LAB.2

Tablet Production Methods

Direct compression

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Tablet production methods

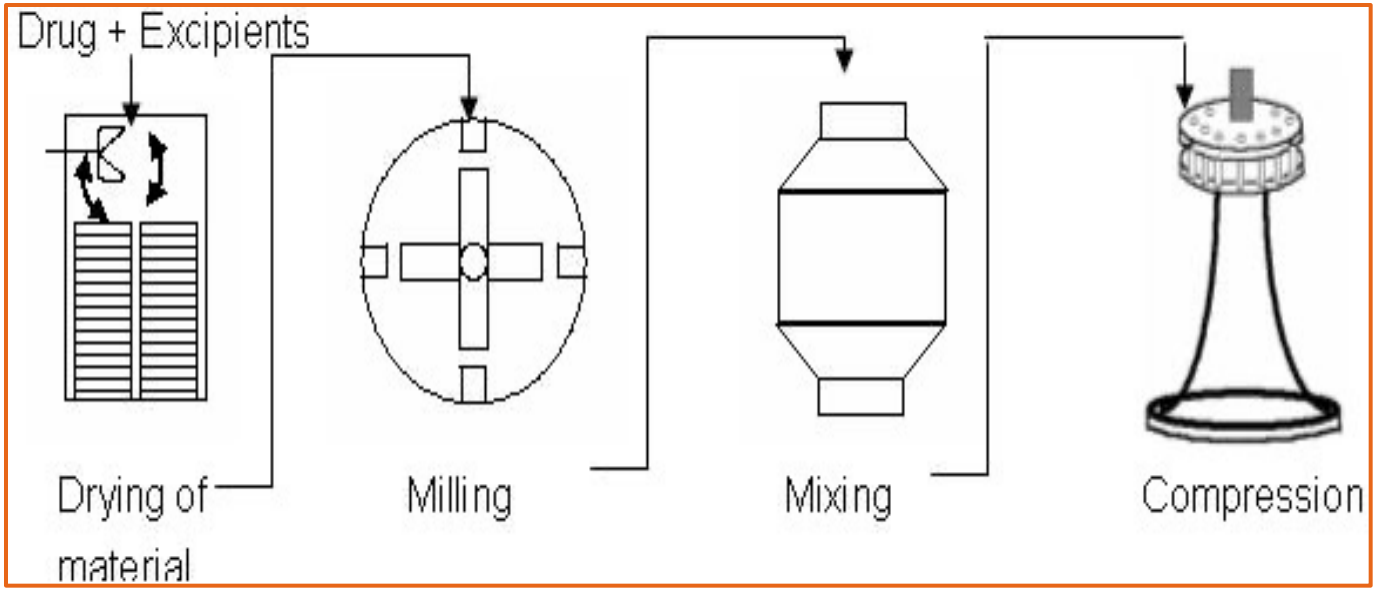
- There are three methods of tablet manufacture designed to confer these essential attributes to a tablet formulation.
- Wet granulation and direct compression are the most important, with

dry granulation used in some circumstances

- **Regardless whether tablets are made by direct compression or granulation, the first step, milling and mixing, is the same; subsequent step differ.**

Direct compression

- Direct compression is the easiest and most cost-effective process for tablet manufacturing, because it only involves blending and compression.
- Consists of compressing the substances together with any substance of physical property enable to compress directly with good flowability.
- A crystalline structure, is more easily to compress than amorphous form because of the creation of certain cohesive bonds between crystals due to the pressure of compression, whereas in amorphous form it will not.
- Addition of a disintegrant to the formulation will aid to avoid the major problems in disintegration like (long time dissolution and melting).


Drug + Excipients
Drying of material
Milling
Mixing
Compression

- Not all materials can be easily or directly compressed:
  1. Most materials having weak intermolecular attracting forces.
  2. Materials are covered with a film of adsorbed gas that hinder compaction.
  3. Large doses drugs do not lend themselves to this technique due to:

     Need of additives in a ratio of 1:1 for e.g. active constituent 500mg and diluent 500mg so will form (large tab., costly, difficult to swallow and not accepted by patients).
  4. Small doses drugs can't be compressed directly like digoxin because there may be not sure to distribute uniformly.

Ideal direct compression excipients:

It is important to note that many excipients can possess multi-functionality, which is dependent upon the concentration at which they are employed. For example, microcrystalline cellulose can be used as an anti-adherent (5–20%), a disintegrant (5–15%) and as a diluent (20–90%).

- Flowability
- Stable, inert, compatible
- Compressibility
- Particle size should be of high range, to meet the particle size of the drug (be close to it) Otherwise segregation (demixing) will occur leading to lack of content uniformity
- Low cost
- Provide high pressure-hardness profile.

Advantages of Direct Compression:

- Requires fewer unit operations compared with wet granulation (shorter processing time and lower energy consumption)
- Fewer stability issues for actives that are sensitive to heat or moisture
- For certain compounds, faster dissolution rates may be generated from tablets prepared by direct compression compared with wet granulation; for example, norfloxacin
- Fewer excipients may be needed in a direct compression formula

Disadvantages of Direct Compression

- Issues with segregation – these can be reduced by matching the particle size and density of the active drug substance with excipients

- Reactions of excipients with the drug like reaction of spray dry lactose with amine resulting in yellowish discoloration while the original color is brown (incompatibility).

- In general, the drug content is limited to approximately 30% or approximately 50 mg.

- May not be applicable for materials possessing a low bulk density because after compression the tablets produced may be too thin.

- Not suited for poorly flowing drug compounds.

- Static charges may develop on the drug particles or excipients during mixing, which may lead to agglomeration of particles producing poor mixing.

Experiment Part

Aim of experiment :

Preparation of aspirin tablets by direct compression

Preformulation test:

1. Organoleptic properties
   a) (crystalline –tubular or needle shape)
   b) Bitter or slightly acidic taste
   c) Odorless or have odor *due to formation of acetic acid and S.A. in the presence of moisture*.

2. Solubility

- Slightly soluble in water (1:300), highly soluble in organic solvent (1:5-7 alcohol, 2:10-17 ether, 1:17 chloroform).
- P.C. high (high solubility in lipids) and thus having good absorption in GIT wall so it is highly absorbed from stomach but also having good absorption from small intestine due to large surface area.

3. Stability

- (unstable in water) due to decomposition (hydrolysis) so it dissolves in aq. solution of carbonate and alkali hydroxyl with decomposition

Formula

- Aspirin 75mg (active constituent)
- Starch 3mg (disintegrant)
- Lactose 40mg (diluent)
- Mg stearate 2mg (Lubricant)

1. Mix all ingredients together after weighing (aspirin, disintegrant , diluent) for 15 minutes
2. Then add the lubricant and mix for not more than 5 minutes
3. Directly compress

Question : lubricant is added at last step . Why?

Thank you