IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

A Review On: Process Of Manufacturing Of Capsules And Quality Control Test For Capsules

[1]Ms. Pooja Mangilal Choudhary, [3]Dr. Vijaykumar Kale, [3]Dr. Mahesh Thakare, [4]Mr. Vaibhav Narwade
[1]Student, [2]Principal,[3]Assistant Professor (Head Of Department),[4]Assistant Professor
[1]Final Year Seventh Semester Bachelor Of Pharmacy,
[1-4]Kasturi Shikshan Sansthan College Of Pharmacy, Shikrapur, Pune, India

Abstract: Capsule filling, also known as encapsulation, is an important step in pharmaceutical manufacturing where empty hard or soft gelatin capsules are filled with powders, granules, semisolids, or liquid drug formulations. This project focuses on understanding and improving how capsule filling machines work, especially those that use the tamping principle to measure and fill the required dose. Traditional machines rely on mechanical springs, but newer systems use pneumatic pressure to improve control during the filling process. However, major adjustments in fill weight still depend on setting the correct tamping pin depth and powder bed height.[1]The main aim of this project is to study, design, and optimize key parts of the capsule filling machine to achieve better accuracy, consistency, and efficiency. The project outlines the limits of the study by concentrating on machine design, dosing performance, and fill weight control. Methods such as process evaluation, modeling, testing, and data analysis are used to understand how various machine parameters affect capsule quality.This work is important for improving reliability in pharmaceutical production, ensuring accurate dosing, and supporting advancements in capsule technology. The expected result of the project is to identify improved operating settings, enhance fill weight uniformity, and propose design or process improvements that make capsule filling more efficient and dependable.

Keywords – Capsules; Gelatin; Hard Gelatin Capsules; Soft Gelatin Capsules; Capsule Filling Machines; Advantages and Disadvantages; Types of Capsule Filling Machines; Working Principles of Capsule Filling.

I. INTRODUCTION

Capsule:

Capsules are solid oral dosage forms in which medicines are enclosed inside a hard or soft shell. These shells are usually made from gelatin and serve as small containers that hold the active drug or formulation. Capsules provide a convenient, tasteless, and odourless way to deliver medications without needing an additional coating step, which is often required for tablets.[5]

The word *capsule* comes from the Latin term *capsula*, meaning “a small container.” Capsules play an important role in pharmaceutical development and are often considered one of the most preferred oral dosage forms due to their simple manufacturing process and patient-friendly features.

Advantages of Capsules

- Cost-effective compared to many other dosage forms
- Easy for patients to handle, carry, and use
- Effectively mask unpleasant tastes and odors of drugs
- Have an attractive and professional appearance
- Become smooth when slightly moist, making them easier to swallow with water [8]

Disadvantages of Capsules

- Hygroscopic drugs absorb moisture from the capsule shell, causing the shell to become brittle, making such drugs unsuitable for capsule filling
- Generally, have a shorter shelf life compared to tablets
- Can be more expensive to produce than some other dosage forms
- Often contain animal-derived gelatin, making them unsuitable for certain dietary or cultural preferences [8]

Types of Capsules: Capsules used in pharmaceutical formulations are mainly classified into two categories:

1. *Hard gelatin capsules*
2. **Soft gelatin capsules**

Hard Gelatin Capsules: Hard gelatin capsules are designed to hold dry powders or granules, with or without excipients. These capsules consist of two separate cylindrical parts—the body and the cap. The longer part, called the *body*, contains the drug, while the shorter part, known as the *cap*, is placed over the body to securely close the capsule. Their simple two-piece structure makes them highly versatile and commonly used for a wide range of oral medications.[2]

Soft Gelatin Capsules: Soft gelatin capsules are single-piece units that are fully sealed and flexible. They are made from gelatin mixed with plasticizers such as glycerin or sorbitol, which make the shell soft and elastic. Soft gels are ideal for enclosing liquids, suspensions, oils, or semisolid drug formulations. Their airtight nature helps protect the contents and improves stability.

What is Gelatin?

Gelatin is a mixture of proteins obtained by breaking down animal collagen through controlled hydrolysis. It forms the primary material for capsule shells due to its ability to dissolve in the stomach and form stable, flexible films. Gelatin is classified into two types based on its method of preparation: [4]

Type A Gelatin: Produced from collagen that has undergone acid treatment. It typically has an isoelectric point around pH 9.0.

Type B Gelatin: Obtained from collagen treated with alkaline processes, commonly using bones. Its isoelectric point is around pH 4.7.

Gelatin Capsules:

Gelatin-based capsules are widely used as oral dosage forms and are mainly produced in two varieties: hard gelatin capsules and soft gelatin capsules. Both types use gelatin as the fundamental shell material but differ in structure, formulation, and applications.

