Pharmaceutical Excipients

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Pharmaceutical Excipients

- **Definition:**
  
  Excipient is a pharmacologically inactive subs. formulated alongside the active pharmaceutical ingredient (API) of a medication.

- **Purposes served by excipients:**
  
  - Provide bulk to the formulation.
  - Facilitate drug absorption or solubility & other pharmacokinetic considerations.
  - Aid in handling of “API” during manufacturing.
  - Provide stability and prevent from denaturation.
Excipients

- No interaction with drug.
- Pharmacologically inert.
- Feasible
- Stable for handling.
- Cost effective
### A list of Pharmaceutical Excipients used in pharmaceutical preparations

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Fillers:

- Typically fill out the size of a tablet or capsule, making it practical to produce & convenient for the consumer to use.

Function of fillers:

- Add volume and/or mass to a drug subs, so facilitating precise metering & handling in preparation of dosage forms.

Used in tablets and capsules.

Typical features of fillers:

- A good filler should be inert, compatible with the other components, non-hygrosopic, relatively cheap, compactable, and preferably tasteless or pleasant tasting.

Example: Plant cellulose & Dibasic calcium phosphate.
Vegetable fats & oils are used in soft gelatin capsules.
Other e.g.; Lactose, Mannitol, Sorbitol, Calcium carbonate, and Magnesium stearate are used as filler.

**Binders:**

- Binders hold the ingredients in a tablet together.
- Binders ensure that tablets & granules formed with required mechanical strength, & give volume to low active dose tablets.

**Typical features of Binders:**

- A Binder should be compatible with other constituents of formulation & add sufficient cohesion to the powders.

**Classification & examples: according to their application:**

- **1. Solution binders** dissolved in a solvent e.g.; water or alcohol
- **2. Dry Binders** added to powder e.g.; Cellulose, methyl cellulose, Polyvinyl pyrrolidone, and Polyethylene glycol.
**Disintigrants:**

- Disintigrants are substance or mixture of subs. added to the drug formulations, which facilitate dispersion or breakup of tablets & contents of capsules into smaller particles for quick dissolution when it comes in contact with water in the GIT.

- **Ideal properties of disintigrants:**
  - Good hydration capacity,
  - Poor solubility and poor gel formation capacity.

Examples: Polyvinylpyrrolidone, carboxymethyl cellulose, and sodium starch glycolate.
Coating Agents:

Coating is a process by which an essentially dry, outer layer of coating material is applied to the surface of a dosage form and agents used in this process are called coating agents.

Types:

- 3 types of coating agents are used pharmaceutically,
- Film coating.
- Sugar coating.
- Compression coating.

Function of coating agents:

- Protection, Masking, Elegance, Ease of swallowing, and identification.
Sorbents:

- Sorbents are materials that soak up oil from the water.
- **Types & examples of sorbents:**
  - **Natural sorbents:** peat moss, sawdust, feathers & anything else natural that contains carbon.
  - **Synthetic sorbents:** polyethylene and nylon.
- **Functions of sorbents:**
  - Used for tablet/capsule moisture-proofing by limited fl. sorbing (taking up of a liquid or a gas by adsorption) in a dry state.

Antiadherents:

- Anti-sticking agents prevent adhesion of tablet surface to the die walls and the punches.
- **Example:** Water insoluble lubricants as **Magnesium stearate**, talc & starch used as antiadherents.
**Lubricants:**

- Lubricants prevent ingredients from clumping together and from sticking to the tablet punches or capsule filling machine.
- Lubricants also ensure that tablet formation & ejection occur with low friction between the solid and die wall.

**Types:**

- **1. Hydrophilic lubricants:** poor lubricants, no glidant or anti-adherent properties.
- **2. Hydrophobic lubricants:** Most widely used today.

Generally good lubricants & effective at low conc.
- Also have both anti-adherent & glidant properties.
- For these reasons, hydrophobic lubricants used much more frequently than hydrophilic. Example; magnesium stearate.

**Roles of lubricants:**

- **1. True Lubricant Role:** To decrease friction at the interface between a tablet’s surface & die wall during ejection and reduce wear on punches.
2. Anti-adherent Role:
- Prevent sticking to punch faces or in case of encapsulation lubricants. Prevent sticking to machine dosators, tamping pins,

3. Glidant Role:
- Enhance product flow by reducing interparticulate friction.

Example of lubricants: Polyethylene glycol, Magnesium stearate, Stearic acid and its derivatives.

Glidants:
- A substance as colloidal silica that enhance the flow of a granular mixture by reducing inter-particle friction & used in the pharmaceutical production of tablets & capsule.
- Functions: Glidants used to promote powder flow by reducing interparticle friction & cohesion.
- Glidants used in combination with lubricants as they have no ability to reduce die wall friction.
- Example: Fumed silica, talc, & magnesium carbonate.
Preservatives:

- substances that commonly added to various foods and pharmaceutical products in order to prolong their shelf life.
- Preservative system protect the product against microbial proliferation but does not compromise product performance.

