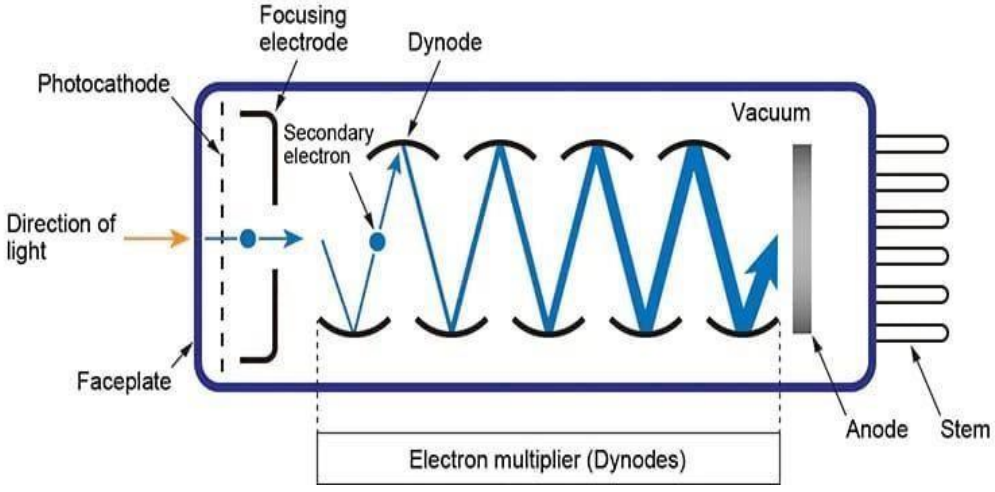

Fig 9. Photo-multiplier tube

5. Recording Devices

In spectrophotometric instruments, the amplifier output is often connected to a recording system, such as a pen recorder or a computer interface. The computer not only plots the spectrum of the analysed compound but also stores the acquired data for further processing and analysis.

Applications

Ultraviolet-visible (UV-Vis) spectroscopy has diverse applications, such as:

- Identification of impurities in samples.
- Determination of structural features of organic molecules.
- Both qualitative and quantitative analysis of compounds.
- General chemical characterization.
- Quantitative estimation of pharmaceutical agents.
- Evaluation of dissociation constants of acids and bases.
- Determination of molecular weight.
- Serving as a detection system in High-Performance Liquid Chromatography (HPLC)

CONCLUSION

Analytical instrument qualification is essential for ensuring reliability, accuracy, and regulatory compliance in modern laboratories. By following DQ, IQ, OQ, and PQ, instruments such as HPLC and UV-Visible spectrophotometers can consistently deliver valid results. Together, these techniques play a vital role in pharmaceutical quality control, clinical diagnostics, environmental monitoring, and food analysis, thereby upholding data integrity and supporting scientific progress.

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Review Article

A Review on Analytical Method Validation as Per ICH Guidelines and Protocols

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ABSTRACT

Analytical method validation is an essential process in pharmaceutical analysis, ensuring that analytical methods are suitable for their intended purpose and comply with International Council for Harmonization (ICH) guidelines. A validation study is designed to provide sufficient evidence that the analytical procedure meets its objectives. These objectives are described with a suitable set of performance characteristics and related performance criteria, which can vary depending on the intended purpose of the analytical procedure and the specific technology selected [8]. The validation process provides documented evidence of accuracy, precision, specificity, linearity, range, detection limit, quantitation limit, robustness, and system suitability. These parameters collectively ensure the reliability and reproducibility of analytical data during drug development, quality control, and regulatory submissions. This review discusses the principles, requirements, and methodology of analytical method validation as outlined in ICH Q2(R1) and the revised Q2(R2) guidelines. Emphasis is placed on the importance of protocol-driven validation and its role in achieving consistent pharmaceutical quality. The discussion also highlights best practices for designing and executing validation protocols, covering both small molecule and biotechnological products [1,2,3].

INTRODUCTION

The primary aim of any pharmaceutical manufacturing unit is to consistently produce medicines of the required quality at the most economical cost [9]. The role of Validation is crucial, as it ensures reliable and repeatable outcomes for both routine analysis and stability testing. This has become increasingly important in the field of quality control and accreditation, particularly with the growing focus on dissolution, testing and impurity profiling in recent years [10]. The concept of validation was first introduced in the United States in 1978.

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VALIDATION:

As defined by the U.S. Food and Drug Administration (FDA), validation refers to a process of production and process control intended to confirm that drug products consistently maintain their identity, strength, quality, and purity. According to the FDA guidelines issued in May 1987, a validation dossier must contain all the necessary data and testing procedures that demonstrate the system and process comply with established requirements [11]. The word validation means assessment of validity or action of proving effectiveness [12].

Analytical methods need to be validated or revalidated.

i.Before their introduction into routine use.

ii. When there is a change in the conditions under which the method was originally validated (for example, use of an instrument with different specifications or samples having a different matrix).

iii. When any changes are made to the method that falls beyond the scope of the initial validation [13].

Significance of Validation:

- Ensures product quality
- Helps achieve time- bound objective
- Enhances process optimization
- Lowers overall quality-related costs
- Reduces errors, mix-ups, and production bottlenecks
- Minimizes batch failures while improving efficiency and productivity
- Decreases rejection rates.
- Increases production output
- Prevents unnecessary capital investments
- Leads to fewer complaints related to process failures
- Lesser need for testing during production as well as in finished products.
- Faster and more dependable commissioning of new equipment.
- Simplified scale-up from development to production stage.
- Easier upkeep and servicing of equipment.
- Better understanding of processes among employees.
- Quicker implementation of automation [9].

Parameters of Analytical Method Validation [22]

The primary purpose of method validation is to demonstrate that an analytical method performs as intended, giving results that are accurate, reliable, and consistent. Validation of analytical methods is carried out in line with the International Council for Harmonization (ICH) guidelines, specifically ICH Q2.

The validation parameters are

• Accuracy

• Precision

• Specificity /Selectivity

• Limit of Detection

• Limit of Quantitation

• Linearity

• Range

• Robustness

• Ruggedness

Accuracy

Accuracy of an analytical method refers to how close the results obtained are to the true or accepted reference value. It indicates the degree of correctness of the analytical procedure. In simpler terms, it measures how close the experimental value is to the actual value. Accuracy is usually expressed as the percentage recovery of a known quantity of analyte within the specified linearity range. [9]

Accuracy of an analytical method is evaluated at different concentration levels (80%, 100%, and 120%) to ensure reliability across the range.

It can be confirmed by comparison with a validated method and should typically be within 3–5% of the true value. As per ICH guidelines, accuracy is assessed using nine determinations at three concentration levels. [17]

The Recovery is determined by the equation:

*Recovery = Analytical Result/True Value * 100%*

Limit: The recovery should be in the range of 98.0% to 102.0%.

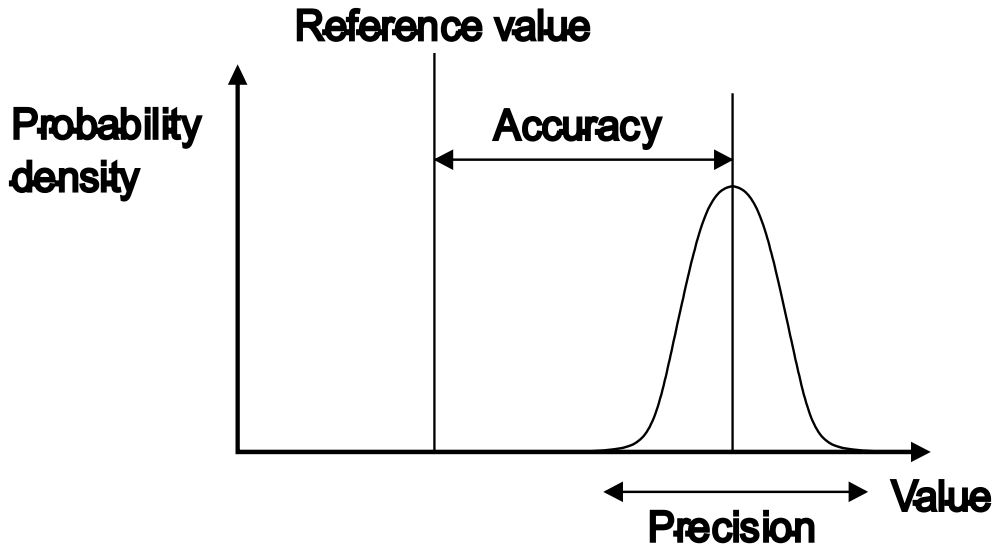

Figure 1

Precision

Precision of an analytical method refers to the closeness of agreement among a series of measurements obtained from multiple analyses of the same homogeneous sample under defined conditions. It indicates the degree of repeatability or consistency of the results when the procedure is repeated. [16]

% RSD =Standard Deviation/Mean x 100

Where, RSD = Relative Standard Deviation

Acceptance Criteria

At each concentration level, the precision of the analytical method should have a coefficient of variation (CV) not greater than 15%. However, for the lower limit of quantification (LLOQ), the CV may be up to 20%, reflecting acceptable variability at low concentration levels. [15]

Specificity / Specificity

Specificity refers to the ability of an analytical method to accurately identify and measure the analyte in the presence of other substances that may be present, such as impurities, excipients, or degradation products. Ensuring specificity is essential during method development and validation, as a lack of it can negatively impact accuracy, precision, and linearity. It should be regularly verified throughout validation and routine application of the method. [18] Selectivity of an analytical method is defined as its ability to accurately measure the analyte in the presence of other components that may be expected to be present in the sample matrix. It represents the method's capacity to resolve and distinguish between different chemical entities. Selectivity is typically assessed by comparing the analytical response of the analyte in the absence and presence of potentially interfering substances, ensuring reliable identification and quantification. [9]

Limit of Detection (LOD)

The Limit of Detection (LOD) is defined as the lowest concentration of an analyte in a sample that can be reliably detected, though not necessarily quantified, under specified experimental conditions. In methods using UV detectors, detecting low-level compounds can be challenging due to gradual changes in detector lamp sensitivity or variations in baseline noise. It is important to ensure that the LOD and LOQ can be consistently achieved with the method. Without a reference standard for an impurity, detection of small peaks may be unreliable. LOD can be estimated using different approaches depending on the type of method:

Visual evaluation – observing the presence of the analyte peak.

Signal-to-noise ratio – comparing the analyte signal to baseline noise.

Standard deviation of the response – using statistical calculations from multiple measurements.[19]

It can be calculated using the formula:

$$LOD = 3.3\ s/S$$

where:

s = standard deviation of the response

S = slope of the calibration curve of the analyte

Limit of Quantitation (LOQ)

The Limit of Quantitation (LOQ) of an analytical method is the lowest concentration of an analyte in a sample that can be determined quantitatively with acceptable precision and accuracy.[18]

It can be calculated using the formula:

$$LOQ=10*s/S$$

where:

s = standard deviation of the response

S = slope of the calibration curve of the analyte

Linearity

Linearity of an analytical method refers to its ability to elicit test results that are directly proportional to the concentration of analyte within

a given range. It is typically evaluated by analysing a series of standard solutions at different concentrations and plotting the corresponding responses to construct a calibration curve. The linearity is then assessed through linear regression analysis, where the slope, intercept, and correlation coefficient of the calibration curve provide quantitative measures of the method's linear response. [19]

Range

The range of a method refers to the time between the highest and lowest concentrations of the analyte for which the procedure has been demonstrated to provide acceptable levels of accuracy, precision, and linearity. The range is normally expressed in the same units as the test results (e.g. percentage, parts per million) obtained by the analytical method. [17]

Minimum specified ranges:

For the assay of drug substance or finished product: 80–120% of test concentration

Content uniformity: 70–130% (or wider if justified)

Dissolution testing: ±20% of the specified range [20]

Robustness

Robustness refers to the ability of an analytical method to remain unaffected by small, intentional variations in method parameters. In the context of HPLC, these variable parameters can include factors such as the flow rate, column temperature, sample temperature, pH, and composition of the mobile phase. [14]

Examples of typical variations are:

- Stability of analytical solutions
- Extraction time.

In the case of liquid chromatography, examples of typical variations are:

- Influence of variations of pH in a mobile phase;
- Influence of variations in mobile phase composition;
- Different columns
- Temperature
- Flow rate.

In the case of gas-chromatography, examples of typical variations are:

- Different columns;
- Temperature;
- Flow rate.

Ruggedness

Ruggedness refers to the ability of an analytical method to produce consistent and reproducible results when subjected to variations that are commonly encountered in different laboratories or by different analysts. It assesses how reliably the method performs under changes such as different operators, instruments, reagents, laboratories, temperatures, or timing. To evaluate ruggedness, the reproducibility of results for the same sample is measured under these varying conditions and compared with the method's precision under standard conditions. This comparison provides an indication of how robust and dependable the analytical method is in practical use. [17]

Acceptance Criteria of Validation for HPLC:

Table 1

S. No	Parameter	Acceptance criteria
1	Accuracy	% Recovery 98 – 102 % %RSD of recovery concentrations must be < 2
2	Precision	RSD < 2%
3	Range	Concentration where data can be reliably detected(80 – 120%)
4	Specificity	No interference
5	Linearity	Correlation coefficient – NLT 0.999
6	Detection Limit	S/N > 2 or 3
7	Quantitation Limit	S/N > 10
8	Ruggedness	Should meet all system suitability parameters
9	Robustness	RSD < 2%

Validation Protocol [7,8]

Validation protocol should include the following points:

- ❖ Objectives
- ❖ Introduction
- ❖ Scope
- ❖ Responsibilities
- ❖ Product details
- ❖ Chemical / reagents
- ❖ Equipment / instruments details
- ❖ Details of analytical method and solution preparation

CONCLUSION

The article emphasizes that analytical method validation is a crucial aspect of the pharmaceutical industry, ensuring that analytical methods are accurate, reliable, and suitable for their intended purpose. It provides a comprehensive understanding of validation, its types, necessity, development procedures, and key parameters such as linearity, LOD, LOQ, range, specificity, robustness, ruggedness, and system suitability. The review aims to guide young researchers in enhancing the quality of analytical method development and validation, thereby ensuring consistency, reliability, and overall quality in drug development and production.

Conflict Of Interest

There is no conflict of interest from all the authors.

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Review Article

An Overview of Liposome

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ABSTRACT

Liposomes are spherical vesicles composed of one or more phospholipid bilayers encapsulating an aqueous core, widely used as drug delivery systems due to their biocompatibility, biodegradability, and capacity to encapsulate both hydrophilic and hydrophobic molecules. Their preparation typically involves lipids (such as synthetic or natural phosphatidylcholines, cholesterol) and aqueous media, employing methods like thin-film hydration, ethanol injection, reverse-phase evaporation, and extrusion. Critical formulation parameters (e.g., lipid composition, lipid-to-drug ratio, chain length, unsaturation, presence of cholesterol) strongly influence properties such as particle size, lamellarity, polydispersity, and encapsulation efficiency. Characterization and evaluation of liposomes involve a set of physicochemical and performance parameters: particle size and size distribution (often via Dynamic Light Scattering), zeta potential (for surface charge and colloidal stability), morphology (by electron microscopy), encapsulation efficiency (percentage of drug loaded), in vitro release profiles, membrane fluidity, and sometimes in vitro/in vivo stability or biodistribution. Optimization of these features is essential for ensuring effective delivery, minimizing toxicity, and achieving controlled release. liposomal properties are highly dependent on both formulation and process variables, a systematic design and thorough analytical characterization are critical in developing clinically viable liposome-based therapeutics.

INTRODUCTION

The name liposome is derived from two Greek words: Lipo = "fat" and Soma = "body". A liposome is the drug delivery system which is structurally seeing like a colloidal, vesicular and made up one or more than one lipid bilayer (outer layer) in which the equal number of aqueous layer (inner layer) is inclosed into it shown in Figure 1 which contains a substance like peptides and protein, hormones, enzymes, antibiotics, antifungal and anticancer agent in this delivery

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system drug achieve the long therapeutic effect for the treatment of particular disease without affected to another part of the body.[1,2] Liposomes are composed of small vesicles of phospholipids encapsulating an aqueous space ranging from about 0.03-to 10 µm in diameter.[3] Liposomes can be produced with various lipid compositions or by different methods, leading to differences in parameters such as size, size distribution, surface electrical potential, number of lamellae, and encapsulation efficiency. Surface modification offers significant advantages in generating liposomes with distinct mechanisms, kinetic properties, and biodistribution profiles. Available products include Doxorubicin (Doxil, Myocet) for Kaposi's sarcoma, Daunorubicin (Daunoxome), and Cytarabine. These artificial microscopic vesicles consist of an aqueous core surrounded by one or more layers of phospholipids and are utilized to deliver vaccines, drugs, enzymes, or other agents to specific cells or organs.[4] Liposomes are nano-sized artificial vesicles characterized by a spherical shape. They can be created from natural phospholipids and cholesterol. When phospholipids interact with water, they immediately form a double-layered sphere.[5] Consequently, Dr. Bauman Cosmetic exclusively creates liposome products that are free from fragrances and artificial preservatives. The same phospholipids that make up the liposome membrane also constitute the walls of skin cells. Likewise, the substance found between skin cells is made up of phospholipids, ceramides, triglycerides, free fatty acids, cholesterol, and water. If skin cells are slightly compromised or if the intercellular substance is diminished due to harsh cleansing practices, liposomes can effectively restore the missing lipids. Thus, the combination of phospholipids, ceramides, and other lipids naturally found in the skin is beneficial. A liposome is a small bubble (vesicle) composed of materials similar to those of the cell membrane. Liposomes can be loaded with medications and utilized to deliver drugs for cancer treatment and other illnesses.[6,7,8]

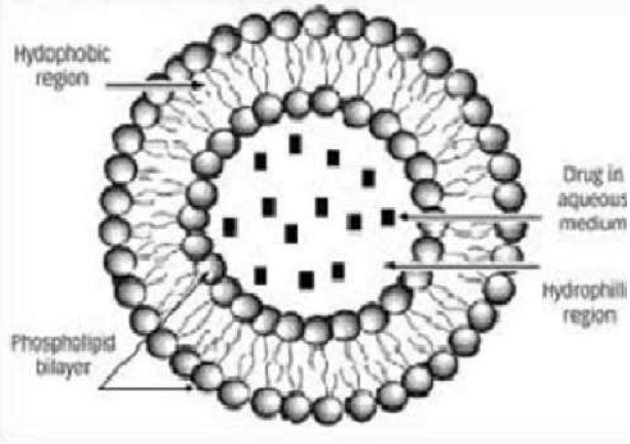

Fig No1: Structure of liposome

Structure of liposomes:[9,10]

Phospholipids

- Naturally occurring phospholipids used in liposome:
  - Phosphatidylethanolamine
  - Phosphatidylcholine
  - Phsphatidylserine

- Synthetic phospholipids used in the liposomes are:

  - Dioleoyl phosphatidylcholine
  - Disteroyl phosphatidylcholine
  - Dioleoyl phosphatidylethanolamine

Cholesterol

Cholesterol can be incorporated into phospholipid membranes at very high ratios, reaching up to 1:1 or 2:1 molar ratio of cholesterol to phosphatidylcholine. As an amphipathic molecule, cholesterol embeds itself within the membrane with its hydroxyl group directed towards the aqueous environment and its aliphatic chain aligned parallel to the acyl chains in the interior of the bilayer. Additionally, it increases the spacing between choline head groups and disrupts the usual electrostatic and hydrogen bonding interactions.

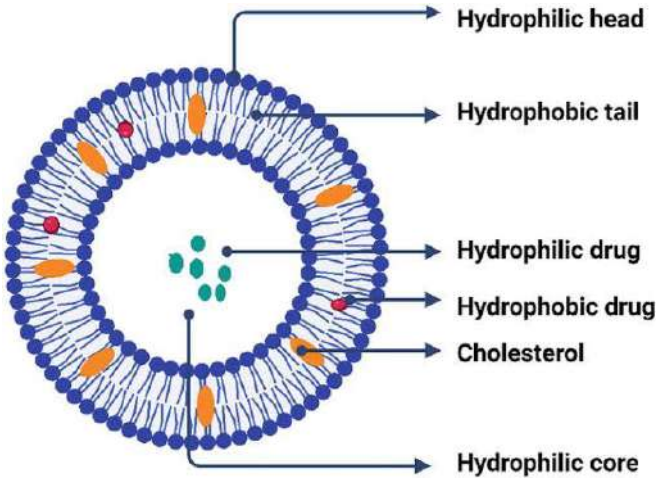

Fig No2: An illustration of liposome and its structural component

History Of Liposome:

Liposomes were initially identified in the mid-1960s by British hematologist Dr. Alec D. Bangham. His research focused on the structure of cell membranes, and he inadvertently discovered liposomes while using an electron microscope. Liposomes are minuscule spherical entities composed of lipid bilayers, resembling the architecture of cell membranes. Dr. Bangham's pioneering research established the groundwork for comprehending and developing liposomes for a variety of applications.[11]

In the subsequent decades, liposomes were acknowledged for their promise in drug delivery. Their capability to encapsulate pharmaceuticals and transport them to targeted areas within the body transformed the landscape of pharmacology. Liposomal drug delivery systems enabled controlled release and minimized the side effects associated with numerous medications.[12]

Over time, liposomes have been utilized not only in drug delivery but also in cosmetics, food technology, and gene therapy. Researchers have created various liposome types featuring different sizes, compositions, and surface modifications to enhance their performance for particular uses.[13,14]

ADVANTAGES:[15,16]

- Some of the advantages of liposome are as follows

- Provides selective passive targeting to tumour tissues (Liposomal doxorubicin).
- Reduction in toxicity of the encapsulated agents.
- Increased efficacy and therapeutic index.
- Increased stability via encapsulation.
- Improved pharmacokinetic effects (reduced elimination, increased circulation life times).
- Flexibility to couple with site specific ligands to achieve active targeting.

DISADVANTAGES:[15,16]

- Short half-life.
- Low solubility.
- Leakage and fusion of encapsulated drug/ molecules.
- Production cost is high.
- Fewer stables.
- Sometimes phospholipids undergo oxidation and hydrolysis-like reaction.

Classification of Liposomes:[17]

A] Based on structure parameter

1. Multilamellar vesicles (MLV) – (> 0.5 mm)
2. Oligolamellar vesicles (OLV) – (0.1-1.0 mm)
3. Unilamellar vesicles (ULV) – (all size ranges)

- Medium Unilamellar vesicle (MUV)
- Small Unilamellar vesicle (SUV) – (20-100 nm)
- Glant Unilamellar vesicle (GUV) – (>1.0 mm)
- Large Unilamellar vesicle (LUV) – (>100 nm)

4. Multivesicular vesicles (MVV) – (>1.0 mm)

B] Based on Method of Preparation

1. Dehydration rehydration method (DRV)
2. SUVs/OLVs made by reverse phase evaporation method (REV)
3. MLVs made by reverse phase evaporation (MLV-REV)
4. Stable plurilamellar. Vesicles (SPLV)
5. Frozen and thawed MLV (FATMLV)
6. Vesicles prepared by Extrusion Technique (VET)

C] Based on Composition and Application

1. CL (conventional Liposomes) - neutral/negatively charged phospholipids and cholesterol
2. Fusogenic Liposomes - RSVE Reconstituted Sendai Virus
3. pH sensitive Liposomes - Using phospholipids such as PE or DOPE with OA
4. Cationic Liposomes - cationic lipids with DOPE
5. Long Circulatory (Stealth) liposomes - Made using cholesterol and 5-10% PEG-DSPE or GM1
6. Immuno-liposomes - With attached monoclonal antibody

Mechanism of formation of Liposome

- As liposomes are made up of phospholipids, they are amphipathic in nature and have ability to binds both aqueous and polar moiety. They have polar head and non-polar tail.
- The polar end is mainly phosphoric acid and it will bound to water soluble molecule.
- In aqueous medium the molecules in self-assembled structure are oriented in such way that the polar portion of the molecule remain in contact with in polar environment and at same time shields the non polar part. Liposomes are formed when the thin films are hydrated and stacks of liquid crystalline bilayers become fluid and swells.
- Once these vesicles get formed, a change in vesicle shape and morphology required energy input in the form of …. Sonic energy to get SUVs and mechanical energy to get LUVs.
- However, in aqueous mixtures these molecules are able to form various phases, some of them are stable and other remains in metastable form.[18,19]

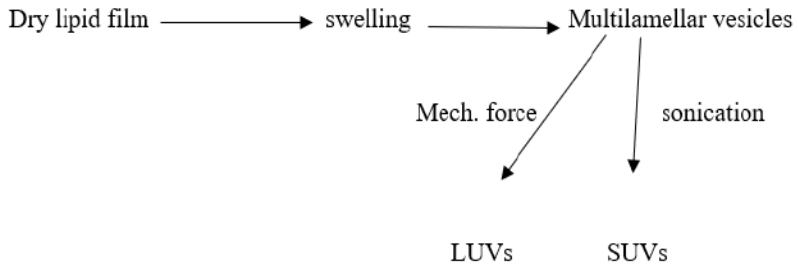

Fig No3: Mechanism of liposome preparation

Method Of Preparation:

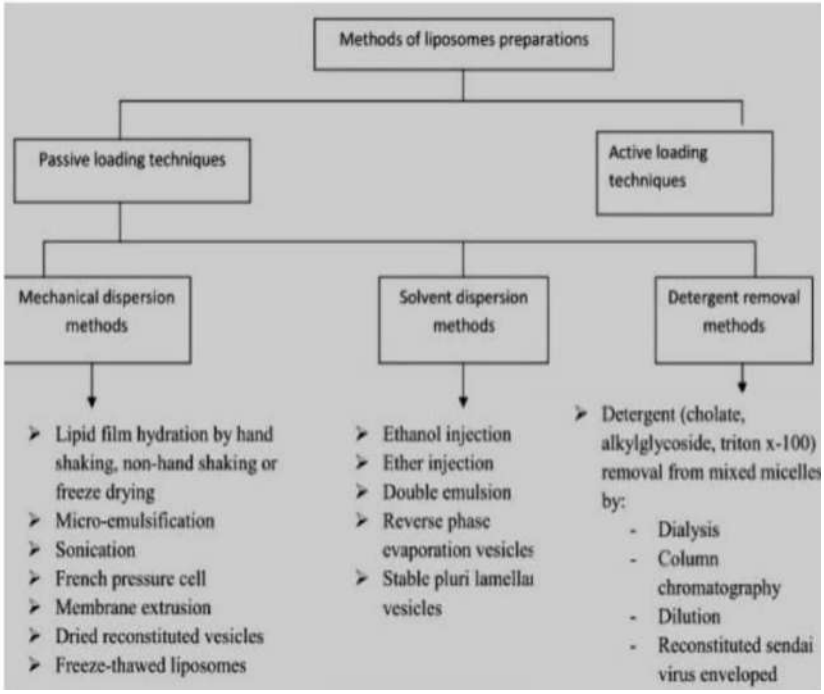

Fig No4: Different Methods of Liposome Preparations

A] Mechanical Dispersion Method

1) Lipid Film Hydration by hand shaking method:[20]

Liposomes were created using a physical dispersion technique with varying ratios of lipids. In this process, the lipids were dissolved in chloroform. This chloroform solution of lipids was spread over a flat-bottomed conical flask. The solution was then evaporated at room temperature without disturbing it. The hydration of the lipid film was performed with phosphate buffer (pH 7.4) while tilting the flask to one side, and the aqueous medium containing the drug to be encapsulated was introduced into the side of the flask as it was slowly returned to an upright position. The fluid was gently allowed to flow over the lipid layer, and the flask was left standing for 2 hours at 37°C for complete swelling; after swelling, the vesicles were collected by swirling the contents of the flask to produce a milky white suspension. The formulations were then subjected to centrifugation. Various batches of liposomes were prepared to identify the optimum formulation.

