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Review Article

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Dosage form Design: From concept to Compliance - Navigating Regulatory Standards and Patient needs

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Abstract

Dosage form design is a pivotal aspect of pharmaceutical formulation, encompassing the meticulous crafting of pharmaceutical products to ensure efficacy, safety, and patient acceptance. This paper comprehensively explores dosage form design, delving into its definition, significance, and multifaceted roles in pharmaceutical development. From therapeutic considerations and biopharmaceutical factors to patient compliance and convenience, every facet of dosage form design is meticulously examined. Therapeutic considerations underscore the need for controlled drug release profiles, optimal bioavailability, precise dosing, and route-dependent administration to maximize therapeutic outcomes and minimize adverse effects. Biopharmaceutical factors, such as drug solubility, permeability, dissolution rate, and absorption site, shape dosage form design strategies to enhance drug performance and bioavailability. Moreover, patient compliance and convenience are pivotal in ensuring adherence to treatment regimens, with considerations ranging from dosage frequency and taste to packaging and patient education. Furthermore, this paper elucidates the intricate interplay between dosage form design and regulatory compliance, emphasizing the importance of adhering to rigorous standards to uphold patient safety and efficacy. By synthesizing theoretical insights with practical applications, this review elucidates the comprehensive approach required for effective dosage form design, encompassing scientific rigor, regulatory adherence, and patient-centric considerations.

Conclusion

This paper underscores the paramount importance of dosage form design in pharmaceutical development, serving as a cornerstone for optimizing therapeutic outcomes, ensuring patient adherence, and advancing public health initiatives. Through a nuanced understanding of dosage form design principles and their implementation, pharmaceutical scientists and healthcare professionals can forge a path toward innovative drug delivery solutions that transcend conventional boundaries and empower patients to achieve optimal health outcomes.

Keywords: Dosage Form Design, Pharmaceutical Formulation, Drug Delivery, Therapeutic Considerations, Patient Compliance

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1. Introduction

1.1 Definition of dosage forms

The physical presentation of a pharmaceutical product containing a specified dose of an active pharmaceutical ingredient (API) combined with other excipients or additives is called dosage form. These dosage forms are intended to administer the medicine to the patient safely, effectively, and conveniently. Examples are capsules, Syrups, Creams, Ointment, Suspension, Emulsion, etc. (1,2)

1.2 Importance of dosage form design-

Dosage form design is critical in pharmaceutical formulations because it directly impacts drug efficacy, patient compliance, and overall therapeutic outcomes. The chosen dosage form affects how the drug is administered, absorbed, and dispersed inside the body, influencing its pharmacokinetics and pharmacodynamics. Proper dosage form design is critical to ensure the drug is safe, stable, and capable of providing the desired therapeutic effect. The route of administration is a major concern in dosage form design. The drug's bioavailability and beginning of its effect can be affected by different routes of administration, such as oral, parenteral (injection), transdermal (patch), or inhalation. Oral drug delivery, for example, may result in first-pass metabolism in the liver, whereas intravenous administration avoids this process, resulting in differing drug quantities and effects. Furthermore, the dosage form must be developed to offer accurate dosing and a constant release profile. (3-5)

The formulation should consider aspects such as drug solubility, stability, and release rate to keep medication levels within the therapeutic range. The dosage form must be developed to offer accurate dosing and a constant release profile. The formulation should consider aspects such as drug solubility, stability, and release rate to keep medication levels within the therapeutic range. The dosage form's design might impact the overall patient experience. Patient acceptability and satisfaction with medication can be influenced by flavour, texture, size, and ease of swallowing. (6-8)

1.3 Role in pharmaceutical development-

The success of a therapeutic product depends on the varied and essential role that dosage form design plays in pharmaceutical development. It entails carefully selecting the ideal dosage form, formulation excipients, and manufacturing methods to achieve the best possible medication administration, bioavailability, stability, and patient acceptance. The dosage form design can strongly impact the drug's performance, safety, and efficacy, as well as patient compliance and overall treatment outcomes. (9-11)

2. Principles of Dosage Form Design (12-18)

Therapeutic considerations- To maintain the safety, effectiveness, and patient compliance of pharmaceutical products, therapeutic considerations in dosage form design involve various elements that must be considered. Creating a drug product in a certain form, such as tablets, capsules, injections, creams, etc., to deliver the medication to the patient most effectively is known as dosage form design. The following are some essential therapeutic factors in dosage form design:

