WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.453
Volume 14, Issue 6, 15-28. Review Article ISSN 2277–7105

A REVIEW ON OMEPRAZOLE ANTACID CAPSULE

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Article Received on
01 February 2025,

Revised on 21 Feb. 2025,
Accepted on 01 March 2025

DOI: 10.20959/wjpr20256-35470

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ABSTRACT

This review explores the formulation, manufacturing, and evaluation of Omeprazole antacid capsules with a focus on both hard and soft gelatin variants. Capsules are a prevalent dosage form that provides advantages like ease of administration, taste masking, and enhanced patient compliance. The document details the structural components, materials, and production techniques, including advancements like rotary die and seamless capsule methods for soft gelatin capsules. Furthermore, the advantages, limitations, and specialized applications of capsules, such as targeted drug delivery and sustained release, are discussed. Quality control tests and regulatory considerations underscore the importance of maintaining efficacy and safety in capsule formulation. This comprehensive review aims to provide insight into the versatile use of capsules in modern pharmaceutical Practices.

1. INTRODUCTION[1]

Capsules are solid dosage forms in which drug substance is enclosed within hard or soft soluble shell. The shells are generally formed from gelatin.

Capsules are of two types

1. **Hard- gelatin capsules:** These consist of two halves that fit together to form a closed container. They typically contain dry medication in powder or pellet form.
2. **Soft- gelatin capsules:** These are usually wider and semi-transparent, containing liquid medication.

1.1 Hard- gelatin capsules[2]

Hard gelatin capsules, also known as hard-shell gelatin capsules or two-piece capsules, are a

popular form of oral dosage used in the pharmaceutical industry. Here are some key points about them:

A. **Structure:** They consist of two cylindrical sections - a cap and a body. The body is filled with the drug substance, and the cap is placed over the body to form a sealed unit.

B. **Materials:** The primary component is gelatin, derived from bovine or porcine sources. Other materials like plasticizers, colorants, and preservatives may be added to enhance performance.

C. **Sizes and Shapes:** Hard gelatin capsules come in various sizes, typically ranging from 000 (largest) to 5 (smallest). The size chosen depends on the dose and density of the medication.

D. **Filling:** They can be filled with powders, granules, pellets, or even mini-tablets. The filling process can be done manually or using automated machinery.

E. **Dissolution:** These capsules dissolve in the stomach within 20 to 30 minutes under normal conditions, releasing the medication for absorption.

1.1.Basic component of hard gelatin capsules[3]

A. Gelatin

Gelatin is by far the most common and most well-known material used to produce hard capsule shells. It is a generic term for a mixture of purified protein fractions. obtained from irreversible hydrolytic extraction of collagen obtained from the skin, white connective tissue, and bones of animals.

B. 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.

C. Colourants

Most frequently, hard gelatin capsules are coloured to enhance the aesthetic properties and also to act as a means of identifying the product. 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.

D. Opacifying agents

Opacifiers (e.g., titanium dioxide) may be included to make clear gelatin opaque. Opaquse capsules may be employed to protection against light or to conceal the contents.

E. 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.

1.1.1.Hard gelatin capsule size and shape [4]:

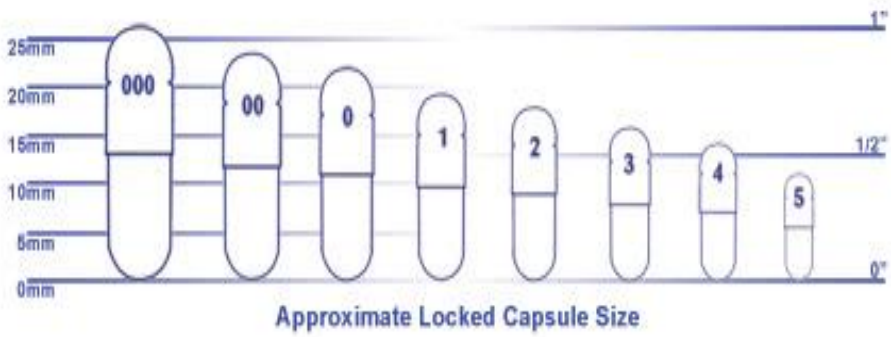

Fig. 1: Hard gelatin capsule size.

Table. 1.1: Size of hard gelatin capsule.

