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REVIEW PAPER

Scope of herbal mucilage in pharmaceutical formulations. A review

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Summary

The aim of the article was to obtain maximum information about plant mucilage, its sources and applications in the pharmaceutical industry. This study focuses on the scientific articles and books available in Internet resources and college library that deal with the sources, applications, extraction and isolation of plant mucilage. Mucilage is obtained mainly from plant sources and can be isolated easily. Due to the low cost, easy availability, non-toxicity, non-irritancy, and biocompatibility, mucilage is of great demand in the field of pharmaceuticals. *Hibiscus rosa-sinensis* L.*, Trigonella foenum-graecum* L.*, Abelmoschus esculentus* L*, Plantago ovata* Forssk. and *Aloe barbadensis* L. are some common sources of mucilage. The isolation methods vary depending on the part of the plant where mucilage is present. It is commonly used as gelling agent, suspending agent, binder, and disintegrant. Since it is hydrophilic in nature, chances of deterioration are higher. In this review, different mucilage sources and their isolation methods are discussed in detail. Mucilage is used as excipient in many formulations of tablets, suspensions, gels, etc. The study explores the potential of plant mucilage as an excipient in pharmaceutical formulations. The biodegradable and biocompatible properties of this inexpensive excipient make it more favourable for the newer formulation development.

Key words: ***mucilage, herbal excipient, suspending agent, binding agent, disintegrating agent***

Słowa kluczowe: ***śluz, roślinne subtancje pomocnicze, środek zawieszający, środek wiążący, środek rozsadzający***

INTRODUCTION

Mucilage, gums and glucans are polysaccharide hydrocolloids which are abundant in nature. Mucilage is the metabolized product produced inside the plant cell, and this process occurs without causing any damage to the plant [1, 2]. The physiological role of mucilage, which is abundant in plants, is unclear in most cases. Different types of mucilage found in plant parts such as rhizomes, roots and seed endosperms may have a large role as energy reserves. However, the mucilage obtained from foliar parts does not

function as a reservoir of carbohydrates. Generally, it is assumed that foliar mucilage is a simple secondary metabolite of plants, although there are investigations that found that mucilages have extremely crucial role in frost tolerance, transport of water and response to wounds. It also has a big role in plant host-pathogen interaction and ionic balance of plant cells. Water-binding capacity of the plant mucilage is high due to the presence of large number of hydroxyl groups present in it. The ability of plants to resist drought is due to this characteristic [1, 3]. Since mucilage is not digested in the small intestine, it moves into the large intestine, where it will be fermented by beneficial intestinal bacteria and converted into gases and substances which then can be absorbed easily [4].

Nowadays, plant-based pharmaceutical excipients are of a great demand and utilized by the researchers in the development of various formulations. The major advantages of the use of this natural resources are that they are renewable and if cultivated properly, give an adequate supply of raw material [5]. They have a wide range of applications as they are used as disintegrants in tablets, gelling agents in gels and suppositories, thickeners and protective colloids in solution dosage forms, etc. [1, 6]. These polymers are applicable in matrix-controlled systems, microspheres, nanoparticles and buccal films for controlling or sustaining the drug release [2]. Mucilage is a substance which is hydrophilic in nature, i.e., either soluble or swell in water, and by addition of alcohol can precipitate into a product with less amorphous or granular mass in nature [1]. Plant components such as leaf cells, seed coats, roots, barks and middle lamella are rich in plant mucilage. It is a semitransparent amorphous substance and polymer of monosaccharides, and majority is found in attachment with uronic acids. Gum and mucilage have similar constituents and on chemical reaction, they yield a combination of sugar and uronic acid [6]. Natural mucilage thus has a wide range of acceptance due to low cost, easy availability, biocompatibility, non-toxicity and least irritancy and thus preferred mostly than synthetic excipients [7].

