PharmD IIIrd Yr

PHARMACEUTICAL FORMULATIONS

TABLET TYPES AND EXCIPIENTS

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TABLET EXCIPIENTS

These are the substances added in the manufacturing of tablet and perform following functions:

- IMPART WEIGHT, ACCURACY, & VOLUME
- IMPROVE SOLUBILITY
- INCREASE STABILITY
- ENHANCE BIOAVAILABILITY
- MODIFY DRUG RELEASE
- ASSIST PRODUCT IDENTIFICATION
- INCREASE PATIENT ACCEPTABILITY
- FACILITATE DOSAGE FORM DESIGN

1. DILUENTS

- Diluents are fillers used to make up required bulk of the tablet when the drug dosage itself is inadequate to produce the bulk.
- Provide better tablet properties such as improved cohesion or to promote flow.

PROPERTIES OF DILUENTS

1. They must be **non toxic**
2. They must be commercially available in **acceptable grade**.
3. Their **cost** must be low
4. They must be physiologically **inert**
5. They must be physically & chemically **stable** by themselves & in combination with the drugs.
6. They must be free from any unacceptable **microbial contamination**.
7. They must not be **contraindicated** by themselves and in comibation with the drug and other tablet components.
8. They must be **color compatible**.
9. They must have no deleterious effect on the **bioavailability** of drugs.

COMMONLY USED:

1. Lactose-anhydrous and spray dried lactose
2. Directly compressed starch
3. Hydrolyzed starch
4. Microcrystalline cellulose-Avicel
(2 grades: pH 101 and pH 102)
5. Dibasic calcium phosphate dehydrate
6. Calcium sulphate dihydrate
7. Mannitol
8. Sorbitol
9. Sucrose
10. Dextrose

2. Binders and Adhesives:

These materials are added either dry or in liquid form to form granules or to promote cohesive compacts for directly compressed tablet.

- **EXAMPLES:**

Natural gums:

Acacia, tragacanth - 10-25% Conc solution

Disadvantages:

- variable in composition and performance, based on their natural origin
- heavily contaminated with bacteria

Solution: When these materials are used, wet granulation masses should be quickly died at 37C to reduce microbial proliferation

- **Cellulose derivatives:** Methyl cellulose, Hydroxy propyl methyl cellulose, Hydroxy propyl cellulose

  Dry: binder properties

  Aqueous solutions: adhesive properties.

- **Natural protein:** Gelatin- 10-20% solution

  Advantage: more consistent material & easier to prepare in solution form.

