Industrial Pharmacy II

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Industrial Pharmacy II

- **This course deals with the pharmaceutical dosage forms.**
- **There are different types of DF, depending on the physical state or route of administration.**
- **Dosage forms are the means by which drug molecules are delivered to sites of action within the body.**
- **Each type has advantages and disadvantages, classification, manufacturing methods, evaluation (Q.C.) and problems.**

As Questions

- **Why we need dosage forms?**
- **What are the differences between dosage form and drug delivery system?**
- **What are the differences between the types of dosage forms?**

Solid Dosage Forms

- Powders and granules
- Capsules
- Tablets

Powders

- Considered as **dosage forms** (dispensed as divided or bulk, administered by oral, pulmonary or topical routes, prepared as granulated (effervescent or non) or not granulated) , lyophilized or non.
- Or as **starting materials** for other dosage forms like tablets, capsules, injections (sterile powders), suspensions (powders ready for reconstitution), DPI.s, nasal ……etc.

- Types of powders depending on p.s., dispensing method and route of administration.
- Advantages and disadvantages??
- General considerations (particle and bulk properties): particle size, shape, poly-dispersity, flowability, density, porosity, compressibility, compactibility, suspendability, penetrability and grittiness.
- For optimization, we need different processing steps like mixing, milling, granulation, drying, lyophilization, microencapsulation and sterilization.

- May be non medicated or medicated containing active ingredients with or without additives (varied with variation of type).
- API of powders may be crystalline (mostly) or amorphous, mainly synthetic.
- Additives may be natural (plant or animal), synthetic or semi-synthetic. Such as:

- **Diluents** or **Bulking powders** such as mono, di or polysaccharides, cellulose derivatives and organic compounds.
- **Glidants** such as talc and stearate derivatives.
- **Moisture-activated adherents** such as Polyox??.
- Others like flavorants, colorants, stabilizers.

Granules

- The granule is defined as a dosage form composed of dry aggregates of powder particles that may contain one or more APIs, with or without other ingredients.
- They may be swallowed as such (directly), dispersed in food, or dissolved in water.
- May be effervescent or non-effervescent.
- Granules are frequently compacted into tablets or filled into capsules, with or without additional ingredients.

- They are irregularly shaped but may be prepared to be spherical.
- They are usually in the 4- to 12-mesh sieve size range, although granules of various mesh sizes may be prepared depending upon their application.
- Granules are prepared by wet methods and dry methods, may be manually or industrially.

Q/ What are the advantages of granules over powders?

(Shape, size, flowability, compressibility, taste, stability, dissolution…..)

Effervescent Granulated salts

- An effervescent dosage form, frequently tablets or granules, contains ingredients that, when being in contact with water, rapidly release carbon dioxide.
- The dosage form is dissolved or dispersed in water to initiate the effervescence prior to ingestion.

- Effervescent salts are granules or (coarse - very coarse) powders containing a medicinal agent in a dry mixture usually composed of **sodium bicarbonate, citric acid, and tartaric acid.**
- When added to water, the acids and the base react to liberate carbon dioxide, resulting in effervescence.
- The resulting **carbonated** solution masks undesirable taste of any medicinal agent.

- **Using a combination of citric and tartaric acids rather than either acid alone avoids certain difficulties.**
- **When tartaric acid is used as the sole acid, the resulting granules readily lose their firmness and crumble.**
- **Citric acid alone results in a sticky mixture difficult to granulate.**
- **Effervescent granules are prepared by two general methods:**

(1) The fusion method **(2) The wet method**

The fusion method:

- The one molecule of water present in each molecule of citric acid acts as the binding agent for the powder mixture.
- The step involves: **milling of citric acid crystals, mixing, drying (at 34-40°C), mixing at wet conditions (massing), wet sieving, drying (not exceeding 54°C).**

- **The wet method:**

- The source of binding agent is not the water of crystallization from the citric acid but the water added as the moistening agent.

- The steps : **milling if needed, mixing, massing, wet sieving and drying.**

Quality control

Bulk Powders

- The pharmacist should compare the final weight of the preparation with the theoretical weight.
- The powder should be examined for uniformity of color, particle size, flowability, and freedom from caking.

Divided Powders

- For divided powders, the pharmacist should individually weigh the divided papers and then compare that weight with the theoretical weight. The packets should be checked to confirm uniformity.

- **As powder incompatibilities or problems, we have:**

1) Eutectics:

Some powders may become sticky or pasty, or they may liquefy when mixed together.

Such as aspirin, camphor, lidocaine and menthol….

Then a bulky powder adsorbent such as light magnesium oxide or magnesium carbonate is added to solve that.

2) Hygroscopic and deliquescent powders:

- Hygroscopic powders will absorb moisture from the air.
- Deliquescent powders will absorb moisture from the air to the extent that they will partially or wholly liquefy.
- Such as Iron and ammonium citrate, Phenobarbital sodium, Pepsin ….
- So it is best to dispense the ingredients in tight containers and incorporate a desiccant packet or capsule when necessary, or dilute the powder with an inert drying powder to reduce the amount of surface area exposed to the moisture.

3) Efflorescent powders:

- An efflorescent powder is a crystalline powder that contains water of hydration or crystallization.

- This water can be liberated either during manipulations or on exposure to a low-humidity environment. If this occurs, the powder will become sticky and pasty, or it may even liquefy.

Such as ferrous sulfate, citric acid, codeine …..

- To solve that:

- Use of an anhydrous salt form of the drug. or
- Include a drying bulky powder.
- Use of a light, non compacting method of mixing the powders.

4) Explosive mixtures:

Some combinations of powders may react violently when mixed together (oxidation-reduction reaction).

Special precautions must be taken if it is necessary to prepare a formulation containing these mixtures.

Ex. ????

5) Incorporation of liquids:

- As in the wet granulation method.

6) Volatile substances