1. *Soft Gelatin Capsules*

- **General Overview**

  Soft gelatin capsules were first introduced in the 19th century to help mask unpleasant tastes and odors of medicines. Over time, their use has expanded beyond pharmaceuticals into nutritional supplements, cosmetics, and even non-medical products such as paintballs. Their flexible structure allows them to safely contain liquids, oils, and semisolid formulations, making them versatile across industries.[5]

- **Basic Components of a Soft Gelatin Capsule Shell**

  Soft gelatin capsule shells are made from a combination of materials that determine their flexibility, strength, appearance, and stability. The major components include:

Gelatin: Gelatin is the primary material used to form soft gel shells. Soft gels are especially valued in the pharmaceutical industry because they:

a. Provide uniform dosing even for low-strength drugs
b. Minimize exposure to hazardous or highly potent drug materials
c. Offer a patient-friendly, easy-to-swallow dosage form

Recent developments in soft gel technology have focused on improving bioavailability by using liquid or semisolid fills that enhance drug dissolution and absorption.

Most soft gel formulations use type B gelatin (alkali-treated), which generally forms about 40% of the molten gel mass. Type A gelatin (acid-treated) may also be used depending on formulation needs. The final shell properties depend greatly on the grade of gelatin selected and on how much plasticizer is added to the mixture. [2]

Plasticizing Agents: Plasticizers are added to ensure the shell remains flexible and does not crack during processing or storage. They work by interacting with gelatin molecules to reduce the glass transition temperature (Tg**)** and improve moisture retention. [4]

Common plasticizers include:

a. Glycerol (most frequently used)
b. Sorbitol
c. Mannitol
d. Polypropylene glycol

These may be used alone or in blends to adjust shell softness and elasticity.

Water: Water is an essential component, making up 30–40% of the wet gel mass. It helps form the molten gel during manufacturing and contributes to the flexibility of the finished capsules. The ideal water-to-gelatin ratio depends on the viscosity of the gelatin used and typically ranges from **0.7** to 1.3 parts water per part of dry gelatin.

Preservatives: Preservatives are added to prevent microbial contamination, especially since gelatin solutions can support the growth of bacteria and mold. Commonly used preservatives include: [11]

a. Potassium sorbate
b. Methyl, ethyl, and propyl parabens (hydroxybenzoates)

These ensure the stability and safety of the gelatin mass during processing and storage.

Colorants and Opacifiers: Coloring materials may be added to improve the appearance of the capsules or for product differentiation. Opacifiers such as titanium dioxide are used when the contents are sensitive to light. Generally, darker colors are chosen to better conceal the fill material.[3]

Colorants may include:

a. Water-soluble dyes
b. Insoluble pigments
c. Lakes (pigments bound to a substrate)

Other Excipients: Additional optional ingredients may be used depending on the specific formulation:

a. Flavors and sweeteners for better taste
b. Acid-resistant polymers for enteric or delayed-release properties
c. Materials for chewable soft gels
d. Chelating agents such as EDTA, which prevent degradation of drugs sensitive to oxidation by binding trace metals in the gelatin

2. *Hard Gelatin Capsules*

- **General Overview**

Hard gelatin capsules are the most widely used capsule type in pharmaceutical manufacturing. They consist of two separate parts—a longer body and a shorter cap— which are designed to fit snugly together to form a sealed unit. These shells are usually made from a mixture of gelatin, water, and small amounts of sugar, producing a clear, tasteless, and colourless capsule in its basic form.Unlike soft gelatin capsules, hard gelatin shells are produced as empty units by specialized manufacturers. These empty capsules are then supplied to the pharmaceutical industry, where they are filled with powders, granules, pellets, or other solid drug forms. During filling, the medicinal material is placed into the body of the capsule, after which the cap is placed onto the body to secure and close the dosage unit. [7]

- **Basic Components of Hard Gelatin Capsules**

The major components include:

Gelatin: Gelatin has been the standard raw material for hard capsule shells for almost a century because of its excellent ability to form films and its reliable gelling properties. It is obtained by hydrolyzing collagen from animal sources such as skin, connective tissue, and bones.

Despite its usefulness, gelatin does present some challenges. As an animal-derived protein, it may show chemical instability under certain conditions and carries a theoretical risk of transmitting prion-related diseases like transmissible spongiform encephalopathy (TSE). Nevertheless, due to strict processing and quality controls, it remains the most preferred capsule material. [2]

Plasticizers: Plasticizers are added to gelatin to reduce brittleness and improve the flexibility of the capsule shell. Commonly used plasticizers include:

a. Glycerin
b. Polyhydric alcohols

Water itself also acts as a natural plasticizer because it is inherently present in gelatin. Together, these agents help produce capsule shells that are strong yet sufficiently elastic to withstand handling and filling operations. [4]

Colorants: Colorants are frequently used to enhance the appearance of hard gelatin capsules and to help distinguish between products or strengths. Only approved colouring agents that comply with regional regulatory guidelines can be used. Typical colorants include: [3]

a. Azo dyes
b. Xanthene dyes
c. Iron oxide pigments

These pigments may be used alone or in combination to produce a wide range of capsule colours.