- **Glucose:** 50% soln in water

  Advantage: low cost

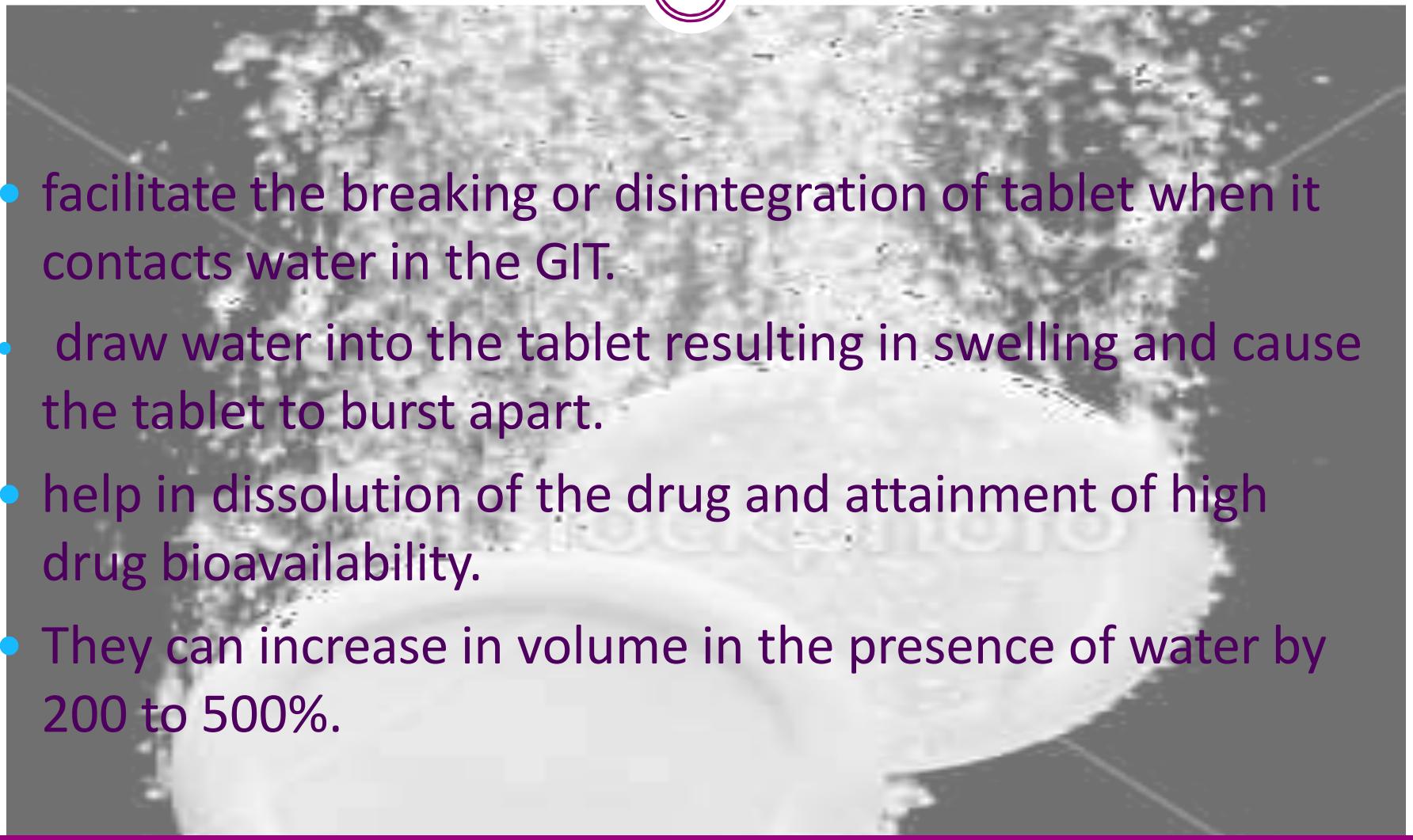
  Disadvantage: bacterial proliferation

- **Synthetic polymer:** Polyvinylpyrrolidone (PVP)- 2% conc.

- **Starch paste:** 10-20% soln

- **Sodium alginate**

3. Disintegrants

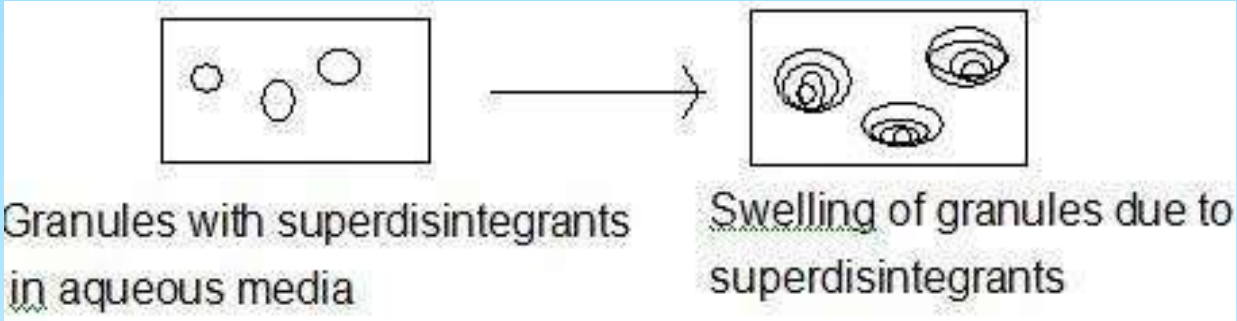


- facilitate the breaking or disintegration of tablet when it contacts water in the GIT.
- draw water into the tablet resulting in swelling and cause the tablet to burst apart.
- help in dissolution of the drug and attainment of high drug bioavailability.
- They can increase in volume in the presence of water by 200 to 500%.

- **Examples:**
- Starch- 5-20% of tablet weight.
- Starch derivatives – low substituted carbo
  1-8% concentration. 4% usually optimun
- Pre-gelatinized starches (5%)
- Clays- Veegum HV and bentonite (10%)
- Microcrystalline cellulose
- Cellulose derivatives- Ac- Di-Sol (internally cross linked sodium carboxymethylcellulose)
- PVP (cross-linked polyvinylpyrrolidone)

Superdisintegrants:

Swells up to ten folds within 30 seconds when contact water.



- **Examples:**

Crosscarmellose- cross-linked cellulose

Crosspovidone- cross-linked povidone (polymer)

Sodium starch glycolate- cross-linked starch.

4. Lubricants, Antiadherents and Glidants:

- **Lubricants** are intended to reduce the friction during tablet ejection between the walls of the tablet and the walls of the die cavity in which the tablet was formed.
- **Antiadherents** are intended to reduce sticking or adhersion of tablet granulation or powder to the faces of the punches or to the die walls.
- **Glidants** are intended to promote flow of granules or powder material by reducing the friction between the particles.