Ideal properties of preservatives:

- Preservative must exert a wide spectrum of antimicrobial activity at low inclusion levels.
- Preservative must maintain activity throughout product manufacture, shelf life and usage.
- Not compromise the quality or performance of product, pack or delivery system.
- Not adversely affect patient safety or tolerance of product.

Examples: Methyl & Ethyl parabens, Propyl paraben, Benzoic acid & its salts, Sorbic acid and its salts.
## Preservatives used in Pharmaceutical Preparations

<table>
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<tr>
<th>Preparation</th>
<th>Preservative</th>
<th>Conc. (% w.v)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injections</td>
<td>Phenol – Cresol-Chlorocresol</td>
<td>0.5- 0.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.1</td>
</tr>
<tr>
<td>Eye drops</td>
<td>Chlorhexidine acetate</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>Benzalkonium chloride</td>
<td>0.01</td>
</tr>
<tr>
<td>Mixtures</td>
<td>Benzoic acid - Alcohol</td>
<td>0.1- 12-20</td>
</tr>
<tr>
<td></td>
<td>Methyl paraben</td>
<td>0.1</td>
</tr>
<tr>
<td>Creams</td>
<td>Parabens</td>
<td>0.1-0.2</td>
</tr>
<tr>
<td></td>
<td>Chlorocresol</td>
<td>0.10</td>
</tr>
<tr>
<td>Tablets</td>
<td>Methylparaben</td>
<td>0.1</td>
</tr>
</tbody>
</table>
Antioxidants:

- An antioxidant is a molecule that inhibits the oxidation of other molecules. Oxidation is a chemical reaction that transfers electrons or hydrogen from a substance to an oxidizing agent.

Ideal Properties of Antioxidants:

- Effective at a low, nontoxic concentration.
- Stable & effective under normal conditions of use, over a wide pH and temperature range.
- Soluble at the required concentration.
- Compatible with a variety of drugs & pharmaceutic excipients.
- Free from objectionable odor and taste.
- Colorless in both the original and oxidized form.
- Nontoxic both internally & externally at the required concentration.
- Unreactive (does not adsorb, penetrate, or interact) with containers or closures.

Reasonable cost

- BHT (Butylated Hydroxy Toluene), BHA (Butyl Hyd Anisol), Sod. sulfite
Sweetening agents:

- Sweetening agents employed in liquid formulations designed for oral administration specifically to increase the palatability of the therapeutic agent.

- **Example:** Sucrouse, Saccarine, Aspertame, Sorbitol.

Uses of sweetening agent:

- The main agents employed in oral preparations are sucrose, liquid glucose, glycerol, sorbitol, saccharin sodium & aspartame.

- **Aspartame** is an artificial sweetening agent. The use of artificial sweetening agents in formulations is increasing.

- Thus use of sugars in oral formulations for children and patients with diabetes mellitus must be avoided.
Flavoring agents:

- Flavoring agents are added to increase patient acceptance.
- The four basic taste sensations are salty, sweet, bitter, sour.
- Certain flavors used to mask these specific taste sensations
  
  **Eg:** Clove oil, citric and syrup, glycerin, rose oil, orange oil, menthol.

Coloring agents:

- The pharmaceutical ingredients that impart the preferred color to the formulation are called coloring agents.
- Two types of coloring agents:
  - 1. Natural Coloring agents:
  - 2. Synthetic coloring agents.
  
  **Eg:**
  - 1. White: Titanium dioxide.
  - 2. Blue: Brilliant blue, Indigo carmine.
  - 3. Red: Amaranth Carmine
  - Yellow: saffron
  - Brown: caramel
Solvents:

- A solvent is a substance that dissolve a solute resulting in a solution. A solvent is usually a liquid but also a solid or gas.

Solvent classification:

- Solvents classified into two groups;
  1. Polar
  2. Non polar

- Polar solvents dissolve polar compound best & non polar solvents dissolve non polar compound best.

Examples & uses of solvent:

- Polar solvent as water in which a drug is freely soluble
- Water –miscible solvent such as Chlordiazepoxide hydrochloride can be used to improve solubility & stability
- Oils used as emulsion, IM. inj. & liquid fill oral preparation
- Aqueous methanol: the standard solvent in samp extraction
- Non-aqueous solvents: glycerol, propylene glycol, ethanol used generally for a lipophilic drug.
**Co-solvents:**

- Co-solvents are defined as water-miscible organic solvents that are used in liquid drug formulations to increase the solubility of poorly water soluble substances or to enhance the chemical stability of a drug.

