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EVALUATION OF MUCILAGE OF CAESALPINIA PULCHERRIMA AS BINDER FOR TABLETS

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ABSTRACT: Water soluble mucilage was isolated from the seeds of *Caesalpinia pulcherrima (Euphorbiaceae)*. The physical Characteristics of the gum such as solubility, swelling index, loss on drying, PH, viscosity and microbiological properties were studied. The gum was found take non-toxic when evaluated for acute toxicity in mile [LD_{50}>5 gm/kg body weight P.O]. The mucilage was evaluated for their granulating and binding properties in tablets, using Diclofenac Sodium as model drug. The mucilage were used at 4 different concentrations viz. 4,6,8 and 10% w/w. Wet granulation techniques was used for preparation of granules. The prepared granules were evaluated for % fines, average particle size, Bulk density and Angle of repose. These properties were compared with starch, which was used as a standard binder at 10% concentration. The tablets were punched by using a cadmach single punch machine and were evaluated for weight variation, Hardness, friability and Disintegration time. The *Caesalpinia pulcherrima* mucilage was found to possess excellent binding property and could be used as a binder in conventional tablet formulation.
KEY WORDS: *Caesalpinia pulcherrima*, mucilage, Binder.

INTRODUCTION

Binders are agents used to impart cohesive qualities to the powdered material during the production of tablets. They impart cohesiveness to the tablet formulation, which ensures that the tablet remains intact after compression as well as improving the free flowing quality [1]. Mucilages are most commonly used adjuvant in pharmaceutical preparations. They possess a variety of pharmaceutical properties, which include binding, disintegrating, suspending, emulsifying and sustaining properties[2]. Natural mucilage are preferred over semi-synthetic and synthetic materials due to their non-toxic, low cost, free availability, emollient and non-irritating nature[3].

The present study deals with the isolation of the gum from the seeds at *Caesalpinia pulcherrima* and its application as binding agent in tablet formulation. The binding properties of this gum were compared with starch which was used as a standard binder at 10% concentration.

MATERIALS AND METHODS

The plant seeds of *Caesalpinia pulcherrima* were collected from surrounding area of Ramanathapuram District, Tamil Nadu, India. The collected plant was authenticated by Botanical survey of India, Coimbatore, Tamil Nadu, Diclofenac sodium was obtained from Microlabs, Houser, as a gifted sample, Lactose obtained from Moly chem, Mumbai. All other materials used in the study were of analytical grade.

ISOLATION OF MUCILAGE

The seeds of *Caesalpinia pulcherrima* were soaked in distilled water for 24 hours, boiled for 1 hour and kept aside for 2 hours to release mucilage in to water. The material was squeezed in a muslin bag to remove the marc from the filtrate. Then, equal volume of acetone

was added to filtrate to precipitate the mucilage. The mucilage was separated, dried in oven at temperature less than 50°C, powdered and passed through sieve number 80. The powder was stored in desiccator until further use (Yield= 11%w/w) [4, 5, 6.]

PHYSICOCHEMICAL PROPERTIES OF GUM

The physicochemical properties, such as solubility, swilling index, loss on drying, viscosity, pH and microbial load[8] (No. of CFU/gm of gum) were determined according to Indian Pharmacopoeial procedure[7], Using air dried powder of gum. The pH of the mucilage was determined using a digital pH digital meter. The viscosity of 1% gum solution was determined at 25°C using ostwalds viscometer after 24 hr of hydration.

ACUTE TOXICITY STUDY IN MICE

The method was performed according to the OECD test guideline for testing of chemicals TG 423 (OECD 2001). Healthy wistar female rats fasted over night, but allowed access to water ad libitum were randomly divided into 5 groups (n = 3). The control group received water. Groups I-IV were orally treated with *Caesalpinia pulcherrim* aqueous seed extract at the dose of 50, 300, 2000, 5000 mg/kg respectively the animals were observed at 15, 30, 60, 120, and 240 minutes with no intake of food and water and thereafter over a period of 24hrs. The rats were further observed for upto 14days with food and water intake ad libitum and were monitored behavioral changes, body weight, morbidity and mortality.

