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Pharmaceutical characterization of *Prosopis juliflora (sw)* seed mucilage-excipient

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Abstract

The present investigation reports the isolation of mucilage of *Prosopis juliflora (SW)* seed. Physiochemical characteristics of mucilage, such as solubility, swelling index, loss on drying, viscosity, powder porosity, and pH were studied. The mucilage was evaluated for its granulating and binding properties in compressed tablet, using diltiazem HCl as a model drug. Mucilage was used in four different concentrations i.e. 0.25, 0.5, 0.75 and 1.0 % w/v. The properties were compared with xanthan gum, which was used as standard binder at 1.0% w/v concentration. The tablets were prepared and evaluated for content uniformity, hardness, friability, disintegration time and *in vitro* dissolution profile. The tablets had good physiochemical properties, and the drug release was more than 85 % within 3 h.

Key words: *Prosopis juliflora,* mucilage, hydrogel, binder

Introduction

The high cost of imitation polymer and ecological pollution by chemical diligence has made the scientist in budding country to enter into *era*, in which plant products serve as alternative to synthetic products because of local accessibility, environmental gracious nature, subordinate prices and nontoxic compared to imported synthetic products. Today we have number of plant based pharmaceutical excipients such as guar gum, starch, agar, alginate, acacia, cocoa butter, cellulose etc. These natural excipients are used as binder, disintegrant in tablet, protective colloids in suspensions, thickening agent in oral liquids, gelling agent in gels and based suppositories. Similarly many plants restrain mucilage, which provide high concentration of complex sugar and uronic acid unit. Mucilage and gums have been known since ancient times for their medicinal uses. In the contemporary era also they are widely used in the pharmaceutical industries as thickeners, water retention agents, emulsifying agent, suspending agents, binders and film formers (Kapoor et al. 1992, Monif et al. 1992). Apart from its use in finished medicines, newer uses have been found in the preparation of cosmetics, textiles and paint paper, hence the demand for these substances is increasing and new sources are getting

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tapped (Kakrani and Jain 1981, Bhunvara and Khorana 1985). Though, India due to geographical and environmental positioning has traditionally been a good source for such products among the Asian countries, a large quantity of this is still being imported from the European countries to meet up the ever-increasing demand (Whistler 1973). Of all the orally administered dosage forms, tablet is most preferred because of ease of administration, compactness and flexibility in manufacturing. Because of changes in various physiological functions associated with aging including difficulty in swallowing, administration of intact tablet may lead to poor patient compliance and ineffective therapy.

Prosopis juliflora (SW) (Kritikar and Basu 2005) is available locally belonging to the family fabaceae and has not been explored as pharmaceutical excipients. The seed of *Prosopis juliflora (SW)* swells and form gelatinous mass when it comes in contact with water due to its hydrophilic nature. Hence the present work was attempted to evaluate binding properties of seed mucilage of *Prosopis juliflora (SW).*

Materials and Methods

Materials

Prosopis Juliflora (SW) seeds were procured from the forest of KORBA, Chhattisgarh, India. Diltiazem HCl was obtained as gift sample from Active Pharmaceutical Ingredient. All other ingredients were of analytical grade and purchased from Loba chemicals, Mumbai, India.

Isolation of mucilage from Prosopis juliflora (SW) seeds

Prosopis Juliflora (SW) seeds Kernel's powder (20 g) were soaked in cold distilled water (200 mL) and slurry was prepared. Then slurry was mixed with 800 mL of boil distilled water. The solution was boiled for 20 min under stirring condition in water bath. The resulting thin clean solution was kept overnight for settling protein and fibers. The solution is centrifuge at 5000 rpm for 20 min. The supernant was separated and poured in to twice the volume of absolute ethanol by continues stirring to precipitate the polysaccharides. The precipitate was washed with absolute ethanol, diethyl ether and petroleum ether and then dried at 40-45°C and passed through sieve #120 and stored in desiccators until used for further studies (Rao 1946, Rao and Srivastav 1973, Nandi 1975).

Drug-excipient compatibility studies

This study has been done to check whether there is any compatibility related problems are associated with drug and excipients used for the formulation of tablet. The drug and excipients must be compatible with one another to produce a product that is stable, efficacious, attractive and easy to administer and safe. If the excipients are new and not been used in formulations containing the active substance, the compatibility studies are of paramount importance. Thermal analysis and FTIR can be used to investigate and predict any physicochemical interactions between components in a formulation and can therefore be applied to the selection of suitable chemically compatible excipients.