PLANT MUCILAGE – GENERAL INFORMATIONS

Types of mucilage

1. Intracellular mucilage: e.g. Orchid species (corn), *Agropyrum repense* L. Beauvois (bulb), *Alium cepa* (bulb), *Urginea maritima* L, *Aloe* (soccuent part), *Musa paradisiaca* L (pulp).
2. Cell membrane mucilage: e.g. *Althea officinalis* L. (root), *Rhamnus fragula* L. (bark).
3. Secreting hair mucilage: e.g. *Coffea arabica* L. (leaf), *Viola tricolor* L. (leaf) [3].

Advantages of mucilage

- **Biodegradable:** Living organisms are the producers of all naturally available polymers, because of which these biodegradable materials have no harmful impact on humans or nature. Apart from that, mucilage sources are renewable.
- **Biocompatible:** Since carbohydrates are the major part of these herbal material, they are highly biocompatible.
- **Non-toxic:** The nature-friendly characteristic of mucilage makes it non-toxic and non-irritant.
- **Inexpensive**: Mucilage is obtained from natural sources, so it is always cheaper. Compared to that of synthetic material, the production cost is also lower.
- **Environmental friendly**: Mucilage is collected depending on seasonal variations in bulk volumes since the production activities are easy and simple.
- **Availability:** In some developing countries, the authorities encourage the cultivation of plants producing mucilage which makes it easily available.
- **Better patient acceptance:** The chances of side effects occurrence are the lowest in natural mucilage, as compared with synthetic ones.
- **Edible sources:** Mucilage is mostly obtained from edible sources [3, 8].

Disadvantages of natural mucilage

- **Microbial growth:** The water content in the mucilage is generally high, and structurally they are carbohydrates. Therefore, the chance of microbial growth is higher during the processing and production as it gets exposed to the external atmosphere. However, by careful handling and use of antimicrobial agents as preservatives, this can be prevented.
- **Batch to batch yield inconsistency:** The production of mucilage depends on environmental and seasonal factors. Therefore, the production may not always be unique, and variations can occur since mucilage concentration is different during different seasons.

- **Reduced rheology on storage:** In general, the viscosity of mucilage increases on contact with water because of its complicated nature. On storage, the viscosity of mucilage decreases due to the conversion from monosaccharide to polysaccharides and their derivatives [3, 8].

Applications of mucilage

Natural mucilage has a broad diversity of purposes in the pharmaceutical field, especially used as pharmaceutical excipient in many conventional dosage forms. Mucilage obtained from certain plants has demulcent properties, and some can be used as bulk laxatives (Isapgol). It is also used as tablet binder, disintegrant, emulsifier, suspending agent, gelling agent, stabilizing agent, thickening agent and film forming agent in transdermal patches and many other formulations [1, 6].

General method of isolation

The plant material rich in mucilage content is collected and washed to remove the dirt and dried. The material after drying is powdered and soaked in water for minimum of 6-8 hours, and the mixture is warmed for about 30 minutes and kept in rest for the complete release of mucilage. The solution is then filtered through a muslin cloth. To the filtrate, three times the volume of acetone is added, and the obtained mucilage is collected, washed again with acetone and dried in an oven at a moderate temperature. The dried mucilage is comminuted thoroughly, sieved and finally kept in desiccators [9].

Characterization of isolated mucilage [9]

Preliminary confirmative test for dried mucilage

- **Molisch's test:** Sufficient quantity of Molisch's reagent is added into the mucilage powder taken in a test tube. After shaking the components, conc. sulphuric acid is added slowly along the sides of the test tube. Formation of violet ring at the junction of two liquids confirms the presence of carbohydrate in the powder sample.
- **Ruthenium test:** A small quantity of dried mucilage powder is mounted on a slide with ruthenium red solution and observed under microscope. Pink colour of the powder sample confirms the presence of mucilage.

Organoleptic evaluation of isolated mucilage

Prepared plant mucilage is evaluated for organoleptic properties to ensure the quality of product.

