Principles of Dosage Form Design

What is pharmaceutics?

- Understanding the basic physical chemistry necessary for efficient design of dosage forms

  (physical pharmaceutics)

- Design and formulation of medicines

  (dosage form design)

- Small and large scale manufacturing of dosage forms

What is pharmaceutics?

- A medicine/ pharmmaceutical product must administer drug to the body in a safe, efficient, reproducible and convenient manner.
- This means suitable additives (excipient, vehicle) are required to make drugs into dosage forms (formulation).
- There three major considerations in the desing of dosage forms:

1. Physicochemical properties of drugs itself
2. Biopharmaceutical considerations such as administration route of dosage form affects the rate and absorbtion of drug into body
3. Therapeutic considerations of the disease treated which in turn decide the most sutibale dosage form, suitable application routes and dose frequency of drug

Understanding Pharmaceutical Dosage Forms

- Dosage forms are believed to be as old as man himself. Primitive man used various forms of plants and animal parts while the early civilizations used a number of dosage forms – ointments, powders, pills, sugar-based sweet preparations, including syrups, conserves, confections, electuaries etc.

- The potent nature of most active drug substances and their low dose requirement and the need for obtaining a stable, safe and therapeutically effective drug product resultted with dosage forms; **each designed to contain a given quantity of active drug substances for ease and accuracy of dosage administration.**

What are Drugs?

Drug can be defined as:

the medicine or other substance which has a physiological effect when ingested or otherwise introduced into the body.

Under the «Health Topics» title, WHO (World Health Organization) defines drugs under two different subtitles;

- essential medicines,

- pharmaceutical products,

which the latter is commonly called as drug or medicine.

Medicines are the products, used in different ways for;

- protecting the living from disease,
- Used with the aim of diagnosing and treating the diseases,
- Contain one (or more) active ingredient,
- Designed to be easily received by the patient,
- Prepared in the form of a formula (auxiliary substances) which will be effected according to the desired purpose and duration.

What are Pharmaceutical Excipients?

(also called pharmaceutical ingredients)

inactive, non-medicinal substances, intentionally included in a drug product to serve different and specialized pharmaceutical purposes during manufacture, storage or use.

Drug products usually contain other substances (e.g., bulking agents, disintegrants, stabilizers, solvents, lubricants, binders, preservatives etc.) other than the Active Pharmaceutical Ingredient (API), to ensure that the drug product is acceptable to the regulatory authorities and patients in terms of manufacturability, appearance and performance.

What are Dosage Forms?

The term “dosage forms” refers to pharmaceutical preparations or formulations in which a specific mixture of drug substances (active pharmaceutical ingredients) and inactive components (excipients) are presented in a particular configuration to facilitate easy and accurate administration and delivery of active drug substances.

Pharmaceutical products:

More commonly known as medicines or drugs – are a fundamental component of both modern and traditional medicine. It is essential that such products are safe, effective, and of good quality, and are prescribed and used rationally.

