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SEAMLESS CAPSULES: Capsules from the Beyond!

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ABSTRACT

Seamless capsules formed of a shell material encapsulating a core material have been made by using as the shell material film-forming materials such as gelatin and gums. Seamless capsules have a clear and glossy appearance with liquid material encapsulation and show greater bioavailability and flexible adjustment of the dosage.

Encapsulation refers to a variety of dosage forms used to enclose drugs in a relatively rigid shell known as a capsule, enabling them to be taken orally or as suppositories, for example, in the manufacture of pharmaceuticals.

Capsules are divided into two main types: Hard-shelled capsules that contain dry, powdered ingredients or miniature pellets made by extrusion or spheronization techniques.

These are made in two parts: The first half is made of aluminium.

A smaller-diameter "body" that is filled and then sealed with a larger-diameter "cap" attached to a smaller-diameter "body".

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

Seamless capsules come under the category of soft gelatin capsules. The bioavailability of these capsules is found to be more potent than other soft gelatin capsules. Some of these capsules show resistance to high temperatures whereas, some can withstand the acidic pH of the stomach, there are still some that show rapid dissolution i.e., they dissolve in the mouth itself. Due to these factors, this type of capsule can be considered superior to the rest.

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KEYWORDS: *Capsules, seamless, soft gelatin, bioavailability, encapsulation*

METHODS AND MATERIALS

Introduction: -

Capsules are solid dosage forms in which the drug substance is contained within a hard or soft soluble shell, typically formed from gelatin.

Capsules have become a popular dosage form due to their smooth, slippery, easily swallowed, and tasteless shell for drugs, in addition to having the advantages of simplicity, ease of use, and portability; the last advantage is particularly beneficial for drugs with an unpleasant taste or smell.

Gelatin when comes in contact with water has the property of disintegrating thereby releasing the medicament.[10]

They are economically produced in large quantities and a wide variety of colors, and they generally guarantee prompt availability of the contained drug since there are no excipients and little pressure is required to compact the material. [[1]]

Fig 1: Capsules

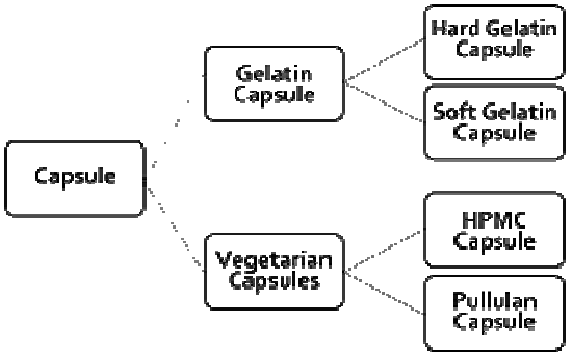
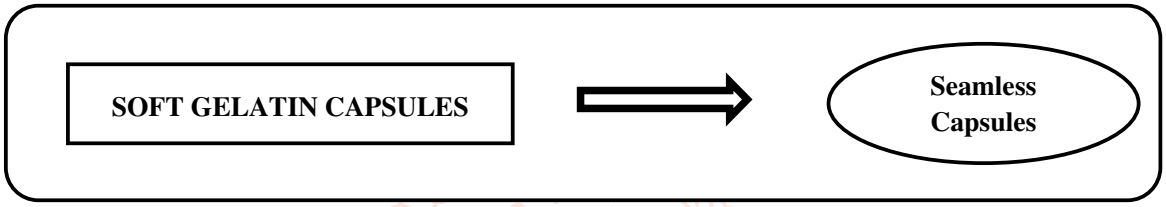


Fig 2: Classification of capsules

Soft Gelatin Capsules



Soft gelatin capsules are made up of a hermetically sealed outer shell of gelatin that encloses a liquid or semisolid medicament in the unit dosage.

Soft gelatin capsules are a completely sealed dosage form that cannot be opened without damaging the capsules.

Soft gelatin capsules are thicker than hard capsules and require additional ingredients such as glycerin to achieve their soft texture.

To achieve better absorption, they contain active ingredients such as suspension, solutions, or emulsion. [9]

Depending on the formulation, the thickness of the capsule, its elasticity, and the degree of residual moisture can be adjusted. [[5]]

These capsules are used for pharmaceuticals that are commercially available in soft capsules, such as cyclosporine, declomycin, chlorotrianisene, digoxin, vitamin A, vitamin E, and chloral hydrate. [[2]]

One such type of soft gelatin capsule is a **seamless capsule.**

SEAMLESS CAPSULES

These capsules are made using the ability of liquids to form a spherical shape due to interfacial tension.

