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Review Article

A REVIEW ON NATURAL POLYMER

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ABSTRACT

Pharmaceutical formulation contains two ingredients one is the active ingredient and other is a polymer. A polymer help in the manufacturing of dosage form and it also improves physicochemical parameters of the dosage form. Polymers play an important role in any dosage form. They influence drug release and should be compatible, non-toxic, stable, economic etc. They are broadly classified as natural polymers and synthetic polymers. They have wide range of applications so selection of polymer is the main step in designing any dosage form. Nowadays, due to many problems associated with drug release and side effects manufacturers are inclined towards using natural polymers. Natural polymers are basically polysaccharides so they are biocompatible and without any side effects. This review discusses various natural polymers, their advantages, their extraction process and role of natural polymers in designing novel drug delivery systems.

Key words: *Natural polymer*

INTRODUCTION

Polymer were defined as 'the substance used as a medium for giving a medicament', that is to say with simply the functions of an inert support of the active principle or principles. The specific application of natural polysaccharide polymers in pharmaceutical formulations include to aid in the processing of the drug delivery system during its manufacture, protect, support or enhance stability, bioavailability or patient acceptability, assist in product identification, or enhance any other attribute of the overall safety, effectiveness or delivery of the drug during storage or use.

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Today we have several pharmaceutical polymer of plant origin, like starch, agar, alginates, carrageenan, guar gum, xanthan gum, gelatin, pectin, acacia, tragacanth, chitosan and cellulose. These natural polymer find applications in the pharmaceutical industry as binding agents, disintegrates, sustaining agents, protective's, colloids, thickening agents, gelling agents, bases in suppositories, stabilizers, and coating materials.

The advantages of natural plant-based polymer include that they are of low cost, natural origin, fairly free from side effects, biocompatible, and bio-acceptable, with a renewable source, environmental friendly processing, local availability, better patient tolerance, as well as public acceptance. Polymers are also sometimes used to bulk up formulations that contain very potent active ingredients, to allow for convenient and accurate dosage. Depending on the route of administration, and form of medication, different polymer may be used. To stabilize the active ingredient, polymer are added, ensuring that the active ingredient stays "active", and, just as importantly, stable for a sufficiently long period of time that the shelf-life of the product makes it competitive with other products. Polymer also can serve to mask an unpleasant taste or texture and help ensure that the right amount of the API makes it to the right spot in the body at the right time. [1,2].

COMMONLY USED NATURAL POLYMER

Natural polymer are widely used in modified drug delivery system and some of them are mentioned below-

GUAR GUM

Nonproprietary Names

BP: Guar galactomannan

PhEur: Guar galactomannanum

Synonyms

E412; Galactosol; guar flour; jaguar gum; Meyprogat; Meyprodorss; Meyprofin.

Biological source

Guar gum obtained from the refined endosperm of the seeds of Cyamopsis tetragonolobus L. Taub.

Description

Guar gum occurs as an odorless or nearly odorless, white to yellowish-white powder with a bland taste

Chemical composition [3].

Chemically, guar gum is a polysaccharide composed of the sugars, galactose and mannose. The backbone is a linear chain of β 1, 4-linked mannose residues to which galactose residues are 1,6-linked at every second mannose, forming short side-branches.

Manufacturing Process

Stepwise process

Guar Seed

- First, Guar Pods are dried in sunlight, manually separated from the seeds.
- The Guar seeds are supplied to the industry for processing.
- Guar by-products, churi and korma are used for Cattle feed.

Undehusked Guar Splits

- The Guar gum is commercially extracted from Guar seeds essentially by a mechanical process of roasting, differential attrition, sieving and polishing.
- The seeds are broken and the germ is separated from the endosperm.
- Two halves of the endosperm are obtained from each seed and are known as Undehusked Guar Splits.

Refined Guar Splits

Refined Guar Splits are obtained when the fine layer of fibrous material, which forms the husk, is removed and separated from the endosperm halves by polishing.

Guar Powder

The refined Guar Splits are then treated and finished into powders by a variety of route and processing technique depends upon the end product desired.

