Journal of Applied Pharmaceutical Science Vol. 3 (4 Suppl 1), pp. S44-S47, May, 2013
Available online at http://www.japsonline.com
DOI: 10.7324/JAPS.2013.34.S7
ISSN 2231-3354

A sustained release of tablet granules associated with ZnS nanocrystals using Tamarind seed polysaccharide

Karthikeyan Ganesan[1], Shyam Kumar Rajaram[2*], Arunachalam Chinnathambi[2], Veerlakshmi Murugesan[1], Kasturiprabha Muruganantham[1], Thoufik Rahuman Amanullah[1], Infant Santhose Barthelomai[3], Sathishkumar Chinnasamy[3]

[1]Dept.of Biotechnology, P.S.R. Engineering College, Sivakasi, India -626 140
[2]Dept. of Botany & Microbiology, College of Science, King Saud University, Riyadh, Kingdom of Saudi Arabia 11451
[3]Robust Mushrooms Pvt ltd, Kalayarkoil, Sivagangai,India

ARTICLE INFO

Article history:
Received on: 17/03/2013
Revised on: 19/04/2013
Accepted on: 01/05/2013
Available online: 12/05/2013

Key words:
Tamarind kernel powder, Tamarind Seed Polysaccharide (TSP), ZnS, Sustained Release Matrix Tablets, TEM analysis.

ABSTRACT

Tamarind seed polysaccharide (TSP) isolated from tamarind kernel powder was investigated for sustained release manners of salicylic acid drug. Tablet granules of salicylic acid were prepared, with two different grades of TSP and Cross linked TSP and embedded with chemically synthesized ZnS nanocrystals. Five different formulations made and the drug excipient mixtures were subjected to pre-formulation studies such as physicochemical studies, in vitro dissolution test, disintegration test, angle of repose and drug content. The physicochemical properties of tablets were found within the limits. Formulation F1 and F5 containing TSP and Cross linked were found to release the drug in sustained manner up to 24 hour and were stable under accelerated conditions of temperature for 6 months since there were no significant changes in drug content and physical parameters. This formulation was more comfortable to the user due to less erosion, faster and optimum pH of surrounding medium.

INTRODUCTION

Tamarind seeds or kernel is a byproduct of Tamarind pulp industry is a valuable raw material containing 30% of testa and 70% of kernel (Kulkarni *et al.*, 2002). Tamarind gum is obtained from endosperm of seeds of the tamarind tree, which is a seed gum with potential industrial applications (Shankaracharya, 1998; Gerard, 1980). Tamarind gum is having applications in paper, food, textile industry etc. Recent year's research has been initiated on the use of tamarind gum in pharmaceutical and cosmetic applications. Tamarind kernel powder disperses and hydrates quickly in cold water but does not reach maximum viscosity unless it is heated for 20-30 min. Tamarind gum along with xanthan gum and hydroxyl propyl cellulose (water soluble neutral polymer) used for nasal mucoadhesion studies in powder formulation (Jambhulkar and Shankhapal, 1992, Glicksman, 1986). Tamarind gum was also evaluated in bioadhesive tablets (Takahashi, 2007). Polysaccharide present in tamarind kernel powder is called as tamarind seed polysaccharide.

* *Corresponding Author*
Department of Botany & Microbiology, College of Science, King Saud University, Riyadh, Kingdom of Saudi Arabia - 11451, P.Box.11451

Tamarind seed polysaccharide (TSP) is derived from the seeds of the tree *Tamarindusindica*. TSP is a complex mixture containing a galatoxyloglucan polysaccharide (55-65%), proteins (18-21%), lipids (6-10%) and certain minor constituents e.g. fibers, tannins, ash etc.Tamarind seed polysaccharide is having molecular weight 52350 units and monomer of glucose, galactose and xylose in molar ratio of 3:1:2. It is used as potential polysaccharide having high drug holding capacity for sustained release of verapamil hydrochloride.

It is also used as suitable polymer for sustained release formulations of low drug loading. Tamarind seed polysaccharide could be used for controlled release of both water-soluble and water insoluble drugs (Takahashi 2007; Khanna *et al.*, 1997). There are references showing gum's potential in ophthalmic drug delivery system (Khanna *et al.*, 1997; Wise e*t al.*, 1991; Zimmerman 1981).Although tamarind seed polysaccharide (TSP) is used as ingredient in food material and in pharmaceuticals has not been evaluated as hydrophilic drug delivery system. TSP is a galactoxyloglucan isolated from seed kernel of *Tamarindus indica*. It possesses properties like high viscosity, broad pH tolerance and adhesively (Rao *et al.*, 1946).

