MODULE 2:Tablets

Lecture 2

DISCLAIMER

All the content material provided here is only for teaching purpose

Tablet Ingredients

In addition to active ingredients, tablet contains a number of inert materials known as additives or excipients. Different excipients are:

1. Diluent
2. Binder and adhesive
3. Disintegrents
4. Lubricants and glidants
5. Colouring agents
6. Flavoring agents
7. Sweetening agents

EXCIEPIENTS

- Impart weight, accuracy, & volume(its allow acccuracy of dose)
- Improve solubility
- Increase stability
- Enhance bioavailability
- Modifying drug release
- Assist pdt identification
- Increase patient acceptability
- Facilitate dosage form design

Excipient functions

Component	Function	Examples
Fillers	Increase size and weight of final dosage form	Microcrystalline cellulose, sucrose
Binders	Promote particle aggregation	Pregelatinized starch, hydroxypropyl methylcellulose
Disintegrants	Promote break down of aggregates	Sodium starch glycolate
Flow Aids	Reduce interaction between particles	Talc
Lubricants	Reduce interactions between particles and surfaces of processing equipment	Magnesium stearate
Surfactants	Promotes wetting	Sodium lauryl sulfate, Polysorbate
Modified Release Agents	Influences the release of active	Hydroxypropyl methylcellulose, Surelease,

1. **Diluent:** Diluents are fillers used to make required bulk of the tablet when the drug dosage itself is inadequate to produce the bulk. Secondary reason is to provide better tablet properties such as improve cohesion, to permit use of direct compression manufacturing or to promote flow.

A diluent should have following properties:

1. They must be non toxic
2. They must be commercially available in acceptable grade
3. There 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 all microbial contamination.
7. They do not alter the **bioavailability of drug.**
8. They must be color compatible.

Commonly used tablet diluents

1. Lactose-anhydrous and spray dried lactose
2. Directly compressed starch-Sta Rx 1500
3. Hydrolyzed starch-Emdex and Celutab
4. Microcrystalline cellulose-Avicel (PH 101and PH 102)
5. Dibasic calcium phosphate dehydrate
6. Calcium sulphate dihydrate
7. Mannitol
8. Sorbitol
9. Sucrose- Sugartab, DiPac, Nutab
10. Dextrose

2. Binders and Adhesives: These materials are added either dry or in wet-form to form granules or to form cohesive compacts for directly compressed tablet.

Example:

- Acacia, tragacanth- Solution for 10-25% Conc.
- Cellulose derivatives- Methyl cellulose, Hydroxy propyl methyl cellulose, Hydroxy propyl cellulose
- Gelatin- 10-20% solution
- Glucose- 50% solution
- Polyvinylpyrrolidone (PVP)- 2% conc.
- Starch paste-10-20% solution
- Sodium alginate
- Sorbitol

3. Disintegrants: Added to a tablet formulation to facilitate its breaking or disintegration when it contact in water in the GIT.

Example:

- Starch- 5-20% of tablet weight.
- Starch derivative – Primogel and Explotab (1-8%)
- Clays- Veegum HV, bentonite 10% level in colored tablet only
- Cellulose
- Cellulose derivatives- Ac- Di-Sol (sodium carboxy methyl cellulose)
- Alginate
- PVP (Polyvinylpyrrolidone), cross-linked

4. Superdisintegrants: Swells up to ten fold within 30 seconds when contact water.

Example:

- Crosscarmellose- cross-linked cellulose, Crosspovidone- cross-linked povidone (polymer), Sodium starch glycolate- cross-linked starch. These cross-linked products swells with in 30 seconds when in contact with water.
- A portion of disintegrant is added before granulation and a portion before compression, which serve as **glidants or lubricant.**

5. Lubricant and Glidants: Lubricants are intended to prevent adhesion of the tablet materials to the surface of dies and punches, reduce inter particle friction and may improve the rate of flow of the tablet granulation.

Glidants are intended to promote flow of granules or powder material by reducing the friction between the particles.

Example:

- Lubricants- Stearic acid, Stearic acid salt - Stearic acid, Magnesium stearate, Talc, PEG (Polyethylene glycols), Surfactants
- Glidants- Corn Starch –5-10% conc., Talc-5% conc., Silica derivative - Colloidal silicas such as Cab-O-Sil, Syloid, Aerosil in 0.25-3% conc.

6. Coloring agent: The use of colors and dyes in a tablet has three purposes:

(1) Masking of off 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 are used in tablet preparation – FD &C and D & C dyes. These dyes are applied as solution in the granulating agent or Lake form of these dyes. Lakes are dyes absorbed on hydrous oxide and employed as dry powder coloring.