- **Drug Release Profile:** To have the desired therapeutic impact, the drug's release from the dosage form must be controlled and consistent. The pharmacokinetics and therapeutic needs of the medicine can be accommodated by adjusting the drug release rate.
- **Bioavailability:** The dosage form needs to guarantee that the right amount of the medication is absorbed and readily available where needed. Elements like solubility, dissolving rate, and permeability can influence the bioavailability of a medicine.
- **Dosage Accuracy:** The dosage form must allow for precise dosing so that patients always receive the correct medication dosage.
- **Route of Administration:** The absorption and distribution of medications can be affected by the method of administration (oral, parenteral, topical, etc.). The best route should be selected based on the drug's properties and the patient's state.
- **Safety and Tolerance:** The dosage form should be created to reduce side effects and improve patient security while taking medications.
- **Special Population Considerations:** To accommodate their particular needs and restrictions, dosage forms for some groups, such as children or elderly patients, may need to be modified.
- **Manufacturing considerations:** The dosage form should be commercially producible, with quality and consistency upheld throughout.
- **Drug-Drug Interactions:** When designing a dosage form, it is important to consider drug interactions, particularly when a patient takes several medications simultaneously.
- **Packaging and Storage:** The dosage form should be shielded from external elements like light, moisture, and temperature that could impact the stability of the medication.
- **Regulatory Compliance:** To guarantee the safety and efficacy of the product, dosage form design must abide by regulatory standards and specifications established by health authorities.

Biopharmaceutical factors- Because they directly impact the drug's absorption, distribution, metabolism, and excretion (ADME) in the body, biopharmaceutical variables are very important for designing dosage forms. Pharmaceutical scientists can customize the dosage form to improve drug performance by being aware of these parameters. Here are some important biopharmaceutical elements to consider when designing dosage forms: (19-25)

- **Drug Solubility:** A drug's solubility, both in its dosage form and at the site of absorption, impacts how easily and quickly it dissolves. Drugs with poor solubility may need unique formulation methods to improve their solubility and bioavailability.
- **Drug Permeability:** A drug's ability to pass through biological membranes and enter the bloodstream impacts how well it is absorbed. Specific formulation techniques may be necessary to increase absorption for medications with low permeability.
- **Drug Dissolution Rate:** A drug's absorption depends on how quickly it dissolves from the dosage form. To sustain therapeutic levels in the body, dosage forms must ensure the medication dissolves at the best possible rate.
- **First-Pass Metabolism:** The degree of first-pass metabolism in the liver should be considered for medications taken orally, as this can lower the drug's bioavailability.
- **pH Sensitivity:** Some medications may have pH-dependent solubility or stability. To maximize absorption, dosage forms can be created to release the medication in particular parts of the gastrointestinal tract.
- **Food Effects:** Food in the stomach might affect how well a medicine is absorbed. Creating dosage forms that reduce how much food affects a drug's bioavailability might be necessary.

Site of Absorption: Choosing the right dose form and delivery strategy depends on whether the medicine is absorbed mostly through the gastrointestinal tract or other routes (such as the skin for transdermal delivery).

- **Patient variability:** Variability in the patient's characteristics, including age, genetics, and illness states, might affect drug absorption and metabolism. To account for these variances, dosage forms ought to be created.

Patient compliance and convenience- Patient compliance and convenience are crucial considerations in dosage form design since they directly impact a patient's willingness to follow the advised course of treatment. Patients are more likely to take their medication as directed when they find the dosage form simple to use and manage, improving treatment effectiveness. In designing dose forms, keep the following factors in mind for patient compliance and convenience: (26-31)

- **Route of Administration:** The best route of administration can impact patient adherence. Compared to injections or complicated delivery systems, oral dose forms (such as tablets, capsules, and liquids) are typically more convenient and well-tolerated by patients.
- **Dosage Frequency:** Reducing the number of daily doses can help patients adhere to their medications. As it decreases the likelihood of missing doses, once-daily dosing is typically preferable over multiple daily doses.
- **Dosage Regimen Flexibility:** By providing dosage forms with various strengths, doctors can modify the dose schedule to meet the individual demands of each patient, making it more convenient for them.
- **Taste and odour:** Regarding oral dose forms, taste and odour significantly influence patients' acceptance. Particularly in juvenile and geriatric groups, medications that have disagreeable tastes or overpowering scents are more likely to be rejected.
- **Size and Shape:** The dimensions of pills or capsules can influence how easily a patient can take them. Smaller medication amounts or other dosage forms (such as chewable pills or oral disintegrating tablets) may be an option for patients with trouble swallowing.
- **Packaging:** Patient compliance may be affected by convenient and user-friendly packaging. Blister packs or unit-dose packaging can aid patients in remembering when they should take their medications.
- **Combination products:** Consolidating several medications into a single dosage form can help patients take fewer pills overall and streamline their medication schedule.
- **Instructions for Use:** If necessary, patients can comprehend how to take the drug properly by reading clear and concise instructions and drawings.
- **Minimizing Side Effects:** Dosage forms intended to reduce side effects can increase patient comfort and treatment plan adherence.
- **Patient Education:** In addition to dose form design, patient education regarding the value of adherence and the potential advantages of the treatment can positively impact compliance.
- **Accessibility and Portability:** Patients benefit more from portable and easy-to-carry dose forms, particularly those with hectic schedules or regular travelers.
- **Special Populations:** Dosage forms should be created with certain patient populations in mind, such as children or the elderly, considering their needs and restrictions.

