International Journal of Research in Pharmacy and Pharmaceutical Sciences
www.pharmacyjournal.in
ISSN: 2455-698X
Received: 14-11-2025, Accepted: 15-12-2025, Published: 30-12-2025
Volume 10, Issue 4, 2025, Page No. 149-159

Formulation development in drug product design: A review

Apeksha P Patil[1*], Deepali K Patil[1], Supekar Madhuri Vijay[2]
[1] Research scholar, Department of Pharmacy, Siddhi's Institute of Pharmacy, Nandgaon, Murbad, Maharashtra, India
[2] Assistant Professor, Department of Quality Assurance, Siddhi's Institute of Pharmacy, Nandgaon, Murbad, Maharashtra, India

Abstract
Formulation development is a critical phase in the creation of products across various industries, including pharmaceuticals, cosmetics, food, and agrochemicals. It involves a systematic and scientific approach to designing formulations that achieve desired properties, performance, and stability. In the pharmaceutical and biotechnology sectors, formulation development plays a key role in determining the success, patentability, and lifecycle of a drug product. As the demand to accelerate drug discovery and clinical trials grows, many companies delegate parts of formulation development to specialized teams or external partners. Large pharmaceutical organizations often establish dedicated departments for the physical characterization of drug substances and formulation studies to streamline processes and reduce development timelines. The concept of pre-formulation, introduced around the 1950s, marked a pivotal stage in industrial pharmaceutical development. It focuses on understanding the physicochemical and biopharmaceutical properties of drug substances to design suitable formulation strategies and delivery methods. Overall, formulation development bridges the gap between drug discovery and commercialization, ensuring product efficacy, safety, and stability.

Keywords: Formulation development, drug discovery and clinical trials grows, ensuring product efficacy, pharmaceutical and biotechnology sector

Introduction

Cosmetics represent a vast category of health and beauty products that serve purposes far beyond simply enhancing physical appearance. While they are often used to modify or highlight one's look, cosmetics also play an important role in skincare and overall body care. Many of these products contribute to personal hygiene, protect the skin, and add a pleasant fragrance to one's presence. Formulated from a wide range of chemical compounds both naturally derived and synthetically produced -cosmetics fulfill diverse functions such as cleansing, safeguarding, and maintaining the body and skin. In contemporary society, they have become an indispensable part of daily routines. Their importance grew significantly after World War Il, when experts in medicine and social sciences recognized that cosmetics not only improve appearance but also influence psychological well-being and skin health. They help preserve skin elasticity, delay wrinkles, prevent infections, and protect against sun damage. The use of cosmetics dates back thousands of years, with ancient civilizations like the Egyptians and Sumerians employing them. In Europe, cosmetic practices continued through the Middle Ages, including face whitening and the application of rouge. However, cultural attitudes toward cosmetics have shifted over time, with certain periods in Western history discouraging their use. Today, the cosmetic industry covers the production and distribution of a wide spectrum of products. This includes makeup items such as foundation and mascara, skincare essentials like moisturizers and cleansers, hair care products including shampoos, conditioners, and dyes, as well as toiletries such as soaps and bubble baths Prominent companies in this sector include Johnson & Johnson, L'Oréal, Gillette, Nivea, and Chanel. India, meanwhile, has made remarkable progress in technological innovation across multiple fields, including medical science. During the COVID-19 pandemic, the country showcased notable advancements and proactive measures to protect public health. To sustain such progress, it is essential that the legal framework continues to evolve in step with the rapidly changing landscape of medical science. Formulation development is a critical and multidisciplinary process within pharmaceutical science that involves converting a pharmacologically active drug molecule into an effective, safe, stable, and acceptable dosage form suitable for patient use. It begins with comprehensive pre-formulation studies, where the physicochemical properties of the active pharmaceutical ingredient (API)—including solubility, pKa, partition coefficient, crystal form, hygroscopicity, compatibility with excipients, and stability under various environmental conditions—are thoroughly evaluated. These characteristics influence the choice of excipients, such as diluents, binders, disintegrants, lubricants, preservatives, solvents, and stabilizers, which collectively enhance the drug's manufacturability and performance. Formulation development aims to overcome biopharmaceutical challenges like poor solubility, low permeability, rapid degradation, or erratic absorption, often through advanced strategies such as solid dispersions, nanoparticles, liposomes, controlled-release systems, and polymer-based delivery systems. It also integrates Quality by Design (QbD) principles, where critical quality attributes (CQAs), critical material attributes (CMAs), and critical process parameters (CPPs) are identified and optimized using scientific tools such as Design of Experiments (DoE)

AIM

Formulation development aims to create safe, effective, and stable pharmaceutical products ensuring optimal therapeutic outcomes, regulatory compliance, and market success.

Objectives

a. Efficacy and Therapeutic Targeting
b. Stability and Shelf Life
c. Safety and Toxicity Prevention
d. Patient Compliance and Acceptability
e. Manufacturability and Scalability
f. Regulatory Compliance
g. Cost-Effectiveness
h. Innovative Drug Delivery Systems
i. Environmental and Sustainability Considerations
j. Customization for Special Populations.

Introduction to Formulation Development

Formulation development is a crucial stage in the process of designing and creating a product, particularly in industries such as pharmaceuticals, cosmetics, food, and agrochemicals. It involves the systematic and scientific approach to developing a formulation that meets specific requirements and objectives. The formulation is essentially the composition of ingredients and their respective quantities to achieve the desired properties, performance, and stability of the final product.