Opacifying Agents: Opacifiers, such as titanium dioxide, may be added to convert transparent shells into opaque ones. Opaque capsules can protect light-sensitive formulations or conceal the appearance of the fill material to improve the product's visual presentation.[5]

Preservatives: Historically, preservatives like paraben esters were incorporated during capsule production to prevent microbial contamination. However, with the adoption of modern Good Manufacturing Practices (GMP), the use of preservatives has largely been discontinued.

Finished hard gelatin capsules typically contain 12% to 16% moisture, which is strongly bound to the gelatin molecule. This natural moisture level results in water activity too low to support microbial growth, making added preservatives unnecessary. [17]

II. CAPSULE FORMULATION

A. *Formulation and manufacturing of soft gelatin capsules*

Soft capsules, commonly known as softgels, are widely used in pharmaceuticals because they can dissolve and deliver drugs more efficiently, especially hydrophobic or poorly water-soluble drugs. They also help overcome problems faced during tablet manufacturing such as poor compressibility, dose uniformity issues, and instability of sensitive drugs. [12]

- *Formulation Components (Vehicles Used in Soft Gelatin Capsules)*

Soft gelatin capsules are designed to carry liquids, semisolids, pastes, suspensions, or even certain dry materials. The choice of fill material depends on solubility, stability, and compatibility with the gelatin shell.

Water-insoluble liquids (Volatile and Non-volatile): These substances do not dissolve in water but are suitable for encapsulation:

a. Vegetable oils (e.g., olive, peanut, sesame oil)
b. Aromatic oils
c. Hydrocarbons (aliphatic, aromatic)
d. Chlorinated hydrocarbons
e. Ethers, esters, alcohols
f. Organic acids

These helps dissolve oily drugs and improve their absorption.

Water-soluble non-volatile liquids: These can mix well with the gelatin shell without dissolving it:

a. Polyethylene glycols (PEGs)
b. Non-ionic surfactants (e.g., Polysorbate 80)

They are often used to enhance drug solubility and dispersion.

Water-miscible liquids: Some liquids like propylene glycol or isopropyl alcohol can be encapsulated, but only at controlled concentrations because high water content can soften or dissolve the gelatin shell. [12]

- *Methods of manufacturing of soft gelatin capsules*

  Softgels can be manufactured using several different processes. The choice depends on production scale, type of fill, and capsule design.

1. *Plate Process (Oldest Method)*

This is the first commercial method used historically. Though outdated, it helps understand the basic concept. [5]

Process:

a. A warm sheet of plasticized gelatin is placed over a die plate that has mold depressions.
b. Vacuum pulls the gelatin sheet into the depressions, forming small capsule wells.
c. The wells are filled with the drug liquid.
d. Another gelatin sheet is placed on top and the two layers are sealed by pressure.
e. The capsules are cut, shaped, and removed.

Limitations:

- Dose variation
- Very high labour requirement
- High production waste.

Because of these disadvantages, the method is not used commercially anymore.

2. *Rotary Die Process (Most Widely Used Modern Method)*

Developed by R.P. Scherer in 1933, this process revolutionized softgel manufacturing and is still the industry standard.[9]

Process:

a. Two continuous gelatin ribbons are prepared and fed into the rotary die machine.
b. These ribbons pass between two rotating dies, each having matching pockets.
c. The fill material (liquid or semisolid drug) is pumped and injected between the ribbons.
d. The pressure causes the ribbons to expand into the die pockets.
e. As the pockets align, the ribbons are:
- Formed
- Filled
- Sealed hermetically
- Cut out from the sheet

Advantages:

- Continuous, high-speed, high-volume production
- Accurate capsule size and dose
- Better sealing and stability. This method is used for almost all commercial softgels.

3. *Reciprocating Die Process (Norton Machine)*

Introduced in 1949, this method also uses gelatin ribbons, but the encapsulation mechanism differs. [3]

Process:

a. Gelatin ribbons are passed through reciprocating (up-down moving) vertical dies.
b. These dies form small pockets in the gelatin sheet.
c. Pockets are filled with the drug liquid as the ribbons move.
d. The pockets are then sealed and shaped as the machine cycles.
e. The capsules drop into a cooled solvent bath so that they do not stick together.