Stability and shelf-life- To guarantee that pharmaceutical goods keep their quality, efficacy, and safety beyond the designated storage term, stability, and shelf life are crucial in dosage form design. The capacity of a drug product to maintain its desirable properties, such as potency, purity, and physical qualities, over its shelf life is referred to as stability. Several important stabilities and shelf-life factors in dosage form formulation are listed below: (32-39)

- **Drug degradation:** Dosage forms should be created to reduce drug degradation over time. Temperature, humidity, light exposure, oxygen, and other variables can cause the medicine to degrade chemically or physically, reducing its effectiveness or raising safety questions.
- **Container closure system:** Choosing the right container and closure is essential for limiting the entry of contaminants such as oxygen, moisture, and other substances that could compromise the stability of the medicine. To protect the dosage form, containers must be properly sealed and inert.
- **Excipient Compatibility:** The excipients used in the dosage form must be compatible with the medication and must not interfere with the active component or contribute to its deterioration.
- **pH Considerations:** The pH needs to be carefully regulated for liquid dosage forms to avoid chemical instability or drug deterioration.
- **Oxidation:** Some medications are vulnerable to oxidation, which can result in deterioration. Antioxidants or appropriate packaging could be required to prevent oxidation.
- **Temperature and Humidity:** Stability studies should be used to determine the optimal storage conditions for the dosage form. The drug's sensitivity to changes in temperature and humidity must be considered.
- **Photostability:** To make sure the medication is stable when exposed to light, photostability testing is required for medicines that are exposed to light, such as oral liquids or topical preparations.

- **Accelerated Stability Studies:** These studies entail exposing the dosage form to greater temperatures and humidity to evaluate and forecast the stability of the dosage form over a shorter period and at room temperature throughout the anticipated shelf life.
- **Real-Time Stability Studies:** To conduct these studies, the dosage form must be kept by approved storage guidelines for the duration of its shelf life.
- **Batch-to-Batch consistency:** To maintain consistent product quality, dosage form design should provide batch-to-batch uniformity instability.
- **Shelf-Life Determination:** Stability data from accelerated and real-time experiments are used to determine the drug product's expiration date or shelf life.
- **Regulatory requirements:** Regulatory bodies need stability data to support a drug product's claimed shelf life. Receiving marketing permissions depends on meeting these standards.
- **Packaging compatibility:** To avoid any concerns with leaching or degradation, the dosage form must be compatible with the packing material.

3. Preformulation Studies (40-46)

Drug characterization and physicochemical properties- Before a drug candidate is turned into a dosage form, it must first thoroughly study its physicochemical and biological properties as part of formulation research. These investigations carried out in the early stages of drug development are crucial for creating an acceptable and efficient dosage form. Drug characterization aims to understand the drug's behavior, stability, and compatibility with excipients, which enables formulation scientists to create a dosage form that maximizes drug distribution and bioavailability. Several important elements of drug characterization in pre-formulation studies are listed below:

- Solubility- To choose the best solvent for formulation development, it is essential to ascertain the drug's solubility in a variety of solvents. Special methods may be necessary to improve the solubility and bioavailability of poorly soluble medicines.
- Particle Size and Morphology: Assessing the drug's particle size and shape is critical because it can affect the dissolving rate, stability, and flow characteristics throughout the formulation process.
- Polymorphism: Since different crystal forms might have varied physicochemical properties, such as solubility and stability, it is crucial to recognize and characterize the various polymorphic forms of the medication.
- Melting Point: Knowing a drug's melting point aids formulation development in choosing the best processing techniques.
- Chemical Stability: Determining the drug's chemical stability under various environmental circumstances (such as temperature, humidity, and light) enables the selection of the best packaging and the identification of potential degradation pathways.
- pH-dependent Solubility: Some medications have pH-dependent solubility, which is essential for creating dosage forms that maximize drug absorption.
- Partition coefficient (Log P): Determine the drug's lipophilicity (Log P) to forecast how it will behave when partitioned in biological membranes, which will affect how well it is absorbed and distributed.
- Dissolution Rate: Analyzing a drug's rate of dissolution in various media might reveal information about how it is released from dosage forms.
- Hygroscopicity: Studying the drug's hygroscopic characteristics is crucial for formulation development and packaging issues.
- Excipient Compatibility: It's critical to evaluate a drug's compatibility with the numerous excipients used in dosage forms to avoid problems that could compromise the stability and effectiveness of the medication.
- Salt selection: Choosing the right salt form for the medicine can increase its solubility and stability.
- Permeability: Understanding a drug's permeability will help you choose the best route of administration and create effective drug delivery systems.

3.1 Excipient compatibility *(47, 48)*

To determine whether the active pharmaceutical ingredient (API) and different excipients that might be employed in the formulation of the finished medicinal product are compatible, an excipient compatibility study is carried out as part of pre-formulation studies, a crucial stage in the development of new drugs. Excipients, which are inert chemicals, are used in pharmaceutical formulations to enhance the drug's stability, solubility, bioavailability, and other properties. The excipient compatibility study seeks to uncover any interactions between the API and excipients that can impair the medicinal product's quality, efficacy, or safety.

The excipient compatibility study in preformulation is explained in detail below:

- Selection of excipients- Finding and choosing excipients that are often used in pharmaceutical formulations and are appropriate for the target therapeutic product is the first stage. Depending on the dosage form (such as tablets, capsules,

creams, etc.), these excipients may include fillers, binders, disintegrants, lubricants, preservatives, and more.

- Excipient Mixture Preparation: To replicate the formulation, each chosen excipient is combined in a specified ratio with the API. To see if any effects depend on concentration, these combinations are typically created at various concentration levels.
- Compatibility testing: Compatibility testing entails putting API-excipient mixtures under various stresses that resemble the circumstances that are anticipated for storage and production. Typical sources of stress include:
    - Temperature: To hasten any potential degradation events, samples are kept at high temperatures (e.g., 40–60°C).
    - Humidity: Humidity-controlled settings are used because some excipients may interact with the API in the presence of moisture.
    - pH: To determine the effects of acidity or alkalinity on the API-excipient mixtures, various pH levels are investigated.
    - Light: For pharmaceutical drugs stored in clear containers, exposure to light is important.
    - Oxidation: To determine how susceptible the API-excipient mixtures are to oxidation; oxidative stress is created.

3.2 Analytical Techniques (49)

Following exposure to stress conditions, the API and excipients are monitored, and any changes are detected using a variety of analytical methods. High-Performance Liquid Chromatography (HPLC), Fourier Transform Infrared Spectroscopy (FTIR), Differential Scanning Calorimetry (DSC), and others are frequently used analytical techniques.

- Stability Assessment: The outcomes of the analytical testing are used to determine how long the API-excipient mixtures will remain stable. The mixtures are carefully examined for any substantial deterioration, impurity production, or physical changes.
- Formulation optimization: Using the findings of the compatibility research, appropriate excipients and their concentrations can be selected to produce an improved drug formulation that guarantees stability and preserves the desirable properties of the therapeutic product.

4. Formulation Development (50, 51)

4.1 Formulation components and excipients

Pharmaceutical formulations are created as part of dosage form design to provide the patient with the active pharmaceutical ingredient (API) in a secure, efficient, and practical way. A carefully thought-out dosage form ensures the medication is stable, simple to administer, and has the desired therapeutic impact. There are two key elements in the design of dosage forms:

- **Active pharmaceutical ingredient:** The main element responsible for the therapeutic effect of the medicine is known as the active pharmaceutical ingredient (API). The chemical or biological material exhibits pharmacological activity. The design of dosage forms must consider the API's purity, potency, and stability, which must be chosen carefully.
- **Excipients:** The final dosage form comprises excipients, which are inert components or additives coupled with the API. They accomplish a variety of things, such as:
    - **Enhancing drug stability:** Some excipients stabilize, stopping the API's deterioration or chemical reactions over time.
    - **Increasing medication solubility:** Some excipients can make pharmaceuticals that aren't very soluble more soluble, which increases absorption and bioavailability.
    - **Altering drug release:** Excipients can regulate the pace at which an API is released into the body, which affects how long the drug remains active.
    - **Masking disagreeable tastes:** To improve patient acceptance, excipients can help mask or neutralize the flavour of some medications.
    - **Improving texture and appearance:** Excipients can enhance the dosage form's texture, colour, and appearance.
    - **Aiding in manufacturing processes:** Excipients can make the manufacturing of dosage forms easier, including the compression of tablets and the filling of capsules.

