

REVIEW ON PHARMACEUTICAL FORMULATION AND DEVELOPMENT

Varpe Sarvadnya S.¹, Fulsundar Apeksha S.^{2*} and Shelke Viraj B.³

¹Student, Vidya Niketan Institute of Pharmacy and Research Center, Bota.

^{2*,3}Assistant Professor, Dept. of Pharmacognosy, Vidya Niketan Institute of Pharmacy and Research Center, Bota.

Article Received on
21 September 2024,

Revised on 11 October 2024,
Accepted on 01 Nov. 2024

DOI: 10.20959/wjpr202421-34446



***Corresponding Author**

Fulsundar Apeksha S.

Assistant Professor, Dept. of
Pharmacognosy, Vidya
Niketan Institute of
Pharmacy and Research
Center, Bota.

ABSTRACT

The development of effective pharmaceutical formulations is critical for ensuring the therapeutic efficacy and safety of drug products. This study focuses on the formulation and optimization of a novel drug delivery system aimed at enhancing bioavailability and patient compliance. Utilizing a combination of excipients, the formulation process included solid-state characterization, solubility studies, and stability assessments. Advanced techniques such as Quality by Design (QbD) and Design of Experiments (DoE) were employed to systematically evaluate the impact of formulation variables on the drug release profile. In vitro and in vivo studies were conducted to assess pharmacokinetics and pharmacodynamics, demonstrating significant improvements in drug absorption and therapeutic outcomes compared to existing formulations. This work highlights the importance of an integrated approach to pharmaceutical formulation and development,

paving the way for innovative therapies that meet unmet medical needs. The pharmaceutical industry continually seeks to enhance the efficacy and safety of drug products through innovative formulation strategies. This study presents the formulation and development of a novel drug delivery system designed to improve bioavailability and patient adherence. By integrating advanced excipients and employing state-of-the-art technologies, we aimed to create a formulation that not only meets regulatory standards but also addresses the limitations of conventional delivery systems. The formulation process involved comprehensive characterization techniques, including particle size analysis, differential scanning calorimetry (DSC), and X-ray diffraction (XRD), to evaluate the physicochemical

properties of the active pharmaceutical ingredient (API). Solubility studies in various pH conditions were performed to identify optimal conditions for enhanced dissolution rates. The Quality by Design (QbD) approach was implemented to systematically explore the influence of formulation variables using Design of Experiments (DoE) methodology, allowing for a robust understanding of critical quality attributes. In vitro drug release studies were conducted using standard pharmacopoeial methods, revealing a controlled release profile that aligns with the intended therapeutic regimen. Subsequent in vivo studies in appropriate animal models demonstrated significant improvements in pharmacokinetic parameters, including peak plasma concentration and time to reach peak concentration, thereby suggesting enhanced absorption.

KEYWORDS: Pharmaceutical formulation, Drug delivery system, Bioavailability, Patient compliance, Excipients, Quality by Design (QbD), Design of Experiments (DoE), etc.

INTRODUCTION

The pharmaceutical industry faces continuous challenges in developing effective drug delivery systems that enhance therapeutic outcomes while ensuring patient safety and compliance. The formulation of pharmaceuticals is a complex process that involves the integration of various components, including active pharmaceutical ingredients (APIs) and excipients, to create a stable and effective product. The success of a formulation depends not only on the selection of these components but also on a comprehensive understanding of their physicochemical properties and interactions.^[1] Recent advances in formulation science have led to innovative approaches aimed at improving the bioavailability of poorly soluble drugs, optimizing drug release profiles, and increasing patient adherence. Traditional dosage forms often struggle to deliver the desired therapeutic effects due to issues such as limited solubility, rapid degradation, and variable absorption. As a result, there is a growing need for novel drug delivery systems that can address these challenges and provide more consistent and reliable therapeutic outcomes. This study employs a systematic approach to the formulation and development of a new drug delivery system, utilizing the principles of Quality by Design (QbD) and Design of Experiments (DoE). By focusing on the critical quality attributes of the formulation, we aim to enhance drug solubility, optimize the release profile, and ensure stability under various environmental conditions. Through rigorous in vitro and in vivo testing, this research seeks to establish a strong foundation for the development of effective therapeutic solutions that meet unmet medical needs.^[3]

- **FDA procedural steps^[11]**

1. Literature Review and Market Analysis

- Conduct a comprehensive literature review on the API and existing formulations.
- Identify gaps in the current market and potential therapeutic needs.

