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# Applications of Mucilages in Drug Delivery - A Review

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**Abstract:** With the increasing interest in polymers of natural origin, the pharmaceutical world has compliance to use most of them in their formulations. Moreover, the tremendous orientation of pharma world towards these naturally derived polymers has become a subject of increasing interest to discover, extract and purify such compounds from the reported origin. In the present review we have discussed mucilage, as a potent candidate to be used in various pharmaceutical formulations. We have also compiled the various sources which may lead to significant mucilage production and also the extraction procedure. The various properties have been dealt in detail, which makes it a potential candidate to be used as pharmaceutical excipient.

**Key words:** Mucilage · Natural polymer · Pharmaceutical application · Pharmaceutical excipient

## INTRODUCTION

In recent years, plant derived polymers have evoked tremendous interest due to their diverse pharmaceutical applications such as diluent, binder, disintegrant in tablets, thickeners in oral liquids, protective colloids in suspensions, gelling agents in gels and bases in suppository [1]; they are also used in cosmetics, textiles, paints and paper-making [2]. These polymers such as natural gums and mucilage are biocompatible, cheap and easily available and are preferred to semi synthetic and synthetic excipients because of their lack of toxicity, low cost, availability, soothing action and non irritant nature [3-6]. Demand for these substances is increasing and new sources are being developed. India, because of its geographical and environmental position, has traditionally been a good source for such products among the Asian countries. Still, large quantities are imported from Europe to meet increasing demand.

**Mucilage in Plant Parts:** Polysaccharide hydrocolloids including mucilages, gums and glucans are abundant in nature and commonly found in many higher plants. These polysaccharides constitute a structurally diverse class of biological macromolecules with a broad range of physicochemical properties which are widely used for various applications in pharmacy and medicine. Although mucilages can occur in high concentrations in different plant organs, their physiological function in most cases is unclear. Mucilages found in rhizomes, roots and seed endosperms may act primarily as energy reserves whereas foliar mucilages appear not to serve as storage carbohydrates [7]. Generally, it has been assumed that foliar mucilages are merely secondary plant metabolites, but there are reports [8] that they may play a role in frost tolerance, water transport, wound responses, plant host–pathogen interactions, the ionic balance of plant cells and as carbohydrate reserves. Due to the high concentration of hydroxyl groups in the polysaccharide, mucilages generally have a high water-binding capacity and this has led to studies of their role in plant water relations. It has been suggested that the ability of mucilage to hydrate may offer a mechanism for plants to resist drought [9]. By the term "mucilage in plants" is meant those substances which are soluble, or at least swell very perceptibly in water and which, upon the addition of alcohol, are precipitated in a more or less amorphous or granular mass. Mucilage originates in the plant either as a part of the contents of the cell or as a part of the wall thereof. When it occurs as a part of the cell contents (as cell- sap), mucilage is produced either as an

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"Auscheidung" from the protoplasm, or it may possibly arise in some cases as a disorganization product of some of the contents. When it occurs as "membrane mucilage," it owes its origin to several causes, viz.: either as a form of secondary thickening or addition product to the wall; or as a metamorphosis of the cell wall, at least in part. In the later case it may arise either as a disorganized intracellular product of the primary wall as an intercellular substance; or of the subsequent lamellae making up the pith, medullary ray, parenchyma and other cells. In addition to these two well authenticated cases of the origin of mucilage, viz., as a cell contents and cell membrane; we have mucilage given out by some secreting hairs (glands). In such instances we can simply say that the mucilage appears between lamellae of cutin on the one hand and of cellulose on the other hand [1, 10].

For convenience, the following table, containing some of the important official plants yielding mucilage and different plant parts rich in mucilage:

**Intra Cell Mucilage:**

| Source | Part |
|---|---|
| *Orchids* sp. | Corn |
| *Agropyrum repens*, L., Beauvois. | Rhizome |
| *Urginea maritime*, L., Baker (Squill) | Bulb |
| *Allium* sp. (onion, garlic) | Bulb |
| *Viola tricolor*, L. | Stem, leaf, flower, stamens |
| *Hagenia abyssinica*, Bruce, Gmelin | Flower-stalks |
| *Musa paradisiacal* | Pulp |
| Aloe | Succulent plant |

**Cell-Membrane Mucilage**
**Secondary Wall Mucilage:**

| Source | Part |
|---|---|
| *Althaea officinalis*, L. | Root |
| *Cinnamomum* sp. | Bark |
| *Rhamnus frangula*, L. | Bark |
| *Sassafras variifolium*, Salisbury. | Bark of Root |
| *Ulmus fulva*. | Inner Bark |
| *Barosma betulina*, Thunberg. | Leaves |
| *Linum usitatissimum*, L. | Seed-coat |
| *S. nigra*, L., *Sinapis alba*, L. | Seed-coat |
| *Cydonia vulgaris*, L. | Seed-coat |

**Metamorphosis of Cell-Wall**
**Pith and Medullary Ray Cells:**

- *Astragalus* sp., yielding Tragacanth.

