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CHEWABLE SOFT GELATIN CAPSULES: A REVIEW OF MANUFACTURING TECHONOLOGY

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ABSTRACT

This study aims to create and assess chewable soft gelatin capsules, designed as a user-friendly dosage form that facilitates administration, particularly for pediatric and geriatric patients. Traditionally, soft gelatin capsules are utilized to deliver liquid or semi-solid active pharmaceutical ingredients (APIs) within a gelatin shell. This research, however, concentrates on a chewable version that aims to enhance adherence among individuals who experience difficulties with swallowing. In this formulation, the gelatin shell is modified to ensure easy chewing while preserving the stability and bioavailability of the active ingredients contained within. A variety of excipients, such as plasticizers and sweeteners, are optimized to provide an enjoyable taste and texture, while also ensuring the capsules maintain their structural integrity. The evaluation of these capsules includes assessments of their mechanical properties, disintegration time, taste-masking effectiveness, and the release profile of the active ingredients.

INTRODUCTION

Chewable forms represent a distinctive category of dosage forms that offer numerous benefits. They serve as a highly convenient oral dosage option for children. Chewable capsules play a vital role in the development of nutraceutical formulations. This dosage form effectively addresses issues related to swallowing difficulties. Capsules are characterized as solid unit dosage forms containing medications, typically presented as small gelatin shells that enclose precisely measured drug substances. They hold a crucial place in drug development and are often regarded as the primary oral dosage form due to their

manufacturing advantages over other forms. Gelatin possesses the ability to disintegrate upon contact with water, facilitating the complete release of the medication. Alternatives to gelatin, such as denatured gelatin, methyl cellulose, and polyvinyl alcohol, can also be utilized for capsule shell production. A chewable soft gel capsule is designed to encapsulate orally ingestible products.

This capsule features an outer shell composition that includes at least one type of gelatin, constituting 20% to 60% of the total shell weight, ideally between 30% and 47%. It also contains a plasticizer to enhance flexibility, starch, an anti-tacking and softening agent to prevent stickiness, and water.[1] The chewable soft gel capsule is well-suited for encapsulating medicinalsubstances.

They are mainly two forms of capsules in pharmaceutical product,

- Hard capsule
- Soft capsule

HARD CAPSULE

Hard capsules are typically used for encapsulating dry solid active ingredients. They are constructed in two parts: a body and a cap, which facilitates the filling process. These capsules are designed to hold dry, powdered substances or small pellets produced through methods such as extrusion or spherization. The design features a smaller-diameter body that is filled and subsequently sealed with a larger-diameter cap. The exterior of a hard capsule consists of two interlocking halves that create a sealed enclosure, while the interior is filled with dry medication in either powder or pellet form. Additionally, some hard capsules are designed to contain liquid medication, referred to as liquid-filled hard capsules (LFHC).

SOFT CAPSULE

Soft gelatin capsules possess a thicker structure and necessitate the inclusion of extra components like glycerin to achieve their pliable consistency. These capsules are particularly well-suited for containing liquid or semi-solid substances, which makes them an excellent choice for administering oil-based formulations. Their primary function is to facilitate the absorption of liquids, specifically oily emulsions.[3]

SOFT GELS

Capsule shell composition

Capsule shells can be categorized into vegetarian and non-vegetarian types based on their source. Gelatin capsules are usually derived from animal sources, while HPMC or starch-based capsules are considered vegetarian. Capsules are composed of either gelatin (in hard or soft forms) or non- gelatin shells, which are typically produced through the hydrolysis of collagen (using acid, alkaline, enzymatic, or thermal methods) from animal sources or from cellulose.[4]

Composition

- Gelatin
- Plasticizer
- Other compounds

GELATIN

Gelatin is a water-soluble protein that can also dissolve in glycerin or propylene glycol (PG), but it remains insoluble in alcohols and other non-polar solvents like acetone and chloroform. When dissolved in water, gelatin adopts a triple helix configuration composed of three α-chains. This unique property makes gelatin an ideal material for capsules, as it can transition from a liquid toa solid state at temperatures slightly above room temperature. The stability of gelatin is attributed to the presence of amino acids that form hydrogen bonds within its structure, which in turn influences the strength of the seal in soft gel capsules and the overall functionality of the soft gel capsule shell. Gelatin is a high molecular weight polypeptide sourced from collagen, the main protein found in animal connective tissues such as bone, skin, and tendons. Gelatin gels can be produced from various sources, including bovine, pig skin, or fish skin, and can vary in Bloom strength, with options of 160 g, 200 g, or 260 g.[22]

Gelatin source

- Bovine-Bovine skin, Bovine lime, Yak skin
- Porcine-Pig skin.
- Marine-Tuna skin(fish), (fish), Saithe skin(fish), Sponge collagen.
- Poultry-Chicken tendon, Chicken skin.