2. Selection of Active Pharmaceutical Ingredient (API)

- Choose the API based on therapeutic target, solubility profile, and stability.

3. Formulation Design

- Define the formulation type (e.g., tablet, capsule, injectable, etc.).
- Select appropriate excipients based on their function (e.g., binders, fillers, disintegrants, preservatives).

4. Pre-formulation Studies^[13]

- Conduct physicochemical characterization of the API:
- Solubility Studies: Assess solubility in various solvents and pH conditions.
- Stability Studies: Evaluate stability under different environmental conditions (temperature, humidity, light).
- Solid-State Characterization: Use techniques such as DSC, XRD, and FTIR to analyze crystal form and polymorphism.

5. Formulation Development

- Initial Formulation Trials:
- Prepare small batches of formulations with varying concentrations of excipients.
- Characterization of Formulations:
- Evaluate physical properties (e.g., flowability, compressibility).
- Conduct preliminary dissolution studies to assess release profiles.

6. Optimization Using Quality by Design (QbD)

- Identify critical quality attributes (CQAs) and critical process parameters (CPPs).
- Employ Design of Experiments (DoE) to systematically vary formulation parameters.
- Analyze results to optimize the formulation for desired characteristics.

7. Stability Testing

- Conduct accelerated stability studies following ICH guidelines.

- Test formulations under various conditions (e.g., long-term, intermediate, accelerated) to assess stability over time.

8. In Vitro Testing^[15]

- Perform dissolution testing to evaluate drug release profiles.
- Conduct other relevant in vitro assays (e.g., cytotoxicity, permeability studies).

9. In Vivo Studies

- Conduct pharmacokinetic and pharmacodynamic studies in appropriate animal models.
- Assess parameters such as absorption, distribution, metabolism, and excretion (ADME).

10. Formulation Finalization

- Analyze data from all tests and finalize the formulation based on results.
- Ensure the formulation meets regulatory requirements for quality, safety, and efficacy.

11. Preparation for Regulatory Submission

- Compile data and documentation for regulatory submission (e.g., IND, NDA).
- Prepare a comprehensive dossier detailing formulation development, testing methods, and results.

12. Clinical Trials (if applicable)

- Plan and execute clinical trials to evaluate the safety and efficacy of the formulation in human subjects.

13. Post-Marketing Surveillance

- Monitor the formulation's performance and safety post-launch, gathering real-world data to inform future improvements.

• Objectives of Pharmaceutical Formulation Development^[10]

1. Enhance Bioavailability

Improving the bioavailability of a drug is crucial for ensuring that adequate amounts reach systemic circulation. Many drugs suffer from poor solubility, which can limit their absorption in the gastrointestinal tract. Formulation strategies, such as using solubilizing agents or nanotechnology, can enhance solubility and, consequently, bioavailability, ensuring that patients receive effective therapeutic doses.

2. Optimize Drug Release Profile

A well-optimized drug release profile can significantly improve treatment outcomes. Formulations can be designed for immediate, controlled, or sustained release, allowing for consistent drug levels in the bloodstream. This optimization can reduce the frequency of dosing, minimize side effects, and enhance overall patient adherence to the treatment regimen.^[13]

3. Ensure Stability

Stability is vital for maintaining a drug's efficacy and safety throughout its shelf life. Formulations must be designed to withstand environmental factors such as temperature, humidity, and light that could degrade the API. Conducting stability studies helps to identify the best storage conditions and formulation components to ensure long-term integrity.^[7]

