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Study of Rheological properties of Psyllium polysaccharide and its evaluation as Suspending agent

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Abstract: Excipients are an integral part of any drug delivery system and though the market is flooded with an array of excipients for widely different applications, cost is a major deterrent, especially in a country like India. The objective of the present study was to investigate indigenous plant sources containing polysaccharides, devise a cost effective extraction procedure and evaluate its use as a multi-functional excipient. Psyllium seed husk has been traditionally used as a bulk laxative in India. Recent studies have also pointed out their cholesterol lowering effect. However the mucilaginous components of the seeds have not yet been investigated as a pharmaceutical excipient. In the present research, spray dried extract obtained from psyllium seeds was used. Paracetamol was selected as drug and mucilage of psyllium polysaccharide (PPS) were prepared in different concentrations. The rheological properties of the mucilage were studied and important parameters like thixotropic nature, hysteresis loop were observed. The results were compared with standard suspending agent sodium carboxymethyl cellulose (Na CMC). Paracetamol suspension was prepared and evaluated for pH, viscosity, resuspendability and sedimentation volume. The Psyllium polysaccharide (PPS) mucilage was found to have a promising potential for its use as a suspending agent.
Key words: Psyllium, rheology, suspending agent, thixotropy.

Introduction

Psyllium is the common name used for the several members of the plant genus *Plantago* [1]. The isapghula husk is derived from the dried ripe seeds of *Plantago ovata* Forsk. The seeds of psyllium are used commercially for the production of mucilage. The mucilage is obtained from the seed coat by mechanical milling of the outer layer of the seeds. It forms a mucilaginous gel by absorbing water. The gel nature and composition of psyllium polysaccharide (PPS) extracted from the seeds of *P.ovata* has been reported in the literature [2, 3]. Psyllium has been reported as a medicinally active natural polysaccharide. It has been used for the treatment of constipation [4, 5], diarrhea [6], inflammatory bowel disease [7], obesity in children and adolescents [8], high cholesterol [9] and diabetes [10].

Studies have been conducted to fractionate the polysaccharide from the seed husk and evaluate its gelling ability. However no studies have been conducted to evaluate the properties of the polysaccharide present in the seeds. Thus the present study focuses on the use of the mucilaginous components of the seeds as suspending agent, compared with sodiumcarboxymethyl cellulose as a standard suspending agent.

Materials and Methods

Psyllium seeds were procured locally and authenticated at the Agarkar Research Institute, Pune. Paracetamol, sodium CMC, sugar, sorbitol, sodium saccharin, citric acid, disodium EDTA, methyl paraben,

propyl paraben, sodium citrate and tween 80 were sourced locally and were of AR grade.

Extraction of Seed gum:
Psyllium seeds were dispersed in deionized water, kept on water bath at 80˚C, with occasional stirring for 2 h and allowed to cool to room temperature and kept overnight for soaking. 0.5 M NaOH was added while stirring (200 rpm for 15 min) to separate the sticky mucilage (PPS) from seeds and resulting solution passed through 12 # sieve. Filtrate was reprecipitated by 2M HCl, washed with deionized water and separated by centrifugation (3000 rpm for 15 min). It was dried in tray drier at 50-60 ˚ for 48 h. Yield was found to be 70%.The crude extract was dispersed in 0.5N NaOH and spray dried under the following conditions: Inlet temperature: 120 °, Outlet temperature: 100 °, Aspiration rate: 40 %, Feed rate: 10 ml/min, Atomization: 2 psi.

Solubility profile:
The solubility of polysaccharide was evaluated 10 ml of various solvents such as acetone, alcohol, ether, chloroform, dichloro methane, dimethyl amine, trimethyl amine, diethyl ether, ethyl acetate, DMSO and water by adding PPS in increments of 0.1g

Swelling Index:
Swelling behavior of polysaccharide as function of pH was studied. It was allowed to swell for 24 h in different pH solutions such as 0.1 N HCl, phosphate buffer pH 6.8, deionized water and 0.5 M NaOH. For this, 1 g of PPS was added in 25 ml solvent in a stoppered flask and kept overnight with intermittent shaking. Volume occupied by the PPS was measured and swelling index calculated from the initial and final volume PPS [11].