Lubricants:

-Stearic acid salts – Calcium and Magnesium stearate

- Stearic acid – it is less effective lubricant than stearic acid salts and also has a lower melting point.

-Talc – it contains trace quantities of iron, therefore it should be considered carefully.

-PEG-- The finer the particle size of the lubricant, the more effective the lubricant action.

- Antiadherents:

Starch, talc , magnesium stearate

- Glidants:

Corn Starch – 5-10% conc.

Talc- 5% conc

Silica derivatives - Colloidal silicas such as Cab-O- Sil in 0.25-3% conc.

5. Coloring agents:

PURPOSE:

(1) Masking of color drugs

(2) Product Identification

(3) Production of more elegant product

•All coloring agents must be approved and certified by FDA.

Two forms of colors t preparation –

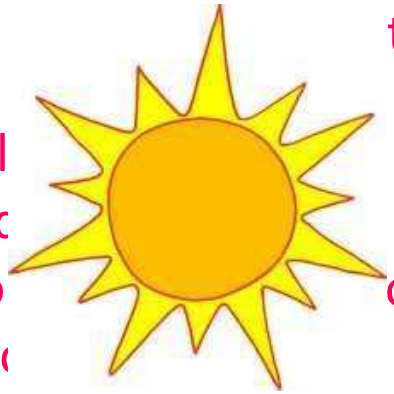
FD &C and D & C

These dyes are appl the granulating agent or

Lake form of these c

Lakes are dyes abso oxide and employed as

dry powders for col



• **Example:**

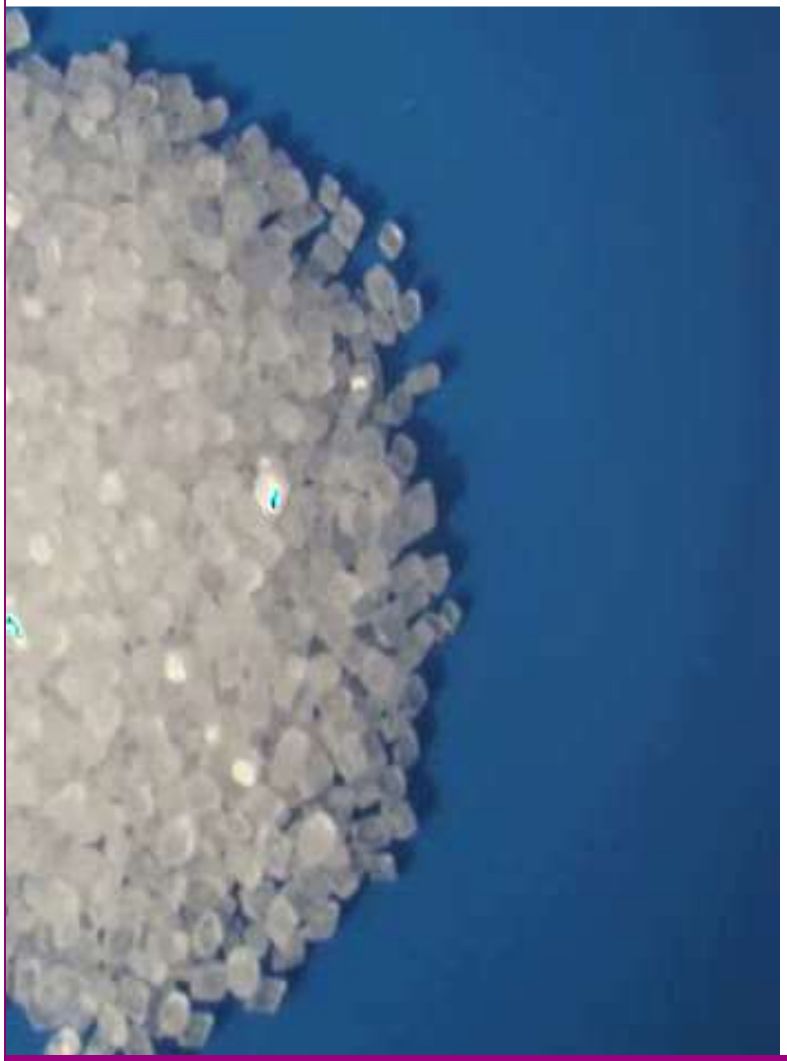
FD & C blue 2 - Indigo carmine

In any colored tablet, the formulation should be checked for resistance to color changes on exposure to light.