Size	Volume in ml	Size in mm
000-Largest	1.37	26.3
00	0.95	23.7
0	0.68	21.8
1	0.50	19.2
2	0.37	18.3
3	0.30	15.3
4	0.21	14.7
5-Smallest	0.15	11.9

1.1.2.Manufacture of Hard Gelatin Capsules[5,6]

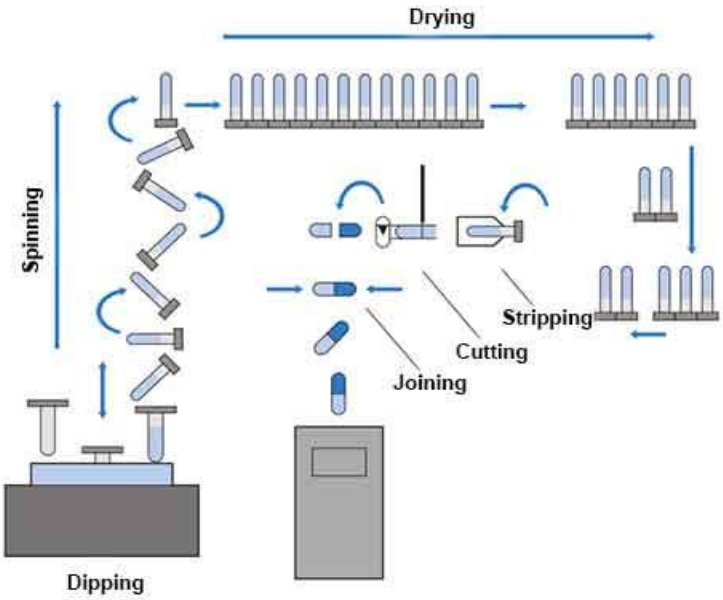

Fig. 2: Hard gelatin capsule manufacturing instrument.

Hard gelatin capsules are manufactured using a dip- coating method and the various stages involved are as follows

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 rows on 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 the 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.

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, pharmacists, nurses, doctors, caregivers. and patients.

1.2 Soft- gelatin capsules[7,8,9]

The term 'soft gelatin capsules' is commonly abbreviated to 'soft gels',

Over recent years, new drug molecules have tended to be more hydrophobic and therefore less soluble in aqueous systems.

In the case of drugs for oral administration, it is becoming more difficult to formulate poorly water-soluble drugs into products from which the drug is fully released and well absorbed.

One of the best methods to overcome this problem is to make a liquid formulation containing the drug.

In order to convert this liquid formula into a solid dosage form, it may be encapsulated into soft gelatin capsules.

1.2.1.Basic component of soft gelatin capsules[10,11]

Typical Soft gel shells are made up of gelatin, plasticizer and materials that impart the desired appearance and some flavors.

A. Gelatin

Most commonly alkali processed gelatin (type B) - 40% of the wet molten gel mass. Type A acid processed gelatin can also be used.

B. Plasticizers

Plasticizers are used to make the Soft gel shell elastic and pliable. They usually account for 20-30% of the wet gel formulation. The most common plasticizer used in soft gels is glycerol. Sorbitol and propylene glycol are also frequently used, often in combination with the glycerol. In soft gelatin capsule the amount of plasticizer and gelatin ratio is 0.8:1.

C. Water

Water usually accounts for 30-40% of the wet gel formulation. Its presence is important to ensure proper processing during gel preparation and encapsulation.

D. Colorants/Opacifiers

Colorants and Opacifiers are used in low concentrations in the wet gel formulation. Colorants are used to impart desired shell color for product identification. Opacifiers are used to produce opaque shell.

1.2.2. Soft gelatin capsule size and shape

Fig. 3: Soft gelatin capsule size and shape.

