Lecture 6

CAPSULES

Hard gelatin Capsule

CAPSULES

- Solid dosage form
- The drug is enclosed within either a hard or soft shell.

shell is typically made of gelatin blends (gelatin, sugar and water), small amount of certified dyes, opaquants, plasticizers and preservatives.

Advantages

- Elegance, ease of use and portability
- Provide a smooth, slippery, easily swallowed and tasteless shell for drugs (having unpleasant taste or odor).
- Produce ready availability of the contained drug.

Disadvantages

Not usually used for administration of extremely soluble materials such as potassium chloride, potassium bromide and ammonium chloride since sudden release of such compounds (fluids) from capsule could results in irritating the stomach (N & V) by dissolving the salt and creating highly concentrated solution.

Not suitable containers for efflorescent materials (powders that contain water of hydration that dissolve gelatin when water is lost) especially when stored in low humidity conditions. Such as codeine phosphate.

Not to be used for deliquescent materials (adsorb or hygroscopic powders) since they may dry the capsule shell to excessive brittleness when moisture is extracted from shell into the powder to dissolve it and form solution. Such as phenobarbital sodium.

MATERIALS

- Capsules made from methylcellulose, PVA, and denatured gelatin to modify their solubility or produce enteric effect.
- Gelatin is a heterogeneous product derived by irreversible hydrolytic extraction of treated animal collagen.
- Common sources of collagen are animal bones, and frozen pork skin.

There are two main types of gelatin:

- Type A: Derived from an acid treated precursor and exhibits an isoelectric point (with zero electrophoretic mobility related with pH and physical properties of gelatin molecules in solution) in the region of pH (9).
- Type B: Derived from alkali treated precursor and exhibit isoelectric point in the region of pH (4.7).
- Capsule may be made from both types of gelatin or as available and difference in physical properties of either types are slight.

√ Blends of bone and pork skin gelatins of relatively high gel strength are normally used for hard capsule production.

√ The bone gelatin produces tough , firm film but tend to be hazy and brittle.

√ The pork skin gelatin contributes to plasticity and clarity to the blend , reducing haze or cloudiness in the finished capsule.

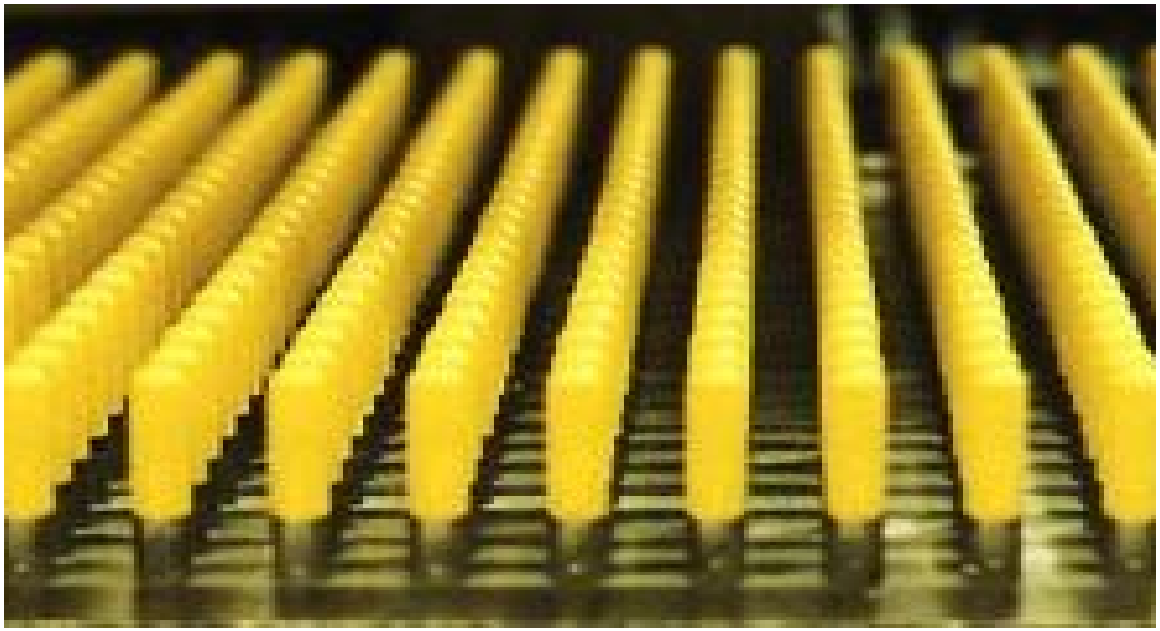
HARD CAPSULES

Method of production

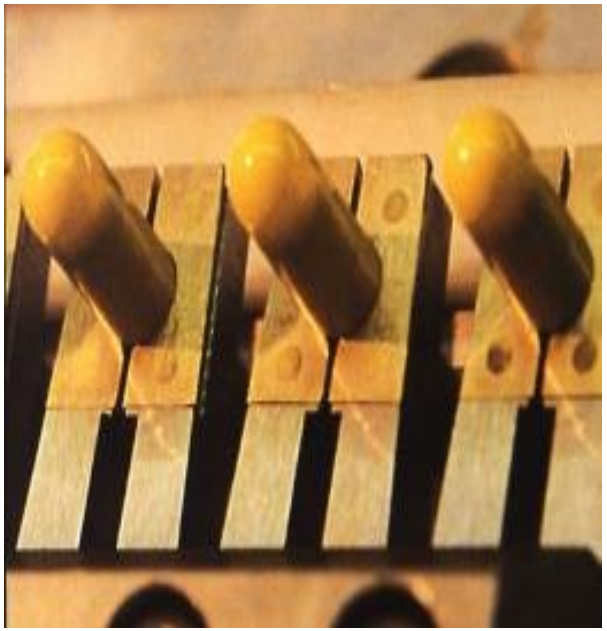
Empty gelatin capsules are produced by completely automatic machine consists of mechanisms for automatically dipping, spinning, drying, stripping, trimming and joining the capsules.