Application [4]

- Guar gum is a galactomannan, commonly used in cosmetics, food products, and pharmaceutical formulations.
- It has also been investigated in the preparation of sustained-release matrix tablets in the place of cellulose derivatives such as methylcellulose.
- In pharmaceuticals, guar gum is used in solid-dosage forms as a binder and disintegrant
- In oral and topical products as a suspending, thickening, and stabilizing agent,and also as a controlled-release carrier.
- Guar gum has also been examined for use in colonic drug delivery
- Guar-gum-based three-layer matrix tablets have been used experimentally in oral controlled-release formulations.

PECTIN

Nonproprietary Names

USP: Pectin

Synonyms

Citrus pectin, E440, methopectin, methyl pectin, methyl pectinate, mexpectin, pectina, pectinic acid.

Biological source

Pectin is obtained from the inner portion of the ring of citrus fruits like lemon, orange etc and vegetative matter like sunflower, papaya, guavas, mangoes, etc.

Description

Pectin occurs as a coarse or fine, yellowish-white, odorless powder that has a mucilaginous taste.

Chemical composition

Pectin, also known as pectic polysaccharides, is rich in galacturonic acid. Several distinct polysaccharides have been identified and characterized within the pectic group.

Sources and production

- Apple 1-1.5%
- Cherries 0.4%
- Orange 0.5-3.5%
- Citrus peels 30%

Extraction of pectin from Citrus peels

Pectin is extracted by adding hot dilute acid at pH-values from 1.5 – 3.5. During several hours of extraction, the protopectin loses some of its branching and chain-length and goes into solution. After filtering, the extract is concentrated in vacuum and the pectin then precipitated by adding ethanol or isopropanol. An old technique of precipitating pectin with aluminium salts is no longer used (apart from alcohols and polyvalent cations; pectin also precipitates with proteins and detergents).

Alcohol-precipitated pectin is then separated, washed and dried. Treating the initial pectin with dilute acid leads to low-esterified pectins. When this process includes ammonium hydroxide, amidated pectins are obtained. After drying and milling, pectin is usually standardized with sugar and sometimes calcium-salts or organic acids to have optimum performance in a particular application. [5].

Extraction of pectin from Orange Peels

Extraction of pectin from dried orange fruit peel was carried out by microwave assisted extraction technique. 25 g of dried orange peel was cut into small pieces and soaked in 200 ml of distilled water for 2 h in a 1000 ml beaker. Its pH was adjusted to 4.5 by using 10 % tartaric acid solution and subjected to microwave irradiation at 160 W for 10 min. It was then filtered while hot; filtrate was cooled and poured into a beaker containing 600 ml of acetone to precipitate out pectin. The precipitated pectin was then separated by vacuum filtration and washed with acetone to make the pectin free from acidic ions. Pectin thus obtained was completely dried at 37º C in a hot air oven.

Application

- Pectin has been used as an adsorbent and bulk-forming agent, and is present in multi-ingredient preparations for the management of diarrhea, constipation, and obesity;
- It has also been used as an emulsion stabilizer
- Experimentally, pectin has been used in gel formulations for the oral sustained delivery of ambroxol
- Pectin gel beads have been shown to be an effective medium for controlling the release of a drug within the gastrointestinal (GI) tract.
- It has also been used in a colon-biodegradable pectin matrix with a pH-sensitive polymeric coating, which retards the onset of drug release, overcoming the problems of pectin solubility in the upper GI tract
- Pectin have been used as a component in the preparation of mixed polymer microsphere systems with the intention of producing controlled drug release [5, 6].

CHITOSAN

Nonproprietary Names

BP: Chitosan hydrochloride

PhEur: Chitosani hydrochloridum

Synonyms 2-Amino-2-deoxy-(1,4)-b-D-glucopyranan; deacetylated chitin; deacetylchitin; b-1,4-poly-D-glucosamine; poly-D-glucosamine; poly-(1,4-b-D-glucopyranosamine).

Biological source

Chitosan is obtained by the alkaline deacetylation of chitin

Description

Chitosan occurs as odorless, white or creamy-white powder or flakes. Fiber formation is quite common during precipitation and the chitosan may look 'cotton like'.