6. Flavoring agents:

- Used in chewable tablets or tablets intended to dissolve in mouth.
- Flavor oils are used and are added to tablet granulations in solvents, are dispersed on clays and other absorbents or emulsified in aqueous granulating agent.
- The maximum amount of oil that can be added is 0.5 -0.75%.

7. Sweetening agents:



Used only in chewable tablets to exclude or limit the use of sugar in the tablets.

Examples:

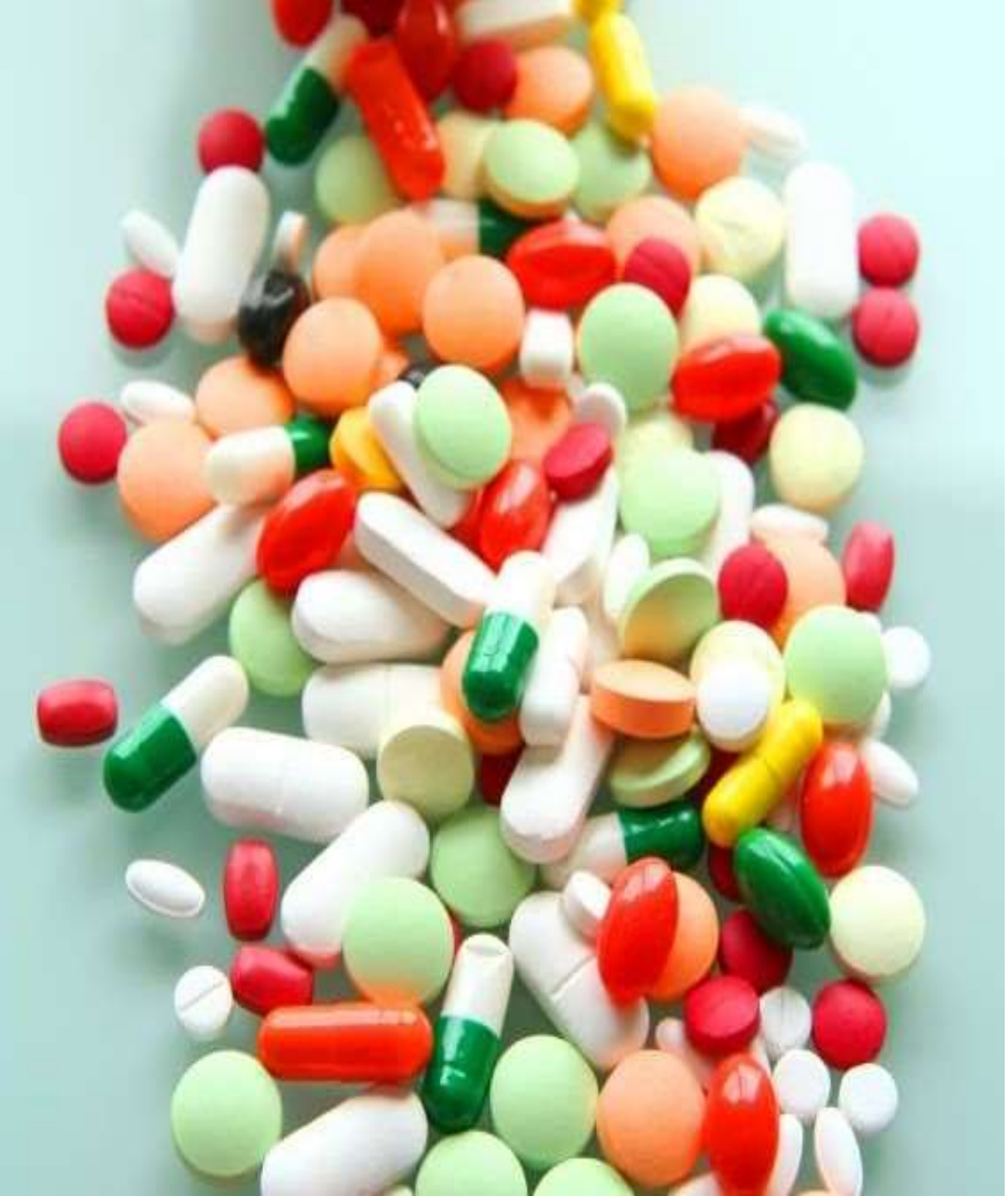
- Saccharine (artificial): 500 times sweeter than sucrose

  Disadvantage: Bitter after taste and carcinogenic

- Aspartame (artificial):

  Disadvantage: Lack of stability in presence of moisture.