- **Solubility:** Solubility of isolated mucilage is determined by dissolving the mucilage in various solvents.
- **pH**: pH of isolated mucilage (1%) is determined by digital pH meter.
- **Swelling index**: In a measuring cylinder of 25 ml, 1 g mucilage is taken and dissolved in 25 ml of distilled water. This is shaked well in each 10 minutes interval for next 1 h and is allowed to stand for 3 hours. Swelling index is calculated using the following formula:

$$SI = \frac{final\ volume \times 100}{final\ volume}$$

- **Viscosity**: Viscosity is determined using Brookfield viscometer.
- **Moisture content**: 1 g of mucilage sample is taken in a watch glass and this is placed in a hot air oven. The sample is then allowed to dry at 105°C and it is weighed in each 5-minute interval until it reached a constant weight. The percent loss of moisture on drying is calculated using the following formula:

$$LOD = \frac{weigh\ of\ water\ in\ sampe \times 100}{weigh\ of\ dry\ sample}$$

SOURCES OF PLANT MUCILAGE

The most important sources of plant mucilage are described below (tab. 1).

Aloe vera

Aloe barbadensis L. which belongs to the family of *Aloaceae* is rich with mucilage. The minor burns and inflammatory diseases can be treated by this mucilage and is also used to develop anti-inflammatory and antidiabetic-controlled release formulations. The matrix forming ability of the mucilage is found responsible for this controlled action [10-16].

Asario

Mucilage is obtained from the kernels of *Lepidium sativum* L. plants of family *Brassicaceae.* The

chemical constituents of *Lepidium* plant includes fatty acids, essential amino acids, proteins and carbohydrates [17, 18]. A comparative study with guar gum explains the good physical properties of cress seed mucilage [19]. *Lepidium sativum* is used as a natural super-disintegrant in the formulation of aceclofenac fast dissolving tablets, and the results shows that it is a good disintegrating agent than other synthetic disintegrant [20].

Asparagus

The mucilage is obtained from the roots of *Asparagus racemosus* Willd. of family *Asparagaceae*, also known as satavari, aheruballi, asparagus and asparagus root. The major chemical constituents include polycyclic alkaloid, asparagamine A, steroidal saponins, shatavaroside A, shatavaroside B, filiasparoside C, shatavarins, immunoside and asparanin A [21-23]. The mucilage obtained from roots is identified as a perfect tablet binder in the uncoated tablet formulations, and it also possess good disintegrating properties [24].

Cactus

The botanical name is *Opuntia ficus-indica* L. and belongs to the family *Cactaceae*, also known as prickly pear, spineless cactus or cactus pear. The water content is very high which is nearly 85%. The major chemical constituents are proteins, fatty acids, linoleic acid, flavonoids such as quercetin, isorhamnetin, and kaempferol [25-27]. The mucilage is used as an edible coating over various pharmaceutical formulations [28, 29].

Cassia

The seed of *Senna tora* L. produces mucilage which contains 1–2% volatile Cassia oil. The plant belongs to *Fabaceae* family [30], and this mucilage is reported to have therapeutic activities such as tonic and stimulant [31], and these are good to use as suspending agent and binding agent in medicinal formulations [32].

Clove basil

The seeds rich in mucilage content are obtained from the plants of *Ocimum gratissimum* L. which belongs to the family *Labiatae*. In some places they are known as clove basil and ram tulasi. Clove basil is an erect, much-branched, aromatic shrub mainly grown in tropical areas. The major chemical constituents are essential oil mainly eugenol, D-germacrene and (Z)-β-ocimene. It can be used as an aromatic, stimulant, antispasmodic and antiseptic herb that repels insects, expels internal parasites and lowers fever. The leaves and stems are used in the treatment of chest colds, fever, headache, impotence, flatulence, diarrhoea, dysentery and worms in children. Externally, the leaves are used to treat rheumatism and lumbago [33]. As per the study conducted by Matyasoh *et al.*, the essential oil obtained from the leaf has shown marked antibacterial activity [34]. The powders of *Ocimum gratissimum* mucilage and *Ocimum gratissimum* seed have been studied for their effectiveness as disintegrating agent and have found to be effective in low concentrations (5%), and they have showed better drug release in comparison with marketed formulations [35]. Mucilage extracted from the seeds were used as a pharmaceutical binder, and it was found that *Ocimum* mucilage could be an alternative to acacia [36]. Mucilage can also be used as suspending agent, and studies revealed that as a suspending agent, it is a very good adjuvant, and it is comparable with tragacanth and sodium CMC [37].