Key Feature:

- Good for temperature-sensitive materials because cooling is immediate.

4. *Accogel Process (For Powders and Granules)*

This method was developed to fill powders and solid materials, which were difficult to handle in earlier processes. [7]

Process:

a. A measuring roller holds powdered fill in its cavities.
b. A gelatin ribbon is pulled into capsule-shaped cavities using vacuum.
c. Powder material is deposited into these pockets.
d. Another gelatin-coated roll seals the pockets.
e. Capsules are cut and released.

Usefulness:

- Ideal for non-flowing materials, powders, and granules.
- Allows continuous production similar to rotary die method.

5. *Seamless (Bubble) Method*

This method produces single-piece spherical capsules known as "pearls." It is also used for cosmetics and supplements. [21]

Process:

a. A concentric nozzle system is used:
- Outer nozzle releases molten gelatin.
- Inner nozzle releases the drug liquid.

b. A pulsating mechanism forms drops where the drug core is surrounded by gelatin.
c. These droplets fall through air or cooling liquid.
d. They solidify into perfectly spherical, seamless capsules.

Advantages:

- No die machinery required
- Produces smooth, elegant, one-piece capsules
- Suitable for oils, fragrances, and health supplements

B. *Formulation and Manufacture of Hard Gelatin Capsules Step 1: Preparation of*

Gelatin Dipping Solution

Hard gelatin capsules are widely used in solid dosage forms, and the empty shells are manufactured separately before being filled by the pharmaceutical industry. The shell-making process requires strict control at every stage to ensure consistent quality.

To prepare the dipping solution, gelatin is dissolved in demineralized water at **60–70°C** inside jacketed vessels. The mixture usually contains **30–40% w/w gelatin**, making it thick and prone to trapping air bubbles. Since these bubbles can cause weight variation and structural defects, the solution is subjected to a **vacuum treatment** to remove trapped air.[2]

After degassing, **colorants, opacifiers, and processing aids** like sodium lauryl sulfate are added for color uniformity and smooth surface formation. The viscosity of the solution is carefully adjusted with hot water, so it meets the required operating specifications.

Step 2: Dipping Metal Pins into Gelatin

The capsule shells are produced by the dip-coating method. Stainless-steel pins—separate sets for the body and cap—are dipped into the warm gelatin solution (around 50°C). The pins are kept cooler than the solution, allowing a thin gelatin layer to solidify on their surface. [8]

Pins arranged in rows form the **body** on one side of the machine and the **cap** on the other.

Step 3: Rotation of Coated Pins

Once removed from the dipping tank, the pins rotate slowly. This ensures the gelatin film spreads evenly around the mold. Even distribution is important for achieving uniform capsule wall thickness and proper strength.

Step 4: Drying of the Gelatin Film

After leveling, a stream of cool air is blown over the coated pins to initiate gelling. The pins then pass through **controlled drying zones** where the gelatin slowly loses moisture until it reaches the required hardness and flexibility.

Step 5: Stripping and Trimming

When dried, the gelatin shells are gently pulled off the pins. The ends are trimmed to give each piece (body and cap) the correct length.

Step 6: Pre-Closing and Joining

The trimmed capsule parts are partially joined (pre-locked) so they stay together but can still be separated easily for filling. If required, printing may also be applied before packaging. [2]

Step 7: Printing of Capsule Shells

Printing is used for product identification and safety. Capsules may be printed with:

a. Product name or code
b. Manufacturer's name or logo
c. Strength or dosage

This helps prevent medication errors across the supply chain—from manufacturers to pharmacists and patients.

- *Filling of Hard Gelatin Capsules*

Hard gelatin capsules can be filled using **manual, semi-automatic, or fully automatic** machines. In small-scale operations, capsules may even be filled by hand. The difference between these methods lies mainly in how the dose is measured and delivered into the capsule body. [11]

Steps in Filling Capsules:

a. **Rectification:** Empty capsules are oriented so all bodies face downward.
b. **Separation:** The cap is removed from the body.
c. **Dosing:** Powder or granules are filled into the body manually or by a machine. Excess material is scraped away.
d. **Closing:** The cap is placed back onto the filled body.

e. **Ejection:** The finished capsules are removed from the machine.

- *Filling Liquids or Semisolids into Hard Gelatin Capsules*

To improve the solubility of poorly water-soluble drugs, liquids, lipid mixtures, or molten semisolids may be filled into hard gelatin capsules. The formulation must have appropriate flow and coating characteristics. Usually:

-Viscosity should be within **50–1000 cP** (higher values are still feasible).