- Mannitol



TYPES & CLASSES OF TABLETS

CLASSIFICATION

TABLETS ARE CLASSIFIED ON THE BASIS OF:

-ROUTE OF ADMINISTRATION OR FUNCTION

-TYPE OF DRUG DELIVERYSYSTEM THEY REPRESENT WITHIN THAT ROUTE

- FORM AND METHOD OF MANUFACTURE

1.ORALLY INGESTED TABLETS:

- Over 90% of tablets manufactured are ingested orally.
- These are designed to be swallowed intact, with exception of chewable tablets.

Compressed Tablets or Standard Compressed Tablets:

- These are standard uncoated tablets made by compression using wet granulation, direct compression or double compression.
- Provide rapid disintegration & drug release.
- Mostly intended to exert local action in GIT.
- Typically include water insoluble drugs such as antacids and adsorbents.
- Other drugs having systemic effect have some aqueous solubility, dissolve from tablet and disintntegrate tablet fragments in GI contents and are then absorbed and distributed in the body.

Multiple Compressed Tablets:

There are 2 classes of multiple compressed tablets:

1. layered tablets
2. compression coated tablets

-Both types may be either two component or three component systems: two or three layer tablets, a tablet within a tablet or a tablet within a tablet within a tablet.

-Both types usually undergo a light compression as each component is laid down, with the main compression being the final one.

-The layered tablet is preferred to the compression coated tablet because surface contact between layers is lessened and production is simpler and more rapid.

ADVANTAGES:

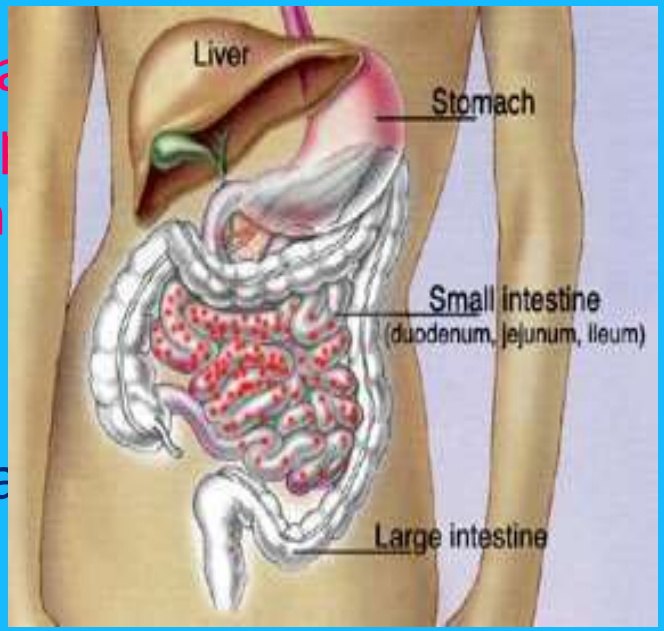
-Separate physically or chemically incompatible ingredients.

-Produce prolonged action products.

Delayed Action and Enteric Coated Tablets:

- Delayed action tablets are intended to release a drug after some delay or after the tablet has passed through one part of GI tract into other.
- The enteric coated tablet is the most common example of a delayed action type product.
- The **polymers** used in enteric coating a insoluble in gastric media that have a p dissolving as the tablets enter duoden

- Cellulose acetate phthalate
- Polyvinylacetate phthalate
- Hydroxypropylmethyl cellulose phthala



Advantages:

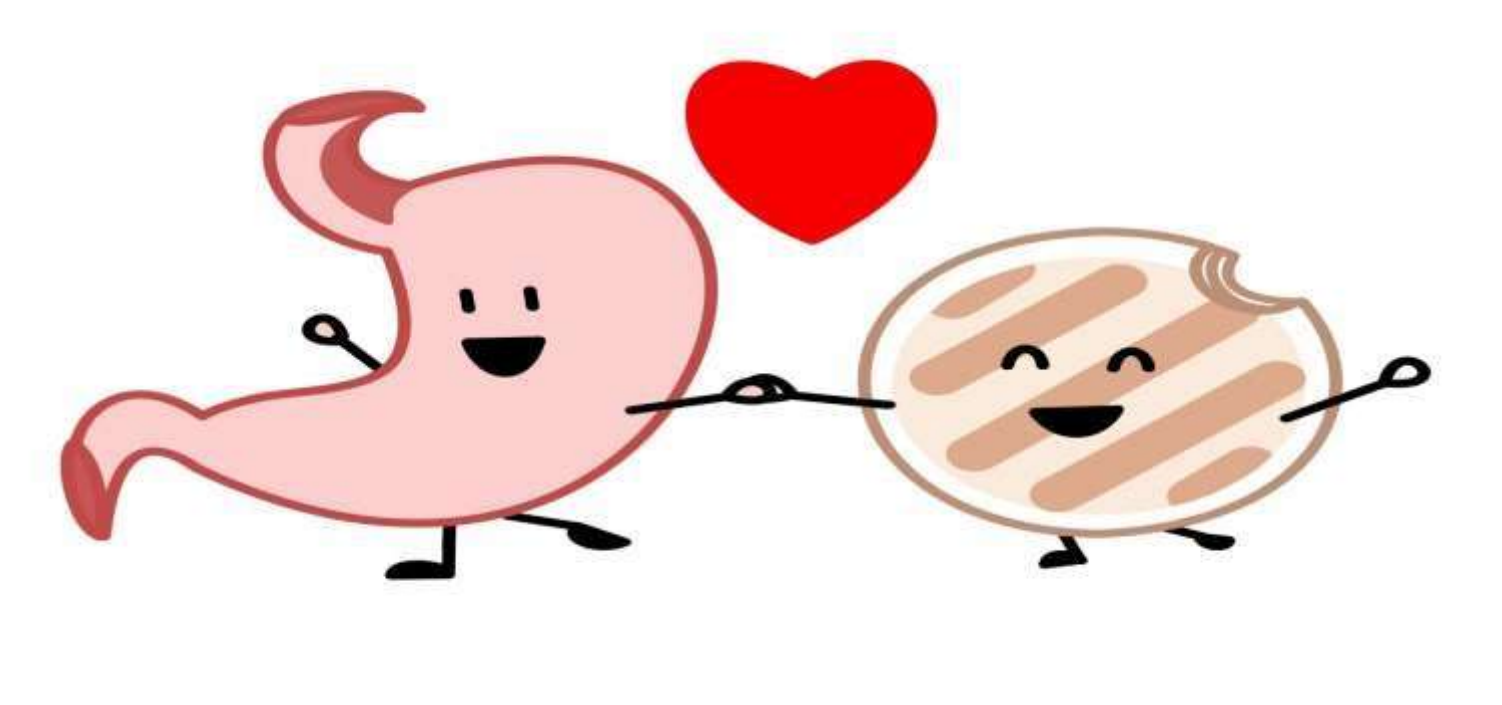
Enteric coated tablets are used for drugs such as:

-Drugs irritating to gastric mucosa which include aspirin and strong electrolytes such as NH4CL.

- Drugs that are destroyed by low pH of stomach

- Drugs that cause nausea and vomiting if released in stomach

-Drugs that are to be released undiluted and in highest possible concentration within intestine



Sugar-coated Tablets:

- an elegant, glossy, easy-to-swallow tablet dosage form.
- they permit separation of incompatible ingredients between coating and core, and utilized in preparing many multivitamin and multivitamin mineral combinations.

Disadvantages:

- The process is time consuming and require skilled coating artisans.
- Sugar coatings typically double tablet weight.
- They are easily mistaken for a candy by children.

The use of water soluble polymers, automated-spray coating equipment, and high-drying-efficiency sidevented coating pans have greatly reduced some of these disadvantages, resulting in:

- more elastic and mechanically stable coatings
- coat weight may be 50% or less of the core weight
- the process may be completed in a day or less.

Film-Coated Tablets:

-These are an alternative to sugar coated tablets in which drug is not required in the coating.

-The film coating composition consists of one or more polymers, a plasticizer for the polymer and a surfactant, all delivered to the tablets in solution from an organic or aqueous solvent.

Polymers used: hydroxypropyl cellulose, hydroxypropyl, methylcellulose, 30% ethylcellulose dispersion (Aquacoat),

Advantages:

- tasteless.
- tablet coating operation takes only one or two hours.
- better mechanical strength of the coating based on elasticity & flexibility of polymer coating.
- little increase in tablet weight than sugar-coated
- ability to retain debossed markings on the tablet
- avoidance of sugar, which is contraindicated in diet of some people.

Disadvantages:

- less attractive and elegant in physical appearance than sugar coated.

Chewable Tablets:

Intended to be chewed in the mouth prior to swallowing and are not intended to be swallowed intact.

Examples:

-Chewable aspirin tablet for children use.

-Antacid tablet

Advantage:

provide a unit dosage form of medication whic
can be easily administered to infants and children
or to the elderly, who may have difficulty swallowing a tablet intact.