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 (Sano *et al.,* 1996), muco adhesivity, biocompatibility (Burgalassi *et al.,* 1996), high drug holding capacity (Kulkarni*et al.,* 1997) and high thermal stability(Saettone *et al.,* 1997). This led to its application as excipient in hydrophilic drug delivery system (Burgalassi *et al.,* 1996; Kulkarni *et al.,* 1997).Since TSP is an important excipient, in the present study, we tried to evaluate and investigate the applicability and synthesis of ZnS by using tamarind seed polysaccharide, in preparation of hydrophilic matrix tablets comparing with standard polymers with an objective to evaluate the suitability of tamarind seed polysaccharide as pharmaceutical excipient.

MATERIALS AND METHODS

Tamarind kernel powder (Grade A) was obtained from Sooraj Trading Co, K.G.F. Karnataka, India. Salicyclic acid from Qualigens (India) was purchased. Salicylic acid was used as model drug for formulation of sustained release tablet granules. This salicylic acid is used for the treatment of psoriasis and other hyperkeratosis disorders.

Preparation of tamarind kernel powder (TKP)

Raw seeds of Tamarind were dried in sun light for two days and the whole seed was broken into small pieces and ground into a fine powder. Distilled water was taken in a beaker and the required amount of fine powder of Tamarind seed was added to give a solution concentration of 4% (w/v). The solution was heated to 80-100°C with a constant stirring to avoid layer formation on the surface for 2 h, and subsequently filtered using glass wool to discard the un-dissolved fraction. The un-dissolved material contained approximately 25% of the dry weight substance. Then the dried materials are called Tamarind kernel powder (TKP).

Isolation of tamarind seed polysaccharide

TSP was prepared following methods by Rao *et al.,* 1973 and Khullar *et al.,* 1998 in three batches on a laboratory scale. To 20g of tamarind kernel powder, 200ml of cold distilled water was added and slurry was prepared.

The slurry was poured into 800ml of boiling distilled water. The solution was boiled for 20 minutes under stirring condition in a water bath. The resulting thin clear solution was kept overnight so that most of the proteins and fibers settled out. The solution was then centrifuged at 5000 rpm for 20 minutes. The supernatant was separated and poured into twice the volume of absolute ethanol by continuous stirring. The product was pressed between felt. The precipitate was washed with absolute ethanol, diethyl ether and petroleum ether and then dried at dried at 50-60^{o}C under vacuum. The dried material was ground and sieved to obtain granules of different particle size range. The particle size range of 150-75microns was used for preparation of tablets.

Cross linking of TSP

10 gm of TSP (soaked in water) and sodium hydroxide (50 ml, 1n, 54^{o} C) were mixed with a glass rod. After homogenization (15min), 0.5ml epichlorohydrin (6g/100g of TSP) was slowly added with continuous homogenization (15min). The gel was then neutralized with acetic acid and washed three times through a sintered glass filter with a solution of water/acetone (60:40 v/v). In the final step, the resulting solid gel was washed with pure acetone a filter. The polymer was air dried at room temperature for 72hrs and stored in airtight container.

Preparation of tablet granules

The total weight of the tablet granules (without magnesium stearate) was 250mg for drug: polymer ratio of 1:4 and 300 mg for drug: polymer ratio of 1:2. The ingredients in mixture for 5 min before and after adding of magnesium stearate.

Formulation Composition

Formulation Ingredients (mg/tab)	F1	F2	F3	F4	F5
Salicylic acid	50	50	50	50	50
TSP	200	200	180	160	-
Cross linked TSP	-	160	180	200	200
Lactose	20	40	60	80	100
Magnesium stearate	2.5	2.5	2.5	2.5	2.5

Evaluation of tablet granules pH

The surface pH of the tablet granules was determined in phosphate buffer pH 6.2 in order to examine the possibility of any irritation in the oral cavity. The tablet granules were kept in contact with phosphate buffer pH 6.2 for 2hr and pH was noted by using universal pH paper.

Angle of repose

For determination of angle of repose (θ), the granules were poured through the walls of a funnel, which was fixed at a position such that its lower tip was at a height of exactly 2.0cm above hard surface.

The granules were poured till the time when upper tip of the pile surface touched the lower tip of the funnel. The tan-1 of the (height of the pile / radius of its base) gave the angle of repose.