Drug development is a high trend in the pharmaceutical and Biotechnology industries. With growing responsibilities to study drugs candidates from discovery to human Clinical Trials as soon as possible, most pharmaceutical and biotech companies are providing a portion of the development of their potential new drugs. Formulation can determine patentability, lifecycle the success of a pharmaceutical product.

In large pharmaceutical companies, specific departments may exist as the physical Characterization of drug substances and formulation issues. In many cases, various department are work at deferent places so there handling is very much important by single authority so that the development get speed up and the formulation development timeline decreases. the concept of pre- formulation was known to us around 1950 as result of focus industrial pharmaceutical product development. it is stage of the pharmaceutical product development during which the physicochemical properties of the drug of drug substance are characterized and established the psychochemical and biopharmaceutical properties gives appropriate formulation and delivery methods. Formulation development is a critical and multidisciplinary process within pharmaceutical science that involves converting a pharmacologically active drug molecule into an effective, safe, stable, and acceptable dosage form suitable for patient use. It begins with comprehensive pre-formulation studies, where the physicochemical properties of the active pharmaceutical ingredient (API)—including solubility, pKa, partition coefficient, crystal form, hygroscopicity, compatibility with excipients, and stability under various environmental conditions—are thoroughly evaluated. These characteristics influence the choice of excipients, such as diluents, binders, disintegrants, lubricants, preservatives, solvents, and stabilizers, which collectively enhance the drug's manufacturability and performance. Formulation development aims to overcome biopharmaceutical challenges like poor solubility, low permeability, rapid degradation, or erratic absorption, often through advanced strategies such as solid dispersions, nanoparticles, liposomes, controlled-release systems, and polymer-based delivery systems. It also integrates Quality by Design (QbD) principles, where critical quality attributes (CQAs), critical material attributes (CMAs), and critical process parameters (CPPs) are identified and optimized using scientific tools such as Design of Experiments (DoE).

Definition

Pharmaceutical formulation development links the discovery of a new drug substance to the successful development of a commercial drug product. Formulation development scientists must determine the most appropriate route to achieving effective drug delivery based on patient need, and then optimize the formulation's characteristics based on knowledge of the drug product's bioavailability and processing requirements

Concepts of Cgmp

Current Good Manufacturing Practices (cGMP) Concepts: The essence of cGMP lies in fostering product quality, ensuring compliance with regulations, and promoting the growth of pharmaceutical companies. By adhering to cGMP guidelines, companies create a foundation for increased production and heightened safety standards. This commitment to maintaining specified standards not only enhances the company's image but also boosts product sales through improved quality. The application of cGMP reduces problems during formulation development, expediting the overall process. The emphasis on quality and continuous improvement leads to a rise in customer satisfaction, as products meet consistent standards. Overall, cGMP serves as a guiding framework that not only ensures adherence to regulatory requirements but also accelerates the development of high-quality pharmaceutical products, resulting in a positive impact on both company reputation and market success.

Steps in Formulation Development

1. **Identification and characterization of drug:** The identification of characterization of drug is so much important because it very much affect the final product and also the effect of various characters make drug more potent or toxic.

2. **Excipients Compatibility Study:** More the excipient compatible with drug more the chances of drug formulation success and effect of drug also increase.

3. **Formulation development:** The next stage deals with the formulation development so that witch chemicals go with witch and witch excipients is suitable for drugs.

4. **Formulation Optimization:** In this stage formulation like vaccine are produces this type of formulation have lots of studies than normal formulation and large amount of the knowledge needed. Formulation optimization is a systematic process of refining the qualitative and quantitative composition of a drug product (the formulation) and its manufacturing process to achieve desired attributes, such as maximum stability, appropriate release rate, improved bioavailability, and patient acceptability

5. **Formulation Evaluation:** The evaluation studies help to improve the already, made formulation by changing the part of formulation like the vehicle type.

Formulation Evaluation. Formulation evaluation involves rigorously testing the optimized formulation to confirm it meets all necessary quality, performance, and safety standards before moving to large-scale production.

1. Physical Characterization
2. Drug Release Performance
3. Dissolution Testing
4. Impurities and Degradation Products
5. Microbial Testing

Stability Studies: It deals with the stability of the formulation by doing various tests so that the stability of formulation increase it also helps to improves the shelf life of formulation Stability studies are essential to determine how the quality of the drug product varies with time under the influence of various environmental factors, such as temperature, humidity, and light. This data establishes the shelf life and recommended storage conditions.

Types of Studies

1. Accelerated Stability

Purpose: To rapidly predict the chemical and physical stability and degradation profile of the drug product over a shorter time period. The data is used to establish a tentative shelf- life early in the development process.

Conditions: The product is stored under exaggerated/elevated stress conditions, primarily higher temperature and humidity than normal storage

2. Long-Term (Real-Time) Stability

Purpose: To confirm the proposed shelf-life and establish the final storage conditions by observing the drug product's characteristics under the actual expected storage environment. This provides the most definitive evidence of stability.

Conditions: The product is stored under the recommended normal storage conditions for the intended market.

Duration: Must cover the full proposed shelf-life (e.g., 2, 3, or 5 years). Testing is performed at specified intervals (e.g., every 3 months in the first year, every 6 months in the second year, and annually thereafter).

3. Intermediate Stability

Purpose: This study is triggered when significant change occurs during the 6-month accelerated stability study. It serves as a moderate bridge between the accelerated and long-term data.

