

Mucilages and Their Pharmaceutical Applications: an Overview

Yashpal Singh Sangwan*¹, Savita Sngwan¹, Pawan Jalwal², Krishna Murti¹, Manish Kaushik¹

¹ P.D.M. School of Pharmacy, Safidon, Jind (Haryana) India

²Department Baba Mastnath institute of research and sciences, Asthal boher, Rohtak, India

Summary

In recent years there have been important developments in different dosage forms for existing and newly designed drugs and natural products, and semi-synthetic as well as synthetic excipients often need to be used for a variety of purposes. Gums and mucilages are widely used natural materials for conventional and novel dosage forms. These natural materials have advantages over synthetic ones since they are chemically inert, nontoxic, less expensive, biodegradable and widely available. They can also be modified in different ways to obtain tailor-made materials for drug delivery systems and thus can compete with the available synthetic excipients. With the increasing interest in polymers of natural origin, the pharmaceutical world has compliance to use most of them in their formulations. 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 types of mucilage used as pharmaceutical excipients. 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.

Correspondence Author

*Yashpal Singh Sangwan

Asst. Professor

P.D.M. School of Pharmacy

Karsindhu (Safidon) India

Email: sangwan.yashpal@gmail.com

Phone No: +91-9812384235

Introduction

Mucilages are naturally occurring, high-molecular-weight (approximately 200,000), polyuronides consisting of sugar and uronic acid units [1]. These are esters of sulphuric acid, wherein ester group is a polysaccharide complex [2]. Chemically, mucilages resemble gums and pectins but differ in their physical properties. Gums swell in water to form sticky, colloidal dispersions and pectins gelatinize in water, while mucilages form slippery, aqueous colloidal dispersions [3-4]. Gums are considered to be pathological products formed upon injury of the plant or owing to unfavourable conditions such as drought, by a breakdown of cell walls (extracellular). On the other hand mucilage is regarded as normal physiological product of metabolism formed within the cell or deposited on it in layers. Mucilages in plants are thought to aid in water storage and seed germination, and to act as a membrane thickener and food reserve. Among the richest sources of mucilages are cacti (and other succulents), and flax seeds. Mucilages are found in nearly all classes and parts of plants, usually in relatively small percentage. The various parts of plants from which mucilage is obtained are cell wall of seed (eg. isabgol, linseed, tamarindus), endodermis (fenugreek), leaf epidermis (senna), bark (cinnamon, slipper-elm) and special secretion cell (squill). Mucilage is also extracted from algae (agar, chondrus) and fungus (conidia of *Magnaporthe grisea*) [3].

Natural gums and mucilages have been widely explored as pharmaceutical excipients. These are widely used in the pharmaceutical industry as thickener, emulsifier, stabilizer, gelling agent, granulating agent, suspending agent, binder, film former, disintegrant and as sustained release matrix. Demand for these natural sources is increasing and new sources are being developed. Natural gums and mucilages are preferred over semi-synthetic and synthetic excipients in the field of drug delivery because they are cheap and easily available, have soothing action and non-irritant nature. Further, they are eco-friendly, capable of multitude of chemical modifications, potentially degradable and compatible due to their natural origin [5-7].

Isabgol mucilage:

The biological name of isabgol is *Plantago ovata* (family- Plantaginaceae). The seed and husk of the isabgol are widely used in pharmaceutical industry as demulcent, emollient, laxative, as an adjunct to dietary and drug therapy on lipid and glucose levels, in patients with type II diabetes [8], and in the treatment of dysentery. The seed and husk of the isabgol contains mucilage which is present in the epidermis of the seed. It is official in IP, BP, and USP. It is used in food and pharmaceuticals at a dose level of 5-6 g twice a day [9]. The mucilage of isabgol consists of pentosan and aldobionic acid, which on hydrolysis yields arabinose, galactose, galactouronic acid and rhamnose. The isabgol mucilage has a swelling factor of 10-14 [2].