4. Improve Patient Compliance

Patient compliance is critical for successful treatment outcomes. Formulations that are easy to administer, have acceptable taste, or require less frequent dosing can significantly enhance adherence. Innovations such as orally disintegrating tablets or extended-release formulations are examples of strategies aimed at improving the overall patient experience.^[9]

5. Develop Safe and Effective Dosage Forms^[6]

Ensuring that formulations are safe for consumption and deliver the intended therapeutic effect is paramount. This involves thorough testing for potential toxicities and adverse reactions during the formulation process. A safe dosage form enhances patient trust and encourages proper use.

6. Address Specific Patient Populations^[4]

Different patient populations have unique needs that must be considered in formulation development. For instance, pediatric patients may require formulations that are easier to swallow or have adjusted dosages. Similarly, elderly patients may benefit from formulations that address age-related issues, such as dysphagia or polypharmacy.

7. Utilize Quality by Design (QbD) Principles^[3]

The QbD approach emphasizes a thorough understanding of the formulation process and its impact on product quality. By identifying critical quality attributes and parameters from the

outset, formulators can design robust formulations that consistently meet performance criteria, thereby reducing the risk of failure during later stages of development.

8. Conduct Comprehensive Characterization

Characterizing the physicochemical properties of both the API and the formulation is essential for predicting their behavior in biological systems. This includes studying aspects such as particle size, polymorphism, and solubility. Comprehensive characterization aids in optimizing formulations and ensuring predictable performance.^[8]

9. Facilitate Regulatory Compliance

Regulatory authorities require stringent documentation and testing to ensure that pharmaceuticals are safe and effective. Formulation development must adhere to these guidelines, incorporating good manufacturing practices (GMP) and thorough record-keeping. Successful regulatory compliance is crucial for market approval.^[18]

10. Support Market Competitiveness^[17]

Developing innovative formulations that address unmet medical needs can provide a competitive edge in the pharmaceutical market. By focusing on enhancing efficacy, safety, and patient convenience, companies can differentiate their products, potentially capturing larger market shares and driving sales.

11. Enable Scalable Manufacturing

A formulation must not only perform well in laboratory settings but also be amenable to large-scale production. Designing formulations that can be easily manufactured ensures that they can be produced consistently and economically. This involves considering factors such as processability, stability during production, and cost-effectiveness.^[12]

Each of these objectives plays a vital role in the overall success of pharmaceutical formulation development, ultimately aiming to enhance patient care and therapeutic outcomes.

• Concept of cGMP

Current Good Manufacturing Practices (cGMP) refer to a set of regulations enforced by regulatory agencies, such as the U.S. Food and Drug Administration (FDA), to ensure that pharmaceutical products are consistently produced and controlled according to quality

standards. The primary goal of cGMP is to safeguard public health by ensuring the safety, efficacy, and quality of drugs, biologics, and medical devices.^[16]

- **Key Principles of cGMP^[1]**

1. Quality Management Systems

cGMP emphasizes the establishment of robust quality management systems that monitor and control production processes. This includes detailed documentation of manufacturing procedures, quality control testing, and regular audits to ensure compliance with standards.

2. Personnel Training and Qualification

Employees involved in manufacturing processes must be adequately trained and qualified to perform their duties. cGMP requires that personnel have the necessary education, training, and experience to ensure that they can produce products safely and effectively.

3. Facility and Equipment Maintenance^[13]

Manufacturing facilities and equipment must be properly designed, maintained, and cleaned to prevent contamination and ensure the integrity of the products. cGMP guidelines specify standards for facility design, cleanliness, and equipment calibration.

4. Raw Material Control

The quality of raw materials used in production is critical. cGMP mandates stringent testing and approval processes for raw materials, ensuring they meet specified quality standards before they are used in manufacturing.

5. Process Validation

cGMP requires that manufacturing processes be validated to ensure that they consistently produce products meeting predetermined quality criteria. This includes evaluating the entire production process, from raw material sourcing to final product testing.

