DOSAGE FORM DESIGN

Swetha V, Yashika S B, Hemalatha K\*

Saveetha College of Pharmacy, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Thandalam, Chennai, Tamil Nadu-602105, India

# ABSTRACT:

Dosage form comprises of active and inactive ingredients. Dosage formulation are alternate modalities developed for highest therapeutic response. The medicine must be compatible with proper quality control measures. Drug formulation rationally designed by inventive computer aided drug design. Desired products are maintained with specialization at different fundamentals. Desired product under general analytics was successive batch by the manner which is treated additionally illustration are included in illness. Preformulating studies dealing with physical description providing specific modification, heat of vaporization involving vapor pressure, membrane as barrier for active and inactive diffusion and stability testing to check specification of drug.

**Keywords:** Dosage form, Formulation, Preformulating, Solubility, Stability

# INTRODUCTION:

Drug substances are a component of pharmaceutical formulations that also include one or more recipients or other pharmacological ingredients. drugs that are manufactured with various dose forms and feature specialised activities. Basic characteristics including physical nature, physiological nature, stability, efficacy, and safety are considered for proper drug design.

**Drug stability**

The degree to which drug ingredients persist within predetermined bounds. Pharmaceutical products have the capacity to maintain their chemical, physical, and microbiological characteristics within predetermined bounds for the course of their shelf lives.  
**DRUG FORMULATION:**

To create a given final product, active drug substance is combined with other ingredients while taking into account factors like pH, solubility, and particle size.

**DRUG DESIGN:**

New drugs are rationally designed using an inventive approach based on an understanding of their biological targets. Computer-aided drug design is the term for drug development using computer modelling.  
**EFFICACY OF DRUG DOSAE FORM:**

According to pharmacology, the drug's greatest response is referred to as its efficacy.

# GENERIC ANALYSIS:

**Before the medication is created into a dosage form, the preferred product type must be determined. The development of several initial product formulations, investigation of these formulations for the desired features (such as medication release profile, bioavailability, and clinical efficacy), pilot plant studies, and scaleup are then required. The product's primary formulation is chosen because it best satisfies the goals of the product. Every new batch of the product must conform to the requirements outlined in the fundamental recipe.**

1. **How it is handled:**

**Although taking medications orally is the most patient and practical way to do so, tablets and capsules are usually made for oral use. Additional Examples of Conditions Affecting Treatment Dosage The condition includes nausea, vomiting, and motion sickness.**

1. **The patient's age and projected condition:**

**Infants and kids of all ages can take the same liquid pediatric formulation, and the dosage will depend on how much is given. Pharmaceutical liquids rather than solid versions are suggested for oral delivery in infants and children under the age of 5. These liquids, which are flavored syrups, aqueous solutions, or suspensions, are typically put directly into the mouths of babies and young children using a dropper, spoon, or oral dispenser or mixed into their food. The dosage form's shape is also influenced by the target patient's age.**

# Need for dosage form DESIGN and convertion of drug to

# dosage form

* **Drugs with dosage forms, such as tablets, capsules, and syrups, must be able to provide exact amounts safely and easily.**
* **After oral administration, protection against stomach acid**

**Example: Tablets with an enteric coating**

* **Protection against atmospheric gases like oxygen and moisture**

**Example: A sealed or covered capsule vehicle you'd like to possess,**

**for instance, like: suspension**

**need for conversions:**

1-Accurate dose.

2-Protection e.g., coated tablets, sealed ampoules.

3-Protection from gastric juice.

4-Masking taste and odor (to make palatable).

5-Placement of drugs within body tissues.

6-Sustained release medication.

7-Controlled release medication.

8-Optimal drug action.

9-Insertion of drugs into body cavities (rectal, vaginal)

10-Use of desired vehicle for insoluble drugs.