Cordia

The mucilage collected from raw fruits of *Cordia obliqua* Willd. has wide pharmacological activities such as expectorant, diuretic, anthelmintic and astringent. Some investigations revealed that this mucilage can be used for treating infections in urinary tract [38-40]. The binding and gelling characteristics make it suitable to be used as binding and matrix forming agents in various tablet formulations, especially those are meant to achieve controlled or sustained delivery [41, 42]. The botanical profile indicates that the cordia plant is the member of *Boraginaceae* family [38].

Dillenia

The mucilage is obtained from the fruits of *Dillenia indica* L. of the family *Dilleniaceae,* also known as elephant apple. The major chemical constituents include flavonoids, steroids, triterpenoids, phenolics, saponins, fixed oil, etc. [43]. The mucilage obtained can be used as a good mucoadhesive agent in the formulation of nasal gels of domperidone and oxytocin [44-46]. *Dillenia indica* mucilage is also used for the development of controlled release formulations [47].

Fenugreek

The source of fenugreek mucilage is the *Trigonella foenum-graecum* L. seeds. It belongs to the family of *Fabaceae* [5]. Major chemical constituents are fibres, flavonoids, polysaccharides, saponins, fixed oils and some limited identified alkaloids namely trigonelline and choline [48]. The mucilage content is very high in fenugreek which water insoluble but able to form a thick and jelly mass on contact with water. Fenugreek seed mucilage is often utilized in external gel preparations because of its easy availability, low cost and non-irritant nature. The mucilage of fenugreek contains a polysaccharide called galactomannan, which passes through the GIT undigested because of its property of remaining unabsorbed in gastric environment [4]. Use of fenugreek in food prevents gastrointestinal disorders like intestinal gas, lifestyle-dependent diseases such as diabetes and chronic diseases like arthritis, cancer, etc.

The possibility of fenugreek mucilage to be used as disintegrant has studied for metformin hydrochloride oral dissolving tablet. As compared to croscarmellose sodium, a broadly used synthetic superdisintegrant, mucilage from fenugreek has showed better results in disintegration value [49]. The mucilage obtained from fenugreek seed is used in the fast dissolving tablet formulation of antihypertensive drug, valsartan as disintegrating agent [50].

Antioxidant and emollient properties of this mucilage make it suitable for topical applications which are meant for wound healing, improving whiteness of the skin, skin conditioning and for treating wrinkles. Waqsi *et al.* have successfully formulated a highly stable water in oil emulsion containing fenugreek seed extract for topical application [51].

Ficus reticulata

Mucilage is obtained from the ripe fruits of *Ficus reticulata* Miq. of the family *Moraceae*. Studies reveal that this fruit mucilage appears to be suitable to be used as a matrix former in the manufacturing of transdermal patches due to its better physical and mechanical properties [52].

Fish berry

Cocculus hirsutus L. leaves which belongs to *Menispermaceae* family is an abundant source of *Cocculus* mucilage. The plant is also known indian cockle. Since the obtained polysaccharide is non-toxic to the skin, it is used therapeutically as emollient. Some attempts revealed that the mucilage can also be used as demulcent [11]. It shows superior anti-inflammatory property as compared to some other marketed anti-inflammatory formulations [53].

Hibiscus

Hibiscus rosa-sinensis L. and *Hibiscus sabdariffa* L. are abundant in mucilage, which is a characteristic property of the plant family *Malvaceae*. It is also known as Chinese hibiscus, China rose or shoeblack plant and is widely grown throughout the tropics and subtropics. The therapeutic activities of this mucilage include healing of various topical issues such as burns, wounds, etc. to the gastric diseases like dysentery. There are also studies that show this mucilage is used as a natural excipient in many formulations [54, 55]. The mucilage isolated from hibiscus is used as a sustained as well as rate controlling matrix for the release of various medicaments such as diclofenac sodium [56, 57, 58]. Studies have found that *Hibiscus* mucilage can be used as suspending agent and also superdisintegrant in tablet formulations [59-64].

