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Development and Formulation of Capsules

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Abstract: *Historically, the most convenient and commonly employed route of drug delivery has been by oral ingestion. Oral drug delivery has been known for decades as the most widely utilized route of administration among all the routes that have been explored for the systemic delivery of drugs via various pharmaceutical products of different dosage forms. It is considered as the most natural, uncomplicated, convenient and safe route.*

Keywords: Solid Oral Dosage.

I. INTRODUCTION

Solid Oral Dosage Forms

Historically, the most convenient and commonly employed route of drug delivery has been by oral ingestion. Oral drug delivery has been known for decades as the most widely utilized route of administration among all the routes that have been explored for the systemic delivery of drugs via various pharmaceutical products of different dosage forms. It is considered as the most natural, uncomplicated, convenient and safe route

Capsules are solid dosage forms in which drug is enclosed within either a hard or soft soluble shell. The shells are generally made up of gelatin. The capsules may be regarded as the container drug delivery system for powder and non powder filling such as tablets, capsules pellets.

Advantages of Solid Oral Dosage Forms

- They are the most stable dosage form with respect to their physical, chemical and microbiological attributes.
- Provide an accurate, stable dose with greatest precision and least content variability, easy to use, handle and to be carried by the patient.
- They are attractive and elegant in appearance.
- The manufacturing cost of tablets is low as compared to other dosage form and their manufacturing speed is also quite high.
- The packaging and shipping of tablets is comparatively easy and cheap.

The unpleasant taste and odor of medicament(s) can be easily masked

- The incompatibilities of medicament(s) and their deterioration due to environmental factors are less.
- They are more suitable for large scale production.
- Their identification is probably the easiest because of variety of shapes and colors.
- They are formulated with certain special release profile products such as enteric or delayed realise products.

Disadvantages of Solid Dosage Form

- Drugs that are amorphous in nature or have low density character are difficult to be compressed into tablet.
- Hygroscopic drugs are not suitable candidate for compressed tablets.
  • Drugs having poor wetting properties, slow dissolution profile and high optimal gastro intestinal absorption are difficult or impossible to formulate as a tablet.
- Drugs having bitter taste and objectionable odor require special treatment like coating or encapsulation which may increase their production cost.
- Some drugs which preferably get absorbed from the upper part of GIT may cause bioavailability problem in tablet dosage form.
- Capsules cannot be used for extremely soluble materials such as potassium chloride, potassium bromide.
- Capsules cannot be used for highly efflorescent or deliquescent fill materials.(1)

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II. MANUFACTURING OF CAPSULES

Immediate-release or Altered release hard gelatin capsules require the following common operations.

- Rectification body end downward orientation.
- Separation of caps from body .
- Dosing of fill material (powder or non powder filling)
- Replacement of caps and ejection of filled capusules.
- Finishing includes de-dusting and polishing.

Capsules are a unique dosage form with a long history of use in pharmacy. The original patent was issued in 1834 to a Parisian pharmacist, Joseph Gérard Dublanc, and pharmacy student, François Achille Barnabé Mothès, for the invention and manufacture of gelatin capsules.1 The basic idea of a capsule is to enclose the drug or active pharmaceutical ingredient (API) in an odorless, tasteless, elegant, easy-to-swallow, and easy-to-fill shell. Today there are two main types of capsules: the hard gelatin capsule and the soft gelatin capsule, often called softshells.

From a drug delivery point of view, capsules have many advantages. For immediate-release (IR) dosage forms, a key step is the breakdown of the capsule shell, which is analogous to disintegration in a tablet. For capsules, this occurs readily; see the discussion of gelatin cross-link in Section.Thus, capsules are ideally suited for IR delivery. In addition, capsules can be used for other types of release profiles as well. In addition to dry powder fills, multiparticulate beads can be filled into capsules. For example, morphine sulfate has a short half-life, and with an IR delivery system, it requires dosing every 8 hours, but with a controlled-release dosage such as Avinza or Kadian, it can be dosed once a day., which is a big advantage in terms of compliance. For patients in an institutional environment, it has greater convenience for the nursing staff. In addition, with multiparticulate beads, you can have a mixture of beads with different release rates. If you look at the initial phase of the plasma concentration versus time pharmacokinetic profile., you can see the initial onset is the same as the oral solution. This is because the coated beads are mixed with uncoated beads for rapid onset of pain relief. In addition to putting multiparticulate beads in a capsule, with modern filling equipment, you can also fill capsules with other dosage forms such as mini tablets and all possible combination of beads, tablets, capsules, powders, and even liquids.

III. OVERVIEW OF CAPSULES

Capsules are solid dosage forms in which medicinal agents and/or inert substances are enclosed in a small shell of gelatin. Gelatin capsule shells may be hard or soft, depending on their composition.