Preparation of Calibration curve of Paracetamol:
50 mg of paracetamol was dissolved in 10 ml 0.1 N NaOH and subsequently diluted to 100 ml using 0.1 N NaOH. This solution was further diluted with 0.1 N NaOH to produce 2-20 µg/ml of paracetamol. Absorbances of these solutions were noted using UV/VIS spectrophotometer (JASCO) at the λ_{max} of 257 nm using 0.1 N NaOH as blank.

Preparation of PPS Mucilage for Rheological Studies:
The mucilage of PPS was prepared in distilled water in strengths of 2, 2.5,3 and 10% w/v. The mucilage was homogenized using tissue homogenizer to break any lumps and subjected to rheometry studies.

Preparation of Paracetamol Suspension:
Sugar was dissolved in water with slight heating over water bath. Other water soluble ingredients including sorbitol 70 % (to prevent gelling), methyl paraben (as preservative), disodium EDTA, citric acid, sodium citrate (as buffer), tween 80 (as wetting agent) were dissolved in it. Water insoluble ingredients including paracetamol, sodium saccharin, propyl paraben were then dispersed in it with trituration using mortar pestle with addition of suspending agent. The volume was made up with sufficient quantity of purified water. The resulting suspension was further homogenized using a tissue homogenize for 30 min at 10,000 rpm. The two suspending agents, PPS and sodium CMC were employed at different concentrations such as 0.5%, 1%, 1.5% and 2% as shown in Table 1.

Evaluation of Paracetamol Suspension: [12, 13]
The suspensions were evaluated for pH, density, particle size, viscosity, assay, in-vitro dissolution profile, sedimentation volume and resuspendibility. Viscosity was measured using Brookfield viscometer. Density was measured using specific gravity bottle. Sedimentation volume was measured by carefully introducing the suspension in a measuring cylinder of 100ml and observing rate of sedimentation after every 30 min for 48h. Resuspendability was determined by subjecting the settled suspension to cyclomixer. Particle size was measured by optical microscopy.

Results and Discussion

Polysaccharide was found to be soluble in strong ammonia solution and dimethyl sulfoxide after 15 min sonication at room temperature. The polysaccharide was insoluble in acetone, alcohol, ether, chloroform, dichloro methane, dimethyl amine, trimethyl amine, diethyl ether and ethyl acetate. It was found to be soluble in DMSO, ammonia solution and 0.5% NaOH. It was found to form a gel when exposed to aqueous environment such as water and 0.1N HCl. Swelling profile of polysaccharide was evaluated (Fig.1). The maximum swelling was found in phosphate buffer pH 6.8 with 1572 % swelling, whereas no swelling was observed in 0.5 M NaOH. The extensive swelling that PPS exhibits in water and 0.1N HCl is indicative of its hydrogel nature which can be exploited to design sustained release dosage forms. Swelling could be a result of entanglement of the polysaccharide chains and development of intra- and inter-molecular hydrogen bonds between the polysaccharide and water causing more and more water to be entrapped within the macromolecular chains.

Table 1: Formulae of paracetamol suspensions

Ingredients (g)	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8
Paracetamol	6.25	6.25	6.25	6.25	6.25	6.25	6.25	6.25
Sugar	156.25	156.25	156.25	156.25	156.25	156.25	156.25	156.25
Sorbitol 70%	25	25	25	25	25	25	25	25
Sodium saccharine	0.375	0.375	0.375	0.375	0.375	0.375	0.375	0.375
Sodium EDTA	0.0625	0.0625	0.0625	0.0625	0.0625	0.0625	0.0625	0.0625
Citric acid	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Sodium citrate	0.375	0.375	0.375	0.375	0.375	0.375	0.375	0.375
Methyl paraben	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Propyl paraben	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05
Tween 80	-	0.002	-	0.002	-	0.002	-	0.002
PPS/Na CMC*	1.25	1.25	2.5	2.5	3.75	3.75	5	5
Purified water	200 ml qs	200ml qs	200 ml qs	200 ml qs	200 ml qs	200 ml qs	200 ml qs	200 ml qs