In one of the study, standardization of isabgol mucilage was done. It was observed that the aqueous dispersion (1%, w/v) of mucilage has a pH of 4-5 and contains not more than 0.01% (w/v) crude fibres. The kinematic viscosity of (0.5%, w/v) aqueous dispersion was found to be 4-6 centistokes. The mucilage was found to contain not more than 0.1% (w/w) of chloride and 20 ppm of heavy metals [1]. On comparative evaluation, isabgol mucilage (0.5%, w/w) was found to possess higher suspending and emulsifying power than methylcellulose (1%, w/v) and tragacanth (1%, w/v) aqueous suspensions. Further, the binding power of aqueous dispersion (2%, w/v) of isabgol was found to be equivalent to the methylcellulose and tragacanth [10].

The disintegrating property of *Plantago ovata* mucilage was evaluated by preparing dispersible tablet of nimesulide using wet granulation technique. The study revealed that the mucilage is effective at low concentration as superdisintegrant. Further, the results revealed that disintegrant property of isabgol mucilage is equivalent to Ac-Di-Sol and superior to sodium starch glycolate [11].

Similar results were obtained in another study, whereby fast dissolving tablets of aceclofenac were prepared by direct compression method employing microcrystalline cellulose as a diluent and isabgol or Ac-Di-Sol or sodium starch glycolate as the disintegrant. The study attributed the better disintegrating property of isabgol mucilage over the Ac-Di-Sol and sodium starch glycolate, to the higher swelling index of isabgol mucilage as compared to the Ac-Di-Sol and sodium starch glycolate [12].

Apart from the disintegrating property, the psyllium husk has also been evaluated as a sustained release agent. The capsules containing sustained release granules and tablets of amoxicillin trihydrate were formulated using various combinations of psyllium husk and HPMC K4M. It was observed that in case of granules, a faster release of amoxicillin occurred from the formulation containing only psyllium husk as the release retardant while use of a combination of psyllium husk and HPMC K4M provided a sustained release of the drug. The incorporation of HPMC K4M into psyllium husk granule was observed to reduce the immediate swelling of the matrix and thus reduce its release [13].

The laxative and cholesterol-lowering activity of the psyllium husk is reported to be due to its gel-forming ability. A method of extracting gel forming fraction of psyllium husk has been described in one of the patent claim. The method involves suspending the husk in dilute aqueous alkali, followed by separation of alkali-soluble fraction and acidifying to a pH of 4.5, which yields the gel and an acid – insoluble fraction. The gel fraction can be dehydrated by washing with organic solvents and dried. Further, the patent describes the use of gel forming fraction of psyllium husk in the form of tablets, capsules or liquid dosage form for its laxation and hypocholesterolemic effects [14-15].

In an attempt to modify the chemical and physical properties of psyllium husk, graft copolymer of psyllium mucilage and polyacrylamide was synthesized using ceric-ion induced redox polymerization. The grafted copolymer was found to dissolve faster than psyllium mucilage in water and had a higher intrinsic viscosity than the mucilage. The grafted copolymer was reported to be better flocculating agent than mucilage in effluent treatment [16-17].

Tamarind seed mucilage:

Tamarind mucilage also known as tamarind seed polysaccharide (TSP) is amorphous polysaccharide extracted from seeds of *Tamarindus indica* (family Leguminosae). The seed powder of tamarind consists of 35% husk and 65% kernel. The kernel of tamarind comprises of about 55-65% galactoxyloglucan polysaccharide [18]. The mucilaginous polysaccharide is extracted by precipitation from aqueous solution by addition of organic solvents. The polysaccharide is composed of backbone of (1→4)-β-D-Glucans substituted with side chain of α-D-Xylopyranose linked (1→6) to glucose residues. The glucose, xylose and galactose units are present in the ratio of 2.8:2.25:1 [19]. Solutions of tamarind seed mucilage are highly viscous and characterized by Non-Newtonian, pseudoplastic flow properties. Tamarind seed mucilage

exhibits wide pH tolerance, biocompatibility and biodegradability [20]. It is used as thickening, stabilizing and gelling agent [21].

