Recent Findings, Application and Future Direction of Natural Extracts: Mucilage

Vandna Choudhary[1], Shilpa Sharma[2], Sankalp Vashishtha[1], Amita Malik[3*]

[1]Department of Chemistry, IFTM University, Moradabad, UP, India.
[2]Department of Chemistry, Manav Rachna University, Sector-23, Faridabad, India.
[3]Department of Chemistry, Dyal Singh College, New Delhi-110003, India.

ABSTRACT

Mucilage is a natural biopolymer present in plants. These have found a variety of applications in different areas of agriculture, food, and pharmaceuticals as binders, diluents, viscosity enhancers, stabilizers, disintegrators, solubilizers, emulsifiers, granulating and thickening agents, and suspending and gelling agents. These natural polysaccharides possess a high molecular weight and have gained attention due to their availability, low cost, and structural versatility. They possess remarkable properties to be used as green and renewable alternatives for developing polymers for requirement-based applications. Natural mucilage has been used as such for different applications. The mucilage-developed hydrogels offer valuable properties when compared with the hydrogels of synthetic origin. Moreover, they are biodegradable, biocompatible, and non-toxic, and simple modifications can be performed to achieve materials that can be used for a few high-end biomedical applications, viz. drug delivery, tissue engineering, and wound management. Mucilage-based hydrogels are one area that can cater to the needs of the above-mentioned applications. The review has been compiled to cover the various aspects of tailoring the mucilage using physical and chemical methods for modification to prepare hydrogels. Graft polymers, co-polymers, interpenetrating, and semi-interpenetrating polymers can be developed with different properties suitable for biomedical applications. The innovations carried out in these areas and their medical applications are covered in this paper.

Key Words: *Mucilage, Hydrogel, Biocompatibility, Drug delivery, Tissue engineering, Wound management*

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INTRODUCTION

Natural materials were used for many biomedical purposes, attracting attention all over the world. People's interest has shifted to naturally occurring biopolymers like mucilage that are derived from plant because of the dangers that synthetic polymers pose to human health [1]. These mucilages can be obtained from various plant components. These mucilages have specific health advantages, such as the ability to regulate diabetes, possession of anti-cancer qualities, and boosting immunity. Consequently, these natural polymers are increasingly being studied because of their potential to manufacture a wide range of materials depending on their characteristics and molecular weight. For their use in medication delivery, these natural polymers have been incorporated into several solid, liquid, and semi-solid formulations. Natural and manufactured polymers have both been utilized. Both synthetic and natural polymers have been employed, however, reports suggest that synthetic polymers are hazardous, expensive, and have other problems with the environment [2]. The effectiveness and usability of plant-based polymers in various pharmaceutical dosage forms, such as matrix-controlled systems, film coating agents, microspheres, and viscous liquid formulations, such as ophthalmic solutions, suspensions, and implants, have been established [3]. These have also been used as emulsifiers, suspending and gelling agents, stabilizers, disintegrators, binders, and viscosity enhancers. These natural polymers, however, present several potential difficulties, such as being produced in small quantities and mixtures; they are structurally complex because they vary depending on the

Corresponding author: Amita Malik
Address: Department of Chemistry, Dyal Singh College, New Delhi-110003, India.
E-mail: ✉ amitamalik@dsc.du.ac.in
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location of the plants and season; as a result, isolating and purifying them is a time-consuming and expensive process. Mucilage from plants can produce gels and is naturally hydrophilic. These plant-based ingredients can take the place of artificial additives. Mucilage from plants forms gels and is naturally hydrophilic. The ingredients of this plant can replace artificial ingredients. Mucilage is a phenomenon of polysaccharide found mainly in higher plants, with various phytochemical properties that make it attractive for medicinal and medicinal products [4]. Mucilage is a complex polysaccharide with a branched structure and a monomeric structure. L-arabinose, D-xylose, D-galactose, L-rhamnose and galactose units and other bioactive components such as alkaloids and steroids [5]. Mucus hydrolysis produces the sugars xylose, glucose, and mannose, which are pentose and hexose. Some swell while others dissolve in water. Alcohol can be used to precipitate polysaccharides with different structures. There are amorphous and high molecular weight (about 200,000) polyglycosidic acid polymers made from sugar and uronic acid units [6]. Value (ionic and non-ionic), shape (linear and branched), origin (plant, animal, and microbial origin), and chemical structure are often used to classify mucus (homoglycans and heteroglycans). Mucilage bears some chemical similarities to gums and pectins, but has a different physical structure. Slime produces a homogeneous hydrocolloid dispersion, while water-swellable gum produces a colloidal dispersion. Gums are extracellular polymers produced when plants or trees are damaged by degradation of their cell walls due to poor quality [7]. On the other hand, mucus is a product of normal metabolism produced or stored in cell layers. Mucus is commonly found in rhizomes, roots, and seed endosperms as energy reserve sources; in contrast, leaf mucus does not appear to be a stored source of carbohydrates. The high concentration of hydroxyl groups in polysaccharides causes mucus to hold more water. Mucilage is used as a membrane, as an aid to seed germination, and as a storage medium for water and food [8].