FTIR spectroscopy

The IR spectral analysis of a drug and other excipients were taken using press pellet technique (using KBr). The IR spectra were determined by using 1601 PC Shimadzu UV Spectrophotometer (Willard et al. 1988, Beckett and Stenlake 2004, Tayed and Vavia 2005, Sharma 2009).

Differential scanning calorimetry studies (DSC)

DSC was performed on a Shimadzu DSC-60 (Shimadzu Limited Japan). A 1:1 ratio of drug and excipient was weighed into aluminum crucible and sample was analyzed by heating at a scanning rate of 10°C/min over a temperature range 20°-300°C under a nitrogen flow of 40mL/min. Reproducibility was checked by running the sample in triplicate (Murli Mohan 2001).

Preliminary phytochemical screening of isolated mucilage

The phytochemical properties such as presence of carbohydrate, protein, flavanoids, sterols, alkaloids, tannins, saponins and terpenoids were determined (Kokate 2006).

Physicochemical properties of dried mucilage

The physicochemical properties such as solubility, pH and viscosity of dried mucilage were determined at 20°C. The loss on drying, total ash content, acid insoluble ash and water soluble ash were determined according to Ayurvedic Pharmacopoeia of India (A.P.I) (Ayurvedic Pharmacopoeia of India 1999).

Microbiological properties

Microbial Lload

Preparation of inoculums

1g powder of *Prosopis juliflora (SW)* mucilage was suspended in 10 mL of sterile water (inoculum). 1 mL of inoculum was transferred to 99 mL dilution blank (sterile water) which was diluted inoculum.

Plate count technique

Inoculum (1 mL) and diluted inoculum (1 mL) were transferred to separate petridishes 9 to 10 cm in diameter. After addition of both the inoculum to the plate, 20 mL of agar medium (40-45°C) was poured into the each plate. Both the plates were gently rotated for through distribution of inoculum throughout the medium and solidified (Michael and Pelezar 1993).

Preparation and evaluation of granules

Diltiazem HCl (DTZ) was used as model drug to formulate the granules. Microcrystalline cellulose was used as disintegrant, were lactose and aerosil was used as diluents and lubricant respectively. Binder solution was prepared by dissolving the mucilage of *Prosopis juliflora (SW)* (MPJ) in water at 0.25%, 0.50%, 0.75% and 1.0% w/v concentrations. The batch size was 100 g. The drug, lactose, aerosil, and MCC were mixed thoroughly and sufficient volume of 20 mL of 0.25%, 0.50%, 0.75% and 1.0% w/v mucilage of MPJ was added slowly to powder blend, and kneading was performed for near about 10 min until the formation of wet mass with enough cohesiveness. The wet mass forced through the sieve # 16 and dried at 40-45°C in hot air oven for 3 h. The dried granules were received through sieve #. 20. The prepared granules were then evaluated for percentage of fines, particles size and flow properties by measurement of angle of repose (Banker and Neil 1987, Indian Pharmacopeia 1996, Gordon et al. 1999). The bulk and tapped densities of the granules were then assessed in accordance with the USP XXV tapped volume meter appartus compressibility index of the granules was determined by Carr's compressibility index (Shah et al. 1997, Reddy et al. 2003, Aulton 2007, Martin et al. 2008).

Preparation and evaluation of tablet

The lubricated granules were compressed into tablet using 8 mm standard concave punch with 10 station single rotary Clit (Jemkay) machine and keeping average weight 200 mg. The prepared tablets were evaluated for content uniformity, hardness, disintegration time and *in vitro* dissolution profile using method specified in Indian pharmacopeia (Indian Pharmacopeia 1996).

Table 1. Composition of Tablet Formulation

Ingredient	Seed mucilage of *Prosopis juliflora (SW)* as binder				Xanthan gum
	F1	F2	F3	F4	F5
DTZ	50 mg	50 mg	50 mg	50 mg	50 mg
MPJ (%W/V)	0.25%	0.5%	0.75%	1.0%	1.0%
MCC	Q.S	Q.S	Q.S	Q.S	Q.S
Lactose	Q.S	Q.S	Q.S	Q.S	Q.S
Aerosil	4 mg	4 mg	4 mg	4 mg	4 mg
Total weight	200 mg	200 mg	200 mg	200 mg	200 mg

Accelerated stability studies

Formulation were stored at various temperature *viz.* 25°C/60% RH, 30°C/65% RH and 40°C/75% RH as per ICH guidelines and various physicochemical parameter (appearance, percentage drug content and release profile) were monitored periodically for 3 months (Amin and Kohli 2003).

