Review Article

Tamarind Kernel Gum: An Upcoming Natural Polysaccharide

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ABSTRACT

Polymers are complex carbohydrates having good mechanical properties for application as fiber, films, adhesives, rheology modifiers, hydrogels, emulsifiers, and drug delivery agents. Tamarind seed polysaccharide (TSP) is a glucosaminoglycan derivative extracted from the kernel of seeds of *Tamarindus indica* Linn., Family Leguminosae. A polymer consists of cellulose-type spine that carries xylose and galactoxylose substituents. It can be used as a binder in tablets, as a mucoadhesive for buccal or sublingual delivery of drugs, in gastro-intestinal targeting as a bioadhesive tablet, and for ocular delivery of drugs for achieving zero-order controlled release. They also act as a carrier for delivery of certain drugs. TSP future perspective is wide application as a promising polymer in pharmaceutical industry as a novel carrier of drugs in various bioadhesive and other sustained release formulations.

Introduction

Over the last two decades, mucoadhesion has become of interest for its potential to optimize localized drug delivery, by retaining a dosage form at the site of action (e.g. within gastrointestinal tract) or systemic delivery, by retaining a formulation in intimate contact with the absorption site (e.g. the buccal cavity). Various studies have been conducted on buccal delivery of drugs using mucoadhesive polymers including mainly polysaccharides.[1] Polysaccharides are relatively complex carbohydrates. They provide good mechanical properties for applications as fibers, films, adhesives, rheology modifiers, hydrogels, emulsifiers, and drug delivery agents. For instance, some polysaccharides have proven to enhance the contact between drug and human mucosa due to their high mucoadhesive properties.[2] Polysaccharides, such as cellulose ethers,[3] xanthan gum,[4] scleroglucan,[5] locust bean gum,[6] and gaur gum,[7] are some of the natural polysaccharide which have been evaluated in the hydrophilic matrix for drug delivery system. Although tamarind seed polysaccharide (TSP) is used as an ingredient in food material but as novel drug delivery system in pharmaceuticals formulations, it has not been extensively evaluated till date. TSP is a galactoxyloglucan isolated from seed kernel of *Tamarindus indica*. It possesses properties like high viscosity, broad pH tolerance and adhesivity.[8] This led to its application as stabilizer, thickener, gelling agent, and binder in food and pharmaceutical industries. In addition to these, other important properties of TSP have been identified recently. They include non-carcinogenicity,[9] mucoadhesivity, biocompatibility,[10] high drug holding capacity,[11] and high thermal stability.[12] This led to its application as excipient in the hydrophilic drug delivery system.[10,11]

A biodegradable glycosaminoglycan and a galactoxyloglucan polysaccharide extracted from tamarind (*Tamarandus indica* Linn. Family, Leguminosae) called as TSP has been found to have a wide application in pharmaceutical industry. Polysaccharides, such as hydroxy ethyl cellulose, ethyl cellulose and TSP, may be expected to reside in the area for relatively prolonged periods, in virtue of their mucoadhesivity and/or viscosity, which slows down the clearance from the site of application which can be utilized to reduce the hepatic first pass metabolism and local degradation of the drug.[2] The present article section includes the different extraction methods which will be best suited for the laboratory and commercial isolation of polysaccharide for the novel drug delivery system and its wide applications in pharmaceutical industry for the future benefits.

History

Tamarind, commonly known as *Imli*, is a rich source of tamarind gum or tamarind kernel powder which came into commercial production in 1943 as a replacement for starch in cotton sizing in Indian textile market.[13] Method of isolation and extraction of TSP was first devised in laboratory by Rao *et al*. 1945,[8] improved by Srivastav *et al*. 1973,[14] and further modified by Nandi *et al*. 1975[15] on a laboratory scale. Thereafter, a number of methods were given as a modified parent method that is best suited for the commercial or laboratory scale by a number of workers. TSP has the ability to form gels in the presence of sugar or alcohol and can be used to form pectin like gels in jams, jellies and other preserves.[16] TSP is found to be free from carcinogenicity in mice.[9]

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Origin

Tamarind is amongst most common and commercially important large evergreen tree that is grown abundantly in the dry tracks of Central and South Indian states, and also in other South East Asian countries.[17]

Following parts of fruit of *Tamarindus indica* L. Family - Leguminosae are commercially very important:

1. Pulpy portion of the fruit mainly used as acidulate in Indian recipes.
2. Tamarind gum is obtained from the kernel of the seeds powder.

