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Review Article

A Review on Gelatin Production and a Special Type of Hard Gelatin Capsules With Their Packaging and Storage

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Abstract:

In this review it is explained about production of gelatin and a special type of hard gelatin capsules with their packaging and storage. Capsules are solid dosage preparations that contain a soft soluble shell of gelatin that encloses the drug substance(s) and/or excipients whereas hard capsules are made up of two pieces that resemble cylinders that are closed at one end: the longer piece is called the "body," and the shorter piece is called the "cap." A variety of formulation types, the majority of which are meant for oral administration, can be filled into capsules. Special applications include capsules that can be added to diagnostic kits, loaded into dry powder inhalers and occasionally soft-shell capsules meant to be inserted as suppositories into the vagina or the rectal cavity. Gelatin or another appropriate polymeric material is typically used to create the sell, which produces an elegant, tasteless, odourless, simple, and easily swallowed dosage form without the need for a second coating step. Capsules can be categorized as hard or soft depending on the makeup of the capsule shell. There was also emphasis on the different packaging and storage techniques.

Keywords: Capsules, Manufacturing, Formulation, Quality control tests, Packaging and storage.

Introduction:

Gelatin, also known as gelatine (Latin: gelatus, meaning "stiff" or "frozen"), is a transparent, flavourless, and colourless food ingredient that is typically made from collagen extracted from animal tissues. When dry, it is brittle; when wet, it become s rubbery. Following hydrolysis, it can also be referred to as hydrolyzed collagen, collagen hydrolysate, gelatine hydrolysate, hydrolyzed gelatine, or collagen peptides. It is frequently used as a gelling agent in food, drinks, pills, pharmaceuticals, vitamin or medication capsules, papers, films for photography, and cosmetics.

Gelatinous substances are defined as those that function similarly to gelatin or that contain gelatin. Gelatin is an irreversibly hydrolyzed form of collagen in which the hydrolysis breaks down protein fibrils into smaller peptides. The molecular weight of the peptides varies widely, contingent on the physical and chemical denaturation processes. Desserts with gelatin, most gummy candies, marshmallows, ice creams, dips, and yoghurts all contain gelatin.(Source:) For cooking, gelatin is available as sheets, granules, and powder. While some instant varieties can be added to the meal right away, others need to soak in water beforehand.

Physical properties of gelatin

Collagen that has been removed from skin, bones, cartilage, ligaments, and other tissues is partially hydrolyzed to create gelatin, a protein product. Collagen strands naturally bond together via molecular bonds, but these bonds break down into a form that rearranges more readily. When heated, gelatin melts, and when cooled again, it solidifies. It creates a semi-solid colloidal gel when combined with water.

Production of gelatin

Commercial gelatin is produced from meat and leather industry by products, primarily split cattle hides, pork skins, and cattle and pig bones. The common misconception is that hooves and horns are used for special purposes. In order to extract the dried collagen hydrolysate, various curing, acidic, and alkali processes are used to prepare the raw materials. It takes several weeks to complete the process.

Colorants

A pharmaceutical product's colour has a big impact on how you use it. The main purpose of colour is to identify a product during every step of its production and usage. By facilitating product differentiation, it helps the manufacturing company's operators adhere to GMP standards. The colorants that can be used in capsules are of two types: **water soluble dyes orin soluble pigments.** Dyes and pigments are combined as solutions or suspensions to create a variety of colours. The three most often utilized dyes are quinolone yellow, indigo carmine, and erythrosine. During the manufacturing process, colourants are added to the gelatin solution to give the capsules their colour.

Gelatin Production Processes

Degreased dried crushed bone	Pigskins
⇩	⇩
Acid Treatment	Chopping
⇩	⇩
Lime treatment	Water wash

