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TAMARIND SEED POLYSACCHARIDE (TSP) - AN ADAPTABLE EXCIPIENT FOR NOVEL DRUG DELIVERY SYSTEMS

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ABSTRACT

Controlled release drug delivery systems are gaining importance in the last few decades for their clinical benefits which are not obtained from conventional oral drug delivery. Hydrophilic matrices involving natural polysaccharides are an interesting option for developing sustained release formulation. One of such polysaccharides is Tamarind seed polysaccharide (TSP) isolated from seed kernel of Tamarindus indica. Although TSP is used as an ingredient in food materials, it has not been extensively evaluated till date for its utility in pharmaceuticals formulations. So, this review mainly focuses on the utility of TSP as an excipient in novel drug delivery systems.

Keywords: TSP, Controlled delivery, Polysaccharides, Kernel.

INTRODUCTION

In the recent years, considerable attention has been focused on the development of controlled drug delivery systems for the sake of convenience and ambulatory patient compliance, which is a problem normally, associated with some class of drugs such as NSAIDs, anti-hypertensive, anti-asthmatic and antipyretic drugs. Among all the methods, matrix dissolution controlled using swellable hydrophilic gums have been extensively investigated [1]. Polymers are used to control the release of drugs from different dosage forms administered orally. An ideal matrix formulation should contain polymers and diluents at amount as little as possible, releasing the drug in a sustained release profile over a reasonable length of time and preferably with zero order kinetics [2].

Hydrophilic matrices are an interesting option when developing an oral sustained release formulation. The drug release from such matrices can be controlled through their physical properties. Polysaccharides are the choice of materials among the hydrophilic polymers used because they are nontoxic and acceptable by the regulating authorities. The various polysaccharides used in drug delivery application are cellulose ethers, xanthan gum, locust bean gum and guar gum. Another natural polysaccharide, Tamarind seed polysaccharide (TSP) which is obtained from the seed kernel of Tamarindus indica, possesses properties like high viscosity, broad pH tolerance, noncarcinogenicity, mucoadhesive nature, and biocompatibility. It is used as stabilizer, thickener, gelling agent and binder in food and pharmaceutical industries. The TSP constitutes about 65% of the tamarind seed components [3].

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 [4]. Method of isolation and extraction of TSP was first devised in laboratory by Rao et al. 1945 [5], improved by Srivastav et al. 1973 [4] and further modified by Nandi et al. 1975 [7] 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,

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jellies and other preserves.40 TSP was tested and found to be free from carcinogenicity in mice [7].

Origin

Tamarind is very 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 [8]. Tamarind products are widely used in Asia and also used in some part of Africa. The Pulpy portion of the fruit is mainly used as acidulate in Indian recipes. Tamarind gum is obtained from the kernel of the seeds powder. In Asian countries [9], especially India, tamarind is mainly cultivated and used as an acidulant, gelling, and acidifying agent [10]. Tamarind gum along with xanthan gum hydroxypropyl cellulose is used for nasal mucoadhesion studies in powder formulation [11]. Tamarind gum is also used in formulation of bioadhesive tablet [12].

Tamarind seed polysaccharides

Over the last two decades, mucoadhesion has attracted considerable attention for a range of reasons like its potential to optimize localized drug delivery by retaining a dosage form at the site of action (e.g. within gastrointestinal tract) and in case of systemic delivery by maintaining the formulation in intimate contact with the absorption site (e.g. the buccal cavity, stomach). Various studies have been conducted on buccal delivery of drugs using muco-adhesive polymers mainly polysaccharides [13]. Polysaccharides are relatively complex carbohydrates. They provide good mechanical properties for applications as fibres, 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 [14]. Polysaccharides, such as cellulose ethers [15], xanthan gum [16], scleroglucan [17], locust bean gum [18] and gaur gum [19] are have been evaluated as hydrophilic matrices for delivering the drug. Although tamarind seed polysaccharide (TSP) is used as an ingredient in food materials, it has not been extensively evaluated till date for its utility in pharmaceuticals formulations. TSP is a galactoxyloglucan isolated from seed kernel of Tamarindus indica. It possesses properties like high viscosity, broad pH tolerance and adhesivity [5]. These properties 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 which include non-carcinogenicity [7], mucoadhesivity, biocompatibility [20], high drug holding capacity [21] and high thermal stability [22]. These led to its application as excipient in the hydrophilic drug delivery system [20,21].