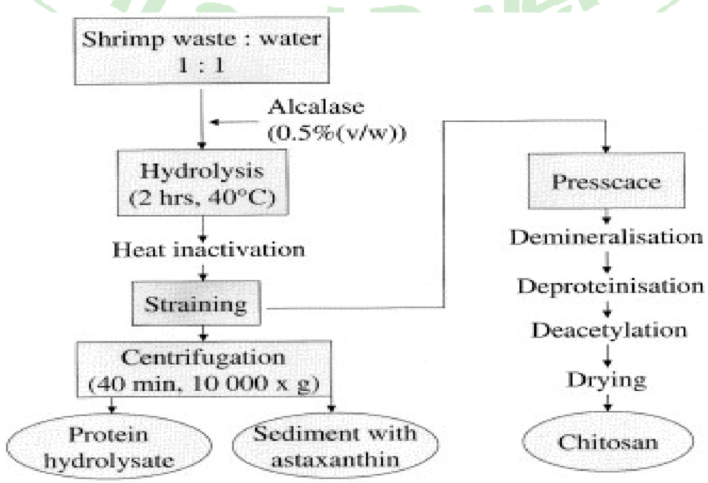
Chemical composition

Chitosan has a rigid crystalline structure through inter and intra molecular hydrogen bonding. Chitosan molecule is copolymer of N-acetyl-D-glucosamine and D glucosamine.

Extraction process

Chitin is mainly recovered from shrimp and crab shells. The major shell components are chitin, proteins, lipids, pigments and trace elements.

Chitin, calcium carbonate and proteins account for about 90% of the dry weight of the shell. In order to obtain purified chitin, it must be separated from the proteins, minerals and other components. This separation is achieved in three steps: (1) demineralization to eliminate the calcium carbonate,(2) deproteinisation, and (3) elimination of lipids and decolourisation.



Application

- Chitosan is used in cosmetics and is under investigation for use in a number of pharmaceutical formulations.
- It is use as a component of mucoadhesive dosage forms rapid release dosage forms improved peptide delivery, colonic drug delivery systems, and use for gene delivery
- Chitosan has been processed into several pharmaceutical forms including gels, films, beads, microspheres, tablets, and coatings for liposomes. [7, 8].
- Furthermore, chitosan may be processed into drug delivery systems using several techniques including spray-drying coacervation, direct compression, and conventional granulation processes.

XANTHAN GUM

Nonproprietary Names

BP: Xanthan gum

PhEur: Xanthani gummi

USPNF: Xanthan gum

Synonyms

Corn sugar gum; E415; Keltrol; polysaccharide B-1459; Rhodigel; Vanzan NF; Xantural.

Biological source

Xanthan gum is a polysaccharide secreted by the bacterium Xanthomonas campestris

Description

Xanthan gum occurs as a cream- or white-colored, odorless, free-flowing, fine powder

Chemical composition

Xanthan is long chain polysaccharides with large number of trisaccharides side chain. The side chains are composed of two mannose unit and one glucuronic acid unit.

Preparation

The polysaccharide is prepared by inoculating a sterile aqueous solution of carbohydrate(s), a source of nitrogen, dipotassium phosphate, and some trace elements. The medium is well-aerated and stirred, and the polymer is produced extracellularly into the medium. The final concentration of xanthan produced will vary greatly depending on the method of production, strain of bacteria, and random variation. After fermentation that can vary in time from one to four days, the polymer is precipitated from the medium by the addition of isopropyl alcohol, and the precipitate is dried and milled to give a powder that is readily soluble in water or brine.In the United States, the manufacture of one kilogram of cheese creates nine kg of the byproduct whey, for which the USDA sought to find more uses. Whey is composed mostly of water and lactose, so researchers developed a strain of *X. campestris* that would grow on lactose rather than glucose. The newly developed lactose-using bacteria produced 30 g/L of xanthan gum for every 40 g/L of whey powder. Whey-derived xanthan gum is commonly used in many commercial products, such as shampoos and salad dressings. [9].