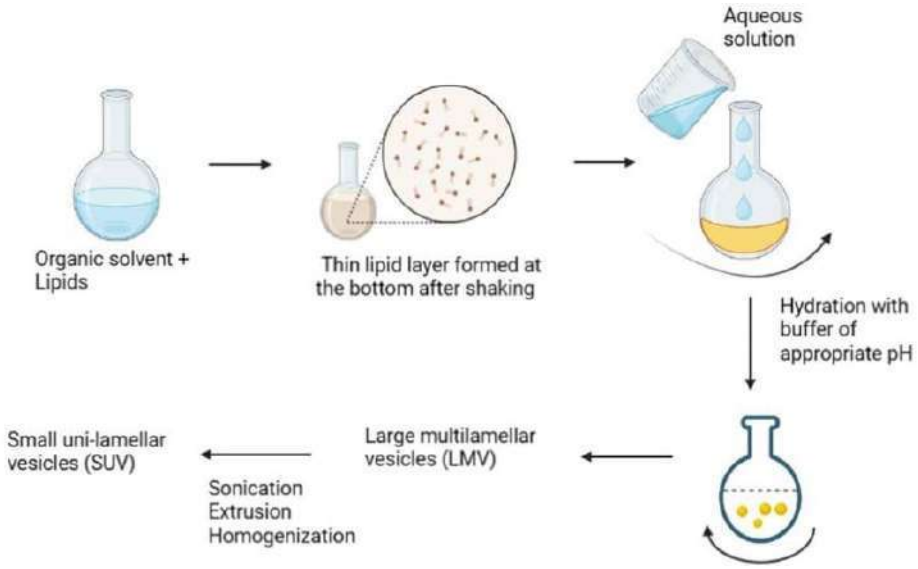

Fig No5 : Lipid Film Hydration method

2) Micro-emulsification:[21]

"Micro fluidizer" is used to prepare small MLVs from concentrated Lipid dispersion. Micro fluidizer pumps the fluid at very at very high pressure (10,000 psi), through a 5 micrometer orifice. Then, it is forced along defined micro channels which direct two streams of fluid to collide together at the right angles at a very high velocity, there by affecting an efficient transfer of energy. The lipids can be introduced into the fluidizer, either as large MLVs or as the slurry of un hydrated lipid in organic medium. The fluid collected can be recycled through the pump and interaction chamber until vesicles of spherical dimensions are obtained. diameter After a single pass, the size of vesicles is reduced to a size 0.1 and 0.2um .

3) Sonication:

This is the procedure by which Multi Lamellar Vesicles (MLVs) are converted into small Uni Lamellar Vesicles (SUVs). Ultrasonic irradiation is applied to the MLVs to produce the SUVs. Two techniques are utilized: a) Probe sonication method, and b) Bath sonication method. The probe

method is used for dispersion and requires high energy for small volumes (for instance, high concentrations of lipids or a viscous aqueous phase), while bath sonication is better suited for larger volumes of diluted liquids. The probe tip sonicator delivers a substantial amount of energy to the liquid dispersion but can lead to overheating of the liposomal dispersion, resulting in lipid degradation. Additionally, the sonication tip may introduce titanium into the liposome dispersion, which can be removed through centrifugation before use. For these reasons, bath sonicator tend to be more commonly employed. The sonication of MLVs is performed by either placing the dispersion in a bath sonicator or immersing the probe tip into the test tube containing the dispersion (for a duration of 5-10 minutes). Following sonication, the resulting dispersion is centrifuged, and as illustrated in the diagram, the SUVs will remain at the top while the smaller MLVs and aggregated lipids settle at the bottom. The upper layer consists of a pure dispersion of SUVs with varying diameters, as size is influenced by factors such as composition, concentration, temperature, duration of sonication, volume, and sonication tuning.

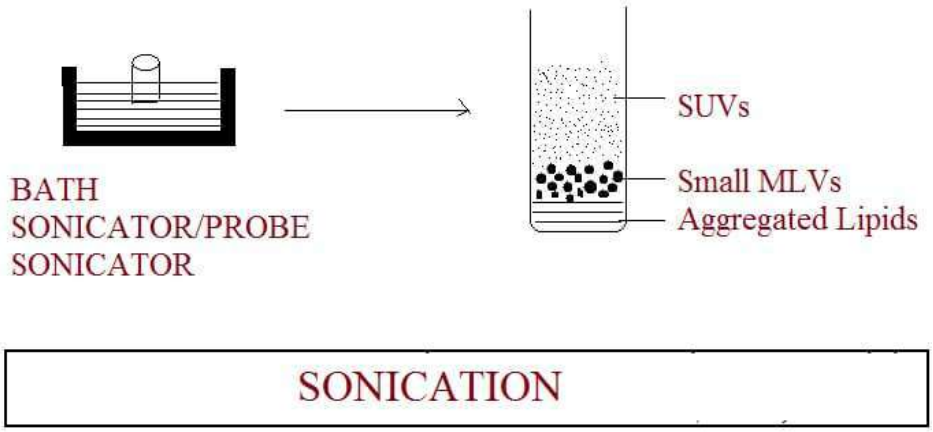

Fig No6 : Method of preparation of liposomes by sonication

4) French-Pressure Cell :[22,23]

The French pressure cell technique consists of extruding MLV through a small orifice. A key characteristic of the French pressure vesicle method is that proteins do not seem to be significantly altered during the process, unlike in sonication. This technique involves gentle handling of sensitive substances. It offers several benefits compared to sonication. The resulting liposomes are generally larger than the small unilamellar vesicles produced by sonication. However, the method has some limitations, such as the difficulty in achieving high temperatures and the relatively small working volumes, which are capped at about 50 ml.

5) Membrane Extrusion :

This technique can effectively process both LUVs and MLVs. The liposome size is minimized by gently forcing them through a membrane filter with a specific pore size, achieved at much lower pressures (<100 psi). During this process, the contents of the vesicles are exchanged with the dispersion medium as the phospholipid bilayers break and reseal while passing through the polycarbonate membrane. Liposomes generated through this method are referred to as LUVETs. This technique is the most commonly utilized method for producing SUVs and LUVs for both in vitro and in vivo research.

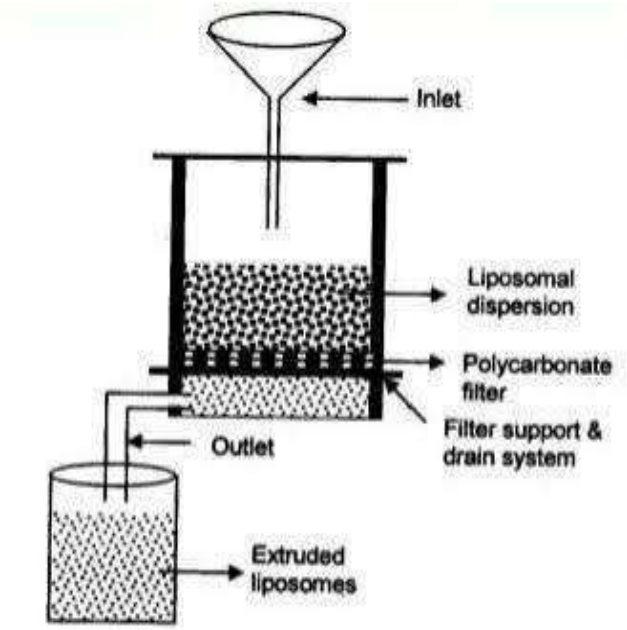

Fig No7 : Liposome Prepared by Membrane Extrusion method

6) Dried Reconstituted Vesicles:

This method starts with freeze drying of a dispersion of empty SUVs. After freeze drying the freeze dried membrane is obtained. Then these freeze dried SUVs are rehydrated with the use aqueous fluid containing the material to be entrapped. This leads to formation of the solutes in oligolamellar vesicles.

7) Freeze Thaw Sonication:

This method is based upon freezing of a unilamellar dispersion(SUV). Then thawing by standing at room temperature for 15min.Finally subjecting to a brief Sonication cycle which considerably reduces the permeability of the liposomes membrane. In order to prepare GIANT VESICLES of diameter between 10 and 50um, the freeze thaw technique has been modified to incorporate a dialysis step against hypo- osmolar buffer in the place of sonication. The method is simple, rapid and mild for entrapped solutes, and results in a high proportion of large unilamellar vesicles formation which are useful for study of membrane transport phenomenon. This method is based upon freezing of a unilamellar dispersion(SUV). Then thawing by standing at room temperature for 15min. Finally subjecting to a brief Sonication cycle which considerably reduces the permeability of the liposomes membrane. In order to prepare GIANT VESICLES of diameter between 10 and 50um, the freeze thaw technique has been modified to incorporate a dialysis step against hypo- osmolar buffer in the place of sonication. The method is simple, rapid and mild for entrapped solutes, and results in a high proportion of large unilamellar vesicles formation which are useful for study of membrane transport phenomenon.[3,24,25]

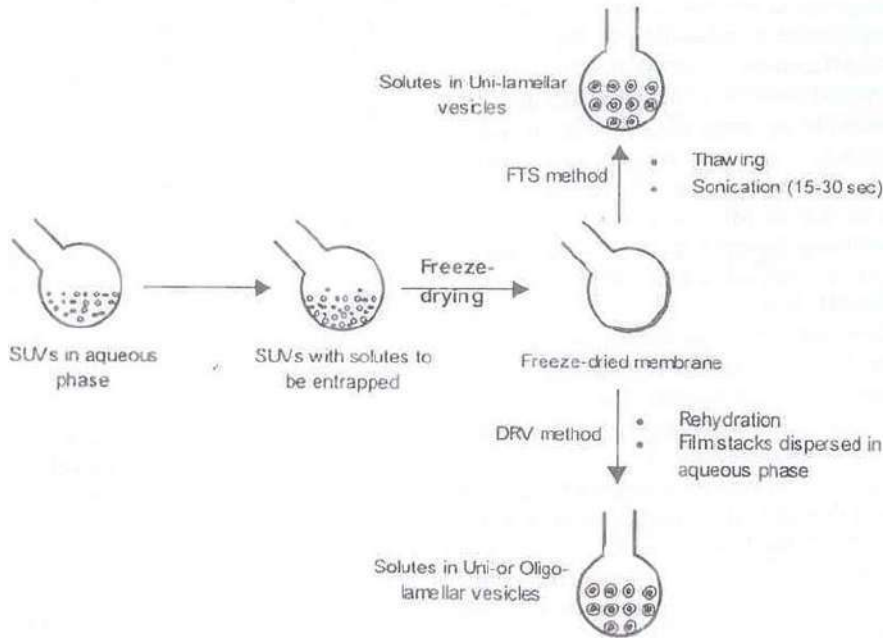

Fig No8: Liposome Prepared by Dried Reconstitute Vesicles/Freeze Thaw Sonication Method

B] Solvent Dispersion Method

1) Ethanol Injection Method :[26]

A lipid solution containing ethanol is quickly injected into a large amount of buffer, resulting in the immediate formation of MLVs. The challenges associated with this method include a heterogeneous population size (ranging from 30 to 110 nm), a very low concentration of liposomes, difficulties in completely removing all ethanol due to its formation of an azeotrope with water, and the risk of inactivating various biologically active macromolecules even with minimal ethanol exposure.

2) Ether Injection Method :

A lipid solution in diethyl ether or an ether/methanol combination is gradually added to an aqueous solution containing the material intended for encapsulation at a temperature of 55-65°C or under reduced pressure. Removing the ether under vacuum afterwards results in the creation of liposomes. The key disadvantages of this method include a heterogeneous particle

size distribution (ranging from 70 to 190 nm) and the exposure of the encapsulated compounds to organic solvents or elevated temperatures.

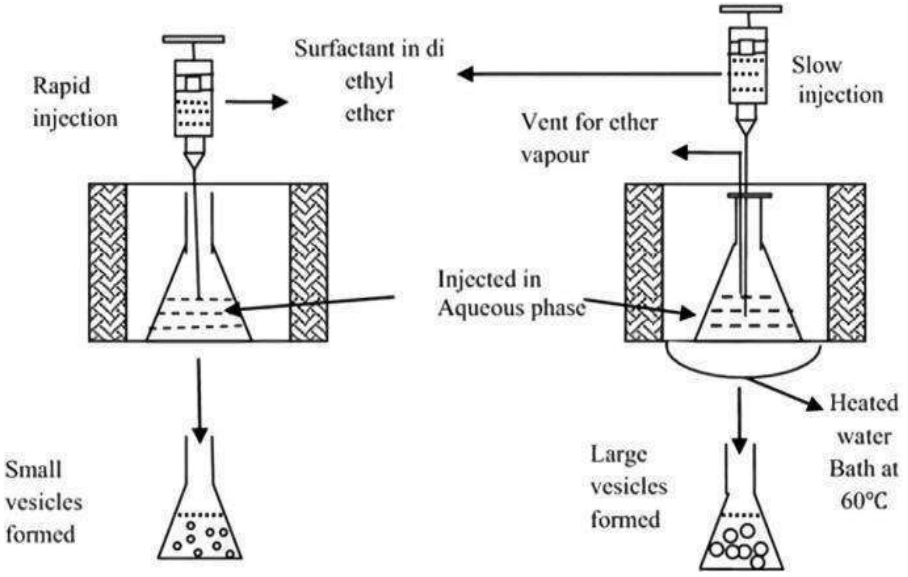

Fig No9 : Liposomes prepared by (1) Ethanol injection and (2) Ether injection method

3) Reverse Phase Evaporation Method :[27]

Initially, a water-in-oil emulsion is created by briefly sonicating a biphasic system that includes phospholipids dissolved in an organic solvent (such as diethyl ether, isopropyl ether, or a combination of isopropyl ether and chloroform) along with an aqueous buffer. The organic solvents are subsequently eliminated under low pressure, leading to the development of a thick gel. Liposomes are produced when the remaining solvent is effectively removed through ongoing rotary evaporation under reduced pressure. This technique can achieve a high encapsulation efficiency of up to 65% in a medium with low ionic strength, for instance, 0.01M NaCl. This method has been utilized for encapsulating both small molecules and large macromolecules. A significant drawback of this technique is that it exposes the encapsulated materials to organic solvents and to short intervals of sonication.

C] Detergent Removal Method :[28]

Detergents at their critical micelle concentrations have been utilized to solubilize lipids. As the detergent is eliminated, the micelles gradually become more enriched in phospholipids and ultimately merge to create IUVs. The removal of detergents can be achieved through dialysis. The benefits of the detergent dialysis method include high reproducibility and the generation of liposome populations that are uniform in size. The primary disadvantage of this technique is the potential for residual detergent(s) remaining within the liposomes. A commercial device known as LIPOPREP (Diachema AG, Switzerland), which is a type of dialysis system, is available for detergent removal. Other methods that have been employed for detergent removal include (a) Gel Chromatography using a Sephadex G-25 column, (b) the adsorption or binding of Triton X-100 (a detergent) to Bio-Beads SM-2, and (c) the binding of octyl glucoside (a detergent) to Amberlite XAD-2 beads.

Evaluation Of Liposome[29]

The liposomal formulation and processing for a designated purpose are defined to guarantee their consistent performance both in vitro and in vivo. The characterization parameters for evaluation can be categorized into three stages: physical, chemical, and biological parameters. Physical

characterization focuses on evaluating aspects such as size, shape, surface characteristics, and drug release profiles. Chemical characterization involves studies that determine the purity and potency of various lipophilic components. Biological characterization parameters aid in establishing the safety and appropriateness of the formulation for therapeutic use. Some of the parameters include:[28]

Characterization of Liposome Structure

Morphology:

- Transmission Electron Microscopy (TEM): Provides high-resolution images of liposome size, shape, and lamellarity.
- Scanning Electron Microscopy (SEM): Offers surface information and morphology details.

Size and Size Distribution:

- Dynamic Light Scattering (DLS): Measures particle size, size distribution, and polydispersity.
- Nanoparticle Tracking Analysis (NTA): Tracks and sizes individual liposomes in a liquid suspension.

Zeta Potential:[30]

- Electrophoretic Light Scattering: Determines the surface charge of liposomes, which affects stability and colloidal behavior

Lipid Composition Analysis:

- High-Performance Liquid Chromatography (HPLC): Identifies and quantifies lipids in liposomal formulations.

Liposome Properties:

Encapsulation Efficiency :

- UV-Visible Spectroscopy or Fluorescence Spectroscopy: Measures the concentration of encapsulated drugs or molecules.

Stability:

- Assessing changes in size, poly dispersity, and zeta potential over time under various storage conditions (e.g., temperature, pH).

Drug Release Kinetics:

- In vitro release studies to determine the rate and extent of drug release from liposomes.

Biological Evaluation:[31]

In vitro Cell Studies:

- Cell viability assays (MTT, Alamar Blue) to assess liposome cytotoxicity.
- Cellular uptake studies to evaluate liposome internalization and drug delivery efficiency.

In vivo Studies:

- Animal models to evaluate the pharmacokinetics, biodistribution, and therapeutic efficacy of liposomal drug formulations.

Biocompatibility and Toxicity Assessment:

- Hemolysis Assay: Measures the potential for liposomes to cause red blood cell damage.
- Immunogenicity Assessment: Investigates the immune response to liposomes.

Drug Release Studies

- Dialysis Method: Evaluates drug release kinetics under sink conditions by dialyzing liposomal suspensions against a release medium.
- Franz Diffusion Cell: Measures drug permeation through a membrane to mimic transdermal drug delivery.

Surface Modification Analysis

- Surface Characterization: Techniques like X-ray Photoelectron Spectroscopy (XPS) and Fourier-Transform Infrared (FTIR) spectroscopy to analyze modifications made to the liposome surface.

Marketed Formulations of Liposomes:[18]

Product	Drug	Company
Ambisome™	Amphotericin B	Nexstar pharmaceuticals Inc., CO
Abelcet™	Amphotericin B	The Liposome Company, NJ
Amphocil™	Amphotericin B	Sequus pharmaceuticals, Inc., C.A
Doxil™	Doxorubicin	Sequus pharmaceuticals, Inc., C.A
Daunoxome™	Daunorubicin	Nexstar pharmaceuticals, Inc., CO
Mikasome™	Amikacin	Nexstar pharmaceuticals, Inc., CO
DC99™	Doxorubicin	Liposome CO., NJ, USA
Epaxel™	Hepatitis A Vaccine	Swiss Serum Institute, Switzerland
ELA-Max™	Lidocaine	Biozone Labs, CA, USA

Applications Of Liposome:

Drug Delivery:[32]

- Liposomes are commonly used as drug delivery vehicles to encapsulate and deliver both hydrophobic and hydrophilic drugs.
- They can improve drug solubility, stability, and bioavailability.
- Liposomal drug formulations can target specific tissues or cells, reducing systemic side effects.

Vaccines:[33]

- Liposomes are used as adjuvants or carriers for vaccines to enhance immunogenicity.
- They can improve antigen delivery to immune cells, leading to a stronger immune response.

Cosmetics and Skincare:

- Liposomes are utilized in cosmetics and skincare products for controlled release of active ingredients, such as vitamins and antioxidants.
- They can enhance the penetration of ingredients into the skin, improving their efficacy.

Gene Delivery:[34]

- Liposomes can be used to deliver genetic material, including DNA and RNA, for gene therapy applications.
- They protect and facilitate the transport of genetic cargo into target cells.

Diagnostics:

- Liposomes can serve as carriers for contrast agents in medical imaging, such as magnetic resonance imaging (MRI) and ultrasound.

- They enable targeted imaging of specific tissues or cells.

Cancer Therapy:[35]

- Liposomal formulations of chemotherapy drugs, like Doxil (liposomal doxorubicin), are used to treat cancer.
- They can improve drug circulation time and reduce damage to healthy tissues.

Food Technology

- Liposomes are applied in the food industry for encapsulating and protecting sensitive ingredients, such as vitamins, flavors, and antioxidants.
- They can improve the stability and bioavailability of these additives in food products.

Biotechnology

- Liposomes are used in research and biotechnology applications for drug screening and delivery to cells in vitro.
- They are valuable tools for studying cell membrane interactions and drug transport mechanisms

Transdermal Drug Delivery:[36]

- Liposomal formulations can be applied topically to deliver drugs through the skin.
- They offer controlled release and can avoid the first-pass metabolism in the liver.

Personal Care Products

- Liposomes are employed in personal care products such as sunscreens and moisturizers to enhance the delivery of active ingredients.

Veterinary Medicine

- Liposomes are used in veterinary medicine for drug delivery to animals, similar to their applications in human medicine.

Environmental Remediation:

- Liposomes can be utilized for the controlled release of remediation agents in environmental cleanup efforts.

Intracellular Delivery:[37]

- Liposomes are valuable tools in research for delivering molecules into specific organelles within cells.

Nutraceuticals:[33]

- Liposomes are used to enhance the bioavailability of nutraceutical compounds in dietary supplements.

Wound Healing

- Liposomal formulations can be applied to wound dressings to promote the controlled release of wound-healing agents.

CONCLUSION

Liposomes are a promising and groundbreaking system for delivering drugs, with numerous applications in the pharmaceutical sector. Extensive studies over the years have shown their ability to address many challenges linked to conventional drug delivery methods. Liposomes have become an encouraging category of drug delivery systems that provide considerable benefits for improving the effectiveness and safety

of various medications. Although challenges persist, ongoing innovations and improvements in liposomal technologies offer great potential for the future of drug delivery within the pharmaceutical domain. Liposomes offer an exciting and adaptable strategy for drug delivery, with the capacity to transform the pharmaceutical landscape by enhancing drug effectiveness, minimizing side effects, and allowing targeted therapies. Further progress in liposomal technology is expected to broaden their application across a diverse array of medical uses.

Conflict Of Interest

The authors declare that there is no conflict of interest.

ACKNOWLEDGMENT

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ASSURING ASEPTIC INTEGRITY: UNIFIED STRATEGIES FOR CLEANING VALIDATION, ENVIRONMENTAL SURVEILLANCE

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ABSTRACT

Assuring aseptic integrity is a critical component of sterile pharmaceutical manufacturing and depends on two interrelated programs: cleaning validation and environmental surveillance. Cleaning validation ensures that equipment, surfaces, and systems are free from residues of previous products, cleaning agents, and microbial contaminants. Environmental surveillance monitors the manufacturing environment to detect and control microbial and particulate contamination that could compromise product sterility. Current regulatory guidelines, including FDA (2020) and EU Annex 1 (2022), emphasize an integrated, risk-based approach linking these two systems. Unified strategies involve scientifically justified cleaning procedures, effective disinfectant rotation, monitoring of high-risk areas, trend analysis, and the use of rapid microbiological methods (RMMs) for timely decision-making. Biofilm control in water systems and cleanroom surfaces remains a major challenge requiring continuous improvement. Data-driven environmental monitoring programs help identify contamination sources and ensure consistent compliance with aseptic standards. The harmonization of cleaning validation results and environmental monitoring data supports root-cause investigations, corrective and preventive actions (CAPA), and continuous process improvement. Together, these strategies build a robust contamination control framework that maintains product safety, efficacy, and regulatory compliance.

KEYWORDS: Aseptic integrity, cleaning validation, environmental surveillance, contamination control, sterile manufacturing, risk-based approach, biofilm control, FDA guidance.

INTRODUCTION

Validation of cleaning is a crucial component of GMP, or good manufacturing procedures. The primary regulatory concern with cleaning validation is cross-contamination of the intended therapeutic material by cleaner agent residues or an active pharmaceutical component from a previous batch.[1] Producing goods with the specified qualities and attributes consistently at the lowest possible cost is the main objective of any pharmaceutical facility.[2] The quality of a product should always be the primary consideration. As a result, pharmaceuticals need to be created that can deliver a consistent therapeutic effect in a mass-producible formulation while maintaining the highest standards of quality in the final product. A product must undergo validation in order to be authorized for commercialization.[3]

Ted Byers and Bud Loftus, two FDA employees, proposed validation as a way to improve the quality of medications in the middle of the 1970s. Numerous sterility problems in the high-volume parenteral sector prompted its design.[4] "Value is documented evidence that provides a high degree of assurance that a specific process will consistently produce a product that meets its predetermined specifications and quality attributes," according to the U.S. Food and Drug Administration (USFDA).[5] According to current good manufacturing practice (cGMP) guidelines, cleaning procedures should be followed for each step of the production, handling, storage, and distribution of active pharmaceutical ingredients. To ensure that there is no substantial risk of contamination, cross-contamination, or carryover to API quality, cleaning procedures should be confirmed.[6]

Documented evidence that a system or piece of equipment can be cleaned regularly to specified and agreed limitations is known as cleaning validation. It is necessary to validate a cleaning procedure to make sure it conforms with all relevant rules and regulations. The primary benefit of carrying out such validation work is locating and fixing any potential flaws that have already been identified and could compromise the efficacy, safety, or quality of subsequent batches of pharmaceutical items made inside the machinery. Tr.[7] Cleaning procedures must strictly follow methods of execution that have been thoroughly planned and validated.[8]

Cleaning validation confirms the cleaning method's "efficacy" in removing pollutants, preservatives, excipients, degradation products, and product residues. It also confirms that any potential microbiological contaminants are controlled. But it is imperative to ensure that there is no chance of *Surabhdahiya@dpsru.edu.in is the author of the correspondence. Cleaning Validation of cross-contamination of active chemicals. It is imperative that cleaning practices follow exacting requirements that have been carefully specified and tested.[9]

Cleaning validation is required to discuss techniques that have been deemed appropriate in order to ensure uniformity and consistency. As with other process validation, it is important to understand that there may be multiple approaches to process validation when it comes to cleaning validation. Any validation process's ultimate test is if scientific evidence demonstrates that the system regularly performs as anticipated and generates a result that regularly satisfies preset requirements.[10]

The CGMP parameter that is most commonly used and well-known is Pharmaceutical Process Validation. The regulations pertaining to process validation are part of the quality system (QS). It is the aim of a quality system to produce goods that are suitable for their intended usage. Process validation refers to how consistently the validation documents that must be included with the file submitted for a marketing licence are presented. Any manufacturing process can benefit from process validation, which is designed to assist producers in comprehending the requirements of their quality management system (QMS) for process validation. The FDA states that a number of important factors, such as the choice of quality processes and in-process and end-product testing, are crucial for ensuring the quality of products. The word "validation" was first used in the 1960s.[11]

An estimated 47.8 million Americans acquire foodborne illnesses from tainted food and drink, a prevalent and significant issue that claims more than 1,000 lives each year. Foodborne illness can be caused by bacteria, viruses, or parasites. Viruses are the most common infectious agents linked to foodborne illness outbreaks, with bacteria coming in second. Although bacteria can contaminate food at any stage of the food chain, the majority of outbreak-related diseases are linked to foods that have undergone minimal processing. For example, a food item that isn't KEYWORDS The consumer is more susceptible to foodborne infection or poisoning if there is cross-contamination, environmental monitoring, food contact surfaces, Listeria, Salmonella, or norovirus that requires additional inactivation measures (such as thermal treatment) before consumption. Food processing facilities must regularly prevent and control any microbial hazards in order to reduce this risk to the public's health. However, because of the variety of pathogen reservoirs and growth conditions, monitoring and controlling microbes in the food manufacturing environment has proven to be an ongoing issue. Animal reservoirs are frequently a source of bacteriological infections, including Salmonella and Escherichia coli, which can contaminate through evisceration processes and be shed by the microbiota of their faeces in the lower GI tract. Humans could be the main reservoir, or other diseases, like Listeria monocytogenes, could be present everywhere in the environment. Because of the variety of reservoirs, a complex system is needed to stop germs from entering the food processing facility. However, foodborne bacteria can spread through several routes besides direct transmission from a specific reservoir. The spread of bacteria across a food processing facility is often made worse by cross-contamination.[12]

MATERIALS AND METHOD

The methods and materials used in cleaning validation and environmental surveillance aim to ensure that pharmaceutical manufacturing processes maintain aseptic integrity by controlling contamination from equipment, personnel, and the production environment.