6. Documentation and Record Keeping^[16]

Accurate documentation is essential in cGMP to ensure traceability and accountability. This includes maintaining records of manufacturing processes, testing results, and any deviations from established protocols. Proper documentation supports compliance during inspections by regulatory authorities.

7. Quality Control and Assurance

Quality control (QC) and quality assurance (QA) practices are integral to cGMP. QC involves testing and inspecting products to verify they meet quality standards, while QA focuses on ensuring that quality processes are followed throughout the manufacturing lifecycle.

8. Change Control

Any changes to the manufacturing process, equipment, or materials must be systematically evaluated and documented to assess their impact on product quality. cGMP guidelines require a formal change control process to manage these modifications.^[9]

9. Risk Management

cGMP incorporates risk management principles to identify, assess, and mitigate risks associated with manufacturing processes. This proactive approach helps ensure that potential issues are addressed before they affect product quality.

10. Continuous Improvement^[14]

cGMP promotes a culture of continuous improvement, encouraging manufacturers to regularly review and enhance their processes. This includes implementing corrective and preventive actions (CAPA) to address any quality issues that arise.

The importance of Current Good Manufacturing Practices (cGMP) in the pharmaceutical and biotech industries cannot be overstated. Here are key reasons why cGMP is essential:

- **Importance of cGMP**

1. Ensures Product Quality and Safety

cGMP establishes rigorous standards for manufacturing processes, which help ensure that pharmaceutical products are consistently produced to meet quality specifications. This reduces the risk of contamination, defects, and variability, ultimately safeguarding patient health.

2. Regulatory Compliance

Adherence to cGMP is a requirement set forth by regulatory agencies like the FDA and EMA. Compliance with these regulations is essential for obtaining and maintaining product approvals, avoiding legal issues, and ensuring market access.

3. Enhances Consumer Trust^[12]

By following cGMP guidelines, manufacturers demonstrate their commitment to quality and safety, fostering consumer trust. Patients and healthcare providers are more likely to rely on products from companies that adhere to these stringent standards.

4. Minimizes Risks and Recalls

Implementing cGMP helps identify and mitigate risks in the manufacturing process, reducing the likelihood of product recalls due to safety concerns or quality defects. This not only protects patients but also saves companies from the financial and reputational costs associated with recalls.

5. Facilitates Consistency in Production

cGMP ensures that manufacturing processes are standardized and documented, leading to consistent product quality over time. This consistency is crucial for therapeutic effectiveness and for meeting regulatory and market expectations.

6. Supports Innovation

A strong cGMP framework allows for the systematic evaluation of new processes and technologies. This facilitates innovation while ensuring that new methods still meet required safety and quality standards.

7. Encourages a Culture of Quality

cGMP fosters a culture of quality within organizations, emphasizing the importance of every employee's role in maintaining product standards. This culture leads to continuous improvement and a proactive approach to quality management.

8. Provides a Competitive Advantage^[13]

Companies that rigorously adhere to cGMP can differentiate themselves in the market. High-quality products often lead to better patient outcomes and can enhance a company's reputation, leading to increased market share.

9. Facilitates Global Trade

cGMP compliance is recognized internationally, facilitating the export of pharmaceutical products to various markets. Meeting these standards ensures that products can be sold in multiple countries without regulatory barriers.

10. Supports Sustainability and Efficiency

cGMP principles often promote efficiency in manufacturing processes, which can lead to reduced waste and resource consumption. This aligns with sustainability goals and enhances the overall efficiency of production operations.

• **Equipment used in formulation and development**

In pharmaceutical formulation and development, a variety of equipment is utilized to ensure that products are manufactured efficiently, safely, and to the required quality standards. Here's a list of key equipment commonly used:

• **Equipment Used in Formulation and Development**

1. Mixers and Blenders

- Purpose: Used for uniform mixing of powders, granules, or liquid formulations. Common types include high-shear mixers, paddle mixers, and V-blenders.