Isapgol

The isapgol mucilage which consists of pentason and aldobionic acid is obtained from the seed husk of plant *Plantago ovata* Forssk. of the family *Plantaginaceae*. This is also known as psyllium, blond psyllium and ispaghula [65].

Arabinose, xylose and traces of other sugars which are present in this polysaccharide mucilage constitute its gel forming fraction. The mucilage coated on isapgol seeds is released by soaking it in hot water. When the seeds are boiled in water, the husk greatly expands, since it contains 25–30% mucilage [66, 67]. It is a broadly using laxative. Other gastric problems like colon cancer, ulcerative colitis, etc. can be treated by this herbal mucilage [68]. Its ability to act as both suspending and disintegrating agent makes it suitable to use as pharmaceutical excipient [69-71].

Linseed

Linum ussitatissimum L. which belongs to the family *Linaceae,* is an excellent source of mucilage. Ghumann *et al.*, successfully loaded metformin hydrochloride in *Linum ussitatissimum* seed mucilage-alginate mucoadhesive microspheres [72]. Along with

polyvinyl alcohol as co-polymer, *Linum ussitatissimum* mucilage was utilized to form nanofibers by Hadad *et al.* [73].

Mimosa

Mimosa seed mucilage is isolated from the plant *Mimosa pudica* L. of family *Mimosaceae*. The synonyms of this plant include sleepy plant, sensitive plant, action plant, touch-me-not, shame plant. d-glucuronic acid and d-xylose are the chief components of this mucialge. The seed mucilage has a property of swelling rapidly by absorbing water which results in the formation of a gel like gummy mass [11, 74]. It can be used as tablet disintegrant and binder [75] and also it is established as a sustained-release excipient [76] and buccoadhesive polymer [77].

Okra

Fresh fruit of the plant *Abelmoshcus esculentus* L. which belongs to the family *Malvaceae* is the source of this mucilage. Okra, bhindi and ladie's finger are synonymous names of this plant. The main chemical constituents include polysaccharides consisting of D-galactose, L-rhamnose, L-galactouronic acid, cellulose, hemicelluloses and lignin with some fractions of glucose, mannose, arabinose and xylose.

It has both food and medicinal applications. Mucilage from okra is employed against gastric disorders, which have an inflammatory and irritating nature and are also used to lower sugar level in systemic circulation by regulating the sugar absorption rate from the intestinal tract [78, 79]. Since this mucilage has a satisfactory pH and organoleptic characteristics, it is advisable to use as a pharmaceutical excipient [2].

Mucilage extracted from the pods of okra is used as a disintegrating agent within the formulation of dispersible tablets of aceclofenac by Kumar *et al.* in their study, and it has been found that this mucilage may be an excellent disintegrant at lower doses (4%) in comparison with standard disintegrants [80]. Okra mucilage is used as a binder in various concentrations within the preparation of paracetamol tablets [81, 82]. Okra mucilage has been developed into an edible film and it possess all the good characteristics of edible films [83].

In a study, Rao *et al.* have made an effort to develop sustained release anti-inflammatory matrix tablets using diclofenac sodium as a drug and gum acacia and okra gum as release modifiers. The study has been confirmed that okra gum is an excellent sustain releaser than standard formulation [84]. A tablet formulation aimed to target colon region using okra polysaccharide as a carrier is successfully developed by Ilango *et al.* [85]. Okra-based nutraceutical formulation is also developed for diabetes. A controlled release matrix tablet is developed with the aid of okra mucilage as matrix forming excipient [86]. Okra mucilage is used as a suspending agent in the formulation of paracetamol suspensions, which shows that it is a very good adjuvant [87].

Poinciana

The mucilage is isolated from the seeds of *Caesalpinia pulcherrima* L. of the family *Fabaceae*, which is also known as peacock flower. The major chemical constituents include diterpeniods, phenols, alkaloids, pulcherrimin-A, coumarin and flavanoids. The mucilage possesses good binding property [88, 89] and it can be also used as a carrier for the development of microspheres [90].