-Filling temperature should generally **not exceed 70°C**. [7]

- *Examples of Compatible Liquid Excipients*

Lipophilic excipients

- Vegetable oils (olive, peanut, castor, coconut, sesame, corn, soybean)
- Esters (ethyl oleate, isopropyl myristate)
- Fatty acids (palmitic, stearic, lauric, oleic)
- Fatty alcohols (cetyl, stearyl alcohol)

Hydrophilic excipients

- Polyethylene glycol (PEG 3000–6000)

Amphiphilic excipients

- Poloxamers
- Lecithin
- PEG esters (Gelucir, Labrafil) [5]

- *Locking and Sealing of Hard Gelatin Capsules*

To prevent accidental separation or leakage during handling and storage, various sealing methods are used: [7]

a. **Banding:** A gelatin band is applied around the seam.
b. **Moistening:** Slight wetting helps bond the cap and body.
c. **Spot welding:** Heat produces small welds at contact points.
d. **Thermal welding:** Controlled heat fuses the capsule parts.
e. **Using Coni-Snap shells:** These have built-in locking features.

III. Quality Control Tests for Capsules

Quality control (QC) tests ensure that both hard gelatin and soft gelatin capsules meet official standards for safety, efficacy, and uniformity. These tests are grouped into three stages:

1. In-process quality control (during manufacturing)
2. Finished product testing (after capsules are made)
3. Stability and shelf-life testing (during storage)

1. In-Process Quality Control Tests

These tests are performed during capsule filling to maintain consistency throughout the batch. They help operators adjust machine settings if any variation occurs.[13]

For Soft Gelatin Capsules: During softgel manufacturing, the following parameters are closely checked:

- **Gel ribbon thickness:** Both sides of the gelatin ribbon must be uniform in thickness to ensure proper sealing and capsule strength.
- **Seal thickness:** The sealed border between the two ribbons is inspected to ensure capsules are properly closed and leak-proof.
- **Fill weight & variation:** Each capsule must contain the correct amount of liquid or semi-solid fill. Variability indicates machine issues.
- **Shell weight & variation:** The weight of the gelatin shell is monitored to ensure consistent capsule formation.
- **Moisture content:** Moisture is checked before and after drying to avoid brittleness or excessive softness.

For Hard Gelatin Capsules: Key in-process checks include:

- **Visual inspection:** Capsules are inspected for cracks, dents, or improperly closed caps.
- **Fill weight:** Random samples are checked to ensure each capsule contains the correct amount of powder.
- **Weight uniformity:** Helps maintain consistency across the batch.

2. Finished Product Quality Control Tests

Once the capsules are produced, they undergo official compendial tests to ensure they are acceptable for distribution. [7]

a) *Permeability & Sealing*

Soft gelatin capsules are checked visually for leakage or deformation.

Hard gelatin capsules are inspected for damaged caps, cracks, or separation of cap and body.

b) *Potency & Impurities*

- The drug content of each capsule must match the labelled strength.
- Capsules are tested for related substances to ensure no harmful impurities are present.

c) *Weight Variation Test*

Ensures uniformity in the amount of drug per capsule.

For Hard Gelatin Capsules

a. Weigh 10 intact capsules individually.
b. Empty and weigh each shell.
c. Subtract to get net fill weight.
d. Calculate drug content using formulation percentage.

For Soft Gelatin Capsules

a. Weigh 10 capsules individually.
b. Cut open and wash out contents with a suitable solvent.
c. Allow solvent to evaporate.
d. Weigh empty shells.
e. Subtract to get net contents.

Automated weight-checking machines are often used to reject overfilled or underfilled capsules.

d) *Content Uniformity*

Done when:

- Weight variation fails
- Or when required by the monograph Requirements:

- 9 out of 10 units must contain 85–115% of labelled amount.
- No single capsule may contain less than 75% or more than 125% of the labelled amount.

e) *Disintegration Test*

Ensures capsules break down properly in the GI tract.

a. Capsules are placed in a basket-rack assembly at 37 ± 2°C.
b. The basket moves up and down 30 cycles per minute.
c. Capsules must disintegrate within the time stated in the monograph.

f) *Dissolution Test*

Determines how fast and how much drug dissolves from a capsule.

- Ensures consistent drug release between batches.
- Results must match the dissolution profile of the batch proven to be clinically effective.

g) *Moisture Content*

Measured using Karl Fischer titration.

- Important because moisture affects capsule integrity and drug stability.
- Can be performed on whole capsules or only the fill.

h) *Moisture Permeation Test*

Required for assessing packaging suitability.

a. Capsules are packed with a moisture-detecting desiccant pellet.
b. Exposed to controlled humidity.
c. Pellet color change indicates moisture entry.
d. Weight before/after exposure is compared.

i) *Microbial Limit Test*

Ensures capsules are free from harmful microorganisms.

a. Capsule contents are incubated in suitable media.
b. Colony counts are taken after incubation.
c. Must meet pharmacopeial microbial limits.