Application

- Xanthan gum is widely used in oral and topical pharmaceutical formulations, cosmetics, and foods as a suspending and stabilizing agent.
- It is also used as a thickening and emulsifying agent.
- Xanthan gum has also been used to prepare sustained-release matrix tablets.
- Xanthan gum has been incorporated in an ophthalmic liquid dosage form, which interacts with mucin, thereby helping in the prolonged retention of the dosage form in the precorneal area.
- Recent studies have revealed that xanthan gum can also be used as an excipient for spray-drying and freeze-drying processes for better results.
- Xanthan gum can be used to increase the bioadhesive strength in vaginal formulations and as a binder in colon specific drug delivery systems.
- Xanthan gum is also used as a hydrocolloid in the food industry, and in

cosmetics it has been used as a thickening agent in shampoo.

SODIUM ALGINATE

Nonproprietary Names

BP: Sodium alginate

PhEur: Natrii alginas

USPNF: Sodium alginate

Synonyms

Algin; alginic acid, sodium salt; E401; Kelcosol; Keltone; Protanal; sodium polymannuronate.

Biological source

Sodium alginate is a salt of alginic acid. It is the purified carbohydrate product obtained from brown algae Laminaria species.

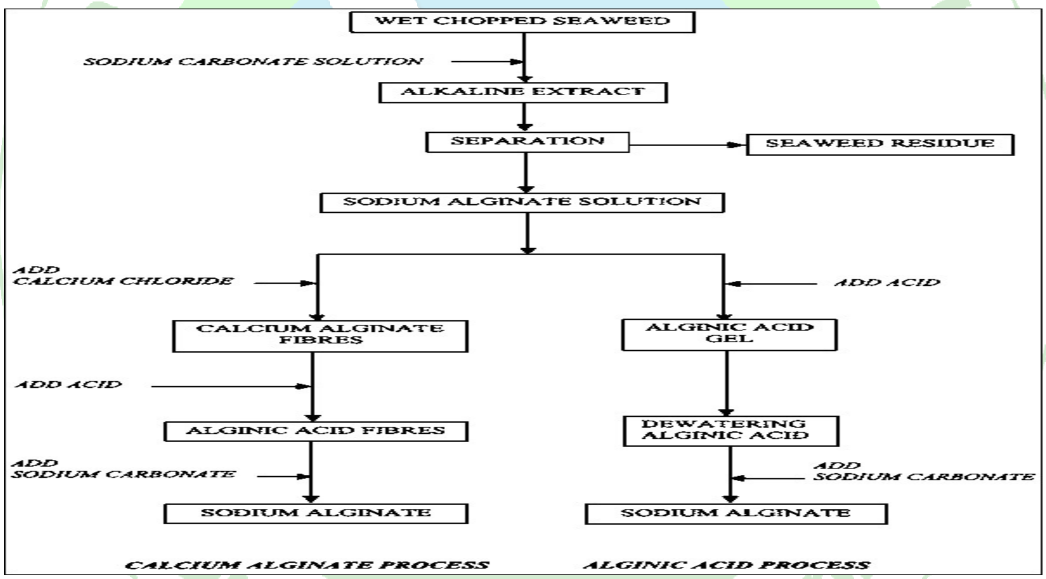
Description

Sodium alginate occurs as an odorless and tasteless, white to pale yellowish-brown colored powder.

Chemical composition

These polymer consist two different monomer in varying proportion namely D-mannuronic acid and L-gluoronic acids linked 1, 4 glucosidic bond as block of only D-mannuronic acid and L-gluoronic acids in homopolymer or alternating the two in heteropolymeric blocks.

Extraction process



Application

- Sodium alginate is used in a variety of oral and topical pharmaceutical formulations. In tablet formulations, sodium alginate may be used as both a binder and disintegrant it has been used as a diluent in capsule formulations.
- Sodium alginate has also been used in the preparation of sustained release oral formulations
- In topical formulations, sodium alginate is widely used as a thickening and suspending agent in a variety of pastes, creams, and gels, and as a stabilizing agent for oil-in-water emulsions.
- Recently, sodium alginate has been used for the aqueous micro encapsulation of drugs in contrast with the more conventional micro encapsulation techniques which use organic-solvent systems.
- It has also been used in the formation of nanoparticles.
- Other novel delivery systems containing sodium alginate include ophthalmic solutions that form a gel in situ when administered to the eye an in situ forming

gel containing paracetamol for oral administration,

- Sodium alginate has been used in combination with an H2-receptor antagonist in the management of gastro esophageal reflux, and as a haemostatic agent in surgical dressings Sodium alginate is also used in cosmetics and food products; [11].