Results and Discussion

Drug-excipient compatibility studies

The dried and coarsely powdered seeds of *Prosopis juliflora (SW)* yielded high percentage (19.8% w/v) of mucilage using ethanol as mucilage precipitating solvent. The thermograms of drug and MPJ shows that there is no change in melting point which confirms that there is neither change in crystallinity of the drug nor any interaction Fig. 1, further drug polymer interaction was checked by comparing the IR spectra of the physical mixture of drug with the MPJ used with the IR spectrum of pure drug. IR spectral assignments for drug reveals that it gives characteristic peaks at 3056 cm^{-1}, 3035 cm^{-1}, 2966 cm^{-1}, 2837 cm^{-1}, 2393 cm^{-1}, 1740 cm^{-1}, 1679 cm^{-1}, 839 cm^{-1}, and 781 cm^{-1} frequencies in the region of 400 cm^{-1} to 4000 cm^{-1} (Mazzo et al. 2005). Frequencies of functional groups of pure drug remained intact in physical mixture containing MPJ Fig. 2; so it was concluded that there was no major interaction occurred between the drug and MPJ used in the study.

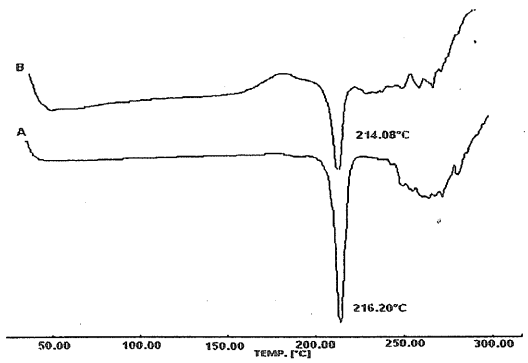

Figure1. DSC of, A) pure drug DTZ and B) Formulation F4

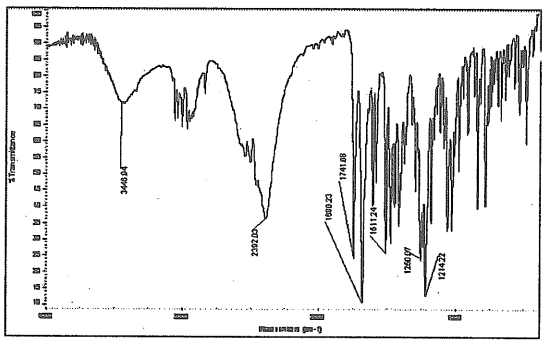

Figure 2. FTIR spectrum of physical mixture of DTZ with excipients used

Preliminary Phytochemical Screening of Isolated Mucilage

The phytochemical screening of natural mucilage confirmed polysaccharides in nature Table 2. The physicochemical and microbiological properties of MPJ were determined. The MPJ completely soluble in warm water, swelling index, viscosity obtained 33% and 3.65cps. The pH of the mucilage was found to be 5.6 were very near to neutral it may be less irritating on gastrointestinal tract and hence gum is suitable for uncoated tablet Table 3.

Table 2. Data Showing, Preliminary Phytochemical Screening of Isolated Mucilage

Active constituent	"MPJ" Mucilage
Carbohydrate	+
Protein	-
Flavanoids	-
Tannins	-
Saponins	-
Sterols	-
Alkaloids	-
Terpenoids	-

+ Present, - Absent.

Table 3. Physicochemical properties of MPJ mucilage

Parameter	Results
Solubility	Soluble in cold water and hot water forming viscous colloidal solution
Swelling index (%)	33.0 ± 0.15
pH	5.6
Viscosity (0.15%w/v solution)	3.65 cps
Specific gravity (g/mL of 0.15%w/v solution)	0.9975
Loss on drying (%)	8.2 ± 0.02
Total ash (%)	7.72± 0.13
Acid insoluble ash (%)	0.57± 0.05
Water soluble ash (%)	6.532± 0.08

*All values are mean ± S.D. for n=3

Microbiological properties

The extracted and purified natural gum were evaluated for microbial load, MPJ shows 100 CFU per gram of gum which shows mucilage were under microbial limit Table 4.

Table 4. Technological characterization of microbial load

Natural gum	No. CFU/mL	Microbial load (No. of CFU/g of gum)
"MPJ"	12	100

Physicochemical properties of dried mucilage

The prepared granules were evaluated for percentage of fines, flow properties, the result are shown in Table 5. It was observed that percentages of fines were reduced as the concentration of MPJ was increased. The percentage of fines was little higher in granules prepared using 0.25% of mucilage as binder. The flow properties of granules were determined by angle repose which was found to be 32° to 22°. Hence all the granules exhibited good flow properties. Bulk densities of the prepared granules were found to decrease slightly by increasing the concentration of MPJ. This result may be due to the formation of larger agglomerates and decrease in fines in the granules, as increasing MPJ concentration. The result of compressibility index indicates decrease in flow ability with increasing MPJ concentration. However, all formulation showed good flow properties. In general compressibility index values upto 15% result in good to excellent flow properties. All these result indicates that the granules possessed satisfactory flow properties and compressibility.

