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CAPSULE AS A SOLID DOSAGE FORM: A REVIEW

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ABSTRACT

Manufacturing of capsules is a special pharmaceutical unit operation in pharmaceutical industries. A number of modified techniques are used for production of capsules. This article concerns with production of capsule dosage form which has numerous advantages over other dosage forms. The object is to be present a review &to discuss aspects of production in terms of pharmaceutical unit operation; i.e., the technical operations of capsules preparation that comprise the various steps involved in production of capsules. Mainly a systemic approach should be followed during the production of capsules &various parameters should be maintained in the production.

INTRODUCTION:

Manufacturing section of pharmaceutical industry decide the economic health of the organization. It has to follow several regulations as per GMP. Regular monitoring in every stage of production which starts from receiving of the material from the store & ends until the final pack reach the NDP, is to be performed by the production, QA &QC departments. Requirement of quantum of production is as per production schedule submitted or decided by the logistics department.

Responsibility of the production department is not only to fulfill the target but also to maintain the quality requirements as per GMP &to follow the norms let down by Quality Assurance Department.

The two main types of capsules are:

Hard-shelled capsules: which are typically made using gelatin and contain dry, powdered ingredients or miniature pellets made by e.g. processes of extrusion or spheronisation. These are made in two halves: a lower-diameter "body" that is filled and then sealed using a higher-diameter "cap".

Soft-shelled capsules: primarily used for oils and for active ingredients that are dissolved or suspended in oil.

Advantages of Capsules:

1. Better bioavailability expected than tablet because they release drugs rapidly &is not compacted.
2. They are much more flexible to formulate compared to tablet – they are easily compounded, there is no need to form a compact resistant to handling, unique mix fills is possible, they have important roles in drug development &clinical trial phases (as drug can be administered W/O any additives)
3. They provide good barriers to atmospheric02.
4. They are elegant, hence more patient compliant.
5. They are portable dosage form.
6. They provide a smooth, slippery, easily swallowed &tasteless shell for drugs.
7. They can make any drug administrative as tasteless &odorless dosage form.
8. They can be economically produced in large quantities, &in wide range of colors.

Disadvantages of Capsules:

1. Capsules may be difficult to formulate with very bulky materials as size is limited.
2. Capsules filling equipment is slower than tableting equipment.
3. They are more costly than tablet; however, this should be judged on a case-by-case basis, tablet may be more expensive also.
4. There is concern over maintaining proper shell moisture constant. Usually, shell moisture content 13-15% W/W &should be stored (unprotected) at a relative humidity of 45-65%. It is too dry; it will become brittle/easily fractured. If too damp, they become soft and sticky. Also, highly hygroscopic drugs/efflorescent/deliquescent material may be quite difficult to formulate, as they may softer/make the shell brittle respectively.
5. Cross linking of gelatin may occur by reacting c the contents leading to change in flexibility of the shell &its reduced solubility.
6. Highly soluble salts (KCl, KBr, NH4Cl) should not be administered in capsules, as their rapid release cause gastric irritation due to localized highconcentration.
7. Suppliers of shell may belimited.
8. HGC (&also tablet) may get lodged in the esophagus &may have consequentialproblems.

Types ofcapsules:

Hardcapsules;

Softcapsules;

Modified-releasecapsules

Administration – Usually orally for both HGC & SGC. HGC are formulated at least 10 times more than SGC. Some SGC may be used for rectal/vaginal insertions for localaction.Some soft-caps are available for ophthalmic administration after cutting a part of the producing shell of these special shaped capsules.

Visual inspection

Unpack and inspect at least 20 capsules. They should be smooth and undamaged. Evidence of physical instability is demonstrated by gross changes in physical appearance, including hardening or softening, cracking, swelling, mottling or discoloration of the shell.

Uniformity of mass

Capsules comply with the test for 5.2 Uniformity of mass for single-dose preparations, unless otherwise specified in the individual monograph.