1.2.3. Manufacture of Soft Gelatin Capsules[12,13,14]

Soft gels are manufactured using the following methods

A. Plate process

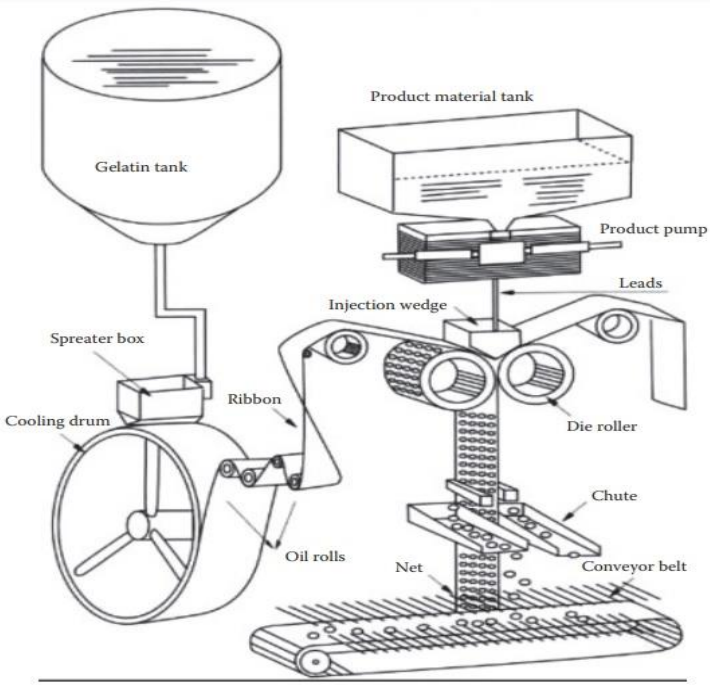

Fig. 4: Plate process equipment.

This is the oldest commercial process used in the manufacture of soft gelatin capsules. In this process, a warned sheet of plain or coloured plasticized gelatin over plate having a number of depression or moulds or numerous die pockets. By applying vacuum, the sheet is drawn into these depressions ne pockets to form capsule wells. The capsule wells are then filled with medication-containing liquid. A second sheet of gelatin is carefully placed on top of the filled wells followed by the top plate of the mould. Pressure is then applied to the combined plate to form, seal and cut the capsules into individual units. This method is used for small scale preparation of soft gelatin capsules and capsules formed generally, had one fiat side.

The major problems with this method of manufacturing soft gels were the lack of dosage uniformity. high manufacturing losses, and its labour-foost-intensiveness. This equipment is no longer available.

B. Rotary Die Process

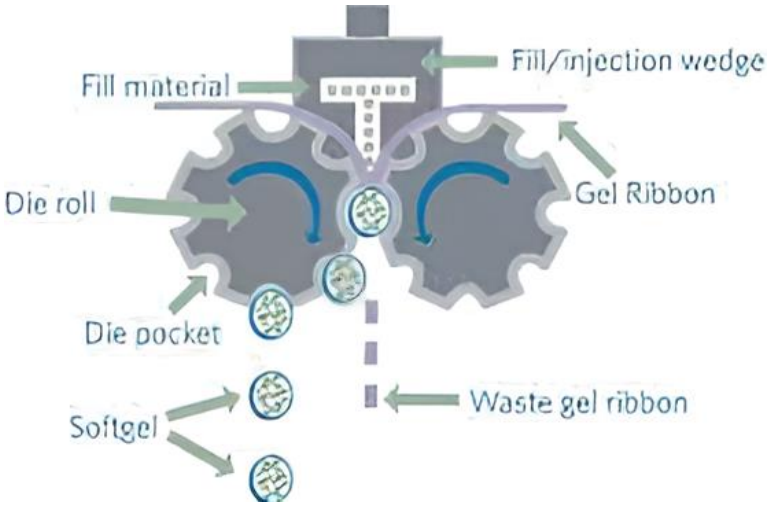

Fig. 5: Rotary Die instrument.

Most soft gelatin capsules are prepared by the rotary die process, a method developed and perfected in 1933 by Robert P. Scherer. This process almost eliminated all the problems associated with the plate process and produced. soft gelatin capsules with improved uniformity and high standards of accuracy.

In this process, two gelatin ribbons (prepared in the rotary die machine) are continuously and simultaneously fed with the liquid, semiliquid or passe fill between the rollers of the notary die mechanism. The Forced injection of the feed material between the two ribbons causes the gelatin to swell into the left and right-hand die pockets which govern the size and shape the soft gels as they converge. As the die rolls rotate. the convergence of the matching dies pockets hermetically seals and cuts out the filled capsule.

C. Reciprocating Die Process (Norton Capsule Machine)

This continuous soft gelatin capsule processing technology was developed by Norton Company in 1949. This process sis similar to rotary process in that ribbons of gelatin are formed and used to encapsulate the fill, but it differs in the actual encapsulating process. The gelatin ribbons are fed between set of vertical dies that continually and close to form rows of pockets in the gelatin ribbons. These pockets filled with the medication and are sealed, shaped, and cut out of the film as they progress through the machinery. As the capsules are cut from the ribbons, they fall into a cooled solvent bath that prevents the capsules from adhering to one another.