Table 5.Technological characterization of granules using *Prosopis juliflora (SW)* mucilage as binder.

Properties	Seed mucilage of *Prosopis juliflora (SW)* as binder				Xanthan gum
Concentration	0.25%	0.50%	0.75%	1.00%	1.00%
Percentage of fines (%)	24.50	23.40	21.10	19.40	18.06
Angle of repose	32.56°	30.40°	26.64°	22.42°	25.84°
Mean particle size (mm)	0.34	0.31	0.33	0.32	0.34
Percentage friability (%)	0.75	0.62	0.54	0.46	0.35
Disintegration time in min.	8	9	11	14	13
Loose Bulk density (g/cm^2) ±SD	0.600±0.05	0.573±0.03	0.560±0.06	0.543±0.01	0.532±0.04
Tapped bulk density (g/cm^2) ±SD	0.652±0.04	0.607±0.01	0.588±0.02	0.582±0.01	0.580±0.02
Compressibility index (%)	7.97±0.78	7.92±0.24	7.62±0.05	7.61±0.04	7.08±0.07
Content uniformity (%) ± SEM	99.6±0.44	100.2±0.54	100.1±0.52	101.4±0.51	101.0±0.70
Hardness (kg/cm^2) ± SEM	4.90±0.44	5.80±0.04	6.20±0.08	6.40±0.07	6.8±0.10

*All values are mean ± S.D. for n=3

In vitro evaluation of tablets

To understand the release profiles of the drug from the tablets, Four batch of tablets were prepared using MPJ at four different concentration (0.25, 0.5, 0.75, 1.00%w/v) xanthan gum mucilage (1.00%w/v) was used as standard binder for comparison. The prepared tablets were evaluated for content uniformity, hardness, friability, disintegration time, dissolution profile. All the batches of tablet exhibited good uniformity in content. Hardness of tablet increased with increase in concentration of mucilage. The tablet prepared with 1.00%w/v MPJ showed the hardness nearly equal to the tablet prepared by using 1.0% w/v of xanthan gum mucilage. The percentage friability values were slightly decreased as increase in concentration of mucilage. Through increase in hardness of tablet, increase in concentration interestingly showed decreased in disintegration time of tablet. *In vitro* dissolution study showed that drug release from the

tablets prepared by using mucilage at four different concentrations was more than 85% in 3h (Fig. 3).

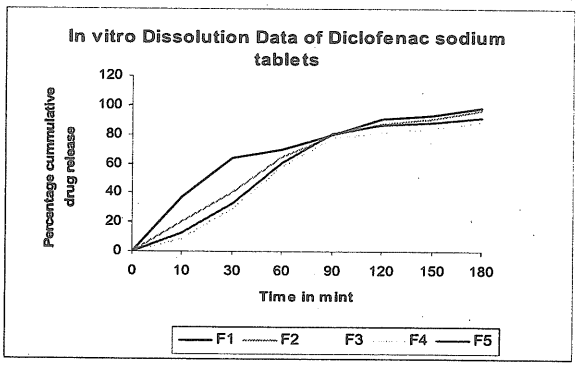

Figure 3. *In vitro* dissolution profile of DTZ tablets prepared with seed mucilage of *Prosopis juliflora (SW)* (MPJ) as binding agent.

Accelerated stability studies

The stability study of optimized batch was carried out at 25°C/60% RH, 30°C/65% RH and 40°C/75% RH as per ICH guidelines. The tablets formulation F1 and F4 were found to be stable at such condition and other parameters were found to be unaffected, but the parameters of formulation F2 and F3 were out of pharmacopoeial limits. They exhibited less hardness and poor drug release pattern

Summary

From the above study, we can conclude that *Prosopis juliflora (SW)* mucilage can be used as a binder in formulation of uncoated tablets. Increase in concentration of mucilage increases the hardness and decrease the disintegration time. This property of mucilage can overcome the friability problems of orodispersible tablets. . It can also be used for sustaining the drug release from tablets, since the prepared tablets using seed mucilage of MPJ produced a sticky film of hydration on the surface. Moreover it may prove economical as binding property of 1% w/v *Prosopis juliflora (SW)* (MPJ) mucilage is almost equivalent to 1.0% w/v Xanthan gum mucilage.

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