CARRAGEENAN

Nonproprietary Names

USPNF: Carrageenan

Synonyms

Chondrus extract; E407; Gelcarin; Genu; Hygum TP-1; Irish moss extract; Marine Colloids; SeaSpen PF; Viscarin.

Biological source

Carrageenans are a family of linear sulfated polysaccharides that are extracted from red seaweeds.

Description

Carrageenan, when extracted from the appropriate seaweed source, is a yellow-brown to white colored, coarse to fine powder that is odorless and tasteless.

Chemical composition

There are three main commercial classes of carrageenan:

Kappa: Forms strong, rigid gels in the presence of potassium ions; it reacts with dairy proteins. It is sourced mainly from Kappaphycus alvarezii.

Iota: Forms soft gels in the presence of calcium ions. It is produced mainly from Eucheuma denticulatum

Lambda: Does not gel, and is used to thicken dairy products. The most common source is Gigartina from South America.

Production

- Semi-refined

This is only performed using *E. cottonii* or *E. spinosum*. The raw weed is first sorted and crude contaminants are removed by hand. The weed is then washed to remove salt and sand, and then cooked in hot alkali to increase the gel strength. The cooked weed is washed, dried, and milled. *E. spinosum* undergoes a much milder cooking cycle, as it dissolves quite readily. The product is called semi-refined carrageenan, Philippines natural grade or, in the U.S., it simply falls under the common carrageenan specification.

cleaned & washed seaweed
↓
Extraction m
↓
coarse filtration → seaweed residue
↓
fine filtration → used filter aids
↓
------------ concentration --------↓
preparation with Kcl | preparation with alcohol
↓ | ↓
gel pressing | ssalcohol recovery
↓ | |
drying | |
↓ | ↓
milling | drying
↓ | ↓
blending | milling
↓ | ↓
gel refined carrageenan | blending ↓

refined carrageenan

- Refined-

The essential difference in the refining process is that the carrageenan is first dissolved and filtered to remove cell wall debris. The carrageenan is then precipitated from the clear solution either by isopropanol or by potassium chloride.

- Mixed processing

A hybrid technology in which seaweed is treated heterogeneously as in the semi refined process exists, but alcohol or high salt levels are used to inhibit dissolution. This process is often used on South American seaweeds and gives some of the cost benefits of semi refined processing, while allowing a wider range of seaweeds to be processed. However, the naturally low cellulose levels in some South American seaweed allow them to be heterogeneously processed and still be sold under the EU refined specification. [12].

Application

- Carrageenan is used in a variety of non parenteral dosage forms, including suspensions, emulsions, gels, creams, lotions, eye drops, suppositories, and tablets and capsules.
- Carrageenan can be used in formulations for oral and buccal drug delivery.
- Incorporation of carrageenan into tablet matrices with various drugs and other excipients to alter release profiles has been studied, illustrating that the carrageenan have good tablet-binding properties
- Carrageenan has been used for the micro encapsulation of proteins and probiotic bacteria.
- It has also been used as beads in the preparation of controlled release systems.

GELATIN

Nonproprietary Names

BP: Gelatin

JP: Gelatin

PhEur: Gelatina

USPNF: Gelatin

Synonyms

Byco; Cryogel; gelatine; Instagel; Solugel.

Biological source

Gelatin is a project obtained by the partial hydrolysis of collagen, derived from the skin, white connective tissue, tendons, ligament and bone of ox (B0s tourur linn), sheep (ovis aries linn), etc

Description

Gelatin occurs as a light-amber to faintly yellow-colored, vitreous, brittle solid. It is practically odorless and tasteless and is available as translucent sheets and granules, or as a powder