D. Accogel Process

Although the rotary die process and reciprocating die process were capable of producing soft gelatin capsules containing oily liquids and pustes, Loderle Laboratories in 1949 developed accogel process, a continuous process that produces soft gelatin capsules containing powders and granules.

The process involves a measuring roll that holds the fill Formulation in its cavities under under the vacuum and rotates directly above the elasticized sheet of the gelatin ribbon. The ribbon is drawn into the capsule cavities of the capsule die roll by vacuum. The measuring rolls empty the fill material into the capsule-shaped gelatin cavities on the die roll. The die roll then converges with the rotating scaling roll covered with another sheet of elasticized gelatin. The convergence of two rotary rolls creates pressure to and cut the formed capsules.

E. Seamless Process (Bubble Method)

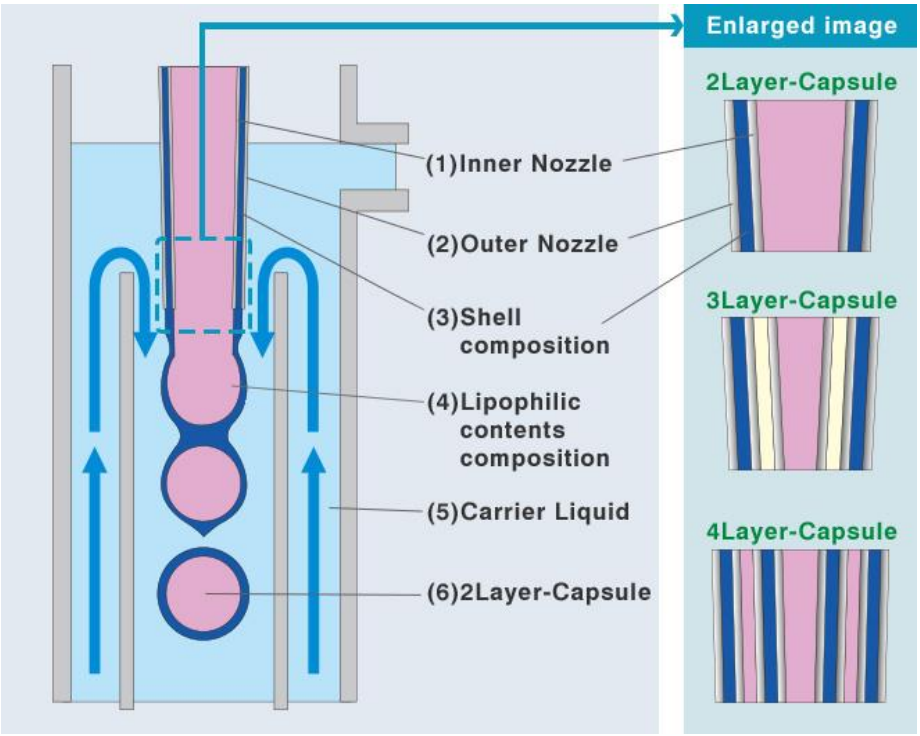

Fig. 6: Seamless capsule manufacturing.

The seamless technique produces one-piece soft gelatin capsules without the use of dies. The process is often referred to bubble method that creates seamless, spherical soft gelatin capsules called pearl.

In this process, a molten gelatin stream flows though the outer nozzle of a concentric tube a

constant rate, and the medicated liquid formulation is dispensed through the inner orifice by means me of a precision metering pump. The emerging stream is broken up into an intermittent but steady flow of uniform-sized by pulsating mechanism, leading to the formation of droplets enveloped in molten gelatin. The formed capsules are quickly removed from the nozzle, slowly congealed, and automatically ejected from the system.

1.3 Advantages of Capsule

- Capsules are tasteless, odorless and can easily be administered.
- Combination of powders we can use
- There are attractive in appearance.
- The drugs having un-pleasant odor and taste are enclosed in a tasteless shell.
- They can be filled quickly and conveniently.
- Physician can change the dose and combination of drug according to patient requirement.
- They are economical.
- They are easy to handle and carry.
- They are smooth, become very slippery when moist and can be easily swallowed.
- The capsules release the medicament as and when desired in gastro-intestinal tract.
- Capsules are made from gelatin and hence they are therapeutically inert.
- Packaged and shipped by manufacturers at lower cost less breakage than liquid forms.