Dissolution test

A sample of 5 ml was withdrawn at an interval of l5min, 30min, lhr, 2hrs, 4hrs, 8hrs, l2hrs, l6hrs, 20hrs and 24hrs respectively. The samples were replaced with fresh dissolution medium each time. The samples were filtered through 0.45trn membrane filter. Samples were suitably diluted with 2mlof f. c. phenol reagent (diluted to 1:2 with distilled water) and 2rn1 of 20 % sodium carbonate solution and the volume made up to 10 ml with dissolution media. The resultant samples were analyzed at 760 nm against reagent blank.

$$\% \text{ Absorbance} = \frac{\text{Absorbance of sample} \quad X\ 100}{\text{Absorbance of Standard}}$$

Disintegration test

Disintegration is evaluated to ensure that the drug substance is fully available for dissolution and absorption from the gastrointestinal tract. Disintegration time was measured for tablet granules by inserting disks using 900ml purified water at 37±2ºC in disintegration apparatus using British Pharmacopoeia.

Drug content

The drug content in each formulation was determined by triturating 20 tablets and powder equivalent to average weight was added in 100ml of 0.1N hydrochloric acid, followed by stirring for 30 minutes. The solution was filtered through a 0.45µ membrane filter, diluted suitably and the absorbance of resultant solution was measured spectro photometrically at 265nm using 0.1 ml hydrochloric acid as blank.

Preparation of ZnS nanoparticle

To the TSP add 300 ml of distilled water and stir well till it get dissolved. It was maintained at pH of about 2. 100mg of Zinc acetate was added and stirred well. Boil for few minutes and cool. This was centrifuged at 5000rpm for 10 min and the supernatant was collected. 100mg of Na_2S was taken in separate test tube, dissolved in 1ml distilled water, stored at -20 for 5min. Then, this was added to the supernatant with constant stirring using centrifuged at 15000rpm for 10min. The pellet was collected and dried. The ZnS nanoparticle containing TSP were caste over glass slides to produce thin film form. The size of the particle was controlled by maintaining pH. The chemical reaction occurs as follows. Then, the sample was given to the TEM analysis for ZnS structure characterization**.**

$$(CH3\ COO)_2Zn + Na_2S \longrightarrow ZnS + 2\ \ CH_3COO\ Na$$

RESULTS AND DISCUSSION

The present work intended at demonstrated and enhancing the successful preparation of sustained release tablets from TSP. Further it was aimed to study the potential of a novel mucoadhesive tamarind gum and well established mucoadhesive ZnS to enhance the accessibility of the drug. The prepared formulations were characterized for the clarity, drug content, gelation and mucoadhesive strength. The clarity of the formulations, determined by the visual examination against white and black backgrounds under illuminated conditions, was found to be good. The drug release from the tablets prepared using tamarind seed polysaccharide was slow and spread over 24 hrs, depending upon the concentration used, whereas drug release from all the tablets prepared employing various polymers. The sugar content in Tamarind kernel powder (TKP) was estimated as 80% by using Anthrone method, as glucose standard graph as reference. The protein content in TKP was estimated as 15% by using Biuret method as BSA standard graph as reference. SDS–PAGE analysis of the fractions indicated that protein was presented in the TKP sample. Formulations of salicylic acid tablet granules were prepared with varying concentration of ingredients TSP, cross linked TSP, microcrystalline cellulose, and magnesium stearate were used as diluents. For each formulation, blend of drug and excipients were prepared and evaluated for various parameters as explained earlier. Furthermore, it is reported to be a mucomimetic, mucoadhesive and bioadhesive, which further justifies its sustaining of miotic effect for longer period (Ghelardi *et al.,* 2000). Polymer is based on polysaccharide consisting of cellulose like backbone that carries xylose and galactoxylose substituents, chemical residues similar to those of mucin MUC-1 and episialin (Hilkens *et al.,* 1992). There are reports indicating that being similar to mucins, it helps to bind to the cell surface and intensify the contact between drugs and the adsorbing biological membrane (Burgalassi *et al.,* 2000). As previously reported for ocular delivery of ofloxacin and gentamicin (Gheraldi *et al.,* 2000), another study demonstrated that it enhances transcorneal disposition and intraaqueous penetration of rufloxacin in healthy rabbits when administered topically in a drop regimen (Wise *et al.,* 1991). The surface pH of all formulations was found in between 6 to 7 except F4, F5which were showing the pH less than 5. The surface pH of all formulations was found in range except F4, F5 Showing the pH less than 5 because of carboxylic acids group present in, TSP polymers. These results reveal that formulations provide an acceptable pH in the range of salivary pH (5.5-7.0) cannot produce irritation to the buccal mucosa (Table-1).A similar release pattern was reported for pilocarpine, wherein the initial fast release (burst effect) decreased with an increase in polymer concentration from alginate systems (Cohen *et al.*,1997).