*F1-F8 Formulations containing 0.5%, 1%, 1.5% and 2% PPS mucilage with and without Tween 80
*F9-F16 Formulations containing 0.5%, 1%, 1.5% and 2% PPS mucilage with and without Tween 80

Table 2: Evaluation of suspensions

Formulation.	Resus (sec)	% release	
		10 min	20 min
F_1	45±0.040	75.23±0.053	97.56±0.053
F_2	40±0.055	83.06±0.062	96.17±0.029
F_3	33±0.044	78.53±0.031	98.10±0.05
F_4	29±0.029	85.97±0.043	97.05±0.043
F_5	25±0.040	77.19±0.025	95.06±0.053
F_6	20±0.029	84.03±0.05	96.15±0.044
F_7	17±0.059	79.17±0.044	98.19±0.040
F_8	13±0.05	85.17±0.066	98.07±0.062
F_9	-	75.17±0.053	97.06±0.025
F_{10}	-	75.05±0.062	98.19±0.044
F_{11}	-	68.15±0.033	95.17±0.029
F_{12}	-	67.57±0.044	97.07±0.053
F_{13}	-	67.08±0.029	98.19±0.067
F_{14}	-	74.17±0.025	97.07±0.033
F_{15}	-	65.17±0.045	98.07±0.044
F_{16}	-	67.37±0.053	99.15±0.043

Resus- Resuspendability, n = 3, *n =500

Table 3: Evaluation of suspensions 9 (n = 3)

No	Sedimentation Volume (ml)	Viscosity (cps)	No	Sedimentation Volume (ml)	Viscosity (cps)
F_1	0.16±0.040	20.21±0.044	F_9	-	158.25±0.045
F_2	0.14±0.033	21.89±0.055	F_{10}	-	158.92±0.031
F_3	0.42±0.043	25.97±0.033	F_{11}	-	767.13±0.034
F_4	0.38±0.036	26.98±0.067	F_{12}	-	768.39±0.08
F_5	0.53±0.044	32.86±0.025	F_{13}	-	1124.98±0.043
F_6	0.52±0.043	32.99±0.070	F_{14}	-	1127.32±0.027
F_7	0.65±0.043	37.52±0.034	F_{15}	-	1395.77±0.065
F_8	0.59±0.036	38.21±0.036	F_{16}	-	1396.43±0.036