This section describes the essential materials, sampling and analytical methods, and the workflow used to validate cleaning and monitor aseptic conditions.[13]

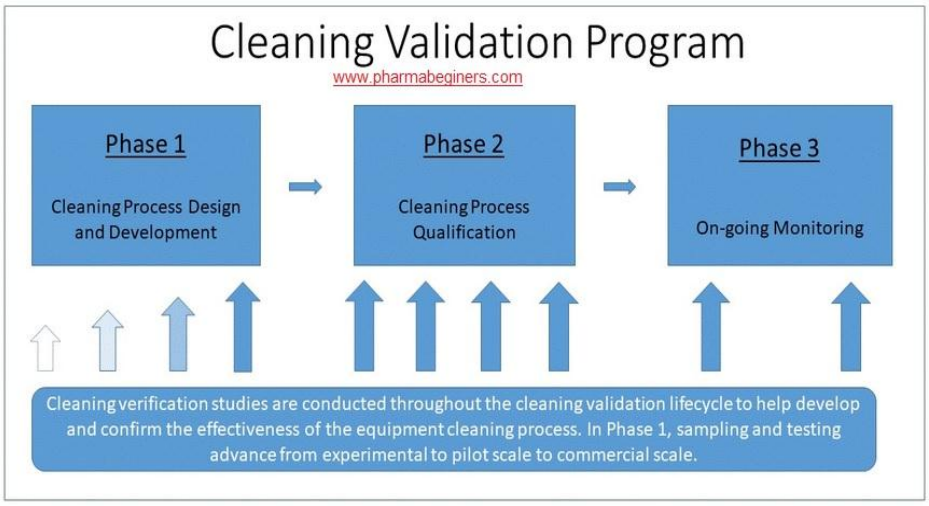

Fig. 1: Phases of Cleaning Validation.

MATERIA

Table 1: Material For Cleaning Validation.

Category	Example/ Description
Equipment	Mixing Tanks, Filling Lines, Reactors, Pipelines, Filtration Units, Isolators, And Cleanroom Surfaces**.**
Sampling Tool	Sterile Cotton Or Polyester Swabs, Stainless-Steel Templates (25 Cm^2), Sterile Containers For Rinse Samples, Contact Plates, Settle Plates.
Cleaning Agent	Purified Water (PW), Water For Injection (WFI), Isopropyl Alcohol, Sodium Hydroxide, Citric Acid, Or Surfactant-Based Detergents.
Disinfectant	Hydrogen Peroxide, Peracetic Acid, Ethanol, Quaternary Ammonium Compounds.
Analytical Reagent	Methanol, Acetonitrile, Phosphate Buffers, And Standards For HPLC/TOC Analysis.
Environmental Monitoring Media	Tryptic Soy Agar (TSA) Plates, Sabouraud Dextrose Agar (SDA), Air Samplers, Particle Counters.
Documentation	Cleaning Validation Protocols, Sampling Records, Equipment Logs, And Environmental Monitoring Data Sheets.

METHOD

A. Cleaning Validation

Cleaning validation confirms that the cleaning procedure removes all chemical and microbial residues to acceptable levels.[14]

Steps

1. Preparation And Planning

- Identify Equipment And Define Scope.
- Develop Cleaning Validation Protocol And Acceptance Limits.

2. Selection of Worst-Case Conditions

- Choose The Most Difficult-To-Clean Product Based On Solubility, Toxicity, And Equipment Design.

3. Execution of Cleaning Procedure

- Follow Standard Operating Procedures (Sops) For Manual Or Automated Cleaning.
- Record Parameters Like Time, Temperature, Detergent Concentration, And Rinse Volume.[16]

4. Sampling Methods

- Swab Sampling: Physical collection from defined surface area.
- Rinse Sampling: Collection of rinse water for analysis.
- Visual Inspection: Preliminary check for visible residues.[15]

5. Analytical Methods

- HPLC: Quantitative detection of product residues.
- TOC Analysis: Total organic residue measurement.
- UV Spectrophotometry: Rapid detection of UV-absorbing compounds.
- Microbial Count Test: Swab or contact plate test for microbial contamination.

6. Data Analysis and Evaluation

- Compare analytical results with acceptance criteria (MACO limits).
- Document three consecutive successful runs to confirm consistency.[16]

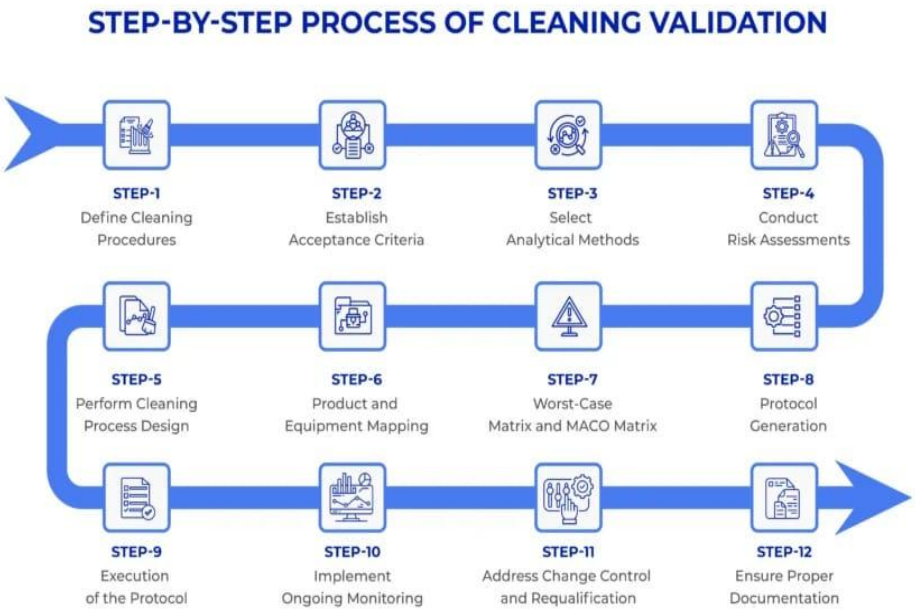

Fig. 2: Process of Cleaning Validation.

B. Environmental Surveillance

Environmental surveillance monitors the cleanroom environment to ensure aseptic control.

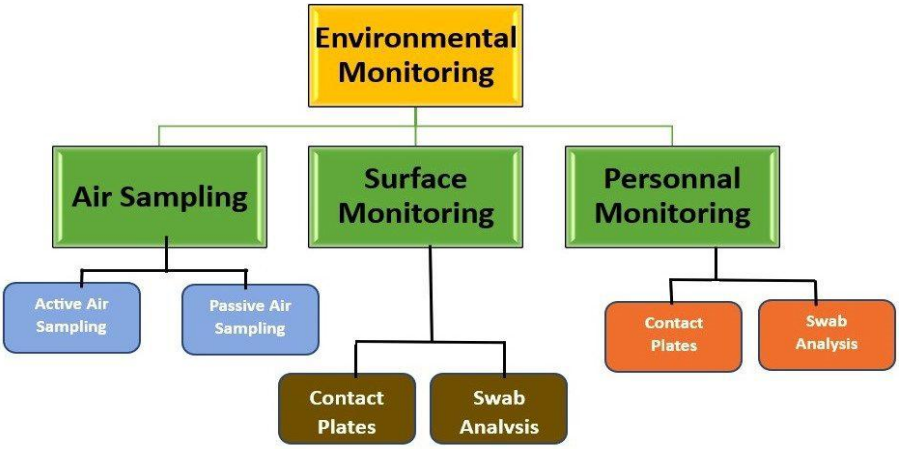

Fig. 3: Methods Used for Environmental Monitoring.

Key Monitoring Parameters

- Airborne particulate count (using particle counters)
- Viable microbial count (using air samplers or settle plates)
- Surface monitoring (swab or contact plate method)
- Personnel monitoring (finger dab or garment plate testing)

Frequency

- Routine (daily or weekly) monitoring in aseptic areas.
- Additional monitoring after equipment maintenance or process changes.

Evaluation

- Results are compared to the alert and action limits specified in EU GMP Annex 1 (2022).
- Deviations trigger investigation and corrective action

Data Interpretation and Documentation

- All analytical and environmental data are compiled into a Cleaning Validation Report and Environmental Monitoring Report.
- Deviations are documented, investigated, and corrective actions implemented.
- Validation is approved by the Quality Assurance (QA) department and reviewed periodically.[17]

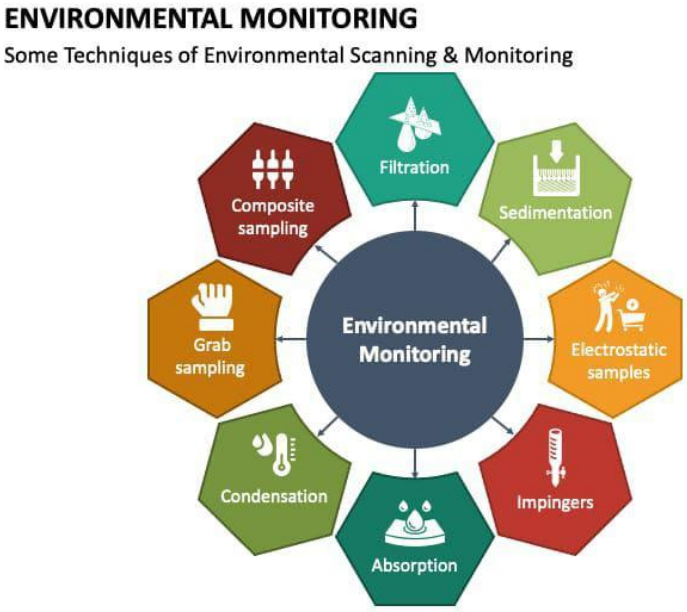

Fig. 4: Various Techniques For Environmental Monitoring.

FIGURE REFERENCE

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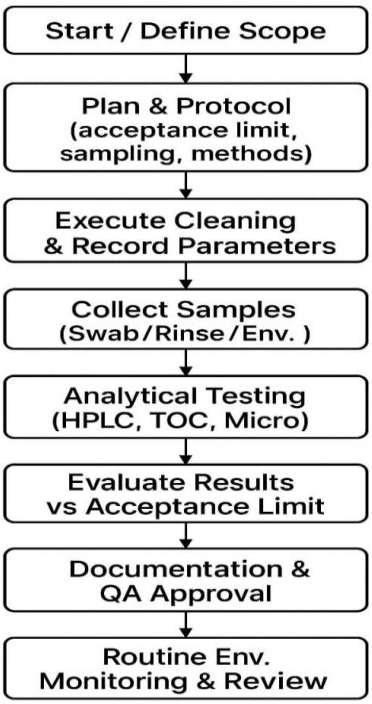
Flow Chart: Cleaning Validation and Environmental Surveillance Process.



RESULT AND DISCUSSION

Result

A. Cleaning Validation

Swab and rinse sampling confirmed that chemical residues and microbial contamination were below allowable limits (API < 10 ppm, CFU < 1/25 cm^2).

Three consecutive validation runs verified consistency and reproducibility of cleaning efficiency.

B. Environmental Surveillance

Airborne particles, viable microbes, and surface contamination were within EU GMP limits.

Personnel monitoring results confirmed proper aseptic practices during operations.

DISCUSSION

The integration of cleaning validation and environmental monitoring ensured equipment cleanliness and environmental sterility—key factors for maintaining aseptic integrity.

Analytical methods like HPLC and TOC proved effective, sensitive, and compliant with FDA and WHO standards.

Low chemical residue levels correlated with low microbial counts, confirming effective contamination control.

Continuous environmental monitoring supported proactive risk management and CAPA implementation,

aligning with EU GMP Annex 1 (2022) and WHO TRS No. 1025 (2020) guidelines.

CONCLUSION

1. Ensures Product Safety and Quality: Cleaning validation guarantees that equipment and processes consistently meet predetermined cleanliness standards, reducing the risk of cross-contamination and ensuring therapeutic efficacy.
2. Regulatory Compliance: Both cleaning validation and environmental surveillance are critical for complying with cGMP and FDA/EU regulations. Proper documentation and validated procedures support regulatory audits and marketing approvals.
3. Systematic and Reproducible Approach: The combined use of swab/rinse sampling, analytical testing, and environmental monitoring ensures that cleaning processes are scientifically validated and reproducible across multiple production batches.
4. Continuous Improvement: Regular environmental surveillance and trend analysis enable early detection of contamination risks, supporting preventive measures and CAPA initiatives for ongoing quality improvement.
5. Holistic Risk Mitigation: Together, these processes minimize chemical and microbiological hazards, protect patient health, and maintain the integrity of pharmaceutical manufacturing.

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Review Paper

An Overview on UV Spectroscopy with Applications

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ABSTRACT

Ultraviolet (UV) spectroscopy is a vital analytical technique used across chemistry, pharmaceuticals, and biological sciences for qualitative and quantitative analysis. It is based on the absorption of ultraviolet light (200–400 nm) by molecules, leading to electronic transitions from lower to higher energy states. The technique follows Beer-Lambert's law, which establishes a linear relationship between absorbance and concentration, making it suitable for precise quantitative measurements. A typical UV-Vis spectrophotometer consists of a radiation source, monochromator, sample cell, detector, and recording system. Common light sources include deuterium and tungsten lamps, while prisms or diffraction gratings serve as monochromators to isolate specific wavelengths. Detectors such as phototubes and photomultiplier tubes convert transmitted light into measurable signals. UV spectroscopy finds wide applications in quantitative chemical analysis, pharmaceutical quality control, biochemical research, and environmental monitoring. Its simplicity, accuracy, and cost-effectiveness make it indispensable for determining molecular structure, concentration, and purity, supporting research and industrial processes with high analytical precision and reproducibility.

INTRODUCTION

Spectroscopy is the technique which measures the Electromagnetic radiations (EMR) which is emitted or absorbed by molecules or atoms or ions of a sample when it moves from one energy state to another energy state and Electromagnetic radiation is a type of energy such as UV rays, Infrared rays, Micro-waves, Radio-waves, X-rays, Gamma rays and visible light etc.

Ultraviolet (UV) spectroscopy is one of the most widely employed analytical techniques in modern chemistry and pharmaceutical sciences. It is a type of absorption spectroscopy which involves the interaction of ultraviolet light, typically in the wavelength range of 200–400 nm, with a substance to study its electronic structure. When UV light passes through a sample, some of it is absorbed, causing the electrons in the molecules to move from a lower energy level (ground state) to

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a higher energy level (excited state), producing a distinct absorption spectrum. This spectrum serves as a molecular fingerprint that helps in the identification, purity assessment, and quantitative determination of chemical compounds.

Principle

The principle of UV-Vis spectroscopy is Based on the principle of absorption of UV light by chemical compounds, which result in production of different Spectra and the spectra arise from the transition of an electron within a molecule from ground state to excited state. When the molecules absorb UV radiation frequency the electron in that molecule undergoes transition from ground level to higher energy level cause electronics transition.

Electronic Transitions

When a molecule absorbs UV light, electronic transitions occur — electrons jump to higher energy orbitals. Molecules that have π-electrons (in double bonds) or non-bonding electrons (lone pairs) can easily absorb UV radiation. This absorption results in different types of transitions depending on the kind of electrons involved:

1. Σ → σ* (sigma to sigma star)
2. N → σ* (non-bonding to sigma star)
3. Π → π* (pi to pi star)
4. N → π* (non-bonding to pi star)

These transitions differ in energy, arranged as:

Σ–σ > n–σ > π–π* > n–π***
(from highest to lowest energy required).

Beer-Lambert's Law

This absorption process is mathematically represented by the Beer–Lambert Law, which defines a direct proportionality between absorbance (A) and the concentration (C) of the absorbing species in the solution,

Beer – Lambert's law states that;

When a beam of monochromatic radiation is passes through the absorbing medium, then the decrease in the intensity of the radiation is directly proportional to the thickness/pathlength as well as concentration of the solution.

The Beer -Lambert's law can be expressed as :

$$A \; a \; c \times l$$

$$A = \varepsilon \times c \times l$$

Where,

A=Absorbance ε=Molar absorptivity c= concentration l= pathlength According to this law, absorbance increases linearly with concentration within a specific range, which makes UV spectroscopy a reliable quantitative method for solution analysis.

Instrumentation

The essential parts of a spectrophotometer are :

1. Radiation Source
2. Monochromator
3. Sample cell
4. Detector
5. Recordings system

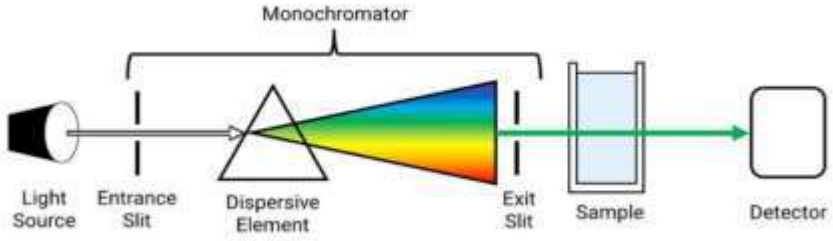

Fig.1. A basic block diagram of the elements in a spectrometer.

Radiation Source

In UV-Vis spectroscopy, the selection of a light source is crucial for accurate and reliable measurements.

The light source used in UV-Visible spectroscopy should give a steady and uniform intensity of light for all wavelengths. However, maintaining this uniformity is challenging. Therefore, to cover the full range of wavelengths—from ultraviolet to visible and sometimes even near-infrared regions—spectrophotometers usually use a combination of two different light sources.

Common light sources used in UV-Vis Spectrophotometers

Light Source	Principle of Operation	Key Applications
Hydrogen Discharge Lamp	Gas discharge through low-pressure hydrogen; emits continuous UV (190–400 nm)	Historically used in UV spectrophotometry; now mainly for calibration due to less stability.
Deuterium Arc Lamp	Gas discharge using deuterium (isotope of hydrogen); continuous UV emission	Preferred UV source (approx. 190–400 nm) in UV-Vis spectrophotometers; offers continuous, stable, long-lasting output.
Xenon Arc Lamp	High-pressure gas discharge in xenon; broad spectrum across UV, visible, near-IR	High-intensity, sunlight-like output; used in fluorescence spectroscopy, solar simulators, and high-intensity UV-Vis applications.
Mercury Arc Lamp	Electric discharge through mercury vapor; emits sharp spectral lines	Valuable for instrument calibration using characteristic UV/visible lines (e.g., 254 nm, 365 nm); also employed in germicidal UV for sterilization.

Monochromator

Monochromator is also known as Wavelength selectors. Used to isolate the desired wavelength of radiation from wavelength of continuous spectra.

Components of Monochromator

- **Entrance Slit:** It narrows the incoming light beam to prevent overlapping of different wavelengths, ensuring a clean input for analysis.
- **Collimating Mirror (Concave):** It straightens the diverging light rays from the entrance slit into parallel beams, which is essential for accurate wavelength separation.
- **Prism or Grating:** This component disperses the parallel light into its individual wavelengths by bending (prism) or diffracting (grating) the light, separating colors like a rainbow.
- **Focusing Mirror or Lens**: It refocuses the dispersed light onto the exit slit, directing the selected wavelength precisely.

- **Exit Slit:** It allows only the desired narrow band of wavelengths to pass through, blocking the rest, to deliver pure monochromatic light.

TYPES OF MONOCHROMATOR

- **Prism Monochromator:** Prism works by refraction. Different wavelengths of Light are bent at It is a transparent container that holds the sample being measured They are typically constructed from materials like quartz, glass, or plastic different angles as they pass through the prism material. (e.g., quartz for UV, glass for visible)
- **Diffraction Grating Monochromator:** Diffraction Grating works by diffraction and interference. A grating has thousands of finely ruled parallel lines. Light striking these lines is diffracted, and different wavelengths interfere constructively at different angles, spreading the light into a spectrum.

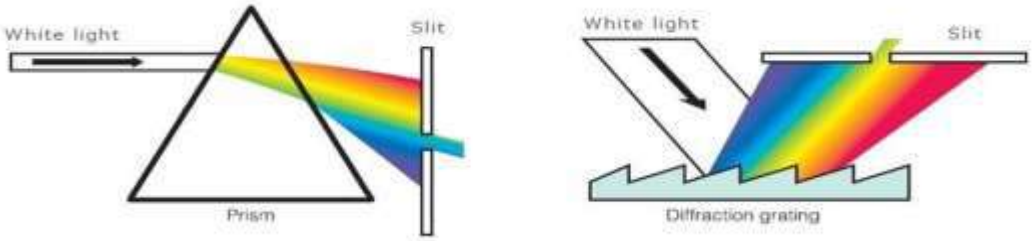

Fig. 2 Working of Monochromators

Sample cell

In UV-Vis spectrophotometry, a sample cell, also known as a *cuvette*, it is a transparent container that holds the sample being measured They are typically constructed from materials like quartz, glass, or plastic.

Fig. 3 Sample holder (Cuvette)

Detectors

A UV-Vis spectrophotometer, the detector is the component responsible For converting the light that has passed through the sample into a measurable electrical signal. This signal is then processed to determine the amount of light absorbed or transmitted by the samples.

Here are the common types of detectors used:

1. Photovoltaic Cell (Photocell)
2. Phototube (Photocell)
3. Photomultiplier Tube (PMT)

Photovoltaic cell (photocell)

Working Principle: Based on the photovoltaic effect light falling on a semiconductor generates electron–hole pairs, producing an electric current.

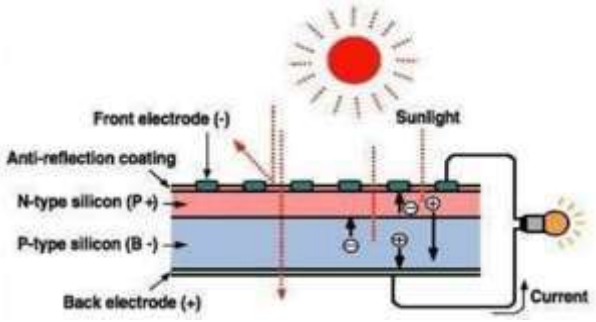

Fig. 4 Photovoltaic cell detector

Photomultiplier tube (PMT)

Working Principle: Also based on the photoelectric effect but with electron Multiplication. The photoelectrons emitted from the cathode strike a series of Dynodes, each releasing multiple secondary electrons, resulting in a large Amplified current.

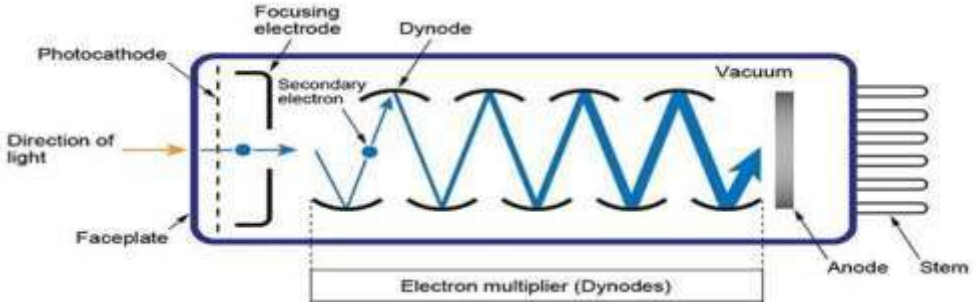

Fig. 5 Photomultiplier tube detector

Phototube (Photoemissive Cell)

Working Principle: Works on the photoelectric effect – light photons strike a Photosensitive cathode, releasing electrons, which are collected at an anode

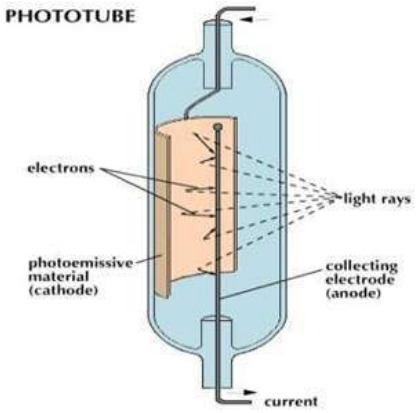

Fig. 6 Phototube detector

Working

Working principle of a spectrophotometer is based on the following steps:

Blank (measure of the intensity of light transmitted through the solvent):

1. The solvent (e.g. water or alcohol) is added into a suitable, transparent and not absorbing container – a cuvette.
2. A light beam emitted by the light source passes through the cuvette with the solvent.
3. The intensity of the transmitted light at different wavelengths is then measured by a detector and recorded.

Sample determination:

1. A sample is dissolved in the solvent and added into the cuvette.
2. A light beam emitted by the light source passes through the cuvette with the sample.
3. When passing through the cuvette, the light is partially absorbed by the sample molecules in the solution.
4. The transmitted light is then measured by the detector.
5. The light intensity change at different wavelengths is calculated by dividing the transmitted intensity of the sample solution by the corresponding values of the blank.

Applications

A. Quantitative Chemical Analysis:

In chemistry labs, UV spectrophotometry is used to measure how much of a substance (solute) is present in a solution. The Beer-Lambert Law explains that the amount of light absorbed by a

solution is directly related to the concentration of the absorbing substance. This allows scientists to accurately determine concentrations.

B. Biochemical and Biomedical Research:

In biology and medicine, UV spectrophotometers are used to study important molecules like proteins and nucleic acids (DNA and RNA). They help identify, measure, and monitor any structural changes in these biomolecules.

C. Pharmaceutical Analysis:

In the pharmaceutical industry, UV spectrophotometry is used to check the concentration of active pharmaceutical ingredients (APIs) in drug formulations. This ensures that medicines contain the correct amount of each ingredient.

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EXPLORING DOCUMENTATION IN MODERN PHARMACEUTICAL PRODUCTION AND MARKETING

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ABSTRACT

In the pharmaceutical industry, documentation is a key element of quality, safety, and compliance, and includes the master formula record (MFR), which is prepared by the research and development department and includes detailed information about the exact ingredients, raw material specifications, and the manufacturing steps required to create a product, the batch manufacturing record (BMR), which is a historical document that contains information about each step of the manufacturing process for an individual batch, including raw materials, equipment, and operators to ensure traceability, and standard operating procedures (SOPs), which provide written, step-by-step instructions for routine operations that help ensure accuracy, productivity, and consistency in pharmaceutical practices. Regulatory authorities at the national and international level also take a vital role in protecting public health by assessing the safety, efficacy, and quality. Additionally, dossiers serve as official submissions to these authorities, containing comprehensive information on product safety, efficacy, manufacturing, labelling, and compliance, thereby enabling approval for international marketing. Collectively, these documentation practices form the backbone of modern pharmaceutical production and marketing, ensuring high-quality medicines and global regulatory compliance.

KEYWORDS: Indian regulatory authorities, CDSCO, USFDA, GMP, Integrated system.

INTRODUCTION

The pharmaceutical sector is one of the most highly regulated industries worldwide. Documentation provides a scientific and legal record of every step in drug development, production, and marketing. Regulatory agencies such as the FDA, EMA, and CDSCO emphasize strict adherence to documentation to ensure patient safety and public trust. Studies indicate that inadequate documentation is one of the leading causes of regulatory observations, warning letters, and product recalls, making it a critical area of focus in modern pharmaceutical practice.[1-3]

Master Formula Record (MFR)

The MFR provides the approved set of instructions for manufacturing a specific pharmaceutical product. It specifies raw materials, their quantities, equipment requirements, and detailed steps of the process. By serving as the "master plan," the MFR ensures uniformity across all manufactured batches. Literature highlights that MFRs play a key role in maintaining Good Manufacturing Practices (GMP) and minimizing variability, thereby ensuring consistent quality of marketed products.[1-4]

Batch Manufacturing Record (BMR)

The BMR is derived from the MFR and serves as the real-time record of each production batch. It documents operator activities, equipment used, in-process checks, and final product testing. Research shows that electronic batch records (eBMRs) improve efficiency, reduce transcription errors, and facilitate regulatory audits. Review-by-exception (RBE) approaches, enabled by eBMR, allow faster batch release and improve compliance outcomes in global manufacturing facilities.[2-5]

Standard Operating Procedures (SOPs)
SOPs are structured documents that define standardized methods for routine tasks, including equipment cleaning, sampling, and quality testing. They act as training tools for staff and minimize errors due to inconsistent practices. Strong SOP management is vital for regulatory inspections and operational efficiency. Studies report that integration of SOPs with digital quality management systems (QMS) supports continuous improvement, audit readiness, and global harmonization in pharmaceutical operations.[6]

Regulatory Affairs and Dossier Preparation
Regulatory documentation ensures that products meet international requirements for safety, efficacy, and quality. The Common Technical Document (CTD) developed by the International Council for Harmonisation (ICH) provides a standardized format for submissions worldwide. Its electronic form (eCTD) is now mandatory in major markets such as the USA, EU, and Japan. Research emphasizes that well-structured dossiers reduce review time, accelerate market entry, and strengthen the global competitiveness of pharmaceutical firms.[3-7]

Modern Trends in Documentation
Pharmaceutical documentation is undergoing a digital transformation. Integrated systems such as Manufacturing Execution Systems (MES), Laboratory Information Management Systems (LIMS), and Enterprise Resource Planning (ERP) platforms enable real-time data management. Blockchain technology is also being explored to enhance supply chain traceability and prevent falsification. Studies indicate that digitized documentation improves compliance, reduces costs, and enhances data integrity, though validation and regulatory acceptance remain challenges.[2-5-8]

METHODS AND MATERIAL

Master formula record
Master Formula Record (MFR): Preparation and Structure
A Master Formula Record (MFR) is a critical document in pharmaceutical manufacturing, detailing the formulation and manufacturing process for a specific product. It serves as a reference for creating Batch Manufacturing Records (BMRs) and ensures consistency, quality, and regulatory compliance.