Tamarind products are widely used in Asia and also used in some part of Africa. In Asian countries, especially India, tamarind is mainly cultivated and used as an acidulant, gelling, and acidifying agent.[18] Tamarind gum along with xanthan gum hydroxypropyl cellulose is used for nasal mucoadhesion studies in powder formulation.[19] Tamarind gum is also used for as a bioadhesive tablet.[20]

Methods of isoltion and extraction

Method 1[21]

200 g of tamarind seeds are soaked in double distilled water and boiled for 5 h to remove the outer dark layer. When the outer dark layer is removed, to the inner white portion sufficient amount of double distilled water was added and boiled with constant stirring to prepare the slurry. Now cool the resultant solution in refrigerator so that most of the undissolved portion settles down. The supernatant liquid can be separated out by simple decantation or best by centrifugation at 500 rpm for 20 min. After this, the solution is concentrated on a water bath at 60°C to reduce the volume to one-third of the initial volume. Now cool the solution and pour into 3 volumes of acetone by continuous stirring. Precipitates obtained were washed with acetone and drying in vacuum at 50-60°C.

Method 2[22]

Tamarind seeds were collected and dried in sunlight. The kernels are than crushed to fine powder. 20 g of fine kernel powder was added to 200 ml of cold distilled water to prepare slurry. The slurry obtained is than poured into 800 ml of boiling distilled water and are boiled for 20 min on a water bath; a clear solution was obtained which was kept overnight. The thin clear solution was than centrifuged at 5000 rpm for 20 min to separate all the foreign matter. Supernatant liquid was separated and poured into excess of absolute alcohol with continuous stirring. Precipitates were obtained which were collected by a suitable method and washed with 200 ml of absolute ethanol and dried at 50°C for 10 h. Store the polymer obtained in a dessicator.

Method 3[23]

This method is patented in United States by Jones *et al*. It involves the separation of tamarind kernel powder on the basis of their size distribution. Tamarind kernel powder was defatted by using C-6 or C-8 aromatic hydrocarbons or C-1 or C-2 or above halogenated lower hydrocarbons or C-1 or C-5 mono or dihydroxy alcohols, e.g. ethylene dichloride, heptanes, or toluene. (For defatting, Crude TKSP is suspended in suitable solvent to extract fat that is mechanically recovered by filtration or centrifugation and dried.) After drying, HiSil or other silicaceous materials like CabOSil improve the flow properties of powder. The powder is further grounded by using Hammer mill or Pin mill that will reduce the size of the powder below 100 μm. The powder is further air classified by using suitable air classifier (The Walther type 150 laboratory air classifier, The Alpine Mikroplex model 400, MPVI Air Classifier). Three fractions of the powder were obtained after air classifications:

1. 10-20% of fine fraction rich in protein.
2. 60-80% of moderately fine fraction rich in polysaccharides.
3. 10-20% of the coarser fraction rich in mechanical properties.

TSP can be isolated from the moderately fine powder fraction of the powder obtained after air classification.

Chemical composition and chemical structure

The composition of tamarind kernel powder, the source of gum resembles cereals with 12.7-15.4% of protein, 3-7.5% of oil, 7-8.4% of crude fiber, 61-72.2% carbohydrates, and 2.45-3.3% of ash. All of this was measured on dry weight basis.[13] Chemically, tamarind kernel powder is a highly branched carbohydrate polymer. TSP is a polymer with an average molecular weight of 52350 Daltons and a monomer of mainly three sugars-glucose, galactose and xylose in a molar ratio of 3:2:1.[24] A polymer consists of cellulose-type spine which carries xylose and galactoxylose substituents. About 80% of glucose residues are substituted by xylose residues (1-6 linked), which themselves are partially substituted by *p*-1-2 galactose residues. The exact sequential distribution of branches is not known.[25] TSP is a branched polysaccharide with a main chain of β-D-1-glucopyrynosyl units, with a side chain consisting of single D-xylopyranosyl unit attached to every 2nd, 3rd and 4th D glucopyrynosyl unit through 1-6 linkage as in Figure 1.[13]

Native TSP is shown to exhibit a strong tendency to self-aggregation when dispersed in aqueous solvents. The aggregates consist of lateral assemblies of single polysaccharide strands, showing a behavior that could be well described by the wormlike chain[26] or the Kuhn's model. Static light scattering data on these particles show that their stiffness is determined by the number of aggregated strands. High degree of substitution of glucan chain produces a stiff

