Review Article

A Review on Lemon Seed Mucilage as A Pharmaceutical Aid

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ABSTRACT

Mucilage is a thick and glue-like substance observed in various parts of the plant such as roots, seeds, rhizomes etc. Mucilage contains Proteins, enzymes, muscle fibres, polysaccharides and gummy exudates. As consider as synthetic polymer, natural polymer having low cost, non-toxic, biodegradable, biocompatibility is higher. Lemon is fulfilled useful in pharmaceutical formulation development having various pharmaceutical aids. Lemon seed mucilage is innovated as pharmaceutical aid in disintegrating agent. Because of disintegrating property of lemon seed mucilage having site to increase solubility of BCS class 2 drugs.

Keywords: Lemon seed, Mucilage, Pharmaceutical aid.

INTRODUCTION

The traditional use of excipients in drug formulations was to act as inert vehicles to provided necessary weight, consistency and volume for the correct administration of the active ingredient, but in modern pharmaceutical dosage forms they often fulfil multi-functional roles such as modifying release, improvement of the stability and bioavailability of the active ingredient, enhancement of patient acceptability and ensure ease of manufacture. New and improved excipients continue to be developed to meet the needs of advanced drug delivery systems. [1]

Both synthetic and natural polymers have been investigated extensively. The synthetic polymers have certain disadvantages such as high cost, toxicity, environmental pollution during synthesis, non-renewable sources, side effects, and poor patient compliance. However the use of natural polymers for pharmaceutical applications is attractive because they are economical, readily available, low cost, non-toxic and capable of chemical modifications, potentially biodegradable and with few exceptions and also biocompatible. [2]

Proteins, enzymes, muscle fibres, polysaccharides and gummy exudates are the natural polymers being used effectively in pharmaceutical dosage forms. [3]

Natural gums (gums obtained from plants) are hydrophilic carbohydrate polymers of high molecular weights, generally composed of monosaccharide units joined by glucocidic bonds. They are generally insoluble in oils or organic solvents such as hydrocarbons, ether, or alcohols. Gums are either water soluble or absorb water and swell up or disperse in cold water to give a viscous solution or jelly. On hydrolysis they yield arabinose, galactose, mannose and glucuronic acid. Based on solubility in water gums are classified as soluble, insoluble and partially soluble gums. Certain gums dissolve in water to form a transparent colloidal solution (e.g. Gum Arabic). Gums such as gum tragacanth, gum karaya do not dissolve in water but swell up into a jelly-like mass. However, if sufficient amount of water is added they yield a thick transparent solution. Partially soluble gums first form a swollen jelly by dispersing in water and become solution on addition of more water. Gum resins are a combination of resins and true gums with a mixture of characteristics of both. Certain gum resins contain small amount of essential oil they are called oleo-gum resins. Small quantities of resins exude on the surface of the trunk due to injury by wind, fire, lightening or wound caused by animals. [4]

Natural gums including acacia, ghatti, karaya, locust bean, albizia, khaya, guar, tragacanth and xanthan, are obtained as exudates or extractives from the bark of stems, branches and roots of various plants. Plant families no table for the production of gums are Anacardiaceae, Combritaceae, Meliaceae, Rosaceae and Rutaceae. Various reasons have been advanced for the production of gums by plants, including: as products of normal plant metabolism; as a protective mechanism against a pathological condition afflicting the plant; and as a consequence of infection of the plant by microorganisms.[5]

The plant based polymers have been studied for their application in different pharmaceutical dosage forms like matrix controlled system, film coating agents, buccal films, microspheres, nanoparticles, viscous liquid formulations like ophthalmic solutions, suspensions, implants and their applicability and efficacy has been proven . These have also been utilized as viscosity enhancers, stabilisers, disintegrants, solubilisers, emulsifiers, suspending agents, gelling agents, bioadhesives & binders. [6, 7]

In this review, we described the developments in natural gums and mucilages for use in the pharmaceutical sciences.

Mucilage

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. [8] 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 drough. [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. [8, 9]

Lemon seed mucilage

Hetero-polysaccharide mucilage was extracted from the seed coats of different citrus rootstocks viz. Rough lemon, Sachtion citmmelo and Yuma citrange for investigating its biochemical and molecular properties. Investigations showed that the mucilage contained (mg/g) starch 3.13-5.04, maltose 3.23-4.31, glucosamine 0.017-0.289, D-xylose 0.059-0.107 and total soluble sugars 8.13-11.82, Specific enzyme activities were 16.98-35.96, 30.60-98.45, 42.00-73.98, 660.98-738.35 and 7.660-19.27 IU mg-1 of protein for protease, amylase, catalase, peroxidase and superoxide dismutase, respectively. Proximate analysis showed 12.85-13.94% moisture, 11.25-14.06% crude protein, 0.31-0.86% crude lipid, 1.31-2.69% crude fibre, 2.95-3.45% ash and 81.48-91.49 kJ100 g-'energy.