Most filled capsules are intended to be swallowed whole. However, it is fairly common in hospitals and extended care facilities for a care giver to open capsules or crush tablets to mix with food or drink, especially for children or other patients unable to swallow solid dosage forms. This should be done only with the concurrence of the pharmacist, since the drug release characteristics of certain dosage forms can be altered and can adversely affect the patient's welfare.(2)

Capsules

Capsules are defined as unit solid dosage form of medicaments available as small containers (shells) made up of gelatin enclosing accurately measured drug substances. The term capsule is derived from the Latin word capsula, meaning a small container. Capsule occupy a significant position in the drug development. They are often believed as the primary oral dosage form because of their manufacturing process compared to other dosage forms. Gelatin has the property of disintegrating when it comes in contact with water, thereby releasing the medicament completely. Instead, of gelatin, denatured gelatin, methyl cellulose and polyvinyl alcohol can also be used to make the capsule shells.[7] There are mainly two types of capsules which are:

Hard-shelled capsules, which contain dry, powdered ingredients or miniature pellets made by e.g. processes of extrusion or spheronization. These are made in two halve smaller diameter "body" that is filled and sealed using large diameter cap.

Both of these classes of capsules are made from aqueous solutions of gelling agents, such as animal protein (mainly gelatin) or plant polysaccharides or their derivatives (such as carrageenans and modified forms of starch and cellulose). Other ingredients can be added to the gelling agent solution including plasticizers such as glycerin or sorbitol to decrease the capsule's hardness.

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Capsule types

There exist various capsule types in scholarly articles, they are; the soft gelatin and hard gelatin capsules, Hydroxypropylmethyl cellulose (HPMC) capsules, Polyvinyl alcohol (PVA) capsules, starch capsules. These can be summarized as the gelatinous and non gelatinous capsules

Gelatin capsules

This category of capsules is basically made from gelatin; they can either be soft or hard gelatin capsules.

Soft gelatin capsules

General aspects

Originally developed in the 19th century to mask unpleasant taste and odour of drug substances, soft gelatin capsules are used in many applications, for pharmaceutical, health and nutrition products, cosmetic applications and even recreational products such as paint balls

In the pharmaceutical field soft gelatin capsules are increasingly being chosen for strategic reasons (line extension), technological issues (high content uniformity of low-dose drugs), safety aspects (reduced operator and environmental contamination with highly potent or cytotoxic compounds) and consumer preference (easy to swallow). The most interesting advances have recently been made in the area of developing liquid and semi-solid formulations in a soft gelatin capsule to address particular bio-performance issues, namely increased bioavailability and decreased plasma variability by improved solubility and absorption-enhancing techniques.(3)

Special types of hard gelatin and soft gelatin capsules Altered Release The rate of release of capsule contents can be varied according to the nature of the drug and the capsule excipients. If the drug is water-soluble and a fast release is desired, the excipients should be hydrophilic and neutral. If a slow release of water-soluble drug is desired, hydrophobic excipients will reduce the rate of drug dissolution. If the drug is insoluble in water, hydrophilic excipients will provide a faster release; hydrophobic and neutral excipients will slow its release. A very rapid release of the capsule contents can be obtained by piercing holes in the capsule to allow faster penetration by fluids in the gastrointestinal tract, or by adding a small quantity of sodium bicarbonate and citric acid to assist in opening the capsule by the evolution of carbon dioxide

Expicients used in Caspules

Plasticizer

Plasticizer Plasticizers are added to gelatin to reduce the rigidity of the polymer and make it more pliable. Common examples of plasticizers are glycerine and polyhydric alcohol. Water is also a good plasticizer and is naturally present in the gelatin

Colurants

Most frequently hard gelatin capsules are colured to enhance its appearance .Colorants used must meet the regulatory requirements of those countries where the product will be sold.Examples of commonly used capsule colourants include synthetic dyes such as azo dyes and xanthene dyes. Iron oxide pigments are also used.

Opacifying agents

These are used to give opacity to the gelatin film. E.g. Titanium dioxide.Opacifying agents are added in formulation to avoid photo degradation of light sensitive material. The concentration of oompacifying agent in formulation may be upto 0.5%

Chelating agent

Iron is always present in raw gelatin and it should contain iron more than 15 ppm.Hence chelating agent are added to prevent chemical degradation of oxidation sensitive material. Chelating act by preventing complex formation of an iron molecule with other materials of formulation.