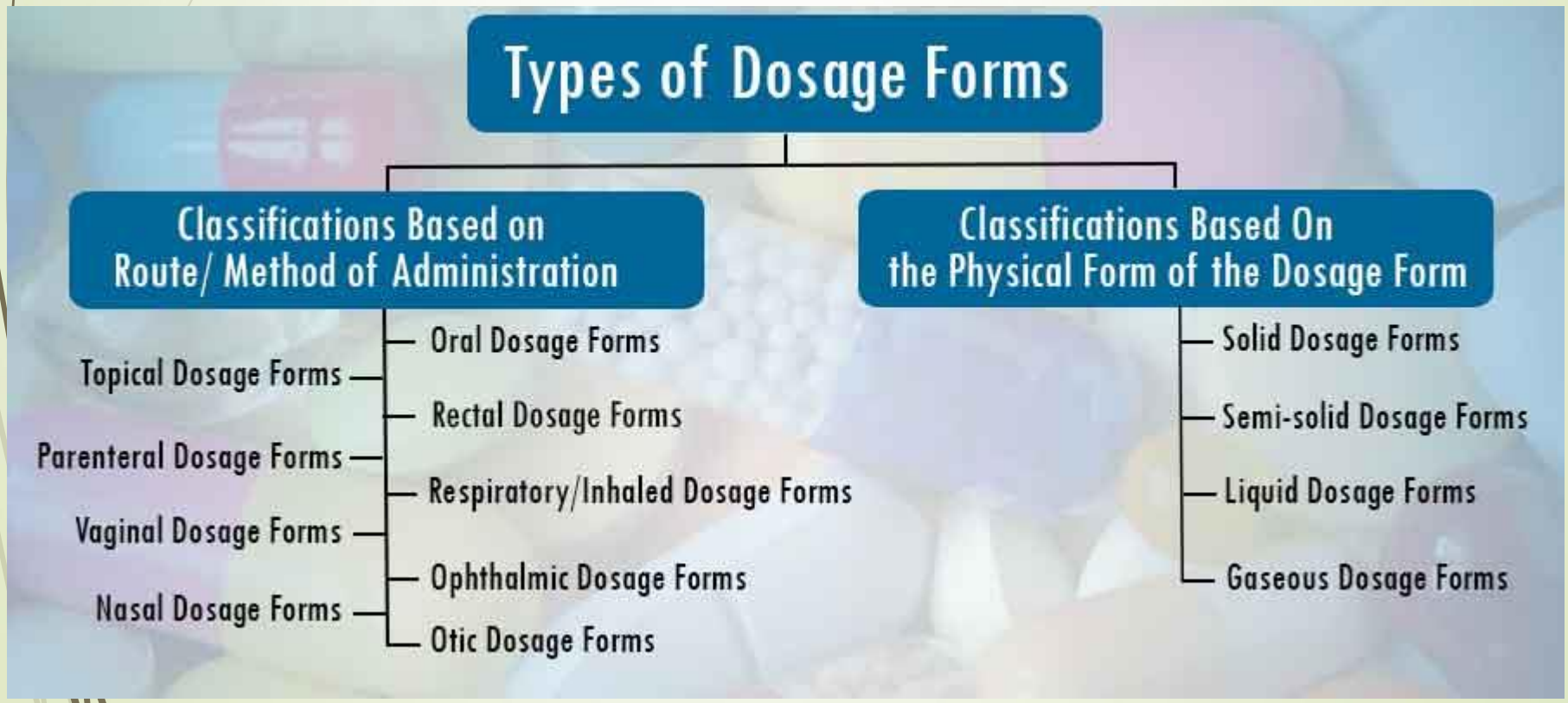
The Need for Dosage Forms

Apart from ensuring safe and convenient delivery of the required dose of drug substances to the sites of action, dosage forms are needed for the following additional reasons:

1.To achieve rapid onset of action following drug delivery e.g., parenteral dosage forms, inhalational/ respiratory dosage forms.
2.To mask the undesirable taste or offensive odour of a drug substance e.g., capsules, taste masked suspensions, coated tablets, etc.
3.To achieve improved bioavailability, modified disposition as well as drug targeting e.g., Nanosuspensions.
4.To provide drug products that are stable, effective and safe for consumption under specified suitable storage conditions e.g., powders for reconstitution.

5. To protect the drug molecules from the destructive influence of gastric juice following oral administration of the dosage form e.g., enteric-coated tablets.
6.To provide drug products that bypass the first pass metabolism e.g., injections, topical dosage forms etc.
7.To provide drugs with predetermined rate and prolonged therapeutic effect over an extended period of time e.g., modified-release tablets, capsules and suspensions.
8.To provide drug products that bind to a specific physiological site of action e.g., targeted-release tablets, capsules etc.
9.To provide useful dosage form for administering poorly water-soluble or insoluble drugs in an appropriate vehicle e.g., suspensions.
10.To provide sterile, clear and particulate free liquid dosage forms of substances e.g., injections and eye drops.

Classifications/ Types of Pharmaceutical Dosage Forms



Pharmaceutical dosage forms are classified either based on the methods/route of administration or based on the physical form of the dosage form.

A. Classifications of Dosage Forms Based on Route/ Method of Administration

B. Classifications of Dosage Forms Based On the Physical Form of the Dosage Form

A. Classifications of Dosage Forms Based on Route/ Method of Administration

The route of administration for a drug product is usually determined by the physicochemical characteristics of the drug molecule. Dosage forms are classified based on the route of administration into:

a. Oral
b. Topical
c. Rectal
d. Parenteral
e. Respiratory/Inhaled
f. Vaginal
g. Ophthalmic
h. Nasal
i. Otic

a. Oral dosage forms

Oral dosage forms comprise pharmaceutical formulations taken orally for systemic effects. They are absorbed through the various epithelia and mucosa of the gastrointestinal tract at varying rates with the exception of drugs that are absorbed in the buccal cavity. Examples include tablets, capsules, suspensions, lozenges, pills, granules, powders, emulsions etc.

b. Topical dosage forms

These include drug molecules that are in a suitable solid base (e.g., powders and aerosols), semi-solid base (e.g., ointments, creams, foams, gels, poultice and pastes), or in liquid form (e.g., solutions, suspension of solids in aqueous solutions or emulsions) which possesses either hydrophobic or hydrophilic properties. These drugs are applied to the skin or other topical surfaces (such as the eye, ear and nose) mainly for local action. Systemic drug delivery can also be achieved using topical preparations (e.g., transdermal patches), though absorption is often poor and erratic.