Common excipients include, for example: (52, 53)

- **Binders:** Hold the components of solid dosage forms, such as tablets, together.
- **Disintegrants:** Encourage the digestive tract to break up tablets or capsules.
- **Lubricants:** Prevent the formulation from sticking to the manufacturing machinery.
- **Fillers and diluents:** Give the formulation more bulk.
- **Coatings:** Give tablets and capsules a layer of protection or regulate drug release.
- **Preservatives:** To stop microbiological growth in liquid compositions, use preservatives.
- **Sweeteners:** Make oral liquid drugs taste better.

- **Emulsifiers and surfactants:** Emulsifiers and surfactants facilitate the development of stable suspensions or emulsions.
- **pH modifiers:** Modify the formulation's pH to enhance the stability or absorption of the medicine.

4.2 Techniques for formulation development (54-56)

Establishing a formula for dosage form design that delivers the active pharmaceutical ingredient (API) in the intended way while being secure, reliable, and safe requires a sequence of methodical procedures. The following are some essential methods and actions in the formulation development process:

- **Preformulation studies-** Pre-formulation studies entail a thorough examination of the API's physicochemical characteristics. These studies offer important information about the API's solubility, stability, excipient compatibility, and ideal processing conditions. Pre-formulation studies include a variety of methods, including:
  - **Solubility studies:** Studying an API's solubility in several solvents will help you choose the best formulation strategy.
  - **Solid state characterization:** Analyze the API's crystallinity, polymorphism, and particle size to see how these factors may affect its stability and bioavailability.
  - **Compatibility studies:** Determine whether the API and excipients are compatible to prevent interactions that can jeopardize the stability of the formulation.
  - **Selection of dosage the** most suitable dosage form is chosen by the results of the pre-formulation investigations and therapeutic needs. Tablets, capsules, oral liquids, parenteral solutions, topical creams, and other dose forms are typical.
- **Excipient Selection and Optimization:** When designing dosage forms, excipient selection is crucial. Excipients are chosen according to how well they work with the API and provide the needed functionality. Optimization entails identifying the excipient concentrations and combinations that work best to obtain the required formulation qualities. (57)
- **Manufacturing Process Development:** Process development entails specifying the manufacturing methods and conditions necessary to create the dosage form consistently and reproducibly. Process development techniques include: (58)
- **Granulation techniques:** Wet granulation, dry granulation, or direct compression for tablet formulations.
  - **Coating techniques:** Film coating or enteric coating for tablets and pellets.
  - **Emulsification methods:** High shear mixing, homogenization or micro fluidization for emulsions.
  - **Lyophilization:** Freeze-drying to produce stable parenteral formulations.
  - **Scale-Up and Technology Transfer:** The procedure is scaled up from laboratory to commercial production following successful formulation development. During large-scale production, effective technology transfer assures constant product quality.

4.3 Stability testing and optimization

Designing dosage forms with stability testing and optimization in mind will help guarantee that the finished product is safe, effective, and of acceptable quality for its shelf life. Testing for stability entails determining how different environmental conditions will affect the formulation over time. The main steps in stability testing and optimization for dosage form design are as follows: (59-60)

- **Study Design and Protocol Development** (61) The stability testing procedure needs to be thoroughly thought out and based on industry best practices as well as legal requirements. The testing settings, storage requirements, sampling intervals, and analytical techniques to be applied for evaluation should all be specified in the protocol.
- **Stress Testing:** To produce degradation, the formulation is put through accelerated circumstances including high temperature, humidity, light exposure, and oxidation. This makes it possible to identify degradation pathways and degradation byproducts.
- **Real-Time Stability Studies:** Real-time stability studies entail keeping the created product for a long time (usually up to two years) under approved storage conditions, such as refrigeration or room temperature. At regular intervals, samples are taken and examined for changes in their physical, chemical, and microbiological characteristics.
- **Intermediate Stability Studies:** Between real-time and accelerated settings, intermediate stability studies can be carried out. These investigations offer further information about the stability profile of the product and can help with formulation optimization.
- **Development of Analytical Methods:** Validated and appropriate analytical techniques are crucial for stability testing. These techniques must be precise, sensitive, and able to measure both the API and any potential degradation products.
- **Evaluation of Physicochemical Parameters:** The formulation is examined for changes in appearance, colour, pH, dissolution, content homogeneity, and particle size during stability

testing. These assessments support the monitoring of chemical and physical stability.