The capsule's diameter can be as small as 1 mm to as large as 10 mm.

The size of the capsule, its thickness, and the hardness of the shell can also be easily adjusted.

They can also be mixed and blended into other products as small, granulated capsules.

Advantages of seamless capsules [3]

- Prevention of oxidation (e.g. fatty acids, fish oils, etc.)
- Suitable for thermolabile and volatile materials
- A single soft capsule can be used for combination drugs that are not desired to be mixed.

FEATURES AND BENEFITS

- Flexibility in diameter and shell thickness –
  Seamless capsules can be produced in 1mm – 10mm in diameter and in several tens of micrometers – many thousands of micrometers in shell thickness, to suit various ingredients and uses.
- Broad range of dissolving times –
  Seamless capsules can be designed to dissolve in the body for several seconds to several hours depending on the ingredients' properties.

- Flexibility in product design –
  Heat-resistant capsules protect the contents without rupturing the shell even at high temperatures, as the capsules contain oil-based substances in an aqueous solution. Beverages, lotion, and shampoo are examples of applications.

SHAPES OF SEAMLESS CAPSULES

A. External Shell

- Edible elastic shell that is made of gelatin, starch, agar-agar, carrageenan, etc.
- Several tens of micrometers to several thousands of micrometers in thickness.
- The shell can be blended with colourings, preservatives, fragrances, and flavourings. It can also be applied with various types of coating.

B. Contents

- Drug substance stability is one of the studies that influence the selection of oily bases for pharmaceutical products.
- Corn oil, soybean oil, sesame oil, cottonseed oil, safflower oil, wheat germ oil, and middle chain triglycerides are some of the vegetable oils used.[4]
- Solid fat that dissolves with low heat (< 60 degrees Celsius)
- Powder (in oil suspension)

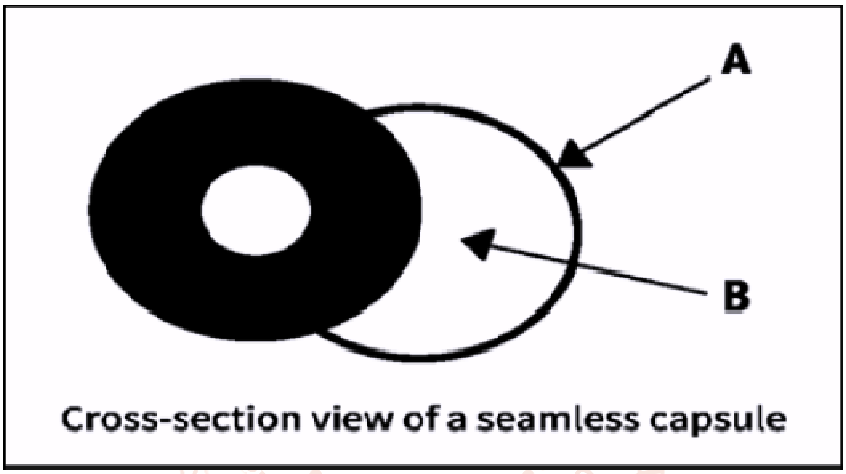


Fig 3: cross-section view of a seamless

TYPES OF SEAMLESS CAPSULES

1. Enteric Seamless and Soft Capsules (uncoated)

- Capsules that pass through the stomach to dissolve in the intestines.
- These capsules are made of natural raw materials and are designed to pass through the stomach and dissolve in the small intestine to exert their effects while maintaining the pleasing appearance of conventional seamless capsules and soft capsules.

2. Ultra-Rapid Dissolution Seamless Capsules

- Instant dissolution when placed in the mouth Seamless capsules that leave no residual shell after dissolution.
- Regular seamless capsules have an external shell that is about 400mm thick, but this capsule has reduced the shell thickness to only 100mm, allowing it to dissolve quickly in the mouth with no remaining shell.
- Moreover, it preserves the flavour of the products for a long time allowing the creation of products such as seasoning oil, bath additives, and mouth fresheners using this property.

