DOSAGE FORM DESIGN

Abstract

Designing pharmaceutical dosage forms is a crucial field that tries to provide convenient, reliable, and safe drug delivery systems. By spanning the gap between active medication ingredients and their administration, this multidisciplinary sector ensures the best possible therapeutic results. Drug qualities, patient characteristics, administration method, release kinetics, and manufacturing considerations are taken into account while designing dosage forms. The design must take into consideration the various demands of patients across age groups, from difficulties with compliance in young children to changes in drug absorption in geriatric populations. The best dosage forms should be stable, easy to administer safely, accurate in their dosing, and well tolerated by patients. Dosage form design is primarily driven by biopharmaceutics, a patient-centred approach, release kinetics, excipient selection, manufacturing, safety, and cost-effectiveness. Novel possibilities for adjusting drug administration to specific needs have been made possible by cutting-edge technologies and personalised medicine. Dosage forms are classified depending on their physical form and mode of administration and include solid, liquid, semi-solid, and gaseous forms. Pre-formulation studies are necessary for gathering important data on the properties of the medicine and its interactions with excipients. Pharmaceutical researchers working with clinicians have the potential to develop revolutionary medication delivery methods, improving patient care and treatment effectiveness.

Keywords: Dosage form, pre-formulations, route of administration, patient care

Objectives: After completing this chapter students would be able to know

- A comprehensive overview of dosage

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form design in the pharmaceutical industry.

- Characteristics of dosage forms, the need for their design, and the principles that guide the formulation process.
- Types of dosage forms based on their physical form and route of administration, outlining their merits and demerits.
- The concept of pre-formulation, emphasizing its significance in gathering essential information about drug properties before formulating dosage forms.
- The primary goal is to convey the importance of dosage form design in pharmaceutical development and how it contributes to safe, effective, and convenient drug delivery to patients.

I. INTRODUCTION

Pharmaceutical dosage form design is a multidisciplinary field that focuses on creating safe, effective, and convenient drug delivery systems for patients. It plays a pivotal role in the development of pharmaceutical products, bridging the gap between active drug substances and their administration to achieve desired therapeutic outcomes. The design of dosage forms encompasses a wide range of factors, including drug properties, patient characteristics, and route of administration, release kinetics, and manufacturing considerations. Regardless of age, drugs must be correctly formulated before being administered to patients. Paediatric patients encounter the formulator with some particular challenges with regard to compliance and treatment effectiveness. Children's drugs must be developed and supplied by pharmaceutical companies and compounding pharmacies because there are not enough drug products accessible for them.

Modern medicine places a great deal of importance on pharmaceutical dosage form design, which enables healthcare professionals to customise therapies to specific patient needs and increase therapeutic efficacy. By combining scientific knowledge, cutting-edge research, and innovative technologies, dosage form designers aim to optimize drug delivery, thereby maximizing drug bioavailability and minimizing adverse effects. From pediatric patients with specific compliance challenges to geriatric populations with altered drug absorption, dosage form design must address the diverse requirements of patients across different age groups. As drug development continues to advance and novel therapeutic agents emerge, dosage form design remains at the forefront of pharmaceutical innovation. With the evolving landscape of personalized medicine, the demand for tailor-made dosage forms has grown, necessitating collaboration among experts from various fields, including pharmaceutical sciences, chemistry, biology, engineering, and clinical medicine. This interdisciplinary approach ensures that pharmaceutical dosage form design is a comprehensive and adaptable process, responsive to the evolving needs of patients and the medical community.

Advancements in pharmaceutical technology have broadened the possibilities for dosage form design, allowing for the development of innovative delivery systems that can improve treatment outcomes and enhance patient experiences. From conventional tablets and capsules to more complex formulations like nanoparticles, liposomes, and transdermal patches, each dosage form design serves a unique purpose in meeting the diverse requirements of modern therapeutics. Furthermore, personalized medicine and targeted drug delivery have emerged as promising frontiers in dosage form design. Tailoring drug delivery to individual patient needs can improve treatment efficacy, reduce side effects, and optimize therapy for specific conditions.

1. **What are Dosage Forms?** The term "dosage forms" refers to pharmaceutical preparations or formulations that present a specific combination of active pharmaceutical ingredients (active ingredients) and inactive ingredients (excipients) in a specific configuration to enable easy and precise administration and delivery of active pharmaceutical ingredients.

   Excipients are pharmacologically inactive compounds that are frequently used in dosage forms as carriers of the active pharmaceutical ingredients (API). APIs are pharmaceutically active bulk drugs that give the intended pharmacological effect.