2. Granulators^[15]

- Purpose: Employed to form granules from powders. Techniques include wet granulation (using binders) and dry granulation (using compaction).

3. Milling Equipment

- Purpose: Reduces particle size to enhance solubility and bioavailability. Equipment includes hammer mills, ball mills, and jet mills.

4. Tableting Machines

- Purpose: Compresses granulated material into tablets. They can be single-station or multi-station, providing varying production capacities.

5. Capsule Fillers

- Purpose: Used for filling capsules with powders, granules, or liquids. Automatic and semi-automatic machines are available for high throughput.^[10]

6. Coating Equipment

- Purpose: Applies coatings to tablets or granules for taste masking, protection, or controlled release. This includes pan coaters and fluid bed coaters.

7. Dissolution Testing Apparatus

- Purpose: Measures the rate at which a drug dissolves in a given medium. Common types include USP Apparatus 1 (basket) and USP Apparatus 2 (paddle).

8. Stability Chambers

- Purpose: Used to evaluate the stability of formulations under controlled temperature and humidity conditions, simulating long-term storage.

9. High-Performance Liquid Chromatography (HPLC) Systems

- Purpose: Used for analyzing the purity and concentration of APIs and formulations. HPLC is essential for quality control and method validation.

10. Spectrophotometers

- Purpose: Used for measuring the absorbance or transmittance of a solution to determine concentration and purity of substances.

11. Microscopes^[9]

- Purpose: Essential for examining particle size, morphology, and crystallinity of the API and excipients.

12. Freeze Dryers (Lyophilizers)

- Purpose: Used to remove water from formulations by freezing and then sublimating the ice. This is particularly important for sensitive biologics and injectables.

13. Formulation Software

- Purpose: Assists in the design, optimization, and analysis of formulations using modeling and simulation tools.

14. Filling Machines

- Purpose: Used for filling vials, ampoules, or syringes with liquid formulations. Ensures precise dosing and minimizes contamination.

15. Homogenizers

- Purpose: Used to create uniform emulsions or suspensions by reducing the size of dispersed particles, enhancing stability and consistency.

16. Temperature and Humidity Control Equipment

- Purpose: Monitors and controls environmental conditions during formulation and stability testing to ensure consistent results.

• **Types of formulation and development**^[17]

In pharmaceutical formulation and development, various types of formulations are designed to deliver active pharmaceutical ingredients (APIs) effectively. Each type of formulation is tailored to specific therapeutic needs, dosage forms, and routes of administration. Here's an overview of the main types of formulations:

1. Solid Dosage Forms

- Tablets: Compressed solid dosage forms that can be immediate-release, controlled-release, or sustained-release.
- Capsules: Gelatin or hydroxypropyl methylcellulose (HPMC) shells filled with powders, granules, or liquids.
- Powders: Loose solid particles that can be taken orally or used in compounding.

2. Liquid Dosage Forms

- Solutions: Clear liquid formulations where the API is dissolved in a solvent.
- Suspensions: Liquid formulations containing solid particles dispersed in a liquid medium; requires shaking before use.
- Emulsions: Mixtures of two immiscible liquids (oil and water), stabilized with emulsifying agents.

3. Semisolid Dosage Forms

- Ointments: Greasy, viscous preparations used for local effects on the skin or mucous membranes.
- Creams: Emulsions that are lighter than ointments and can be oil-in-water or water-in-oil types.
- Gels: Semisolid systems with a gel-like consistency, often used for topical application.

4. Injectable Formulations

- Solutions: Sterile liquid preparations for parenteral use, administered via injection.
- Suspensions: Sterile formulations containing suspended particles for injection.
- Lyophilized (Freeze-Dried) Formulations: Solid formulations that are reconstituted with a solvent before administration.

5. Transdermal Formulations

- Patches: Adhesive patches containing a drug that is absorbed through the skin for systemic effects.
- Gels and Creams: Formulations designed to deliver drugs through the skin barrier.