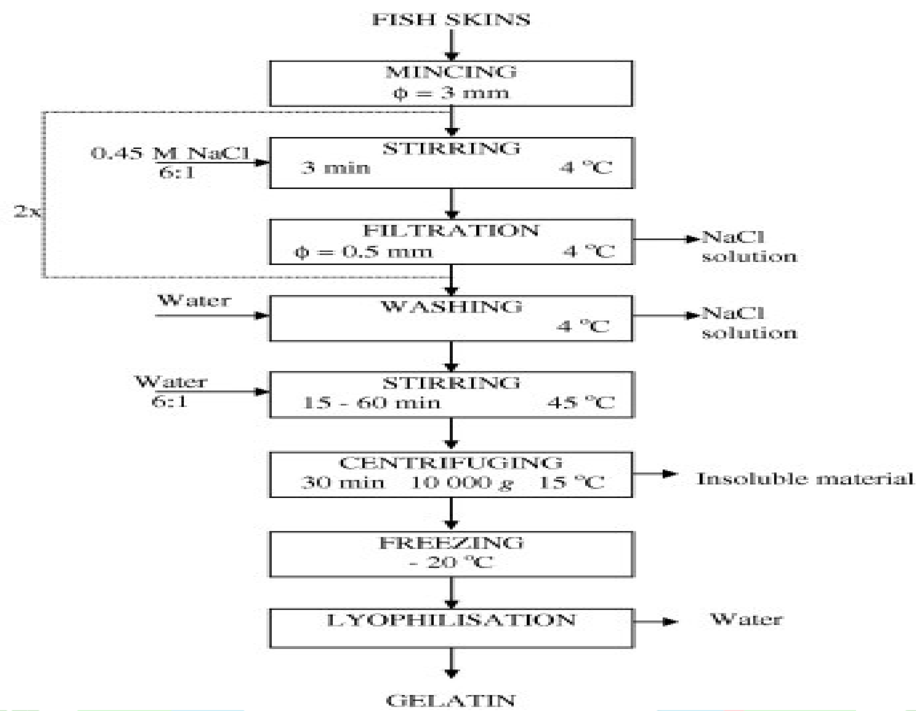
Chemical composition

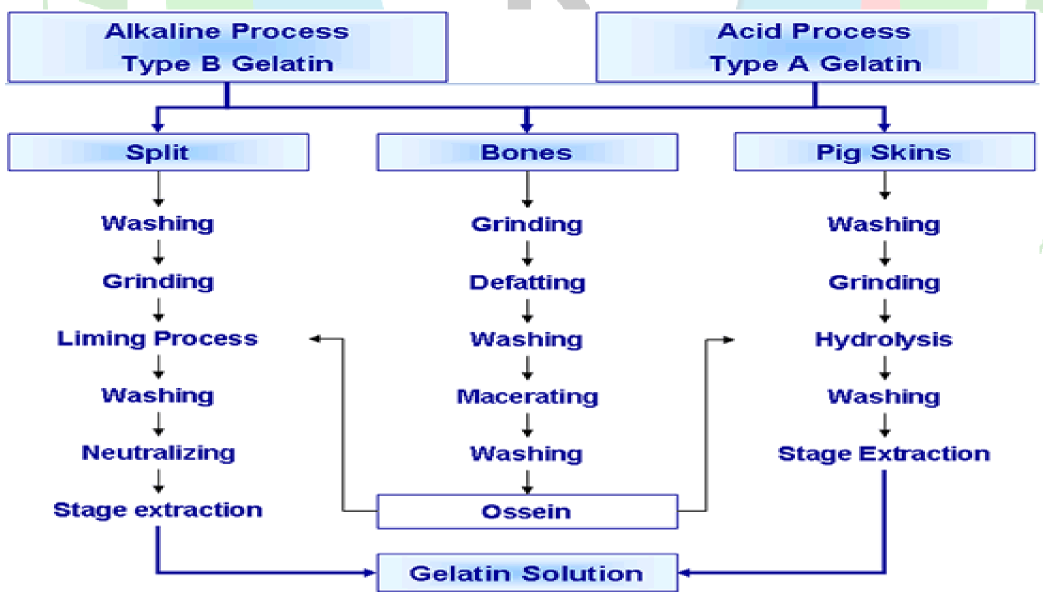
Gelatin mainly consists of protein glutin which on hydrolysis gives a mixture of amino acids like glycine, alanine, leucine, aspartic acid, argentine, lysine valine, cystine etc.