# FIGURE 1: **TYPES OF DOSAGE FORM :**

|  |  |  |
| --- | --- | --- |
| Types of dosage form  1.Solid dosage form:    Tablets, capsules, chewing gum, pellets.  2.Liquid dosage form:  Solutions, elixirs, syrups.  3.Semi- solid dosage form:  Cream, gel, liniment, lotion.  4.Gaseous dosage form: | Merits  1.Dose accuracy  2.stability of drug  3.uniformity of dose  4.reproductivity  1.easy to swallow  2.easy to manufacture  3.fast absorption  4.improves bioavailability  1.easy to use  2.more stable that liquid  3.avoidance of first pass metabolism  4.patient convenience  1.easy to handle and convenient  2.withdrawal of dose without contamination  3. provides medication to local area | Demerits  1.non suitable for unconscious  2.formulations complications  3. not preferable for acid labile and stomach irritant drug.  1.non uniformity of dose  2.bulky  3.less stability  4. unsuitable for unpleasant taste.  1.difficult to handle  2.chances of contamination  3. may cause irritation and staining.  1.Expensive  2.may create environmental hazards.  3. non reliable performance. |

FIGURE 2: **MERITS AND DEMERITS OF DOSAGE FORMS**

# PREFORMULATION STUDIES:

It involves the physiochemical property related to drug molecule providing the sense of modification to show better performance.

1. **Physical description:**

Dealing with studies of physical, chemical, and pharmaceutical properties which relate molecule by providing specific modification to show better performance.

1. **Heat of vaporization:**

The amount of heat that is required to convert of the liquid substance into a vapor form, without involving the temperature increase. Heat of vaporization involving the vapor pressure as important factor in dosage form like Nasal inhalants and Aerosols form. Carmustine drug exhibits large (or) greater vapor pressure while the temperature tend to be increased, while cisplatin, cyclophosphamide are lesser than that.

1. **Particle size:**

Particle size distribution is the measurement which defines the total no. of particles to present according to their size. They can be spherical, non- spherical with various length and width measurement. Particle size distribution play vital role in affiling the physiochemical properties lie bioavailability, color, texture, stability, spianolactone, nitrofurantoin, procaine penicillin are certain drugs which influenced as oral absorption.

1. **Solubility:**

Solubility is the important property influencing physical, chemical nature of drug substance, specifically in the aqueous solution/aqueous system. When drug entering the systemic circulation in body the drug must be soluble. While insoluble drug substances show the incomplete absorption in body.

1. **Membrane permeability:**

Membrane permeability is the drug substance crossing the biological membranous layer to produce the biological response at a site.

Membrane acts as barriers against lipid which permit soluble drug molecules through passive diffusion. This property permits both active and passive diffusion.

1. **Partition coefficient:**

It is defined as the ratio of the concentration of drug substance in a mixture of two immiscible solvent attaining the state of equilibrium. It is specifically given for the in-ionized dug with ionized drug species concentration. It measures the lipophilic character of drug, studies about ADME of drug.

1. **Stability testing:**

Quality of drug products are shifted by environmental factors lie temperature, humidity, light, pressure that are tested by stability testing. Stability testing Is a “re-testing” process done for check in the specification of given drug substances.

# DESIGN FOR CONTROLLED RELEASE IN DRUG DELEIVEY SYSTEM

Aim:

It enables the therapeutic effect in body by improving its efficacy and safety over controlled time and specific place of release/site of action in body.

* It is maintaining the state of equilibrium at levels of drug substance in blood fluid and in all tissues for exceeded time period.
* It gives the précised in reproducibility in the drug release of pharmacokinetics reaching at a desired concentrated level.
* Sustained release provides the constant rate of drug in the human body known to be zero order dissolution.
* This design over the dosage form implies the release of specific dose having therapeutic effect over desired zone and optimal serum –drug concentration.

Mechanism of controlled release that:

includes the degradation, swelling, diffusion active efflux.

Advantages of controlled system:

* Maintains the levels with desired range.
* Avoids over dosing.
* Prevention /reduction of side effects
* Reduces dose frequency.

E.g.

Drug delivery releases the drug at steady rate into extravascular region of body including transdermal patches, intramuscular implantable pumps and intramuscular depot injections.