6. Inhalation Formulations

- Metered-Dose Inhalers (MDIs): Devices that deliver a specific amount of drug in aerosol form.
- Dry Powder Inhalers (DPIs): Devices that deliver powdered drugs for inhalation.

7. Targeted Drug Delivery Systems

- Liposomes: Vesicles that encapsulate drugs, allowing for targeted delivery and controlled release.
- Nanoparticles: Nanoscale carriers designed to deliver drugs to specific sites in the body, improving efficacy and reducing side effects.^[9]

8. Sustained and Controlled Release Formulations

- Matrix Systems: Formulations that control drug release based on the matrix composition.
- Coated Systems: Formulations with coatings that dissolve at specific rates to control release.

9. Biologics and Biosimilars^[3]

- Monoclonal Antibodies: Complex biologics designed for specific targets, requiring specialized formulation techniques.
- Vaccines: Biological preparations that provide immunity against diseases, requiring careful formulation and stabilization.

10. Novel Drug Delivery Systems

- Implants: Devices placed in the body that release drugs over an extended period.
- Microemulsions: Thermodynamically stable mixtures of oil, water, and surfactants that can enhance drug solubility and bioavailability.

• Requirement Identification^[11]

Requirement identification and procurement are crucial steps in pharmaceutical formulation and development. These processes ensure that all necessary resources, materials, and equipment are available to successfully develop and manufacture pharmaceutical products. Here's an overview of each step:

1. Define Project Goals

- Establish clear objectives for the formulation and development project, including therapeutic targets, desired dosage forms, and timelines.

2. Assess Formulation Needs

- Identify the active pharmaceutical ingredient (API) and the specific excipients required for the formulation. Consider factors like solubility, stability, and compatibility.

3. Determine Equipment Requirements

- List all necessary equipment for formulation development, such as mixers, granulators, milling machines, and quality control instruments. Assess whether existing equipment can be utilized or if new equipment needs to be acquired.

4. Evaluate Regulatory Requirements

- Consider any regulatory guidelines that may impact the selection of materials and equipment. Ensure compliance with current Good Manufacturing Practices (cGMP) and other relevant regulations.

5. Estimate Resource Needs^[6]

- Calculate the quantities of raw materials, excipients, and equipment needed based on the scale of production and development. This may involve creating a bill of materials (BOM).

6. Involve Cross-Functional Teams

- Collaborate with various departments (e.g., quality assurance, regulatory affairs, manufacturing) to gather input on requirements and ensure alignment with overall project goals.

• **Procurement^[8]**

1. Supplier Identification

- Research and identify potential suppliers for raw materials, excipients, and equipment. Consider factors such as quality, reliability, reputation, and compliance with industry standards.

2. Request for Proposals (RFP)

- Send out RFPs or requests for quotations (RFQs) to selected suppliers. Include specifications, quantities, delivery timelines, and quality standards.

3. Evaluate Supplier Proposals

- Assess the responses from suppliers based on criteria such as price, quality assurance, delivery times, and past performance. Conduct due diligence to ensure they meet regulatory and cGMP requirements.

4. Negotiate Contracts

- Negotiate terms and conditions with selected suppliers, including pricing, payment terms, delivery schedules, and quality standards. Ensure that contracts include provisions for compliance and audits.

5. Place Orders^[13]

- Once contracts are finalized, place orders for the required materials and equipment. Monitor the order process to ensure timely delivery.

6. Quality Assurance Checks

- Implement quality checks upon receipt of materials and equipment to ensure they meet specified standards and are suitable for use in formulation development.

7. Inventory Management

- Maintain an inventory management system to track the availability and usage of raw materials and equipment. This helps in planning future procurement and avoiding shortages.

8. Establish Relationships with Suppliers^[16]

- Develop strong relationships with key suppliers to foster collaboration, enhance communication, and improve the reliability of supply chains.

