EXCIPIENTS

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- **flavors** and **sweeteners.**
- **Colorants**
- **Preservatives**
- **Antioxidants**
- **chelating agents**
- lubricants

- **Not all salts are salty but their taste is function of both cation and anion.**
- Salty tastes :NaCl, KCl, NH_4Cl and by NaBr, KBr.
- ammonium give bitter and salty sensations.
- **potassium iodide** and **magnesium sulfate** (epsom salt) are predominantly bitter.

- In general, low-molecular-weight salts are salty, and high-molecular-weight salts are bitter.

- With organic compounds, increase number of hydroxyl groups (—OH) increase the sweetness of the compound.

FLAVORING PHARMACEUTICALS

- **To liquid** mask **taste**.
- **Chewable tablets**, such as antacid and vitamin products, usually are **sweetened and flavored** to improve acceptance.
- Organic compounds: Increase number of **hydroxyl** groups (-OH) **increase sweetness** of compound.
- **Sucrose**(**8 -**OH), sweeter than **glycerin**(3-OH)
- In general: organic esters, alcohols, and aldehydes are pleasant to the taste
- volatile, affect odor and flavor of preparations

- **Many nitrogen-containing** (e.g., quinine) **bitter**, but other nitrogen-containing (e.g., **aspartame**) are **sweet**.
- Even **simple structural change alter taste**.
- D-Glucose is **sweet**, but L-glucose has slightly **salty.**

- **saccharin** is very **sweet** but **N-methyl-saccharin** is **tasteless**.

- **Selection of appropriate flavor depends on several factors:**

A: Taste of drug.

1. **cocoa-flavored** masking bitter.
2. Fruit or citrus flavors sour or acid-tasting.
3. cinnamon, orange, raspberry, make preparations of salty drugs
4.

- B: The age

1. **Children prefer sweet candy-like with fruity flavors.**
2. **Adults prefer less sweet with tart flavor**.
3. soybean and oils; carriers include water, ethanol, propylene glycol, glycerin, and emulsifiers.

Dry carriers include maltodextrins, corn syrup, modified starches, gum, salt, sugars, and whey protein.

Flavors degrade by **light, temp, oxygen, water, enzymes**

Artificial flavor: Any substance used to give flavor that is not derived from spice, fruit or fruit juice, vegetable or vegetable juice, herb, bark, bud, root, leaf eggs, dairy

SWEETENING PHARMACEUTICALS

- **saccharin** excreted **unchanged** by kidneys.
- **Cyclamate**, is **metabolized**, in GIT, and excreted by kidneys.
- **Aspartame** breaks down to three basic components: amino acids **phenylalanine** and **aspartic acid**, and **methanol**. are metabolized through regular pathways in the body.

- metabolism to phenylalanine.
- use of aspartame by persons with **phenylketonuria** (PKU) is discouraged.
- diet foods and drinks must bear label **warning** not be consumed by such individuals.
- They cannot metabolize phenylalanine adequately, so they undergo an increase in the serum levels of the amino acid (hyperphenylalaninemia). result in **mental retardation** and can affect the fetus of a pregnant woman who has PKU.

- Acesulfame potassium, a non nutritive sweetener Structurally similar to saccharin, it is 130 times as sweet as sucrose and is excreted unchanged in urine.

- **Acesulfame is more stable than aspartame at elevated temperatures** use in candy, chewing gum, and instant coffee and tea.

- Stevia powder30 times as sweet as sucrose.used in both hot and cold preparations.

COLORING PHARMACEUTICALS

- sulfur (yellow), riboflavin (yellow), cupric sulfate (blue), ferrous sulfate (bluish green), cyanocobalamin (red), and red mercuric iodide (vivid red).
- **most pharmaceutical colorants in use synthetic, a few are natural mineral and plant sources**.
- ferric oxide mixed with zinc oxide to give calamine pink color.
- 0.0005% to 0.001% FD&C, D&C, dyes or lake.
- **30 to 60 coats:tablet dyes**. With **lakes, fewer** color coats are used

- ointments, suppositories, and ophthalmic and parenteral products **assume the color of their ingredients and do not contain color additives.**

PRESERVATIVES

- **Ophthalmic and injectable preparations, sterilized by physical methods (autoclaving for 20 minutes at 15 lb pressure and 121°C, dry heat at 180°C for 1 hour, or bacterial filtration) during manufacture.**
- **syrups, emulsions, suspensions, and some semisolid creams** protected by addition of antimicrobial preservative
- **hydroalcoholic and most alcoholic preparations not require addition of preservative** when the alcoholic content is sufficient to prevent microbial growth.

- **15% V/V alcohol will prevent microbial growth in acid media and 18% V/V in alkaline media.**
- elixirs, spirits, and tinctures, are self-sterilizing and do not require additional preservation.

PRESERVATIVE SELECTION SHOULD

- **prevents growth** of microorganisms.
- **Soluble in water** to achieve adequate concentrations in aqueous phase.
- Concentration of preservative does not affect safety of patient.
- has **adequate stability** and not reduced in conc by decomposition during desired shelf life of preparation.
- **compatible** with all formulative ingredients.
- The preservative **does not advers**ely affect container or closure.

GENERAL PRESERVATIVE CONSIDERATIONS

- intravenous preparations given in large volumes as blood replenishers or nutrients not contain bacteriostatic additives.
- Microorganisms **molds, yeasts (acid** medium).**bacteria**favoring slightly **alkaline** medium.
- few microorganisms grow **below pH 3 or above pH 9**
- Aqueous preparations are within favorable pH range must be protected against microbial growth.

- Preservative must **dissolve in sufficient conc** in **aqueous phase** of preparation.
- , only **undissociated fraction** of preservative possesses preservative capability, because the ionized portion is incapable of penetrating the microorganism.
- preservative selected must be largely undissociated at pH of the formulation prepared.

- Acidic preservatives **benzoic**, **boric, and sorbic acids** more **undissociated** more effective as the medium is made more **acid.** Conversely, **alkaline preservatives** are less effective in acid or neutral media and more effective in **alkaline media**.
- if formula interfere with solubility or availability of preservative t, its chemical conc may **misleading**, because it may not be a true measure of the effective concentration.

- tragacanth, **attract and hold preservative**, such as the **parabens and phenolic** rendering them unavailable for preservative function.
- preservative **must not interact with container**, such as a metal ointment tube or a plastic medication bottle, or closure, such as a rubber or plastic cap or liner.

MODE OF ACTION

1. **Modification of cell membrane permeability**.
2. **Lysis and cytoplasmic leakage** Irreversible coagulation of cytoplasmic constituents (e.g., protein precipitation)
3. **Inhibition of cellular metabolism**, such as by interfering with enzyme systems or inhibition of cell wall synthesis
4. **Oxidation** of cellular constituents
5. **Hydrolysis**

PRESERVATIVES CONCENTRATIONS

- benzoic acid (**0.1% to 0.2%).**
- sodium benzoate (**0.1% to 0.2%)**
- alcohol (15% to 20%),
- phenol (0.1% to 0.5%),
- cresol (0.1% to 0.5%),
- benzalkonium chloride (**0.002% to 0.01%)**
- combinations of methylparaben and propylparaben (0.1% to 0.2)against fungus.

- **Preservative in ophthalmic preparation**

must have **low degree of irritant** qualities, like **chlorobutanol**, **benzalkonium** chloride.