- **Identification of Degradation Products:** This step is essential if degradation occurs. The degradation products are characterized, and their effects on safety and efficacy are understood using mass spectrometry, NMR, and other analytical techniques.
- **Statistical analysis:** Stability data is frequently submitted to statistical analysis to identify patterns and forecast shelf life. This can be accomplished by using statistical methods like regression analysis and the Arrhenius equation.
- **Optimization:** The formulation might need to be improved if stability problems are found during testing. This may entail modifying excipient concentrations, manufacturing procedures, or packaging to increase stability.
- **Determination of Shelf-Life:** The dosage form's shelf life is established using stability data. The term "shelf life" refers to how long, under specific storage conditions, the product is anticipated to maintain acceptable quality standards.
- **Stability Report:** Based on the stability testing results, conclusions, and recommendations, a thorough stability report is produced. This report is necessary for continuing quality control and regulatory submissions.

5. Quality Control and Assurance (62-63)

5.1 In-process controls

Process controls in dosage form design refer to the methodical steps and inspections carried out during manufacturing to guarantee the pharmaceutical product's consistent quality, safety, and efficacy. These controls aid in locating and addressing potential differences or deviations throughout production, eventually creating a trustworthy and repeatable dosage form. The following are some crucial elements of dosage form design process controls:

- **Standard Operating Procedures (SOPs):** For every stage of the production process, well-defined, validated SOPs are established. These SOPs specify the precise procedures, tools, supplies, and essential variables to be applied during manufacturing.
- **In-Process Testing and Quality Checks:** Critical metrics and attributes are monitored during various phases of the production process by in-process testing. Examples include monitoring blend uniformity, tablet weight, hardness, friability, disintegration time, and content uniformity while making tablets.
- **Monitoring of Process Parameters:** Process parameters that could have an impact on the final product's quality are closely watched and managed. Mixing time, temperature, pressure, drying time, and compression force are a few examples of these parameters.
- **Real-time process monitoring:** Using specialized sensors and tools, some processes can be continually observed in real-time. Real-time monitoring provides prompt modifications to maintain product quality by allowing for the immediate detection of deviations.
- **Statistical Process Control (SPC):** It is the use of statistical methods to track the production process and spot patterns or deviations that could point to possible problems. Data analysis and potential corrective action are done using control charts and other SPC tools.

5.2 Finished product testing (64-65)

An essential step in the production of pharmaceuticals is finished product testing in dosage form design. Before being made available for use and distribution, the final dosage form must undergo a few tests and studies to guarantee its quality, safety, and efficacy. The testing is done according to industry norms and recognized regulatory rules. These are some essential components of testing a finished product:

Identity and Appearance: To make sure the product is what was intended, the identity is checked. Checking the product's look, colour, shape, and any distinctive identifying characteristics is part of this process.

- **Assay or Content Uniformity:** The active pharmaceutical ingredient's (API) composition is assessed to make sure it falls within the predetermined range. Testing for content uniformity is crucial for solid dosage forms like tablets and capsules.
- **Dissolution Testing:** The rate at which the API is released from the dosage form is determined by dissolution testing. It is especially important for oral solid dose forms because it evaluates how readily the medicine can be absorbed.
- **Disintegration Time:** For solid dosage forms, disintegration time testing is done to make sure that the product disintegrates into tiny pieces within a predetermined amount of time, allowing for adequate drug release and absorption.
- **Weight Variation:** To maintain uniformity throughout the production process, the weight of each dosage unit (such as a tablet or capsule) is checked.
- **Friability & hardness:** Friability and hardness tests are performed on tablets to determine how well they will endure handling and transportation without cracking or disintegrating.
- **pH (for Oral Solutions):** To make sure they fall within the appropriate range for stability and patient tolerance, oral solutions and suspensions may be subjected to pH testing.

- **Sterility testing (for Parenteral Products):** Parenteral products, including injectables, must go through sterility testing to make sure they are free of microbial contamination.
- **Particulate Matter (for Parenteral Products):** Patients may be in danger if there are any visible particulates in parenteral products.
- **Microbiological Testing:** To ensure products fulfil the necessary microbial limits, products intended for topical or ophthalmic use are subjected to microbiological testing.
- **Endotoxin testing (for Parenteral Products):** Endotoxin testing is performed on parenteral products to determine whether endotoxin levels are within acceptable ranges.
- **Packaging Integrity:** The product's packaging is examined to ensure it is not tampered with and preserves product quality over its shelf life.