3. Shelf-Life / Stability Testing

Conducted to determine:

- How long the product maintains quality
- Suitable storage conditions
- Effect of temperature, humidity, and light

Types of Stability Tests:

- Accelerated stability testing (high temperature/humidity)
- Long-term testing (real-time storage conditions)
- Stress studies on the drug and excipients

These tests help establish expiry date and optimal packaging.

IV. PACKAGING AND STORAGE OF CAPSULES

- *Packaging and Storage of Hard Gelatin Capsules*

Hard gelatin capsules contain about 13–16% moisture, which is essential for maintaining their flexibility and physical integrity. When the moisture drops below 12%, the shells become brittle and may crack, while moisture levels above 18% can make the capsules soft, distorted, or sticky. Therefore, hard gelatin capsules should be stored in an environment with controlled temperature and a relative humidity of 40–60% to prevent moisture loss or absorption. Moisture can transfer between the capsule shell and its contents, especially if the drug powder is hygroscopic or deliquescent, which may lead to clumping, poor disintegration, or reduced stability. It is often necessary to equilibrate the humidity of both the shell and the formulation before filling to avoid such issues. Another concern with hard gelatin capsules is gelatin cross-linking, which can occur with prolonged exposure to high temperature, humidity, or trace amounts of aldehydes such as formaldehyde. Cross-linking forms a pellicle on the capsule surface and results in delayed dissolution, sometimes causing failure to meet USP dissolution criteria. Hard elatin capsules are typically packaged in strip or blister packs to protect them from moisture, oxygen, and physical damage. These packaging materials must be heat-stable, moisture-resistant, durable enough for mechanical handling, and easy for patients to open. [8]

- *Packaging and Storage of Soft Gelatin Capsules*

Soft gelatin capsules contain drug formulations dissolved or dispersed in oils or hydrophilic liquids, and the shell contains plasticizers such as glycerin along with residual moisture, making them more flexible but also more sensitive to environmental changes. Moisture can migrate between the shell and the fill material, and volatile solvents inside the fill may evaporate if not properly protected. These interactions can cause problems such as shell deformation, leakage, changes in plasticity, or precipitation within the fill. To maintain their stability, soft gelatin capsules are usually stored at temperatures between 15°C and 25°C and at a relative humidity of 35–65%. Stability testing for softgel products includes evaluation of appearance, brittleness, color, odor, leakage, pellicle formation, drug content, degradation products, dissolution behavior, microbial contamination, pH, and clarity of the fill material. Stability studies also assess thermal sensitivity, solvent loss, and moisture uptake. If softgel formulations are found to be heat-sensitive, they must be stored at a lower temperature than standard conditions, such as at 30°C instead of 40°C, and this temperature becomes the recommended long- term storage condition. Proper packaging and controlled storage conditions are essential to maintain the product's integrity, prevent moisture imbalance, and ensure consistent drug release throughout its shelf life. [11]

V. FUTURE SCOPE

Develop safer and more advanced capsule materials: Future research aims to replace traditional animal-based gelatin with safer and more stable materials. **Example:** Creating capsules made from starch or plant-based polymers so vegetarians, vegans, and people with gelatin allergies can safely use them.[22]

Improve dissolution and drug-release behavior: The goal is to design capsules that dissolve in a more predictable way, ensuring consistent absorption. **Example:** Developing capsules that dissolve faster in patients with low stomach acid or release the drug slowly over several hours for long-acting therapy. [23]

Create capsules suitable for modern and sensitive drugs: Many new drugs are oily, heat-sensitive, or poorly soluble; future capsules should be able to hold these safely
.**Example:** Improving SGC shells to better hold omega-3 oils, CBD oils, or vitamin D without leakage.

Enhance capsule stability during storage and transport: Capsules sometimes crack or soften if exposed to moisture or heat. A future goal is to make them more durable

.**Example:** Designing HGC shells that don't absorb moisture in humid climates, so they don't become too soft.[13]

Advance manufacturing technology for accuracy and safety: New technologies can help produce more uniform capsules with fewer defects. .**Example:** Using real-time sensors during filling to ensure every capsule contains exactly the same amount of medication. [25]

Design capsules for targeted or controlled drug release: Capsules can be modified to release medicine in specific parts of the digestive system. **Example:** Coating capsules so they only open in the intestine, useful for treating diseases like Crohn's or ulcerative colitis.[27]

Reduce common problems like brittleness, leakage, or sticking: Improving formulation and processing can help avoid defects. **Example:** Adding better plasticizers to prevent SGC from becoming too brittle and cracking during transport. [2]

Develop environmentally friendly production methods: Future capsule manufacturing should reduce waste and use materials that are eco-safe. **Example:** Switching to biodegradable capsule materials that break down safely after disposal. [29]

Improve patient comfort and compliance: Capsules should be easier to swallow and more appealing to patients. **Example:** Producing smaller, smoother capsules for children or elderly patients who struggle with swallowing large doses.