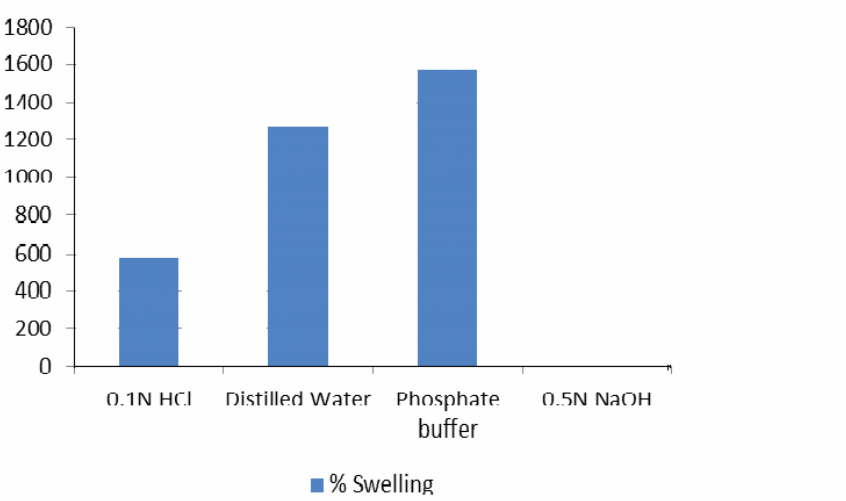

Figure 1: Swelling index

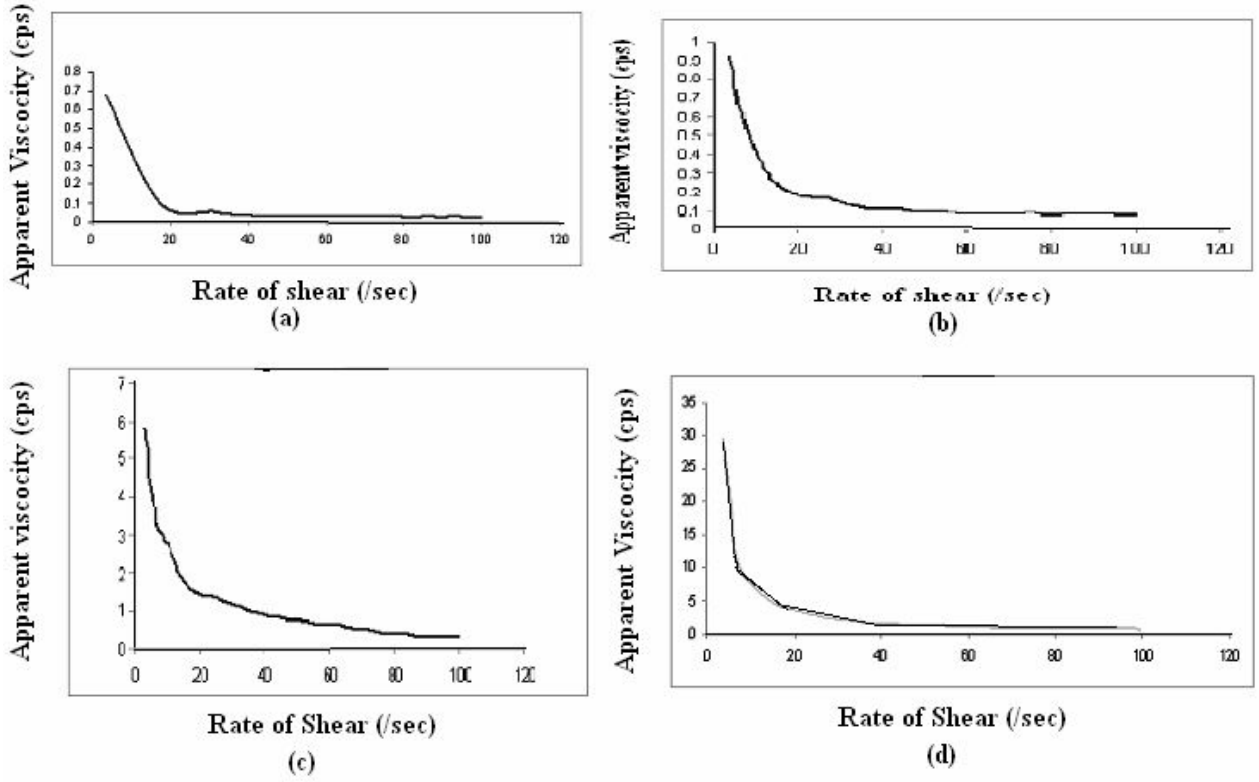

Fig. 2: Apparent Viscocity vs. rate of shear
(a):2% (b):2.5% (c):3% (d):10%

Rheology is an important physical property affecting the physical stability and ease of use of any liquid and semi solid preparation. The PPS mucilage of all strengths were found to have shear thinning properties as evident from the graphs of apparent viscosity vs. rate of shear indicating pseudoplastic behaviour which is characteristic of polymeric systems (Fig. 2).The curved graphs indicate that the apparent viscosity continuously decreased with increasing rates of shear and reached a constant value at shear rates greater that 40/sec.