2. **Characteristics of Ideal Dosage Forms:** Dosage forms are pharmaceutical preparations designed to deliver a specific dose of medication to patients in a safe, effective, and convenient manner. These dosage forms come in various shapes, sizes, and formulations to cater to different patient needs, drug properties, and administration routes.

Many factors influence the characteristics of ideal dosage forms. An Ideal dosage forms should be:

- Easy and safe administration
- Easy to handle
- Accuracy and precision
- Stability and compatibility
- Appropriate route of administration
- Patients acceptance and compliance
- Rapid and predictable onset of action
- Biocompatibility
- Easy to reproduce and manufacture
- Having the long shelf life, reducing the need for frequent replacements.
- Economical to patients
- An ideal dosage form should be environmentally friendly, with minimal impact on the ecosystem during manufacturing and disposal.

3. **The Need for Dosage Forms**

- The strength and low dosage of the majority of medications in use today exclude (rather than permit) any notion that the general public might safely derive the proper amount of a drug from bulk material.
- The majority of medications are administered in milligram (mg) doses, which are much too small to be measured on any scale but a delicate prescription or electronic analytical scale.
- The production of solid dosage forms like tablets and capsules with filler or diluents is necessary when the drug dose is tiny in order to make the dosage unit large enough to be picked up with the fingertips.

In addition to offering a method for the safe and straightforward distribution of the proper amount, dosage forms are necessary for a variety of other reasons as well.

- To ensure the safe and convenient delivery of a precise dosage
- To protect drug components (sealed ampoules, coated tablets) against the harmful effects of humidity or ambient oxygen.
- To safeguard the medication from the damaging effects of stomach acid following oral delivery (enteric coated tablets)
- To decrease the salty, bitter, or unpleasant taste or aroma of a pharmacological substance (in capsules, coated tablets, or flavouring syrups)
- To offer liquid formulations (suspensions) of substances that are either unstable, insoluble in the proper medium, or unstable.

- Rate-controlled medicine delivery employing a range of controlled-release pills, capsules, and liquids
- To make sure that topical medications (such as ointments, creams, transdermal patches, and solutions for the eyes, ears, and nose) have the best possible pharmacological activity at the sites of topical administration.
- To enable the direct administration of a medicine into the bloodstream or body's tissues (injections), as well as into a body orifice (rectal or vaginal suppositories),
- To make it feasible to implant pharmaceuticals, ensuring that inhalation therapy (using inhalation aerosols) produces the most potent medication activity.
- Numerous dosage forms also make it simple to identify drugs due to their distinctive colours, shapes, or distinguishing markers.

Table 1: Dose of the Some Drugs

Drugs	Usual Dose (mg)	Category of the Drugs
Acetaminophen	500-1000	Analgesic, Antipyretics
Aspirin	81-325	Nonsteroidal Anti-Inflammatory Drug (NSAID)
Levothyroxin	0.10	Anti-ulcerative
Digoxin	0.25	Cardiotonic
Metformin	500-1000	Anti-diabetic (Oral)
Amlodipine	5-10	Anti-hypertensive (Calcium channel blockers)
Prazosin HCL	2	Anti-hypertensive
Omeprazole	20-40	Anti-ulcerative
Clonazepam	1	Anti-convulsant
Risperidone	2	Anti-psychotic
Nifedipine	10	Anti-hypertensive (Calcium channel blockers)
Ibuprofen	200-800	Nonsteroidal Anti-Inflammatory Drug (NSAID)
Chlorapheniramine maleate	4	Anti-histaminic

4. A Dosage form must be Properly Designed and Manufactured, and it Requires:

- Considering the physical, chemical, and biologic features of all medicinal products and pharmaceutical ingredients that will be used in the manufacturing of the product
- The medicine and pharmaceutical ingredients must be compatible with each other in order to produce a medicinal substance that is stable, efficient, appealing, easy to use, and safe.
- The product must be manufactured with the appropriate quality controls and packaged in materials that preserve the stability of the product.
- To ensure the product has the greatest shelf life possible, it should be labelled to encourage proper use and stored properly.

5. Principles of Dosage Form Design: The principles of dosage form design serve as fundamental guidelines for developing pharmaceutical formulations that deliver drugs effectively, safely, and conveniently to patients. These guidelines are based on an in-depth

knowledge of the characteristics of the medication, the desired therapeutic result, and patient needs. Here are the key principles of dosage form design:

- **Biopharmaceutics and Pharmacokinetics:** Dosage form design starts with a clear understanding of the drug's biopharmaceutical characteristics, such as solubility, permeability, and stability. These properties influence drug absorption, distribution, metabolism, and excretion. Pharmacokinetic considerations help in determining the appropriate route of administration, dosage regimen, and release kinetics to achieve the desired drug concentration and duration of action.