Disadvantage:

Bitter or foul tasting drugs can not be given by this dosage form

2. TABLETS USED IN THE ORAL CAVITY

Buccal and Sublingual tablets:

•Small, flat tablets, intended to be held between cheek and teeth or in the cheek pouch (buccal tablets) or beneath the tongue (sublingual tablets).
•Release drug contents for absorption directly through oral mucosa.
•Designed not to disintegrate but to slowly dissolve, over a 15 to 30 min period.
•Produce systemic drug effects as the drug is absorbed from oral mucosa to directly to general circula
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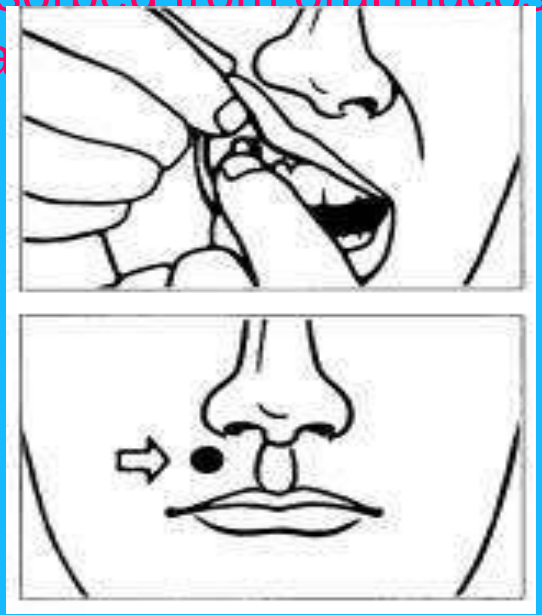


TROCHES AND LOZENGES:

- Disc shaped solid dosage forms containing **medicinal agent** & **flavoring substance** in a hard candy or sugar base.
- Intended to exert a **local effect** in the mouth or throat.
- Commonly used to treat **sore throat** or to control coughing in normal cold.
- May contain local anesthetics, antiseptics, antibacterials, demulcents, astringents and antitussives.
- Designed not to disintegrate but to dissolve or slowly erode over a period of **30 min** or less in mouth.
- Lozenges: also called pastilles or cough drops. They may be made by compression but are usually formed by fusion or by a candy-molding machine.
- Troches: are made by compression.

DENTAL CONES:

-Designed to be placed in the empty socket remaining following a tooth extraction.

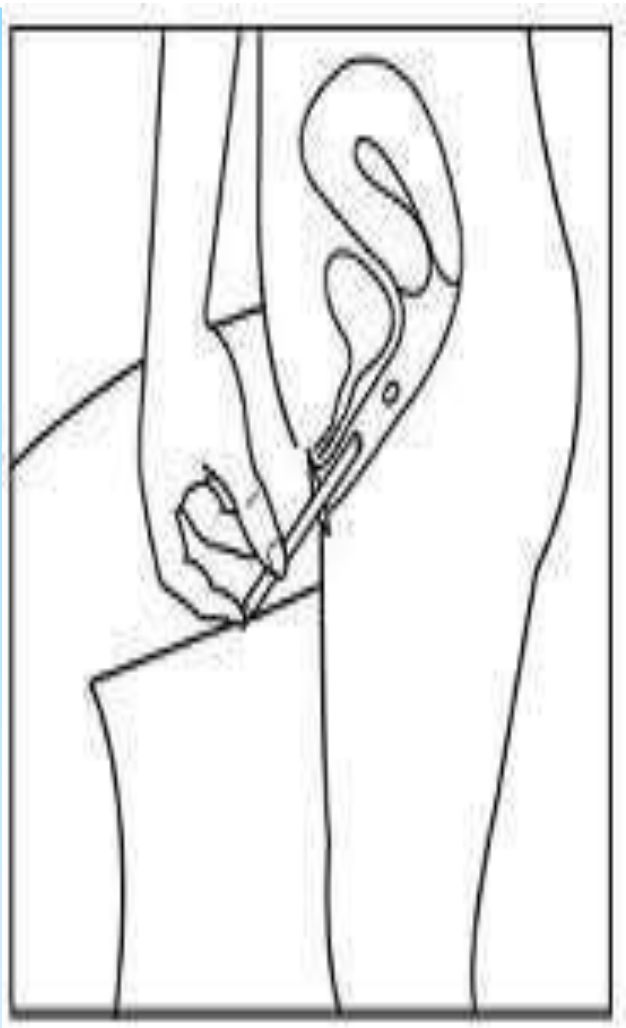
-It is formulated to dissolve slowly in presence of a small volume of serum/ fluid over a 20 or 40 min period.

Uses:

-To prevent multiplication of bacteria in the socket by employing a slow releasing antibacterial.

-To reduce bleeding by containing an astringent or amino acid.