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 soditun 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. [10]

Honey Locust Gum

It is known botanically as *Gleditsia triacanthos*, and belongs to the order Leguminosea (suborder Mimoseae). The gum is obtained from the seeds of the plant. The seed contains proteins, fats, carbohydrates and fibers. Honey locust gum was used to produce matrix tablets at different concentrations (5% and 10%) by wet granulation method using theophylline as a model drug. [11]

Cordia Mucilage

Cordia Mucilage is obtained from raw fruits of *Cordia obliqua*, willed family Boraginaceae. The mucilaginous substance of the fruit used as gum an expectorant and is effective in treating the disease of the lungs and the raw gum can be used beneficially in gonorrhoea. [12]

Ocimum Mucilage

Ocimum mucilage is obtained from the seeds of *Ocimum americanum* commonly called as *Ocimum canum* belongs to the Family: Lamiaceae (Labiatae). Seeds are having Nutlets with narrowly ellipsoid, punctulate black. Polysaccharides composed of xylose, arabinose, rhamnose and galacturonic acids. [13] Pharmacognostic and phytochemical evaluation of Ocimum *americanum* were studied. Mucilage from the seeds of *Ocimum americanum* was explored as a tablet disintegrant. [14]

Mimosa Mucilage

Mimosa pudica, commonly known as sensitive plant belongs to family Mimosaceae. Mucilage of M. pudica is obtained from seeds, which is composed of d-xylose and d glucuronic acid. Mimosa seed mucilage hydrates and swells rapidly on coming in contact with water. A controlled delivery system for diclofenac sodium using Mimosa seed mucilage was studied. [15]

Dendropthoe Mucilage

Dendropthoe Mucilage is obtained from dried as well as fresh stem parasite of *Dendrophthoe falcate* (Loranthaceae) on *Magnifera indica.* [16] Mucilage is plant products similar to the gum regarded to be the normal products of plant metabolism. Mucilages are produced inside the cells of the plant. Mucilage forms slimy masses with water, but not dissolves. Mucilages are esters of sulphuric acid where in ester group is a polysaccharide complex. [17] Mucilage of Dendropthoe falcata was evaluated as a binder for pharmaceutical dosage forms. [18]

Mimosa scabrella

Mimosa scabrella, highly hydrophilic galactomannan is obtained from the seeds of *Mimosa scabrella* (a brazilian leguminous tree called bracatinga) of the Mimosaceae family. Its seeds provided 20–30% of galactomannan (G) with a mannose: galactose ratio of 1.1:1. In an independent study directly compressed theophylline tablets, containing commercial xanthan (X) (Keltrol) and a highly hydrophilic galactomannan (G) from the seeds of *Mimosa scabrella* as release-controlling agent was studied.[19]

Cassia Tora Mucilage

Cassia tora mucilage derived from the seeds of *Cassia tora*, belongs to Caesalpiniaceae is a wild crop and grows in most parts of India as a weed and locally known as charota. Cassia is used as tonic, carminative and stimulant. Cassia

contains 1-2 % volatile cassia oil which is mainly responsible for the spicy aroma and taste. The primary chemical constituents of Cassia include cinnamaldehyde, gum, tannins, mannitol, coumarins and essential oils (aldehydes, eugenol, and pinene); it also contains sugars, resins and mucilage among other constituents. [20]

Binding properties of seed mucilage of *Cassia tora was* evaluated and compared with common natural agents such as Acacia, guar gum and xanthan gum. [21] Suitability of Cassia tora mucilage as a suspending agent in sulphadimidine suspension was studied and compared to the relatively common natural agents. [22]

Isapghula Mucilage

Psyllium seed husks, also known as ispaghula, isabgol, or simply as psyllium, are portions of the seeds of the plant *Plantago ovata*, (genus plantago), a native of India and Pakistan. Gel forming fraction of the alkaliextractable polysaccharides is composed of arabinose, xylose and traces of other sugars. They are soluble in water, expanding and becoming mucilaginous when wet. Seeds are used commercially for the production of mucilage. It is white fibrous material, hydrophilic in nature and forms a clear colourless mucilaginous gel by absorbing water. Psyllium seed husk has been successfully evaluated as binder, disintegrant, release retardant and also pH sensitive novel hydrogels using N, N methylenebisacrylamide as crosslinker and ammonium persulfate (APS) as initiator for model drugs (tetracycline hydrochloride, insulin and tyrosine), for colon specific drug delivery systems. [23, 24]

Hibiscus Mucilage

Hibiscus rosasinensis Linn of the Malvaceae family is also known as the shoe flower plant, China rose, and Chinese hibiscus. Mucilage of *Hibiscus rosasinensis* contains L-rhamnose, D-galactose, D-galactouronic acid and D-glucuronic acid. [25] In a study the use of mucilage for the development of sustained release tablet. [26] Mucilage of Hibusccus subjected to toxicity studies for its safety and preformulation studies for its suitability as a disintegrating agent. [27]