- **Patient-Centered Approach:** Patient preferences and needs are central to dosage form design. User-friendly and patient-accepted formulations enhance compliance and treatment outcomes. Dosage forms should be easy to administer, taste pleasant (if applicable), and tailored to meet the specific needs of different patient populations (e.g., children, elderly).

- **Route of Administration:** The choice of the most suitable route of drug delivery is crucial. Different routes, such as oral, parenteral, topical, and inhalation, offer distinct advantages and challenges. The route selected should align with the drug's properties and the desired therapeutic effect.

- **Release Kinetics:** Controlling the drug release profile is essential for achieving the optimal pharmacokinetic behavior. Different release kinetics, such as immediate-release, sustained-release, and targeted-release, are utilized to match the drug's therapeutic requirements.

- **Excipient Selection and Compatibility:** Excipients play a critical role in dosage form design. They aid in drug delivery, improve stability, and provide desirable formulation characteristics. Excipient selection should consider their compatibility with the drug substance and each other to ensure a stable and effective formulation.

- **Manufacturing and Quality Control:** Dosage forms must be designed with manufacturability in mind. Robust manufacturing processes and strict quality control measures are essential to ensure consistency, reproducibility, and compliance with regulatory standards.

- **Safety and Tolerability:** Dosage form design should prioritize patient safety and tolerability. The formulation should minimize the risk of adverse effects and toxicity by considering the excipients' safety profile and the route of administration.

- **Stability and Shelf-Life:** Proper formulation and packaging are essential to maintain the drug's stability throughout its shelf-life. Factors such as temperature, humidity, and light sensitivity must be considered to prevent degradation and loss of potency.

- **Cost-Effectiveness:** While designing dosage forms, cost-effectiveness should be considered to ensure affordable and accessible medications without compromising quality and efficacy.

- **Emerging Technologies and Personalized Medicine:** Advancements in technology, such as nanotechnology and 3D printing, offer innovative opportunities for dosage form design. Personalized medicine, based on individual patient characteristics and genetic profiles, is also shaping the future of pharmaceutical formulations.

Adhering to these principles ensures that pharmaceutical dosage forms are designed to meet the specific needs of patients, optimize drug delivery, and contribute to improved therapeutic outcomes and patient well-being.

6. Primary Reasons for Designing a Dosage Form

- **Protection**

  - To shield medications (such as coated tablets, capsules, and ampoules) from the elements such as air oxygen, temperature, and humidity.
  - To prevent acid-labile medications from degrading in the stomach due to gastric acid (Enteric coated).
  - To prevent the chemical interaction and ensure the stability of the drugs
  - Design the dosage forms in a way to prevent microbial contamination as it can compromise drug safety and efficacy
  - Mechanical Protection: Certain dosage forms, including tablets with protective coatings, are made to resilient physical stress during handling and transportation, lowering the likelihood that the medication will break or be harmed.
  - Inhalation protection: For example, metered-dose inhalers and dry powder inhalers are made to protect the medication throughout administration, making sure the right dose reaches the respiratory system's intended site of action.
  - Parenteral protection: Parenteral administration dosage forms, such as ampoules or vials, are designed to keep sterility and avoid contamination during storage and administration.

- **Improve Therapeutic Activity**

  - To provide the ideal pharmacological action to the intended site (Transdermal patches, Transdermal ointments)
  - Direct insertion of medications into body orifices (rectal, vaginal suppositories)
  - To provide the optimal drug action in the bodily tissues or blood stream (such as, for injections, inhalants, and aerosol inhalation).
  - To give prolonged release administration of drugs with a rate-controlled drug action.
  - To increase the bioavailability of medications with a narrow window of absorption (Gastroretentive administration)

- **Patient Compliance**

  - Provide unit dose (Tablet, Capsule) to ensure dose accuracy.
  - A decrease in dosage frequency (Prolonged release and Sustained release)
  - Masking the bitter and unpleasant taste or aroma of the medicine (film-coated tablet, capsules, suspension, emulsion)

- Medication delivery into human tissues and cavities (otic, rectal, vaginal, buccal, and sublingual routes).
- Easy administration and handling (chewable tablets)