Conditions: Storage conditions are less stressful than accelerated conditions but more stressful than long-term conditions.

Parameters Monitored

4. Dissolution profile

Definition: Dissolution stability is not a separate study type but a critical quality attribute that is monitored at every time point in all the stability studies (Accelerated, Long-Term, and Intermediate)

- **Basic Techniques**

Standard Operating Procedure (SOP) and Handling Guidelines for Pharmaceutical Equipment

Table 1: Tablet compression machine

SOP :	Handling Guidelines:
❖ Pre-use Inspection and Calibration: - Verify cleanliness, inspect tooling, and calibrate the machine. ❖ Tooling Setup: - Load correct tooling and align according to specifications. ❖ Production Monitoring: - Continuously monitor tablet parameters such as weight and hardness. ❖ Cleaning and Maintenance: - Thoroughly clean and lubricate the machine after each production run.	❖ Calibration and Operation: - Operate with calibrated tools for precision. ❖ Reporting Deviations: - Promptly report any deviations observed during production. ❖ Maintenance Procedures: - Ensure adherence to proper cleaning and maintenance procedures.

Table 2: Capsule filling machine

Sop:	Handling Guidelines:
❖ Pre-use Inspection and Loading: - Perform inspection, load empty capsules into the machine. ❖ Adjustments and Monitoring: - Adjust machine settings, monitor capsule filling for accuracy. ❖ Cleaning and Sanitization: - Thoroughly clean and sanitize the machine after production.	❖ Accuracy in Filling: - Ensure precise capsule filling during operation. ❖ Documentation of Adjustments: - Document adjustments made during the process. ❖ Proper Cleaning Procedures: - Adhere to proper cleaning procedures post-production.

Table 3: Tablet coater

SOP:	Handling Guidelines:
❖ Verification and Loading: - Verify cleanliness, load tablets evenly into the coating drum. ❖ Coating Process: - Set coating parameters, monitor the process for uniformity. ❖ Post-coating Inspections: - Conduct inspections for weight gain and appearance. ❖ Cleaning: - Clean the coater thoroughly after each coating cycle.	❖ Coating Solution Preparation: - Follow guidelines for preparing the coating solution. ❖ Documentation: - Document coating parameters and deviations. ❖ Ventilation during Operation: - Ensure proper ventilation during the coating process.

Table 4: Fluidized Bed Dryer

SOP:	Handling Guidelines:
❖ Pre-use Inspection and Loading: - Inspect, load wet granules into the drying chamber. ❖ Drying Parameters: - Set parameters, monitor the drying process. ❖ Moisture Content Checks: - Perform checks to ensure desired dryness. ❖ Cleaning: - Clean the dryer thoroughly after each drying cycle.	❖ Granule Loading: - Ensure proper loading of wet granules. ❖ Documentation of Drying Parameters: - Document parameters and deviations. ❖ Thorough Cleaning Procedures: - Follow detailed cleaning procedures post-use.

Table 5: Extruder and spheronizer

SOP:	Handling Guidelines:
❖ Pre-use Inspection and Loading: - Inspect, load granulation material into the extruder. ❖ Extrusion and Spheronization: - Set parameters, monitor the extrusion and spheronization process. ❖ In-process Checks: - Conduct checks for pellet size during operation. ❖ Cleaning: - Clean both the extruder and spheronizer thoroughly.	❖ Adherence to Techniques: - Adhere to proper extrusion and spheronization techniques. ❖ Documentation of Steps: - Document deviations, cleaning steps, and adjustments. ❖ Detailed Cleaning Procedures: - Follow detailed cleaning procedures post-use.

Table 6: PH meter

SOP:	Handling Guidelines:
❖ Calibration: - Calibrate using standard buffer solutions. ❖ Rinsing and Immersion: - Rinse electrode with distilled water before and after use, immerse in the sample. ❖ Recording and Maintenance: - Record pH values, conduct regular maintenance.	❖ Proper Rinsing: - Use distilled water for rinsing the electrode. ❖ Storage: - Store the pH meter properly, protecting the electrode. ❖ Reporting Irregularities: - Report any irregularities promptly for corrective action.

Table 7: High-speed mixer

SOP:	Handling Guidelines:
❖ Pre-use Inspection and Loading: - Inspect, load ingredients into the mixing vessel. ❖ Mixing Parameters: - Set parameters, monitor the blending process. ❖ In-process Checks: - Conduct checks for mixture homogeneity. ❖ Cleaning: - Thoroughly clean the mixer.	❖ Operating at Recommended Speeds: - Operate the mixer at recommended speeds. ❖ Documentation: - Document mixing parameters and deviations. ❖ Thorough Cleaning Procedures: - Follow detailed cleaning procedures post-use.

Experimental

1. Preformulation Studies and Preparation of Preformulation Data Sheet

a. Introduction to Preformulation

The idea of pre-formulation comes from a focus on the development of pharmaceuticals in the industry, where the physical and chemical properties of drug substances are examined and understood. Pre-formulation studies refer to lab investigations that help determine the characteristics of the active substance and other ingredients (excipients).

Goals and Objectives

1. **Compatibility and Stability:** Check how well the drug works with common ingredients and ensure the product remains stable over time.

2. **Processing and Storage Insights:** Understand how to process and store the drug to maintain its quality.

The physicochemical characteristics of drug substances are essential considerations in pharmaceutical development. These characteristics influence the formulation, stability, and performance of drugs.