Phoenix Mucilage

Phoenix mucilage is obtained from the dried fruit of *Phoenix dactylifera* was brown colour date fruit composed of amino acids and proteins, carbohydrates, fatty acids, salts and minerals, and dietary fibre. Carbohydrates make up to 44 - 88% of the fruit which include mainly reducing sugars such as fructose, sucrose, mannose, glucose and maltose in addition to small amounts of polysaccharides such as pectin (0.5 - 3.9%), starch and cellulose. The protein content is approximately 2.3 - 5.6% with 23 amino acids which include alanine, aspartic acid, serine, glutamic acid, threonine, proline and glycine. Binding properties of date palm mucilage was successfully evaluated. [28]

Fenugreek mucilage

Trigonella foenum-graceum, commonly known as Fenugreek, is an herbaceous plant of the leguminous family. Fenugreek seeds contain a high percentage of mucilage (a natural gummy substance present in the coatings of many seeds). Although it does not dissolve in water, mucilage forms a viscous tacky mass when exposed to fluids. Like other mucilage containing substances, fenugreek seeds swell up and become slick when they are exposed to fluids. [29]

Ability of the husk to form mucilage, its binding properties in solid dosage forms was studied. [30] Mucilage derived from the seeds of fenugreek evaluated as a matrix formulation containing propranolol hydrochloride. Methocel K4M was used as a standard controlled release polymer for comparison. [31] Gelling potentials of Fenugreek mucilage was evaluated. [32]

Tamarind Seed Polysaccharide

Tamarind seed polysaccharide obtained from the seed kernel of *Tamarindus indica*, possesses properties like high viscosity, broad pH tolerance, noncarcinogenicity, mucoadhesive nature, and biocompatibility. The tamarind seed polysaccharide constitutes about 65% of the tamarind seed components. [33] It is a branched polysaccharide with a main chain of -d-(1,4)-linked glucopyranosyl units, and that a side chain consisting of single d-xylopyranosyl unit attached to every second, third, and fourth d-glucopyrnosyl unit through an -d-(1,6) linkage. One d-galatopyranosyl unit is attached to one of the xylopyranosyl units through a -d-(1, 2) linkage. [34]

In a stud tamarind seed polysaccharide obtained from tamarind kernel powder and this was utilized in the formulation of matrix tablets containing Diclofenac Sodium by wet granulation technique and evaluated for its drug release characteristics. [35] Another study on Pilocarpine *in-situ* gelling solution based on alginate along with novel bioadhesive tamarind gum. [36] Potentials of tamarind seed polysaccharide to act as a biodegradable carrier for colon specific drug delivery was studied. [37]

Tamarind seed polysaccharide

It is a galactoxyloglucan. Sumathi et al. isolated tamarind seed polysaccharide from tamarind kernel powder and studied the sustained release behavior of both water-soluble and water-insoluble drugs from tamarind seed polysaccharide. Acetaminophen, caffeine, and theophylline were used as water-soluble drug whereas salicylic acid and indomethacin as water-insoluble drug. It was founded that the mechanism of release of soluble drugs was anomalous whereas water-insoluble drug showed zero order release behaviour. [38]

Hibiscus rosasinesis mucilage

It was suggested that this mucilage could be utilized as release-retarding excipient to get sustained release for upto 12 hr, when 1:1.5 ratio of drug:mucilage was used. [39]

The suitability of hibiscus rosasinesis mucilage as a binding agent in the formulation of tablet dosage form was examined. From the results of studies it was revealed that hibiscus rosasinesis mucilage had good binding efficacy and could be used as release-retarding agent. [40]

Leucaena leucocephala seed polysaccharide

This seed polysaccharide is isolated from seed kernel of *Leucaena leucocephala*. Jeevanandham et al. suggested the use of Leucaena leucocephala seed polysaccharide for sustain-release of drug. This studied the sustained release behaviour of Leucaena leucocephala seed gum on both water-soluble and water-insoluble drug. [41] Deodhar et al. used Leucaena leucocephala gum as a tablet binder. [42] Pendyala et al. suggested that Leucaena gum have potential for its use in tablet formulation as a disintegrant.[43]

Other examples of seed mucilages

Mucilage	Biological name and family	Pharmaceutical use
Aloe	*Aloe species* Liliaceae	i. Gelling agent ii. sustained release agent
Bavchi	*Ocimum canum* Gigarginaceae	i. Suspending agent ii. emulsifying agent
Shatavari	*Asparagus racemosus* Aapocynaceae	i. Binding agent ii. sustaining agents
Tamarind	*Tamarindus indica* Leguminoseae	i. Binding agent ii. Emulsifier iii. suspending agent iv. sustaining agents
Cactus	*Opuntia ficus-indica*	i. Gelling agent

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