Polysaccharides, such as hydroxy ethyl cellulose, ethyl cellulose and TSP are expected to reside in the target area for relatively prolonged periods, in virtue of their mucoadhesivity and/or viscosity, which slows down the clearance from the site of application and this can be utilized to reduce the hepatic first pass metabolism and local degradation of the drug [14]. There are three different extraction methods which will be best suited for the laboratory and commercial isolation of polysaccharide.

Methods of Isolation and Extraction of TSP

Large scale

Method 1 [26]

200 g of tamarind seeds must be soaked in double distilled water and boiled for 5 h to remove the outer dark layer. After removing the outer dark layer, sufficient amount of double distilled water should be added to the inner white portion and boiled with constant stirring inorder to obtain 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 to be concentrated on a water bath at 60°C to reduce the volume to one-third of its initial volume. Now the solution is to be cooled and poured into 3 volumes of acetone by continuous stirring. Precipitates obtained must be washed with acetone and dried in vacuum at 50-60°C.

Method 2 [27]

Tamarind seeds must be collected and dried in sunlight. The kernels should be crushed into fine powder. 20 g of fine kernel powder is to be added to 200 ml of cold distilled water to prepare slurry. The slurry obtained must be poured into 800 ml of boiling distilled water and boiled for 20 min on a water bath to obtain a clear solution which must be kept aside overnight. The thin clear solution was then 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 obtained 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 [24]

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 (TKP) 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 TKP is suspended in a suitable solvent to extract fat that is mechanically recovered by filtration or centrifugation and dried. After drying, HiSil or other silicaceous materials like CabOSil are used to 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 mm. The powder is further air classified by using suitable air classifier.

Laboratory Scale

Method 1

This method 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

This method 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

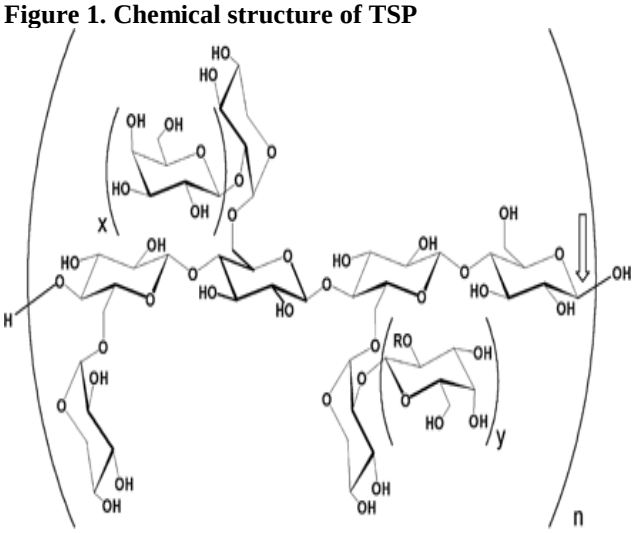
It is the most rapid and appropriate method for the isolation and purification of TSP. This is the best method and utilizes very less or no exposure of the crude material to chemicals. It involves much of the physical methods like air separation and processes for the isolation, but it utilizes a complicated and sophisticated apparatus and machinery, so it is not suited for the laboratory extraction but it is a good method for the commercial extraction [24].

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 [4]. 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. 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. TSP is a branched polysaccharide with a main chain of Â-D-1-glucopyrynosyl units, with a side chain consisting of single D-xylopyranosyl unit attached to every 2nd, 3rd and 4th D glucopyrynosyl unit through1-6 linkage as in Figure 1 [5].

Native TSP is shown to exhibit a strong tendency to self-aggregate when dispersed in aqueous solvents. The aggregates consist of lateral assemblies of single polysaccharide strands, showing a behaviour that could be well described by the wormlike chain 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 extended conformation for tamarind polysaccharide molecule, with large volume occupancy in a solution [8].

Figure 1. Chemical structure of TSP



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 [4]. Chemical residues are similar to that of mucin MUC-1 and Epsialin [25]. 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 [26]. In addition, it is non-toxic and non-irritant with a haemostatic activity. It is a galactoxyloglucan, belongs to the xyloglucan family, and possesses properties such as non-Newtonian rheological behaviour, mucomimetic, mucoadhesive and pseudo plastic properties [21,29].