1.4 Disadvantages of Capsule

- **Less Durable:** Capsules are generally less stable than tablets and can be affected by environmental conditions such as humidity and temperature.
- **Shorter Shelf Life:** They tend to expire more quickly than tablets.
- **Higher Cost:** Capsules are often more expensive to manufacture, which can make them pricier for consumers.
- **Limited Dosage Capacity:** Capsules cannot hold as much medication as tablets, which can be a limitation for higher doses.
- **Potential Allergens**: Some capsules contain gelatin, which is derived from animal products and may not be suitable for vegetarians or those with certain dietary restrictions.
- **Splitting Issues:** Capsules cannot be split evenly, making it difficult to adjust doses.

1.5 Application of Capsules[15]

Capsules have several specialized applications beyond standard oral drug delivery. Here are

some notable ones

- **Inhalation Therapy:** Capsules are used in dry powder inhalers for respiratory conditions like asthma and COPD. The medication is released as a fine powder when the capsule is punctured.
- **Diagnostic Kits:** Capsules can be used to deliver reagents in diagnostic kits, ensuring precise and convenient application.
- **Suppositories:** Soft gelatin capsules can be used for rectal or vaginal insertion, providing an alternative route of administration for certain medications.
- **Targeted Drug Delivery:** Capsules can be designed to release their contents at specific sites within the gastrointestinal tract, enhancing the effectiveness of the medication and reducing side effects.
- **Personalized Medicine:** Advances in capsule technology allow for the development of personalized medicine, where capsules are tailored to the specific needs of individual patients.
- **Nutritional Supplements:** Capsules are widely used for dietary supplements, vitamins, and herbal products.
- **Enteric Coated Capsules:** Coating of cellacephate (cellulose acetate phthalate) and mixture of waxes with fatty acids or their esters is given.
- **Sustained Release Capsules:** Finely powdered drug first converted to pellets pellets are coated with protective coating that delay the release of drug. 30% uncoated pellets 30% coated pellets that release drug at 4 hrs. & 8 hrs. interval & 10% neutral pellets to fill the capsule.
- **Rectal Capsules:** Soft gelatin capsules as substitute for rectal & vaginal suppositories. Pear shaped
- **Capsule Containing Ophthalmic Ointments:** Ophthalmic ointments are sterile to keep that ointment sterile during their storage & & later use it is required to be filled in a single dose container. Intended for single application to eye. The capsule is puncture with sterile needle a& instilled into eye & shell is discarded

1.6 Evaluation of Capsules[16]

Evaluating capsules involves several quality control tests to ensure they meet the required standards for safety, efficacy, and stability. Here are some key tests performed during the evaluation of capsules:

- **Weight Variation Test:** Ensures that each capsule contains the correct amount of active ingredient. This is done by weighing individual capsules and comparing them to the average weight.
- **Content Uniformity Test:** Measures the consistency of the active ingredient within a batch of capsules. This ensures that each capsule contains a uniform amount of the drug.
- **Disintegration Test:** Determines the time it takes for a capsule to break down into smaller particles. This is important for ensuring that the drug is released properly in the body.
- **Dissolution Test:** Measures the rate and extent to which the active ingredient is released from the capsule and becomes available for absorption.
- **Moisture Content Test:** Assesses the amount of moisture in the capsule shell and the contents. Excess moisture can affect the stability and integrity of the capsule.
- **Stability Testing:** Evaluates the capsule's ability to maintain its quality over time under various environmental conditions such as temperature and humidity.
- **Microbial Content Test:** Ensures that the capsules are free from harmful microorganisms.

CONCLUSION

Capsules represent a pivotal advancement in pharmaceutical dosage forms, offering a versatile solution for drug delivery. Their ability to encapsulate a wide range of active ingredients, coupled with tailored manufacturing techniques, ensures precision and adaptability for various therapeutic needs. Despite some limitations, such as susceptibility to environmental factors and higher production costs, their benefits—ranging from enhanced patient compliance to targeted drug delivery—underscore their value. Future developments in capsule technology, particularly for personalized medicine and complex formulations, will likely further solidify their role in healthcare. This review highlights the innovation and meticulous quality standards that drive the success of capsule-based drug delivery systems.

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