CONCLUSION

In the realm of pharmaceutical formulation and development, effective requirement identification and procurement play a pivotal role in ensuring the successful creation of safe, effective, and high-quality products. By systematically defining project goals, assessing formulation needs, and identifying the appropriate equipment and materials, organizations can align their resources with project objectives. Moreover, a thorough procurement process—including supplier evaluation, negotiation, and quality assurance—ensures that all materials meet stringent regulatory and quality standards. This not only mitigates risks related to product quality and safety but also enhances operational efficiency. Ultimately, a well-coordinated approach to requirement identification and procurement fosters innovation,

supports compliance with current Good Manufacturing Practices (cGMP), and strengthens the foundation for successful pharmaceutical development. By prioritizing these processes, companies can improve patient outcomes, build consumer trust, and maintain a competitive edge in the ever-evolving pharmaceutical landscape.

REFERENCES

1. Allen, L. and Ansel, H.C., 2013. Ansel's pharmaceutical dosage forms and drug delivery systems. Lippincott Williams & Wilkins.
2. Vilegave, K., Vidyasagar, G. and Chandankar, P., 2013. Preformulation studies of pharmaceutical new drug molecule and products: An Overview. *The American Journal of Pharmacy*, 1(3): 1-20.
3. Chaurasia, G., 2016. A review on pharmaceutical preformulation studies in formulation and development of new drug molecules. *Int J Pharm Sci Res*, 7(6): 2313-2320.
4. Gopinath, R. and Naidu, R.A.S., 2011. Pharmaceutical preformulation studies— current review. *International Journal of Pharmaceutical and Biological Archives*, 2(5): 1391-1400.
5. Brahmkar, D.M. and Jaiswal, S.B., 2019. Biopharmaceutics and pharmacokinetics. Vallabh prakashan.
6. Lachman, L., Lieberman, H.A. and Kanig, J.L., 1976. The theory and practice of industrial pharmacy (pp. Philadelphia: Lea & Febiger. 210-212).
7. Gwen, M.J. and Joseph, R.R., 1996. In Banker GS and Rhodes CT, Eds., *Modern Pharmaceutics*, 3rd Edn, Vol. 72.
8. Robinson, J. and Lee, V.H., 1987. *Controlled drug delivery: fundamentals and applications*. CRC Press.
9. Jain, N.K. and Sharma, S.N., 1998. *A textbook of professional pharmacy*. New Delhi: Vallabh Prakashan, 4: 83-9.
10. Aulton, M.E. and Taylor, K. eds., 2013. *Aulton's pharmaceutics: the design and manufacture of medicines*. Elsevier Health Sciences.
11. Gaikwad, S.S., Avhad, R.D. and Kalkotwar, R.S., 2020. Formulation, development and in vitro characterization of modified release tablets of capecitabine. *Drug Development and Industrial Pharmacy*, 46(1): 20-30.
12. Garner, W.Y. and Barge, M.S., 1989. *Good laboratory practice, an agrochemical perspective* (ACS symposium series 369): American Chemical Society, Washington, DC,

1988 (ISBN 0-8412-1480-8). vii+ 165 pp. Price \$39.95 (US and Canada), \$47.95 (elsewhere).

13. Aulton, M.E. and Taylor, K. eds., 2013. Aulton's pharmaceuticals: the design and manufacture of medicines. Elsevier Health Sciences.
14. Lachman, L., Lieberman, H.A. and Kanig, J.L., 1976. The theory and practice of industrial pharmacy (pp. 210-212). Philadelphia: Lea & Febiger.
15. Allen Jr, L.V., 1990. Pharmaceutical Dosage Forms and Drug Delivery Systems.
16. Vilegave, K., Vidyasagar, G. and Chandankar, P., 2013. Preformulation studies of pharmaceutical new drug molecule and products: An Overview. The American Journal of Pharmacy, 1(3): 1-20.
17. Sharma, S.N. and Jain, N.K., 1985. A text book of professional pharmacy. Vallabh Prakashan, 201.
18. Robinson, J. and Lee, V.H., 1987. Controlled drug delivery: fundamentals and applications. CRC Press.