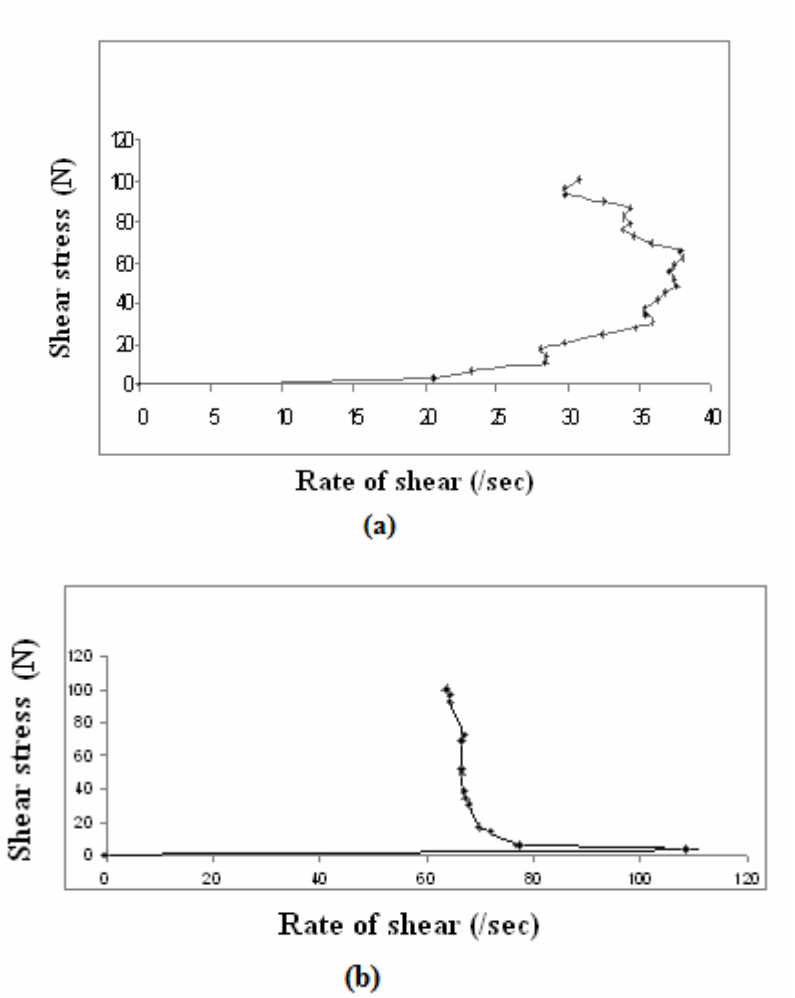

Figure 3: Shear stress vs. Rate of Shear
(a):2% PPS mucilage(b):10% PPS mucilage

The rheogram (Fig. 3) for shear rate vs. shear stress for 10% PPS mucilage showed a characteristic spur value indicating a sudden breakdown in structure followed by a significant increase in shear rate with moderate increase in shear stress. At higher strength the mucilage has a very rigid structure which can be attributed to the formation of hydrogen bonds between the polysaccharide and water. The spur value was found to be greater than 100/sec. However at lower strengths, spur value was absent which was indicative of the greater structural flexibility. Thixotropy is another important rheological property which influences the physical stability of a suspension. The mucilage of 3% and 10% strength were subjected to increasing and decreasing shear rates and the rheogram was plotted (Fig. 4**).** Presence of a hysteresis loop was indicative of thixotropic nature of the mucilage. It was evident that structural breakdown took place as the shear rate was increased but the recovery of the structural rigidity was not instantaneous. The area of the hysteresis loop is indicative of degree of thixotropy .The area of hysteresis loop for the 3% mucilage was found to be 450 sq.units whereas for the 10 % mucilage it was 368 sq.units. The area was calculated using the planimeter method. The mucilage of lower strength had greater degree of thixotropy than the 10 % mucilage. This is can be attributed to the gel like rigid structure of the 10% mucilage leading to lesser breakdown in structure during shearing. However the presence of hysteresis loop is itself is a desirable feature even when formulating a gel.