# formulation additives: for designing of solid, liquid, semisolic dosage form:

## **solid dosage form**

**Solid dosage forms make a significant contribution to medical care, and a sizable population depends on them for good health. Tablets, capsules, freeze-dried (lyophilized) powders, powder aerosol formulations, spray-dried powders, etc. are all examples of solid dosage forms in general. Patients and healthcare professionals can benefit greatly from solid dose forms like pills, granules, and powders. All the solid dosage forms make use of various additives, such as lubricants, binder, and diluents.**

Depending upon their use in solid dosage forms additives are classified as follows:

**Diluents/fillers:**

When the amount of the active ingredient in the formulation is reduced, these additions increase the dosage form's bulk content. Example: mannitol, sorbitol, sucrose, dibasic calcium phosphate dihydrate, immediately compressible starch, hydrolysed starch, MCC, and lactose, among other cellulose derivatives.

**Wetting Agents:**

In solid dosage form wetting agents aid water uptake by reducing surface tension and thereby enhancing disintegration and dissolution. Example: Sodium lauryl sulphate.

**Chelating Agents:**

Chelating agents tend to respond with overwhelming metal particles inactivating their synergist action in the oxidation of medicaments by forming soluble complexes. Example: ethylenediaminetetraacetic acid, glycine, citric acid, or tartaric acid, etc.

**Lubricants:**

Lubricants are intended to decrease the friction between surfaces in mutual contact like tablets and die cavity. It works to make efficient ejection of tablet from die cav- ity. Example: stearic acid salt, surfactants, waxes, etc.

**Glidants:**

Glidants are used to improve the flowability of granular mixture by reducing interparticle friction and that is used in the pharmaceutical production of tablets and capsules. Actually, glidants, lubricant, and antiadherent have a close relationship because in different concentration glidants work as lubricants and antiadherents. Example: talc, corn starch, etc.

**Binders:**

These may be dry powders or liquid, they are added at a specific stage in wet granulation to promote formation of granules or to provide cohesive force between particles during direct compression for mechanical strength. Example: cellulose, methyl cellulose, polyvinyl pyrrolidine, polyethylene glycol (PEG), gelatine, polyvinylpyrrolidone, hydroxypropyl methylcellulose, sucrose, starch, etc.

**Disintegrants:**

Disintegrants are added to the formulation to facilitate the fragmentation of the tablet and capsule into smaller particles that will provide increased surface area

|  |  |  |
| --- | --- | --- |
| Sr.No. | Name | Recommended concentration |
| 1.  2.  3.  4.  5.  6.  7.  8.  9.  10. | Benzyl alcohol  Benzalkonium chloride  Butyl paraben  Chlorobutanol  Meta cresol  Chlorocresol  Methyl paraben  Phenyl ethyl alcohol  Propyl paraben  phenol | 0.5 to 10%  0.01%  0.015%  0.25 to 0.5%  01 to 0.25%   * 1. to 0.18%   0.01to 0.5%  0.25 to 0.002%  0.005 to 0.002%  0.065 to 0.02% |

figure 3: **preservatives of solid media**

## LIQUID DOSAGE FORMS

Compared to solid dosage form, liquids are processed and formulated as solutions, suspensions, and emulsions according to the dosage form required or API solubility and stability. Powder may also be delivered as syrups, solutions, suspensions, and emulsions by reconstitution in which powder and vehicle are combined prior to delivery.

**Aqueous Vehicles:**

Water (SWFI, WFI, USP purified water), propylene glycol, ethyl alcohol, glycerine.

**Oily Vehicle:**

Vegetable oils, mineral oils, organic oily bases or emulsified bases. Solubilizers: Breaking the hydrogen bond between the particles so they get soluble in water. Solubility can be modified by use of cosolvent, pH change, complex formation, or the use of surfactants. Example of solubilizers in LDF are ethanol

**Natural Sweeteners:**

Sucrose, lactose, mannitol, etc.

**pH Modifiers and Buffering Agents:**

Buffers used to control or prevent changes in the formulation pH which could prevent and increase the stability.