Cacti (and other succulent plants) and flax seeds are two of the finest sources of mucilage. Mucilage is almost always present in a limited quantity in all plant parts and classes. Mucilage can be extracted from different plants, including the walls of seeds (such as isabgol, flaxseed, and tamarind), inner bark (fenugreek), leaf epidermis (cassia), bark (cinnamon and slipper elm), and specialized secretory cells (squill). Mucilage can also be obtained from fungi and algae (agar and Chondrus) (conidia of Magnaporthegrisea). Along with proteins, resins and tannins, homopolysaccharides or heteropolysaccharides are the main components of mucilage. These can be modified to form hydrogels, which are materials made from a combination of synthetic and natural polymers. These materials have a long history of developing hydrophilic polymer-based materials for biomedical applications such as drug delivery, therapy, and tissue engineering. These drugs have cross-links of hydrophilic polymers that allow them to absorb a lot of water, swell and retain their three-dimensional structure [9]. According to the swelling rate, they can be divided into low (20-50%), medium (50-90%), high (90-99.5%) and over 99.5% superabsorbent. Having the same stability, hydrogels are generally non-toxic, soft, porous, and strong, making them useful for medical applications. They also have important properties such as flexibility, biocompatibility and biodegradability. Thanks to the principle of osmosis, hydrogels can absorb more than 400 times their own weight in water, and hydrogels adhere to water molecules through hydrogen bonding [9]. The gums can be modified to form different types of hydrogels. This could expand research into the development of hybrid-based hydrogels for a variety of applications. Although mucilage is only found in the seeds, leaves, roots and fruits of the plant in insects, it can be used for many purposes due to its differences in its chemical properties.

The purpose of this review is to describe the classification, extraction, chemical composition, characterization of various samples and some new research products used in a variety of biological and health [9].

Mucilage extraction and characterization

Since the plants' many sections all contain mucilage, mucilage extraction presents several difficulties. The characteristics of the extracted mucilage depend on the method of extraction because it is a natural substance. To attain the best outcomes and mucilage qualities, the extraction procedure and conditions must be standardized and improved. Simple classic soxhlet extraction using heat energy, microwave extraction, and ultrasonic extraction are some of the procedures used. Two key processes in the extraction process are grinding and maceration, which is then followed by precipitation. It is preferable to soak the material before maceration. There is a need to improve extraction efficiency and speed during the maceration process. Methods include hot water extraction, solvent extraction, acid/alkali extraction, and hot water extraction. To enhance mucilage extraction, several chemicals, including acid solutions, ammonium oxalate, and EDTA, have been utilized. When mucilage is obtained from various plant parts, its quality with regard to purity, viscosity, and other elements has to be examined. The quality of the mucilage is further impacted by temperature and agitation [10, 11]. We can define and improve the processes for extracting mucilage from different natural sources. The primary components of mucilage extracts are polysaccharides and proteins. The literature listed below explores various extraction techniques from various plants.

- *Calendula flower (Calendula officinalis)*

The Compositae family includes the fragrant annual plant calendula, also known as pot marigold. Although widespread all over the world as an ornamental plant, the homeland of the marigold is the Mediterranean region (although some say it originated in Egypt). The dried flowers of calendula contain essential oil, various bitter compounds, various carotenoids, mucilage, plant resins, various polysaccharides, plant acids and various alcohols, saponins, other glycosides and more types of sterols.In addition to monosaccharides, the ethanol extract of the plant's inflorescence revealed the existence of polysaccharides with a (13)-D-galactam backbone and short side chains at C-6, including araban- (13)-araban, and alpha-L-rhamnan, (13)-araban.Calendula is extracted by allowing the flowers to dry in the sun for ten days. To extract the slime, soak in water for 5-6 hours, boil for 30 minutes and leave for an hour. The filtrate is then sieved or filtered through cheesecloth and treated with ethanol. The precipitated mucus is dried at 35°C, crushed and sieved. This method yielded 9-11% of the C. flower fraction. Each plant piece was precisely weighed using a digital scale before being extracted continuously at room temperature while being occasionally shaken by hand using n-hexane, dichloromethane, acetone, ethyl acetate, methanol, and distilled water. Each solvent extraction required two days to complete. A rotary evaporator was then used to vacuum-evacuate the filtered solvent until it was completely dry. The extract has yields of 8.32%, 5.09%, 5.70%, 0.71%, 15.27%, and 12.99% (w/w) respectively. The Calendula mucilage's FT-IR spectra exhibit oscillations in the C-C bond stretching as well as a broad intermolecular O-H hydrogen bond peak at 2424.98 cm^{-1} and a sharp peak at 1621.94 cm^{-1}. Aliphatic C-N vibration accounts for 1202 cm^{-1}, while C = C bending vibration accounts for 616.28 cm^{-1}. Alkane experiences expansion and contraction of 2453 cm^{-1} by C–H and 1704 cm^{-1} by C = O [12].