c. Rectal dosage forms

These are solutions, suppositories or emulsions administered rectally for local rather than systemic effect. These formulations can also be used to deliver drugs that are inactivated by gastrointestinal fluids when administered orally or when the oral route of the patient is precluded.

d. Parenteral dosage forms

These are usually sterile, particulate free and non-pyrogenic solutions or suspensions (of drugs in water or other suitable physiological acceptable vehicles) that are injected into the body using syringe and needle, infusion set etc.

e. Respiratory/Inhaled Dosage Forms

This is a type of dosage form where drugs are delivered in gaseous, aerosol mist or ultrafine solid particle form into the lungs. These classes of dosage form are mainly for direct treatment and management of respiratory diseases. Examples include nebulizers, powder aerosols and pressurized metered dose aerosols.

f. Vaginal dosage forms

These are dosage forms that are intended to be used in the vaginal cavity for either contraception, induction of labour, treatment of vaginal infections or local menopausal symptoms. Commonly used vaginal dosage forms include creams, tablets, vaginal gels and pessaries, suppositories, foams, ointments, tampons and inserts. Others include vaginal rings, vaginal films etc.

g. Ophthalmic Dosage Forms

These are principally sterile solutions, ointments and suspensions, essentially free from particles or substances that might irritate the eye. They are meant to be gently applied to the eyelids or placed in the pocket between the eyelids and the eyeball. Ophthalmic dosage forms are commonly used to treat local ocular disorders, e.g. infection and inflammation; or intraocular disorders e.g. glaucoma.

h. Nasal dosage forms

Nasal formulations are non-sterile aqueous-based systems that are instilled within or sprayed into the nasal cavity from a dropper or from a plastic squeeze bottle. They are predominantly employed for the treatment of local disorders – infections, congestion, and allergic rhinitis. Nasal preparations when absorbed through the nasal mucosa to achieve systemic effect.

i. Otic dosage forms

These are non-sterile aqueous solutions, or solutions prepared with glycerin or other solvents and dispersing agents that are instilled into the ear canal for the treatment of local disorders.

B. Classifications of Dosage Forms Based On the Physical Form of the Dosage Form

This class comprises the following dosage forms.

a. Solid
b. Semi-solid
c. Liquid,
d. Gaseous

a. Solid Dosage Forms

These comprise drug products with definite shape and volume. They constitute approximately 90% of all dosage forms clinically used to provide systemic administration of therapeutic agents. This class broadly encompasses two types of formulation – tablets and capsules. Others include powders, granules etc.

b. Semi-solid dosage forms

These preparations applied on the skin or to the mucous membrane to achieve local or systemic effect. Examples include ointments, pastes, creams, gels etc. Semi-solid dosage forms have many characteristics in common – consistency, presentation, preservation requirement, and also route of administration which is mainly topical.

c. Liquid Dosage Forms

These include drug products administered in the form of solutions, suspensions, colloidons, emulsions etc. Liquid dosage form can be sterile or non-sterile depending on the route of administration.

d. Gaseous dosage forms

This class comprises drug products that are packaged under pressure in a holder with a ceaseless or restricted conveyance valve framework. The gas inside contains restoratively dynamic medicaments that are released upon activation of an appropriate valve system. Examples include aerosols, nebulizer, sprays, inhalers etc.

General Considerations in Dosage Form Design

A suitable dosage form design includes

a. Preformulation Studies

These studies are designed to identify those physical and chemical properties of a candidate drug molecule which may affect the development of a safe, stable and efficient dosage forms with good bioavailability.

Commonly evaluated parameters during preformulation studies include – particle size and size distribution, solubility, dissolution behaviour, stability, refractive index, partition coefficient, drug-excipient compatibility, crystal form, surface properties, etc.

b. Biopharmaceutical Considerations

These studies are carried out to evaluate the rate and extent at which candidate drug molecule becomes available at the site of action. The aim is to achieve optimal therapeutic activity for the patient by modifying the delivery pattern of a drug molecule to systemic circulation.

The major biopharmaceutical considerations include

i. Pharmacodynamic Considerations
•Therapeutic objective.
•Toxic effect.
•Adverse reactions of candidate drug molecule.

ii. Drug Consideration
•Physicochemical characterization of the candidate drug molecules.

iii. Drug Product Consideration
•Bioavailability of candidate drug molecule.
•Pharmacokinetics of candidate drug molecule.
•Route of administration for the candidate drug molecule.
•Desired drug dosage form and
•Desired dose of the candidate drug molecule.

iv. Patient Consideration
•Compliance and acceptability of the final drug product

v. Manufacturing Considerations
•Cost
•Availability of pharmaceutical raw materials
•Stability and quality

c. Formulation and Development

This stage involves the actual combination of candidate drug molecule with various excipients and also optimizing the concentration at which each excipient is used. The choice of excipients depends on the properties of the drug molecule and the nature of the intended drug product.