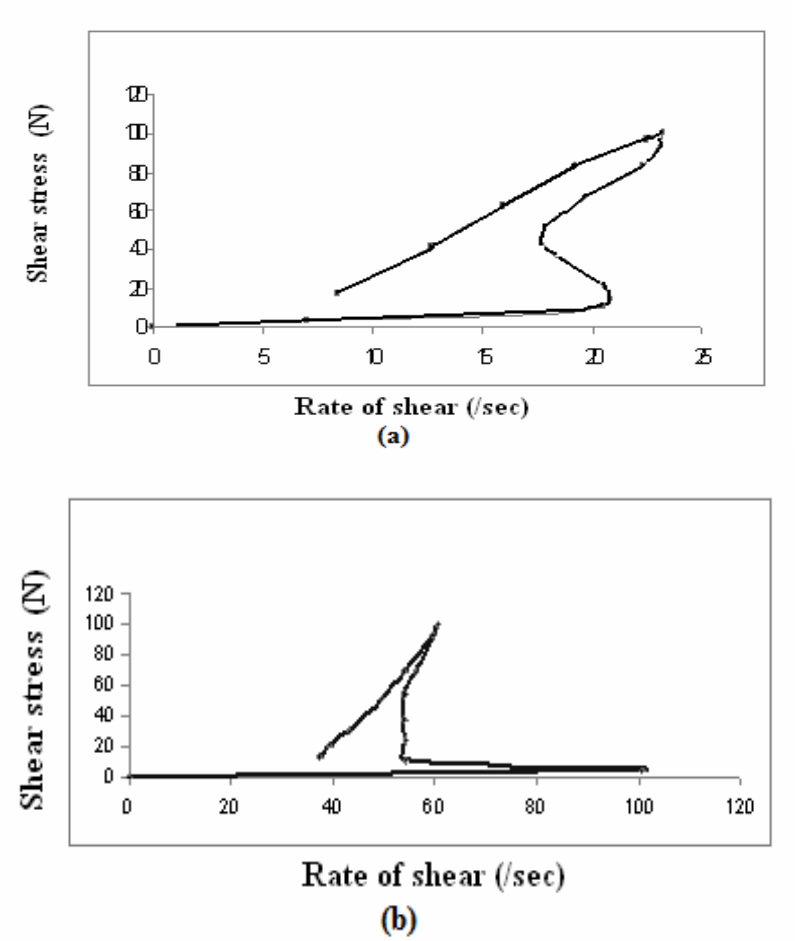

Figure 4: Hysteresis loop-- (a)3% PPS mucilage (b)10% PPS mucilage

The results of rheological studies of the PPS mucilage revealed that at concentrations greater than 5% it was more useful as a gelling agent and hence for its evaluation as a suspending agent, lower strengths ranging from 1.25-5% were used. For these studies suspensions were prepared containing paracetamol as a model drug with different concentrations of PPS. Comparisons were drawn with similar concentrations of sodium CMC as model suspending agent (1.25-5%) (Table 2 & 3).The suspensions were evaluated for various parameters such as pH, viscosity, particle size, resuspendability, percent release, sedimentation volume and assay for drug content. All the formulations contained 91-95% drug which was within compendia limits. The pH of the formulations ranged from 6-7.5 and particle size between 25-35µ. There was no evidence of agglomeration of the particles due to entanglement in the polymeric chains of both PPS and sodium CMC..A direct relationship was observed between the concentration of PPS and viscosity. Viscosity of suspension containing low concentration of the PPS mucilage was low and so sedimentation was faster resulting in more compact sediment. Hence the time for resuspendability was also higher at lower concentration of PPS i.e. 45 sec. An inverse relationship was observed between resuspendability and concentration of PPS. The sedimentation volume is the ratio of ultimate height of sediment to the initial height of the total suspension. Sedimentation volume for the PPS suspension was found to be in the range of 0.5-0.7 which indicated reasonably good resuspendability. In case of suspensions prepared using sodium CMC the viscosity ranged from 158-1400 cps and the sedimentation volume was equal to one thus indicating superior suspendability. No interference was evident in the release of drug as seen by the in vitro dissolution profile with 98% drug being released within 20 min.

Thus, we can conclude that the polysaccharide extracted from psyllium seeds was found to have shear thinning as well as thixotropic properties. The rheogram showed a characteristic spur value indicative of sudden breakdown of structure. Paracetamol suspension prepared using PPS as suspending agent compared favourably with those prepared with sodium CMC. Future research could be aimed at derivatizing the polysaccharide to improve

its utility as a pharmaceutical excipient in general and as suspending agent in particular.

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