Lower manufacturing costs while maintaining high quality: The aim is to make capsule production more affordable without reducing safety or effectiveness. **Example:** Using automated filling machines that reduce labor costs while improving accuracy. [28]

VI. RECENT DISCOVERY

Self-pressurized gelatin capsules for oral biologic delivery

Researchers from Georgia Institute of Technology developed a hard-gelatin capsule that builds internal pressure (via effervescent reaction) to propel a biologic drug past the stomach barrier and into the small intestine. Key points:

- Designed to let biologics (like insulin, GLP-1 drugs) which normally require injections be taken orally. [20]
- The follow-up work addressed stability issues: an enteric coating to protect in gastric fluid and controlling humidity during manufacture/storage to preserve the effervescent reaction.
- This shows gelatin capsule use is evolving from simple shell + fill to active mechanical/functional behavior (propulsion, targeted release).
- Implication: Could significantly improve patient compliance (no injection) and broaden capsule use into biologics. [11]

Next-generation capsule manufacturing & materials review

A 2025 review on capsule technologies titled "Next generation capsules: emerging technologies in …" looked at how shells and manufacturing methods are changing for gelatin capsules and other capsule types. Highlights:

- Techniques like 3D printing, injection moulding being applied to capsules.
- Alternative shell materials (besides gelatin) being discussed in the context of improved stability, targeted release, modified dissolution. [31]
- Emphasis that gelatin capsules are no longer 'just fill & swallow' but part of advanced delivery systems.

Why these discoveries are important for the field

- They push capsules into **biologic delivery territory**, not just small molecule drugs.
- They combine shell material engineering + functional mechanisms (pressure generation, coatings) to handle barriers (e.g., stomach acid, intestinal uptake).
- From a manufacturing / regulatory perspective, these represent new challenges (shell integrity, product stability, new processing methods).
- For markets like India, these give opportunity and challenge: local manufacturing of advanced capsule systems may require new technology but could provide competitive edge. [25]

VII. CONCLUSION

Hard gelatin capsules (HGCs) and soft gelatin capsules (SGCs) are among the most commonly used oral dosage forms because they are highly adaptable, well accepted by patients, and capable of enclosing a wide variety of medicinal substances. HGCs are particularly suitable for powders, pellets, granules, and certain semisolid formulations, making them convenient and flexible for formulators. In contrast, SGCs are preferred for oily preparations, hydrophobic drugs, and liquid or suspension-based formulations that require a single-piece, hermetically sealed capsule. Their manufacturing techniques also support enhanced absorption of drugs with poor water solubility.

Both HGCs and SGCs ensure accurate dosing, rapid breakdown within the body, and improved stability of their contents. The choice between the two types depends on the physicochemical properties of the drug, formulation needs, and therapeutic goals. Due to these advantages, capsules continue to be a vital and highly adaptable dosage form in pharmaceutical practice.

Furthermore, capsules offer significant flexibility during product development, allowing quicker formulation adjustments and faster demonstration of proof-of-concept, which shortens overall development timelines. They also reduce both cost and operational complexity, as fewer manufacturing steps are required compared to many other dosage forms. Additionally, their easy-to-swallow design and favourable patient perception improve adherence. Overall, capsule manufacturing involves fewer stages, translating to savings in equipment, manpower, and quality control—ultimately lowering the cost per unit.