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Preservatives

Preservatives (often parabens esters) were formerly added to hard capsules as an in-process aid in order to prevent microbiological contamination during manufacture. Manufacturers operating their plants to Good Manufacturing Practice (GMP) guidelines no longer use them. In the finished capsules, the moisture levels, 12–16% w/ v, are such that the water activity will not support bacterial growth because the moisture is too strongly bound to the gelatin molecule

Coating capsules

Coating is done to enhance appearance to improve taste and to prevent relase of drug in stomach .It also delay relasing of drug until it reaches to selective target site

IV. TYPES OF CAPSUELS

1. Sustainable relase capusles

Provides the ability to maintain a constant level of medication within the body. Sustained release matrix tablet can be prepared in two ways, one is direct compression of the powder blend containing the drug, polymer and other additives, and another one involves granulation prior to compression. Selection of the proper method depends on the properties of the drug, polymer and other ingredients. Finely powders drug is converted into pellets by attaching sugar moiety.Then pellets are trated wiith coating to controll release of drug

2. Liquid filled hard gelatin capsules

It is generally accepted that many of today‟s NCE‟s (New Chemical Entities) are poorly water soluble and the classical methods, such as reduction in particle size are no longer adequate to achieve satisfactory drug adsorption from a solid oral dosage form. One of the most promising strategies to deliver these insoluble compounds is using dissolved systems like using lipids, liquids or semi-solids to formulate new products. Two-piece hard-shell capsules are one of the most logical approaches when choosing the best dosage form to deliver these new liquid formulations.

3. Non-Gelatin Capsules

Traditionally, gelatin has been used almost exclusively as shell-forming material of capsules. In the recent advancements, non-gelatin capsules have been discovered, which do not contain gelatin as it‟s shell-forming agent. Under this category of capsules are the HPMC, PVA and starch capsules

4. HPMC Capsules

The commercial and neutraceutical markets have driven the development of alternative forming materials for traditional capsule shell material gelatin according to need. Formulator requires a non-cross-linking capsule that is well characterized, compatible with current excipients and assays, and has a gelatin-like dissolution. Marketing prefers a capsule that meets the dietary and cultural needs of patients. Manufacturing needs a capsule with gelatin-like performance that can run on existing filling equipment. Regulatory wants a capsule polymer that has a proven safety record and wide regulatory acceptance. Clinicians need to be certain that patient compliance is assure

5. PVA Capsules

International Patent Application WO 9 755 3723 describes the preferable use of polyvinyl alcohol (PVA) and optional use of some other materials, all being film-forming polymers that lack the gelling properties that are necessary for soft capsule production using the conventional rotary die process. The invention therefore provides the use of preformed rolls of nearly water-free plasticized films that may be fed to a rotary die encapsulation unit for soft capsule production. To render the film material more flexible and to assist the seam formation at temperatures depending on the film composition, the films are partially spray solvated prior to encapsulation. PVA films according to this invention may be composed of 70–75% w/w PVA, 10–15% w/w glycerol and 5–10% w/w starch,

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6. Starch Capsules

It can be formulated with conventional plasticizers such as glycerol, sorbitol, etc. (10–60% w/w of dry shell) and water to form a molten mass that can be extruded to set within less than 20 secs producing mechanically strong, elastic films on temperature-controlled casting drums. Sealing may be performed at temperatures between 25 and 80°C, by a fusion process comparable to the one observed with soft gelatin capsules. After drying, mechanically strong and highly elastic products can be achieve

Prototype capsules with lipophilic fill formulations are shiny with high appearance stability on storage. The capsule shells do not show crosslinking and exhibit a greater mechanical stability than soft gelatin shells when exposed to elevated humidity and temperature, i.e. even under hot and humid storage conditions they may not become sticky. Formulation approaches with hydrophilic fills are expected to be as challenging as for soft gelatin capsules. Oxygen permeability is comparable to gelatin-based shells. The dissolution mechanism is completely different to the one of a soft gelatin capsule. On contact with an enzyme-free aqueous medium at 37°C, the capsule shell only swells, at a rate and to an extent depending on the type and concentration of electrolytes present.

V. CAPSULE FORMULATION

Hard gelatin capsule formulation

It is estimated that the utilization of hard gelatin capsules to prepare solid dosage forms exceeds that of soft gelatin capsules by about 10-fold. Hard gelatin capsules are fabricated and supplied empty to the pharmaceutical industry by shell suppliers and are then filled in a separate operation

Manufacture of Hard Gelatin Capsules: Hard gelatin capsules are manufactured using a dip-coating method and varoius methods are involved as.

Step 1: Preparation of the gelatin solution (dipping solution)

A concentrated solution of gelatin is prepared by dissolving the gelatin in demineralized water which has been heated to 60–70°C in jacketed pressure vessels. This solution contains 30 – 40% w/w of gelatin and is highly viscous, which causes bubbles as a result of air entrapment. The presence of these bubbles in the final solution would yield capsules of inconsistent weight and would also become problematic during capsule filling and upon storage. To remove the air bubbles, a vacuum is applied to the solution; the duration of this process varies with batch size. Following the above steps, colourants and pigments are added to attain the desired final capsule appearance. At this stage, other processing aids may be added, such as sodium lauryl sulfate, to reduce surface tension. The solution viscosity is measured and adjusted as needed with hot demineralized water to achieve the target specification.