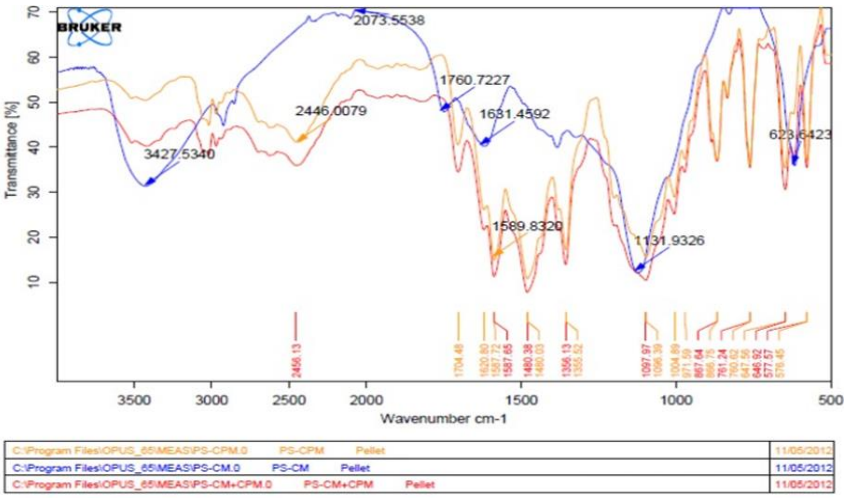

Figure 1. FTIR spectra of Calendula mucilage

- *Basil seed (BSM) (Ocimum sanctum)*

When the polysaccharide component of BSM (basil seed mucilage) was examined, two main portions were found. The first one is the 43% of glucomannan that is acid stable, which makes up the central core and has a glucose to mannose ratio of 10:2. The second one has 14 glycosidic linkages, an acidic side chain at the C2 and C3 carbons, and also contains 24.29% xylan. The second one contains an acidic side chain at the C2 and C3 carbons and contains 24.29% xylan with 14 glycosidic connections. A highly branched arabino-galactan and a little amount of glucan (2.31%) have also been reported [13]. Galactose, arabinose, mannose, glucuronic acid, rhamnose, galacturonic acid, and glucose are some of the carbohydrates found in BSM. The mucilage around the outer layer is present in the seeds of Ocimum basillicum Linn. Mucilage that has been isolated has the significant flaw of swelling yet remains attached to the seeds. As a result, alternative approaches were explored to separate the seed mucilage since typical methods for mucilage separation do not apply to it [14, 15].

Extraction of Ocimum basillicum Linn: Basil polysaccharide seeds are extracted using various methods and solvents to produce slime through a hydrothermal process. As a result of folding the muslin cloth with the addition of ethanol and acetone, slime precipitated from the filtrate at yields of 36.19% and 14%. Higher ethanol yields have been found when comparing different methods of extracting slime from hot distilled water to equivalent amounts of ethanol [16]. The distinctive bands can be seen at approximately 3455.13, 2926.01, and 1674.19 cm^{-1} in the FTIR spectrum of BSM in **Figure 2** above. These bands, which contain hydroxyl (-OH) stretching, C-H stretching of the CH_2 groups, and -COO (asymmetric

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vibrations) groups, are frequently observed in polysaccharides [16]. The distinctive bands can be seen at approximately 3455.13, 2926.01, and 1674.19 cm^{-1} in the FTIR spectrum of BSM in **Figure 4** above. These bands, which contain hydroxyl (-OH) stretching, C-H stretching of the CH_2 groups, and -COO (asymmetric vibrations) groups, are frequently observed in polysaccharides [16].

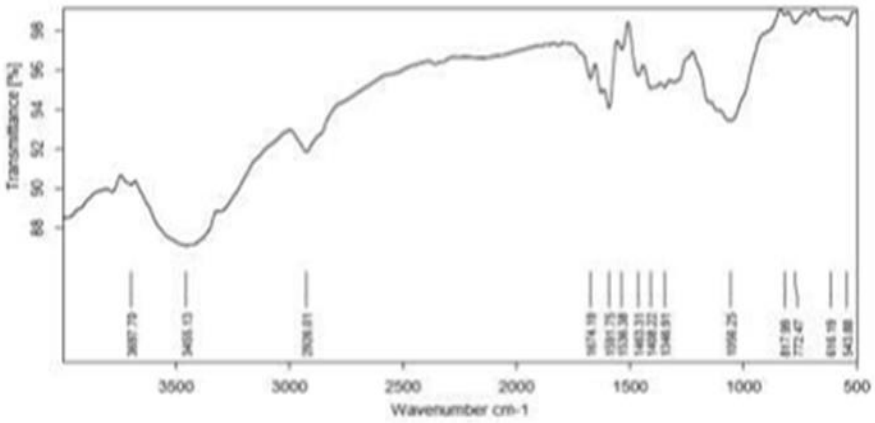


Figure 2. FT-IR spectra of Basil seed mucilage

- *Chia seeds (Sativa hispanica)*

It is an angiosperm of the Lamiaceae family, found in the tropics and subtropics. Researchers have become interested in chia seed mucilage because it is biocompatible and biodegradable [17]. Lin *et al*. (1994) have determined what polysaccharides' fundamental structural units are. As a tetrasaccharide with a branch from b-D-xylopyranosyl on the backbone and a 4-O-methyl-D-glucuronopyranosyl residue. By acid hydrolysis in a 2:1:1 ratio, the monosaccharides 4-O-methyl-D-glucuronic acid, D-xylose, and glucose were produced. Using distilled water, the mucilage of chia seeds was removed from the whole seed (water: seed ratio of 10:1–30:1). The extraction process took place at 30-80°C with stirring lasting 2-4 hours. In a standard hot air oven, the aqueous suspension was dried at 50 °C. 6.97% is the extraction yield [18]. Munoz *et al*. extracted chia seed mucus using distilled water, while the seed-to-water ratio, pH, and temperature were changed to examine the mucus' microstructure. The collected mucus aqueous solution was dried at 50°C, after being stirred continuously for two hours during the experiment. After two hours of hydration, the weight of the seeds in all ratios remained constant, but the amount of mucilage produced increased as the temperature rose from 200 °C to 800 °C. The yield is increased from 6% to 22% [19]. The chia mucilage FTIR spectrum is shown below in **Figure 3**. The common peak of polysaccharide was shown as a broad stretch between 1000 and 1200 cm^{-1} at a peak of 2928.64 cm^{-1}, which displays the C-H stretch. A minor peak associated with O-C-O asymmetric stretching, exhibited at 1153.29 cm^{-1}, indicated the presence of xyloglucan in the mucilage sample, while the peak at 1026.74 cm^{-1} mimics the C=O link from the alcohol group. The stretching visible at 1420 cm^{-1} (1409.41) is related to the symmetrical COO-link vibrations, whereas the peak at 1656.62 cm^{-1} is predominated by the secondary structures of the chia protein [19].