1. **Solubility:** The ability of a drug to dissolve in a particular solvent, typically water. Solubility affects the drug's absorption and bioavailability.

2. **Partition Coefficient:** Indicates the distribution of a drug between an organic solvent and water, providing insights into its affinity for lipids or aqueous environments.

3. **Melting Point:** The temperature at which a solid drug changes from a solid to a liquid state. This information is crucial for formulation and manufacturing processes.

4. **Particle Size and Shape:** The size and shape of drug particles influence their surface area, dissolution rate, and bioavailability.

The physicochemical characteristics of drug substances are essential considerations in pharmaceutical development. These characteristics influence the formulation, stability, and performance of drugs. Here are some key physicochemical characteristics:

1. **Solubility:** The ability of a drug to dissolve in a particular solvent, typically water. Solubility affects the drug's absorption and bioavailability.

2. **Partition Coefficient:** Indicates the distribution of a drug between an organic solvent and water, providing insights into its affinity for lipids or aqueous environments.

3. **Melting Point:** The temperature at which a solid drug changes from a solid to a liquid state. This information is crucial for formulation and manufacturing processes.

4. **Crystallinity:** Describes the arrangement of molecules in a crystal lattice structure. Amorphous and crystalline forms can impact the drug's stability and dissolution rate.

b. Identification and Characterization of Drug Using Ftir, Dsc & Uv

1. Fourier-Transform Infrared Spectroscopy (FTIR)

The detector measures the combined signal intensity as a function of the Moving Mirror's position (time). This raw, time-domain signal, which contains the signature of all absorbed frequencies simultaneously, is called the Interferogram. The maximum intensity occurs at the Zero Path Difference (ZPD) when the two mirrors are equidistant from the beam splitter

- **Purpose:** Identifies functional groups in the drug molecule.
- **Method:** Measures absorption of infrared light by the drug.
- **Results:** Provides a unique fingerprint spectrum for drug identification.

Application

1. Identification of Functional Group.
2. Qualitative Analysis of Drugs.
3. Quantitative Analysis.
4. Detection of Impurities & Degradation Products.
5. Polymer and Excipient Characterization.

2. Differential Scanning Calorimetry (DSC)

Differential Scanning Calorimetry (DSC) is a powerful thermal analysis technique used to measure the heat flow associated with material transitions as a function of temperature or time. It is widely used in pharmaceuticals, polymers, and materials science to study thermal events such as melting, crystallization, glass transitions, and chemical reactions.

- **Purpose:** Determines thermal properties like melting points and heat flow.
- **Method:** Measures heat changes as the drug is heated or cooled.
- **Results:** Reveals thermal transitions, aiding in drug characterization.

Application

1. Determination of Melting Point (Tm).
2. Purity Analysis.
3. Glass Transition Temperature (Tg).
4. Polymorphism Identification.
5. Drug–Excipient Compatibility Studies.

3. Ultraviolet (UV) Spectroscopy

Principle

The principle of UV-Vis spectroscopy is based on the interaction between light energy and matter, specifically the excitation of electrons in molecules.

Absorption of Energy: When a molecule absorbs a photon of UV or visible light, the energy from the photon causes an electron to move from a lower energy level (the ground state) to a higher energy level (the excited state).

The Beer-Lambert Law

The quantitative power of UV-Vis spectroscopy is derived from the Beer-Lambert Law, which states that the absorbance of a solution is directly proportional to the concentration of the absorbing species and the path length of the light through the solution.

- **Purpose:** Assesses the drug's electronic transitions.
- **Method:** Measures absorption of UV light by the drug.

- **Results:** Identifies specific wavelengths absorbed, aiding in drug characterization.

Fig 1: Ultraviolet (UV) Spectroscopy

Application

1. Qualitative Analysis (Identification of Drugs)
2. Detection of Impurities
3. Dissolution and Release Studies
4. Determination of pKa Values
5. Kinetic Studies

c. Physical Properties and Physical Forms

1. Physical Properties

The physical properties with organoleptic properties of the candidate drug molecule and excipients such as color odor taste by just analyzing them various properties of the drugs are shown like when analyzing odor, the constituents present can be determined by checking colour one can determine the impurities.

2. Physical Form

2.1 Crystalline: it has repetitious spacing of constituent's atom or molecules in dimensional array it is more stable than amorphous

2.2 Amorphous: Does not have any fixed internal shape

2.3 Particle size & shape: It is most important characteristics it affects the bulk properties of the substance like test colour performance, efficiency, solubility, stability uniformity and texture the particle size is obtains by surface area formulae

2.4 Flow Properties: It is critical in tablet orientation in case of large doses the powder should have proper flow properties it is found out by the cars index ANGEL OF REPOSE: TAN Θ= H/R Θ= angle of repose, H=height of pile, R=radius of pile. CARRS INDEX= tapped density -poured density /tapped density *100

2.5 Solubility profile: It is based on the lipophilicity and hydrophilicity of the drugs.

pKa + pKb = pKw**,**

3. Formulations of Conventional Drug Delivery Systems

A drug delivery system involves the absorption of a drug across a biological membrane. In contrast, a targeted release system delivers the drug in a specific dosage form. Conventional drug delivery systems encompass various methods for administering drugs into the body. These classical approaches are commonly employed when the objective is rapid drug absorption, necessitating a quick release.

1. Tablets

Definition: Compressed solid dosage forms containing medicaments used for diagnosis or treatment.