**Properties of co-solvent:**

- Co-solvents increase the solubility of a drug.
- An ideal co-solvent should possess values of dielectric constant between 25 and 80. The most widely used system that will cover this range is a water/ethanol blend.
- Should not cause toxicity or irritancy when administrated for oral or parental use.
- Examples: *sorbitol, glycerol, propylene glycol & syrup*. 
Chelating agents:

- Molecules that are capable of forming complexes with the drug involving more than one bond; it’s a complex compound contains one or more ring in its structure.

- For example: ethylene diamine is bidentate and ethylene diamine tetraacetic acid is hexadentate.

- Example and uses:
  - EDTA: ethylene diamine tetraacetate used for estimation of metals ions.
  - EDTAH4: ethylene diamin tetraacetic acid used for softening water.
  - Calcium Disodium Edetate: used in treatment of heavy metal poisoning mostly caused by lead.
  - Disodium Edetate: used in hypercalcemic states. Also useful in the treatment of cardiac arrhythmias.
Buffering agents:
These are materials which, when dissolved in solvent will enable the solution to resist any change in pH should an acid or an alkali be added. The choice of suitable buffer depends on the pH and buffering capacity required.

- **Properties of buffering agents:**
  - should have a low toxicity.
  - should be buffered at the range of 7.4 as pH of body is 7.4.
  - should be non-irritant.

- **Examples of buffering agent**
  - Most of buffering system based on carbonate, citrates, gluconates, lactates, phosphates, or tartrates.
**Viscosity imparting agents:**

- Agents used to increase or decrease the viscosity of a liquid either to serve as adjacent for palatability or to improve pour ability. They are also called thickening agents.

- Viscosity imparting agents are of two types:
  
  1. **Viscosity modifier:** decrease the viscosity of a liquid to improve pour ability and make it more palatable.
  
  2. **Viscosity enhancer:** increase the viscosity of a liquid to improve pour ability and make it more palatable.

- Most commonly used viscosity imparting agents are:
  
  - Hydroxy ethylcellulose
  - Hydroxy propylmethylcellulose
  - Methyl cellulose
  - Polyvinyl alcohol
  - Polyvinyl pyrrolidone.
Humectant:
- A humectant attracts & retains the moisture in the nearby air via absorption, drawing the water vapor into and/or beneath the organism/object's surface.
- Humectants absorb water vapors from atmosphere till a certain degree of dilution is attained.
- Aqueous sol. of humectants reduce the rate of loss moisture.
- Ideal properties of humectants:
  - Must absorb moisture from atmosphere & retain the same under normal conditions of atmospheric humidity.
  - Should be colorless or not of too intense color.
  - Should have good odor and taste.
  - Should be nontoxic and nonirritant.
  - Should be noncorrosive to packaging materials.
  - Should not solidify under normal conditions.
  - Should not be too costly.
Classification of humectants with examples:

- **3 types** of humectants as inorganic humectants, metal organic humectants and organic humectants.

  1. **Inorganic humectants:**
     - Calcium chloride is an example. It has compatibility problems and corrosive in nature, so not frequently used in cosmetics.

  2. **Metal organic humectants:**
     - Sodium lactate is limited used in cosmetics because of compatibility problems, corrosive nature and pronounced taste.

  3. **Organic humectants:**
     - These are widely used in cosmetics.
     - They include polyhydric alcohols, their esters and ethers.
     - The most commonly used organic humectants are glycerol, ethylene glycol, polyethylene glycol (PEG), diethylene glycol, triethylene glycol, propylene glycol, dipropylene glycol, glycerin, sorbitol, mannitol, glucose.
**Surfactants:**

- Compounds that lower surface tension (or interfacial tension) between two liquids or between a liquid & a solid and increase the solubility. Also known as surface active agents.

**Properties of surfactants:**

- A surfactant must fulfill 2 structural requirements:
  1. A surfactant must contain a **lipophilic region**.
  2. A surfactant must contain a **hydrophilic region**.

- Both hydrophilic & lipophilic region must be balanced, then will be concentrated at an interface and therefore surface tension will be lowered.
Types of surfactants:

- 4 types of surfactants based on charge of the hydrophilic region:
  - 1. **Anionic surfactant** (the hydrophilic region is negatively charged i.e. an anion)
  - Sodium lauryl sulphate: used as excipient on dissolved aspirins.
  - 2. **Cationic surfactant** (hydrophilic region is positively charged i.e. a cation)
  - Cetyl trimethyl ammonium bromide (cetrimide) - is an effective antiseptic agent against bacteria and fungi.
  - 3. **Non-ionic surfactants**:
    - **Tween 80** (polyoxyethylene sorbitol monooleate)- Polysorbate 80 is an excipient that is used to stabilize aqueous formulations of medications for parenteral administration.
  - 4. **Amphoteric surfactant**:
    - **Lecithin**: act as a wetting, stabilizing agent and a choline enrichment carrier, helps in emulsifications and encapsulation, and is a good dispersing agent. N-dodecyl alanine.
References:


4. www.wikipedia.com
THANK YOU