Uniformity of content

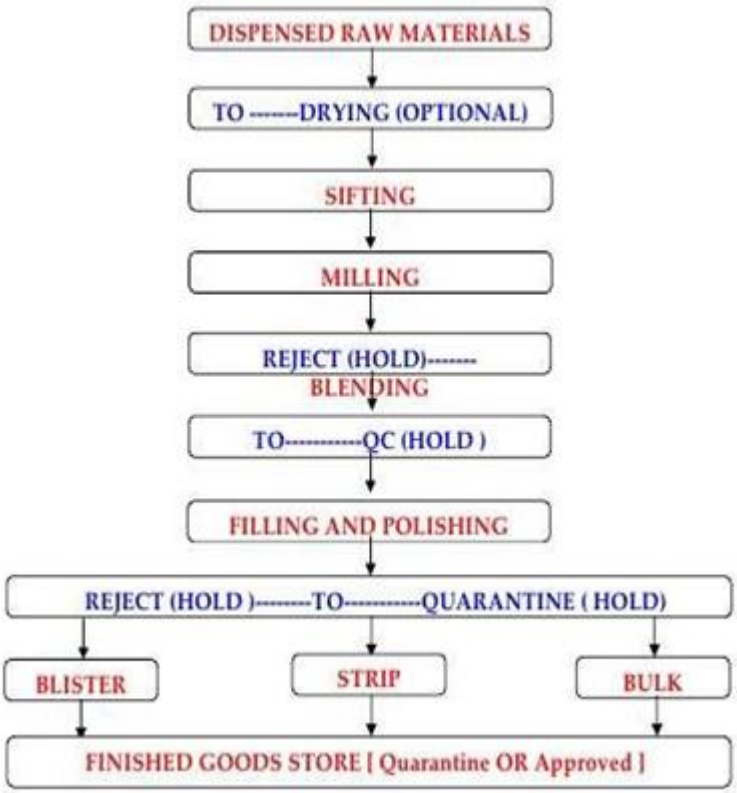
Where a requirement for compliance with the test for 5.1 Uniformity of content for single-dosepreparations is specified in an individual capsule monograph the test for 5.2 Uniformity of mass forsingle-dose preparations is not required.

Fig.1: Process flow chart for capsule

Shell composition of hard gelatin capsules:

Gelatin is the most important constituent of the dipping solutions, but other components may also be present.

1. Gelatin
2. Colorants
3. Opaquingagent
4. Preservatives
5. Water



Steps in HGC shell manufacture:

DIPPING: Pairs of SS pins dipped into a solution of gelatin to simultaneously form cap & body of the capsules. Pins at ambient temperature(22 degree C), lubricated c a patented mold release agent, is dipped in dipping solution maintained ay 50 degree C. Film casting time is

approx. 12S but increase c sizecapsules.

ROTATION: After dipping pins are withdrawn from dipping solution, elevated &rotated 2.5 times until they face upward. The rotation distributes gelatin uniformly over the whole pin surface giving uniform thickness &prevents formulation of a lead at the tip. Then a blast of cool air sets the film.

DRYING: The set gelatin film coated pins then pass thru a set of 4 drying ovens. Dryingis done by dehumidification (using large quantity of dry air) & a few degree rise in temperature (excess temp would melt the shells). Rapidly drying should be avoided to prevent case-handling. Over drying would cause film-cracking/brittleness (due to shrinkage). Under drying cause a toopliable.

STRIPPING: Pairs of bronze jaws (softer than SS) strip the cap & body of capsules from the pins.

TRIMMING: The two parts are firmly held in a rotating collect & a knife trims the shells to accurate size.