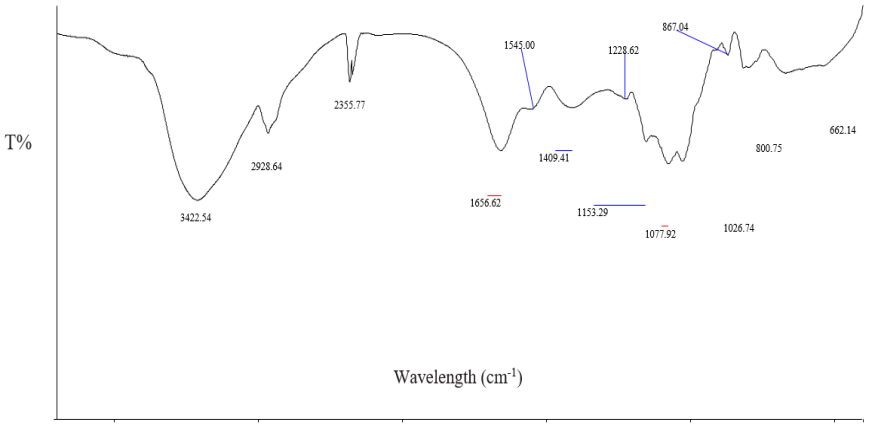


Figure 3. FT-IR spectra of chia mucilage

- *Okra (Abelmoschus esculentus)*

The monocotyledonous plant known as okra, belongs to the Malvaceae family and is mostly grown in temperate, tropical, and subtropical climates. Protein, fiber, calcium, iron, and zinc are just a few of the essential elements found in okra. It also has low amounts of anti-nutrients and good mineral bioavailability [20]. It has been established that okra extract contains acidic polysaccharides made up of several sugars, including galactose, rhamnose, galacturonic acid, galactose, glucose, and glucuronic acid [21]. Okra mucus has polysaccharides that have repeating units of (1-2) rhamnose and (1-4) galacturonic acid residues [22].

Okra (Abelmoschus esculentus) was washed, dried for 24 hours in the shade, and then dried at between 30 and 40°C until totally dry. The fruit powder was mixed continuously for 4 hours at 60°C. The yield of mucus was found to be 11.44% when the concentrated solution was filtered through a muslin cloth and chilled to 4°C to 6°C utilizing a water-based extraction technique [23]. From powdered pods, aqueous okra mucilage was extracted in a beaker with distilled water (30:1 ratio). To extract mucus, the swollen powder was slowly agitated with a magnetic stirrer for three hours at 700 rpm and 55°C. The thick okra extract was separated using a white muslin cloth (mucus). At a ratio of 3 parts acetone to 1-part mucus extract, acetone was added while stirring to precipitate mucus. After that, 1 part of 96% v/v ethanol was added to eliminate any remaining contaminants, such as pigments. The collected mucus was then dried for 4 hours at 100 °C to produce a yield of 6–7% [22, 23] **(Figure 4)** shows the FTIR spectrum of okra mucilage. The complex C-O band expansion and contraction of the tightly bound polysaccharide, as well as the spectral region of 1035.77 cm^{-1}, were caused by the C-O-C group of the polysaccharide and the C-O bond of the alkyl aryl ether at 1246.02 cm^{-1}.Free alcohol, O-H in-plane bend at 1373.32 cm^{-1} The OH bend is at 1413.82 cm^{-1}, the -CH_3 bend is at about 1598.99 cm^{-1}, the C = O of the carboxylic acid group is at 1724.36 cm^{-1}, the alkane C-H stretch is at 2926.01 cm^{-1} (medium), and the alcohol O-H stretch is at 3269.34 cm^{-1} (sharp, medium).