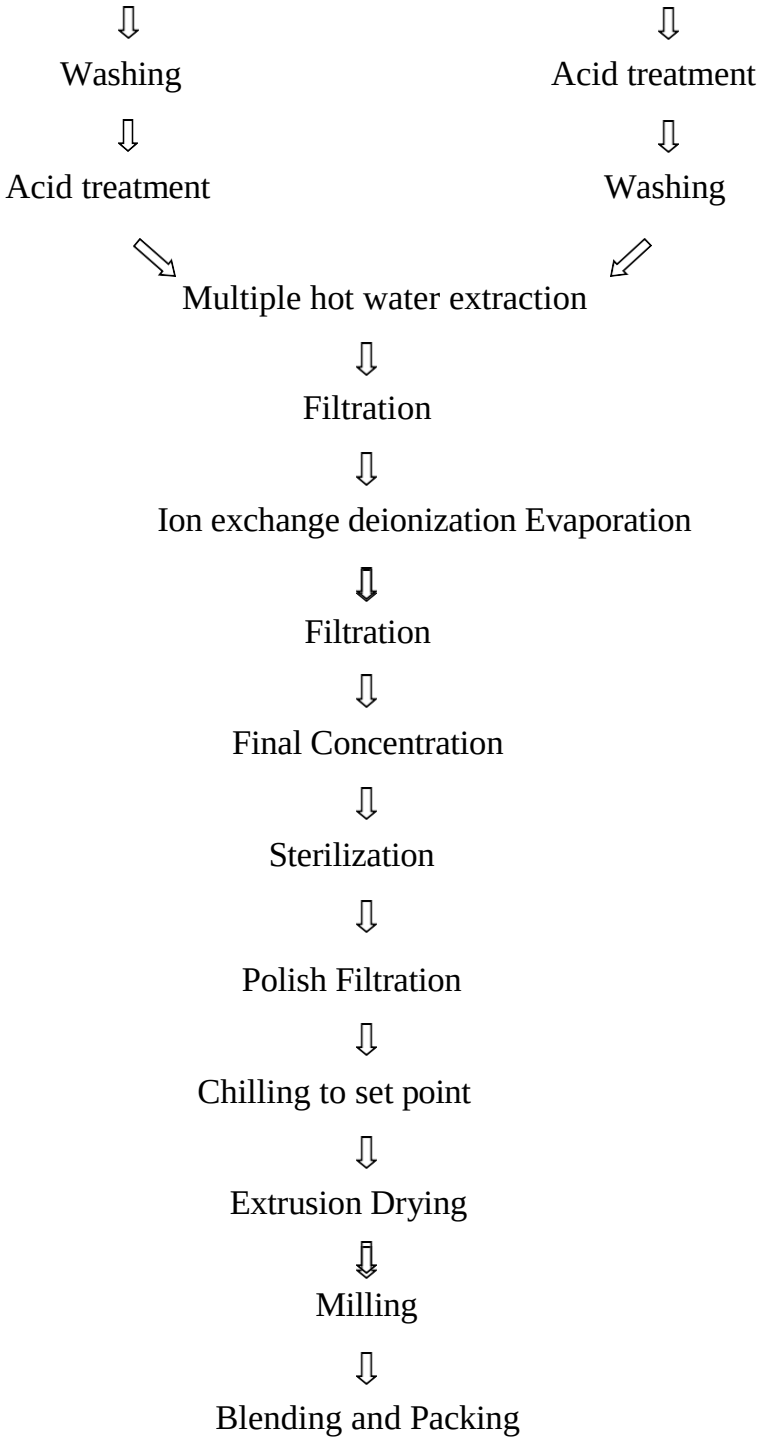

Figure1: Flow chart for gelatin production process

Process aids

During the manufacturing of capsules, the gelatin solution is supplemented with surfactants and preservatives to facilitate processing. Bacterial growth thrives in gelatin solutions at temperatures lower than 55 C. To stop microorganisms from growing until the gelatin film's moisture content is less than16%w/v, preservatives are added to the colourant and gelatin solutions. With time, the bacterial population will decrease at moisture contents below that threshold. The following substances are added as preservatives: sulphur

dioxide in the form of sodium salts bisulfite or metabisulfite .Sodium lauryl sulphate, which serves as a wetting agent and 0.15% w/w in some hard gelatin capsules, makes sure that the lubricated metal moulds are evenly coated after being dipped into the gelatin solution. It is possible to administer powders, semisolids, and liquids using capsules, which come in a variety of sizes and shapes. Moreover, precisely measured doses for vaginal or rectal administration can be obtained by using capsules.