Types: Compressed, multiple compressed, repeat action delayed release, sugar-coated, film-coated, buccal, sublingual, troches, dental.

Methods: Made by molding, compressing, wet granulation, and dry granulation.

Machines: Single station, multi-station tablet compressing machines.

Evaluation: Thickness, weightUniformity, Hardness, Friabi lity, DisintegrationTest, Dissolution Test.

2. Capsules

Definition: Pharmaceutical dosage forms where drugs are enclosed in a gelatin shell or other suitable material.

Types: Hard gelatin, soft gelatin, enteric coating, sustained release, rectal, vaginal.

Formulation Methods: Punch methods, volume fill, tamping, wax fill.

Machines: Fully or semi-automatic vibration-assisted tablet filling machines with doster, auger dosing disc.

Evaluation: AppearanceTest, MoistureContent, Capsule Shell'Integrity, Microbial Testing.

3. Oral Liquids

Definition: Homogeneous liquid preparations for oral administration.

Types: Syrups, elixirs, linctuses, mixtures, oral solutions, oral suspensions, emulsions, drops.

Formulation Methods: Mixing, volumetric methods, diaphragm methods, time-flow methods.

Evaluation: Appearance, Viscosity, Stability Studies, pH Measurement, Sedimentaion volume.

4. Ophthalmic Preparations

Definition: Specialized dosage forms designed for instillation onto the external surface of the eye.

Types: Anti-angiogenic, miscellaneous, anaesthetics, etc

Evaluation: Clarity Test, Sterility Test, Viscosity Test, Assay / Drug Content.

5. Parenteral

Definition: Sterile drug products presented as solutions, suspensions, emulsions, or reconstituted lyophilized powder for injection.

Types: Liquid, powder, emulsion, suspension, oily, infusion for injection Considerations: Formulated in a sterile environment with proper cleanliness; high risk of complications if contamination occurs.

Formulation of Novel Drug Delivery System

A cutting-edge approach in pharmaceuticals, the Novel Drug Delivery System utilizes advanced technologies to overcome limitations of traditional methods. It aims to enhance drug efficacy, safety, and precision through controlled release, targeted delivery, and improved bioavailability.

1. **Controlled Drug Delivery System:** A Controlled Drug Delivery System (CDDS) is a sophisticated pharmaceutical formulation designed to release the active pharmaceutical ingredient (API) at a predetermined rate and/or to a specific target location for a defined period of time.

Aims to release a precise therapeutic dose in a specific area over time.

Types: Diffusion-controlled, dissolution-controlled.
Example: Drug-eluting stents.

Application
1. Chronic Disease Management.
2. Pain Management.
3. Cancer Therapy.
4. Hormone Therapy.
5. Transdermal Drug Delivery.

2. **Nano Carriers:** A nanocarrier is a nanoscale vehicle engineered to transport, encapsulate, or conjugate with a therapeutic agent (like a drug, protein, or gene) for its targeted delivery within the body. These sophisticated materials are typically colloidal structures with one or more dimensions in the nanometer range (generally 1 to 1000 nm, though often limited to 200 nm for better systemic circulation)

Deliver drugs to specific targets for site-specific delivery.
Types: Liposomes, phytosomes, nanoparticles, microsphere s.
Example: Liposomal doxorubicin.

Application
1. Targeted Drug Delivery
2. Cancer Treatment
3. Enhancement of Drug Solubility & Bioavailability
4. Vaccine Delivery
5. Gene Delivery

3. **Vesicular Drug Delivery System:** A Vesicular Drug Delivery System (VDDS) involves the encapsulation of an active pharmaceutical ingredient (API) within a vesicular structure, which is a highly organized assembly typically composed of one or more concentric lipid or non-ionic surfactant bilayers enclosing an aqueous core. The term "vesicular" refers to these microscopic, sack-like structures (vesicles), which act as drug carriers.

Enhances bioavailability and reduces toxicity by targeting specific sites.
Method Pioneered by: Bingham in 1965.
Example: Lipid-based vesicles.

Application
1. Ocular Drug Delivery.
2. Pulmonary Drug Delivery.
3. Anti-inflammatory Drug Delivery.
4. Cosmetics & Dermatology.
5. Brain Targeting.

4. **Transdermal Drug Delivery System and Implants:** A Transdermal Drug Delivery System (TDDS) is a non-invasive dosage form designed to deliver a therapeutically effective amount of drug across the intact skin and into the systemic circulation (bloodstream) for a sustained period. The most common form of TDDS is the transdermal patch.

Delivers a therapeutic dose across the skin. Example: Nicotine patches.
Implants Example: Subdermal contraceptive implants.

Application
1. Systemic Delivery of Drugs
2. Hormone Therapy
3. Hypertension Management
4. Motion Sickness
5. Pain Management

Evaluation
The assessment of medications is an ongoing process that commences prior to dispensing and extends throughout and after the dispensing period. This continual review plays a vital role in identifying and addressing any issues related to the use of drugs.

a. Solid Dosage Form
- **Dissolution Test:** The dissolution test is a crucial evaluation for solid dosage forms, providing insights into how a drug is released from its formulation. This test is essential for understanding the drug's efficacy and bioavailability. It is a fundamental aspect of drug development, helping ensure pharmaceutical quality, regulatory compliance, and optimal formulation.