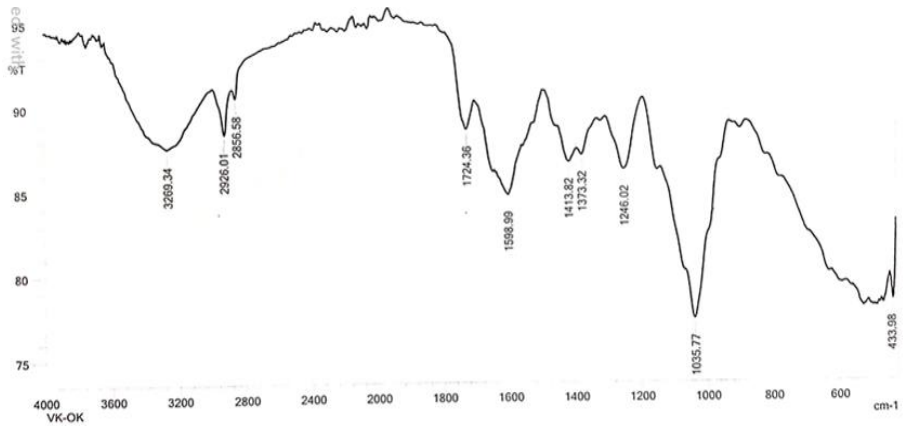


Figure 4. FT-IR spectra of okra mucilage

- *Flaxseed seed mucilage*

Linum usitatissimum L., also referred to as flax, is a plant used for its fiber and oil. The flaxseed hull and endosperm are two of the six layers that make up flaxseed. The mucilage oozes on the surface as the seed layer becomes moist. There are roughly 60–70% carbohydrates and 4–20% proteins in it. Due to its high concentration of ALA, a crucial omega-3 fatty acid, dietary fiber, and natural phenolic antioxidants, the use of flaxseed in food and food products has been rising. These phytochemicals, which include flavonoids, lignins, phenolic acids, and cinnamic acids, act as antioxidants and influence cell growth and survival. The majority of the mucilage is made up of polysaccharides, which, upon hydrolysis by an acid, are converted to galactose, xylose, arabinose, rhamnose, galacturonic acid, and possibly traces of D-glucose [24]. The heterogeneous polymer known as FSM (Flaxseed Mucilage) is made up of neutral arabinoxylan (75%) and rhamnogalacturonan (25%). The rhamnogalacturonan contains L-rhamnose, D-galactose, D-galacturonic acid, and L-fructose acid, whereas the arabinoxylan contains xylose, arabinose, and galactose. It has been reported to be help treat heart disease and colorectal cancer, as well as having therapeutic efficacy in lowering blood glucose and cholesterol. It has a high viscosity in aqueous solutions and an excellent ability to retain water and swell [24]. Additionally, due to its unique nutritional value as a dietary fiber and its gelling properties, researchers have shown a keen interest in its possible medicinal applications [25]. Mucilage extraction from flaxseeds was soaked in 500mL of the water. After 48 hours, the soaked seeds were boiled for 15 minutes in deionized water, and the mucilage was then filtered through the muslin fabric. The mucilage was precipitated from the filtrate by adding ethanol and centrifuging at 1000 rpm. The mucilage can be,

precipitated in and then dried at 40 °C to obtain a constant weight. The yield was 8% [25, 26].

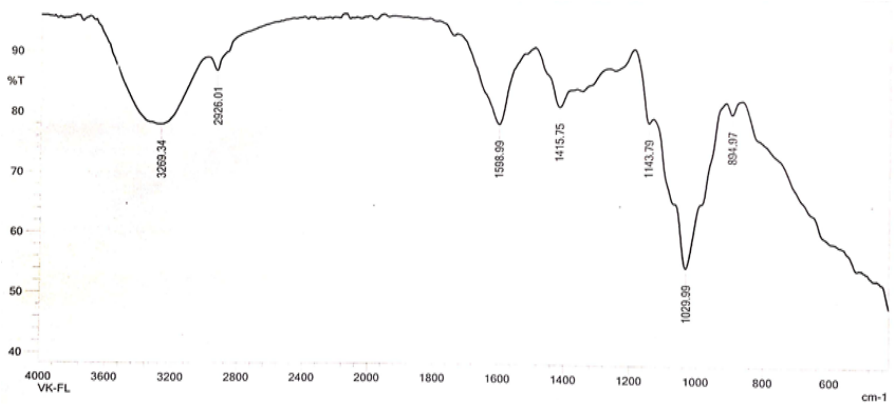


Figure 5. FT-IR Spectra of flax seed mucilage

Flaxseed mucilage FTIR spectrum shown above in **Figure 5**. OCH_3 group presence at 894.97 cm^{-1} region, C-O bond stretching of C-O-C group in polysaccharide at 1029.99 cm^{-1} region, C-O bond stretching of aliphatic ether at 1143.79 cm^{-1} region, O-H bending of alcohol at 1415.75 cm^{-1} regions, C=C stretching of alkene at 1598.99 cm^{-1} regions, C-H stretching of alkane at 2926.01 cm^{-1} regions(medium) (sharp, medium).

Mucilage-based hydrogels(polymeric materials)

Hydrogels

Hydrogel describes three-dimensional network structures created by the hydrophilic groups or domains present in a class of synthetic and/or natural polymer networks that can absorb and retain a significant amount of water upon hydration**.** The natural polymers used are the naturally occurring polysaccharides and proteins. The polysaccharides constitute the cellulose and the hemicellulose, which can be either of plant or animal origin. These polymers, in combination with synthetic polymers, lead to the formation of hybrid polymer gels, which can be tailored to achieve hydrogels for high-end biomedical applications like drug delivery, tissue engineering, and wound care, to name a few. Mucilage from plants contains a class of polysaccharides that can be modified to prepare different hydrogels with improved properties. The methods used for modification can be either physical or chemical methods [27]. The three-dimensional network formed due to these modifications leads to the formation of hydrogels by linking macromolecular chains together, leading to progressively larger branches, which decrease the solubility of polymers and are referred to as ‘gel points."Physical linking can be sub-categorized as strong physical gels and weak physical gels. Chemical linking includes the formation of polymers by crosslinking the polymeric chain or by grafting [27].

In the physical method, polysaccharides present in mucilage form a cross-linked network with a counter-ion at the surface. High counter-ion concentrations will require longer exposure times to achieve complete cross-linking of the polysaccharides. These are also of different types and have been reported as heating and cooling, ionic interaction and complex coacervation, H-bonding, maturation (heat induces aggregation), and freezing.

Chemical methods involve the grafting of monomers onto the backbone of the polymers or the use of a cross-linking agent to link two polymer chains. The cross-linking of natural and synthetic polymers can be achieved through the reaction of their functional groups (such as -OH, -COOH, and $-NH_2$) with cross-linkers such as aldehydes (e.g., glutaraldehyde, adipic acid dihydrazide). There are a number of methods reported in the literature to obtain chemically cross-linked permanent hydrogels. Among other chemical cross-linking methods, interpenetrating networks (polymerizing a monomer within another solid polymer to form an interpenetrating network structure) and hydrophobic interactions (incorporating a polar hydrophilic group by hydrolysis or oxidation followed by covalent cross-linking) are also used to obtain chemically cross-linked permanent hydrogels. Chemical crosslinking can be carried out using chemical initiators, while radiation grafting can be carried out using radiation as an initiator. The radiation can be gamma radiation, UV, photochemical, microwave, or an electron beam. The activation sites formed on the polymer can lead to the attachment of functional monomers, resulting in the formation of grafted polymers with different properties depending on the functional monomers used [27, 28].

