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Alteration in Drug Release Due to Tamarind Kernel Powder and Its Polysaccharide as Binders

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ABSTRACT

Many natural, synthetic and semi-synthetic polymeric substances are being used in various pharmaceutical preparations as excipients for various purposes and different polymers show different properties like modification in drug release pattern. In the current experiment, it was hypothesized that these polymers may impart an effect on dissolution profile of drugs even when used in small amounts like binders. Tamarind kernel powder and its isolated polysaccharide in predetermined concentrations were used as binders in the formulation and dissolution profiles obtained from them were compared with a conventional binder in immediate release tablet formulation. Depending upon concentration and the material used as a binder, release profile was altered in a typical manner. Thus it is important to keep a close eye on release pattern of any drug when any polymer is newly being used in any dosage form for any purpose.

INTRODUCTION

The patients who are on continuous medications mostly stick to the brand to which they are consuming since a long time. It has been proposed that changing merely the brand of medication with same drug content may show variations in pharmacokinetic responses. Among various factors which may be held responsible for the same, the liability of change in release of drug from the same type of dosage form may also lie with the excipients used in formulations. It is hypothesised that not only the excipients that are used in larger proportions like diluents or matrix forming agents influence the release of the drug but also the excipients which are used in smaller amounts may show a modification in release pattern of the drug. Tablets have always remained a choice of the dosage form and immediate release tablets are most widely used. Powder of Tamarind kernel and its polysaccharide have earlier been used as drug release modifiers as well as binders in conventional and extended-release tablet formulations.[1,2]

Tamarind (*Tamarindus indica* Linn.) is one of the important economic trees of India. Tamarind seeds are one of the side products of the agriculture industry. They are inexpensive and are available throughout the year in India.[3] They are used as a famine food and for cattle in several states in our country. Tamarind kernel powder (TKPW) is prepared from seeds of Tamarind by roasting them to remove the brown testa, followed by grinding the cream coloured Kernel. TKPW and Tamarind kernel polysaccharide (TKPL) [4] form fluids of high viscosity at lower concentrations have broad pH tolerance, adhesivity and serve as a good creaming agent for the concentration of rubber latex and in industrial adhesives. The composition of tamarind kernel varies with habitat and geographical distribution. TKPW and TKPL find extensive application in the textile industry where it is widely used in sizing of artificial silk, cotton, and jute. Utilization of renewable biomass like Tamarind seeds for commercial applications has been envisaged as a modern system to conserve energy. Agricultural residues, forest wastes and side products containing various types of polysaccharides, which comprise the bulk portion of the vegetable kingdom, are the most readily available and renewable natural resources available to human beings.[5] The choice of the material used by the industry is usually governed by the relative costs, the cost of downstream processing and the availability of the material. Various pharmaceutical applications of Tamarind gum include dissolution improvement, mucoadhesion, bioadhesion, ophthalmic drug delivery and few more.[6]

The polysaccharide of tamarind kernel is referred as D-Galacto-D-xylo-D-glucan or simply Galactoxyloglucan (GXG). The ratio of Glucose: Xylose: Galactose is found to be 3: 2: 1 and the tentative value of molecular weight of polysaccharide is 115,000.[7] (Fig.1) While considering monomer of GXG, three molecules of Glucose are connected to each other with 1β4 linkage. One molecule each of Xylose is connected with 6α1 linkage to two out of three glucose molecules and one molecule of Galactose is connected with 2β1 linkage to one molecule of Xylose out of two.[8] Polysaccharides have always remained the choice material as binding agents due to their non-toxicity and acceptance by various regulating authorities. Various other natural binders used in the tablet are acacia, gelatin, starch paste.

Taking into consideration the above facts, the study of TKPW and TKPL as a binder in tablet formulation was undertaken. TKPW was the material of our choice because of its low cost, easy availability, high content of complex polysaccharide of galactoxyloglucan type and very little variation in its composition. In this paper, an attempt is made to correlate the modification imparted in the release of drug when TKPW and TKPL used as binders.

MATERIALS AND METHODS

Tamarind kernel powder was kindly gifted by Chhaya Industries, Barshi, Maharashtra (India). All other chemicals used were of analytical grade. Proximate analysis of Tamarind kernels was done for non-fibre carbohydrates, [9] proteins, [10] crude fibre, lipids, and ash with standard methods.[11]

Isolation of TKPL

TKPW was used as a starting material for isolation of TKPL. A paste of the powder in ten times its weight of cold water was added to thirty times its weight of boiled water, boiled for thirty minutes, strained through a muslin cloth and allowed to stand overnight. This was then decanted and poured into twice its volume of ethanol to precipitate Tamarind Xyloglucan as a fibrous mass. The precipitate was collected in a cloth bag and dried in an oven at 55˚C and finally powdered in a dry grinder mixer. The powder obtained with this procedure was a pale creamy white substance without taste and odour.[12]

Preparation of TKPW and TKPL paste:

Weighed amounts of TKPW and TKPL were added to the respective amount of distilled water separately, stirred properly and warmed till a smooth paste was formed. Both these pastes were prepared in 5% and 10% concentrations.