Packaging and storage of capsules

The best way to store capsules is in tightly sealed glass or plastic containers that are kept in a cool environment. Compared to cardboard boxes, these containers are easier to handle and transport, and they shield the capsules from dust and moisture. A packet containing a desiccant, such as silica gel or anhydrous calcium chloride, may be placed in vials containing highly hygroscopic capsules to stop the capsules from absorbing too much moisture. Nowadays, capsules come in strip packaging, which makes counting and identifying them easier and allows for hygienic handling of medications.

Gelatin capsules that have been empty should be kept at room temperature and humidity level constant. Low humidity can lead to drying and cracking of the capsules, while high humidity can cause the capsules to soften. When capsules are stored in glass containers, they are shielded from dust and excessive humidity. The qualities of the medications that filled the capsules determine how long they should be stored. Hard gelatin capsules with semisolid fillings should not be kept in direct sunlight as this could cause the contents to melt or become softer.

Capsule Administration

Generally speaking, swallowing capsules ranging in size from No. 5 to No. 0 is not too difficult. Several patients might find it challenging to swallow the No. 00 and No. 000 capsules. If this happens, the patient might be instructed to slide the capsule over mucous membranes by placing it on the back of the tongue before consuming a liquid or by briefly immersing the capsule in warm water before taking it.

Special types of hard gelatin capsules

Altered Release: Depending on the medication and the excipients in the capsule, the rate at which the contents release can be adjusted. In case the medication is soluble in water and rapid release is required, neutral and hydrophilic excipients should be used. Hydrophobic excipients will slow down the rate of drug dissolution if a gradual release of a water-soluble medication is required. Hydrophilic excipients will accelerate the release of a drug that is soluble in water, while hydrophobic and neutral excipients will cause the drug to dissolve more slowly. One way to achieve an extremely quick release of the contents of the capsule is to puncture holes in it so that fluids in the gastrointestinal tract can enter it more quickly, or you can add a tiny amount of citric acid and sodium bicarbonate to help the capsule open more quickly.

Adding sodium lauryl sulphate can increase water penetration into the capsule and accelerate dissolution by 0.1to1%. The active medication can

be combined with different excipients, such as sodium alginate or cellulose polymers (methylcellulose), if a slower release of the medication is required. When the percentage of polymer or alginate increases in comparison to water-soluble ingredients like lactose, the rate of release generally slows down. It should be noted that it can be challenging to forecast a drug's precise release profile and to get consistent results from batch to batch. Furthermore, controlled bioequivalence studies are the only way to demonstrate dependable, consistent blood levels and duration of action. Furthermore, because the toxic and therapeutic doses are so close together, many drugs have narrow therapeutic indices. As a result, impromptu attempts to change release rates in this way ought to be avoided.

Coating capsules: Coatings have been applied haphazardly to improve appearance, mask taste, and stop medication release in the stomach (enteric coated products). The majority of capsule coatings call for sophisticated formulation knowledge and equipment used in manufacturing facilities for quality control. It is possible to coat capsules to postpone the release of the active medication until a particular area of the digestive system is reached. These materials are used because they are insoluble in acids but soluble in alkali solutions. Several of the more recent coating materials erode over time when exposed to gastrointestinal contents as opposed to over a pH gradient, making them time-erosion- dependent as opposed to acid-base-dependent. Furthermore, there are several more recent materials with dependable pH solubility profiles.

Enteric-coated capsules: Enteric-coated capsules fragment in the intestine but do not dissolve in the stomach. The enteric-coated tablets have essentially replaced them. Commercially available coatings include cellulose acetate phthalate and wax-fatty acid and/or esters mixtures.

Generally speaking, applying a coating calls for expertise and extra tools. Although a general coating can be used, it is probably best reserved for less critical medications. Experience is frequently required for particular formulations based on the demands of the doctors and the requirements of the individual patients. Several coating methods may be used and are described as follows:

Beaker-flask coating: A tiny amount of the coating material should be added to the flask and heated slowly until it melts. To begin applying the coating, add a few capsules, take the flask off the heat source, and rotate it. Add a few more drops of melted coating material on a regular basis while rotating. The only thing needed to prevent the capsules from clumping and adhering to one another is the addition of extremely tiny amounts.

Dipping: In a beaker, heat the coating material to the lowest possible temperature. Using tweezers, dip each capsule individually, letting the coating cool before dipping again until a thick enough layer forms.