- *Interpenetrating polymer (IPN) and Semi-interpenetrating polymers (semi- IPN)*

Interpenetrating polymer networks (IPNs) consist of two or more bonds and are crosslinked with or without the presence of covalent bonds. These bonds cannot be separated unless chemical bonds are broken. The main aim of IPNs is to improve at least one property of their

constituent networks. The types of IPN are: (i) when both network precursors are mixed and the two networks are synthesized at the same time by independent, non-interfering routes such as chain and stepwise polymerization; and (ii) when a single network is swollen into a solution containing a mixture of monomer, initiator, and activator, with or without a cross-linker. If a cross-linker is present, fully-IPN is produced, while in the absence of a cross-linker, a network having linear polymers embedded within the first network is formed (semi-IPN or pseudo-IPN). The networks that constitute the IPN can be identical, i.e., homo-IPN, or different, hetero-IPN34. They can be obtained by undergoing either chemical or physical polymerization. They have properties that can differ between macromolecular constituents. These polysaccharides are abundant, available from renewable sources, and have a large variety of compositions and properties that may allow appropriately tailored chemical modifications [29, 30].

These hydrogels are made mostly of polysaccharides and proteins and their derivatives, which are natural polymers. Hydrophilic functional groups found in synthetic polymers include -COOH, -OH, -$CONH_2$, -SO_3H, amines, R_4N^+, ether, and others. The main categories are synthetic hydrophilic polymers, proteins, and polysaccharides. Sometimes the crosslinking in polymeric materials happens within the polymer itself [30].

- *Stimuli responsive polymers responsive polymers*

Stimuli-responsive polymers are types of polymers that are sensitive to external stimuli. These polymers respond as per the external environmental change. This behavior is due to the functional groups present in the polymer. Different functional groups respond to different stimuli like pH, temperature, light, magnetic, and electric properties [31]. These polymers have gained interest due to their potential biomedical applications in different areas like drug delivery vehicles, cell adhesives, sensors, biomimetic tissues, etc. Different polymers have been used in synthesizing stimuli-responsive polymers. Different hydrophilic and hydrophobic polymers have been used in preparing polymers with single, dual, or multi-responsive properties. Different mucilage extracts have been used in preparing stimuli responsive polymers. Various synthetic and natural materials have been used in synthesizing smart materials for biomedical applications. Among natural sources, polysaccharides have gained attention due to their remarkable biological and low toxicological activities. Polysaccharide-based hydrogels are an ideal candidate for the development of sustained/controlled release oral drug delivery systems, and the release of drugs from such systems mainly depends upon the swelling ability of polysaccharides. Any change in the composition of the surrounding environment may affect the swelling of polysaccharides and, hence, the drug-releasing ability. The presence of salt in food, concomitant administration with alcohol, and a low pH in the GI tract may affect the release of drugs. Therefore, it is of utmost importance to study the swelling-deswelling behavior of BSH under different conditions [31].

- *Grafted polymers*

Grafting is the process by which one substance is covalently linked to another. This will increase the hereditary properties of the main segment. It is a useful technique as it can help modify the properties of the polymeric material. This can be done through different processes like ionic grafting, photochemical grafting, grafting through enzymes, microwaves, and gamma radiation. Recent developments in polymer grafting have resulted in improved surface properties, making them suitable for biomedical applications. This grafting on mucilage was first performed on acrylic acid and psyllium mucilage using an initator (potassium persulfate) and cross-linker (hexamethylene tetraamine), which resulted in grafted polymers with improved surface properties [32]. Grafting needs three processes: free radicals, radiation, and enzymes. Among the three methods, free radical grafting is the best as it produces high yields with better grafting efficiency.

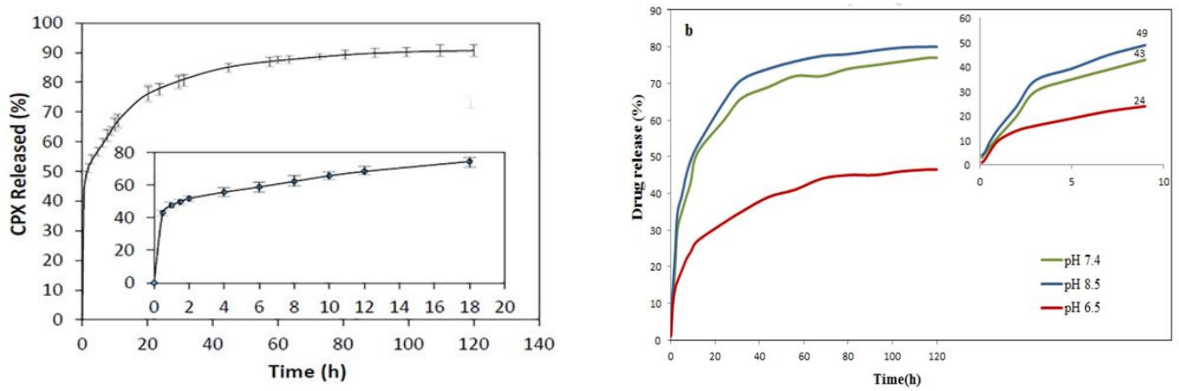
Mishra *et al*. reported the synthesis of grafted okra using polyacrylamide. The grafting was carried out with acrylonitrile using redox initiator ceric ammonium nitrate/nitric acid. The synthesis was conducted in the nitrogen (N_2) atmosphere. Grafting improved the okra mucilage by introducing more reactive sites without altering the molecular mobility of chelating groups of polysaccharides [33]. Nandi *et al*. carried out microwave-assisted grafting of okra mucilage with methacrylic acid and CAN and potassium persulfate (PPS) as the free-radical initiator. The mucoadhesive potency of the obtained graft copolymer was analyzed. These find applications in drug delivery in the form of buccal patches, nanocomposite films, binders, and mucoadhesive gels [32].