7. Flavoring agents: For chewable tablet- flavor oil are used

8. Sweetening agents: For chewable tablets: Sugar, mannitol.

- Saccharine (artificial): 500 time's sweeter than sucrose
- Disadvantage: Bitter aftertaste and carcinogenic
- Aspartame (artificial)
- Disadvantage: Lack of stability in presence of moisture.

9. Wetting Agents

- Water molecules attract each other equally in all directions. Water molecules on the surface, however, can only be pulled into the bulk water by water molecules underneath, since there are no water molecules to pull in the opposite direction. The surface tension of water is strong enough to support the weight of tiny insects such as water striders.

- The surface tension in action can be visualized by placing a small drop of alcohol on a thin layer of water. Alcohol with lower surface tension mixes with water causing reduction in the surface tension in the local region. Owing to the higher surface tension of water in the neighbor, water is pulled from the alcohol dropped region into the neighbor, and this leads to the formation of a dry spot in the middle of the water layer.

Lactose

- Two forms of lactose are anhydrous or hydrous form
- Hydrous form undergoes maillard reaction leading to browning and discoloration of certain drugs, hence anhydrous form is preferred.
- But anhydrous form picks up moisture when exposed to humidity.
- In wet granulation, hydrous lactose of two varieties are used 60-80 mesh (coarse) and 80-100 mesh (regular) grade.
- Lactose formulation show good release.
- Low cost diluent.
- But may discolor in presence of amine drug bases or salts of alkaline compounds

Spray dried lactose

- Lactose is placed in aqueous solution, removed impurities and spray dried
- Mixture of large alpha monohydrate crystals and spherical aggregates of smaller crystals
- Good flowability but less compressibility
- Poor dilution potential
- Less compressibility upon initial compaction
- Problem of browning due to contamination of 5-hydroxyfurfural which was accelerated in the presence of basic amine drugs and catalyzed by tartarate, citrate and acetate ions

- Fast-Flow lactose (early 1970s)
  - Spherical aggregates of microcrystals lactose monohydrate
  - Held together by a higher concentration of glass (amorphous lactose)
  - Much more compressible
  - Highly fluid
  - Non hygroscopic
  - Tablets are three to four times harder than regular spray dried

- Tabletose: aggromerate form of lactose
  - More compressible than spray dried but less compressible than Fast Flo lactose

Starch

- Can be corn, wheat or potatosource
- USP grade of starch has poor flow & compression characteristics
- Also has high moisture content between between 11& 14 %.
- Specially dried starches also have standard moisture level of 2-4%
- Therefore used in wet granulation

Dextrose

- 90-92% dextrose, 3-5% maltose and the remainder higher glucose polysaccharides
- Available both anhydrous and a hydrate product
- Excellent compressibility and good flow
- Contain 8-10% moisture and may increase hardness after compression
- Largest particle size, therefore blending problem may occur
- Cerelose is also avilable

Powders intended for compression into tablets must possess two essential properties

- **Powder fluidity or flowability**
  - The material can be transported through the hopper into the die
  - To produce tablets of a consistent weight
  - Powder flow can be improved mechanically by the use of vibrators, incorporate the glidant
- **Powder compressibility**
  - The property of forming a stable, intact compact mass when pressure is applied is called powder compressibility
- **Easily mixed with other particles**
- **Homogenous colouring etc**
- **Friction and adhesion properties**

- **Single punch machine**
- **Multi-station rotary presses**
- The head of the tablet machine that holds the upper punches, dies and lower punches in place rotates
- As the head rotates, the punches are guided up and down by fixed cam tracks, which control the sequence of filling, compression and ejection.
- The portions of the head that hold the upper and lower punches are called the upper and lower turrets
- The portion holding the dies is called the die table

- The upper punches enter a fixed distance into the dies, while the lower punches are raised to squeeze and compact the granulation within the dies
- After the moment of compression, the upper punches are withdrawn as they follow the upper punch raising cam (H)
- The lower punches ride up the cam (I) which brings the tablets flush with or slightly above the surface of the dies
- The tablets strike a sweep off blade affixed to the front of the feed frame (A) and slide down a chute into a receptacle
- At the same time, the lower punches re-enter the pull down cam (C) and the cycle is repeated

References

- The theory and practice of Industrial pharmacy, by Leon Lachmann and Herbert A.Lieberman,3rd edition, Page no: 294 to 336.
- The science and practice of pharmacy by Remington, Volume I, Page no: 905 to 916.
- Indian pharmacopoeia 2010, volume-2, Page no: 751 to 754.