Table. 1: Pre compression studies of the prepared granules.

Code	pH	Angle of repose (θ)	Taste
F1	6.1	27.258±0.352º	Bitter
F2	5.8	24.215±0.390º	Bitter
F3	5	27.120±0.525º	Slightly bitter
F4	4	24.526±0.437º	Slightly Bitter
F5	4	27.050±0.252º	Slightly Bitter

Powders with angle of repose close to 25ºC correspond to good flow properties whereas angle near to 50ºC is characteristics of cohesive powders. The results of angle of repose indicate good flow properties of the granules. Generally, compressibility index values up to 15% result in good to excellent flow. At first sight these observations are justified on the fact that we have already discussed while understanding its potential for *in vitro* drug release, i.e. the tamarind gum is good viscosity enhancer and hence it prevents the spillage of the ocular solution out of *cul de sac* thereby preventing loss by drainage and reduction of wash out of topically administered drug (Glicksman 1986; Khanna *et al.,*1997; Takahashi *et al.,*2007).In the present study of *in vitro* dissolution studies of various formulations at different time interval are reported. In phosphate buffer pH 6.2 a cumulative percent drug release of less than 55.50% was obtained even after 2 hours of dissolution for F1 of salicylic acid. The results are much in agreement with the pH-sensitive nature of cross linked TSP. This value suggests that sufficient taste masking has been achieved

and that the bitter taste of drug will not perceived while the tablet is in mouth after oral intake. Almost 99% of drug was found to be released after 60 minutes of dissolution. The *in vitro* disintegration time (DT) of the tablet granules was found to less than 30 sec. All the formulations showed enhanced dissolution rate as compared to pure salicylic acid the results were shown Table-2.

Table. 2: Pre compression studies of the prepared formulations.

Code	Dissolution (%)	Disintegration (sec)	Drug content
F1	87.563	22	49.26±0.15
F2	81.145	210	49.61±0.35
F3	95.222	30	49.80±0.20
F4	95.596	40	49.92±0.42
F5	92.997	100	49.34±0.25

The drug content was found in the range of 93.2 % - 99.1% (acceptable limit) and the parameters were found well within the specified limit for tablets granules. Good uniformity in drug content was found among the formulations, and percentage of drug content was more than 95%. All the tablet formulations showed acceptable pharmacotechnical properties. The drug content varied between 49.26 to 49.92 mg in different formulations with low coefficient of variation (C.V. < 1.0%), indicating content uniformity. The nanostructure observed from TEM (Model JEOL JEM-100cx) shows the size of thenanocrystalline to be spherical in shape and size of the crystal. The TEM micrographs of ZnS in TSP matrix are depicted (Figure-1).

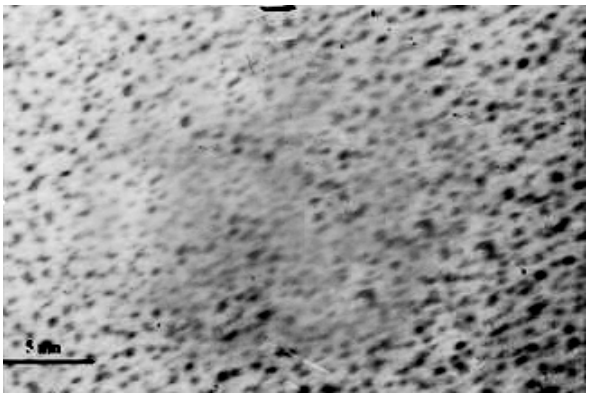

Fig. 1: Zns nanocrystal.

CONCLUSION

In conclusion, the formulation and assessment of extended release tablets were prepared by the trial and error method. The prepared tablets shown reasonable results for various physicochemical evaluation tests and TSP or Cross linked TSP were found to be appropriate as bases for preparing hydrophilic tablet matrices and a stable sustained release dosage form containing the drug salicylic acid and hence it won't be good emotion for patient in mouth. So, it was implemented in to tablet preparation. Sustained release granules preparation and ZnS synthesis performed efficiently by using TSP.

Thus, Tamarind seed polysaccharide was found to be an effective release retarding and rate controlling polymer and is appropriate for the design of oral sustained release tablets.