Application

- Gelatin is widely used in a variety of pharmaceutical formulations, including its use as a biodegradable matrix material in an implantable delivery system although it is most frequently used to form either hard or soft gelatin capsules.
- Gelatin is also used for the microencapsulation of drugs, where the active drug is sealed inside a microsized capsule or beadlet,
- Other uses of gelatin include the preparation of pastes, pastilles, pessaries, and suppositories. In addition, it is used as a tablet binder and coating agent, and as a viscosity-increasing agent for solutions and semisolids.
- Therapeutically, gelatin has been used in the preparation of wound dressings and has been used as a plasma substitute,.
- Gelatin is also widely used in food products and photographic Emulsions [13].

Extraction process





AGAR

Nonproprietary Names

JP: Agar

PhEur: Agar

USPNF: Agar

Synonyms

Agar; Bengal isinglass; Ceylon isinglass; Chinese isinglass; E406; gelosa; gelose; Japan agar; Japan isinglass; layor carang

Biological source

Agar is dried gelatinous substance, obtained from, Gelidium amansil Lamouroux, Glidium cartilagineum Gall etc.

Description

Agar occurs as transparent, odorless, tasteless strips or as a coarse or fine powder. It may be weak yellowish-orange, yellowish-gray to pale-yellow colored, or colorless. Agar is tough when damp, brittle when dry.

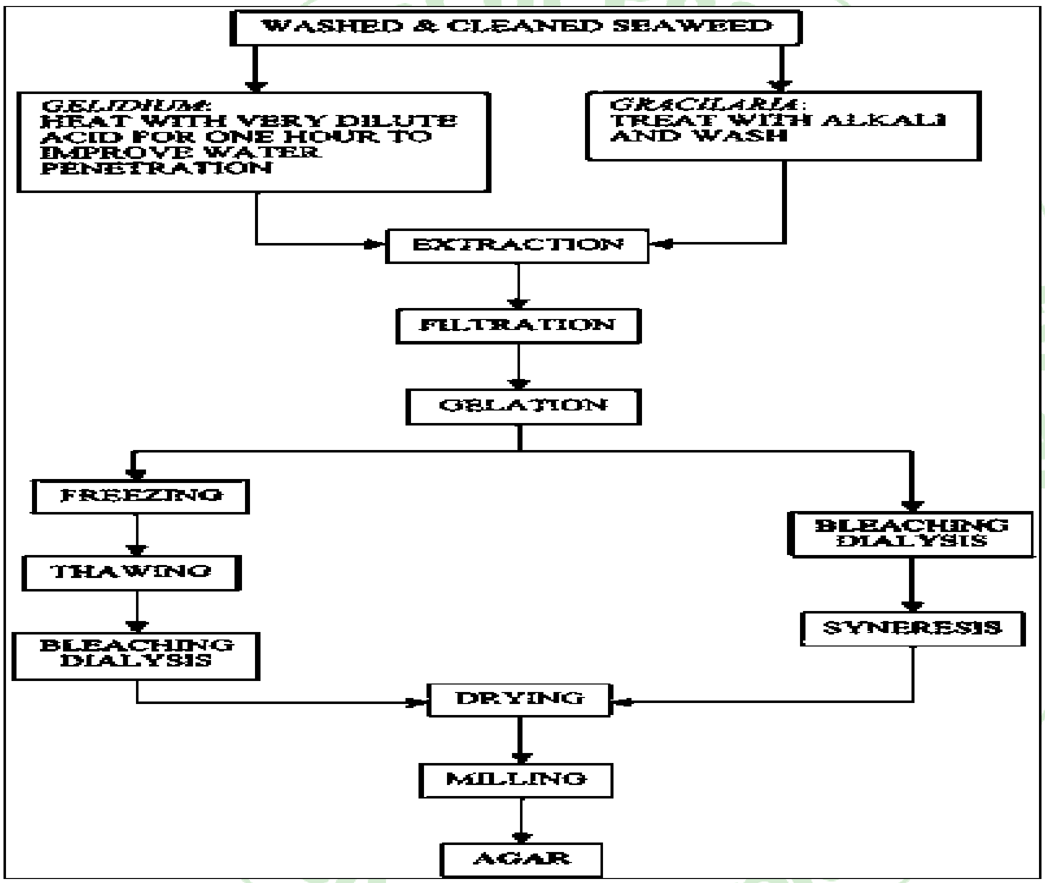
Chemical composition

Heterogeneous polysaccharides consisting of two components

(a) Agarose (70%),

(b) Agaropectin (99%)