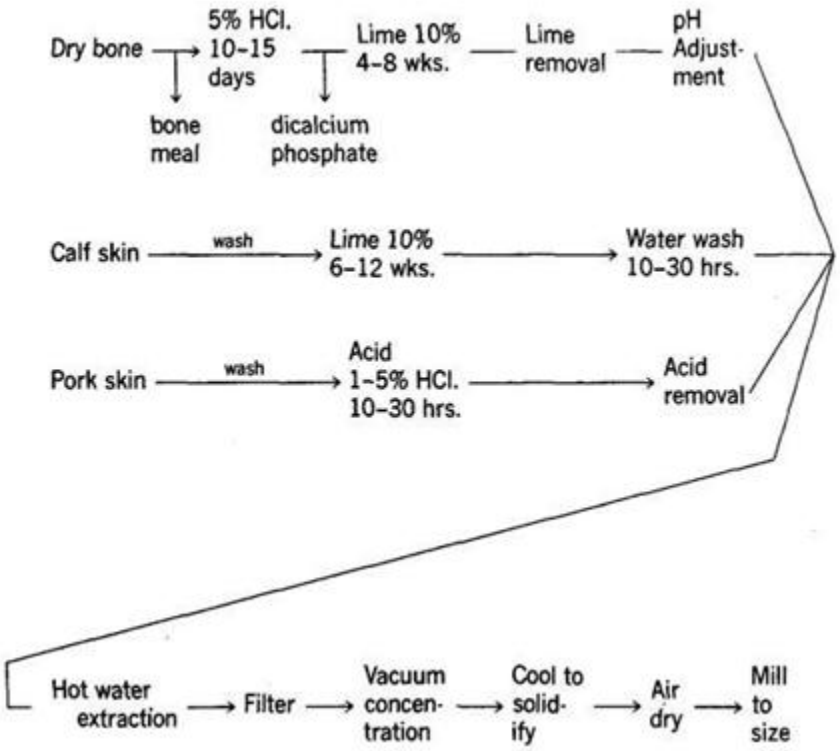


Fig.2: Process of gelatin manufacturing

JOINING: The cap & body are aligned &joined concentrically in channels by slowing pushing thentogether.

SORTING: Immediately prepared capsules have a moisture content of 15-18% W/W. The final adjustment to moisture content occurs during sorting step. In the step the defective shells are sorted out &discarded.

PRINTING: In some cases capsule shells may be printed before filling due to faster handling &since loss. Printing is done on offset rotary presses output rates as high as 0.75 million/hr. Pinting is done either axially or radially on the shells.

The substances are mixed together so as to form a eutectic mixture, then an absorbent like magnesium carbonate or kaolin is added.

1. **Addition of inert powders –** when the quantity of the drug to be filled in capsules is very small and it is not possible to fill this much small amount in capsules then inert substance or diluents is added so as to increase the bulk of the powder, which can be filled easily incapsules.
2. **Use of two capsules** – some of the manufacturers separate the incompatible ingredients of the formulation by placing one of the ingredients in smaller capsule, and then placing this smaller capsule in a larger capsule containing the other ingredients of theformulation.
3. **Filling of granular powder** – some powders which lack adhesiveness and most granular powders are difficult to fill in the capsules by punch method because they are not compressible and flow out of the capsule as soon as they are lifted from the pile of powder into which they are punched. To overcome this difficulty the non-adhesivepowders should be moistened with alcohol and the granular powders should be reduced to powder before filling intocapsules.

Formulation design of HGC powders:

The majority of products filled in HGC is powders &are required to be released as quickly as possible. The nature of contentsdetermine drug release rate from capsules. A formulator in preparing a formation needs to consider–

1. The nature of theAPI
2. The nature &type of excipients,&
3. The fillingprocess.

The use & section of individual components in a capsule mix may be discussed briefly –

API – The importantproperties of the drug are its particle size &aqueous solubility. Smaller particles may dissolve quickly, but may aggregate making the dissolution fluid to wet it difficult. The available SA of the drug is, therefore, more

important. Then total SA in capsulesdissolution.

The amount & type of the API influences size of capsules as well as nature & amount of excipients,. Drug doses < 10mg are better formulated as tablet than capsule.

Flow properties may also be important. Both dissolution characteristics as well as flow properties may be improved by granulation.

Fillers: They are needed to increase the bulk of theformulations.

E.g. – Starch, lactose, DCP; MCC Pregelatinized starch (starch 1500) Spray processed lactose (Fast Flo) Unlimited DCP-dihydrate(DiTab)

The fillers improve flow &compactibility while maintaining the basic propertiesof original malts.

Fillers, However may □/□ the drug dissolution from capsules; hence their judicious slection & drug-filler interactions must be studied for developing a formulation.