Preparation and evaluation of tablets:

Various tablet formulations containing 300 mg of Paracetamol with a final weight of 350 mg were formulated by wet granulation method, using 35 mg starch powder as a diluent and Talc as a lubricant. 15 mg each of TKPW and TKPL pastes were used as test binders which were compared with 10% starch paste as a standard. Tablets were prepared using single punch hand operated tablet punching machine fitted with flat faced round punches. The diameter of tablets was 13 mm which was kept constant throughout the study. Formulated tablets were evaluated for drug content uniformity, weight variation, hardness, thickness, disintegration time and dissolution. The dissolution test was carried out with USP type II apparatus using 900 ml of 0.1 N HCl (pH 1.2) as dissolution medium at 50 RPM for 120 min. Sampling was done at fixed intervals of 15 min each. These observations were recorded in triplicate and their average was taken into consideration.

RESULT AND DISCUSSION

The proximate analysis of TKPW used in the present study showed the presence of 68% non-fibre carbohydrates, 15% protein, 8% crude fibre, 7% lipids, 2% ash. Tablets prepared using above discussed formula passed all the tests for immediate release tablets. Tablets were elegant in appearance and without manufacturing defects. The hardness of the tablets increased with increase in the concentration of binders. The hardness of tablets prepared by using TKPW was comparable with conventional tablets while that of tablets prepared using TKPL was found to be lesser. The percent friability of tablets with TKPW as a binder was comparable with tablets having conventional binder while that of TKPL was more than rest of the tablets. Values obtained after evaluation of tablets are tabulated in Table No. 1.

The dissolution profile of prepared tablets showed significant observations. For comparison, 10% starch paste which is conventionally and widely used as a binder is used. And the release pattern obtained from it was considered as a standard. As seen in Fig. 2, release pattern of Paracetamol with the use of 5% TKPW as a binder was similar to the pattern of

10% starch paste and it showed improvement in the release of drug during 45-120 min. When TKPW was used in 10% concentration it showed more retardation of drug release in first 45 min in contrast to 5% concentration but finally at 90-120 min it matched to tablets with a higher concentration of TKPW.

Use of 10% TKPL as a binder showed the highest modification in release pattern and presented a sigmoid curve. During the first hour, it released less than 50% of total drug content. However irrespective of variations in concentrations of TKPW and TKPL in the tablet, the drug release at a time point near to 90 min was almost same. When 5% TKPL was used as a binder it showed a linear release pattern with lesser fluctuations. From Fig. 2 it is clear that during the first hour of release all the tablets showed different release concentrations but at a time near to 90 min all tablets released drug near to 85-90%.

CONCLUSION

Many natural and synthetic polymers are used as release modifiers in pharmaceutical preparations. Most of them are used either as a matrix and/or in higher concentrations. From above observations, it is clear that TKPW and TKPL show a modification in the release of drug even when used in minor concentrations. As their concentration increases, they show more and more retardation in drug release. TKPL shows more modification in drug release than TKPW, probably because of its purity. TKPW and TKPL retard the drug release at lower concentrations but release almost all the drug at a point near to 90 min, which may be due to some peculiar property is shown by the polymer getting dissolved in the medium. It is thus concluded that polymers show some change on the release profile of drugs even when used at lower concentrations. This may be the answer as to why merely changing brand of the drug with same drug content gives modification in the pharmacokinetic response of the drug since different pharmaceutical manufacturers use different excipients in their formulations.