3. Heat Resistant Seamless Capsules

- Heat resistant up to 120 degrees Celsius.
- Unlike traditional capsules, this type of seamless capsule has a unique shell structure that allows for higher temperatures.
- Hence, they can be used in a wide variety of applications such as soups, beverages, candies, and ice cream because they can withstand heat, moisture, and pressure processes both fresh and dried varieties can be produced, making them suitable for a wide variety of uses.

Fig 4: Seamless Capsules

MANUFACTURING OF SEAMLESS CAPSULES

Soft gelatin delivery system is a unitary tube, made up of gelatine outer layers, that contains the active ingredients in solution, suspension, or paste form. The soft gelatin capsule may have many shapes and sizes, depending on the structure.

Hydrophobic drugs can lead to poor bioavailability. These drugs will not dissolve well in water, gastric, or intestinal fluid, and when they are mixed in solid dosage forms, the dissolution rate may be slow, absorption may vary, and the bioavailability may be poor.

Bioavailability is enhanced in the presence of fatty acids, e.g., mono or diglycerides. Fatty acids can solubilize hydrophobic substances in the gut and facilitate faster absorption. Unlike other soft gelatin capsules, these capsules deliver drugs in solution and also offer a solid dosage form.

Hydrophobic drugs are dissolved in a hydrophilic solvent, which, when crushed or chewed, releases the drug immediately to form a gastric juice solution ready for absorption from the gastrointestinal tract into the bloodstream.

Consequently, the desired therapeutic effects are quickly delivered.

As a fine particle cloud, acid-soluble compounds may remain in solution and acid-insoluble compounds may precipitate as a fine particle, but they re-dissolve quickly and result in a high degree of bioavailability.

Soft gel development time is shorter due to fewer bioavailability issues, and such solutions can be offered at a fraction of cost.

Ibuprofen soft gelatin capsules, on the other hand, have a shorter time to reach peak plasma concentration and a higher peak plasma concentration than a marketed tablet formulation.

Cyclosporin can provide therapeutic blood levels that are not achievable in tablet form.

Similarly, oral hypoglycaemic glipizide in soft gelatin capsules is also known to have better bioavailability results than tablet form.

Soft gel delivery systems can also include phospholipids, polymers, or natural gums to entrap the drug active in the gelatine layer with an outer coating to achieve desired delayed/controlled release effects.[11]

ENCAPSULATION THEORY: -

Principle-

From the nozzle, the core solution and shell solution are ejected simultaneously. Mini capsules are formed as a result of the surface tension effect between different solutions. The shell solution is solidified to form a shell in the cooling solution.

Here's an overview of how encapsulation theory intersects with seamless capsule manufacturing:

- Encapsulation concept: - Encapsulation involves enclosing one substance within another, often to protect the encapsulated substance, control its release, or facilitate its delivery to a specific target. In pharmaceuticals, a shell or matrix is used to contain active pharmaceutical ingredients.

- Shell material selection: - The selection of materials for capsule shells is guided by encapsulated theory. The materials must meet strict criteria for safety, biocompatibility, stability, and manufacturability. Synthetic materials such as Hydroxypropyl methylcellulose, or HPMC, are used in capsule manufacturing.
- Manufacturing techniques: - The development of manufacturing processes for seamless capsules is informed by encapsulated theory. Injection molded, dip molded, and capsule-in-capsule technology are some of the techniques used to create capsules with precise dimensions, uniform thickness, and smooth surfaces.
- Drug encapsulation and release: - Drug release and drug stability can be improved with the help of Encapsulation theory. It's possible to protect sensitive APIs from degradation caused by environmental factors, pH changes, or enzymatic activity in the gastrointestinal tract with the help of the encapsulated APIs.
- Targeted delivery strategies: - Strategies for drug delivery using capsules are covered in encapsulated theory. The capsule's contents can be released at specific locations within the body, allowing for targeted therapy and avoiding systemic side effects.

Fig 5: Encapsulation machine

Construction-

1. Vibrator:

Obtains uniform size and weight. Adapt the rate of capsule droplet formation.

Using the vibrator, we can achieve uniform pressure.

It is located on the top of the encapsulation unit, i.e., the vibrator is mounted on the top of the machine.

2. Core-Liquid Inlet:

The vessel holds the core liquid by the core liquid inlet, and the system's core liquid is introduced into the system.

3. Shell Liquid Inlet:

Shell liquid is introduced into the system through the shell liquid inlet, where it covers the inlet conical vessel containing core liquid.

4. Nozzle Unit:

It is the bottom of the conical vessel where shell liquid meets core liquid in a spherical shape.