COMPOSITION OF SOFT GELATIN CAPSULES:

Like hard gelatin shells, the basic component of soft gelatin shells is gelatin; however, the shell has been plasticized by the addition of glycerin, sorbitol or propylene glycol. Other components may includedyes,opacifiers, preservativesand flavors. The ratio of dry plasticizer to dry gelatin determines the hardness of the shell and can vary from 0.3-1.0 for a very hard shell to 1.0-1.8 for a very soft shell. Up to 5% sugar may be included to give a 'chewable' quality to the shel.

MANUFACTURE OF SOFT GELATIN CAPSULES:

PLATE PROCESS:

The oldest commercial process, this semi-automaticbatch process hasbeen supplantedby more modern, continuous process. Equipment for the plate process is no longer available. In general, the processinvolved

I. placing the upper half of the plasticized gelatin sheet over a die plate containing numerous thepockets,

II. application of vacuum to draw the sheet into the diepockets,

III. filling the pockets with liquid orpaste,

IV. folding the lower half of the gelatin sheet back over the filled pockets,and

V. Inserting 'sandwich' under a die press where the capsules are formed and cutout.

ROTARY DIE PROCESS:

The first continuous process is the rotary die process, which was invented in 1933 by R.P. Scherer. Aside from its being a continuous process, the rotary die process reduced manufacturing loses to a negligible level and constant variation to a ± 1-3% range, both major problems with earlier processes. In this process the die cavities are machined into the outer surfaces of two roller form the light side of the capsules; the die pockets on the right hand roller form the right side of the dye capsules. The dye pockets on the two rollers. The die pockets on the left hand roller form the left side of the capsules; the die pockets on the right hand roller form the right side of the dye capsule.Thedye pockets on thetworollers match as the rollers rotate. Two plasticized gelatin ribbons are continuously and simultaneously fed with the liquid or paste fill between the rollers of the rotary die mechanism. The forceful injection of the feed material between the two ribbons causes the gelatin to swell into the left and right-hand die pockets as theyconverge.As thedierolls rotate, the convergence of the matching die pockets seals and cut out the filled capsules.

Manufacturing Steps of Soft Gelatin Capsule:

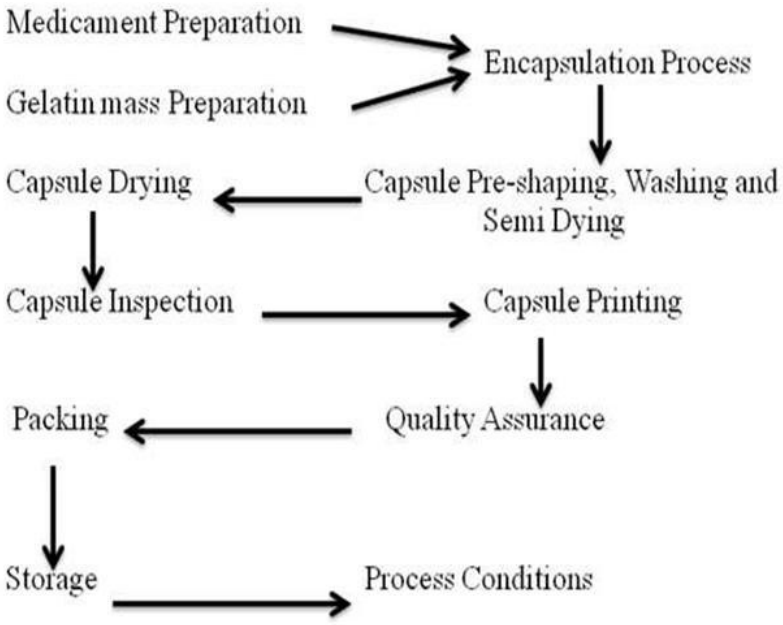


Fig. 3: Manufacturing Steps of Soft Gelatin Capsule

Modified-releasecapsules:Pancoating:

The pan coating process, widely used in the pharmaceuticalindustry, is among the oldest industrial procedures for forming small, coated particles or tablets. The particles are tumbled in a pan or other device while the coating material is appliedslowly.