Pharmaceutical applications

TSP is an interesting candidate for pharmaceutical use. It is used 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 wet granulation as well as direct compression methods. The results indicated that tamarind seed polyose could be used as binder for wet granulation and direct compression tabletting methods [30].

Table 2. Pharmaceutical applications of TSP

S. No	Dosage form	Applications	Comments	References
1	Verapamil HCL	As a drug release retardant	TSP can be used as sustained release component	[21]
2	Terbutaline sulphate Tablet	As a binder for tablet prepared by wet granulation and direct compression methods	It can be used as binder as well as a polymer for sustained release formulations of low drug loading	[40]
3	Diclofenac sodium Spheroids	Polysaccharide hydrogel was used as release modifier	Formulation follows zero order release pattern over 8 hrs with improved bioavailability.	[10]
4	Tablet (water soluble & water insoluble drugs)	As a carrier polysaccharide	Anomalous release of water soluble drugs, Zero order drug release for water insoluble drugs	[39]
5	Caffeine tablet	As a carrier polysaccharide	Anomalous drug release	[37]
6	Nifedipine mucoadhesive tablet	As a mucoadhesive and sustained release component	More comfortable to the user to do less erosion, faster hydration rate, and optimum pH of surrounding medium	[42]
7	Metronidazole Mucoadhesive buccal Patches	As a mucoadhesive and sustained release component	TSP might be well utilized to develop a buccal drug delivery system with required mucoadhesive strength.	[41]
8	Ketoprofen Diclofenac sodium	Assess the release behaviour of drugs, from cross linked tamarind seed polysaccharide	This study confirmed that the crosslinked TSP can be used as an effective release retardant and can be successfully used in commercial products.	[38]

As a mucoadhesive polymer

TSP is used for production of thickened ophthalmic solutions having a pseudo plastic rheological behaviour and mucoadhesive properties. The solution is used as artificial tear and as a vehicle for sustained release ophthalmic drugs. TSP is an adhesive thereby prolongs the retention time of formulation onto the surface of eye unlike other eye preparations. 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's eye [31]. It also increases the resident time of the drug to the cornea, e.g. Â-blockers. The effect of an ophthalmic preparation containing timolol and TSP on intra-ocular pressure was evaluated in rabbits and found to decrease considerably.

In sustained drug delivery

It is a potential polysaccharide having high drug holding capacity which sustained the 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 [32]. Sustained release behaviours 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 selecting sparingly soluble drugs such as indomethacin along with TSP. The rate of release can be controlled by using suitable diluents such as lactose and microcrystalline cellulose [34]. 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. 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 increased the intraocular penetration of rufloxacin in both infected and uninfected

eyes. Polysaccharide allowed sustained reduction of S. aureus in cornea to be achieved even when the time interval between drug administrations was extended. These data suggest 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] 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 [21].

In controlled release of spheroids

TSP was used as release modifier for the preparation of diclofenac sodium spheroids using the extrusion spheronization technique with microcrystalline cellulose as a spheronization enhancer. It was found that release was sustained over a period of 7.5 h^{59} .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].

Colon targeting

The potential use of TSP as a carrier for colonic drug delivery was demonstrated [35]. Matrix tablets were prepared 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 colon indicating that TSP can be used as a carrier for colonic drug delivery [38].

Bio-adhesive tablet

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

As a suspending agent

The Tamarind seed polysaccharide (TSP) possesses properties like high viscosity, broad pH tolerance, no carcinogenicity, mucoadhesive nature, and biocompatibility. Since suspensions are thermodynamically unstable, it requires a suspending agent which reduces the rate of settling and permits easy redispersion of any settled particulate matter. R. Deveswaran et.al. has done an attempt to use this polysaccharide as suspending agent in the formulation of Nimesulide suspension. They found that the TSP powder can be used as an effective suspending agent [38-42].

CONCLUSION

Polysaccharides are the choice of materials among the hydrophilic polymers used because they are nontoxic and acceptable by the regulating authorities. A novel polysaccharide named tamarind seed polysaccharide is now being used as an excipient in the hydrophilic drug delivery system because of its properties which include non-carcinogenicity, mucoadhesivity, biocompatibility, high drug holding capacity and high thermal stability. There is a need to carry out further research on the efficacy of TSP as an excipient in pharmaceutical formulations.

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