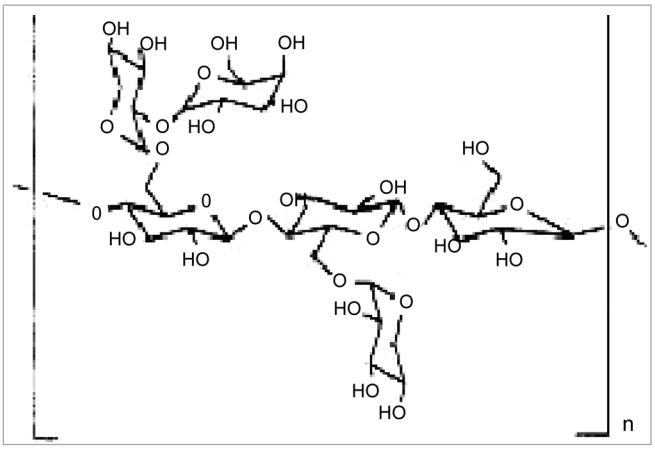

Figure 1: Average primary structure of tamarind seed polysaccharide. The cellulose type backbone is substituted by xylose (a 1-6) and galacto (8 l-c2) xylose (cu 1-6) residues[27]

extended conformation for tamarind polysaccharide molecule, with large volume occupancy in a solution.[16]

Chemical struture of tamarind seed polysaccharide

General properties of tamarind seed polysaccharide

Purified TSP is a high-molecular-weight, neutral branched polysaccharide consisting of cellulose like backbone that carries xylose and galctoxylose substances.[12] Chemical residues are similar to that of mucin MUC-1 and Epsialin.[28] It is insoluble in organic solvents and dispersible in warm mater to form a highly viscous gel as a mucilaginous solution with a broad pH tolerance and adhesivity.[8,29-30] In addition, it is non-toxic and non-irritant with a haemostatic activity.[29] It is a galactoxyloglucan, belongs to the xyloglucan family, and possesses properties such as non-Newtonian rheological behavior, mucomimetic, mucoadhesive and pseudo plastic properties.[12,31]

Pharmaceutical applications

TSP is an interesting candidate for pharmaceutical use, e.g. as a carrier for variety of drugs for controlled release applications. Many techniques have been used to manufacture the TSP-based delivery systems [Table 1] which makes it an exciting and promising excipient for the pharmaceutical industry for the present and future applications.

Binder in tablet dosage form

Evaluations of tamarind seed polyose as a binder for tablet dosage forms was taken up for the weight granulation as well as direct compression methods. The results indicated that tamarind seed polyose could be used as binder for weight granulation and direct compression tableting methods.[32]

In Ophthalmic drug delivery

TSP is used for production of thickened ophthalmic solutions having a pseudoplastic rheological behavior and mucoadhesive properties. The solution is used as artificial tear and as a vehicle for sustained release ophthalmic drugs. The concentrations of TSP preferably employed in ophthalmic preparations for use as artificial tears, i.e. products for replacing and stabilizing the natural tear fluid, particularly indicated for the treatment of dry eye syndrome are comprised between 0.7% and 1.5% by weight. The concentrations of tamarind polysaccharides compromised between 1 to 4 % by weight is preferably employed in the production of vehicles (i.e. delivery system) for ophthalmic drugs for prolonging the prevalence time of medicaments at their site of actions.[33]

In sustained drug delivery

It is used as potential polysaccharide having high drug holding capacity for sustained release of verapamil hydrochloride. The release pattern was found to be comparable with matrices of other polysaccharide polymers such as ethyl cellulose, hydroxyethyl cellulose, and hydroxypropylmethyl cellulose, as well as the commercially available sustained release tablets.[30] Sustained release behaviors of both water-soluble (acetaminophen, caffeine, theophylline and salicylic acid) and water-insoluble (Indomethacin) drugs on TSP was examined. Studies showed that TSP could be used for controlled release of both water-soluble and water-insoluble drugs. Zero-order release can be achieved taking sparingly soluble drugs such as indomethacin fromTSP. The rate of release can be controlled by using suitable diluents such as lactose and microcrystalline cellulose.[32] For water-soluble drugs, the release amount can also be controlled by partially cross-linking the matrix. The extent of release can be varied by controlling the degree of cross-linking. The mechanism of release due to effect of diluents was found to be anomalous and was due to cross-linking.