**Antimicrobial Preservatives:**

Preservative used in preparation to prevent the growth of microbes so it should be of wide spectrum. It should be nontoxic, no sensitizing, compatible with other additives, and have no taste and odour, e.g., parabens (0.015%0.2% w/v.), Phenol, benzyl alcohol (2%), chlorocresol, etc.

**Suspending Agent and Viscosity Modifying Agent:**

Cellulose derivatives: MCC (and derivatives such as carboxymethylcellulose (CMC)); Clays: magnesium aluminium silicate; sodium alginate, xanthan gum, carbomer povidone, tragacanth, guar gum; colloidal silicon dioxide; BHA, BHT, EDTA; fumaric acid tartaric acid, ascorbic acid, alpha tocopherol, citric acid.

A diagram of a substance

Description automatically generated

Figure 4: liquid dosage forms

## semisolid dosage from

It contains a major portion of pharmaceutical formulations. It is used to deliver a drug by way of skin, cornea, rectal tissue, nasal mucosa, vagina, buccal tissue, urethral mem- brane, and external ear lining. But topically applied drugs have some problems in their permeation, but to minimize this issue additives play a vital role in delivering the drug in an efficient manner Additives work on the physical properties of the vehicle, which make them capable to change the stratum corneum property, e.g., alcohol, or the mucosa to deliver the drug effectively. Semisolid dosage forms usually are intended for localized drug delivery. Semisolids have rheological properties in which they impart solid-like properties until they are disturbed; disturbance easily breaks down particle forces. Semisolids includes creams, ointments, pastes, and gels.

**Bases:**

The base is the central ingredient used in semisolid dosage formulation. Base of ointment does not merely act as the transporter of the drug but influences the absorption of drug. Bases are categorized as follows:

**Water-soluble base:**

They are mixtures of high and low MW PEG which have the general formula CHCH2 CH2OCH2 CH2OH. The CH2OH. The characteristics of these bases are:

* Low molecular weight as liquids; those with moderately higher molecular weight are unctuous and the high molecular weight are solids.
* No water is required for their preparation.
* Suitable combination of high and low molecular weight PEG yield material having ointment-like consistency. It melts when applied to the skin.
* Presence of many polar groups make it water soluble.
* Also called greaseless ointment bases.

**Water-miscible bases:**

Excess of water is used to make them soluble, that is why formulation using these bases can be removed after use or application, e.g., cetrimide, cetomacrogol. For o/w type, e.g., antifungal benzoic acid ointment.

Importance of water-miscible bases:

* Promptly miscible with the exudates.
* Reduced impedance with ordinary skin functioning.
* Effective in touch with the skin, in view of their surfactant content.
* Elevated corrective agreeableness, and it makes less probability of the patients discontinuing treatment.
* Easy expulsion from the hair

## STABILITY STUDIES

**DRUG AND DRUG PRODUCT STABILITY:**

**There are five types of stability.**

Chemical: Active ingredients retain chemical integrity and labeled potency within the specified limits.

Physical: Original physical properties, appearance, palatability, uniformity dissolution and suspend ability are retained.

Microbiologic: Sterility/resistance to microbial growth.

Therapeutic: Therapeutic effect remains unchanged.

Toxicologic: No significant increases in toxicity occurs.

**Results:**

 The proper design and formulation of a dosage form requires consideration of the physical, chemical, and biological characteristics of all of the drug substances and pharmaceutical ingredients (excipients) to be used in fabricating the product. The drug and pharmaceutical materials utilized must be compatible and produce a drug product that is stable, efficacious, palatable, easy to administer, and well tolerated. Preformulating factors include physical properties such as particle size, crystalline structure, melting point, solubility, partition coefficient, dissolution, membrane permeability, dissociation constants, and drug stability.

**Conclusions:**

Successful development of a formulation includes multiple considerations involving the drug, excipients, compliance, storage, packaging, and stability, as well as patient considerations of taste, appearance, and palatability.

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