1. Cover Page
Content: Product name, dosage form, strength, batch size, shelf life, storage conditions, MFR number, revision history, and authorization signatures.

2. Product Information
Content: Generic and brand names, label claims, ingredients, description of finished product, packaging specifications, drug schedule classification, and superseded MFR details.

3. Bill of Materials (BOM)
Content: Detailed list of raw materials and packaging materials, including quantities per batch, overages, tolerances, material codes, and specifications.

4. Manufacturing Process
Content: Step-by-step instructions for manufacturing, including equipment and tools required, in-process quality control checks, expected yield and losses, and critical control points.

5. Packaging Instructions
Content: Details on primary, secondary, and tertiary packaging, labeling requirements, sealing and leak testing procedures, and final product inspection criteria.

6. Quality Control Specifications
Content: Finished product specifications, sampling plans and methods, stability data, storage conditions, and references to Standard Operating Procedures (SOPs).

7. Revision History
Content: Version number, date, reason for revision, approved by, and change control references.[9]

Form Number MF-001-V1
Date Original Issue: JULY 2021
Date Revised:
Page 1 of 1

MASTER FORMULA

PRODUCT NAME:			
FORMULA REFERENCE:			
FORM PREPARED BY:			
		LOT NUMBER:	
		THEORETICAL YIELD:	
START DATE:		FINISHED PRODUCT SIZE:	
MIX TANK:		BATCH SIZE IN LBS:	

PRODUCT DESCRIPTION:
Example: Anhydrous emollient skin balm, white in color. Bulk product is manufactured by xxx and packaged in white stick with orange cap. Then sent to third party for label and tag application and shipped to client from there.

RESPONSIBILITY:
The person in charge of making products is responsible for making this product. This formula is confidential, and should not be shared with others outside the company.

MATERIALS/EQUIPMENT/SUPPLIES:
1. Mix tank 3
2. Scale X
3. Bowls
4. Blender
5. Measuring cups/beakers
6. Thermometer

INGREDIENTS:		
Phase A		%
Phase B		%
Ingred #		
Ingred #		
Ingred #		
Ingred #		
Ingred #		
Ingred #		
TOTAL		100.00

Fig 1: Master Formula Record.

Batch Manufacturing Record
A Batch Formula Record (BFR) is a critical document in pharmaceutical manufacturing, detailing the specific formulation and manufacturing instructions for a particular batch. It serves as a comprehensive record of the ingredients, quantities, and processing steps involved in the production of the batch, ensuring consistency, traceability, and compliance with Good Manufacturing Practices (GMP).

Structure and Content of a Batch Formula Record

A well-structured BFR typically includes the following sections.

1. Product Information

Content: Product name, batch or lot number, manufacturing date, expiry date, packaging details (e.g., container type, size, and closure).

2. Formulation

Content: List of all ingredients, including active pharmaceutical ingredients (APIs), excipients, and any other components used.

3. Manufacturing Instructions

Content: Step-by-step instructions for the manufacturing process, including equipment used, operating conditions, and processing times.

4. Quality Control

Content: Specifications and acceptance criteria for raw materials, intermediate products, and finished products.

5. Packaging Instructions

Content: Details on primary, secondary, and tertiary packaging, labelling requirements, sealing and leak testing procedures, and final product inspection criteria.

6. Revision History

Content: Version number, date, reason for revision, approved by, and change control.[9]

	Pharmaceutical Guidelines Delhi, India Batch Manufacturing Record		Page No. 1 of 16
Product	: Atorvastatin Tablets IP 40 mg	**B.M.R. No.**	XX/XXX/000
		B.M.R Revision No./ Date	00/ddmmyyyy
Batch Size	: 2,00,000 Tablets	**Ref. M.F.R. No**	XX/XXX/000
Batch No.	: XXXXX/XX	**M.F.R. Revision No. & Date**	00/ddmmyyyy

Batch Quantity	: 35.00 kg.	**COMPOSITION:** **Each Film Coated Tablet contains:** Atorvastatin Calcium IP Equivalent to Atorvastatin ------ 40 mg Color :Titanium Dioxide IP
Reworking Added (If any)	:	
Theoretical Yield	:	
Mfg. Date:		Exp. Date:
Document issued by: Date:		Document Received by: Date:
This Document Supersedes	: None	
Reason for Change	: New	
Mfg. Licence No.	: XXXX/XX/XXXX	Material code No. - XXXXXXXX
Shelf Life	: 36 Months or expiry of active ingredient whichever is less.	
Storage Condition	: Store in cool, dry & dark place.	
Marketed by	: XYZ Pharmaceuticals Ltd.	
Serial No.	:	

	Granulation	Compression	Coating
Date of Commencement:			
Date of Completion:			
Area Used:			
Previous Product Processed:			
Batch No:			
Checked by Pharmacist: Date:			

This batch has/has not been completed according to the instructions given in M.F.R. No. XX/XXX/00.
Deviation sheet attached: Y/N

Actual Yield:_____Tablets Reworking Generated:_____Kg. Total Yield: _____%	Date of Packing: Quantity:
Final BMR Checked By: Date:	Final BMR Checked By: Date:

Prepared By	Checked By	Reviewed By	Approved By
Quality Assurance	Production	Production Head	QA & QC Head
Date:	Date:	Date:	Date:

Fig 2: Batch Manufacturing Record.

SOP (standard operating procedure)

Steps for Preparing a Standard Operating Procedure (SOP)

Step 1: Identify the Title and Purpose

The SOP should begin with a clear title, unique identification number, version, and effective date. The purpose section explains why the SOP is being developed, ensuring clarity for all users.[11]

Step 2: Define the Scope

The scope specifies where the SOP will apply, what activities are covered, and any limitations. This avoids ambiguity and ensures all relevant processes are included.[12]

Step 3: Assign Roles and Responsibilities

Responsibilities of each individual involved should be clearly defined to promote accountability and proper task delegation.

Step 4: List Materials and Equipment

The SOP must list required raw materials, instruments, and resources. Proper detailing ensures users follow the same standards each time.

Step 5: Write the Procedure

Provide step-by-step instructions in sequential order. This is the core of the SOP, ensuring repeatability and consistency of the process.[10]

Step 6: Include Quality Control and Assurance

SOPs should describe quality checks, acceptance criteria, and corrective actions to ensure data reliability.[12]

Step 7: Add Safety Considerations

Health and safety precautions must be integrated to protect both researchers and the environment during procedure execution.[11]

Step 8: Documentation and Record Keeping

This section outlines how results, deviations, and activities must be recorded and stored for regulatory compliance and auditing.[10]

Step 9: Review and Approval

The SOP should undergo expert review and approval before implementation. Regular revision ensures that it stays updated with regulatory and scientific developments.[11]

SOP Preparation Process

123 LIMITED (COMPANY NAME)

STANDARD OPERATING PROCEDURE

TITLE	:			SOP NO.	:	
DEPARTMENT	:			SUPERSEDES	:	
TARGET AREA	:			EFFECTIVE DATE	:	
PAGE NO.	:			NEXT REVISION DATE	:	
ACCOUNTIBILITY	:	PREPARED BY	REVIEWED BY	APPROVED BY	:	AUTHORIZED BY
NAME	:					
SIGNATURE	:					
DATE	:					
DESIGNATION	:					
DEPARTMENT	:					

1. PURPOSE
2. SCOPE
3. REFERENCES AND RELATED DOCUMENTS
4. ROLES AND RESPONSIBILITIES
5. ABBREVIATIONS
6. PROCEDURE
7. APPENDICES
8. REVISION HISTORY

Fig 3: SOP Sample.

Regulatory Bodies

Pharmaceutical regulatory agencies are regulatory bodies or authorities that have jurisdiction over the process of developing, improving, preparing, manufacturing, producing, and managing the quality and efficacy of pharmaceutical supplements.

It is morally and legally required that the appropriate steps be taken to ensure the highest quality, safety, and effectiveness of pharmaceutical products, even though no product is completely safe or effective in every situation.

INDIAN REGULATORY AUTHORITIES

Central drug standard control organization

Regulatory agencies provide strategic, tactical, operational, and practical data, guidance, and support to expedite the development and delivery of safe and effective healthcare products to people worldwide.

As the Central Drug Authority for carrying out the duties delegated to the Central Government by the Drugs and Cosmetics Act, the Central Drugs Standard Control Organization (CDSCO) is in charge of six zonal offices, four sub-zonal offices, eleven port offices, and six laboratories.

Key responsibilities of CDSCO

1. regulatory oversight of clinical trials, new drug approval, and drug imports.
2. meetings of the Drugs Technical Advisory Board (DTAB) and Drugs Consultative Committee (DCC).
3. Central Authority for Licence Approval.

The approval of licenses for specific drug categories, including blood and blood products, IV fluids, vaccines, and sera, falls under the purview of the Drug Controller General of India. According to the Drug and Cosmetics Act, the Central Authorities are in charge of approving new drugs and clinical trials nationwide, while the State Authorities are primarily in charge of regulating the production, sale, and distribution of drugs.

Ministry of Healthcare and Family Welfare.

A secretary to the Indian government leads each of the four departments that make up the Ministry of Health and Family Welfare.

Departments of Health and Family Welfare; Department of AYUSHD.

Department of Health Research.

Department of AIDS Control.

Department of AIDS Control recently merged with the Department of Health & Family Welfare to become the National AIDS Control Organization (NACO); as a result, the Ministry of Health and Family Welfare consists of the following three departments, each of which is led by a secretary to the Indian government.

Departments of Health & Family Welfare

Department of AYUSH (Ayurveda, Yoga & Naturopathy, Unani, Siddha, and Homoeopathy)

Department of Health Research.[13]

Country	Regulatory Body
United States of America	Food and Drug Administration
United Kingdom	Medicines and Healthcare Products Regulatory Agency
Australia	Therapeutic Good Administration
India	Central Drug Standard Control Organisation
Canada	Health Canada
Europe	European Medicines Agency
Denmark	Danish Medicines Agency
Costa Rica	Ministry of Health
New Zealand	Medicines and Medical Devices Safety

Fig 4: Regulatory Bodies of Different Countries.

Dossier

A pharmaceutical dossier is a compilation of in-depth records that offer details about a particular medication.

When submitting the dossier to the regulatory body for approval in any country where a license is needed for the production, marketing, use, distribution, or sale of the license in question, these documents must contain a lot of information. Also referred to as the Marketing Authorization Application (MAA) for the European Union and the New Drug Application (NDA) for the United Nations, dossiers must be prepared using the globally accepted CTD and ACTD formats in order to save time and effort when registering a single drug product in numerous countries.

Contents

Introduction to dossier & registration dossier

Contents of dossier
Goals of dossier
Common dossier used in p'ceutical industry
Description of various format dossier
Dossier management
Compilation Abd review of dossier
Regulatory submissions
Planning and preparation of regulatory submission
Review aspects for regulatory submission
Binders in pharmaceutical industry.[14]

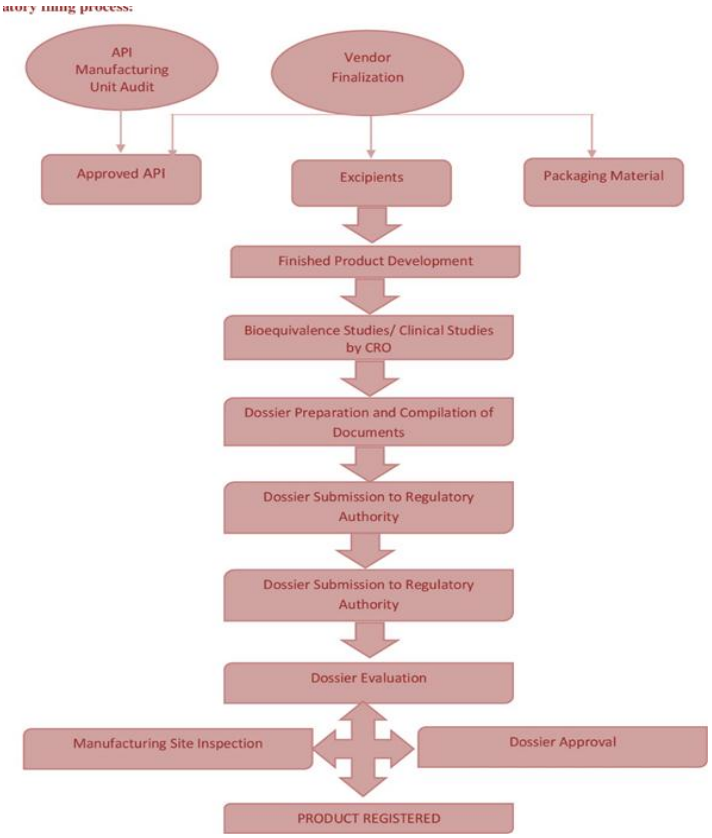

Fig 5: Dossier Process.

RESULTS

From the review and exploration of documentation practices in pharmaceutical production and marketing, the following key results were observed.

1. Types of Documentation Identified.

Master Formula Record (MFR) and Batch Manufacturing Record (BMR) are central to production consistency.

Standard Operating Procedures (SOPs) standardize daily operations.

Regulatory Dossiers (CTD/eCTD) form the basis of drug approval and marketing.

2. Regulatory Requirements

Authorities such as US FDA, EMA, WHO, and CDSCO enforce strict documentation under GMP guidelines.

All documentation must meet principles of accuracy, completeness, traceability, and data integrity (ALCOA+).

3. Current Industry Practices

Paper-based systems are still widely used, but there is a rapid shift toward electronic documentation systems such as Electronic Batch Records (EBR) and Manufacturing Execution Systems (MES).

Documentation plays a dual role: ensuring quality in production and enabling regulatory approval in marketing.

4. Common Issues Identified

Incomplete entries, poor version control, missing signatures, and deviations without justification.

Lack of harmonization in dossier preparation across regions.

DISCUSSION

The results confirm that documentation is not only a regulatory requirement but also a quality tool in pharmaceutical industries. The MFR and BMR ensure reproducibility and traceability of every batch, directly impacting patient safety and regulatory compliance. Literature and industry findings reveal that documentation lapses are a major cause of regulatory observations during inspections, underlining the need for robust systems.

The discussion also highlights a paradigm shift from paper to digital records, driven by regulatory encouragement for data integrity and operational efficiency. Electronic systems minimize transcription errors, enable real-time monitoring, and support global compliance. However, their adoption comes with challenges such as high implementation cost, need for system validation, and user training.

In the marketing domain, dossiers (CTD/eCTD) play a crucial role in gaining market authorization. Variations in regional requirements make harmonization an ongoing challenge, but ICH guidelines have improved global acceptance.

Overall, the exploration shows that modern pharmaceutical companies must balance regulatory compliance, operational efficiency, and technological adaptation. Strong documentation practices are directly linked to product quality, faster approvals, and competitive advantage in global markets.

CONCLUSIONS

Documentation is critical for product quality, patient safety, and regulatory compliance in modern pharmaceutical industries.

MFR and BMR ensure consistency between “what should be done” and “what was done” in production, while SOPs provide operational reliability.

Regulatory dossiers bridge production and marketing, serving as the foundation for global approvals.

Regulatory bodies (FDA, EMA, WHO, CDSCO, etc.) set strict documentation standards; compliance is non-negotiable for market access.

Transition to digital documentation systems improves traceability and efficiency but requires strong validation and training.

The future of pharmaceutical documentation lies in harmonization, digitalization, and integration of regulatory and production systems to enhance efficiency, reduce errors, and accelerate time to market.

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FIGURE REFERENCES
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https://share.google/images/QrUP6NTUUtXyHvN5W

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Review Article

Validation Study on Reported UV Method Used for Estimation of Ibuprofen from Marketed Tablet Preparation

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ABSTRACT

Ibuprofen is non-steroidal anti-inflammatory drug (NSAID) drug which used for relief of symptoms of arthritis, primary dysmenorrhea, and fever and as an analgesic. The aim of this study was to develop highly sensitive, selective and rapid quantitative analytical method for estimation of ibuprofen as well as evaluation of marketed tablet of ibuprofen (Brufen400). The drug shows absorption maxima at 226nm. The liner dynamic response was found to be in the concentration of 2-10µg/ml. The slop, intercept and correlation coefficient were found to be 0.0389, -0.0454 and 0.977091 respectively. The estimated amount of ibuprofen in marketed tablets was found to be 99.80±0.12%. The marketed tablets evaluated for weight variation, hardness, friability, and disintegration time and dissolution study. The tablets show acceptable weight variation as per pharmacopeial specification. Friability shows below 1% indicating good mechanical resistance of tablets. The marketed tablet shows average 5.4 kg/cm² hardness which indicate good strength of tablets. The disintegration time varies from 5.53 min. to 7.34 min. and 97.16% drug release in 50 minutes. The newly developed method and the evaluation of marketed tablets can be used for analysis of ibuprofen of equal significant drug as well as evaluation parameters can be help for quality control and quality assurance of the drug.

INTRODUCTION

Ibuprofen was discovered by Dr. Stewart Adams, a pharmacologist in the Research Department of The Boots Pure Drug company Ltd at Nottingham, UK. Dr. Stewart Adams' aim was to find an analgesic drug which has improved efficacy over aspirin. Dr John Nicholson was the first person to synthesize ibuprofen. When Stewart Adams started his research, at that time aspirin & Cortisone were the standard drugs for treating painful arthritic disease. On the basis of Ibuprofen safety record, The Boots company applied to the

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UK Department of Health & Social Security in August 1978 to allow Ibuprofen for nonprescription sale for the treatment of muscular and rheumatic pain, fever with Unit dose of 200mg and a maximum adult dose of 1200mg.

In 1974. Ibuprofen got FDA approval. Brufen ™ Motrin ™ were used as first line treatment of pain and inflammation. Clearance of both enantiomers of ibuprofen possess a relatively short, approximately 2hours.[2] Ibuprofen is R, S-2-(p-isobutylphenyl) propionic acid, its chemical formula is C13H18O2 and its molecular weight is 206.28. Ibuprofen contains carboxylic group and aromatic ring as shown in Fig No. 1. Its appearance is a white crystalline powder, which is freely soluble in organic solvents like ethanol and acetone.[1] For the administrating of ibuprofen, commonly the oral route is used.[2] Cyclooxygenase is required for the synthesis of prostaglandins through the arachidonic acid pathway. COX converts the arachidonic acid to prostaglandin H2 (PGH2) in the body. Ibuprofen is a nonselective inhibitor of COX, which results in a lower level of prostaglandins in the body. Prostaglandins are important mediators of sensations, such as fever, pain, and inflammation [2], Ibuprofen is used to treat pain and Inflammation which was first NSAID'S.[3]Method including titration[4], HPLC with combined drug studies[5,6,7], HPLC[8], UPLC[9,10], UV spectrophotometric[11,12], First- order Derivative and UV-spectrophotometric Methods[13], GC-MS[14,15] are widely used to determine ibuprofen in single and pharmaceutical dosage form. Bradycardia, hypotension and metabolic acidosis are the side effect of ibuprofen when dose is exceeding 300mg/Kg concentration. [17,18] In rheumatoid patient's liver dysfunction is observed when treated with the lower homolog of ibuprofen; Ibufenac.[19] The objective of the present research work deals with simple, accurate, precise UV spectroscopic method using Absorption Maxima Spectroscopy method for estimation of Ibuprofen in bulk and validated as per ICH guideline.

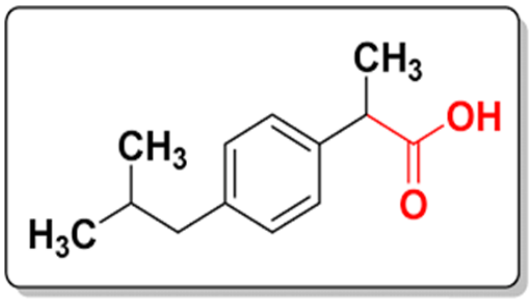

Figure no. 1 Chemical Structure of Ibuprofen

IUPAC Name: (RS)-2-(4-(2-Methylpropyl) phenyl) propanoic acid

Molecular Formula: $C_{13}H_{18}O_2$.

Molecular Weight: 206.28 g/mol

Melting Point: 75-78 °C

Solubility: Practically insoluble in water, highly soluble in organic solvents (e.g., methanol, acetone, NaOH)

Category: Non-Steroidal Anti-Inflammatory Drug (NSAID)

Pharmacokinetics and Pharmacodynamics: Ibuprofen is given as a racemic combination of the R and S enantiomers; the majority of its pharmacologic action is attributed to S-ibuprofen. Alpha-methyl acyl-CoA-racemase, encoded by the gene AMACR, converts about 50–65% of R-ibuprofen to S-ibuprofen via an acyl-CoA thioester in the liver; however, it may also happen in the gut. Oral administration, Ibuprofen is quickly absorbed, reaching peak plasma levels within 1–2 h.. About 90–98% of ibuprofen binds to plasma.

UV – Spectrophotometry

Ultraviolet (UV) spectroscopy is one of the most widely employed analytical techniques in pharmaceutical sciences due to its simplicity, sensitivity, cost-effectiveness, and rapid applicability. The principle of UV spectroscopy is based on the absorption of ultraviolet radiation (200–400 nm) by molecules containing chromophores, leading to electronic transitions. The extent of absorption is directly proportional to the concentration of the absorbing species, as described by Beer–Lambert's law, which forms the theoretical basis for quantitative analysis.

In pharmaceutical analysis, UV spectroscopy plays a crucial role in drug estimation, quality control, dissolution testing, and stability studies. It is particularly useful for the routine determination of active pharmaceutical ingredients (APIs) in bulk drug substances and finished formulations. Compared to other sophisticated techniques such as HPLC or LC-MS, UV spectroscopy offers the advantages of low operational cost, minimal sample preparation, shorter analysis time, and reproducibility, making it suitable for laboratories with limited resources.

Role of UV Spectrophotometry in Routine Quality Control

- **Identification of Drugs** – Confirms the identity of active pharmaceutical ingredients (API) by comparing UV absorption spectra.
- **Assay of Formulations** – Used to estimate the drug content in tablets, capsules, syrups, etc. quickly and accurately.
- **Purity Testing** – Detects impurities and degradation products in raw materials and finished formulations.
- **Dissolution Testing** – Monitors drug release profile from dosage forms during in-process and finished product testing.
- **Content Uniformity** – Ensures uniform distribution of active ingredient in multiple dosage units.
- **Stability Testing** – Assesses the stability of drugs under different environmental conditions (light, heat, pH).
- **Validation of Analytical Methods** – Helps in establishing linearity, accuracy, precision, and sensitivity of QC methods.
- **Cost-Effective and Rapid** – Provides a simple, economical, and fast method suitable for routine QC laboratories.

Analytical Method Validation

Analytical method validation is a documented process ensuring that an analytical procedure is suitable for its intended purpose, delivering reliable, accurate, and consistent results in pharmaceutical, chemical, or clinical laboratories.

Method validation confirms that the chosen analytical procedure can accurately and precisely measure the analyte in a sample without interference or error under actual conditions of use. It is fundamental for regulatory compliance, product safety, and quality assurance in pharmaceuticals and other fields.

Importance of Analytical Method Validation

- Ensures the developed method is accurate, precise, and reliable.
- Provides documented evidence of method suitability as per ICH Q2(R2) guidelines.

- Confirms specificity by ruling out interference from excipients in formulations.
- Establishes linearity for accurate quantification across different concentrations.
- Determines LOD and LOQ for sensitivity of the method.
- Validates precision through intra-day and inter-day reproducibility.
- Demonstrates robustness and ruggedness, ensuring reliability under varied conditions.
- Supports regulatory compliance and acceptance of analytical data.
- Ensures consistency in routine quality control of ibuprofen tablets (Ibufen).

AIM AND OBJECTIVE

AIM: To Validate on reported UV method used for estimation of ibuprofen from marketed tablet preparation.

OBJECTIVE:

1. To determine the lowest amount of analyte that can be detected, but not necessarily quantified, under the stated experimental conditions.
2. To determine the lowest amount of analyte that can be quantitatively measured with suitable accuracy and precision.
3. To obtain consistent, reliable and true data.
4. To demonstrate that it is suitable for its intended purpose.
5. To form a base for written procedure for production and process control which are designed to assure that the
6. drug products have the identity, strength, quality and purity.
7. To hold the quality, safety and efficacy in final product.
8. To control each step of manufacturing process.
9. To produce the best analytical results possible

MATERIALS AND METHODS

Drug Sample: Ibuprofen standard was obtained from a certified pharmaceutical supplier with a declared purity of ≥99%. The sample was stored in airtight containers at room temperature to prevent moisture absorption.

Chemicals and Reagents: All chemicals used were of analytical reagent (AR) grade. 0.1N NaOH, distilled water were used for preparation of solutions. All glassware was thoroughly cleaned, dried, and calibrated before use

Instrumentation

UV-Visible double beam Spectrophotometer (Shimadzu UV-1800), with matching pair of 1 cm quartz cuvettes. All weighing was done on Electronic Analytical Balance (Shimadzu AY-220). To degas the solution Ultrasonicator (Bio-Technics India) was used.

Selection of Solvent

Based on drug profile, the solubility of Ibuprofen was freely soluble in NaOH. So, 1 NaOH was selected as a solvent.

Preparation of Stock solution of Ibuprofen

Standard stock solution of Ibuprofen was prepared by accurately weighing 12mg of Ibuprofen and transferred to 100 ml volumetric flask and volume make up with methanol.

Preparation of sample solution

The equivalent weight of powdered tablets was found to be 12 mg, which was calculated by average weight of 20 tablet, cross multiplication of average weight and label Content of drug, equivalent weight was obtained. Now this 12 mg of powered tablet weighed and transferred to a 100 ml volumetric flask and NaOH was added and filtered with Whatman filter paper. After that volume was made up to mark to get concentration 100ug/ml.

Selection of analytical wavelength

The standard stock solution was taken and spectra was observed from 200 to 400nm in aUV-spectrophotometer.

Method Validation

The method was validated according to ICH Q2 (R1) guidelines for validation of analytical procedures for parameters like linearity, accuracy, precision, LOD, LOQ for the analyte.

Linearity

The Linearity of an analytical procedure is its ability (within a given range) to get test result which are directly proportional to the concentration of analyte within the sample. five different concentrations of ibuprofen covering from 2-10 ug/ml were prepared and analyzed. The linearity was accessed by plotting calibration curve of Ibuprofen.

Precision

The degree of agreement among individual test results when the method is applied repeatedly to multiple sampling of homogenous sample.

LOD and LOQ

The Limit of Detection (LOD) is the smallest concentration of the analyte that gives the measurable response. LOD was calculated using the following formula:

$$LOD = 3.3\ \sigma / S$$

The limit of quantification (LOQ) is the smallest concentration of the analyte, which gives response that can be accurately quantified. LOQ was calculated using the following formula:

$$LOQ = 10\ \sigma / S$$

Where, σ is standard deviation of the response and S is the slope of the calibration curve.

RESULT AND DISCUSSION

Selection of Analytical wavelength

he Spectra of Ibuprofen was observed and highest absorbance was seen at 226 nm.