In ocular drug delivery

Administration of vicosified preparations produced antibiotic concentrations both in aqueous humor and cornea that were significantly higher than those achieved with the drugs alone. The increased drug absorption and the prolonged drug elimination phase obtained with vicosified formulations indicate the usefulness of the TSP as an ophthalmic delivery system for topical administration of antibiotics. Eye drops from TSP are used to treat dry eye syndrome.[12] TSP was used for ocular delivery of 0.3% rufloxacin in the treatment of experimental *Pseudomonas aeruginosa* and *Staphylococcus aureus* keratitis in rabbits. The polysaccharide significantly increases the intraocular penetration of rufloxacin in both infected and uninfected eyes. Polysaccharide allows sustained reduction of *S. aureus* in cornea to be achieved even when the time interval between drug administrations was extended. The results suggested that TSP prolongs the precorneal residence time of antibiotic and enhances the drug accumulation in the cornea, probably by reducing the washout of topically administered drugs.[34]

In controlled release of spheroids

TSP was used as release modifier for the preparation of diclofenac sodium spheroids using the extrusion spheronization

Table 1: Pharmaceutical applications

Dosage form	Application	Comments	References
Terbutaline sulphate tablet	As a binder for tablet prepared by wet granulation and direct compression methods	Can be used as a binder or a polymer for sustained release formulation of low dug loading	Kulkarni, 1998
Diclofenac sodium spheroids	Polysaccharide hydrogel was used as a release modifier	Formulation follow zero-order release pattern over 8 h with improved extend of absorption and bioavailability	Kulkarni, 2005
Tablet (water soluble and water insoluble drugs)	As a carrier polysaccharide	Anomalous release of water soluble drugs Zero-order release of water insoluble drugs	Sumathi and Ray, 2002
Caffiene tablet	As a carrier polysaccharide	Anomalous drug release	Sumathi and Ray, 2002

technique with microcrystalline cellulose as an spheronization enhancer. It was found that release was sustained over a period of 7.5 h.[35] A credible correlation was obtained amongst swelling index, viscosity, and surface roughness of the polysaccharide particles and *in vitro* dissolution profile of spheroids. In the comparative bioavailability study, the developed spheroids have been able to sustain drug release and also were found to improve the extent of absorption and bioavailability of drug (e.g. diclofenac sodium, caffeine, etc.).[36]

Pharmaceutical uses

TSP has promising pharmaceutical uses and is presently under research as a carrier molecule in various drug delivery systems.

Colon targeting

The potential use of TSP as a carrier for colonic drug delivery was demonstrated.[37] They prepared matrix tablets by wet granulation methods using ibuprofen as a model drug. *In vitro* release studies mimicking mouth to colon transit demonstrated the ability of TSP to release the drug at pH 6.8. TSP was remarkably degraded in rat indicating that TSP can be used as a carrier for colonic drug delivery.[37]

Ocular targeting

TSP is an adhesive enabling it to stick to the surface of eye longer than other eye preparations. TSP possesses mucomimetic, mucoadhesive, and pseudo plastic properties. Furthermore, the TSP drops did significantly better job of relieving several key subjective symptoms of dry eye syndrome namely trouble blinking, ocular burning, and having sensation of having something in someone eye.[34] It also increases the resident time of the drug to the cornea, e.g. β-blockers. The effect of an ophthalmic preparation containing timolol and TSP on intra-ocular pressure was evaluated in rabbits and found to decrease considerably.

Bioadhesive tablet

Tablets prepared from the TSP and tamarind gum were evaluated as bioadhesive tablets and was found that the tablets showed longest residence time in oral cavity as compared to that prepared from xanthan gum and carboxycellulose[21] but the unpleasant taste of the former gradually developed.

Laboratory feasibility

All the methods describe above are modification of methods given by Rao *et al*. 1945 for the extraction and isolation of Jellose from tamarind seeds.[8]

Method 1 involves the use of simpler principle and easy to execute on a laboratory scale. It includes implication of methods like distillation, centrifugation, settling, and filtration, but it is time consuming and required at least 2 days to extract tamarind seed polysaccharide.[22] *Method 2* used for isolation of TSP is simpler easy to execute, and utilizes implication of a method like extraction and purification. It is less time consuming and best suited for both laboratory and commercial scales.[23] *Method 3* is the most rapid and appropriate method for the isolation and purification of TSP. It is the best method and utilizes very less or no exposure of the crude material to chemicals. It involves much of the physical methods like air separation[24] and processes for the isolation, but it utilizes a complicated and sophisticated apparatus and machinery, so it is not suited for the laboratory extraction but it is a good method for the commercial extraction.

Future perspective and applications

Seeing the wide application of the tamarind Gum and TSPs in the novel drug delivery systems used in pharmaceutical as well as food industry, it is offering a great application for the drugs which are extensively metabolized in the gastro-intestinal tract and undergoes extensive first pass metabolism after oral administration. So it should be obtained in the purest form by the easiest methods applicable for both the commercial and pharmaceutical use.

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