Pumps are used to pump the core and shell fluids these are ejected into a cooling liquid, forming the seamless mini capsules.

5. Rectifier:

It is used for obtaining a uniform flow of cooling liquid.

Processing steps at the production scale

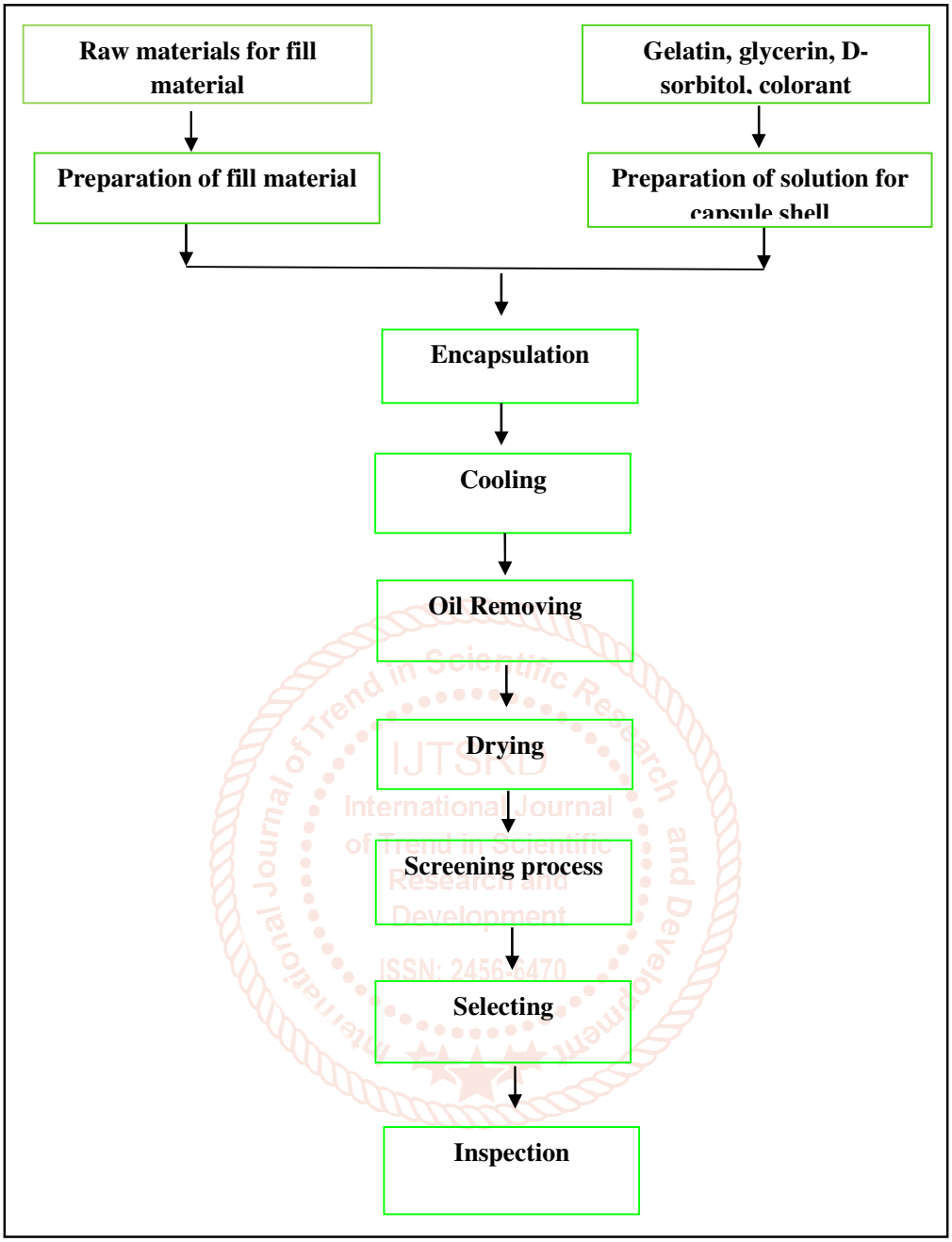


Fig 6: Steps for production of seamless capsule

Processing steps at production scale explanation

- The Gelatin mass and medicine for the capsule fill are prepared before the process begins. The Gelatin powder is heated and stirred under a vacuum. The medicine fill is prepared using standard procedures used in pharmaceutical liquid, paste, or suspension manufacturing. The outer layer of the vessel requires flavors or colors to be added using a turbine mixer and is transferred to mobile vessels. The mass is kept at a constant temperature in a steam-jacketed storage vessel.
- Molten gel is pumped into the machine. At the top of the machine is where this enters. The conical vessel of core material is surrounded by shell material. The vibrator puts appropriate pressure on the material towards the nozzle. The pressure is regulated by a monitor.
- The core material is covered by shell material at the nozzle unit. The size of the capsule can affect the Orifice of the nozzle and the pressure produced. The cooling liquid is regulated by a rectifier. The drying of droplets is done after solidification.