Dissolution Medium: Select a dissolution medium that mimics physiological conditions.
Temperature Control: Maintain the dissolution medium at a specified temperature (typically 37°C).
Sample Withdrawal: Withdraw samples at predefined time intervals.

Analysis: Analyze the drug concentration in the withdrawn samples using suitable methods such as UV-Visible spectroscopy or HPLC.
1. Immediate-Release Tablets (Uncoated): 30 minutes
2. Hard Gelatin Capsules | 20 minutes | Typically in water or a specified medium at 37^0C
3. Plain Coated Tablets | 60 minutes | Tested in water or specified medium at 37^0C

Fig 2: Dissolution Apparatus

Disintegration Test: The disintegration test assesses the time it takes for a tablet or capsule to break down into smaller particles. It plays a key role in ensuring that the medication is effectively broken down, allowing for optimal absorption in the body.

Disintegration Medium: Select a disintegration medium according to pharmacopiea specifications.

Temperature Control: Maintain the disintegration medium at a specified temperature.
Sample Observation: Observe the dosage form for disintegration visually or using appropriate instrumentation.
Record Time: Record the time taken for the dosage form to disintegrate completely.

Fig 3: Disintegration Test

Friability and Hardness Test

1. **Friability Test:** Tumble tablets in a friabilator. Weigh the tablets before and after the test. Calculate the percentage weight loss.

Principle
Tablets are subjected to tumbling and dropping inside a rotating drum. Loss of weight indicates how fragile or robust the tablets are.

Construction (Parts)

1. Rotating Drum
- Transparent cylindrical drum (30–40 cm diameter)
- Contains one plastic/curved baffle to lift and drop tablets.

2. Motor
- Rotates drum at 25 ± 1 rpm.

3. Timer
- Set for 100 revolutions (approx. 4 minutes).

4. Dust Collector (optional)

Procedure
- Select 10 tablets and weigh (W_1).
- Place tablets in drum.
- Rotate for 100 revolutions at 25 rpm.
- Remove tablets, dedust, and weigh again (W_2).

Fig 4: Friability Apparatus

Applications
- Evaluate mechanical strength of tablets.
- Optimize granulation and compression force.
- Quality control in manufacturing.
- Acceptance Criterion
- Stability Testing
- Process Optimization

2. **Hardness Test:** Place the tablet between the platens of a hardness tester. Apply force until the tablet fractures. Record the applied force (hardness).

Fig 5: Hardness Apparatus

Principle
A tablet is placed between two anvils, and a force is applied until the tablet breaks. The force (in kg/cm² or Newtons) is recorded as the hardness.

Procedure
- Place tablet between the anvils.
- Increase pressure gradually.
- Note the force at which the tablet breaks.

Applications
- Ensure tablets are strong enough to handle packaging and transport.
- Maintain proper disintegration and dissolution.
- Adjust compression settings during formulation development.

Variation and Content Uniformity Test

1. Weight Variation Test
Weigh a sample of individual tablets from the batch.
Compare individual tablet weights to establish a weight range. Ensure weights fall within the acceptable range.

2. Content Uniformity Test
Content Uniformity (CU) Test ensures that each individual tablet or capsule contains the correct amount of drug. It is performed by assaying 10 dosage units individually and calculating the percent drug content.

Acceptance Criteria
- Each unit should contain 85–115% of the label claim, with RSD ≤ 6%.
- If limits are not met, assay 20 more units (total 30)
- No unit should be outside 75–125%, and the average should be within 85–115%.

This test is required for low-dose, potent, or narrow therapeutic index drugs to ensure dose accuracy, safety, and therapeutic consistency.

a. Liquid Dosage Form

1. **Leakage Test:** Procedure: Fill 10 containers with the liquid dosage form, invert them for 24 hours, and check for leakage. Additionally, inspect for any leakage around rubber closures.

- **Dye Bath Test:** Procedure: Submerge the container, either empty or filled with the product, in a dye bath. Apply pressure and vacuum, then after the specified time, check for any dye marks, indicating potential leaks.

2. Clarity Test

Procedure: Dilute the liquid preparation and inspect for cloudiness. Use clean water as a control. Observe transparent or white particles against a black background and black or dark particles against a white background.

3. Sterility Test

- **Direct Transfer Method:** Transfer 10% of the sample into 9 ml tubes containing culture medium. Incubate for 14 days and observe for microbial growth.

- **Membrane Filtration Method:**

Pass the sample through a 0.22 to 0.4 µm pore size filter.
Cut the filter into halves, place in culture medium, and incubate for 7 days.
Incubate the other half at a different temperature for an additional 7 days.

4. Pyrogen Testing:

- **Sham Test**

Observe three rabbits for 1 to 3 days.
Check body temperature 30 to 40 minutes prior to the test.
Administer the sample solution (pre-warmed to 37 ºC) and monitor temperature.
A rise of 0.5 ºC within 1 hour passes the test; otherwise, use 5 additional rabbits.

- **LAL Test (Limulus Amoebocyte Lysate)**

Use 0.1 ml of the sample with LAL reagent.
Incubate for 1 hour at 37 ºC and analyze for clot formation due to the properties horseshoe crab gel.
These evaluation tests ensure the quality, safety, and efficacy of liquid dosage forms, covering aspects such as container integrity, clarity, sterility, and absence of pyrogens.

b. Semisolid Dosage Form

- **Viscosity Test**

The viscosity test evaluates the flow characteristics of a semi-solid formulation, indicating its consistency and applicability. Conducted with a calibrated viscometer, the procedure involves placing a weighed sample in the viscometer container, setting it to a specific speed, and recording viscosity after stabilization.