Step 2: Dip-coating the gelatin solution on to metal pins (moulds)

Capsule shells are manufactured under strict climatic conditions by dipping pairs (body and cap) of standardized steel pins arranged in rowson metal bars into an aqueous gelatin solution (25 – 30% w/w) maintained at about 50 ° C in a jacketed heating pan. Because the moulds are below the gelling temperature, the gelatin begins to form a thin gelatin layer or film on the moulds. The rows of pins are arranged so that caps are formed on one side of the machine while bodies are simultaneously formed on opposite side of the machine

Step 3: Rotation of the dip-coated pins

Following adsorption of the gelatin solution on to the surface of the pins, the bar containing the pins is removed and rotated several times to evenly distribute the solution around the pins, correct gelatin distribution being critical to uniform and precise capsule wall thickness and dome strength

Step 4: Drying of the gelatin-coated pins

Once the gelatin is evenly distributed on the mould, a blast of cool air is used to set the gelatin on the mould. At this point, the gelatin is dried, and the pins are then passed through several drying stages to achieve the target moisture content

Step 5: Stripping and trimming

After the gelatin is dried, the capsule is stripped off the mould and trimmed to the proper length

Step 6: Joining of the trimmed capsule shell

Once trimmed, the two halves (the cap and body) are joined to the pre-closed position using a pre lock mechanism. At this point, printing is done if needed before packing in cartons for shipping

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Step 7: Printing

After formation, the capsule shells can be printed to improve identification. Printing can be achieved using one or two colours, containing information such as product name or code number, manufacturer‟s name or logo and dosage details. Printing reduces the risk of product confusion by the numerous handlers and users of the product including manufacturers, pharmacist,nurses and patients.

THE MANUFACTURE OF HARD GELATIN CAPSULE SHELL(4)

Hard gelatin capsule shells are manufactured in two sections, the capsule body and a shorter cap.The two parts overlap when joined, with the cap fitting snugly over the open end of the capsule body. The shells are produced industrially by the mechanical dipping of pins or pegs of the desired shape and diameter into a temperature controlled reservoir of melted gelatin mixture The pegs, made of manganese bronze, are affixed to plates, each capable of holding up to about 500 pegs. Each plate is mechanically lowered to the gelatin bath, the pegs submerged to the desired depth and maintained for the desired period to achieve the proper length and thickness of coating. Then the plate and the pegs are slowly lifted from the Bath and the gelatin is dried by a gentle flow temperature- and humidity-controlled air.

Prepares capsules differentiated from those of other manufacturers (Pulvules, Eli Lilly). Another manufacturer uses capsules with the ends of both the bodies and caps highly tapered (Spansule Capsules, SmithKline Beecham). Yet another innovation in capsule shell design is the Snap-fit,Coni-snap, and Coni-snap Supro hard gelatin capsules.

The original Snap construction enables the two halves of the capsule shells to be positively joined through locking grooves in the shell walls. The two grooves fit into each other and thus ensure reliable closing of the filled capsule. During the closing process, the capsule body is inserted into the cap. With the high-capacity filling rates of the modern capsule filling machines (more than 180,000 capsules per hour), splitting (telescoping) and/or denting of the capsule shell occur with the slightest contact between the two rims when they are joined. This problem, which exists primarily with straight-walled capsule shells, led to the development of the Coni-snap capsule.

CAPSULE SIZES

Empty gelatin capsules are manufactured in various lengths, diameters, and capacities. The size selected for use is determined by the amount of fill materialto be encapsulated. The density and compressibility of the fill will largely determine to what extent it may be packed into a capsule shell For estimation,comparison may be made with powders of wellknown features and an initial judgement made as to the approximate capsule size needed to hold a specific amount of material.However, the final determination may be largely the result of trial and error. For human use, empty capsules ranging in size from 000 (the largest) to 5 (the smallest) are commercially available. Larger capsules are available for veterinary use.For prescriptions requiring extemporaneous compounding, hard gelatin capsules permit a wide number of options for thephysician. The pharmacist may compound capsules of a single medicinal agent or combination of agents at the precise dosage prescribed for the individual patient.

PREPARATION OF FILLED HARD GELATIN CAPSULES

The large-scale or small-scale preparation of filled hard gelatin capsules is divided into the following general steps.

1. Developing and preparing the formulation and selecting the capsule size
2. Filling the capsule shells
3. Capsule sealing (optional)
4. Cleaning and polishing the filled capsules.