Air-suspension coating:

Air-suspension coating, first described by Professor Dale Erwin Wurster at the University of Wisconsin in 1959, gives improved control and flexibility compared to pan coating. In this process the particulate core material, which is solid, is dispersed into the supporting air stream and these suspended particles are coated with polymers in a volatile solvent leaving a very thin layer of polymer on them. This process is repeated several hundred times until the required parameters such as coating thickness, etc., are achieved. The air stream which supports the particles also helps to dry them, and the rate of drying is directly proportional to the temperature of the air stream which can be modified to further affect the properties of the coating.

The re-circulation of the particles in the coating zone portion is effected by the design of the chamber and its operating parameters. The coating chamber is arranged such that the particles pass upwards through the coating zone, then disperse into slower moving air and sink back to the base of the coating chamber, making repeated passes through the coating zone until the desired thickness of coating is achieved.

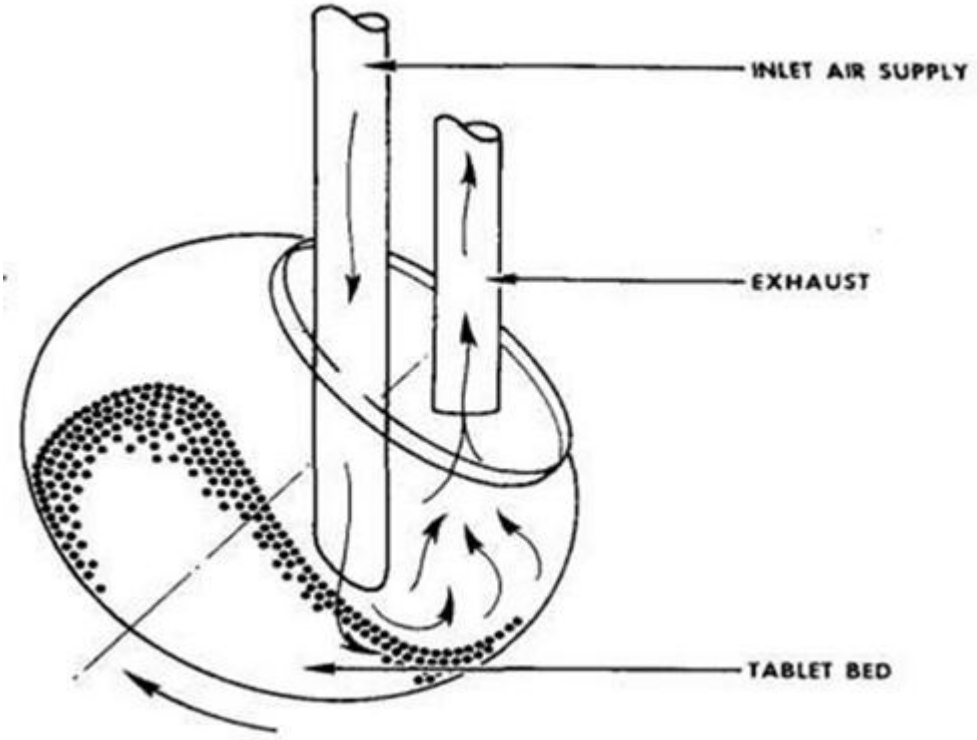


Fig. 4: Standard coating pan

Centrifugal extrusion:

Liquids are encapsulated using a rotating extrusion head containing concentric nozzles. In this process, a jet of core liquid is surrounded by a sheath of wall solution or melt. As the jet moves through the air it breaks, owing to Rayleigh instability, into droplets of core, each coated with the wall solution. While the droplets are in flight, the molten wall may be hardened or a solvent may be evaporated from the wall solution. Since most of the droplets are within ± 10% of the mean diameter, they land in a narrow ring around the spray nozzle. Hence, if needed, the capsules can be hardened after formation by catching them in a ring-shaped hardening bath. This process is excellent for forming particles 400–2,000 μm(16–79 mils)in diameter. Since the drops are formed by the breakup of a liquid jet, the process is only suitable for liquid or slurries.A high production rate can be achieved, up to 22.5 kg (50 lb) of microcapsules can be produced per nozzle perhour.