Linearity

For preparation of dilution 0.2, 0.4, 0.6, 0.8, 1 ml stock solution was pipette out and was transferred to 10 ml Volumetric flask and volume make up with NaOH which results in 2, 4, 6, 8, 10 µg /ml concentration solution, absorbance was observed (Table No. 1) and the method was found linear with correlation coefficient r^2 =0.9989. The calibration curve of Ibuprofen is shown in Fig. No. 3. The slope and intercept are 0.028314 and 0.009733 respectively as shown in Table No. 2.

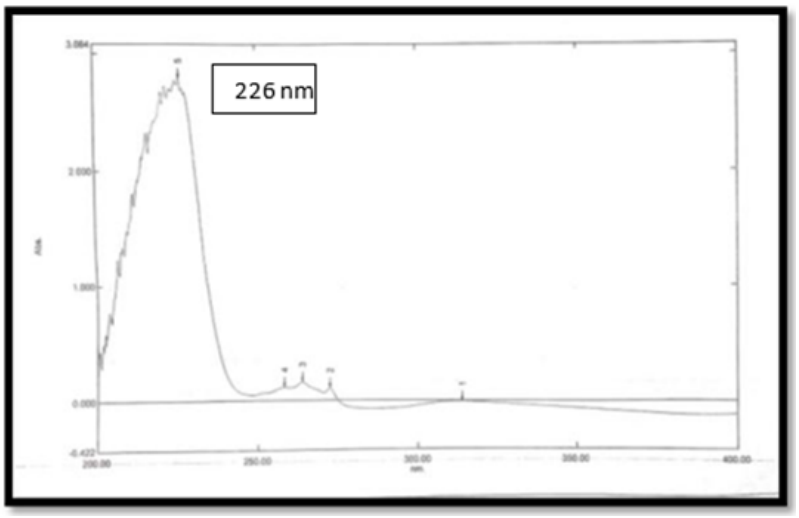

Figure 2 UV absorption spectra 0f IBU at λ-max=226nm

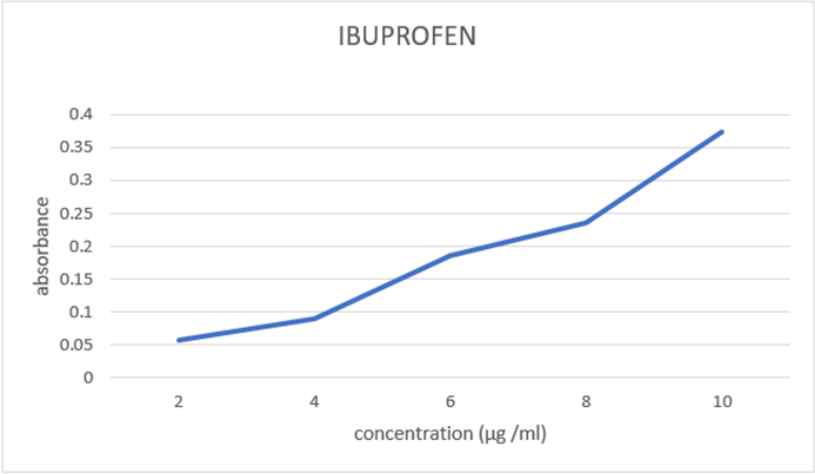

Figure 3 Calibration curve for Ibuprofen

Table no.1: Linearity

Sr. No.	Conc.	Absorbance
1	2	0.057
2	4	0.089
3	6	0.186
4	8	0.235
5	10	0.373

Table No.2: Linear regression analysis by UV.

Sr. No.	Parameters	Absorption Maxima Spectroscopy Method
1	λmax (nm)	226nm
2	Regression equation	0.0389x-0.0454
3	Slope (m)	0.0389
4	Intercept (c)	-0.0454
5	Correlation Coefficient (r^2)	0.977091
6	Limit of detection (LOD)	268.2652

Analysis of Tablet (marketed) Formulation

For analysis of tablet formulation BRUFEN® tablet was taken. The 36ug/ml dilution was prepared and amount of drug present in tablet and %RSD was calculated which is shown in Table No. 3.

Table No. 3: Result of Tablet analysis.

Drug Name	Mean	SD	%RSD
Brufen	0.188	0.126	67.02%

Accuracy

Accuracy was determined at 80%, 100% and 120% level by standard addition method and % recovery was evaluated which is shown in Table No. 4.

Table No.4: Result of Accuracy study.

Level addition	Mean	SD	%RSD
80	100.17	0.2322	0.2318
100	99.93	0.1394	0.1395
120	100.42	0.1743	0.1734

Precision

The results of intra-day precision were expressed as % RSD and it was found to be 1.72 and 0.27 for IBU. The % RSD value indicates the good precision of the method which is shown in Table no.5. The results of inter-day precision were expressed as % RSD. It was found to be 1.72 and 0.27 for IBU respectively. The % RSD value indicates the good precision of the method which is shown in Table No. 5.

Table No.5: Result of Intraday precision.

Sr. No.	Conc. (ug/ml)	Absorbance	Mean	SD	%RSD
1	2	0.057			
2	2	0.059	0.058	0.0010	1.72%
3	2	0.058			
4	6	0.089			
5	6	0.090	0.088	0.0017	1.96%
6	6	0.087			
7	10	0.0373			
8	10	0.0374	0.0374	0.0001	0.27%
9	10	0.0375			

Inter-day precision were evaluated for 2 ,6 ,10 ug/ml for three consecutive days within same environment which is shown in Table No. 6.

Table no.6: Result of Inter-day precision.

Sr. No.	Conc. (ug/ml)	Absorbance	Mean	SD	%RSD
1	2	0.058			
2	2	0.059	0.058	0.0010	1.72%
3	2	0.057			
4	6	0.090			
5	6	0.091	0.089	0.0017	1.96%
6	6	0.088			
7	10	0.0375			
8	10	0.0374	0.0375	0.0001	0.27%
9	10	0.0376			

LOD AND LOQ

Five sets of known concentrations (02-10 µg/ml) were prepared and scanned. By using these spectra, regression equations were obtained. By taking average of slopes and standard deviation of y-intercept, LOD and LOQ were calculated. The values of LOD and LOQ are given in Table 2.

LOD = 3.3 σ /S

LOD = 268.2652

LOD of Ibuprofen was found to be 268.2652 µg/ml.

LOQ = 10 σ/S

LOQ = 812.9248

LOQ of Ibuprofen was found to be 812.9248 µg/ml.

CONCLUSION

In Absorption maxima method methanol was used as solvent and detection was done at 226 nm. The % RSD for all parameters were found within 2%. The result showed that the proposed method was suitable for the accurate, precise and rapid determination of Ibuprofen in its bulk and tablet dosage form. The method was validated as per ICH guidelines.

Conflict Of Interest

There is no conflict of interest from all the authors.

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Advances in Oral Thin Films: Modern Strategies for Patient-Centric Drug Delivery and Global Regulatory Perspectives

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Abstract-

Oral thin films (OTFs) have emerged as a cutting-edge drug delivery platform designed for enhanced patient-centric care. These thin, rapidly dissolving films provide a convenient alternative to traditional oral dosage forms, enabling fast drug release and absorption through the oral mucosa, which bypasses first-pass metabolism and improves bioavailability. OTFs are particularly beneficial for pediatric, geriatric, and dysphagic patients who face difficulties swallowing tablets or capsules. Advances in manufacturing techniques, such as solvent casting, hot melt extrusion, and novel printing technologies including inkjet and 3D printing, have enabled precise dosing, personalized therapies, and rapid onset of action. The films can also incorporate taste masking and controlled release features, further improving patient compliance and therapeutic efficacy. On the regulatory front, global agencies are evolving guidelines to ensure safe, effective OTF quality control and manufacturing standards, fostering wider adoption. The OTF market is rapidly growing, reflecting the increasing demand for user-friendly, efficient drug delivery systems. Future directions explore multilayer films and multi-drug combinations, positioning OTFs as transformative solutions in modern pharmacotherapy and nutraceutical applications. This review elucidates these advances and regulatory perspectives underpinning the OTF landscape today and beyond.

Keywords- Oral thin films (OTF), Patients-Centric Drug Delivery, Fast-Dissolving Films, Regulatory Guidelines, Global Market

1. Introduction

Oral drug delivery is generally convenient, but it can pose difficulties for specific groups, such as pediatric, older adults, and individuals with swallowing disorders (dysphagia). These populations may struggle to swallow conventional dosage forms like tablets and capsules. Even fast-dissolving tablets may present a choking hazard and are not always well accepted by all patients. To overcome these challenges, oral fast-dissolving films (OFDFs) have been developed as a novel solution. These thin, polymer-based films rapidly dissolve upon contact with the tongue, allowing for easy administration without water or chewing. This approach improves patient adherence, especially in elderly individuals taking multiple medications and those affected by conditions such as Alzheimer's disease, Parkinson's disease, and schizophrenia. OFDFs also offer a practical and safe alternative for pediatric patients compared to traditional dosage forms.[1-2]

1.1 Oral Thin Film:

Oral fast-dissolving films or strips are drug delivery systems designed to quickly release the active ingredient by dissolving or attaching to the mucosal surface with the aid of saliva, usually within seconds of being placed in the mouth or on the tongue. The concept of oral thin films was introduced in the 1970s as an innovative dosage form. They were officially introduced to the market in 2004 for systemic drug delivery and have since become widely accepted.[3-5]

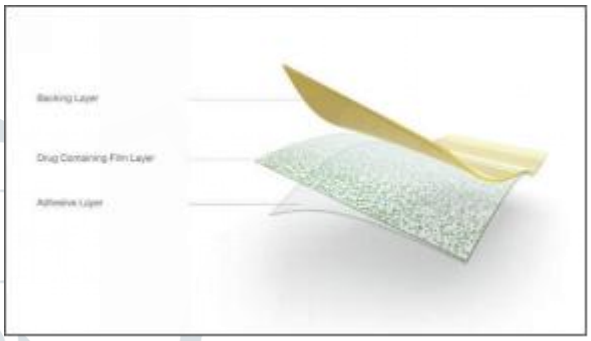

Figure 1: Oral Thin Film

Oral disintegrating or dissolving films (ODFs) are drug delivery systems designed to release the active ingredient rapidly by dissolving or adhering to the oral mucosa with the help of saliva within seconds, owing to the presence of water-soluble polymers, when placed in the mouth or on the tongue. The sublingual mucosa has a thin membrane and is highly vascularized, which allows for rapid absorption and excellent bioavailability. Oromucosal films are considered patient-friendly dosage forms due to their high level of patient acceptance. According to the European Medicines Agency, patient acceptability refers to the ability and willingness to use a medicinal product as intended. This is particularly relevant for populations such as the elderly with swallowing difficulties, infants, young children, and patients who are uncooperative or prone to nausea and vomiting. Although oral solid dosage forms make up around 60% of all dosage types, they present several challenges that can be mitigated through alternative systems like fast-dissolving oral films (FDOFs).The development of fast-dissolving drug delivery systems originated from the need to provide patients with a more convenient way to take medications. FDOFs are ultra-thin films, generally ranging from 5–20 cm^2 in size, containing an active pharmaceutical ingredient. Among the available administration routes, the buccal cavity is especially advantageous for systemic FDOF delivery because of its superior bioavailability, quick onset of therapeutic action, and high treatment adherence, resulting from the rich vascular supply and permeability of the oral mucosa. These films are particularly useful for pediatric and geriatric patients who struggle with swallowing, as well as bedridden patients, those suffering from nausea, diarrhea, allergic reactions, or cough, and individuals with active lifestyles. In addition, FDOFs are effective for achieving localized therapeutic effects, for example, as local anesthetics for toothaches, oral ulcers, cold sores, or teething discomfort.[6-17]

This dosage form consists of an ultra-thin oral strip that quickly disintegrates and dissolves in the mouth, enabling rapid medication release for oromucosal absorption. It offers a shelf life of 2–3 years, depending on the nature of the active pharmaceutical ingredients. Recognized as one of the most advanced solid oral dosage forms, it combines flexibility with patient comfort and enhances the effectiveness of APIs by dissolving within seconds upon contact with saliva, eliminating the need for chewing. Drugs commonly formulated as FDOFs include selective serotonin reuptake inhibitors (such as Fluoxetine and Sertraline), antiemetics (e.g., Ondansetron, Granisetron), 5HT3antagonists (such as Alosetron, Ondansetron, Granisetron, Palonosetron), antiepileptics (including Carbamazepine, Clonazepam, Phenytoin), antimigraine agents (like Almotriptan, Zolmitriptan), and dopamine D1/D2 receptor antagonists (including Bromperidol and Domperidone) Chlorpromazine (CPZ), an antipsychotic and antiemetic used to treat schizophrenia, has not yet been

formulated as an FDOF according to existing literature. Hence, the present study aims to develop and evaluate fast-dissolving oral films for the oro-buccal delivery of chlorpromazine. It's formulated and evaluated but not in marketed.[18-22]

Figure 2 : Fast Dissolving Oral Thin Film

The oral mucosal epithelium is a multilayered structure, about 40–50 cells thick, consisting primarily of carbohydrates and proteins. The mucosa's thickness in regions such as the mouth base, tongue, and gums typically ranges between 100 and 200 µm. Beneath this layer, the submucosa secretes a small quantity of gel-like mucus composed mainly of water (90%–99%) and water-insoluble glycoproteins (1%–5%), along with proteins, enzymes, electrolytes, and nucleic acids. The salivary glands are made up of lobules that produce saliva and parotid secretions, which are delivered through ducts located near the sublingual canals and submandibular teeth. Numerous minor salivary glands are distributed within the lip and cheek mucosa. On average, about 1–2 mL of saliva is secreted each minute. This fluid contains mucus, water, the enzyme amylase, lysozyme, mineral salts, immunoglobulins, and blood-clotting components. Together, mucin and saliva provide a protective barrier for the oral mucosa.[23-24]

The mucosal epithelium consists of two distinct zones: a lipophilic stratified epithelial membrane and hydrophilic intercellular spaces. The oral absorption of many drugs is restricted by enzymatic degradation, first-pass metabolism, and the stomach's acidic environment. Traditionally, these drugs have been delivered through parenteral routes, which often lead to poor patient compliance. To overcome these limitations, the pharmaceutical industry has developed innovative drug delivery systems, including thin, rapidly dispersing or dissolving oral films. Fear of choking, commonly associated with orally disintegrating tablets (ODTs), poses a challenge for some patients. In contrast, oral thin films (OTFs) that dissolves quickly in the mouth offer a more suitable alternative. Once placed on the tongue, OTFs are rapidly hydrated by saliva, resulting in their disintegration or dissolution and facilitating drug release for systemic or local absorption. Additionally, because ODTs are fragile and can break during transport, fast-dissolving OTF systems have emerged as a more durable and patient-friendly option.[25-28]

1.2 Types of Oral Thin Films:

OTFs are classified into 3 types

i. Flash Release
ii. Mucoadhesive Melt Away Wafers
iii. Mucoadhesive Sustained Release Wafers. [29]

- **Advantages**

1. Rapid breakdown within seconds, ensuring a swift therapeutic effect.
2. Simple and convenient to administer.
3. Enhances patient adherence, especially for children, elderly individuals, bedridden patients, and those with psychiatric conditions who are unwilling to swallow tablets.

4. Can be taken without the need for water or chewing.
5. Eliminates the risk of choking.
6. Offers a pleasant taste and texture in the mouth.
7. Requires no specialized training for proper use.
8. Avoids the first-pass metabolism, allowing for a lower dosage and reducing the likelihood of side effects from the active ingredient [30-36]

- **Disadvantages**

1. Requires specialized packaging equipment.
2. Unsuitable for drugs that are unstable or cause irritation at oral pH.
3. Allows administration of only small medication doses, although studies indicate that API content can be increased by up to 50% of the film's weight (for instance, each Gas-X® film strip from Novartis Consumer Health contains 62.5 mg of Simethicone).
4. Being hygroscopic, they pose challenges for long-term storage and protection.
5. Applicable only to drugs that are absorbed through passive diffusion
6. Due to their rapid dissolution, discontinuing the dose once administered is not possible.
7. Not currently recognized in any pharmacopoeia.
8. Manufacturing is more costly compared to orally dissolving tablets.[37 -39]

2. Overview and Mechanism of Oral Thin Film:

Drug absorption in the buccal cavity occurs mainly through passive diffusion of non-ionized molecules via epithelial intercellular spaces, driven by a concentration gradient. The primary pathway involves passive transport of non-ionic compounds across the lipid membrane of the buccal cavity. Similar to other mucosal membranes, the buccal mucosa functions as a lipid-rich barrier, and drugs with higher lipophilicity tend to be absorbed more rapidly. The absorption process in this region can be effectively described by first-order kinetics. Various factors can impede buccal drug absorption. Dearden and Tomlinson (1971) reported that salivary secretion changes the drug concentration within the oral cavity, which subsequently impacts the absorption kinetics from a drug solution. The relationship between salivary secretion and time can be expressed as a linear equation

$$[- dm / dt = Kc/ViVt]$$

Where,
m - Mass of drug in mouth at time
K - Proportionality constant
c - Concentration of drug in the mouth at time
Vi - The volume of the solution put into mouth cavity and
Vt - Salivary secretion rate.[40-42]

2.1 Comparison Between Fast Dissolving Oral Films and Conventional Tablets: [43-45]

Table 1: Comparison between Fast dissolving oral films and Conventional Tablets

Oral dissolving film	Oral disintegrating tablets
It is a film	It is a tablet
Greater dissolution due to greater surface area	lesser dissolution due to less surface area
Better durable as compared to disintegrating tablet	Less durable as compared to oral film
More patient compliance	Less patient compliance as compared to film
Low dose can only be incorporated in film	Higher dose can be incorporated in tablet
No fear of choking	It has fear of choking

3. Preparation Techniques and Technological Innovation:

3.1 Solvent Casting Methods

The solvent casting method is an efficient and straightforward approach for developing fast-dissolving oral thin films. In this technique, water-soluble polymers, active pharmaceutical ingredients, and excipients are mixed to form a viscous solution, which is subsequently spread and dried to obtain thin films with a thickness range of 12–100 µm. Researchers have emphasized that this method is economical, suitable for thermo labile drugs, and yields films with adequate mechanical strength and rapid drug release. Nonetheless, careful control of the solvent selection and solution viscosity is essential to maintain the uniformity and quality of the films.[46]

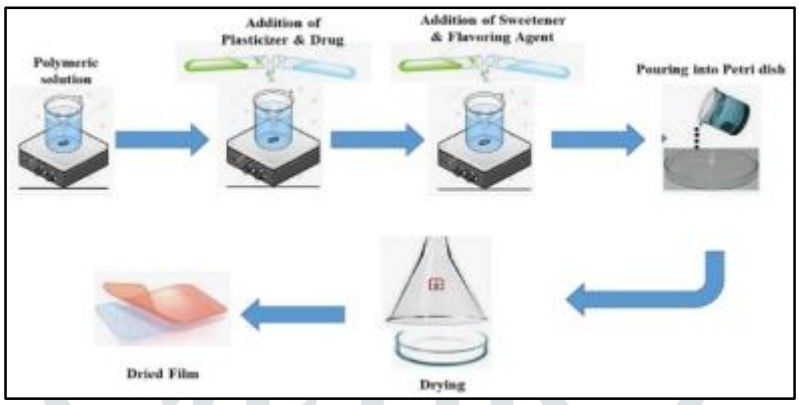

Figure 3: Diagrammatic Representative Solvent Casting Methods

3.2 Hot Melt Extrusion:

The hot melt extrusion technique is a widely used method for producing oral thin films, involving the melting of polymers under controlled heat and pressure to create films. In this process, all components are mixed in their dry form, heated to generate a molten mass, and subsequently cast, cooled, and cut into the desired film shapes. One key advantage of this approach is its ability to produce uniform films without requiring solvents; however, its main drawback is the risk of thermal degradation or loss of activity in heat-sensitive drugs due to elevated processing temperatures. According to Patel et al., while hot melt extrusion is an effective manufacturing method, the solvent casting technique is often favored for oral thin film formulation, as it better accommodates temperature-sensitive compounds and achieves improved film uniformity.[47]

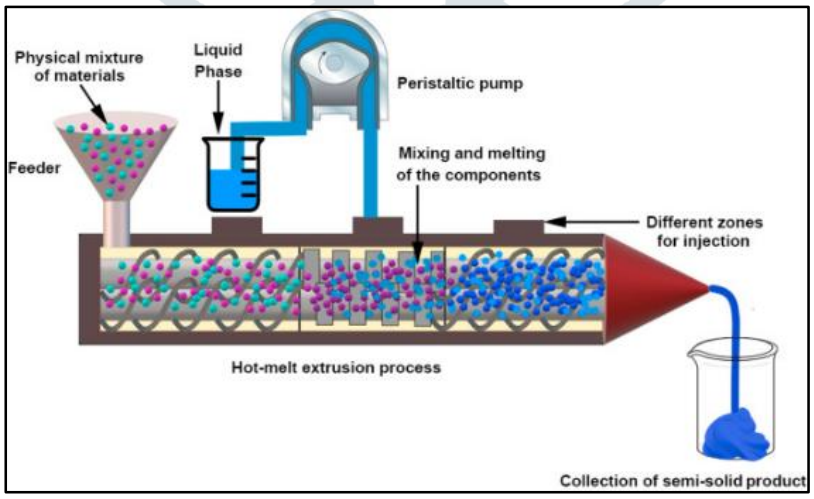

Figure 4: Diagrammatic Representative Hot Melt Extrusion Methods

3.3 Inkjet and 3D Printing:

The study described printing technologies such as 3D printing and inkjet printing as advanced and versatile techniques for producing oral thin films. It was noted that these methods offer precise and individualized drug dosing by depositing drug-containing inks onto appropriate substrates, enabling the creation of patient-specific formulations. In inkjet printing, the active pharmaceutical ingredient is directly printed, whereas flexographic printing applies a polymeric thin film coating onto the substrate. The researchers highlighted that these approaches ensure excellent uniformity, accurate dose control, cost efficiency, and enhanced film stability, making printing technology a valuable tool for developing fast-dissolving oral films.[48]

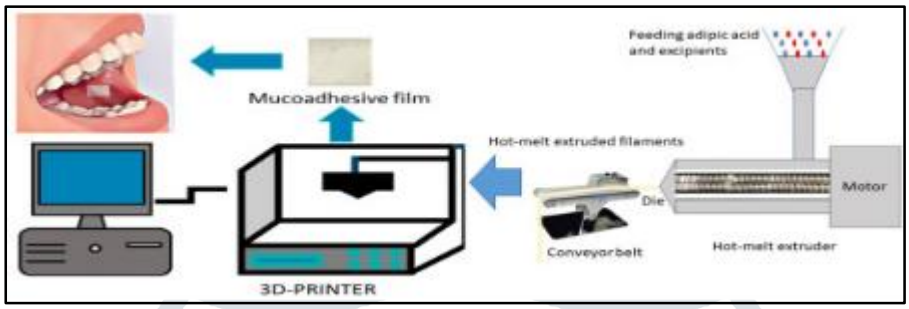

Figure 5: Diagrammatic Representative 3D Printing Technology

3.4 Slot-Die Coating

The slot-die casting technique, employing a doctor blade setup, is a highly effective method for producing thin polymeric films. In this process, a hydrogel is dispensed through a slot-die nozzle onto a plasma-treated PET substrate positioned on a heated platform, resulting in the formation of a uniform film layer. The system comprises rollers, a regulated syringe pump, and an adjustable nozzle that together ensure accurate control of film thickness and coating smoothness. The study indicated that regulating parameters such as deposition rate, temperature, and substrate movement enables the fabrication of transparent films with uniform thickness and high consistency. The authors concluded that slot-die casting is a reliable and scalable technique for producing polymeric thin films suitable for pharmaceutical and biomedical.[49]

4. Polymer and Film Forming Agent:

- Classification Of Polymers Used In Mouth Dissolving Film
- Natural Polymer
- Synthetic Polymer

  Polymer selection plays a vital role in ensuring the successful formulation of oral films, as tensile strength is directly influenced by the type and proportion of polymer used. For optimal performance, the dry film composition should contain at least 45% polymer by weight, with 60%–65% being ideal to achieve the desired mechanical and functional properties. Polymers may be utilized alone or blended to tailor specific film characteristics.

  Given that oral thin films (OTFs) are intended to quickly dissolve and disperse in the oral cavity, film-forming polymers should exhibit water solubility. Additionally, the films must possess enough strength to withstand handling, transportation, and storage without sustaining damage.[51-53]

Table 2: Common Polymers Utilized In Otfs [51-54]

Component	Class	Example
Natural	carbohydrate	Pectin, pullulan , mallodextrin, sodium alginate, and sodium starch glycollate
	protein	gelatin
	resin	Polymerized (new film forming)
Synthetic	Cellulose derivatives	Hydroxy propyl methylcellulose (K50, K3, K15, E5, E3, and E15), carboxy methylcellulose, methylcellulose (A3, A15, and A6), sodium carboxymethyl cellulose, croscarmellose sodium, and microcrystalline cellulose
	Vinyl polymer	Polyvinylpyrrolidone (K90 and K30), polyvinyl alcohol, and polyethylene oxide
	Acrylic polymer	Eudragit (RL-100, 9, 10, 11, 12, and RD-100)

5. Innovation in Drug Loading and Release:

The innovation of micropellet-loaded oral films designed to achieve rapid disintegration along with controlled drug release. The authors highlighted that embedding coated, drug-loaded micropellets within the film matrix helps maintain prolonged drug release and reduces dose dumping. Speer incorporated diclofenac-loaded micropellets using the spheronization technique to enhance the solubility of poorly soluble drugs such as indomethacin. The study emphasized that such films improve stability, safety, and patient compliance. Additionally, the development of pH- and sugar-sensitive layer-by-layer thin films was discussed as a promising approach for controlled drug release, in which environmental pH or sugar concentration regulates drug permeability and release behavior .[55]

6. Mechanical and Physiochemical Characterization:

Mechanical and physicochemical characterization, including thickness, folding endurance, weight uniformity, and moisture sensitivity, are essential for evaluating oral thin films reported that film thickness directly affects drug content and patient comfort, with an optimal range of 50–1000 µm. Flexibility, assessed through folding endurance, reflects the film's mechanical strength, with values above 300 folds indicating high flexibility. Uniform film weight ensures an even distribution of the active drug, while moisture absorption measurements help determine stability under humid conditions. The study concluded that these characteristics are critical for maintaining the quality, durability, and overall performance of oral thin films .[56]

7. Clinical and Therapeutic Application:

Discussed the clinical and therapeutic uses of oral thin films, emphasizing their increasing role in modern healthcare. The researchers noted that oral film technology provides a convenient, patient-friendly, and effective way to administer medication, thereby improving adherence. The study highlighted that these films are successfully used to deliver drugs such as antipsychotics, antihistamines, and analgesics. When formulated with nano-sized particles, oral films further enhance drug dissolution, bioavailability, and therapeutic performance. The authors also proposed that applying this technology to other drug categories, such as antihypertensive and antiulcer agents, could lead to better outcomes for chronic diseases. Overall, the study

identified oral thin films as a promising innovation for advancing drug delivery and promoting patient compliance .[57]

8. Market Trends:

Oral thin film (OTF) drug delivery systems have demonstrated high market acceptance due to ease of patient use and effectiveness, drawing investment from both established and startup pharmaceutical companies. The OTF drug products market grew from around $7.3 billion in 2015 to an estimated $16 billion by 2024, reflecting more than 100% growth within ten years. Although only about 10 prescription OTF products existed by 2015, the number has steadily increased, with ongoing clinical trials and regulatory approvals.

North America remains the leading manufacturer of oral thin films, accounting for approximately 85% market share as of 2015, with notable companies including Pfizer, Novartis, Solvay, Allergan, Sumitomo Dainippon Pharma, and IntelGenx Corp, alongside emerging startups such as FFT Medicals and Cynapsus Therapeutics. Technologies such as MonoSol's PharmFilm and Applied Pharma Research/Labtec's Rapid Film account for nearly 38% of marketed products. The Asia Pacific region, led by India, Japan, and China, is projected to be the fastest-growing area for OTF manufacturing.