DEVELOPING THE FORMULATION AND SELECTING THE CAPSULE SIZE

In developing a capsule formulation, the goal is to prepare a capsule with accurate dosage, good bioavailability, ease of filling and production, stability, and elegance.

In dry formulations, the active and inactive components must be blended thoroughly to ensure a uniform powder mix for the fill. Care in blending is especially important for low-dose drugs, since lack of homogeneity in blending may result in significant therapeutic consequences. Preformulation studies are performed to determine whether all of the formulation’s

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bulk powders may be effectively blended together as such or require reduction of particle size or any other processing to achieve homogeneity.(5)

A diluent or filter may be added to the formulation to produce the proper capsule fill volume.Lactose, microcrystalline cellulose, and starch are commonly used for this purpose. In addition to providing bulk, these materials often provide cohesion to the powders, which is beneficial in the transfer of the powder blend into capsule shells (2). Disintegrants are frequently included in a capsule formulation to assist the breakup and distribution of the capsule's contents in the stomach. Among the disintegrants used are pregelatinized starch, croscarmellose, and sodium starch glycolate.(6)

To achieve uniform drug distribution, it is advantageous if the density and particle size of the drug and nondrug components are similar. This is particularly important when a drug of low dosage is blended with other drugs or nondrug fill (8). When necessary, particle size may be reduced by milling to produce particles ranging from about 50 to 1,000 µm. Milled powders may be blended effectively for uniform distribution throughout a powder mix when the drug's dosage is 10 mg or greater (8). For drugs of lower dose or when smaller particles are required, micronization is employed. Depending on the materials and equipment used, micronization produces particles ranging from about 1 to 20 µm.

In preparing capsules on an industrial scale using high-speed automated equipment, the powder mix or granules must be free-fl owing to allow steady passage of the capsule fill from the hopper through the encapsulating equipment and into the capsule shells. The addition of a lubricant or glidant such as fumed silicon dioxide, magnesium stearate, calcium stearate, stearic acid, or talc (about 0.25% to 1%) to the powder mix enhances fl ow properties (2).When magnesium stearate is used as the lubricant, the waterproofing characteristics of this water-insoluble material can retard penetration by the gastrointestinal fl uids and delay drug dissolution and absorption. A

This may be done to separate chemically incompatible agents or to add premeasured amounts of potent drug substances. Rather than weighing a potent drug, a pharmacist may choose to insert a prefabricated tablet of the desired strength in each capsule. Other less potent agents and diluents may then be weighed and added. On an industrial scale, coated pellets designed for modified release drug delivery are also commonly placed in capsule shells.Gelatin capsules are unsuitable for aqueous liquids because water softens gelatin and distorts the capsules, resulting in leakage of the contents. However, some liquids, such as fixed or volatile oils, that do not interfere with the stability of number of capsules. On an industrial scale, this means hundreds of thousands of capsules.(7)

In community practice, an individual prescription may call for preparation of a few to several hundred capsules. Any slight loss in fill material during preparation and capsule filling will not materially affect an industrial size batch, but in the community pharmacy, a slight loss of powder could result in an inadequate quantity to fill the last capsule. To ensure enough fill in the compounding of small numbers of capsules, the community pharmacist may calculate for the preparation of one or two more capsules than required to fill the prescription.However, this procedure must not be followed for capsules containing a controlled substance,since the amount of drug used and that called for in the prescription must strictly coincide.

The selection of the capsule size for a commercial product is done during product development. The choice is determined by requirements of the formulation, including the dose of the active ingredient and the density and compaction characteristics of the drug and other components. If the dose of the drug is inadequate to fill the volume of the capsule body, a diluent is added. Information on the density and compaction characteristics of a capsule's active and inactive components and comparison to other similar materials and prior experiences can serve as a guide in selecting capsule size .Hard gelatin capsules are used to encapsulate about 65 mg to 1 g of powdered material smallest capsule (No.5) may be expected to hold 65 mg of powder or more, depending on the characteristics of the powder. Oftentimes, in the extemporaneous compounding of prescriptions, the best capsule size to use is determined by trial. Use of the smallest size capsule, properly filled, is preferred. A properly filled capsule should have its body filled with the drug mixture, not the cap. The cap is intended to fit snugly over the body to retain the contents. An easy method to select the proper capsule is to weigh the ingredients for the required number of capsules to be prepared. Place the powders in a graduated cylinder and obtain the volume occupied by the powders.

Divide the volume by the number of capsules to be prepared and this provides the volume that will be occupied by the powder for each capsule. Compare this volume (in mLs) with the appropriate line .and select the size that will accommodate the powder. If the capsule is too large, simply multiply the capsule size in Volume by the number of capsules to be prepared to obtain the final volume of the powder that is required. Then add additional diluent to the

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graduated cylinder containing the other powders to the mark indicated for the total volume of powder required. For documentation, weigh the total powder blend and subtract the initial quantities that were weighed, and the quantity of additional diluent that was added will be obtained. The following examples demonstrate the drug and nondrug contents of a few commercially available capsules.