Formulation steps: -

1. Preparing shell solution-

Various shell solutions are prepared, each according to their intended use, with

appropriate caution being used to keep the gel strength form from decreasing.

2. Encapsulation-
Oil is carefully isolated from the capsule's surface layer, and excessive pressure is carefully avoided.

3. Cooling-
During cooling, the outer layer of the capsules begins to solidify. The capsules have sufficient hardness due to the cooling process, it can be achieved by using coolant solutions.

4. Drying-
The soft capsules are carefully dried in a controlled humid environment.

5. Quality Inspection-
The contents of each capsule are measured according to GMP. [[7]]

Conclusion: -
There are far-reaching benefits to seamless capsule manufacturing.

Their smooth design and advanced manufacturing techniques offer many advantages in the pharmaceutical industry.

A seamless surface that is easier to swallow and less likely to cause irritation, contributes to enhanced patient compliance and comfort.

Moreover, the improved drug stability ensured by seamless capsule manufacturing processes helps maintain the potency and effectiveness of medications over time. This aspect is essential for ensuring the safety and efficacy of pharmaceutical products throughout their shelf life.

For patients with swallowing difficulties or sensitivities, this aspect is crucial.

The pharmaceutical industry's continuous efforts to improve patient outcomes, enhance drug delivery systems, and elevate standards of quality and innovation are reflected in the seamless capsule.

Patients and healthcare professionals alike stand to benefit from safer, more effective, and more user-friendly medication options as pharmaceutical companies increasingly adopt seamless capsule technology.

REFERENCES:

[1] S Arora, GK Jain, FJ Ahmad, VB Hostetler*, JP Stanley*, "Lachman/Lieberman's Theory and Practice of Industrial Pharmacy", CBS Publishers and Distributors Pvt. Ltd., 4th Edition, Page no.: - 546

[2] Pharmaceutical Drugs and Dosage, available at https://www.pharmacy180.com/article/soft-gelatin-capsules-2844/#:~:text=Soft%20gelatin%20capsules%20may%20contain,is%20a%20self%2Dmicroemulsifying%20preconcentrate.

[3] Seamless Mini Capsule, Products, Freund Corporation, Available at http://www.freund.co.jp/english/chemical/trustee/seamless_capsule.html.

[4] Capsule shell material, fill material, drug content. Available at https://www.tokaicap.co.jp/e_develop/02.html

[5] Softgels (Soft Gelatin Capsules) available at http ://www.gelita.com/en/Softgel_Softcapsules

[6] Seamless capsules with a high degree of freedom in product design. Available at http://www.sunsho.co.jp/en/products/seamless capsule.shtml

[7] Seamless Soft Gelatin Capsules Manufacturing Method. Available at https://www.researchgate.net/publication/303285442 SEAMLESS SOFT GELATIN CAPSULES MANUFACTURING METHOD

[8] Gursharan Moonga, Softgel Drug Delivery Systems, innovaro pharma licensing available http://pharmalicensing.com/public/articles/view/948454700_3888452c79360/ softgeldrug-delivery-systems

[9] Garg Deepak, Kishor Kamal, Bilandi Ajay, Kataria Kumar Mahesh, "Soft Gelatin Capsules: Development, Application, and recent Patents", International Research Journal for Inventions in Pharmaceutical Sciences.

[10] Aliyu R. S., Lawal A. M., Chasta P., and Sharma G. K., "Capsules: Types Manufacturing Formulation, Quality Control Test and Packaging and Storage- A Comprehensive Review" World Journal of Pharmaceutical and Life Sciences.

[11] Chetan D. Modi, Dipak Modi, Ankit Patel, P. D. Bharadiya "Innovation in Capsules: Seamless Technology" World Journal of Pharmaceutical Research.