- **pH Test**

The pH test assesses the acidity or alkalinity of a semi-solid dosage form, crucial for skin compatibility and overall stability. Using a calibrated pH meter, the procedure includes immersing the pH electrode into the formulation, recording the stabilized pH reading, ensuring the product falls within an acceptable range for optimal performance and safety.

5. Labelling and Packing:

Pharmaceutical packaging involves the processes and materials used for preparing and distributing pharmaceutical products from production to end consumers.

Types of Packaging

- **Primary Packaging:** Directly contacts drugs (e.g., cap, cap liner, label).
- **Secondary Packaging:** External to primary, adds physical protection (e.g., leaflets, cartons).
- **Tertiary Packaging:** Provides protection during handling, storage, and transportation (e.g., cardboard boxes, wood pallets).
- **Containers:** Ampoules, vials, strip packages, blister packaging, syringes, etc.
- **Container Types:** Airtight, light-resistant, multi-dose, single-dose, well-closed, aerosol

Packaging Materials

- **Glass:** Common for superior protection (e.g., borosilicate, soda lime).
- **Plastic:** Offers versatility with various polymers (e.g., p olyethylene, polystyrene).
- **Metals:** Versatile materials like aluminum and tin for tablets, blisters, tubes, can
- **Paper and Paperboard:** Traditional materials for boxes, sachets, etc.

Evaluation Tests for Packaging Materials

- Identification: Checks appearance of packaging material and its combination with product content.
- Physical Tests: Assess appearance, light absorption, pH, non-volatile matter, residue, heavy metals, etc.
- Chemical Tests: Include pH, chloride, sulfates, alkalinity, compatibility tests for containers.

Labeling of Different Dosage Forms

Labeling involves all written, printed, or graphic information on a drug's immediate container or package. It provides essential details such as product name, drug facts, active ingredients, purpose, warnings, directions, allergic reactions, expiry date, and manufacturing date.

Fig 6: Labeling of Different Dosage Forms

Hands on Activity

Identification and characterization of drug by melting point, solubility, UV spectroscopy:

a. Melting point: The temperature at which a solid melt and becomes a liquid is the melting point. Since this requires that the intermolecular forces that hold the solid together have to be overcome, the temperature. Hence, different compounds tend to have different melting points. Pure samples usually have sharp melting points, for example 149.5-150 C or 189-190 C; impure samples of the same compounds melt at lower temperatures and over a wider range, for example 145-148 Cor 186-189 C.

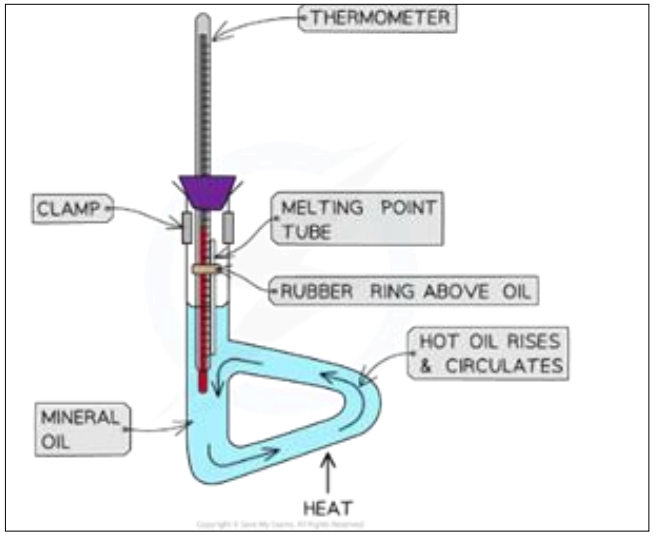

Fig 7: Melting Apparatus

b. Solubility study: The drug-solvent systems through which the drug is delivered helps in the pre-formulation solubility studies. For example, solubility of an orally administered drug in media with isotonic chloride ion concentration and acidic pH can be determined.

Table 8: BCS Classification

Sr. No	BCS Class	Solubility	Permeability	IVIV correlation expectation
1	Class-I	High	High	ivivc if the dissolution is slower than the gastric emptying rate otherwise limited or no correlation
2	Class-II	Low	High	ivivc is expected if the in vitro dissolution rate is similar to the in vivo dissolution rate, unless the dose is very high
3	Class-III	High	Low	permeability is rate determining, limited or no ivivc with dissolution rate
4	Class-IV	Low	Low	Limited or no IVIVC expected

c. UV spectroscopy: Solubility property is essential for developing solutions to be injected either intravenously or intramuscularly. Solubility is a function of chemical structure; salts of acids or bases are the drugs that can achieve the desired degree of water solubility. The analytical method used for measuring solubility can vary according to the drug moiety. If unsaturated conjugation is present in the drug structure, it absorbs visible or UV light, and can be analysed by spectrophotometry. UV–Visible spectroscopy is an analytical technique that measures the absorption of ultraviolet (200–400 nm) and visible light (400–800 nm) by molecules.

Molecules containing chromophores absorb light and undergo electronic transitions such as $\pi \rightarrow \pi^*$, $n \rightarrow \pi^*$, $n \rightarrow \sigma^*$, etc.

Principle

When UV or visible light passes through a sample:
A portion of light is absorbed. Remaining light is transmitted to the detector. Absorbance (A) is directly proportional to: Concentration (c) Path length (l)
where,
A=absorbance
ε=molar absorptivity
c = concentration
l = path length (usually 1 cm)
This is the basis for quantitative analysis.