REFERENCES

Burgalassi S, Panichi L, Saettone MF, Jacobsen J,Rassing MR. Development and in vitro/ in vivo testingof mucoadhesivebuccal patches releasing benzydamine and lidocaine. Int J Pharm. 1996;133:1-7.

Burgalassi S, Raimondi L, Pirisino R, Banchelli G, Boldrini E,Saettone MF. Effect of xyloglucan (tamarind seed polysaccharide) on conjunctiva cell adhesion to laminin and on corneal epithelium wound healing. Eur J Ophthalmol. 2000;10: 71-76.

Cohen S, Lobel E, Trevgoda A,Peled Y. A novel in situ forming ophthalmic drug delivery system from alginates undergoing gelation in the eye. J Control Rel.1997; 44: 201-208.

Gerard T. 1980. Tamarind gum in hand book of water soluble gums and resins, In: Davidson RL, USA: McGraw. Hill Book Cu. 1-23.

Ghelardi E, Tavanti A, Celandroni F, Senesi S. Effect of novel mucoadhesive polysaccharide obtained from tamarind seeds on intraocular penetration of gentamicin and ofloxacin in rabbits. J Antimicrob Chemother. 2000; 46: 831-834.

Glicksman M. Tamarind seed gum in food hydrocolloids. CRC Press Florida, (1986) 3: 191.

Jambhulkar V, Shankhapal KV, Effect of minerals on lipid production by *Rhizopus nigricans* and *Penicillium nigricans* on tamarind kernel powder. J Food Sci Technol. 1992; 29: 333.

Hilkens J, Ligtenberg MJ, Vos HL, Litvinov SV. Cell membrane-associated mucins and their adhesion modulating property.Trends Biochem Sci. 1992;17: 359-363.

Khanna M, Nandi RC, Sarin JP, Standardization of Tamarind seed powder for pharmaceutical use. Ind Drugs.1997; 24: 268-269.

Khullar P, Khar RK, Agarwal SP, Evaluation of guar gum in the preparation of sustained-release matrix tablets. Drug Dev Ind Pharm. 1998; 24:1095-1099.

Kulkarni D, Dwivedi DK, Sarin JPS, Singh S. Tamarind seed polyose: A potential polysaccharide for sustained release of verapamil hydrochloride as a model drug. Ind J Pharm Sci. 1997; 59:1-7.

Kulkarni GT, Gowthamarajan K, Brahamajirao, Suresh B. Evaluation of binding properties of selected natural mucilages. J Sci Ind Res. 2002; 61: 529.

Rao PS, Ghosh TP, Krishna S. Extraction and purification of tamarind seed polysaccharide. J Sci Ind Res (India). 1946; 4:705.

Rao, P.S, & Srivastava, H.C. (1973). Tamarind. In RL Whistler (ed.) Industrial Gums. 2nd ed.(pp 369-411) New York :Academic Press.

Saettone MF, Burgalassi S, Giannaccini B, Boldrini E, Bianchini P, Luciani G. Ophthalmic solutions viscosified with tamarind seed polysaccharide. PCT Int Appl Wo. 1997; 28: 787.

Sano M, Miyata E, Tamano S, Hagiwara A, Ito N, Shirai T. Lack of carcinogenicity of tamarind seedpolysaccharide in B6C3F mice. Food Chem Toxicol. 1996; 34: 463-467.

Shankaracharya NB. Tamarind-chemistry, technology and uses a critical appraisal. J Food Sci Technol. 1998; 35: 193-208.

Takahashi Y, Takeda C, Seto I, Kawano G, Marinda Y. Formulation and evaluation of Lactoferrin bioadhesive tablets. Int J Pharm. 2007; 343: 220- 227.

Wise R, Johnson J, O'Sullivan N, Andrews JM, Imbimbo BP. Pharmacokinetics and tissue penetration of rufloxacin, a long actingquinolone antimicrobial agent. J Antimicrob Chemother. 1991; 28: 905-909.

Zimmerman TJ. Pilocarpine. Ophthalmology, 1981; 88: 85-88.

How to cite this article:

Karthikeyan Ganesan, Shyam Kumar Rajaram,Arunachalam Chinnathambi, Veerlakshmi Murugesan, Kasturiprabha Muruganantham, Thoufik, Rahuman Amanullah, Infant Santhose Barthelomai, SathishkumarChinnasamy., A sustained release of tablet granules associated with ZnS nanocrystals using Tamarind seed polysaccharide. J App Pharm Sci, 2013; 3 (4 Suppl 1): S44-S47.