Parenchyma Cells of Wood and Bark:

- Cherry-gum, yielded by some of the Amygdalaceae.

Various Cells of the Bark:

- *Acacia senegal*, yielding Gum arabic.

Primary Wall as Intercellular Substance:

- Thallus of *Chondrus crispus*, Stackhouse and *Gigartina mamillosa*, J. agardh (Irish moss).

**Secreting Hairs (Drüzenzotten):**

- Leaf and calyx of *Viola tricolor* L.
- Leaf of *Coffea arabica* L.
- Leaf of *Prunus avium*.

**Extraction:** The dry part of subject is extracted with hot distilled water in the proportions of one part of plant material to ten parts of water. The extraction is continued for 24 hours with efficient stirring or shaking and the viscous extract obtained is filtered through muslin, while the material is returned to the vessel for two additional extractions. The polled extracts are then filtered through a bed of glass wool and muslin to remove foreign particles and the filtrate poured into alcohol, which precipitates a fibrous gelatinous product. Filtration, re-solution and reprecipitation of the mucilage may be carried out several times, the product then being precipitated in successive increasing concentrations of alcohol. The precipitated mucilage are then dried at 45-50°C and stored in a desiccator [11].

**Pharmaceutical Application:** Mucilages are most commonly used as adjuvant in pharmaceutical preparations, with wide range of applications such as thickening, binding, disintegrating, suspending, emulsifying, stabilizing and gelling agents. Mucilages may be used as sustained and controlled release formulations [12].

**Binding Agent:** Different mucilages have been used as binding agent in pharmaceutical formulations. Mucilage has good binding properties as compared to many synthetic compounds. Binding property of mucilage was used to determine the ability of mucilage as pharmaceutical excipient in different research papers.

Generally binding and granulating properties are determined with each other in single step. Mucilages from *Asparagus racemosus* and *Cassia sophera* were evaluated as binding agents in tablet formulations and these mucilages were found to be suitable binders for uncoated tablets as compared to starch [13]. Evaluation of *Chlorophytum borivilianum* mucilage as pharmaceutical excipient shows that it can be used as suspending agent as compared to tragacanth and also found to be effective binder [12] *Plantago ovata* and *Trigonella foenum graecum* mucilages have evaluated for binding property in tablet formulation and they show comparable disintegration, hardness and release data as starch [14]. Evaluation of *Delonix regia* endospermic mucilage as tablet binder using calcium carbonate tablets for general appearance, hardness, friability and disintegration shows that this mucilage can be used as a good binder [15]. Seed mucilage of *Vigna mungo* (L.) have been evaluated as a binder in tablet formulations and showed good binding properties [16]. Gum mucilages of *Cissus populnea* and *Acassia senegal* were evaluated for their binding properties using paracetamol tablets and show good binding properties [17]. The seed mucilage of *Caesalpinia pulcherrima* has been successfully evaluated for their granulating and binding properties in tablets, using diclofenac sodium as model drug. The mucilage was found non-toxic when evaluated for acute toxicity in mice ($LD_{50}$>5 gm/kg body weight) [18].

Evaluation of *Cassia angustifolia* seed mucilage using Diltiazem HCl as model drug showed that it has good granulating and binding properties [19]. Mucilage isolated from *Zizyphus jujuba lamk* seed have been used to prepare tablet formulation and further evaluated for their binding properties [20]. In one study mucilage was isolated from seeds of *Prosopis juliflora* (Mimosaceae) and further used to evaluate its binding properties in tablet formulation using diclofenac sodium as model drug. The result determined that the granules prepared using mucilage having excellent flow property and tablets prepared using 8 and 10 % of mucilage shows drug release over a period of 5h [21]. Mucilage extracted from *Plantago psyllium* seeds has been evaluated for its inertness and safety parameters; further binding properties of tablets were assessed using paracetamol as model drug [22]. In one study mucilage was isolated from the seeds of *Caesalpinia pulcherrima* (Euphorbiaceae) and further evaluated for their granulating and binding properties in tablets, using diclofenac sodium as model drug. Results showed that *Caesalpinia pulcherrima* mucilage has excellent binding property and could be used as a binder in conventional tablet formulation [23].