3. TABLETS ADMINISTERED BY OTHER ROUTES

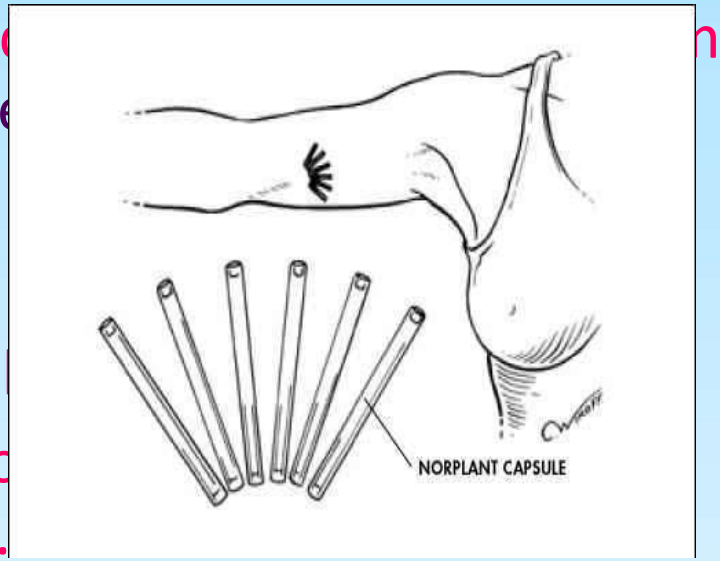


Vaginal tablets / Inserts:

- Uncoated **bullet shaped or ovoid** tablets.
- Designed to undergo **slow dissolution** and drug release in vaginal cavity.
- It may contain antibacterials, antiseptics or astringents to treat vaginal infections such as vaginitis or antifungals to treat fungal infections such as candidiasis or to release steroids for systemic absorption.
- often buffered to promote pH favorable to action of an antiseptic agent.
- Placed in the upper region of vaginal tract by plastic tube inserter.

Implantation/Depot Tablets:

- Small, cylindric or rossete shaped forms, not more than 8mm in length.
- Designed for subcutaneous implantation.
- Provide as constant a drug delivery rate as possible.
- Provide prolonge
  one month to a ye
-
- **Disadvantages:**
- It has safety probl
- Tissue toxicity pro
  implantation site.



4.TABLETS USED TO PREPARE SOLUTIONS:

Effervescent Tablets:

- Designed to produce a solution rapidly with the simultaneous release of CO_2.
  prepared by compressing the active ingredients with mixtures of organic acids such as citric acid or tartaric acid and $NaHCO_3$.
- When such a tablet is dropped into a glass of water, a chemical reaction is initiated between the acid and $NaHCO_3$ to form sodium salt of the acid and to produce CO_2 in water. The reaction is quite rapid and is usually completed within in one minute or less.
- The are packed in hermetic-type foil pouches or are stack-packed in cylindrical tubes with minimal air space.

Examples: Aspirin , saline cathartics

Advantages:

- Provide a mean of extemporaneously preparing a solution containing accurate drug dose.
- They produce pleasantly flavored carbonated drink which assists in masking the taste of certain drugs.

Disadvantages:

- Difficulty of producing a chemically stable product.
- Moisture in air during product preparation may be adequate to initiate effervescent reactivity.
- During the course of reaction, water is liberated which autocatalyzes the reaction.
- Compression of tablet in the hands of the consumer.

Dispensing Tablets:

- Intended to be added to a given volume of water by the pharmacist or the consumer, to produce a solution of a given drug concentration.
- Materials incorporated in dispensing tablets include mild silver proteinate, bichloride of mercury and quarternary ammonium compounds.

Disadvantages:

- Difficuty with dispensing tablets is that some of the components previously used in this dosage form are highly toxic and extremely hazardous and even lethal if mistakenly swallowed.
- Inavailability of sterile water to produce sterile solutions.

Hypodermic Tablets:

They are composed of one or more drugs with other readily soluble water soluble ingredients and are intended to be added to sterile water or WFI.

Advantage:

The physician can carry many vials of tablets in his bag with only one bottle of sterile WFI.

Disadvantage:

The likelihood of administering a nonsterile solution, even though portable sterile filteration equipment exists to help assure sterility.

Tablet Triturates:

- Small, usually cylindric molded or compressed tablets.
- Provide **extemporaneous** method of preparation by the pharmacist.
- The drugs used were potent and mixed with lactose and a binder such as powdered acaia, after which the mixture was moistened to produce a moldable, compactable mass. This mass was forced into holes of a mold board wood or plastic, after which tablets were ejected using a peg board, whose pegs matched the holes in the mold, dried and dispensed.

Disadvantages:

- Unreliable bioavailability.
- Poor content uniformity of tablets containing potent drugs.