In India, investor interest in OTF technology is rising, exemplified by new companies like Aavishkar Oral Strips Pvt. Ltd., NU Therapeutics, ZYM Laboratories, and major manufacturers such as Cipla, Mankind, and Dr. Reddy's Laboratories.[58]

Table 3: Market Comparison

Year	Global OTF Market Value ($ million)	CAGR (2016–2024)	# Prescription Products (2015)	Regional Market Leader	Tech Usage Share (%)	Fastest Growth Region
2007	500	—	—	—	—	—
2010	2,000	—	—	—	—	—
2015	7,338	18.3	10	North America (85.3%)	MonoSol/APR-Labtec (38)	Asia Pacific
2024	15,984	18.3	—	North America, Asia-Pacific rising	—	Asia Pacific (India, Japan, China)

9. Regulatory Guidelines For Oral Thin Film Is Different Regions:

9.1 Regulatory Perspectives:

All industries in the pharmaceutical sector must undertake an initial experimental phase in product design to develop goods that are both acceptable and sustainable. Applying ideas through a structured process ensures that the resulting products meet established quality standards. The manufacture and development of pharmaceutical products are governed by various compendial requirements and are subject to regulations set by national authorities, which are formed after extensive testing. Almost every country has its own regulatory agency that enforces laws, guidelines, and standards concerning drug development, registration, licensing, manufacturing, classification, and marketing. Alongside national agencies, international organizations also work to enhance drug safety by creating guidelines for product approval, distribution, production, pricing control, marketing, advertising, and the protection of intellectual property rights (Franco, 2013). Table 1 offers a detailed reference to regulatory bodies from different nations. Drug regulation entails numerous measures

to safeguard the safety, efficacy, and quality of medications (Wirthumer-Hoche and Bloechl-Daum, 2016). To meet regulatory requirements, pharmaceutical companies must establish a regulatory affairs department that engages in all stages of drug development—from clinical trials through marketing and post-marketing surveillance. This department functions as the connection between regulatory authorities and the pharmaceutical industry (De Frutos, 2013).[59]

Table 4: Regulatory Bodies and Function:

Regulatory bodies	**Function**
International Council for Harmonization**(ICH)**	Technical Requirements for Pharmaceuticals for Human Use: Issues guidelines defining quality, safety, efficacy, and related aspects for developing and registering new medicinal products in Europe, Japan, and the United States.
Central Drugs Standard Control Organization **(CDSCO)**	Ministry of Health & Family Welfare, Government of India: Provides drug regulatory requirements in India.
European Medicines Agency **(EMA)**	Decentralized body of the European Union headquartered in London prescribes guidelines for inspections and general reporting and all aspects of human and veterinary medicines.
US Food and Drug Administration **(FDA)**	Issues regulations, guidelines, notification, news, and other communications
Medicines and Healthcare Products Regulatory Agency **(MHRA)**	Responsible for ensuring efficacy and safety of medicines and medical devices in the United Kingdom; produces news, warnings, information, and publications.
Japanese Pharmaceutical and Medical Devices Agency (**PMDA)**	An Independent Administrative Institution responsible for ensuring the safety, efficacy, and quality of pharmaceuticals and medical devices in Japan.
Health Canada	The federal department responsible for health-related issues in Canada; issues advisories warnings, recalls, reports, publications, activities, legislation, and guidelines

9.2 Regulatory Guidelines for Ofdfs in Different Regions: [60]

Table 5: Regulatory guidelines for OFDFs Region

Regulatory Authority	**Region**	**Key Guidelines and Regulations**	**Functions**
Central Drugs Standard Control Organization (CDSCO)	India	-CDSCO's Schedule M for Good Manufacturing Practices (GMP) -CDSCO's requirements for registration and marketing approval -Indian Pharmacopoeia standards for pharmaceutical products	Provides drug regulatory requirements in India.
Therapeutic Goods Administration(TGA)	Australia	-TGA's Good Manufacturing Practice(GMP) requirements -TGA's guidelines for the registration of therapeutic goods	Assessing new medicines and medical devices before they can be sold.

		-TGA's requirements for complementary medicines	
National Medical Products Administration (NMPA)	China	-NMPA's Good Manufacturing Practice(GMP) regulations -NMPA's guidelines for drug registration and approval -NMPA's technical guidelines for pharmaceutical products	Drafting laws, regulations, and policies related to supervision of drugs, medical devices, cosmetics, and health food, and developing plans for food and drug safety.
National Health Surveillance Agency(ANVISA)	Brazil	-ANVISA's Good Manufacturing Practices(GMP) requirements -ANVISA's regulations for registration and approval of drugs -ANVISA's requirements for labeling and package inserts	Promote public health by regulating, monitoring, and controlling the production, marketing, and use of products and services that impact health, including food, drugs, cosmetics, medical devices, and health services.
South African Health Products Regulatory Authority (SAHPRA)	South Africa	-SAHPRA's Good Manufacturing Practice(GMP) standards -SAHPRA's guidelines for the registration of medicines -SAHPRA's requirements for labeling and package inserts	The national regulatory body for health products, ensuring their quality, safety, and efficacy by monitoring, evaluating, investigating, inspecting, and registering all health-related products, including medicines, medical devices, and clinical trials

9.3 Indian Regulatory Framework (CDSCO):

India’s pharmaceutical regulatory system plays a crucial role in ensuring the safety, efficacy, and quality of medicinal products, thereby contributing significantly to public health protection. This section provides an overview of the organizational structure, functions, and regulatory responsibilities of the Central Drugs Standard Control Organization (CDSCO), the national regulatory authority of India, and the Drug Controller General of India (DCGI), who governs drug approval and regulatory enforcement in the country.[61]

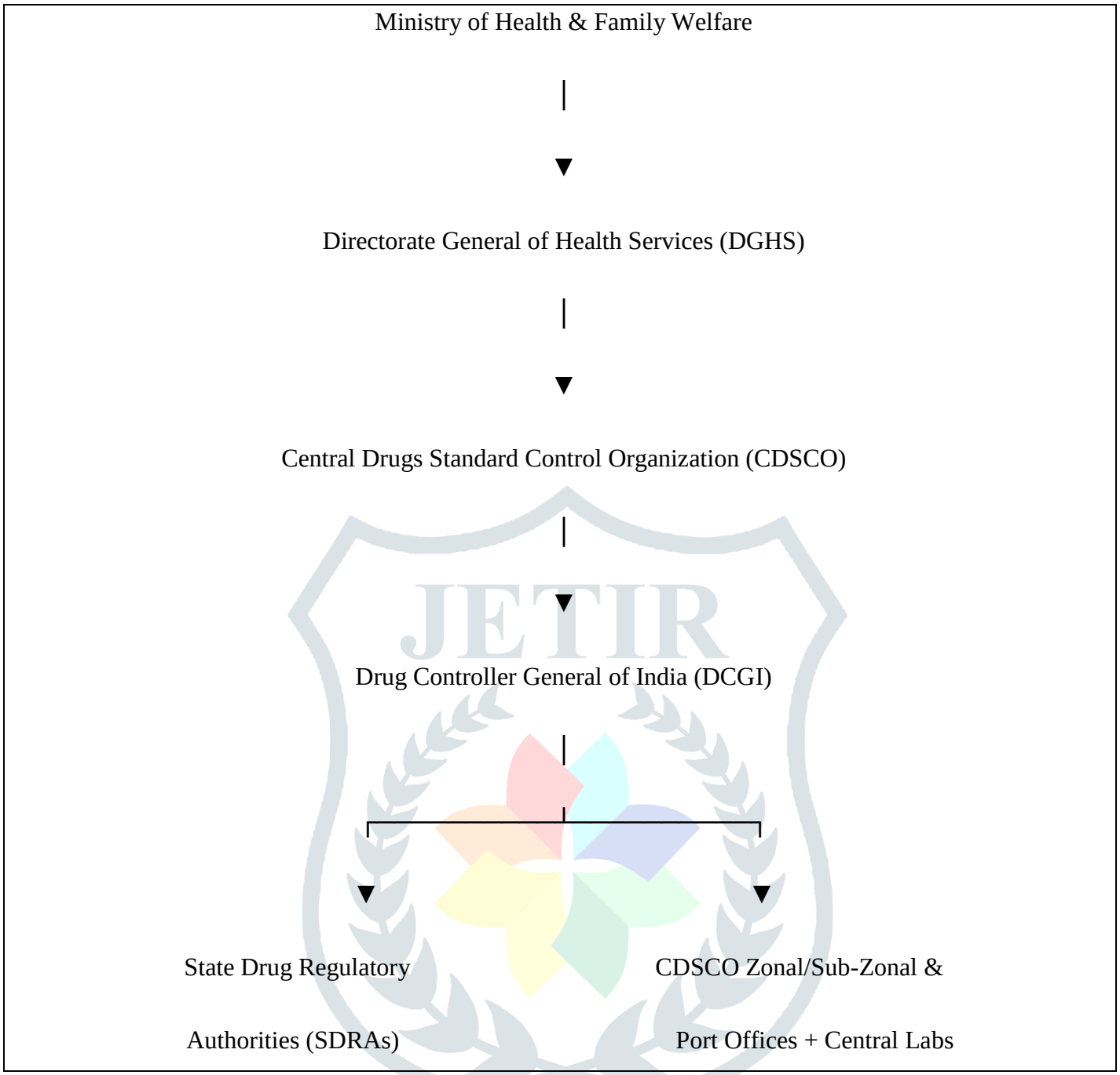

Figure 6: Organizational Hierarchy of Drug Regulation in India

The Central Drugs Standard Control Organization (CDSCO)

The Central Drugs Standard Control Organization (CDSCO) operates under the Directorate General of Health Services, Ministry of Health & Family Welfare, Government of India, and serves as the nation's National Regulatory Authority (NRA). Its headquarters is located at FDA Bhawan, New Delhi, with an extensive network of zonal and sub-zonal offices, port offices, and central laboratories across the country. CDSCO functions under the Drugs and Cosmetics Act, 1940 and the Drugs and Cosmetics Rules, 1945, regulating critical areas including new drug approval, clinical trial authorization, import control, and establishment of drug quality standards. In coordination with State Drug Regulatory Authorities, CDSCO ensures uniform regulatory enforcement nationwide. Additionally, it is responsible for licensing and monitoring high-priority and sensitive biological products such as blood and blood-derived products, vaccines, and intravenous fluids.[62]

Table 6: Comparison of Major Global Drug Regulatory Authorities

Parameter	**CDSCO (India)**	**FDA (United States)**	**EMA (European Union)**
Governing Ministry/Body	Ministry of Health & Family Welfare	U.S. Department of Health & Human Services	European Commission
Key Lead Authority	DCGI (Drug Controller General of India)	Commissioner of Food and Drugs	EMA Executive Director + CHMP
Establishment Year	1940 Act / 1945 Rules	1906 Pure Food & Drugs Act	1995
Primary Responsibilities	New drug approval, clinical trials, import regulation, GMP, pharmacovigilance	Review & approval of drugs/devices, manufacturing oversight, post-market surveillance	Scientific evaluation and supervision of medicinal products within EU
GMP Regulation	Schedule M	21 CFR Parts 210 & 211	EU GMP Guidelines (EudraLex Vol. 4)
Clinical Trial Oversight	Under NDCT Rules (2019) via CDSCO + Ethics Committees	Investigational New Drug (IND) & Institutional Review Boards (IRB)	Clinical Trials Regulation (EU No. 536/2014)
Territory Covered	India	United States	27 EU member states
Marketing Authorization Validity	India-specific	US-specific	EU-wide centralized approval

9.4 Regulatory Challenges: [59]

10. Oral Fast Dissolving Film Packaging:

In the pharmaceutical industry, packaging serves as a vital component in maintaining the stability and therapeutic effectiveness of a product. The protection of rapidly dissolving formulations during manufacturing and storage demands precise processing, careful handling, and frequently, high-cost packaging methods. Several packaging approaches are available for fast-dissolving films (FDFs). These drug delivery systems are typically packaged as single units, with aluminum pouches being one of the most widely used options. A notable innovation in this field is the Rapid Card, an exclusive packaging solution created by APR-Labtec for Rapid films. This credit card-sized system accommodates three films on each side, allowing users to separate and access individual doses with ease. The materials selected for packaging fast-dissolving films must meet

essential criteria, as highlighted in earlier research: Packaging materials should effectively shield the product from environmental factors such as moisture, light, and air, preserving its quality and potency. In compliance with FDA guidelines, all materials used in pharmaceutical and food packaging must be certified for safety and suitability. Tamper-evident features are mandatory to assure product authenticity and safeguard consumers. Packaging substances should undergo stringent safety assessments to confirm they are non-toxic and suitable for use. There must be no physical or chemical interaction between the material and the product throughout storage or distribution. Packaging components must not transfer odors or tastes to the product, maintaining its sensory characteristics.[63-65]

Blister Packs:

Blister packs remain one of the most common formats for oral fast-dissolving films (OFDFs). Each strip contains individual cavities that isolate and protect each dose from environmental exposure. This design enhances dosing accuracy, facilitates easy handling, and guarantees tamper evidence.

Aluminium Foil Pouches:

Aluminium pouches are another excellent option for OFDF packaging, offering superior barriers against moisture, oxygen, and light. Each pouch securely encloses the film units, ensuring long-term stability and product protection. They are especially suitable for storing or distributing multiple OFDF units together.[66-67]

Application of Oral Thin Film:

- Orally dissolving films are used to treat localized discomfort, allergies, sleeping problems, and CNS issues.
- Soluble films are appropriate for topical administration as analgesics or antibacterial agents in wound treatment.
- Orally disintegrating films can be used to improve the bioavailability of medications that are poorly bioavailable.
- Topical application of dissolvable films as analgesics or antibacterial agents for wound treatment is possible.
- Unpleasant medications are hidden in the taste.[68-71]

11. Discussion:

Oral thin films (OTFs) represent a significant advancement in drug delivery systems, offering a patient-friendly alternative to conventional oral dosage forms. Their rapid disintegration, ease of administration without water, and potential for enhanced bioavailability make them particularly suitable for pediatric, geriatric, and dysphagic patients. Recent developments in film-forming polymers, plasticizers, and taste-masking agents have improved OTFs' mechanical strength, flexibility, palatability, drug loading, and stability. Natural and synthetic polymers such as hydroxypropyl methylcellulose (HPMC), pullulan, and polyvinyl alcohol (PVA) are widely used, while nanotechnology-based approaches—including nanoemulsions, solid dispersions, and microneedle-assisted films—enable controlled and targeted drug release.

Regulatory alignment across the US FDA, EMA, and CDSCO is key to ensuring quality, safety, and efficacy. Although classified as oral solid dosage forms, OTFs require specific testing for tensile strength, disintegration time, folding endurance, and dissolution. However, variations in global regulatory standards remain a challenge. Market adoption of OTFs is growing across indications such as migraine, schizophrenia, nausea, and allergy management, with pharmaceutical companies focusing on convenience, adherence, and user experience. Persistent challenges include dose uniformity, limited drug loading capacity, and moisture sensitivity.

Overall, the integration of formulation innovation, regulatory harmonization, and market growth positions OTFs as a promising platform for systemic and local drug delivery. Future research will likely prioritize enhancing drug stability, expanding eligible drug categories and leveraging smart polymer technologies for personalized therapies.

12. Conclusion:

Oral thin film (OTF) technology marks a major advancement in pharmaceutical drug delivery, offering rapid disintegration, improved absorption, and enhanced bioavailability. Its water-free, easy-to-use design benefits pediatric, geriatric, and dysphagic populations, boosting comfort and adherence. Innovations in polymer science and manufacturing methods ensure dose precision, mechanical stability, and scalability. The integration of mucoadhesive and biodegradable polymers improves retention and therapeutic efficiency, while novel designs enable controlled release and stability. Regulatory authorities like the FDA, EMA, and ICH emphasize quality-by-design and bioequivalence to guarantee safety and consistency. These combined developments make OTFs a next-generation platform that blends scientific progress with global regulatory alignment, paving the way for personalized and universally accepted drug delivery systems.

13. Future Scope:

The future of oral thin films (OTFs) is promising, with personalized formulations using advanced 3D printing and inkjet printing technologies enabling tailored doses and drug combinations. Integration of nanotechnology is expected to improve bioavailability and enable targeted delivery. The use of OTFs is also expanding in nutraceuticals and vaccine delivery. The global oral thin film market is projected to grow significantly, driven by increasing patient demand for convenient and effective drug delivery systems.

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A REVIEW ON CALIBRATION OF PHARMACEUTICAL INSTRUMENTS

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ABSTRACT

The present study focuses on the calibration and verification of in-house laboratory equipment, including the pH meter, weighing balance, and UV-visible spectrophotometer, in accordance with Good Manufacturing Practice (GMP) standards and relevant Pharmacopoeial requirements. Accurate and reliable analytical measurements are critical in pharmaceutical and research laboratories, and periodic calibration ensures data integrity, traceability, and compliance with regulatory guidelines. The pH meter was calibrated using standard buffer solutions at pH 4.00, 7.00, and 9.20 under controlled temperature conditions. The weighing balance was verified for accuracy, repeatability, linearity, and eccentricity using certified standard weights, confirming proper performance for routine analytical weighing. The UV-visible spectrophotometer was calibrated. All performance parameters were found to comply with the specified limits. The outcome of this study confirms that all three instruments are fit for routine analytical use, maintain compliance with GMP standards, and provide reliable and reproducible results.

KEYWORDS: Calibration, weighing balance, pH meter, UV spectrophotometer.

AIM AND OBJECTIVE

Aim: To carryout equipment calibration and verification report in compliance with Good Manufacturing Practices standards for in house equipment's.

Objective

- To calibrate and verify the weighing balance by comparing standard weight with reading.
- To calibrate and verify the pH meter.
- To calibrate and verify the UV- visible spectrophotometer.

INTRODUCTION

Calibration is the comparison of an instrument's measurement output to a known reference standard to detect and correct inaccuracies. In the pharma industry, where batch decisions, environmental controls, and quality release hinge on instrument readings, even minor[1] measurement drifts can have serious implications.

Why calibration is critical in pharma

Because medicines are designed to interact with the human body, even minor errors in measurement can have serious health consequences. Regular calibration prevents this by achieving several key objectives:

1. **Ensures accuracy and consistency:** Over time, equipment can "drift," or lose its accuracy, due to wear and tear, environmental changes, or repeated use. Regular calibration minimizes this uncertainty.
2. **Maintains regulatory compliance:** Agencies like the FDA, EMA, and WHO require that all instruments used for manufacturing and testing are routinely calibrated against certified standards.
3. **Provides traceability:** Calibration creates an unbroken chain of comparisons, linking a measurement back to national or international standards, such as those maintained by the National Institute of Standards and Technology (NIST).
4. **Protects data integrity:** Trustworthy data is essential for making informed decisions and releasing products. Calibration ensures the reliability of data from analytical instruments and sensors.
5. **Prevents errors and waste:** A mis-calibrated

instrument can lead to incorrect dosages, [2] batch failures, and expensive product recalls.

OBJECTIVES OF CALIBRATION

The main purposes of calibration are:-

1. To ensure instrument/equipment readings display correct readings each time.
2. To determine how accurate, precise and reliable the measurements produced, as well as the degree of deviations are that are produced.
3. To check how reliable the instrument is by examining if it delivers reproducible results.
4. To assess the degree of drift from accuracy over time.

Weighing Balance

A weighing balance is a precision instrument used to measure the mass or weight of an object. Balances are generally more accurate and sensitive than scales and are essential tools for applications that require a high degree of precision, such as in laboratories.[4] Weighing is a common task in any chemical laboratory and its results may determine the acceptability of the products or outcome of a test. Weighing data are associated with some uncertainty, as this is common with all other working procedures and their data. Also all manufacturer specifications are based on "idealized" weighing conditions. Otherwise, comparisons could not be made between different instruments because the methods actually used in the field often differ from those used by the manufacturer. Hence it is important to have procedures for assuring the quality of these weighing devices in our laboratory conditions. Weighing is an important step in an experiment and its results, from electronic balances or other weighing devices are often of critical importance for next steps of an analysis.[5]

Fig. No.1: Weighing Balance.

The influence factors which are part of the combined measurement uncertainty of a mass determination and their interplay, namely the technical specifications of the balance (Repeatability, nonlinearity, sensitivity tolerance, and temperature coefficient of the[6] sensitivity and the effect of air buoyancy).

PH Meter

pH is defined for compendial purposes as the value obtained using an adequately calibrated[7] potentiometric sensor and measuring system, traditionally known as a "pH meter". pH is a scale that indicates the acidity or alkalinity of a solution. It is defined as the negative logarithm of the hydrogen ion concentration. The pH value expresses the strength of acids and bases in aqueous systems. In simple terms, pH helps to determine whether a solution is acidic, neutral, or basic. The pH value indicates the level of acidity or alkalinity present in a solution. In the context of Pharmacopoeia, specific standards and limits for pH are established for substances where pH is essential for stability or physiological suitability. The pH is determined at 25° ± 2° unless stated in the individual monograph. A potentiometric method can accurately determine a solution's pH level. It combines a pH meter, a reference electrode, and a glass electrode. These electrodes are available in analogue and digital[8] formats, allowing measurement flexibility. Adhere to the manufacturer's instructions to ensure precision when operating the pH meter. Begin by calibrating the device using a primary standard, specifically buffer solution. This is essential for obtaining the correct pH value corresponding to the temperature of the tested solution. The pH measurement is potentiometric, that is, it explains the relationship between the electrode potential and the solution.

Applications of pH Measurement

1. **Biomedical field:** pH meter is used to check how acidic or alkaline blood, organs, and tissues.
2. **Pharmaceuticals: pH plays a role in how well medicines dissolve, stay stable, and get absorbed in the body.**
3. **Food and beverages:** pH control helps to maintain taste, quality, and safety of food, especially during processing methods like pressure treatment.
4. **Textile and dyeing**: The pH of the dye bath affects how strong the colour is and how[9] quickly the fabric gets dyed.

Fig. No.2: pH Meter.

UV Visible Spectrophotometer

A UV-Vis spectrometer can be a relatively inexpensive piece of laboratory equipment and generally has the following basic components; a source of UV-Vis

radiation, a monochromator which ensures the correct wavelength of radiation illuminates the sample, a sample holder, and a detector.[10] It is used to determine the identity, strength, quality, and purity of several compounds. It is a measuring device which is used for quantitative analysis generally used for chemical substance by determining amount of light that is partially[11] absorbed by analyte present in the solution .

Fig. No.3: UV- Visible Spectrophotometer.

UV-visible spectrophotometer investigates the interaction of light radiation with matter in the ultra violet (200-400) and visible (400-800) range. The basic principle involves the absorption of visible and UV radiation is associated with excitation of electrons from low to high energy levels It involves observation of electrons and is also known as electron spectroscopy. It involves the determination of Electromagnetic Radiation (EMR) which is absorbed or emitted when molecules or atoms or ions of the sample move from one energy state to another energy state. It may be from ground state to excited state or from excited state to ground state. It is a physical technique which utilizes light in region of visible,[12] ultraviolet and near infrared areas.

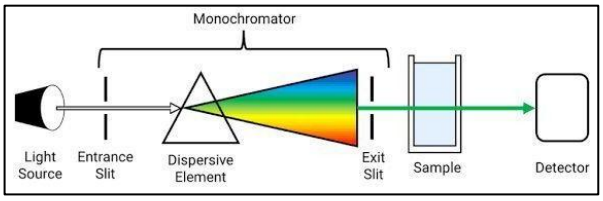

Fig. No. 4: Instrumentation UV- Visible Spectrophometer.

UV spectroscopy quantifies the discrete wavelengths of UV or visible light absorbed or transmitted by a sample in comparison to a reference or blank. This property, intricately linked to the sample's composition, holds the potential to unveil details about the sample's constituents and their concentrations. The outcomes of UV spectroscopy are graphically represented as spectra, providing a visual and quantitative depiction of the spectral data. This review aims to comprehensively explore the principles, applications, and advancements in UV spectroscopy, shedding light on its significance in diverse scientific domains. Through a systematic examination of the literature, we intend to elucidate the pivotal role of UV spectroscopy in analytical chemistry, molecular characterization, and quantitative analysis, offering a nuanced understanding of its contributions to contemporary scientific endeavours.[13]

MATERIALS

Equipment: weighing balance, pH meter, UV spectrophotometer.

Chemicals: buffer capsules, holmium oxide, per chloric acid, holmium perchlorate, potassium dichromate, potassium chloride, sulphuric acid solution, toluene, hexane, distilled water etc.

Apparatus: standard weights, volumetric flask, beaker, measuring cylinder etc.

METHODS

Weighing balance

Pre calibration process

- Before starting the calibration Warm-up the weighing balance for a minimum of 30 to 60 minutes, or as given in operating manual of the weighing balance.
- Keep the standard weights close to the weighing balance at least 30 to 60 minutes before the calibration to get thermal stabilization. Weighing balance & standard weights should be under thermal equilibrium.

For detailed calibration of weighing balance following of the tests are recommended to be performed.

- Repeatability Test
- Eccentricity Test
- Linearity Test

Repeatability Test

"Repeatability is the ability of a weighing balance to repeat the results when same load is applied again and again".

Repeatability test is performed on full and half capacity of the weighing balance, to perform repeatability test two weight are required one of full capacity of weighing balance and one of half of the capacity , for example, for a weighing balance of 200g capacity, weights required for repeatability test will be 200g and 100g.

Following steps to be followed

1. After warm-up, set the balance display to zero.
2. Take the full capacity weight; place it on the weighing balance pan, weight for the display to be stable, note the reading when display is stable.
3. Remove the weight from balance pan and wait for display to return zero, note down the return zero display of the weighing balance.
4. Again place the same weight on balance pan, wait for display to be stable and note down the stable reading
5. Remove the weight and wait for return to zero, note down the reading at no load.
6. Repeat the process at least five times (for batter

results 10 observations are recommended), and calculate the standard deviation.

Repeatability =2 x Standard Deviation / Smallest Net Weight

Acceptance criteria: Not more than 0.1.

Eccentricity Test

"Eccentricity is error due to off centre loading that may occur if measured is not placed in the centre of the weighing balance pan". Always use single weight for eccentricity test Mark five locations on the pan including one centre and four corners for both square and round type pans as shown in figure.

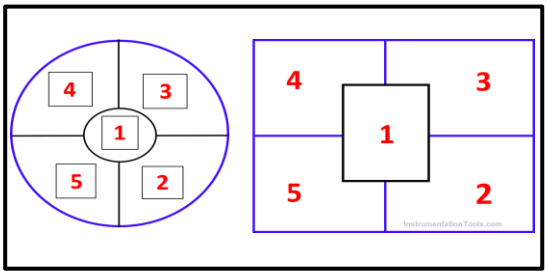

Fig. No. 5: Position of weighing on the weighing pan.

Procedure

1. Tare the weighing balance to zero and place the standard weight in centre position marked as (1), and note down the stable reading, remove the weight
2. Now place the weight at location 2, 3 4 and 5. Note down the readings respectively in same manner as above.
3. Again place the weight in centre and take second observation,
4. Now place the weight at location 5, 4, 3, 2 and note down their readings.
5. Again place the weight in centre and note down third observation at location (1).
6. Calculate average readings for all particular locations, now subtract average values of location 2, 3, 4 and 5 from location 1; maximum difference at any particular location must be within the specified limit to pass the eccentricity test.

Acceptance criteria: Not more than 0.05%.

Accuracy Test/ Linearity Test

The difference between the actual mass of a calibrated weight and its display on the weighing balance is known as the linearity error of that weighing balance. The linearity of the weighing balance determined by successively placing calibrated weights of the known mass value on the balance pan, and observing the difference between actual mass value and the display of weighing balance. The departure of indication from nominal value or the linearity of the weighing balance is measured at sufficiently and equally spaced points over the full ranges of the weighing balance. Usually minimum ten such points are taken.

Procedure

1. Place weight of known mass on the pan, where weight is approximately one-tenth of the range of the balance. Note down the balance reading.
2. Remove the weigh from the pan and then replace it back on the pan and note down the new balance reading. Take the average of these two readings.
3. Remove the weight from the pan and read the zero indication. This reading is average with that in step (i) to give the zero load value.
4. Place the next weight on the balance pan and note down balance reading.
5. Remove this weight momentarily from the pan and then replace it back on the pan and note down the new balance reading. Take the average of this reading and that in previous step.
6. Remove the weight from the pan and read the zero. This reading is averaged with that in step (iii) to give the zero load value.
7. Repeat the above steps with all other weights until the maximum capacity of the balance is reached.