Extraction



Application

- Agar is widely used in food applications as a stabilizing agent.
- In pharmaceutical applications, agar is used in a handful of oral tablet and topical formulations.
- It has also been investigated in a number of experimental pharmaceutical applications including as a sustained-release agent in gels, beads, microspheres, and tablets.
- It has also been reported to work as a disintegrant in tablets.
- Agar has been used in a floating controlled-release tablet; the buoyancy in part being attributed to air entrapped in the agar gel network.
- It can be used as a viscosity-increasing agent in aqueous systems. Agar can also be used as a base for non melting, and non disintegrating suppositories. [14].

STARCH-

Nonproprietary Names

BP: Maize starch, Potato starch, Rice starch, Tapioca starch, Wheat starch

JP: Corn starch, Potato starch, Rice starch, Wheat starch

PhEur: Maydis amylum (maize starch), Solani amylum (potato starch), Oryzae amylum (rice starch), Tritici amylum (wheat starch)

USPNF: Corn starch, Potato starch, Tapioca, Wheat starch

Synonyms

Amido; amidon; amilo; amylum; Aytex P; C*PharmGel;

Biological source

Starch consists of polysaccharide granules obtained from the grains of Maize Zea mays L, or of rice Oryza sativa L, or of wheat Triticum aestivum L or from the tubers of the potato Solanum tuberosum L.

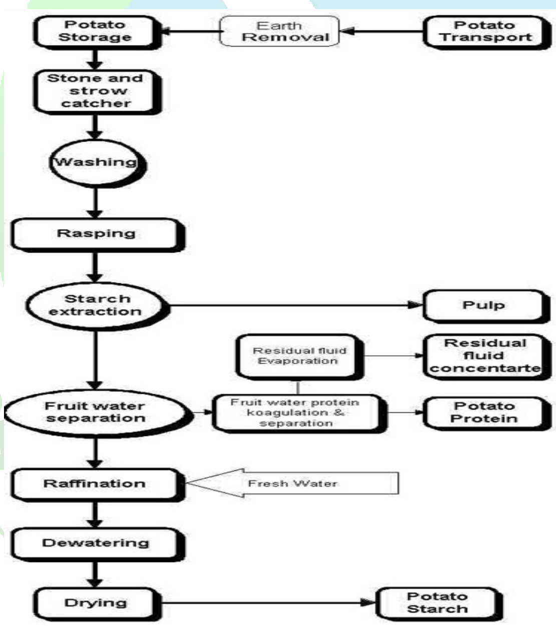
Description

Starch occurs as an odorless and tasteless, fine, white-colored powder comprising very small spherical or ovoid granules whose size and shape are characteristic for each botanical variety.

Chemical composition

Starch contain generally a mixture of two polysaccharides, amylopectin (more than 80%) and Amylose (20%)

Extraction



Application

- Starch is used as an excipient primarily in oral solid-dosage formulations where it is utilized as a binder, diluent, and disintegrant.
- As a diluent, starch is used for the preparation of standardized triturates of colorants or potent drugs to facilitate subsequent mixing or blending processes in manufacturing operations.
- In tablet formulations, freshly prepared starch paste is used at a concentration of 5–25% w/w in tablet granulations as a binder.
- Starch is one of the most commonly used tablet disintegrants at concentrations of 3–15% w/w.
- Starch has been investigated as an excipient in novel drug delivery systems for nasal, oral, periodontal, and other site-specific delivery systems.
- Starch mucilage has also been applied to the skin as an emollient, has formed the

base of some enemas, and has been used in the treatment of iodine poisoning. [15].

CONCLUSION

Polymers play a vital role in the drug delivery. So, the selection of polymer plays an important role in drug manufacturing. But, while selecting polymers care has to be taken regarding its toxicity, drug compatibility and degradation pattern. By this review, we can say that natural polymers can be good substitute for the synthetic polymers and many of the side effects of the synthetic polymers can be overcome by using natural polymers.

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