Applications of mucilage-based polymeric materials

Drug delivery

Mucilages are polysaccharides usually extracted from natural sources and are hydrocolloid compounds. These are compounds with low concentration and high viscosity, making them potent candidates to be used as gels in the pharmaceutical industry in the form of coating agents, nanoparticles, suspensions, implants, and drug delivery systems. Controlled drug delivery is an important factor to be considered for drug delivery systems. Mucilages have shown their potential application as controlled drug delivery systems [34] and sustained drug delivery system.

Ali *et al*. reported the release of the drug cephalexin from magnetically coated mucilage. The mucilage obtained was extracted from basil seeds. The basil plant (Ocimum basilicum L.), a medicinal plant known as tulsi in Hindi, is considered a sacred plant and has been known for its anti-inflammatory and antibacterial properties. The basil mucilage, coated with Fe_3O_4 nanoparticles, possessed magnetic properties. The release trend explained the explosive release of cephalexin for the first 2 hours, which was about 52%, whereas 38% was released for 88 hours. These mucilage-based nanocomposite materials can be used for treating diseases that require longer exposure to drugs **Figure 6a** [34]. Masoomeh *et al*. claimed the development of pH-sensitive films from basil seed mucilage and polyvinyl alcohol (PVA) for wound healing. The optimized film was prepared by varying the concentrations of BSM, PVA, and glutaraldehyde (crosslinker). The incorporation of the drug moiety, tetracyline hydrochloride, accelerated the healing process. The MTT assay was done in order to determine the viability of fibroblast cells. The optimized hydrogel films were non-toxic to human cells, as mentioned in **Figure 6b** [35].



a) b)

Figure 6. Drug release study of basil seed mucilage blend with (a) Fe_3O_4 nanoparticle (b) Polyvinyl alcohol

Muhammad *et al*. designed a drug carrier from flaxseed mucilage and pluronic for the release of the drug docetaxel. Cytotoxicity studies can be done to determine the release efficiency. The minimum toxicity of the drug carrier was found to be 100% at a concentration of 250 µg/ml whereas 82% at 500 µg/ml making it chemotherapeutically effective **(Figure 7)** [36]. Polymeric microspheres were designed using okra mucilage and alginate. Oxcarbazepine was loaded on polymeric microspheres, and a release study was done in the physiological fluid of the gastrointestinal tract (GI tract). The polymeric microspheres prepared from alginate alone and alginate-okra mucilage showed drug release rates of 92.12% (12 h) and 84.47% (24 h), respectively [37]. Therefore, the blend of alginate and okra can be used for sustained drug delivery systems **(Figure 8)**.

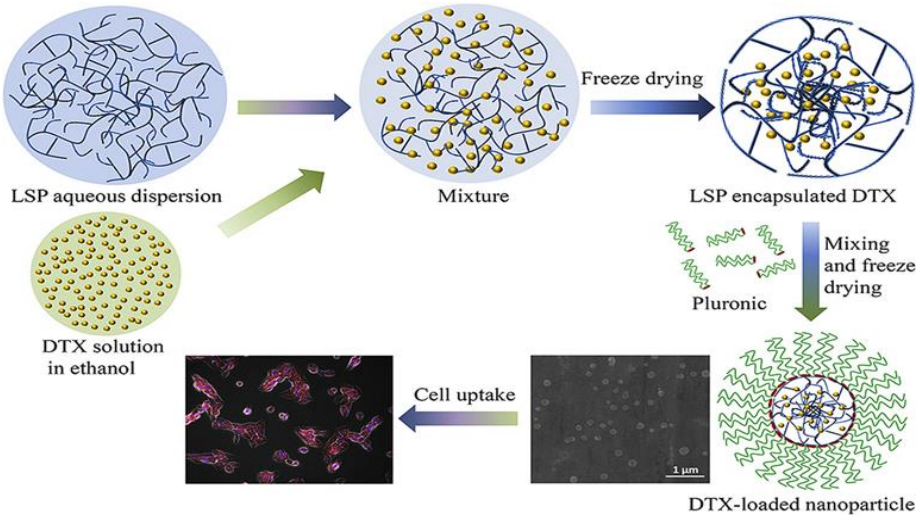


Figure 7. Flaxseed mucilage and pluronic for the release of docetaxel drug [36]