Heads containing 16 nozzles are available.

Vibrational nozzle:

Core-shell encapsulation or microgranulation (matrix-encapsulation) can be done using a laminar flow through a nozzleandan additional vibration of the nozzle or the liquid. The vibration has to be done in resonance with theRayleigh instabilityand leads to very uniform droplets. The liquid can consist of any liquids with limited viscosities

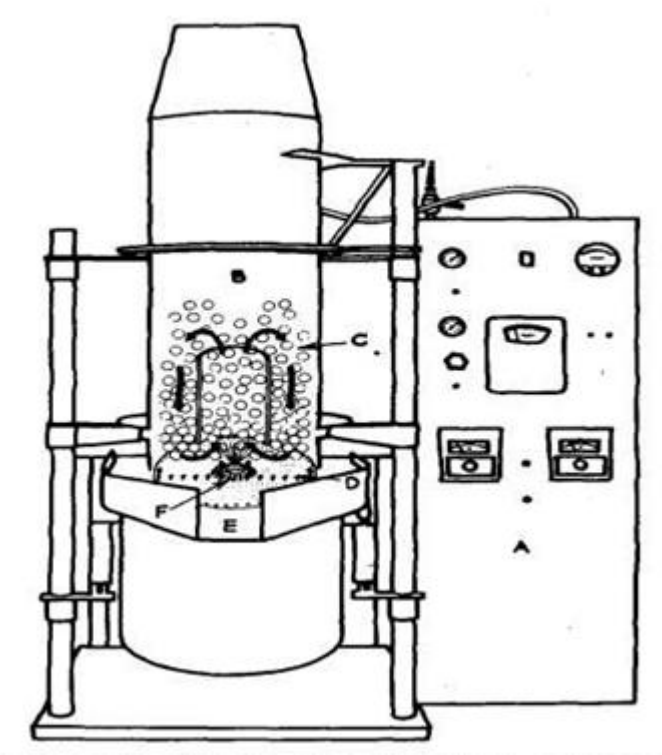


Fig. 5: Wurster Air suspension Apparatus

10,000 mPa·s have been shown to work), e.g. solutions, emulsions, suspensions, melts etc. The soldification can be done according to the used gelation system with an internal gelation (e.g. sol-gel processing, melt) or an external (additional binder system, e.g. in a slurry). The process works very well for generating droplets between 20– 10,000 µm(0.79–393.70 mils),applicationsforsmaller and larger droplets are known. The units are deployed in industries and research mostly with capacities of 1–20,000 kg per hour(2–
44,000 lb/h) at working temperatures of 20–1,500 °C (68–2,732 °F) (room temperature up to molten silicon). Heads are available with from one up to several hundred thousand nozzles.

CONCLUSION:

The report clearly explains the activities, responsibilities of production (capsule) department. The co-ordination with other related department specially quality control, quality assurance &maintenance in an important &essential role to maintain a smooth production. This report is an effort to explain the various utility &functions as has been experienced through an industrial training.

REFERENCES:

1) L. Lachman, H.A. Lieberman, J.L. Kanig (1986), The Theory and Practice of Industrial Pharmacy (Third Edition), pp-374-429

2) Remington – The Science and Practice of Pharmacy, 20th Edition, Volume –1.

3) Modern Pharmaceutics (Fourth Edition, Revised and Expanded) by G. S. Banker, C. T. Rhodes,pp-338-378

4) Ansel's pharmaceutical dosage forms and drug delivery system (Ninth edition), pp-203- 224

5) PHARMACEUTICAL MANUFACTURING ENCYCLOPEDIA (SecondEdition Reprint Edition), volume - 2

6) Pharmaceutics – The Science of Dosage form Design by M.E. Aulton, 2nd Edition.

7) Pharmaceutical Capsules (2nd edition) by Fridrun Podczeck, Brian E.Jones

8) Website:http://apps.who.int/phint/pdf/b/Jb.6.2.1.1.pdf