VI. FILLING HARD CAPSULE SHELLS

When filling a small number of capsules in the pharmacy, the pharmacist may use the punch method. The pharmacist takes the precise number of empty capsules to be filled from the stock container. By counting the capsules as the initial step rather than taking a capsule from stock as each one is filled, the pharmacist guards against filling the wrong number of capsules and avoids contaminating the stock container with drug powder. The powder to be encapsulated is placed on a sheet of clean paper or on a glass or porcelain plate. Using the spatula, the powder mix is formed into a cake having a depth of approximately one-fourth to one-third the length of the capsule body.

Then an empty capsule body is held between the thumb and forefinger and punched vertically into the powder cake repeatedly until filled. Some pharmacists wear surgical gloves or latex finger cots to avoid handling the capsules with bare fingers. Because the amount of powder packed into a capsule depends on the degree of compression, the pharmacist should punch each capsule in the same manner and weigh the product after capping. When nonpotent materials are placed in capsules, When filling a small number of capsules in the pharmacy, the pharmacist may use the punch.(8) method. The pharmacist takes the precise number of empty capsules to be filled from the stock container. By counting the capsules as the initial step rather than taking a capsule from stock as each one is filled, the pharmacist guards against filling the wrong number of capsules and avoids contaminating the stock container with drug powder. The powder to be encapsu-lated is placed on a sheet of clean paper or on a glass or porcelain plate. Using the spatula, the powder mix is formed into a cake having a depth of approximately one-fourth to one-third the length of the capsule body. Then an empty capsule body is held between the thumb and forefinger and punched vertically into the powder cake repeatedly until filled.

Some pharmacists wear surgical gloves or latex finger cots to avoid handling the capsules with bare fingers. Because the amount of powder packed into a capsule depends on the degree of compression, the pharmacist should punch each capsule in the same manner and weigh the product after capping. When nonpotent materials are placed in capsules, the first filled capsule should be weighed (using an empty capsule of the same size on the opposite balance pan to counter the weight of the shell) to determine the capsule size to use and the degree of compaction to be used. After this determination, the other capsules should be prepared and weighed periodically to check the uniformity of the process. When potent drugs are being used,

CAPSULE SEALING

As mentioned previously, some manufacturers make tamper-evident capsules by sealing th jjoint between the two capsule parts. One manufacturer makes distinctive-looking capsules by sealing them with a colored band of gelatin (Kapseals, Parke-Davis). If removed, the band cannot be restored without expert resealing with gelatin. Capsules may also be sealed through a heat-welding process that fuses the capsule cap to the body through the double wall thickness at their juncture (10). The process results in a distinctive ring around the capsule where heat welded. Still another process uses a liquid wet-ting agent that lowers the melting point in the contact areas of the capsule's cap and body and then thermally bonds the two parts using low temperatures (40°C–45°C) (11). Industrial capsule-sealing machines are capable of producing 60,000 to 150,000 gelatin-banded, heat-welded, or thermally coupled capsules per hour depicts a sealed hard gelatin capsule

Although it is difficult and tedious, extemporaneously prepared capsules may be sealed by lightly coating the inner surface of the cap with a warm (9)

CLEANING AND POLISHING OF CAPSULES (10)

Small amounts of powder may adhere to the outside of capsules after filling. The powder may be bitter or otherwise unpalatable and should be removed before packaging or dispensing. On a small scale, capsules may be cleaned individually or in small numbers by rubbing them with a clean gauze or cloth. On a large scale, many capsule-filling

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machines are affixed with a cleaning vacuum that removes any extraneous material from the capsules as they exit the equipment. Figure 7.15 shows industrial cleaning and polishing of filledrd capsules using the Accela-Cota apparatus.

SOFT GELATIN CAPSULES

Soft gelatin capsules are made of gelatin to which glycerin or a polyhydric alcohol such as sorbitol has been added. Soft gelatin capsules, which contain more moisture than hard capsules, may have a preservative, such as methylparaben and/or propylparaben, to retard microbial growth. Soft gelatin capsules may be oblong, oval, or round. They may be single colored or two-toned and may be imprinted with identifying markings. As with hard gelatin capsules, they may be prepared with opaquants to reduce transparency and render characteristic features to the capsule shell.

Soft gelatin capsules are used to encapsulate and hermetically seal liquids, suspensions, pasty materials, dry powders, and even preformed tablets. Soft gelatin capsules are pharmaceutically elegant and are easily swallowed.