Mucilage extracted from seeds of *Cassia auriculata* have been successfully evaluated for their binding properties [24]. Seed mucilage extracted from Cassia fistula Linn. has been evaluated for their binding properties in tablet formulation using diltiazem HCl as model drug. It was observed that increasing the concentration of mucilage increases hardness and decreases the disintegration time in tablets formulation [25].

**Gelling Agent:** Gels are specific pharmaceutical formulation, which are generally applied externally. They are used either topically on the external skin for the control of pain But when they are applied to body cavity, have specific purpose such as improvement of bioavailability, control of side effects and drug targeting. The nasal route of administration, has received a great deal of attention in recent years as a convenient and reliable method not only for local but also for systemic administration of drugs. The nasal cavity offers a number of unique advantages such as easy accessibility, good permeability especially for lipophilic, low molecular weight drugs and avoidance of harsh environmental conditions and hepatic first pass metabolism. It has a potential for direct delivery to the brain and it provides direct contact of vaccines with lymphatic tissue and act as inducer as well as effectors of the mucosal immune system. Highly swellable mucoadhesive gels exhibiting mucoadhesive behavior could be extremely useful in nasal delivery applications. Mucoadhesive agents in their molecular form make intimate contact with mucin of mucosa and then make adhesion with the nasal membrane and finally the mucoadhesive carriers allow the release of drug through nasal membrane in a continuous fashion [26]. Many plants contain mucilages, which provide high concentration of complex sugars. When solutions of polysaccharides (hydrophilic polymer) are mixed, they interact with each other; this can result in an increase in viscosity, which becomes greater than the viscosity of each solution individually. Under certain conditions, they may even form a gel such a phenomenon is often called as rheology synergism [27].

When these mucilage are mixed with water, a protective and soothing preparation results, which can be applied externally. Mucilage of various plants has been used as gelling agent due to its non-toxicity, low cost, free availability, emollient and non-irritating nature [28]. The mucoadhesive strength and viscosity of mucilages are generally found to be higher in comparison to the synthetic polymers, namely hydroxy propyl methyl cellulose (HPMC) and carbopol 934, which are conventionally used for a similar purpose [26]. A revolutionized formulation of oxytocin nasal gel using natural mucoadhesive agent obtained from the fruits of *Dellinia indica.* L. has been already prepared [29]. *Trigonella foenum graceum* L. has been used to prepare intra nasal gel using diazepam as model drug [26]. *In vitro* release of ketoprofen from proprietary and extemporaneously manufactured gels has been studied at Rhodes University, Grahamstown. A water soluble chitosan gel was also prepared for skin hydration and it was characterized and evaluated at Sains University, Malaysia. In the same context Shah and Donovan [30] at University of Iowa studied bio adhesive gels for extended intranasal residence time and optimization of formulation was carried out. Sesbania seed mucilage has been evaluated for its gelling properties [31]. *Anacardium occidentale* mucilage may be used as gelling agent for topical delivery of non-steroidal anti-inflammatory drugs [32].

Different studies are able to demonstrate that due to their good release profile, water-soluble nature, physical stability and spreadibility, mucilage can be a good substitute of synthetic gelling agents.

In one study mucilage extracted from *Alyssum homolocarpum* seed was evaluated for rheological properties. Results obtained showed that extracted mucilage can be used as thickening agent in different formulations [33]. Mucilage obtained from leaf of *Cocculus hirsutus* has been used to prepare gel of flurbiprofen. Study showed that leaf mucilage can be used as base for gel preparation [34].