5.3 Quality standards and regulations (66)

Pharmaceutical dosage forms must be consistent, effective, and safe, and this is made possible by quality standards and laws. The following are some critical elements of quality standards and laws governing dosage form design:

- **cGMP, or current good manufacturing practices:** Pharmaceutical items are continuously produced and monitored following quality standards according to cGMP requirements established by health authorities (such as the FDA and EMA). Dosing form design should follow cGMP criteria to preserve product quality throughout manufacturing.
- **Pharmacopeial Standards:** Monographs providing specifications for different dosage forms, including tests for identity, purity, strength, and quality, are provided by pharmacopoeias (such as the United States Pharmacopoeia and the European Pharmacopoeia). Pharmacopeial standards compliance is necessary for regulatory approval and global acceptance.
- **Quality by Design (QbD):** A systematic approach called QbD emphasizes incorporating quality into the product even before it is designed. To maintain consistent quality, dosage form design should consider critical quality attributes (CQAs) and employ risk-based evaluations.
- **Regulatory Submissions and Approvals:** Before requesting approval for marketing and distribution, dosage form designs must satisfy regulatory standards for safety, effectiveness, and quality. Data from preclinical studies, clinical trials, stability testing, and validation studies should all be included in regulatory submissions.
- **ICH:** A global organization called the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) brings together regulatory agencies and the pharmaceutical industry to create and advance international standards and guidelines for the creation, post-approval, and registration of pharmaceutical products. These recommendations seek to facilitate the global development and registration of medications while ensuring their safety, effectiveness, quality, and performance.

6. Packaging and Labeling (67-69)

Packaging materials selection- The choice of packaging materials significantly impacts the stability, safety, efficacy, and general quality of pharmaceutical goods, making it a crucial component of dosage form design. In addition to assuring patient compliance and convenience, proper packaging helps shield the drug product from external influences like light, moisture, air, and contamination. Here are some important factors to consider when choosing packaging materials for dosage form design:

- **Compatibility with drug substance:** The packaging material should be compatible with the drug substance to prevent interactions that can reduce the product's effectiveness or quality.
- **Protection from light:** Drugs that are sensitive to light need packaging materials that offer sufficient defense against light exposure. For these products, amber or opaque containers are frequently utilized.
- **Moisture Barrier:**

  To avoid loss of effectiveness and physical changes, drugs that are vulnerable to moisture degradation should be packaged in materials with excellent moisture barrier qualities.
- **Oxygen Barrier:** Oxygen-sensitive pharmaceuticals require packaging materials that efficiently limit oxygen permeation to prevent oxidation and ensure drug stability.
- **Chemical and Physical Stability:** Over the course of the drug product's designated shelf life, packaging materials should maintain the physical and chemical stability of the drug product.
- **Tamper-Evidence:** To protect the product's integrity and safety, packaging should be made to show signs of tampering.
- **Child-Resistant Packaging (CRP):** To prevent unintentional consumption, certain medications, especially those that provide a risk to children, may require child-resistant packaging.
- **Dosage form compatibility:** Packaging needs to be compatible with the dosage type, whether it be solid oral pills, capsules, liquids, or injectables.
- **Convenience and compliance:** Compliance and patient convenience are crucial aspects to consider. User-friendly packaging can help patients take their medications more consistently.

- **Environmental impact:** The choice of packing materials is becoming increasingly influenced by sustainability factors. It might be desirable to use recyclable and eco-friendly materials.
- **Storage and transportation conditions:** Packaging should be appropriate for the planned storage and transit conditions to maintain the stability and integrity of the product during distribution.
- **Container Closure Integrity (CCI):** To prevent contamination and maintain the product's sterility, packaging materials must maintain the integrity of the container closure system.
- **Cost-Effectiveness:** To ensure the entire commercial viability of the product, the cost of packaging materials should be considered while preserving quality and safety.