PREPARATION OF SOFT GELATIN CAPSULE

Soft gelatin capsules may be prepared by the plate process, using a set of molds to form the capsules, or by the more efficient and productive rotary or reciprocating die processes by which they are produced, filled, and sealed in a continuous operation

By the plate process, a warm sheet of plain or colored gelatin is placed on the bottom plate of the mold and the medication-containing liquid is evenly poured on it. Then a second sheet of gelatin is carefully placed on top of the medication and the top plate of the mold is put into place. Pressure is then applied to the mold to form, fill, and seal the capsules simultaneously. The capsules are removed and washed with a solvent harmless to the capsules.

On the industrial scale, solid dosage forms are counted by large automated pieces of equipment that count and transfer the desired number of dosage units into bulk containers. The containers are then mechanically capped, inspected visually or electronically, labeled, and inspected once more. Some filled containers are then placed in outer packaging cartons. An industrial counting and filling machine is shown in. Capsules are packaged in glass or in plastic containers, some containing packets of a desiccant to prevent absorption of excessive moisture.

USE OF SOFT GELATIN CAPSULES

Soft gelatin capsules are prepared to contain a variety of liquid, paste, and dry fills. Liquids that may be encapsulated into soft gelatin capsules include the following

1. Water-immiscible volatile and nonvolatile liquids such as vegetable and aromatic oils, aromatic and aliphatic hydrocarbons, chlorinated hydrocarbons, ethers, esters, alcohols, and organic acids.
2. Water-miscible nonvolatile liquids, such as polyethylene glycols, and nonionic surface active agents, such as polysorbate 80.Water-miscible and relatively nonvolatile compounds such as propylene glycol and isopropyl alcohol, depending on factors such as concentration used and packaging conditions.

CONTAINERS FOR DISPENSING CAPSULES

The USP lists specifications prescribing the type of container suitable for the repackaging or dispensing of each official capsule and tablet.Depending on the item, the container may be required to be tight, well-closed, light resistant,and/or all of these.

VII. EVALUATION TESTS FOR CAPSULES.

1. DISINTEGRATION TEST FOR CAPSULES

The disintegration test for hard and soft gelatin capsules follows the same procedure and uses the same apparatus described in the next chapter for uncoated tablets. The capsules are placed in the basket rack assembly, which is immersed 30 times per minute into a thermostatically controlled fl uid at 37°C and observed over the time described in the individual monograph. To satisfy the test, the capsules disintegrate completely into a soft mass having no palpably firm core and only some fragments of the gelatin shell.(11)

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2. DISSOLUTION TEST FOR CAPSULES

The dissolution test for capsules uses the same apparatus, dissolution medium, and test as that for uncoated and plain-coated tablets described in Chapter 8. However, if the capsule shells interfere with the analysis, the contents of a specified number of capsules can be removed and the empty capsule shells dissolved in the dissolution medium before proceeding with the sampling and chemical a denalysis.

3. WEIGHT VARIATION (11)

The uniformity of dosage units may be demonstrated by determining weight variation and/or content uniformity. The weight variation method is as follows.

4. HARDNESS OF CAPUSLES

Ten capsules are individually weighed and their contents removed. The emptied shells are individually weighed and the net weight of the contents is calculated by subtraction. From the results of an assay performed as directed in the individual monograph, the content of the active ingredient in each of the capsules is determined.(11)

5. CONTENT UNIFORMITY

All official capsules must be labeled to express the quantity of each active ingredient in each dosage unit.(11)

6. STABILITY TESTING

Stability testing of capsules is performed as described in Chapter 4 to determine the intrinsic stability of the active drug molecule and the influence of environmental factors such as temperature, humidity, light, formulative components, and the container and closuresystem. The battery of stress testing, long-term stability, and accelerated stability tests help determine the appropriate conditions for storage and the product's anticipated shelf life.(11)

7. MOISTURE PERMEATION TEST

The USP requires determination of the moisture permeation characteristics of single-unit and unit-dose containers to ensure their suitability for packaging capsules. The degree and rate of moisture penetration are determined by packaging the dosage unit together with a color-revealing desiccant pellet, exposing the packaged unit to known relative humidity over a specified time, observing the desiccant pellet for color change (indicating the absorption of moisture), and comparing the pretest and posttest weight of the packaged unit.