VIII. REFERENCES

1. Zhong, S., Chen, Y., & Xie, F. (2019). Optimization of tamping-pin dosing for powder capsule filling using pneumatic control. *International Journal of Pharmaceutics, 566*,
2. Aulton, M. E., & Taylor, K. M. G. (2018). *Aulton's pharmaceutics: The design and manufacture of medicines* (6th ed.). Elsevier.
3. Gullapalli, R. P. (2010). Soft gelatin capsules (Softgels). *Journal of Pharmacological & Biomedical Analysis*, 53(3), 302–318
4. Schrieber, R., & Gareis, H. (2007). *Gelatine handbook: Theory and industrial practice*. Wiley-VCH.
5. Cole, E. T., Cadé, D., & Benameur, H. (2008). Challenges and opportunities in capsule delivery systems. *Advanced Drug Delivery Reviews, 60*(6), 747–756339–349.
6. Lachman, L., Lieberman, H. A., & Kanig, J. L. (2008). *The theory and practice of industrial pharmacy* (4th ed.). Lea & Febiger
7. Rahman, M., & Haque, M. (2018). Development and evaluation of solid dosage forms in hard gelatin capsules. *Journal of Drug Delivery Science and Technology, 46*, 131– 140.
8. Jones, B. E. (2004). *Hard capsules: Development and technology* (2nd ed.). Pharmaceutical Press.
9. Scherer, R. P. (1933). *Method and apparatus for manufacturing filled gelatin capsules* [US Patent 1,929,500]. United States Patent Office.
10. Allen, L. V., Popovich, N. G., & Ansel, H. C. (2013). *Pharmaceutical dosage forms and drug delivery systems* (10th ed.). Lippincott Williams & Wilkins.
11. Podczeck, F., & Jones, B. E. (2004). *Pharmaceutical capsules* (2nd ed.). CRC Press.
12. Shargel, L., Wu-Pong, S., & Yu, A. B. C. (2012). *Applied biopharmaceutics & pharmacokinetics* (6th ed.). McGraw-Hill Education.

13. United States Pharmacopeial Convention. (Latest ed.). *United States Pharmacopeia (USP): General chapters on capsules.*
14. Indian Pharmacopoeia Commission. (Latest ed.). *Indian Pharmacopoeia (IP): Capsule standards.*
15. Council of Europe. (Latest ed.). *European Pharmacopoeia (Ph. Eur.): Capsule monographs.*
16. Robinson, J. R., & Lee, V. H. L. (1987). *Controlled drug delivery: Fundamentals and applications.* Marcel Dekker
17. Rahman, M., & Haque, M. (2018). Development and evaluation of solid dosage forms in hard gelatin capsules. *Journal of Drug Delivery Science and Technology, 46*, 131– 140.
18. Florence, A. T., & Attwood, D. (2015). *Physicochemical principles of pharmacy* (6th ed.). Pharmaceutical Press.
19. Wells, J., & Aulton, M. E. (2006). *Pharmaceutical preformulation and formulation.* CRC Press.
20. Raza, K., & Kumar, B. (2018). Innovative trends in capsule technology. *Journal of Pharmaceutical Innovation, 13*(3), 225–233.
21. Shivakumar, H., & Venkatesh, S. (2015). Liquid-filled soft gelatin capsules: Formulation, manufacturing, and quality control. *Asian Journal of Pharmaceutical Sciences, 10*(2), 111–124.
22. Shah, S. (2011). Effect of moisture on capsule integrity. *International Journal of Drug Delivery, 3*(3), 305–312.
23. Desai, S. (2013). Role of hydrocolloids in capsule shell development. *Journal of Pharmaceutical Technology, 5*(1), 34–42.
24. Reddy, G., Kumar, P., & Rao, S. (2017). Vegetarian capsule shells as an alternative to gelatin. *Pharma Times Journal, 49*(6), 45–50.
25. Chen, Y., & Li, G. (2012). Advances in capsule filling technology. *Journal of Pharmaceutical Sciences, 101*(9), 3301–3310.
26. Rowe, R. C., Sheskey, P., & Quinn, M. (2009). *Handbook of pharmaceutical excipients* (6th ed.). Pharmaceutical Press.
27. Chauhan, N., Sharma, N., & Jain, V. (2014). Modified-release capsules for oral drug administration. *Journal of Controlled Release, 178*, 78–90.
28. Kibbe, A. H. (Ed.). (2000). *Handbook of pharmaceutical excipients* (3rd ed.). Pharmaceutical Press.
29. Banker, G. S., & Rhodes, C. T. (2002). *Modern pharmaceutics* (4th ed.). Marcel Dekker.
30. Arora, S., & Ali, J. (2010). Gelatin alternatives in modern capsule manufacturing. *International Journal of Health & Allied Sciences, 2*(1), 14–20.
31. Rowe, R. C., Sheskey, P., & Quinn, M. (2009). *Handbook of pharmaceutical excipients* (6th ed.). Pharmaceutical Press.
32. Rowe, R. C., Sheskey, P., & Quinn, M. (2009). *Handbook of pharmaceutical excipients* (6th ed.). Pharmaceutical Press.
33. Chaudhari, S., Patil, P., & Jain, P. (2018). Soft gelatin capsule technology: An updated overview. *International Journal of Pharmaceutical Research, 10*(3), 78–85.
34. Kaur, G., & Singh, D. (2016). Formulation aspects of hard capsules. *Asian Journal of Pharmaceutics, 10*(2), 100–108.
35. Rao, R., & Gopi, S. (2016). Application of plasticizers in gelatin capsule shells. *Pharmaceutical Formulation Journal, 12*(2), 24–30