Linearity correction for a weight is calculated as: Standard mass value – Average observed.[14]

Acceptance criteria: Not less than 0.9999.

2) *pH meter*

Procedure

1. Before starting the calibration make sure that the correct mode is selected.
2. Wash the electrode thoroughly with de-Ionized water or a rinse solution. Do not wipe the electrode; this causes a build-up of electrostatic charge on the glass surface.
3. Maintain the temperature of the buffers to 25℃ ± 2°℃.
4. Perform the three point calibration using standard buffers of pH 4.00, 7.00, 10.00.
5. Dip the electrode into the calibration buffer. The end of the electrode must be completely immersed into the sample. Stir the electrode gently to create a homogeneous sample.
6. Press CAL/MEAS key to enter pH calibration mode. The CAL indicator will be shown. The primary display will show the measured reading while the smaller secondary display will indicate the pH standard buffer solution reading.
7. Wait for the measured pH value to stabilize.
8. Press HOLD/ENTER key to confirm calibration. The meter is now calibrated to the current buffer.
9. Rinse the electrode with de-ionized water, which is followed by next buffer solution and place it in the buffer solution.
10. After all calibrations, the meter will return to measurement mode automatically.
11. If needed, press CAL/ MEAS again to stop early.
12. Record all calibration data properly.
13. Change the calibration buffer every week or whenever required and record.[15]

3) *UV Spectrophotometer*

A] Control of Wavelength
B] Control of Absorbance
C] Resolution Power
D] Limit of Stray Light

A] Control of Wavelength

1. Weight accurately 1.0 gm. of Holmium Oxide and dissolve it in 1.4 M Per chloric acid solution. Makeup to 25 ml with the same solvent.
2. Select the method file of CONTROL OF WAVELENGTH in the instrument.
3. After selecting the file press Reference button for baseline correction.
4. Then fill the cuvette with 1.4M Per chloric acid and put in the sample cubicle and press reference to zero.
5. After auto zero put the Holmium perchlorate solution in sample cubicle then press start key.
6. Scan it and verify the wavelength using absorption maxima of Holmium Perchlorate solution.
7. The permitted tolerance is given in below table.

Table No. 1: Permitted Tolerance.

Sr. No.	Maxima Wavelength	Tolerance (nm)
1.	241.15nm	240.15nm to 242.15nm
2.	287.15nm	286.15nm to 288.15nm
3.	361.5nm	360.50nm to 362.50nm
4.	536.3nm	533.30nm to 539.30nm

B] Control of Absorbance

1. Dry a quantity of potassium dichromate by heating to constant weight at 130°C.
2. Weigh & transfer accurately a quantity not less than 57.0 mg & not more than 63.0 mg to 1000 ml volumetric flask. Dissolve & dilute in sufficient 0.005M H_2SO_4 to produce 1000 ml.
3. Measure the absorbance of potassium dichromate solution at the wavelengths given below.
4. Calculate the value of Absorptivity (1% 1cm) for each wavelength.
   A (1% 1cm) = Absorbance X 10000 / Weight of Potassium dichromate in mg.

Acceptance Criteria

Table No. 2: Control of Absorbance.

Sr. No.	Wavelength (nm)	Limit
1.	235.0	122.9- 126.2
2.	257.0	142.8-145.7
3.	313.0	47.0-50.3
4.	350.0	105.6-108.2

C] Resolution power

Record the spectrum of a 0.02% v/v solution of toluene in hexane in the range of 260 nm to 420 nm (before use check the hexane for transmittance, using water as a blank between 260nm to 420nm & use only if transmittance is not less than 97%).

Acceptance criteria

The ratio of the absorbance at the maximum at about 269nm to that at the minimum at about 266nm is not less than 1.5.

D] Limit of Stray Light

Prepare a 1.2 % w/v solution of potassium chloride in water. Measure absorbances of the above solution at 198, 199, 200, 201 and 202 nm using water as blank.

Acceptance criteria: Absorbance must be greater than 2.

OBSERVATIONS AND RESULTS

Weighing balance Model: AB-200
Serial No. : 2401132
Capacity: Max. 200 gm, Min. 0.2gm
Sensitivity: 0.01.

Table No. 3: Repeatability Test.

Sr. No.	Repeatability test			
	Half load		Full load	
	Applied wt.	Indicated wt.	Applied wt.	Indicated wt.
1.	100 gm.	99.39	200 gm.	199.68
2.	100 gm.	99.39	200 gm.	199.63
3.	100 gm.	99.39	200 gm.	199.68
4.	100 gm.	99.40	200 gm.	199.67
5.	100 gm.	99.39	200 gm.	199.68
6.	100 gm.	99.38	200 gm.	199.68
7.	100 gm.	99.38	200 gm.	199.68
8.	100 gm.	99.38	200 gm.	199.67
9.	100 gm.	99.38	200 gm.	199.68
10.	100 gm.	99.37	200 gm.	199.68

Note: Smallest net weight= S.D × 2000

Repeatability (half load) = 2 x Standard Deviation / Smallest net weight
= 2 x 0.008498 / 16.996
= 0.001

Repeatability (full load) = 2 x Standard Deviation / Smallest net weight
= 2 × 0.01567 / 13.34
= 0.002

Result: The repeatability test of weighing balance is passed.

Table No. 4: Eccentricity Test.

Sr.	Pan Position	Indicated wt.			Average	Difference	% Deviation
1	1	99.38	99.39	99.35	99.38	-	
2	2	99.35	99.35	-	99.35	0.03	0.030
3	3	99.33	99.34	-	99.335	0.045	0.045
4	4	99.35	99.35	-	99.35	0.03	0.030
5	5	99.37	99.36	-	99.365	0.015	0.015

$$\% \text{ Deviation} = \frac{\text{Wt.at center} - \text{wt.at coner}}{\text{Wt.at center}} \times 100$$

Result: The eccentricity test of weighing balance is passed.

Table No. 5: Linearity Test.

Sr. No.	Applied wt.	Indicated wt. (gm)	Difference/erro
1	10	10.20	-0.2
2	20	19.60	0.4
3	30	29.56	0.44
4	40	39.69	0.31
5	50	50.30	-0.3
6	60	60.27	-0.27
7	70	69.70	0.3
8	80	80.25	-0.25
6	90	89.70	0.3
10	100	99.39	0.61
11	200	199.68	0.32

Error = Applied wt. - Indicate wt.

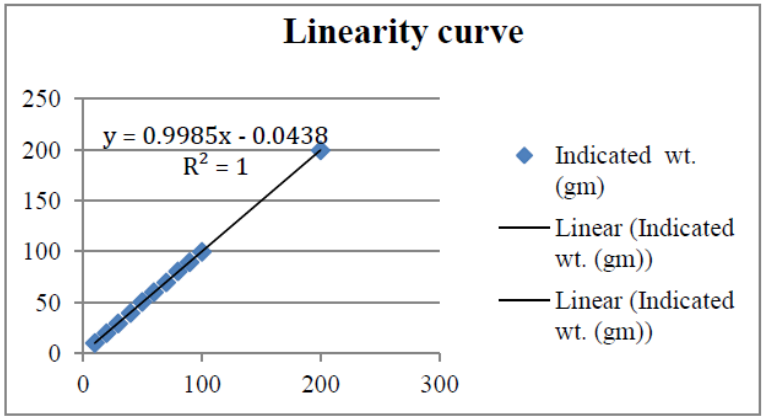

Fig. No. 6: Linearity curve Result: The linearity test of weighing balance is passed.

pH meter
Model: EQ-610

OBSERVATION
Table No. 6: Calibration Result of pH meter.

Standard solution of different pH values	Readings of standard solutions shown by pH meter before calibration	Readings of standard solutions shown by pH meter after calibration
Solution of pH 7	6.19	7.00
Solution of pH 4	3.1	4.00
Solution of pH 10	8.9	9.78

RESULT: The pH meter was successfully calibrated using standard buffers (pH 7, 4, 10).

DISCUSSION

Calibration of the pH meter, weighing balance, and UV–Visible spectrophotometer is essential to ensure accurate and reliable analytical results in pharmaceutical laboratories. The pH meter requires frequent calibration because electrode condition, buffer quality, and temperature can affect readings. The weighing balance is highly sensitive to environmental factors like vibration, air flow, and static electricity, so routine checks with standard weights are necessary. For the UV–Vis spectrophotometer, calibration of wavelength accuracy, absorbance accuracy, and stray light is critical to maintain correct quantitative measurements. Overall, regular calibration of these instruments prevents errors, supports GMP compliance, and ensures consistent quality of pharmaceutical testing.

CONCLUSION

All three instruments pH Meter, Weighing Balance, and UV-Visible Spectrophotometer were found to be within the specified accuracy and performance limits as per GMP and Pharmacopoeial requirements. The equipment is suitable for routine analytical use, ensuring reliability, accuracy and consistency of test results. Regular periodic calibration and verification will continue as per the approved schedule to maintain compliance with GMP standards. All instruments are calibrated.

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Review Article

Performulation Studies In Sustained Release Development with Experimental Insights into Drug Polymer Incompatibility

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ABSTRACT

Preformulation studies are crucial to formulation development because they offer crucial details regarding a drug's physicochemical and compatibility characteristics. In order to create a sustained release bead formulation that would prolong drug release and enhance patient compliance, the current study was conducted on molnupiravir. A controlled release system is necessary for molnupiravir, an antiviral medication with a short half-life, to maintain a constant plasma concentration and minimize frequent dosing. Solubility analysis, partition coefficient determination, melting point, drug stability, and organoleptic evaluation were among the preformulation studies carried out. FTIR spectroscopy techniques were used to evaluate drug-polymer compatibility studies in order to detect any potential interactions. The findings showed no appreciable alterations in the distinctive peaks, demonstrating that molnupiravir is compatible with the chosen polymers, including sodium, ethyl cellulose, and HPMC K4M.

INTRODUCTION

The purpose of drug delivery systems is to deliver therapeutic agents to particular body locations at a predetermined rate and duration in order to produce the best possible therapeutic results. Enhancing patient compliance, lowering dosage frequency, minimizing side effects, and increasing bioavailability are the objectives of a contemporary Novel Drug Delivery System (NDDS). The capacity of advanced delivery systems, such as controlled release or sustained release formulations, to sustain consistent plasma concentrations and extended therapeutic action has made them more significant. 2. . Sustained Release Formulations Are Needed: Multiple daily doses are necessary because conventional dosage forms frequently cause fluctuations in plasma drug levels. To solve this issue, sustained release formulations are created, which release the medication over a longer period of time at a regulated rate. Benefits include: Preserving consistent therapeutic levels; lowering the

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frequency of doses; improving patient compliance; and minimizing adverse effects.

METHOD:

Supplies And Methods: -

SUPPLIES: 1. Molnupiravir, the medication 2. Alginate made of sodium 3. 4. Ethanol. 5. EDTA. Chloride of calcium 6. HPMC 7. . Cellulose8 methyl carboxy cellulose. Procedures for propylene glycol: 1. Organoleptic Properties: Molnupiravir's organoleptic studies include its overall appearance, including its color, nature, and odor. Were conducted and watched. 2. . Identification of Melting Point Range: The USP method was used to determine the melting point. A capillary tube that was sealed was filled with a small amount of molnupiravir. The melting point apparatus was positioned over the tube. Gradually raising the device's temperature allowed for the monitoring of the temperature at which molnupiravir began to melt as well as the temperature at which the entire medication melted. The "open capillary method" is another name for this approach. 3. . Investigation of drug-polymer interaction (FTIR): Fourier transformed infrared spectroscopy was used for FTIR spectroscopy. The wave numbers for the drug and polymer mixture scan ranged from 3971point 35 to 678point 36.

Preparation of molnupiravir microbeads:

Method Used:

Ionotropic – gelation technique Microbeads of molnupiravir were prepared using sodium alginate, sodium carboxy methyl cellulose, HPMC, EDTA and calcium chloride. Weighed quantity of drug and polymer were added to 100ml of sodium alginate solution with stirring about 300 rpm. The resultant solution was added drop wise to 100 ml of calcium chloride solution under constant stirring using 12.7gauge needle syringe. The obtained microbeads were filtered and then dried for 6hrs.

Drug profile:

1 Drug name: Molnupiravir2 IUPAC name: [(2R,3S,4R,5R)-3,4-dihydroxy-5-[4-(hydroxyamino)-2-oxopyrimidin-1-yl]oxolan-2-yl]methyl 2-methylpropanoate3 Structural formula: 4 Empirical formula: C13H19N3O75 Molecular weight: 329.3g/mol6 Class: broad spectrum anti-viral7 Category: Anti-viral agent8 Mechanism of action: Molnupiravir prevents the spread of infection by causing widespread mutations in the replication of viral RNA by RNA-directed RNA polymerase. It undergoes metabolism to produce β-D-N 4-Hydroxycytidine 5′-triphosphate, also known as EIDD-1931 5′-triphosphate or NHC-TP, a ribonucleoside analogue that resembles cytidine. NHC-TP is incorporated into freshly synthesized RNA by the virus's enzyme during replication rather than actual cytidine. Side effects: nausea, diarrhea, and dizziness; 11 uses; COVID-19; POLYMER PROFILE: -1; 9pH1.5-2.510. The structural formula for sodium alginate is: Sodium alginate, Natrii alginas. Hydropropyl Propyl Methyl Celluse, Hypromellose is the name of HPME.

DISCUSSION:

To learn more about Mol crystalline form, which is white to off-white nupiravir's physicochemical characteristics and compatibility with particular polymers, preformulation studies were conducted. The drug's and odorless, was confirmed by the organoleptic evaluation. According to the measured partition coefficient (log P = -0.30), molnupiravir is hydrophilic, which supports the necessity of a sustained release system to extend its therapeutic effect. FTIR analysis of drug and

polymer mixtures revealed no discernible changes in characteristic peaks, indicating that there was no chemical interaction and that the mixtures were compatible with polymers like sodium alginate, ethyl cellulose, and HPMC K4M. These results indicated that the polymers could be used to formulate Molnupiravir beads with sustained release that were made using the ionotropic gelation method. According to the study's findings, molnupiravir can be successfully combined with the chosen excipients to create a stable suspension.

SUMMARY AND CONCLUSION:

Molnupiravir's physicochemical characteristics and compatibility with polymers for formulation of sustained release beads were assessed through preformulation studies. Confirming purity, the drug was discovered to be a white, odorless, crystalline powder with a melting point of 171 °C. In order to sustain extended drug levels, a sustained release system is required, as indicated by the partition coefficient (log P = -0.30), which indicated hydrophilic nature. The compatibility of Molnupiravir with polymers like HPMC K4M, EDTA, propylene glycol, and sodium alginate was confirmed by FTIR spectroscopy analysis, which revealed no appreciable changes in identifiable peaks. According to the reference study, the ionotropic gelation method produced uniform beads with good entrapment and controlled release. The investigation came to the conclusion that molnupiravir is physicochemically stable and compatible with specific polymers, which makes it appropriate for creating a sustained release bead formulation.

RESULT:

Solubility: It was ascertained using the method specified in the material and equipment section of the preformulation. The following table provides an illustration of the findings. 1: Molnupiravir microbead solubility: Test Specification Outcome Solubility: Water and ethanol soluble, insoluble in 2-propanal Compiled (as specified) Melting point: Melting point was ascertained using a melting point apparatus. The following table provides an illustration of the findings. 2: Molnupiravir's melting point: Material: Melting pointResult: Molnupiravir171 0CCompiles (per specification) Drug-polymer interaction (FTIR) study: IN-VITRO Dissolution graph of Molnupiravir: Partition Coefficient: The shake flask method was used to determine it in accordance with the protocol. PHASE CONCENTRATION Aqueous Layer 42ug/mln-octanol Layer 21ug/mlCALCULATION is an example of the results.

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INTEGRATING ANALYTICAL METHOD DEVELOPMENT, SELECTION AND VALIDATION IN NDDS

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ABSTRACT

UV-Visible Spectroscopy is a widely used analytical technique that measures the absorption of ultraviolet and light by chemical substances to determine their concentration and structural properties. It operates by passing light through a sample and recording the absorbance at specific wavelengths. The major components of a UV spectrophotometer include a light source, monochromator, sample cuvette, detector, and display system. The technique is fast, nondestructive, and suitable for routine quantitative and qualitative analysis in pharmaceutical research. The present study focuses on the development and validation of a simple, accurate, and precise UV–Visible spectrophotometric method for the estimation of Samples (Metronidazole). UV spectroscopy is based on the absorption of ultraviolet light (200–400 nm) by molecules, causing electronic transitions from lower to higher energy states. The analysis was carried out using a SHIMADZU UV–Visible double beam spectrophotometer (Model UV– 1900I) with quartz cuvettes. The standard solution of Metronidazole was prepared, and serial dilutions ranging from 0.5 to 2.0 µg/mL were analyzed. The wavelength of maximum absorbance (λ max) was observed at 321 nm. The calibration curve plotted between absorbance and concentration showed a linear relationship in accordance with Beer–Lambert's law, with absorbance increasing proportionally to concentration. The developed method was found to be accurate, reproducible, sensitive, and economical, making it suitable for the routine quality control and quantitative analysis of Metronidazole in bulk and pharmaceutical formulations.[1-2]

KEYWORD: UV Spectroscopy, Beer-Lambert' Law, Electronic Transition, Metronidazole.

INTRODUCTION

Spectroscopy is the technique which measures the Electromagnetic radiations (EMR) which is emitted or absorbed by molecules or atoms or ions of a sample when it moves from one energy state to another energy state and Electromagnetic radiation is a type of energy such as UV rays, Infrared rays, Micro-waves, Radio-waves, X-rays, Gamma rays and visible light etc.

Ultraviolet (UV) spectroscopy is one of the most widely employed analytical techniques in modern chemistry and pharmaceutical sciences. It is a type of absorption spectroscopy which involves the interaction of ultraviolet light, typically in the wavelength range of 200–400 nm, with a substance to study its electronic structure. When UV light passes through a sample, some of it is absorbed, causing the electrons in the molecules to move from a lower energy level (ground state) to a higher energy level (excited state), producing a distinct absorption spectrum. This spectrum serves as a molecular fingerprint that helps in the identification, purity assessment, and quantitative determination of chemical compound.

UV spectroscopy is simple, fast, and non-destructive, making it suitable for routine analysis and monitoring reactions. Key components include a light source, monochromator, sample holder, and detector.

Principle

The principle of UV-Vis spectroscopy is Based on the principle of absorption of UV light by chemical compounds, which result in production of different Spectra and the spectra arise from the transition of an electron within a molecule from ground state to excited

state. When the molecules absorb UV radiation frequency the electron in that molecule undergoes transition from ground level to higher energy level cause electronics transition.[3-4-5]

Electronic Transitions

When a molecule absorbs UV light, electronic transitions occur — electrons jump to higher energy orbitals. Molecules that have π-electrons (in double bonds) or non-bonding electrons (lone pairs) can easily absorb UV radiation. This absorption results in different types of transitions depending on the kind of electrons involved:

1. Σ → σ* (sigma to sigma star)
2. N → σ* (non-bonding to sigma star)
3. Π → π* (pi to pi star)
4. N → π* (non-bonding to pi star) These transitions differ in energy, arranged as:

Σ–σ > n–σ > π–π* > n–π***

(from highest to lowest energy required).

Beer-Lambert's Law

This absorption process is mathematically represented by the Beer–Lambert Law, which defines a direct proportionality between absorbance (A) and the concentration (C) of the absorbing species in the solution,

Beer – Lambert's law states that

When a beam of monochromatic radiation is passes through the absorbing medium, then the decrease in the intensity of the radiation is directly proportional to the thickness/pathlength as well as concentration of the solution.

The Beer -Lambert's law can be expressed as : A a c × l

A= ε ×c×l

Where, A=Absorbance ε=Molar absorptivity

c= concentration l= pathlength

According to this law, absorbance increases linearly with concentration within a specific range, which makes UV spectroscopy a reliable quantitative method for solution analysis.

Fig. 1 & 2: UV Spectrophotometer.

Instrumentation

UV - VIS SPECTROPHOTOMETER

A UV-Vis spectrophotometer is an analytical instrument used to measure the amount of light absorbed by a sample at different wavelengths in the ultraviolet (UV) region (190 to 400 nanometers) and the visible (Vis) region (approximately 400 to700 nanometers) of the electromagnetic spectrum. Its primary function is to determine the concentration of a substance in a solution or to help identify substances based on their unique absorption patterns. It works by passing a beam of light through a sample and measuring how much of that light passes through (transmittance) or is absorbed (absorbance).

The essential parts of a spectrophotometer are

1. Radiation Source
2. Monochromator
3. Sample cell
4. Detector
5. Recordings system

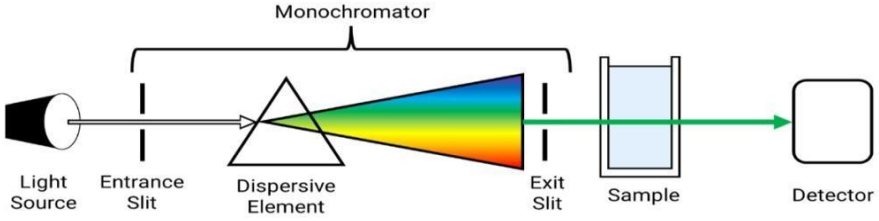

Fig. 3: Working of UV spectrophotometer.

Radiation Source

In UV-Vis spectroscopy, the selection of a light source is crucial for accurate and reliable measurements.

The light source used in UV-Visible spectroscopy should give a steady and uniform intensity of light for all wavelengths. However, maintaining this uniformity is challenging. Therefore, to cover the full range of wavelengths—from ultraviolet to visible and sometimes even near- infrared regions—spectrophotometers usually use a combination of two different light sources.[1-2]

Common light sources used in UV-Vis Spectrophotometers.

Light Source	Principle of Operation	Key Applications
Hydrogen Discharge Lamp	Gas discharge through low-pressure hydrogen; emits continuous UV (190–400 nm)	Historically used in UV spectrophotometry; now mainly for calibration due to less stability.
Deuterium Arc Lamp	Gas discharge using deuterium (isotope of hydrogen); continuous UV emission	Preferred UV source (approx. 190–400 nm) in UV-Vis spectrophotometers; offers continuous, stable, long-lasting output.
Xenon Arc Lamp	High-pressure gas discharge in xenon; broad spectrum across UV, visible, near-IR	High-intensity, sunlight-like output; used in fluorescence spectroscopy, solar simulators, and high-intensity UV-Vis applications.
Mercury Arc Lamp	Electric discharge through mercury vapor; emits sharp spectral lines	Valuable for instrument calibration using characteristic UV/visible lines (e.g., 254 nm, 365 nm); also employed in germicidal UV for sterilization.

Monochromator

Monochromator is also known as Wavelength selectors. Used to isolate the desired wavelength of radiation from wavelength of continuous spectra.

Components of Monochromator

- **Entrance Slit:** It narrows the incoming light beam to prevent overlapping of different wavelengths, ensuring a clean input for analysis.
- **Collimating Mirror (Concave):** It straightens the diverging light rays from the entrance slit into parallel beams, which is essential for accurate wavelength separation.
- **Prism or Grating:** This component disperses the parallel light into its individual wavelengths by bending (prism) or diffracting (grating) the light, separating colours like a rainbow.
- **Focusing Mirror or Lens**: It refocuses the dispersed light onto the exit slit, directing the selected wavelength precisely.
- **Exit Slit:** It allows only the desired narrow band of wavelengths to pass through, blocking the rest, to deliver pure monochromatic light.

TYPES OF MONOCHROMATORS

- **Prism Monochromator:** Prism works by refraction. Different wavelengths of Light are bent at It is a transparent container that holds the sample being measured They are typically constructed from materials like quartz, glass, or plastic different angles as they pass through the prism material. (e.g., quartz for UV, glass for visible)
- **Diffraction Grating Monochromator:** Diffraction Grating works by diffraction and interference. A grating has thousands of finely ruled parallel lines. Light striking these lines is diffracted, and different wavelengths interfere constructively at different angles, spreading the light into a spectrum.

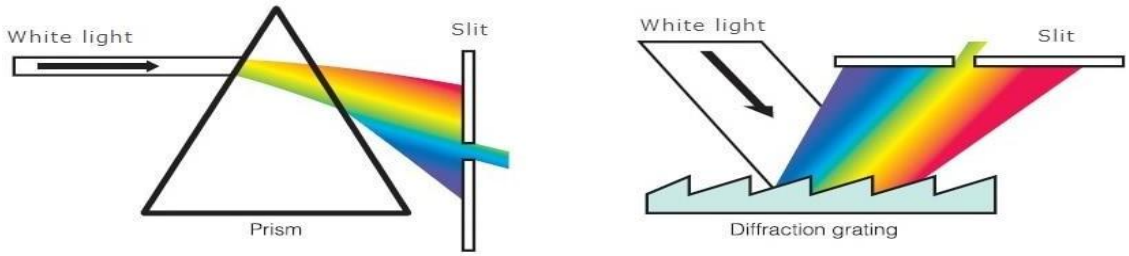

Fig. 4: Working of Monochromators.

Sample cell

In UV-Vis spectrophotometry, a sample cell, also known as a ***cuvette***, It is a transparent container that holds the sample being measured They are typically constructed from materials like quartz, glass, or plastic.

Fig. 5: Sample holder (Cuvette).

Detectors

A UV-Vis spectrophotometer, the detector is the component responsible for converting the light that has passed through the sample into a measurable electrical signal. This signal is then processed to determine the amount of light absorbed or transmitted by the samples.

Here are the common types of detectors used

1. Photovoltaic Cell (Photocell)
2. Phototube (Photocell)
3. Photomultiplier Tube (PMT)

Photovoltaic cell (photocell)

Working Principle: Based on the photovoltaic effect light falling on a semiconductor generates electron–hole pairs, producing an electric current.

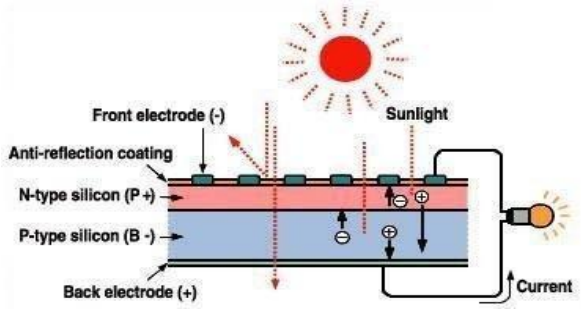

Fig. 6: Photovoltaic cell detector.

Photomultiplier tube (PMT)

Working Principle: Also based on the photoelectric effect but with electron Multiplication. The photoelectrons emitted from the cathode strike a series of Dynodes, each releasing multiple secondary electrons, resulting in a large Amplified current.

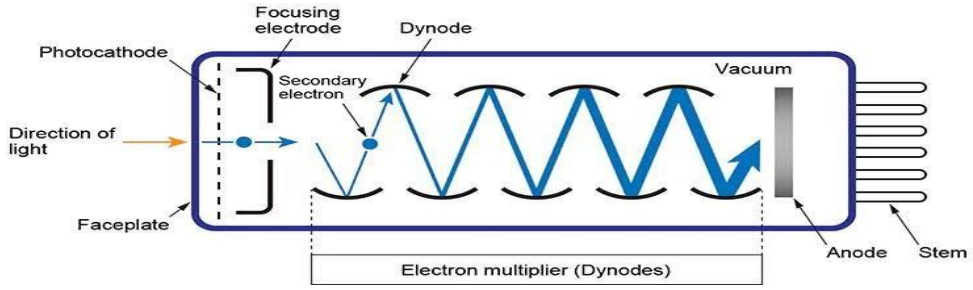

Fig. 7: Photomultiplier tube detector Phototube (Photo emissive Cell).