Instrumentation of UV–Visible Spectrophotometer.

1. Light Sources.
- Deuterium lamp
- Tungsten Halogen Lamp

2. Monochromator.
- Prism Monochromator
- Granting Monochromator

3. Sample Holder / Cuvettes.

4. Detector.
- Photocell
- Photodiode
- Photomultiplier tube
- Silicon diode

5. Readout System

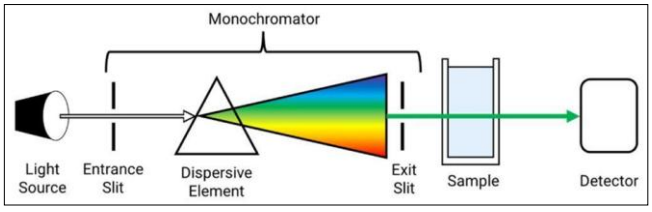

Fig 8: UV Spectroscopy

Applications of UV–Visible Spectroscopy
1. Qualitative Analysis
2. Quantitative Analysis
3. Detection of Impurities
4. Dissolution Testing
5. Kinetic Studies
6. Determination of pKa

Implementation of Domain

The implementation of formulation development begins with pre-formulation activities, including defining project goals and objectives, conducting a literature review, and developing a project plan. Next, the formulation development phase involves API characterization, excipient selection, formulation design, prototype development, and formulation optimization. Analytical method development

and validation are also crucial during this phase. Stability testing is then conducted to evaluate the formulation's stability under various conditions. After successful stability testing, the formulation is scaled up, and a manufacturing process is developed and validated. Regulatory documents are prepared and submitted to regulatory agencies. Post-approval activities include monitoring product quality, implementing changes and updates, and conducting post-marketing surveillance. Throughout the entire process, Quality by Design (QbD) principles and Design of Experiments (DoE) techniques are applied to ensure the development of a robust and efficacious formulation.;

Conclusion

This review study highlights the importance of adhering to Current Good Manufacturing Practice (cGMP) guidelines in the development of pharmaceutical formulations. It emphasizes that the preparation of all formulations must be conducted in accordance with these standards to ensure product quality, safety, and efficacy. To further promote safety, efficiency, and patient compliance, the study stresses the necessity of conducting thorough preformulation studies during the formulation development process. These studies are critical as they provide valuable information on various aspects of the formulation, including stability, solubility, and compatibility of ingredients. In particular, preformulation studies support the development of appropriate In-Process Quality Control (IPQC) tests, which are essential for monitoring the quality of the formulation throughout production. The review also underscores the significance of proper packaging and labelling in maintaining drug stability and prolonging shelf 1

References

1. Hajare A. Industrial pharmacy I. Pune: Nirali Prakashan; p. 1.1–1.40.
2. Patel P. Preformulation studies: An integral part of formulation design. IntechOpen. 2019 Jun 9. Submitted Jul 16, 2018; Reviewed Dec 3, 2018. DOI:10.5772/intechopen.82868.
3. United States Pharmacopeia. Disintegration test and dissolution test. USP–NF. Stage 4 harmonization; Official May 1, 2020, 701–1 to 703–25.
4. Indian Pharmacopeia Commission. Pyrogen testing. Indian Pharmacopeia, Appendix I. British Pharmacopeia 2007. In: Remington: The science and practice of pharmacy, 2007, 1.
5. Mundada AS, Meshram DR, Mishra M, Bhalekar MR, Avari JG. Formulation and evaluation of bitterless rapidly disintegrating tablet of famotidine using ion exchange resins. Int J Pharm Excipients,2008:7:23–5.
6. Shirsand SB, Suresh S, Para MS, Swamy PV, Kumar DN. Plantago ovata mucilage in the design of fast disintegrating tablets. Indian J Pharm Sci,2009:71:41–5.
7. Loyd VA, Nicholas GP, Howard CA. Ansel's pharmaceutical dosage forms and drug delivery systems. 8th ed. London: Lippincott Williams & Wilkins, 2005.
8. Aulton ME, editor. Pharmaceutics: The science of dosage form design. 2nd ed. Sydney: Churchill Livingstone, 2002.
9. McMillan A, Young H. The treatment of pharyngeal gonorrhea with a single oral dose of cefixime. Int J STD AIDS,2007:18:253–4.
10. Preformulation studies in a drug development program for tablet formulations. J Pharm Sci. Jan,1985:74(1):16–20.
11. Jones TM. Preformulation studies. In: Pharmaceutical formulation: The science and technology of dosage forms, 2018, 1–41.
12. Bharate SS, Vishwakarma RA. Impact of pre-formulation on drug development. Expert Opin Drug Deliv,2013:10:1239–1257. Published online Mar 27, 2013.
13. Devangen HK. An important approach for novel drug delivery system. J Biomater Sci Polym Ed. 2020. DOI:10.1080/09205063.2020.1825304.
14. Cooper and Gunn. Dispensing for pharmaceutical students. 12th ed. London, 2008.
15. Vranić E. Sonophoresis—mechanisms and application. Bosn J Basic Med Sci,2004:4(2):25–32.
16. Bharate SS, Vishwakarma RA. Impact of pre-formulation on drug development. Expert Opin Drug Deliv,2013:10:1239–1257. Published online Mar 27, 2013.