- Dipping : Pairs of stainless steel mold pins are dipped into a gelatin solution of controlled viscosity to form caps and bodies .

- Spinning : Pins are usually rotated to distribute gelatin uniformly, during which the gelatin may be set or gelled by a blast of cool air.



- Drying: Pins are moved through a series of controlled air drying kilns (Ovens) for the gradual and precisely controlled removal of water



- Stripping : The capsules are stripped from the pins by bronze jaws.
- Trimming : The capsules are trimmed to length by stationary knives

- Joining : the cap and body are joined and ejected from the machine .
- The entire cycle take 45 min.

√ Thickness of the capsule wall is controlled by :

- Viscosity of the gelatin solution
- Speed and time of dipping

√ Other matters critical to the final dimensions are:

- mold pin dimensions,
- precise drying
- and machine control relating to cut length.

Moisture content in capsules:

√ Empty capsules are usually received moisture content between 12% and 15%.

√ Below 10% moisture content, they become brittle and may shrink to the point of no fitting into the filling equipment.

√ Above 16% moisture content, they may cause problems in the filling equipment, plus a loss of mechanical strength.

Filling Equipments

FILLING OF HARD GELATIN CAPSULES

Various Filling Machine Available...

- Eli-lily and Co.
- Farmatic.
- Hofliger and Karg.
- Zanasi.
- Parke-Davis.

- These machine differ in there design and output

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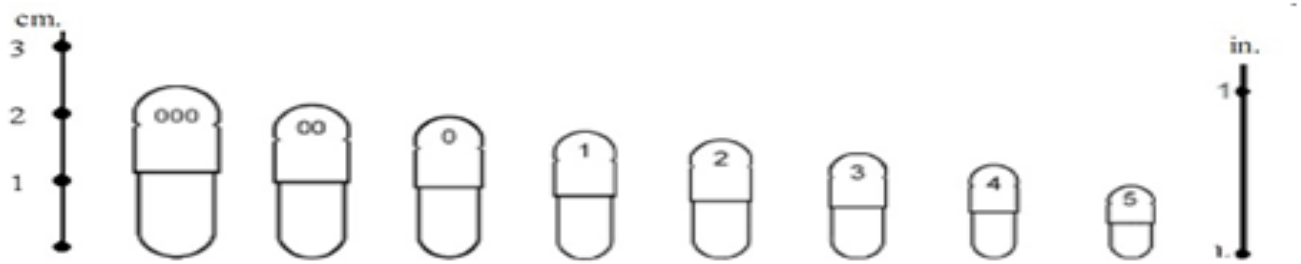
ZANASI AUTOMATIC
CAPSULE FILLING MACHINE

HOFLIGER KARG AUTOMATIC
CAPSULE FILLING MACHINE

SHAPES OF CAPLUSE



*The largest size of the capsule is No: 000.
*The smallest size is No: 5.
*The standard shape of capsules is traditional, symmetrical bullet shape.

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Mostly used capsule sizes for humans range from size 0; the largest to size 5; the smallest.

Formulations

The problems encountered in handling powders during mixing and filling are diverse. Two major ones can be listed:

1. After the powder ingredients have been homogenously blended by a suitable technique, the flow of the resultant mixture must be adequate to ensure delivery of sufficient powder to the capsules at the time of filling .
2. Physical incompatibilities between active ingredients, diluents or between active ingredients and/or diluents and the capsule shell.

Three major considerations for capsule formulations:

1. The powder mix must have the type of flow characteristics required by the equipment. Lubricants such as metallic stearate may be used for such case.

Particle sizes and powder densities of all ingredients should be matched as closely as possible to assist in the prevention of de –mixing .

2. Potential incompatibilities should be anticipated with each new mixture of materials. Reactions at elevated humidities and temperatures should be studied.

3. The choice of excipients should be considered according to their use.

- Such these materials used for improvement of flow characteristics are (glidants and or lubricants) like talc, glycol ester, silicon dioxide and stearic acid.
- Other materials used to control dusting and additional cohesiveness are oils.

Determination of amount of diluents based on:

1. The total amount of material that can be possibly put in the capsule in relation to the amount of active ingredient to be supplied by the capsule.

2. The amounts of lubricant and/or oil (2% or less) that can be used.

Finishing (dusting and polishing):

1. Pan Polishing : Accela-cota pan is used to remove dust and polish. By putting cloth liner to trap the removed dust and gloss the capsules.
2. Cloth Dusting : Capsule are rubbed with cloth.
3. Brushing : Capsule are feed under soft rotating brush.

Storage

Finished capsules normally contain an equilibrium moisture content of 13-16%.

To maintain a relative humidity of 40-60% when handling and storing capsules

Special Techniques

1. Imprinting: operation best performed on empty capsules (to prevent capsule damage) for product identification.

2. Special purpose capsules with special treatment to retard solubility or delay absorption of active ingredient.

e.g.: solubility limits for capsules as follows:

A) water resistance- 20 to 30°C in 15 min.

B) Acid solubility- dissolve in < 5 min in 0.5% aq. HCl at 37°C.

a) Formalin treatment (modify gelatin capsule solubility) by formation of cross linking gelatin films and preventing complete solubility.

b) Various coating to provide modify solubility characteristics like shellac, resins and cellulose acetate phthalate.

Thank you