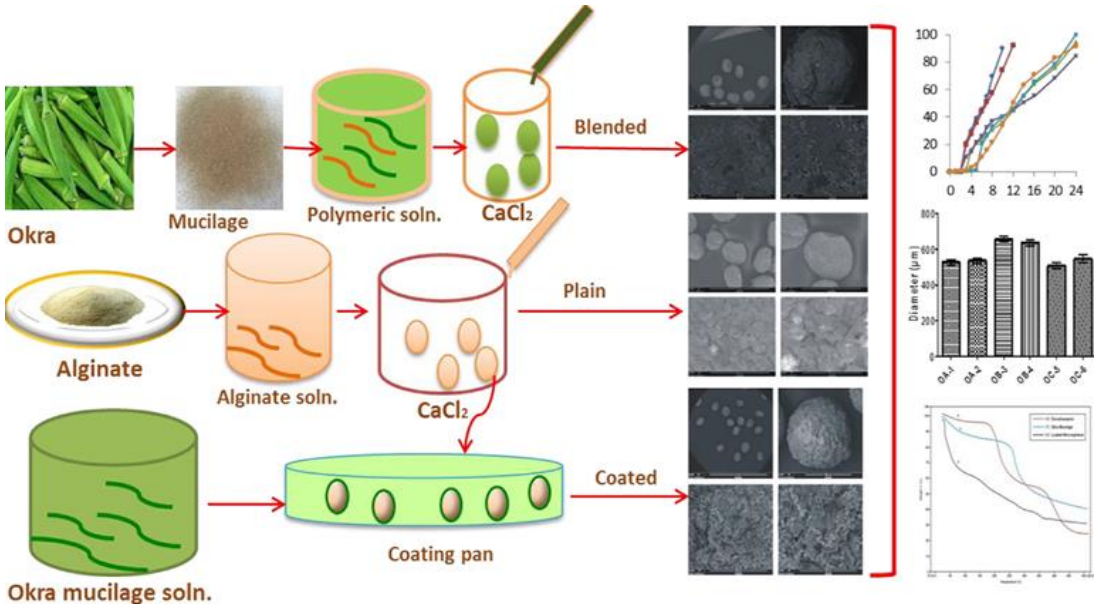


Figure 8. Alginate and okra mucilage-based microsphere for drug delivery [37]

Wound management

Wound healing is a natural process that fixes damaged tissues. Healing is the interaction of a complex cascade of four overlapping events that generate resurfacing, reconstitution, and restoration of the tensile strength of injured skin. It is also a complex and dynamic process of replacing devitalized and missing cellular structures and tissue layers [38]. During the routine wound healing process, the human body can supply all the basic needs unless there are severe skin functional defects or massive fluid losses. However, providing proper pH, humidity, oxygen pressure, and protection against microbial invasion can speed up the wound healing process. Different types of dressings have been used for treating chronic wounds. Hydrogel-based wound dressings are very effective in wound treatments. They allow gaseous exchange from the wound to the outside. They keep the wound moist, absorb body fluids, and maintain a constant temperature. They reduce pain by cooling the wound. They prevent the bacteria and dust from entering the wound surface. Mucilages from different sources have also been used in the healing of wounds. Cellular-based hydrogels and their derivatives are commercially available as wound dressing products in different forms, such as fibers, membranes, and sponges. The porous network can be fabricated from any soft polymer or semi-polymer expressing macroscopic forms of films, beads, papers, gels, microspheres, and even aerogels obtained by the methods of air drying, cryo-desiccation, or supercritical drying, respectively. A wide range of hydrogels with distinct functional junction points of view have been reported [38].

Tissue engineering

Tissue engineering is a developing field in medicine, with a focus on preparing new biomaterials that can mimic functional tissues for particular applications. It is an interdisciplinary research project that involves chemistry, biomaterials, and biological sciences. It mainly aims at implantation, delivery, and placing cells or tissues within different matrices. Tissue engineering follows a biological approach in order to preserve, restore diseased and damaged organs or tissues. Different materials with properties like nontoxicity, biocompatibility, and appropriate mechanical properties are valuable for use in tissue engineering and regeneration purposes. The material matrices with implanted cells helps regenerates tissues. Associated with the different features of the cells in different microenvironments, the regeneration process of the tissue is largely dependent on the biophysical properties of the matrices [38]. Cells and growth factors either adhere to the scaffold surface or get encapsulated within the matrix. In tissue engineering applications, cell-ECM interactions play an important role in day-to-day cellular activity and the wound healing process. The two main elements of the tissues are cells and the extracellular matrix (ECM). Cells regulate body processes, performing normal maintenance and wound healing, while ECM components, composed of a dynamic preparation of polysaccharides and proteins (collagen, elastin, fibrinogen, silk fibroin, elastic, keratin, etc.), serve as the major structural component of the body. Preparing a novel set of tissue replacement pieces and their implementation are areas of medical research. Scaffold design and production are important topics for regenerative medicine and tissue engineering, and their success is a key factor for the overall application [39, 40]. Prakash *et al*., reported the synthesis of a mucilage blend that can be used for tissue engineering applications. The mucilage obtained from jackfruit blended with poly (caprolactone) showed 90% cell

viability results. These mucilage blends claim to be used in cancer treatment and cell growth [41].

CONCLUSION

When it comes to biodegradability and biocompatibility, there is no space for compromise. Even though hydrogels made from biomaterials are more environmentally sustainable, acrylic hydrogels based on petrochemicals still dominate due to various competitive factors. Today cellulose-based hydrogels are used in different industries, including contact lenses, hygiene application, bandages for wounds, tissue engineering, and drug delivery. Natural gums/mucilage have become popular as pharmaceutical excipients because they are affordable, plentiful and non-toxic. For creating new application delivery methods, biotechnological uses, and other delivery systems, it is necessary to develop more natural sources as well as adapt current natural materials. Therefore, natural gums/mucilage and their modifications for the creation of improved drug delivery materials will continue to be an area of interest in the years to come.

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