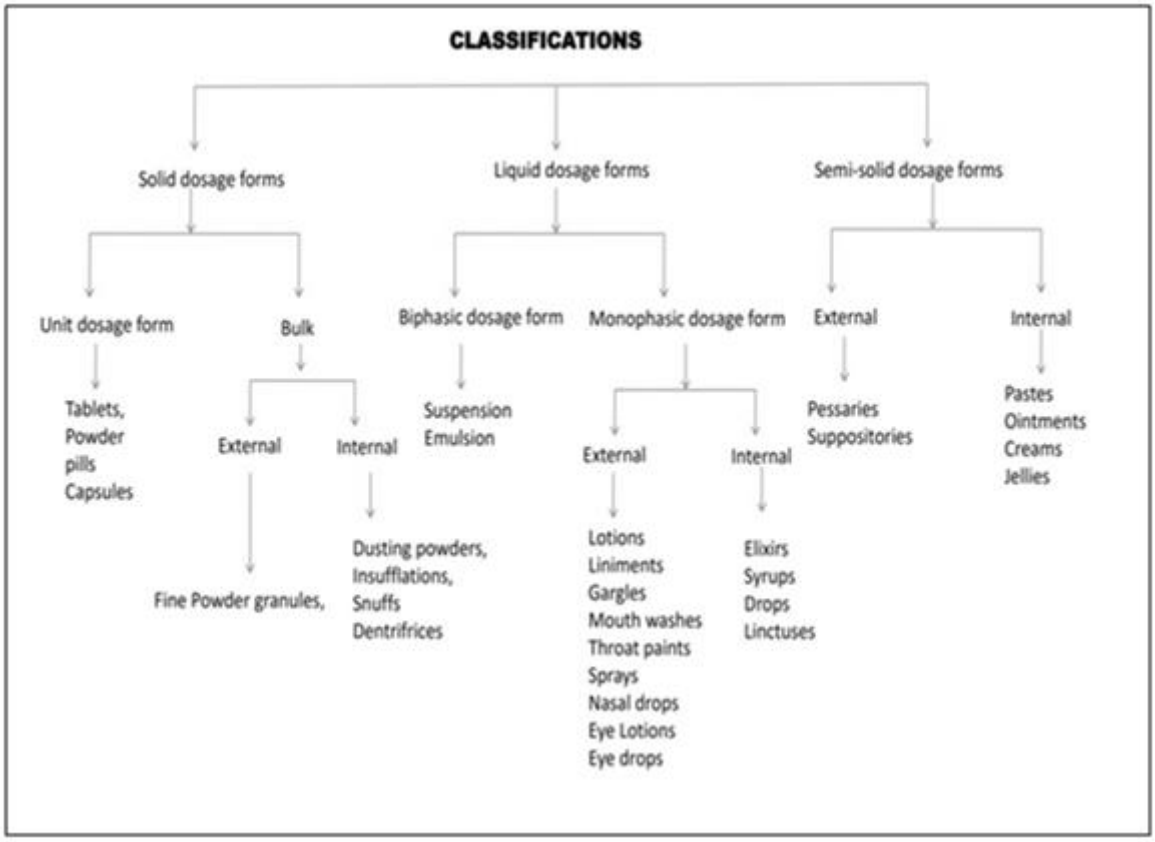

Figure 1: classification of the several dosage forms of medication according to their physical form

7. **Dosage Form Types:** Dosage forms can be categorized into the following groups based on their physical characteristics and methods of administration:

- **On the basis of Physical Form**

  - **Solid Dosage Form:** For instance, pills, powder, capsule, films, lotions, chewing gum, and pellets with conventional and modified release.
  - **Liquid Dosage Forms:** For instance, tincture, injection, mouthwash, gargles, syrup, elixir, spirit, aromatic water, suspension, and emulsion.
  - **Semi-Solid Dosage Forms:** Semisolid dosage form for topical (otic, nasal, vaginal, or rectal) administration to skin and mucous membranes. For instance, pastes, liniments, ointments, creams, and gels.
  - **Gaseous Dosage Forms:** a mixture of a propellant and an active component that, when activated, releases a fine dispersion of solid and/or liquid materials in a gaseous medium. for example an aerosol, inhaler, or nebulizer.