Safed musli

The mucilage is obtained from the dried tubers of the plant *Chlorophytum borivilianum* Santapau & R.R.Fern. of the family *Asparagaceae* commonly known as safed musli. The major chemical constituents include saponins, polysaccharides, sapogenins, fructanans, mucilage, resins, vitamins and proteins [91-93]. The mucilage can be used as a suspending agent and binder [94].

Toddy palm

The mucilage is obtained from the endosperm of *Borassus flabellifer* L. of *Arecaceae* family. It is also known as palmyra palm, toddy palm, wine palm or ice apple. The endosperm of its fruit contains mucilage which can be used as a natural gel former as well as pharmaceutical excipient [95]. It can also be used as a mucoadhesive polymer for buccal drug delivery [96]. The fruit mucilage is often used as novel matrix forming material for sustained drug delivery [97] and potential biodegradable carrier for colon specific drug delivery [98]. Studies reveal that it can be used as a natural suspending agent [99] and also as a matrix former for transdermal delivery of diclofenac [100]. In addition, it is also used as a unique excipient for matrix of ranitidine hydrochloride floating tablet [101].

Table 1.

List of plant mucilages

Sl No.	Botanical name	Common name	Family	Pharmaceutical applications
1.	*Abelmoschus esculentus* L.	Okra	*Malvaceae*	binder in tablets, sustained release
2.	*Aloe barbadensis* L.	Aloe	*Aloaceae*	gelling agent, ling sustained release agent
3.	*Asparagus racemosus* Willd.	Satavari	*Asparagaceae*	binder, disintegrating agent
4	*Borassus flabellifer* L.	Toddy palm	*Arecaceae*	mucoadhesive agent, SR matrix, suspending agent
5.	*Caesalpinia pulcherrima* L.	Poinciana	*Fabaceae*	binding agent
6.	*Chlorophytum borivilianum* Santapau & R.R.Fern.	Chlorophytum borivilianum	*Asparagaceae*	suspending agent, binder
7.	*Cocculus hirsutus* L.	Cocculus	*Menispermaceae*	gelling agent
8.	*Cordia obliqua* Willd.	Cordia	*Boraginaceae*	binding agent
9.	*Dillenia indica* L.	Dillenia	*Dilleniaceae*	controlled release formulations, mucoadhesive agent
10.	*Hibiscus rosa sinensis* L.	Hibiscus	*Malvaceae*	suspending agent, sustained release agent
11.	*Lepidium sativum* L.	Asario	*Cruciferae*	suspending agent, emulsifying agent, controlled release tablets
12.	*Linum ussitatissimum* L.	Linseed	*Linaceae*	controlled release formulations, gelling agent
13.	*Ocimum canum* L.	Ocimum seed mucilage	*Labiatae*	suspending agent, emulsifying agent
14.	*Ocimum gratissimum* L.	Mimosa	*Labiatae*	suspending agent, binding agent
15.	*Opuntia ficus-indica* L.	Cactus	*Cactaceae*	edible coating
16.	*Plantago psyllium* L., *Plantago ovata* L.	Ispagol	*Plantaginaceae*	cathartic, lubricant, demulcent, laxative, sustaining agent, binder, emulsifying and suspending agent
17.	*Senna tora* L.	Cassia	*Fabaceae*	binding agent
18.	*Trigonella foenum graecum* L.	Fenugreek	*Fabaceae*	gelling agent tablet binder, sustaining agent, emollient and demulcent

CONCLUSION

Since abundant in plants, mucilage is a good alternative for various synthetic excipients. Mucilage is widely used as binding agent, gelling agent, suspending agent, emulsifying agent, rate controller, coating agent, etc. Microbial growth and batch to batch variations in the yield are the major challenges facing in the usage of mucilage. However, biodegradable and biocompatible characteristics and the easiness of isolation and availability make mucilage the most favorable alternative.

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Conflict of interest: Authors declare no conflict of interest.

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