Spraying: The coating material is prepared as an alcoholic or ethereal solution and put in a small sprayer (a model aeroplane paint sprayer works well).The capsules are set up in a well-ventilated

area on a screen. Applying the coating material solution in very thin coats and allowing enough time for drying in between coats is done (this step may involve using a hair dryer with caution). Until a sufficient layer has developed, the process is repeated.

Sustained release capsules: There are times when the blood concentration of the medication is too high or too low when using the conventional method of taking a dose three or four times a day. One way to address this and simultaneously lower the daily dose is to take a capsule containing multiple coated pellets that release the medication gradually over an extended period of time. Usually, an adhesive is used to attach the finely powdered drug to sugar granules in order to form pellets. After that, the pellets are coated with protective materials, the thickness of which varies depending on the batch, to postpone the drug's release. After the batches are well combined, the appropriate dosages are put into the capsules. For instance, a mixture might include 10% neutral pellets, which are used only to fill the capsule, 30% coated pellets that release the drug at 4 and 8 hours, and 30% uncoated pellets for immediate release of the drug. To make mixing easier to control and identification simpler, each batch can have a different colour.

Liquid filled hard gelatin capsules

It's widely acknowledged that a large number of today's NCEs (New Chemical Entities) have poor water solubility, making it impossible to adequately achieve drug adsorption from solid oral dosage forms using traditional techniques like particle size reduction. A highly promising approach to delivering these insoluble compounds is the formulation of new products using dissolved systems, such as lipids, liquids, or semi-solids. One of the most sensible methods for determining the ideal dosage form to administer these novel liquid formulations is to use two-piece hard shell capsules. One of the biggest technological advances of the past few years is the ability to package liquids in hard gelatin capsules. The procedure can be kept in-house and scaled up similarly to the hard gelatin capsule powder / pellet filling or tableting processes.

Capsules for packing of ophthalmic ointments

It is imperative that ophthalmic ointments are free of irritation and sterility. As a result, they need to be packaged so that the product keeps its sterility until it is finished. Packing the preparation into single dose containers is the best way to prevent contamination while using it. These days, ophthalmic ointments are frequently filled with soft gelatin capsules. These capsules are designed to be applied to the eye only once.

Cleaning and Packaging

To prevent powders from sticking to the surface and giving the capsules an unpleasant taste and appearance, every effort must be made to reduce the amount of moisture or body oils on them. It is challenging to clean capsules that have become sticky or moist. It is important to handle the capsules in a way that keeps their shine and dryness.

(3) it is possible to prepare four or five capsules before having to start the procedure over. If the capsules have been kept dry, you can shake in cloth that has been shaped into a bag or hammock, or roll between folds of cloth to remove clinging surface powder. Capsules can also be cleaned by gently rolling a container filled with salt, sugar, or sodium bicarbonate after they have been placed inside. The capsules can then be collected by pouring the contents into a sieve with a mesh size of 10 and allowing the "cleaning salt" to flow through the screen. It must be underlined that the capsules must have been kept dry and clean in order for these cleaning techniques to work.

ROTOSORT is a new filled capsule-sorting machine sold by Eli Lilly and Company. It is a mechanical sorting device that removes loose powder, unfilled joined capsules, filled or unfilled bodies, and loose caps. It can handle upto150, 000 capsules per hour, and it can run directly off a filling machine or be used separately.

Recent updates in Capsule technology

New products by Caps gel:

Ocean caps capsules, recently introduced by Caps gel, have all the qualities of traditional gelatin capsules, including appearance, Machin ability, mechanical properties, hygroscopic and oxygen properties, chemical stability, and versatility. They are made from 100% natural fish gelatin derived from farm-raised fish. Moreover, they have no taste and no smell with a fill capacity ranging from 1000 mg to 1400 mg, depending on the density of the liquid fill material, Licaps'new 000 size capsules are perfect for optimizing liquid dosage. The two-piece capsules are specifically made to be sealed, allowing liquids and semi-solids to be safely contained without the need for banding. They come in different colours to suit your needs and are available in gelatin and HPMC (Hydroxy propyl Methyl cellulose) capsules.

Conclusion:

The advantages and characteristics of capsules over tablet dosage forms account for their popularity. The medication is expensive due to its unpleasant taste and bitter coating. While packing such medications into hard gelatin capsules could hide an unpleasant taste or odour and be an economical method that also benefits from a quick start of action.

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