**Suspending Agent:** Suspensions have a number of applications in pharmaceuticals. They are used to supply drugs to the patients in liquid dosage form. If drug is insoluble or poorly soluble, a suspension may be the most suitable dosage form. To improve the stability of this type of formulations, different types of suspending agents are used. Suspending agents may be natural, semi-synthetic and synthetic in nature. Mucilages are used primarily to aid in suspending insoluble substances in liquid formulations; their colloidal character and viscous nature prevent immediate sedimentation. This should be considered that all mucilages are prone to decomposition, showing appreciable decrease in viscosity on storage. Mucilages are cheap and effective natural excipients that can be used as an effective alternative for the formulation of pharmaceutical suspensions. Due to their higher viscosity, mucilages can be a stabilizer of choice in a suspension. Suspending property of mucilages are comparable to different gums, which have been already used in pharmaceutical preparations. *Cassia tora* mucilage have been evaluated for its suspending properties and showed better result than compound tragacanth gum, acacia gum and gelatin [35] Evaluation of *Chlorophytum borivilianum* mucilage using zinc oxide suspension showed good suspending properties and can be used to prepare pharmaceutical suspension [8]. *Abelmoschus esculentus* mucilage also showed good suspending properties when evaluated in paracetamol suspension [36].

**Disintegrant:** Disintegrant are substances or group of substances added to the formulations that facilitate the breakup or disintegration of tablets into smaller particles that dissolve more rapidly than in the absence of disintegrants. Disintegrant have the major function to oppose the efficiency of tablet binder and physical forces that act under compression to form the tablets. Tablet disintegration has been considered as the rate limiting step in faster drug release. Disintegrants are substances that are added to formulations to dissolve more rapidly in aqueous environment [37, 38]. Mucilages have been used as disintegrants due to their swelling properties. They can display good binding property; both of these properties depend upon the concentration of mucilage in formulation. Generally in the 1 to 10% concentration of total tablet weight mucilages can act as binder and above it they act as disintegrant. This is an important parameter to determine the application of mucilage in particular formulation. Mucilages are used as disintegrant in solid pharmaceutical formulations. Many of them are already evaluated for its disintegrant properties and others are in process. *Plantago ovata* mucilage has been evaluated for their disintegrant [39, 40] and superdisintegrant properties [41] Seed mucilage of *Ocimum gratissimum*, [42] *Ocimum americanum* [43] and

*Salicornia fruticosa* (L.) [44] have been used as disintegrant in solid formulations. Studies showed that mucilage obtained from leaves of *Hibusccus rosasinensis* can be successfully used as superdisintegrant in tablet formulation. It was also found that the mucilage extracted is devoid of toxicity [45].

Seed mucilage of *Lepidium sativum* (Cruciferae) was used to prepare fast disintegrating tablets and formulated tablets were compared with tablets prepared using synthetic disintegrant such as sodium starch glycolate, kyron T314 and ac-disol. The results showed that disintegration and mean dissolution time for batch containing 10% mucilage was better than other tablets prepared using different synthetic disintegrating agent [46].

**Sustained Release Polymer:** Among various dosage forms, matrix tablets are widely accepted for oral sustained release as they are simple and easy to formulate. Matrix system is the specific type of release system, which prolongs and controls the release of drug that is dissolved or dispersed. Making drug-embedded matrix tablets through the direct compression of a blend of drug, retardant material and additives is one of the simplest formulation approaches. The inclusion of polymeric materials in a matrix system is a common method of modulating drug release. Various natural gums and mucilages have been examined as polymer for sustained release formulations. The use of natural polymers and their semi-synthetic derivative in drug delivery continues to be an area of active research. Drug-release retarding polymers are the key performers in matrix systems. Various polymers have been investigated as drug retarding agents, each presenting a different approach to the matrix system. Based on the features of the retarding polymer, matrix systems are usually classified into three main groups: hydrophilic, hydrophobic and plastic. Hydrophilic polymers are the most suitable for retarding drug release and there is growing interest in using these polymers in sustained drug delivery [47, 48, 49]. Mucilage from *Aloe barbadensis* Miller have been used as a pharmaceutical excipient for sustained release matrix tablets. Results showed that the dried Abelmoschus esculentus fruit mucilage can be used as a matrix forming material for controlled release matrix tablets [50].

Cactus mucilage has been used to prepare a edible coating in pharmaceutical formulation [51].

In one study buccal discs of fluconazole were prepared using *Mimosa pudica* seed mucilage as bucoadhesive polymer. Results easily predict the fact that mucilage has sufficient bucoadhesive strength and have characteristics to be used as bucoadhesive polymer [52]. Matrix moderated transdermal systems of diltiazem Hcl have been prepared using various proportions of *Ficus reticulata* fruit mucilage. Results easily predict the fact that this fruit mucilage has sufficient properties to prepare transdermal system [53].

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