Carboxymethylation of TSP was carried out to modify its properties. It was observed that the carboxymethylation of TSP increases its solubility in cold water and stability towards microorganisms, and thus slows down its biodegradation.

Graft copolymerization of acrylate polymers on natural gums is frequently used to modify the properties of natural polymers. In one such study, ceric ion-induced graft copolymerization of polyacrylamide on TSP was carried out. However, there was only a slight decrease in the rate of biodegradation of TSP on grafting with polyacrylamide and stability towards microorganisms. It has a high drug loading capacity and thermal stability [22].

In one of the study, release behaviour of drugs of varying aqueous solubility from matrix tablets of TSP was investigated. A zero-order rate of release was observed for sparingly soluble drug like indomethacin, while the mechanism of release of relatively more water soluble caffeine, paracetamol and theophylline was found to be anomalous. The sustaining ability of TSP was further improved by partially crosslinking the mucilage with epichlorohydrin [23].

In yet another study, controlled release spheroids of TSP containing diclofenac sodium were prepared using extrusion-spheronization technique. The spheroids released the drug by zero-order release kinetics and were able to sustain the drug release for 8 h duration [24].

TSP exhibits mucoadhesive properties. It is well tolerated by the corneal and buccal tissue [25-26]. Further, it maintains its characteristic mucoadhesive properties even after autoclaving and at a physiological pH [27]. It has been explored as a tear fluid substitute in keratoconjunctivitis sicca. It was found to reduce the *in vitro* toxicity of ofloxacin, rifloxacin, timolol and merthiolate on human conjunctival cell [28]. *In vivo* evaluation of gentamicin and ofloxacin ophthalmic preparations formulated in TSP vehicle revealed significantly higher intraocular penetration of gentamicin and ofloxacin as compared to TSP free vehicle [29].

Okra mucilage: s

Okra mucilage is obtained from the pods of *Hibiscus esculentus*, a bulky annual plant cultivated throughout the tropical and subtropical areas [30]. Extraction of mucilage involves soaking the pieces of okra fruit in water overnight, followed by filtration through muslin cloth. The okra mucilage is an amorphous polysaccharide composed of D-galactose, L-rhamnose and L-galactouronic acid [31]. A 0.5% (w/v) dispersion of okra mucilage was found to have specific gravity of 0.9975 gm/ml and pH of 4.0 at 20 °C. The microbial count was found to be 200 CFU/gm of the mucilage [32].

Okra mucilage has been evaluated as sustained release matrix [32-35]. In one of the study, sustained release tablets of propranolol hydrochloride with okra mucilage (1:4) were formulated by direct compression technique. The tablets were able to sustain the release for 10 h. The release of propranolol was non-Fickian and the mechanism of release was anomalous.

In another study, okra matrix tablets of paracetamol were prepared by direct compression technique. The okra matrix tablets were found to sustain the release of paracetamol upto 6 h. Combination of okra with sodium CMC or HPMC were tried to achieve zero-order release kinetics. Okra mucilage also possesses mucoadhesive properties, and has been evaluated to

modify the bioadhesive strength of carbopol 941 tablets. The results of the study revealed that the tablets containing carbopol 941 and okra mucilage (1:1) provided the highest bioadhesive strength [36].

Conclusion

Natural gums and mucilages have been widely explored as pharmaceutical excipient. These are widely used in the pharmaceutical industry as thickener, emulsifier, stabilizer, gelling agent, granulating agent, suspending agent, binder, film former, disintegrant and as sustained release matrix. Semi-synthetic derivatives of natural gum and mucilages have been prepared to improve their physio-chemical properties, and thus widening their pharmaceutical applications. There are large numbers of plant yielding mucilage (e.g. *Dillenia*, *Eulophia*, *Opuntia*, *Mimosa* etc.) whose full pharmaceutical potential is not yet explored. The focus should be directed towards the development of these newer excipients, so that they can enter the pharmaceutical industry and newer formulations could be developed and formulation problems could be solved.

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