POLYMER

A plasticizer is an additive incorporated into the gelatin base of capsule shells to enhance

their elasticity and strength. By reducing the likelihood of issues such as adhesion, brittleness, and leakage, plasticizers can also boost production efficiency. These substances are utilized to alter characteristics like flexibility, elasticity, and rigidity, thereby facilitating better handling of the gelatin film during production and ensuring the stability of the final soft gel product throughout its shelf life. Polymers contribute to the elasticity and pliability of the soft gel shell, with water serving as a key plasticizing agent in the formulation. Common plasticizers in soft gels include glycerol, sorbitol, and propylene glycol-400. The selection and quantity of the polymer influence the hardness of the final product and can impact its dissolution, disintegration properties, as well as its overall physical and chemical stability.

COLORANT

Dyes are compounding that dissolve in water, whereas lakes consist of a mixture of insoluble substances. There is a growing trend towards the use of natural colorants, including curcumin, riboflavin, annatto, vegetable carbon, and carotenes, due to their ecological sustainability. A colorant is incorporated into the shell formulation at a concentration of 0.5–1.0% w/w to alter the visual characteristics of the gelatin film, which typically appears transparent and ranges from light amber to light yellow, depending on the type of gelatin used.[5]

OPACIFER

The shell formula incorporates light-sensitive compounds within the filler, given that gelatin allows visible light to pass through. Titanium dioxide is the most frequently used opacifier and serves as a white pigment as well.

SWEETNER

The shell formula incorporates various components, particularly in chewable soft gel products, to enhance palatability by effectively masking the taste and odors associated with medications. Xylitol, a sugar alcohol, serves as both a sweetener and an excipient in pharmaceutical formulations. Sucralose, an artificial sweetener, is utilized as an excipient in certain drug formulations to enhance the flavor of liquid or chewable medications. Common sweetening agents selected include extra fine granular sucrose, acesulfame potassium, aspartame, and sodium saccharin. Sweeteners can be categorized into two main groups: natural and artificial.[7] Natural sweeteners, which contain carbohydrates and provide energy, encompass monosaccharides (such as glucose and fructose), disaccharides (like sucrose and lactose), and polyols, also referred to as sugar alcohols (including sorbitol, xylitol, mannitol,

lactitol, and maltitol). Fructose, a monosaccharide, is naturally present in fruits, honey, certain vegetables,and table sugar.[8]

PRESERVATIVE

They assist in maintaining the stability and safety of the gelatin mass and the product for extended storage periods. Typical preservatives include sorbic acid, sodium benzoate, potassium sorbate, and β-naphthol, with concentrations in the shell ranging from 0.01% to 0.5%. These preservatives are utilized to inhibit microbial growth, such as methyl paraben and propyl paraben.[19]

STEPS IN MANUFACTURING PROCESS OF SOFTGELATIN CAPSULES

Preparation of core material[9]

The filling substance can consist of liquid, semisolid, or suspension forms. The material within the shell enhances the drug's bioavailability, stability, and compatibility. It is essential that the core material is uniform.

Encapsulation process

The encapsulation process initiates with the pumping of molten gel into the machine, resulting in the formation of two slender ribbons of gelatin. These ribbons travel over a sequence of rollers and are continuously directed between two rotating die cylinders, which define the dimensions and contours of the capsules, creating the two halves. Subsequently, the ribbons meet at a fill injector, where a precise volume of the fill material is measured and dispensed by a pump. As thedie assembly rotates, the filled halves of the capsules are sealed together through the application of heat and pressure before being ejected.[9]

Soft gelatin capsules represent a single-unit solid dosage form that contains a liquid or semi-solid filling encased in a one-piece, sealed elastic outer shell. The formulation includes a specific quantity of the active ingredient or extract, along with any necessary adjuvants, all contained within a globular, oval, or alternatively shaped soft shell.[13]