Working Principle: Works on the Working Principle: Based on the photovoltaic effect light falling on a semiconductor generates electron–hole pairs, producing an electric current. Effect – light photons strike a Photosensitive cathode, releasing electrons, which are collected at an anode.[3-4-5]

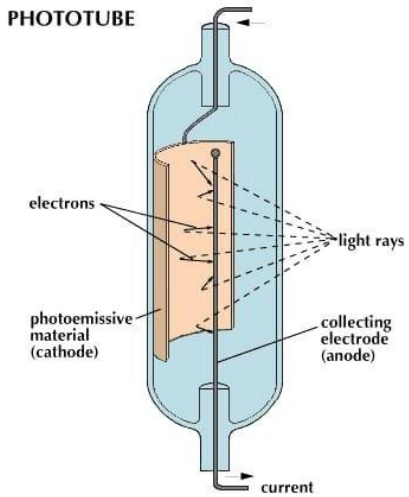

Fig. 8: Phototube detector.

Working

Working principle of a spectrophotometer is based on the following steps:

Blank (measure of the intensity of light transmitted through the solvent):

1. The solvent (e.g. water or alcohol) is added into a suitable, transparent and not absorbing container – a cuvette.
2. A light beam emitted by the light source passes through the cuvette with the solvent.
3. The intensity of the transmitted light at different wavelengths is then measured by a detector and recorded.

Sample determination

1. A sample is dissolved in the solvent and added into the cuvette.
2. A light beam emitted by the light source passes through the cuvette with the sample.
3. When passing through the cuvette, the light is partially absorbed by the sample molecules in the solution.
4. The transmitted light is then measured by the

detector.

5. The light intensity change at different wavelengths is calculated by dividing the transmitted intensity of the sample solution by the corresponding values of the blank.[6]

APPLICATIONS

A. Quantitative Chemical Analysis

In chemistry labs, UV spectrophotometry is used to measure how much of a substance (solute) is present in a solution. The Beer-Lambert Law explains that the amount of light absorbed by a solution is directly related to the concentration of the absorbing substance. This allows scientists to accurately determine concentrations.

B. Biochemical and Biomedical Research

In biology and medicine, UV spectrophotometers are used to study important molecules like proteins and nucleic acids (DNA and RNA). They help identify, measure, and monitor any structural changes in these biomolecules.

C. Pharmaceutical Analysis

In the pharmaceutical industry, UV spectrophotometry is used to check the concentration of active pharmaceutical ingredients (APIs) in drug formulations. This ensures that medicines contain the correct amount of each ingredient.

D. Environmental Monitoring

UV spectrophotometry is also used to test environmental samples, especially water. It helps detect pollutants such as heavy metals and organic compounds, ensuring that water quality.

AIM

To develop and validate a simple, accurate, precise, and sensitive UV-Visible spectrophotometric method for the estimation of sample and to study its analytical, physical, and chemical characteristics according to ICH guidelines.

OBJECTIVE

1. To understand the basic principle of UV–Visible Spectroscopy, which is based on the measurement of light absorbed by molecules in the ultraviolet and visible regions of the electromagnetic spectrum (190–700 nm).
2. To study the instrumentation and working mechanism of the UV–Visible Spectrophotometer, including its main components — light source, monochromator, sample cell (cuvette), detector, and display system.
3. To develop a simple and rapid UV-Visible spectrophotometric method for the estimation of the selected sample.
4. To ensure the developed method is accurate, precise, and sensitive for reliable analysis.
5. To validate the developed method in accordance with ICH (International Council for Harmonization) guidelines.
6. To evaluate the physical and chemical characteristics of the sample.

MATERIAL AND METHOD

Instrument and Material

SHIMADZU UV – visible double beam spectrophotometer model UV – 1900I with 1cm matched quartz cells were used for all the spectral measurements. Chemicals and reagents Distilled water, metronidazole tablets (METROGYL 400). Solvent mixture of methanol and water (80:20) was used as solvent for development of spectral characteristics. All the chemicals used were of analytical grade.

physical and chemical properties of Metronidazole

- Chemical Formula: C6H9N3O3
- Molecular Weight: 171.15 g/mol
- Physical Appearance: White to pale yellow crystalline powder
- Melting Point: Approximately 158–161°C
- Boiling Point: Estimated around 301 °C
- Solubility: Moderately soluble in water (about 1 g/100 mL at 20 °C), soluble in dilute acids and ethanol; very slightly soluble in ether and Chloroform pH of Saturated Solution: Around 5.8 to 6.5
- Odor: Slight odor, bitter and salty taste
- Stability: Darkens on exposure to light, stable under standard conditions but incompatible with strong oxidizing agents
- Density: Approximately 1.4 g/cm³

Structure of metronidazole

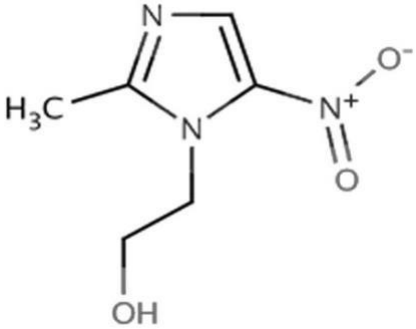

Fig. 9: Structure of Metronidazole.

Fig. 10: Metronidazole Tablets.

Clinical Uses of Metronidazole

- Treatment of amoebiasis (intestinal and hepatic)
- Treatment of trichomoniasis.
- Management of bacterial vaginosis.
- Treatment of anaerobic bacterial infections.
- Used in pseudomembranous colitis (Clostridium difficile infection). Part of ombination therapy for Helicobacter pylori in peptic ulcer disease

Side effects of metronidazole

- Vomiting, Nausea
- Loss of appetite
- Metallic taste in the mouth, Dry mouth
- Abdominal pain or cramps
- Mouth or tongue irritation
- Skin rash or itching[7-8-9]

PREPARATION OF SAMPLE

Preparation of standard stock solution

1. Twenty tablets were weighed accurately and ground into a fine powder.
2. A quantity of the powdered tablets, equivalent to 50 mg of metronidazole, was weighed accurately.
3. This powder was transferred into a 100 ml volumetric flask.
4. The contents were dissolved with sufficient amount of solvent and diluted up to the mark to obtain a sample stock solution
5. The solution was filtered through Whatman filter paper No. 41 to obtain a clear solution.

Preparation of Primary stock solution

6. From the stock solution, 10 ml was pipetted and transfer into a 100 ml volumetric flask and make up the volume with water.
7. Pipette out 1ml of solution and transfer it to the 10ml of volumetric flask. Make up the volume up to the mark by water to get the final dilutions.[10 -11]

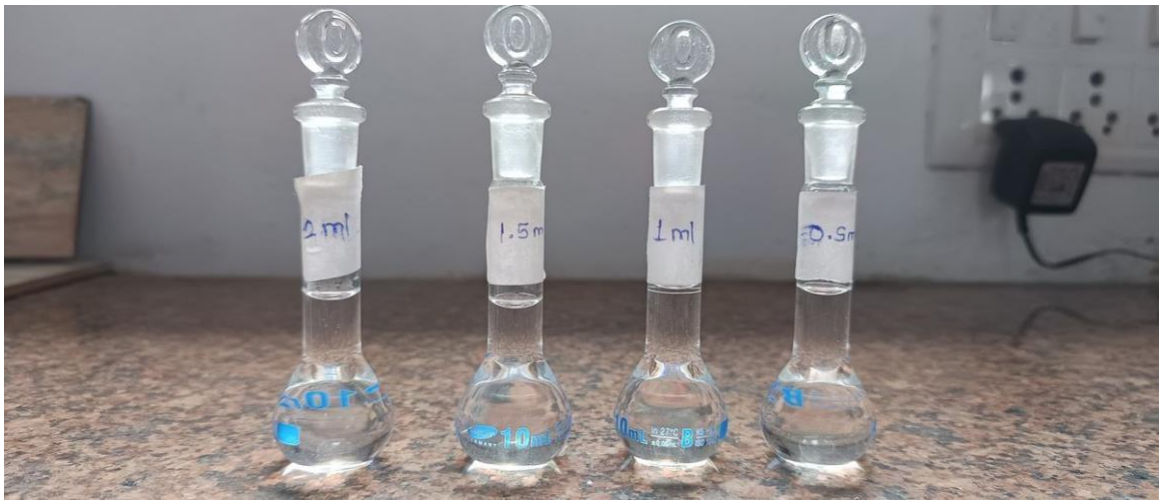

Fig. 11: Solution of different concentration.

Criteria for method selection for metronidazole

The criteria for method selection for metronidazole estimation by UV visible spectroscopy in novel drug delivery systems (NDDS) typically include:

- **Wavelength selection:** Metronidazole shows maximum absorbance (λ max) around 278-320 nm depending on the solvent and formulation type. This wavelength corresponds to its UV absorbance maximum for optimal sensitivity.
- **Linearity**: The method should obey Beer's law within a suitable concentration range (e.g., 5-30 µg/mL or larger ranges like 80%-120% of drug concentration). Correlation coefficient [R^2] values close to 0.999 indicate good linearity.
- **Accuracy and recovery**: Percentage recovery

should be within acceptable limits of around 98-102% to confirm accuracy.

- **Precision**: The method should demonstrate reproducibility and precision with low relative standard deviation (e.g., coefficient of variation below 2%) on replicate measurements.
- **Sensitivity**: The limits of detection (LOD) and quantification (LOQ) should be low enough for the required assay range.
- **Stability**: The sample solution should remain stable for a reasonable period (e.g., 24 hours) to allow consistent readings.
- **Specificity**: The method should clearly differentiate metronidazole from excipients or other formulation components without interference.[10]

RESULTS AND DISCUSSION

A series of standard solutions of Metronidazole was prepared in the concentration range of 0.5–2.0 µg/ml and scanned in the UV region (200–400 nm) to determine the wavelength of maximum absorbance (λ max). The λ max was found to be 321 nm.

A calibration curve was plotted between absorbance (Y-axis) and concentration (X-axis). The curve was found to be linear within the studied concentration range.

OBSERVATION

Sr. No	Concentration	Absorbance
1.	0.5	0.624
2.	1.0	1.246
3.	1.5	1.544
4.	2.0	2.262

Calibration Curve for Metronidazole

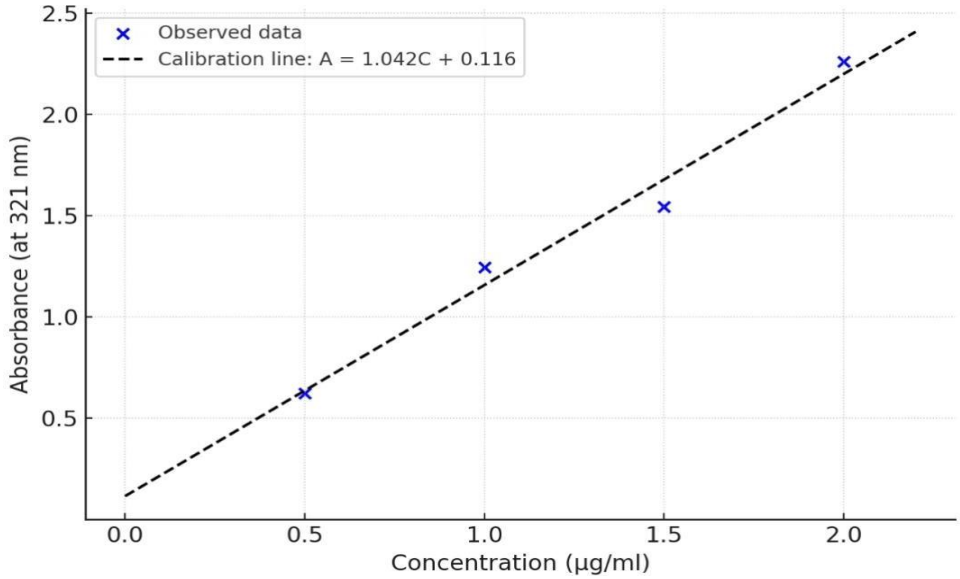

Fig. 12: Calibration Curve of Metronidazole.

Fig. 13: Spectrum Showing absorption maxima for metronidazole.

The UV spectrophotometric method developed for the estimation of Metronidazole showed a clear linear relationship between concentration and absorbance at 321 nm.

The linearity of the calibration curve suggests that absorbance increases proportionally with the concentration, validating the applicability of Beer–Lambert's law in this concentration range. The λ max at 321 nm corresponds to the characteristic absorption of Metronidazole, indicating no interference from excipients or solvent.

Thus, the method is suitable for the routine analysis of Metronidazole in bulk and pharmaceutical dosage forms using UV-visible spectrophotometry due to its simplicity, precision, and reproducibility.

SUMMARY AND CONCLUSION

The present study focused on the development and validation of a simple, accurate, precise, and sensitive UV–Visible spectrophotometric method for the estimation of Metronidazole in bulk and tablet dosage form according to ICH guidelines.

The λ max of Metronidazole was found to be 321 nm using a solvent system of methanol and water (80:20). Standard solutions with concentrations ranging from 0.5 to 2.0 µg/mL showed a linear relationship between absorbance and concentration, confirming adherence to Beer– Lambert's law. The calibration curve demonstrated excellent linearity, indicating the reliability of the method for quantitative analysis.

The developed method was found to be simple, rapid, and reproducible, with no interference from excipients or solvents. The accuracy and precision were within acceptable limits, making the method suitable for routine quality control analysis of Metronidazole in pharmaceutical.

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REGULATORY, USES AND SAFETY ASPECTS OF MICROBEADS SUSTAINED RELEASED SYSTEM IN COSMETICS

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Abstract :
Microbeads, commonly found in cosmetics and personal care items, have attracted considerable interest due to their functional advantages, especially in sustained-release delivery systems. These tiny polymeric particles, which can encapsulate active ingredients, improve product effectiveness by allowing for a controlled and prolonged release while reducing negative side effects. Their growing application in exfoliants, cleansers, creams, and related products has fueled expansion in the global market; nevertheless, the environmental and health risks tied to synthetic microbeads have raised concerns as well. This review brings together existing knowledge about the different types, uses, regulatory frameworks and safety assessment. Regulations from India, the United States, the European Union, United kingdom, China, Thailand and South Korea are analyzed to emphasize the developing compliance requirements and the difficulties that manufacturers encounter.

Keyword : Microbeads, Sustained-release delivery systems, Cosmetics and personal care products, Regulatory frameworks, Safety assessment .

INTRODUCTION

Cosmetics are preparations that have been used by humans for a long time, primarily for regenerative purposes, and are appreciated by both genders. They can be defined as preparations that are typically used externally and can be formulated from a single or combination of substances obtained from either natural or artificial sources.[1] According to Section 3(a) of the Drugs and Cosmetics Act, 1940 “Cosmetic can be explained as a product anticipated for coating, gushed, dispersed or sprayed on, or instigate into, or else dermally used on the humans or any part of the things just mentioned for cleansing, embellishing, enhancing attractiveness, or changing the looks, and includes any product intended for a component of cosmetic”.[2] The use of microbeads is becoming more popular due to improvements in microsphere quality and functionality, an accordingly, they have increasingly been used in food science and separations and as exfoliants in cosmetics and personal care products.[3] Multiple unit dosage forms such as microspheres or micro beads have gained in popularity as oral drug delivery systems because of more uniform distribution of the drug in the gastrointestinal tract, more uniform drug absorption, reduced local irritation and elimination of unwanted intestinal retention of polymeric material, when compared to non-disintegrating single unit dosage form. Microbeads are small, solid and free flowing particulate carriers containing dispersed drug particles either in solution or crystalline form that allow a sustained release or multiple release profiles of treatment with various active agents without major side effects.[4] Microbeads are commonly found in products like facial scrubs, body washes, toothpastes, and creams.[5]

Personal care companies (including Unilever, Target, Johnson & Johnson, Procter & Gamble, and L’Oreal) were somé of the largest producers of microsphere-containing products. In 2014, the global market for microspheres had attained $2.3 billion and was expected to reach $3.5 billion by 2020, registering a compound annual growth rate (CAGR) of 7.8% from 2015 to 2020. The medical technology market segment for microspheres alone was expected to grow from $504 million in 2015 to $810 million in 2020, at a CAGR of 10.0% from 2015 to 2020. However, as synthetic polymers have found widespread application in the global market, they have become more ubiquitous in the environment, leading to increasing concern about their environmental impacts.[6]

TYPES OF MICROBEADS

There are two types of microbeads; microcapsules and micrometrics. Microcapsules are those in which entrapped substance is distinctly surrounded by distinct capsule wall, and micro matrices are those in which entrapped substance is dispersed throughout the matrix. Microbeads are sometimes referred to as microparticles. Microspheres can be manufactured from various natural and synthetic materials. Microbeads play an important role in improving conventional drugs' bioavailability and minimizing side effects.[7-10]

USES OF MICROBEADS

Microbeads have been seen in personal care products such as deodorants, toothpaste, shaving creams etc. Apart from personal care products they are also found in consumer products such as printing toner, cleaning products. They are also part in industrial products such as plastic blasting, textile printing and medical applications. Some of these products are used on a daily basis in our houses that could lead to around 95,000 microbeads particles released to water, as per study. A Canadian Cosmetic, Toiletry, and Fragrance Association (CCTFA) survey says that annual volume of microbeads within Canada ranged from 30 Kg to 68,000 kg per year.[11]

1.In order to provide exfoliation, microbeads are added to toothpaste, face scrubs, soaps, and other cosmetics and personal hygiene items. To make over-the-counter medications simpler to swallow, they could be added.

2.Microbeads are utilised in fluid visualisation, process troubleshooting, microscopy techniques, fluid flow analysis in biological and health science research. [12]

3.Creams and lotions have a smooth texture and are easily spread because of the ballbearing effect caused by sphericity and uniform particle size. Roundness and smoothness can act as lubricants. Cosmetic goods look more appealing when they contain coloured microsphere.[13]

MICROPLASTIC :

Plastic debris is a contaminant of emerging concern that is often discussed in society, science, the media and policy. It is visible to the naked eye and easily linked to our daily lives, which explains part of the public concern. One size fraction of plastic debris is called microplastics.[14-16] The vast majority of microplastics come from the breakdown of larger plastic waste. The diversity of sources is reflected in the heterogeneity of microplastic properties (shape, size, density and polymer type),[17- 19] transport characteristics, and in vivo and in vitro biological effects and therefore also in its risks. [20]

The presence of contaminants in microplastic adds to this diversity.[21] Together with a high probability of being ingested and absorbed by a large range of species, this diversity in multiple dimensions has contributed to the concern that microplastics may constitute a risk to humans and the environment.[14,22-28] Microplastics have been detected in air, soil, fresh water, drinking water, the oceans, aquatic and terrestrial biota, food products, and human placenta and stools.[29]

REGULATIONS OF COSMETIC MICROBEADS:

The Bureau of Indian Standards (BIS) has categorised microbeads as "unsafe" in the year 2017 and proposed a ban on its usage in cosmetics products, however, initially slated to come into effect in the year 2020, the ban has not been implemented so far.[30] Indicating a lackadaisical approach towards this problem which needs prompt corrective action in the form of regulatory framework. Policy and regulations from a few jurisdictions are briefly discussed below before moving on to suggestions for a microplastics framework for India.

The increase in plastic pollution needs a collaborative effort from "regulators, scientists and the general public about how to deal with this problem that affects ecosystems and human health". [31] Due to inadequate awareness among the masses about the dangers of microplastics, enough actions are not being taken to regulate it at all. Before the situation gets any worse, prudent regulatory actions must be taken, the results of which can be observed quickly. The problem of microplastics in India is dire, with an estimated release of "around 391,879 tones of microplastics in the environment by the end of year 2024", which is only set to increase. The Central Pollution Control Board (CPCB) has also "acknowledged the presence of microplastics in India's water bodies and organisms, primarily entering through sewage, wastewater, and surface runoff, due to inadequate filtration in treatment systems and contributions from plastic infrastructure".[32] In terms of composition, the majority of microplastic pollution in India is attributed to the "textiles market, which is dominated by polyester synthetic fibres and the personal care products, 45% of which contains microbeads".

USA: The Microbead-Free Waters Act of 2015 was passed by the US Congress to handle the issue of "microbeads present in the water supply, prohibiting its manufacturing, packaging, and distribution in rinse-off cosmetics and personal care products along with non-prescription drugs containing plastic microbeads".[33] The law aims to reduce microplastic pollution by eventually phasing-out the use of these microbeads in certain products.

UK: The UK government first pledged to ban plastic microbeads in September 2016, following a US ban in 2015. The Environmental Protection (Microbeads) (England) Regulations of 2017 was enacted by the Parliament in 2018, banning manufacture and sale of plastic microbeads used in cosmetics and personal care products. The aim of the law was to protect the environment and the food supply from further pollution by microbeads and to build consumer confidence in products without these harmful particles.[34]

EU: The EU issued a Commission Regulation (EU) 2023/2055 in the year 2023 to "regulate synthetic polymer microparticles also known as microplastics, as substances on their own and in mixtures". This framework falls under the "Registration, Evaluation, Authorization and Restriction of Chemicals or REACH regulation, which protects human health and the environment from the risks that can be posed by chemicals".[35]

CHINA: The Ministry of Ecology and Environment had implemented a phased ban on production and sale of chemicals containing plastic microbeads from the year 2020 onwards in a bid to prevent plastic pollution. Production of daily chemicals containing plastic microbeads, such as rinse-off cosmetics including facial cleansers, shampoos, bath lotions, soaps, and toothpastes, was prohibited nationwide by December 31, 2020.Sales of these products were banned by December 31, 2022, providing a buffer for inventory depletion and supply chain adjustments. [36]

THAILAND: The import, manufacture, and sale of rinse-off cosmetics containing plastic microbeads has been banned by the Ministry of Public Health since the year 2020 to reduce plastic waste and protect the marine environment .The policy, published in the Royal Gazette on December 24, 2019, aligns with Thailand's push against plastic pollution, including oxo degradable plastics, promoting environmental safeguards for ecosystems and public health.[37]

SOUTH KOREA: The Government has banned production and sale of microbeads contained in rinse-off cosmetics in the year 2017. Additionally, a Special Act on Microplastic Reduction and Control has been proposed with the objective to ban manufacture, import, and sale of products with excessive primary microplastics, including spanning cosmetics, health foods, consumer chemicals, quasi-drugs.[38]

INDIA: The regulatory framework in India must be inclusive and all-encompassing in nature containing a suitable definition of microplastics, so that maximum restrictions can be placed on a variety of pollutants i.e. microbeads, microfibres , microspheres, etc. The provisions must contain labelling requirements on products, standard of acceptable levels of microplastics in water, air, soil and food items, along with additional requirements on industries to reduce microplastics. Greenwashing of products to be strictly restricted and ban on intentional microplastic additives in wash-off cosmetic products. Compliance mechanism for industry, to ensure all the requirements are strictly followed, must also be incorporated so that the regulation does not remain a mere toothless document.

Global Regulations on Plastic Microbeads:[33-38]

Country	Law/Regulation	Key Clauses / Provisions	Year Enforced
USA	Microbead-Free Waters Act of 2015	• Ban on manufacturing microbead cosmetics (2017) • Ban on sale (2018) • Defines microbeads <5mm in rinse-off cosmetics	2015
UK (England)	Environmental Protection (Microbeads) Regulations 2017	• Ban on manufacture (Jan 2018) • Ban on sale (June 2018) • Applies to rinse-off cosmetics	2018
EU	Commission Regulation (EU) 2023/2055	• Ban on placing products with added microplastics on market • Applies to cosmetics, detergents, paints, fertilizers • Definition: synthetic polymer particles<5mm	2023
China	Microbead Ban (Ministry of Ecology & Environment)	• Phased ban on production (2020) • Ban on sale (2021) • Targets rinse-off cosmetics	2021-2022
Thailand	Ministry of Public Health Ban	• Ban on import, manufacture, and sale • Applies to rinse-off cosmetics	2020
South Korea	MFDS Microbead Ban	• Ban on production and sale • Applies to rinse-off cosmetics	2017
India	Bureau of India Standards (BIS)	• Ban on its usage in cosmetics products	Not been implemented so far

Table no 1:- Global Regulations on Plastic Microbeads

WAY FORWARD

While research efforts are ongoing to tackle the issue of microplastics and "scientists are exploring plastic-eating microorganisms, along with plastic alternatives, individuals can advocate for reduced plastic manufacturing and more recycling."[39] Better choices can be made by shifting to eco- friendly alternatives such as bioplastics, which are biobased and biodegradable plastics, eventually reducing the use of fossil-based plastic in a bid to achieve sustainability. Meanwhile, policy and regulatory efforts are an aspect that can be strengthened by further putting restrictions in place and bring about a shift in governance. Management of microplastics through a multidimensional approach including technological innovation, improved waste management practices, shift towards sustainable materials and consumption along with stricter regulation seems to be the best foot forward in tacking the menace of microplastic pollution.

SAFETY :

Uses of microplastics in cosmetics have emerged as a major environmental concern. At the same time the popularity and worldwide prominent sale of these cosmetic products containing microplastics make it difficult to eliminate those products from use. Hence a safer substitute is required to replace these environmentally hazardous constituents. World plastics production has experienced almost constant growth for more than half a century, rising from approximately 1.9 tons in 1950 to approximately 330 million tons in 2013[40]. A recent study had revealed that 5.25 trillion plastic particles weighing some 269,000 tons are floating on the surface of the sea [41]. The option to remove the accumulated plastic load from the ocean is time consuming, costly as well as non viable on some aspects. Moreover, this operation will simultaneously remove the normally abundant microscopic yet significant planktons and other flora and fauna from the food chain which may disrupt the entire marine ecosystem [42]. Thus, the only option is to minimize and if possible cease the entrance of more plastic in the lakes, rivers, seas and ocean. Ocean Conservancy, Plastic Pollution Coalition, 5 Gyres, etc organizations are working with the scientists, politicians and industries to aware the public about the problems related with the use and discharge of microplastic beads [43]. As part of the overarching contribution in providing sustainable solutions, representatives of plastics organizations from around the globe have announced a 'Declaration for Solutions on Marine Litter' at the 5th International Marine Debris Conference in Honolulu. The declaration describes steps that the industries will take and suggest approaches and platforms for global cooperation and future partnerships. As of 2015, 60 world plastic organizations from 34 countries signed the pledge. Different multinational companies like Avon, Beiersdorf, Colgate-Palmolive, Henkel, L' Oréal, Oral B, Procter and Gamble, Unilever, etc had announced that they would phase out the use of microplastics in their cosmetics products. Many other personal care product companies are voluntarily phasing out the use of microplastics in their products. Chinese plastic industry associations are the conglomerate of major plastic producers of the world. They have recently joined the global effort to prevent used plastics from entering the environment. New legislations are thus required to chalk-out strategies in manufacturing sustainable and biodegradable plastics, handling plastic products more responsibly after utilizing them during their life cycle through proper recycling, safe disposal and extended responsibility from the producers' end. A possible alternative to traditional microbeads for cosmetics and personal health care products was suggested to be the biodegradable polyhydroxyalkanoate (PHA) microbeads. [44] Being soluble PHAs minimize the potential threats of microplastic beads in the environment. PHAs can biodegrade in either aerobic or anaerobic environments. The authors have also demonstrated the faster biodegradation rate of PHAs in comparison with other traditional synthetic polymers. Havens et al. [45] have applied for a patent on the method for reducing marine pollution using PHA microbeads. They have claimed that the described method by incorporating PHA microbeads into personal care formulations such as exfoliants, cosmetics and toothpaste would reduce aquatic pollution significantly

CONCLUSION

Sustained-release microbeads constitute a significant improvement in cosmetic formulations because they increase product efficacy, improve user experience, and allow for controlled release of active ingredients. Their widespread usage in industrial, cosmetic, and scientific applications demonstrates their usefulness, but growing worries about human exposure and environmental contamination have led to tighter international restrictions and more scientific focus. Although their methods differ, the comparison of regulatory regimes shows that various areas prioritise safety, transparency and compliance. The need for biodegradable microbeads and more robust, welldefined regulatory frameworks is growing as the cosmetics sector shifts to safer and more ecologically friendly formulations. Sustained-release microbeads will continue to be safe, efficient, and ecologically friendly ingredients in cosmetic products if technological developments are in line with legal standards.

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