OFFICIAL AND COMMERCIALLY AVAILABLE CAPSULE

Approximately 200 officially recognized medications in capsule form are listed in the USP. However, many times this number of capsule products are available from various manufacturers for various drugs and in various dosage strengths. Examples of official and commercially available medications in hard and soft gelatin (11)

TECHNIQUES FOR INSPECTING, PACKAGING AND STORING OF CAPSULES

Capsules produced on a small or a large scale should be uniform in appearance. Visual or electronic inspection should be undertaken to detect any fl aws in the integrity and appearance of the capsules. Defective capsules should be rejected. In commercial manufacture, Current Good Manufacturing Practice regulations require that if the number of production flaws is excessive, the cause must be investigated and documented and steps undertaken to correct the problem. In the pharmacy, capsules may be counter In the pharmacy, capsules may be counted manually or by automated equipment. Specially designed trays, such as the type depicted in, are used for counting small numbers of solid dosage units. In using this tray, the pharmacist pours a supply of capsules or tablets from the bulk source onto the clean tray and, using the spatula, counts and sweeps the dosage units into the trough until the desired number is reached. Then the pharmacist closes the trough cover,picks up the tray, returns the uncounted dosage units to the bulk container by means of the lip at the back of the tray, places the prescription container at the opening of the trough, and carefully transfers the capsules or tablets into the container. With this method, the dosage units remain untouched by the pharmacist. To prevent batch-to-batch contamination, the tray must be wiped clean after each use because powder, particularly from uncoated tablets, may

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remain. In some community and hospital pharmacies, small automated counting and filling machines may be used.. Computer-based automated dispensing systems are also available that will fill, label, and check the drug using bar code or video systems.(12)

On the industrial scale, solid dosage forms are counted by large automated pieces of equipment that count and transfer the desired number of dosage units into bulk containers. The containers are then mechanically capped, inspected visually or electronically, labeled, and inspected once more. Some filled containers are then placed in outer packaging cartons. An industrial counting and filling machine. Capsules are packaged in glass or in plastic containers, some containing packets of a desiccant to prevent absorption of excessive moisture.(13)

ORAL ADMINISTRATION OF SOLID DOSAGE FORMS

Solid dosage forms (capsules and tablets) for oral administration are best taken by placing the dose upon the tongue and swallowing it with a glassful of water or beverage, e.g., milk, coffee, juice, tea. Ingesting solid dosage forms with adequate amounts of fluid is important. Some patients attempt to swallow a tablet or capsule without water, but this can be dangerous because of the possibility that it will lodge in the esophagus.Esophageal ulceration can occur with dry ingestion of tablets and capsules, particularly taken just before bedtime. Among the drugs of greatest concern in this regard are alendronate sodium, aspirin, ferrous sulfate, any nonsteroidal anti-infl ammatory drug, potassium chloride, and tetracycline antibiotics.(14)

The proper administration of alendronate sodium tablets (Fosamax, Merck), for example, calls for the tablets to be taken with a full 6- or 8-ounce glass of plain water upon rising in the morning and at least half an hour before taking any food, beverage, or other medication to prevent local irritation of the esophagus and other upper gastrointestinal mucosa. The patient is also instructed not to recline for at least 30 minutes and until after the first food of the day is eaten because of the possibility that the drug will refl ux into the esophagus.(15)

In general, patients with gastroesophageal reflux disease must take their medications with adequate amounts of water and avoid reclining for at least an hour to avoid reflux.

When an ordinary tablet is crushed or a capsule opened to facilitate ease of administration, any unpleasant drug taste may be partially masked by mixing with custard, yogurt, rice pudding, other soft food, or fruit juice. The patient should be advised to consume the entire drug food mixture to obtain the full dose, and to maintain stability, the drug should not be premixed and allowed to set.(16)

If a patient cannot swallow a solid dosage form, the pharmacist can suggest a chewable or liquid form of the drug. If these are not available, an extemporaneously compounded liquid form may be prepared. Extemporaneous compounding involves a pharmacist preparing a dosage form suitable for an individual patient. There are numerous resources available for this very important and expanding part of pharmacy practice(17)

VIII. CONCLUSION

The baisc idea of an capsule is to enclose the drug or active pharmaceutical ingredients in an odourless, tasteless, elegant, easy to swallow and easy to fill shell. Today there are two main types of capsules: the hard gelatin capsule and the soft gelatin capsule, often called soft shells. The pharmaceutical company cannot be imagined without Hard gelatin capsule. These capsuels are majorly used for filling the medicine in the form of dry powder or small pelletes

REFERENCES

[1]. Capsules: Types, Manufacturing, Formulation, Quality Control Tests And, Packaging And Storage - A Comprehensive Review August 2020 By Abubkar Lawal Mohammad.
[2]. Aulton's Pharmaceutic: The Design and Manufacture of Medicines By M.E Aulton.
[3]. Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems: By Loyd V.Allen, Nicholas Popvich.
[4]. Martin A. Diffusion and Dissolution, Physical pharmacy, 3rd Edn; Lea and Febiger.
[5]. Indian Pharmacopoeia: Controller of Publications, Govt. of India, Ministry of Health & Family Welfare, New Delhi, 1, 135, 1996
[6]. Formulation and Evaluation of Hard Gelatin Capsule of Losartan Potassium 2003,Naisarg Pujara.