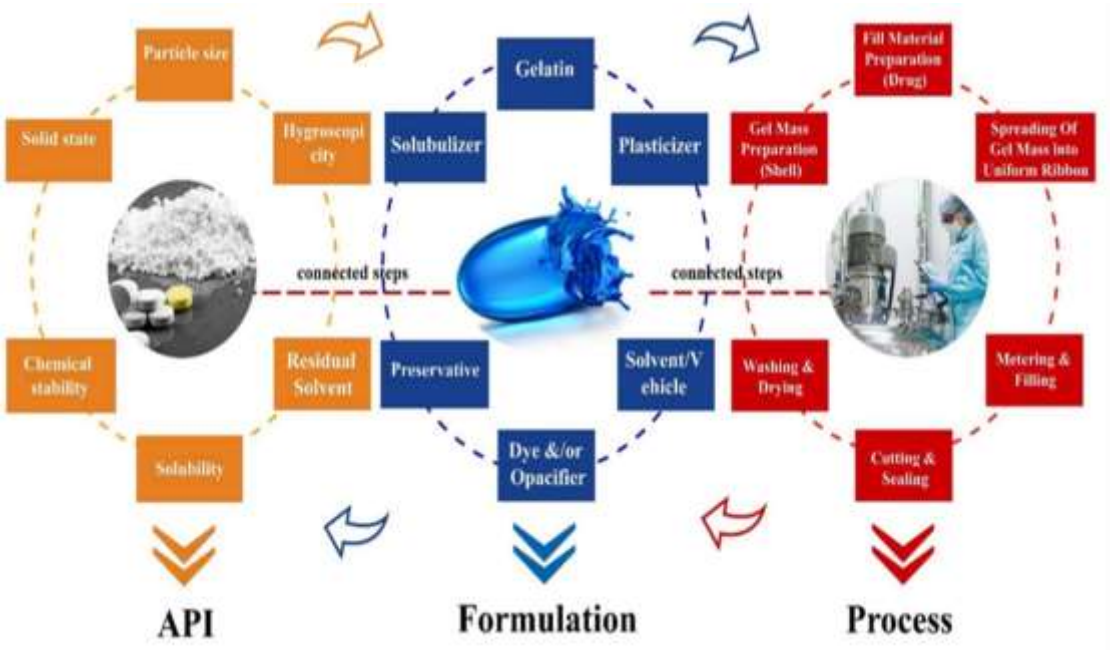
MANUFACTURING CONDITIONS

In the capsulation process, it is essential to maintain the air temperature and humidity at levels of57-59 °F and 20% relative humidity. Drying should occur in an environment set to 25 °F. Common environmental conditions for the production of soft capsules typically range from 78 °Fwith 15% relative humidity to 68 °F with 20% relative humidity.[13]

MANUFACTURING PROCESS OF SOFT GELATIN CAPSULE[10]

Manufacturing process of soft gelatin capsule is divided into the following steps:

1. Gelatin Preparation
2. Material (Fill) Preparation
3. Encapsulation
4. Drying
5. Inspection
6. Polishing
7. Packing



CHEWABLE PRODUCTS

The prevalent methods and formulation development processes utilized in their production are noteworthy. Recent advancements in 3D printing have underscored its potential to address technical challenges and enhance organoleptic properties, which are essential for ensuring efficacy, safety, and patient compliance.[6] Medicated chewing gums feature a chewable gum core that may be coated, consisting of an aqueous insoluble gum base that can be blended with sweeteners and flavoring agents. Chewable tablets are designed to have a pleasant flavor, avoiding any bitterness or unpleasant aftertaste. They offer numerous advantages over other pharmaceutical forms, including ease of administration and the elimination of the need for water. Soft-chew formulations have demonstrated good stability for all three pharmaceuticals over a period of up to 24 months, with the ibuprofen

formulation showing dissolution comparable to that of a standard oral tablet, along with satisfactory microbial stability.[7] This indicates that soft chewable tablet formulations that are easy to swallow, well-masked in taste, and possess an extended shelf life are achievable for various active pharmaceutical ingredients.[14]

MECHANICAL EVALUATION OF SOFTGELATIN CAPSULES[4]

- Tensile Strength Test
- Puncture Strength Test
- Viscosity Test
- Peel Test and Probe Test
- Hardness Test

EVALUATION PARAMETERS OF CHEWABLE CAPSULES

Swelling and erosion studies

The tablets were precisely weighed (W0) and positioned in the basket of the apparatus 1 USP dissolution tester (Erekat DT800). The baskets were subsequently submerged in 500 mL of dissolution medium, rotating at a speed of 100 rpm. Samples were analyzed individually in simulated gastric fluid (SGF) without pepsin (pH 1.2), simulated intestinal fluid (SIF) without pancreatin (pH 6.8), and purified water maintained at 37 ± 0.5 ˚C. At intervals of 2, 5, 10, 20, 60, 120, 180, and 240 minutes, the tablet was extracted from the basket, gently blotted with tissue paper to eliminate excess test liquid, and then reweighed (W1). The experiments were conducted in triplicate.