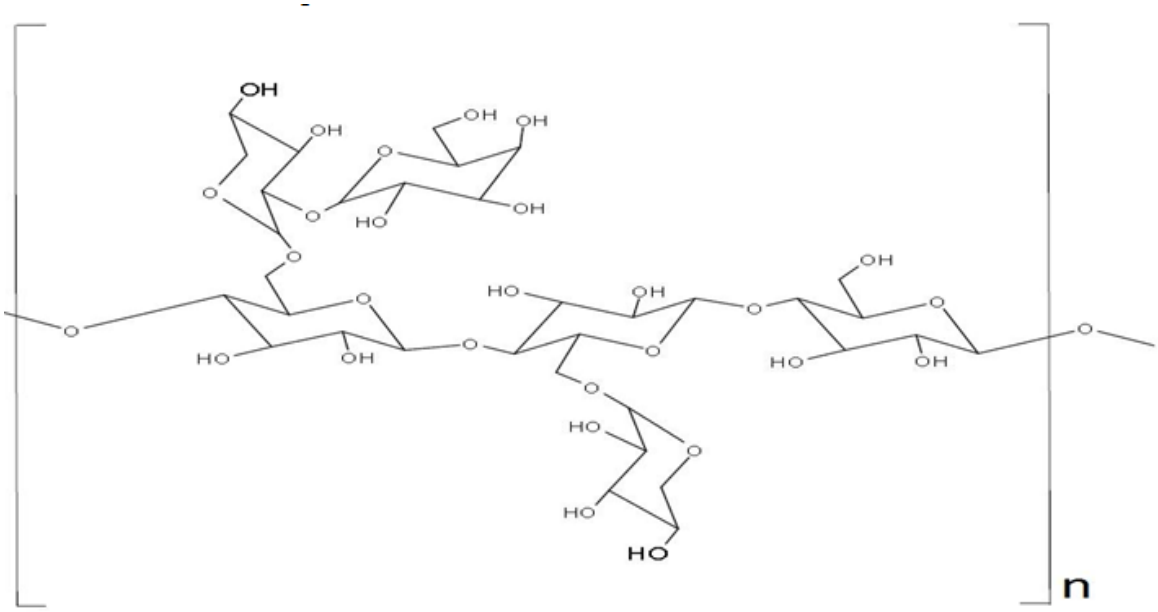

Fig.1 - Structure of Tamarind kernel Galactoxyloglucan

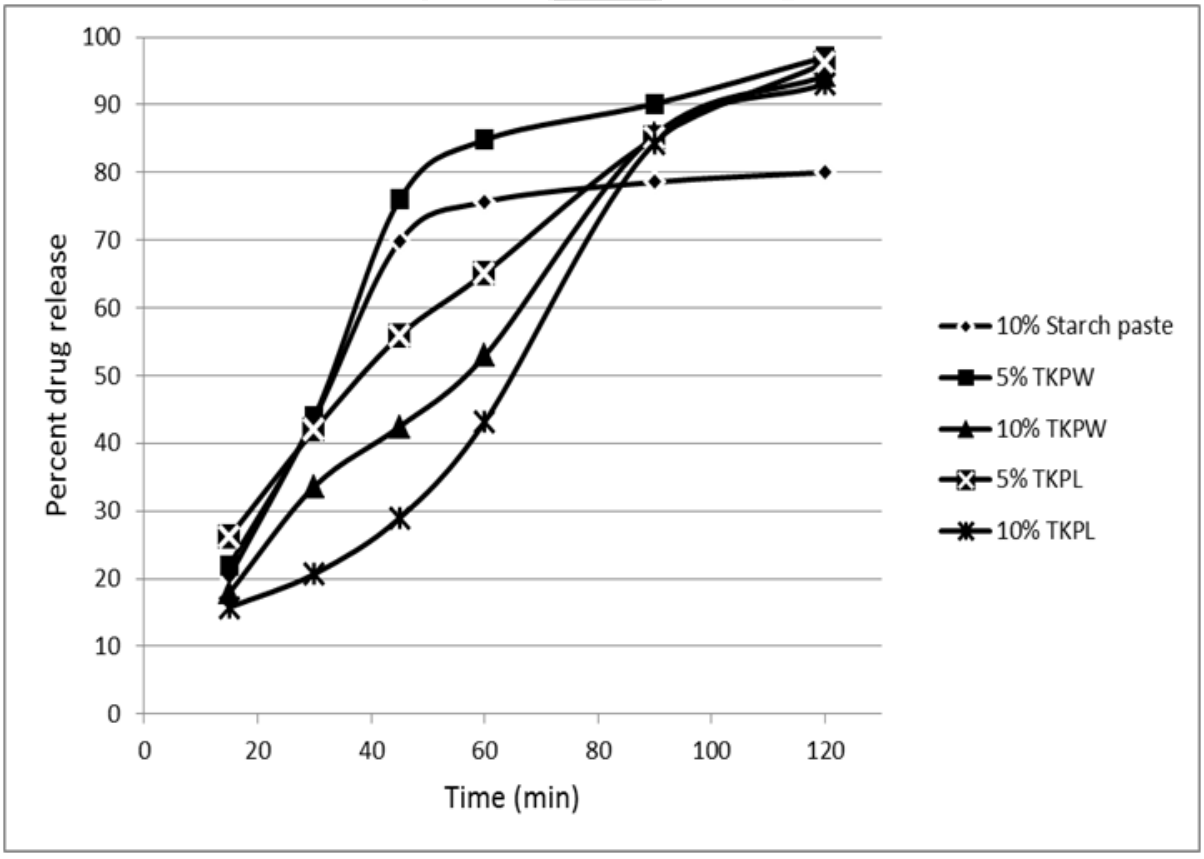

Fig. 2 – Release profile of Paracetamol from different tablets.

Table No.1 – Comparative values of various tablet evaluation parameters.

Sr. No.	Parameter	Values				
		A	**B**	**C**	**D**	**E**
		10% Starch paste	**5% TKPW**	**10% TKPW**	**5% TKPL**	**10% TKPL**
1	Drug content uniformity (%)	98.27	99.01	98.01	98.50	98.39
2	Average weight (mg) (±S.D.)	0.355 (±0.02765)	0.336 (±0.01132)	0.341 (±0.01235)	0.358 (±0.02149)	0.341 (±0.01380)
3	Thickness (mm)	4.3	4.1	4.2	4.3	4.0
4	Hardness (kg/cm^2) (±S.D.)	5.2 (±0.1633)	5.1 (±0.2598)	5.6 (±0.0943)	5.3 (±0.0943)	5.5 (±0.0943)
5	Percent Friability	0.88	0.88	0.9	1.94	1.85
6	Disintegration Time(sec)	250	202	262	210	268

TKPW: Tamarind kernel powder

TKPL: Tamarind kernel polysaccharide

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