6.1 Container-closure systems (70-75)

Different kinds of container closure systems are employed in pharmaceutical dosage form design to package and safeguard the medication product. Depending on the dosage form, medication properties, and intended use, each type of closure mechanism has unique advantages. Pharmaceuticals frequently use the following types of container closure systems:

- **Bottles:** Syrups, suspensions, and solutions are examples of liquid dosage forms that are frequently packaged in glass or plastic bottles. They could feature child-resistant closures, screw caps, or snap caps.
- **Vials:** Small glass or plastic vials are frequently used for sterile liquids, injectable medications, and vaccines. Aluminium caps and rubber stoppers can be used to seal them.
- **Ampoules:** Ampoules are tiny, sealed glass containers that are used to administer single-dose parenteral drugs. They are made to be cracked open as needed, guaranteeing product sterility.
- **Blister Packs:** Individual sections of pre-formed plastic or aluminium called blister packs hold one dose of a solid dosage form (such as tablets or capsules). They provide defense against contamination, moisture, and physical damage.
- **Strip Packs:** Strip packs are made up of single-dose or multiple-dose solid dosage form units that are wrapped in a strip of plastic or aluminum and sealed. They retain the integrity of the product and make dispensing easy.
- **Sachets:** A single dose of powder, granules, or liquid is contained in a compact, sealed sachet composed of paper or plastic. They are frequently employed for oral reconstitution of pharmaceuticals or single-dose oral powders.
- **Aerosol Cans:** The drug product is released as a spray or foam in pressurized cans called aerosols. They are frequently utilized for topical foams, nasal sprays, and inhalers.
- **Tubes:** Flexible containers constructed of aluminum or plastic are employed as tubes to store semi-solid dosage forms such as creams, ointments, and gels. They frequently have flip-top or screw-cap closures.
- **Parenteral cartridges:** Glass or plastic canisters, known as parenteral cartridges, are used in specialized injection devices to administer pre-measured quantities of injectable medications.
- **Prefilled syringes:** Single-dose syringes that have been pre-filled with a specific drug dosage are known as prefilled syringes. They are ready to use, which lowers the possibility of contamination and dosing mistakes.
- **Dropper bottles:** Dropper bottles are tiny containers with an integrated dropper or pipette that are frequently used to administer tiny doses of liquid pharmaceuticals (such as eye drops).

6.2 Labeling requirements

Designing dosage forms with labelling regulations is critical for providing patients, customers, and healthcare professionals with crucial details about pharmaceutical products. The safe and effective use of the medication and compliance with legal requirements are ensured by proper labelling. Following are some important labelling specifications for dosage form design:

- **Name of Drug and Strength:** The label should prominently display the product's generic name and, if relevant, the brand name. Clearly stating the amount of the active ingredient(s) per dosage unit is very important.
- **Dosage Instructions:** On the label, there should be brief and clear dosing instructions that include the frequency and mode of administration.
- **Indications and Usage:** The approved indications for use, which outline the ailments or disorders the medication is licensed to treat, should be included.
- **Contraindications and Warnings:** Important safety warnings and information regarding circumstances in which the medication should not be used (contraindications) should be included.
- **Adverse effects and precautions:** Precautions for certain populations, such as pregnant women and children, should be listed on the label, along with any potential side effects or adverse reactions.
- **Instructions for Handling and Storage:** Appropriate storage conditions should be offered to guarantee product stability. These conditions should include temperature and light needs.
- **Date of Expiry and Lot Number:** The drug product's expiration date and a distinct lot number

should be provided for traceability and quality control purposes.

- **Route of Administration:** The proper method of administration (such as oral, topical, or intravenous) should be explicitly stated on the label.
- **Batch number and Manufacturing information:** For the purposes of product traceability and recall, the batch number and manufacturing details, including the name and address of the manufacturer, are crucial.
- **Barcodes:** To accurately identify products during distribution, barcodes with product information, such as the National Drug Code (NDC) or Global Trade Item Number (GTIN), are useful.
- **Patient Information Leaflet (PIL):** A patient information leaflet must include detailed instructions and vital patient safety information.
- **Child-Resistant Packaging (CRP):** It should be made very apparent on the label whether the product needs to be packaged in a child-resistant manner.
- **Special Handling Instructions (if applicable):** It should be apparent if the product needs treatment, such as refrigeration or light protection.

7. Conclusion

Designing dosage forms is crucial in pharmaceutical development, ensuring safe, efficient, and practical drug administration. Understanding the physicochemical properties of active ingredients is key in selecting appropriate formulations. Patient-centred design improves compliance and therapeutic outcomes by customizing dosage forms to meet diverse patient needs. Technological advancements, especially in nanotechnology and controlled-release systems, have revolutionized dosage form design, enhancing drug release profiles and therapeutic efficacy. Safety considerations are paramount, including precise dosing and compatibility with other medications. Packaging and labelling ensure proper medication use and storage, while adherence to regulatory standards requires thorough testing and validation. Collaboration among clinicians, formulators, scientists, and regulators is essential to creating dosage forms that optimize patient outcomes and advance healthcare globally.

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Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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