The increase in weight percentage resulting from liquid absorption or water uptake was calculated at each time point using the following equation.[12]

$$\% \text{ weight change} = W1 - W0/W0 \times 100$$

Ribbon thickness

The thickness of the gel ribbon from all batches was assessed using a caliper gauge, followed by the calculation of the average thickness.

Viscosity of Gel Mass Preparation[20]

Brookfield Viscosimeter: Ensure the tube is filled with the precise quantity of gel mass, calibrated to 20.0 ± 0.1.

Moisture absorption study

The moisture absorption test serves as a method to evaluate the resistance of B/GFRP bar against the penetration of water molecules in extreme conditions. A higher moisture absorption rate, under identical circumstances, indicates poorer resistance.[15]

Typically, B/GFRP bars are most susceptible to water molecule corrosion in alkaline environments, followed by exposure to aqueous solutions. Research conducted by Wang highlights the significant influence of the pH level in alkaline environments on the permeability of water molecules. Specifically, under consistent conditions, an increase in the pH from 12.7 to 13.4 can lead to a fourfold rise in moisture absorption for GFRP bars and a fifteenfold increase for BFRP bars. Additionally, the moisture absorption of B/GFRP bars is influenced not only by the environmental type but also escalates with higher internal porosity of the FRP bars and risingambient temperatures.[16]

Total soluble solids

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ADVANTAGE[17]

- Easy to consume, flavorless, designed for single-dose use, and resistant to tampering.
- Simple to chew with a pleasant texture in the mouth.
- No water is needed for swallowing, allowing for consumption at any moment.
- Offered in a variety of colors, shapes, and sizes to suit different compounds, including

semi-solids, liquids, gels, or pastes.

- Provides choices for both immediate and delayed drug release.
- Can improve drug absorption by delivering them in a solution or incorporating other agents that facilitate absorption.

MERITS

- This provides a simple method of consumption, particularly beneficial for elderly individuals and children.
- The chewable form facilitates rapid drug release, thereby improving absorption.
- Its chewable nature contributes to a quicker onset of action.
- Additionally, it is convenient for travel and easy to ingest.
- It can be taken without the need for water and is effective in alleviating digestive discomfort.

LIMITATIONS OF USING CHEWABLE SOFTGELS

- Flavor of the medication
- It may cause irritation in the throat and esophagus.
- It can only accommodate a restricted dosage.
- High cost – price of the treatment.
- It is not appropriate for all individuals.

STORAGE CONDITIONS[17]

Soft gelatin capsules typically consist of the active ingredient either dissolved or suspended in oils or water-soluble liquids. The stability of soft gels can be influenced by storage conditions, including temperature, humidity, and exposure to light. It is advised to store empty capsule shells at temperatures ranging from 15 to 25°C, with a relative humidity maintained between 35% and 65%. These conditions aim to reduce moisture absorption or evaporation, thereby preventing alterations in physical dimensions during the encapsulation process.

STABILITY TEST

The rupture test was conducted in accordance with the General Chapter guidelines. Observationsof the capsules were made, and the timing of the shell rupture was documented.

CONCLUSION

The development of chewable soft gelatin capsules represents a significant advancement in patient-centered pharmaceutical formulations, particularly for those who have difficulty swallowing traditional dosage forms. The optimized formulation successfully combines patient compliance with effective drug delivery, offering an improved alternative for pediatric, geriatric, and dysphagic populations.

The study demonstrated that the chewable soft gelatin capsules provide a palatable and convenient dosage form without compromising the stability or bioavailability of the active pharmaceutical ingredients (APIs). Taste-masking agents and sweeteners were effectively incorporated, making the product more acceptable to patients. In-vitro dissolution and stability tests confirmed that the modified capsule meets the required standards for drug release and shelf life under varied conditions.

This formulation approach shows great potential for expanding the use of soft gelatin capsules ina wider range of therapeutic applications, improving both adherence to treatment and patient quality of life.

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