- **On the basis of Route of Administration**

  - **Oral- Through Oral Route**
    - Tablet-buccal, sublingual or orally disintegrating, modified release
    - Capsules- Hard gelatin and soft gelatin
    - Powder
    - Liquid- Monophasic and biphasic

  - **Topical- Applied Over the Skin Surface and Mucosa**
    - Cream, gel, balm, liniment, lotion, ointment
    - Eye drops (opthalmic)
    - Ear drops (otic)
    - Skin patches (transdermal)
    - Vaginal rings

  - **Parenteral-Applied through the Skin**
    - Intramuscular (IM) injection (90^0 angle)- given directly into the muscle
    - Intradermal (IM) injection (10^0-15^0 angle) -given directly in the dermal region of the skin
    - Intravenous (IV) injection (25^0 angle)- is the infusion or injection given directly into the vein
    - Subcutaneous (SC) injection (45^0 angle)- given under the skin into the subcutaneous layer
    - Intraosseous (IO) injection- given directly into the bone marrow
    - Intrathecal (IT) injection- administered around the spinal cord

  - **Inhalational**
    - Instilled through the nasal and pulmonary route. E.g. aerosols, solutions, sprays

  - **Instilled in the Body Cavities:** Suppository, pessary, douche etc..
    - Rectal
    - Vaginal

Table 2: Dosage forms with their Merits and Demerits

Types of Dosage Form	Merits	Demerits
1. Solid dosage forms Tablets, capsules, Lozenges, pellets, Chew gum, Films	1. Accuracy of the dose 2. Uniformity of dose 3. Stability of the drug 4. Easy to handle and transport 5. Reproducibility 6. Cost-effective 7. Can mask unpleasant tastes 8. High mechanical strength	1. Susceptible to degradation by moisture 2. Not suitable for unconscious patients 3. May not be suitable for patients with certain swallowing or gastrointestinal problems 4. Slower onset of action compared to liquid 5. Formulations problems

2. Liquid dosage forms Monophasic: Solutions, Syrups, Elixirs, Liniments, Lotions Biphasic: Suspension, Emulsion	1. Easy to manufacture 2. Convenient to swallow and administer 3. Rapid absorption 4. Quick onset of action 5. High Bioavailability 6. Suitable for various routes of delivery 7. Suitable for certain insoluble drugs 8. Less processing steps 9. Enhanced stability	1. Shorter shelf life compared to solids 2. Chances of non-uniformity of the dose 3. Higher chances of breakage and loss during shipping or transportations 4. Bulky and heavier than solids 5. Light sensitive formulations 6. May require refrigeration before use 7. Unsuitable for unpleasant taste and obnoxious odour drug
3. Semi-solid dosage forms: Creams, gels, lotions, pates, ointments, suppositories etc.	1. Easy to use 2. Higher stability 3. Easy to apply and remove 4. Suitable for localized treatment 5. Avoid first pass metabolism 6. Can incorporate both water and oil	1. Prone to microbial contamination 2. Difficult to handle 3. Some formulations may be less stable 4. May cause staining and irritations 5. Texture and consistency may vary
4. Gaseous dosage forms	1. They are absorbed quickly by the body, as they don't require dissolution like solid dosage forms. 2. Withdrawal of dose without contamination 3. Provides medication to apply on the local area 4. Adjustment of dose is possible (metered valves) 5. Temper proof 6. Targeted delivery to the respiratory system, offering localized treatment for conditions like asthma or COPD. 7. Easy to handle and convenient	1. May create environmental hazards 2. Expensive 3. Difficulty in administration especially in children and elderly 4. Limited formulations 5. Risk of overdose 6. Limited safety

8. **Pre-Formulation Concept:** To create stable, secure, and efficient dosage forms, basic information on the physical and chemical characteristics of the medication ingredient must be gathered. These studies are known as preformulation.

- The drug's identification and the development of analytical procedures are the first two steps in the preformulation study.
- The second step is the study of the drug's physical properties, including its organoleptic properties, physical description, particle size and shape, powder flow properties, melting point, polymorphism, solubility, intrinsic solubility (Co), dissolution, intrinsic dissolution rate, partition coefficient (Log P), wetting, dielectric constant, pKa, and hygroscopicity.
- Investigation on the drug's chemical composition, including hydrolysis, oxidation, drug stability, polymerization, isomerization, racemization, photolysis, decarboxylation, and deamination.
- Study on how drugs interact with excipients.

Table 3: Preformulation Drug Characterization Properties:

Fundamental Properties	Derived Properties
Solubility in solid state and solution Melting point Assay of samples by UV spectroscopy Solubility- aqueous , pKA, salts, solvents, Partition coefficient, dissolution Stability in solution and solid state Assay development	Microscopy- particle size and size distribution Bulk density Flow properties Compression properties Drug-excipient compatibility

II. CONCLUSION

To optimize medication delivery for patient benefit, dosage form design is a dynamic field that integrates a wide range of scientific disciplines and technology. Pharmaceutical research, personalized medicine, and emerging technology will continue to affect dosage form design in the future, resulting in safer, and more effective and patient-friendly drugs. Pharmaceutical scientists and physicians need to work together to capitalise on these breakthroughs and develop transformational medication delivery systems for better patient care.

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