DIFFERENTIAL SCANNING COLORIMETRY

The DSC curve of diclofenac sodium and mixture of mucilage/diclofenac sodium were generated by differential scanning colorimeter (Mettler Toledo DSC 821, Switzerland.) at heating rate of 10°C/minute from 0 – 300 °C under nitrogen atmosphere

PREPARATION AND EVALUATION OF GRANULES

All the materials were passed through a mesh sieve with aperture of 250µm before use. The tablets were prepared by wet granulation method. The compositions of tablets were given in table 1. Diclofenac sodium and lactose were thoroughly mixed and the solution of the mucilage of specified concentration was prepared by dispersing the mucilage in water. The mucilage solutions were used for moistening the powder mixture, for preparing tablets to evaluate the binding potential. The wet mass was then passed through sieve no. 16 and dried at temperature not exceeding 50°C in a hot air oven for 30minute. The dried granules were rescreened through a sieve no 20. The same method was followed in the preparation of standard formulation (ST I) using starch mucilage 10% w/w concentration as a binder.

The granules were evaluated for their particle size, the particle size were estimated by sieving method, sieves were arranged in a nest with coarsest at the top a sample of 15g of the granules were placed on the top sieve. The sieve set were fixed and shaken for a sudden period of time (20minutes) the granule retained on the each sieves were weighed. Frequently, the granules were assigned the mesh number of the screen through which it passed or on which it was retained. It was expressed in terms of arithmetic mean of the two sieves.

TABLE : 1 COMPOSITION OF TABLETS CONTAINING *CAESALPINIA PULCHERRIM* (CP) MUCILAGE AS BINDER

Ingredients	CP I	CP II	CP III	CP IV	CP V	ST I
Diclofenac Sodium	50 mg	50 mg	50 mg	50 mg	50 mg	50 mg
C P mucilage	2%	4%	6%	8%	10%	_
Starch Mucilage	_	_	_	_	_	10%
Talc	2%	2%	2%	2%	2%	2%
Magnesium Stearate	2%	2%	2%	2%	2%	2%
Lactose	q.s	q.s	q.s	q.s	q.s	q.s
Total Weight	220 mg	220 mg	220 mg	220 mg	220 mg	220mg

The flow properties of granules evaluated by the flow rate through a funnel, the compressibility index Hausner ratio was determined. Using the glass funnel specified in the European Pharmacopoeia III the flow rate (g/s) was calculated from the time needed for the entire sample (40 g) to empty from the funnel.

The bulk density was calculated by 15 gm of granules were introduced in to a 100 ml measuring graduated cylinder. The cylinder was fixed on the bulk density apparatus and the timer knob was set for 100 tapings. Then noted the volume continued another 50 tapings and noted the final volume. This volume was noted as bulk volume. Based on the bulk and tap density both the Carr index (%) [(Tapped – Bulk) X 100/Tapped] and Hausner ratio (tapped/bulk) were calculated.

Angle of repose was determined by fixed funnel method[10]. Funnel with the end of the stem cut perpendicular to the axis of symmetry was secured with its tip at a given height (H) above a graph paper placed on a flat horizontal surface. The material was carefully poured through the funnel until at apex of the conical pile so formed just touches the tip of the funnel. The mean diameter (2R) of the base of the powder cone was determined and the tangent of the angle of repose is given by $\tan \alpha = H/R$, where α is the angle of repose. All the results were compared with the standard formulation (ST I).

PREPARATION AND EVALUATION OF TABLETS

The granules were lubricated with 2% w/w magnesium stearate and talc. The tablets were compressed by using Cadmach single punch machine using 6mm round flat faced punches. The tablets of average weights 220mg were prepared. 9 batches of tablets were prepared by using isolated mucilages of five different concentration (2%, 4%, 6% 8% and 10%) were used, starch mucilage (10% concentration) was used as a standard binder for comparison.

The prepared tablets were evaluated for weight variation, hardness, friability and disintegration time. Disintegration time was determined using USP tablet disintegration apparatus (Model ED – 2 Electrolab, Mumbai) using water (900ml) as medium at 37±0.5^{o}C weight variation test was carried out as per IP. Monsanto hardness tester and the Roche friabilater were used to test hardness and friability respectively as per IP.

RESULTS AND DISCUSSION

Mucilage obtained from the *Caesalpinia pulcherrim* seeds was an amorphous free flowing powder with a light brown colour. It exhibited good solubility in water and forms a viscous solution (Table- 2). Lethal effects no were observed after the administration of dose of *Caesalpinia pulcherrim* aqueous extract (50, 300, 2000 and 5000 mg/kg body weight) all animals appeared normal; no behavioral changes in observation period. There were no remarkable changes or difference observed in body weight (Table-3) of the treated rats compared to control. Therefore, the LD_{50} values for oral administration of *Caesalpinia pulcherrim* aqueous extract is greater than 5000mg/kg. DSC thermograms of Dicofenac Sodium and mixture are depicted in figs 1 and 2 respectively. The thermogram of the pure drug exhibited a sharp endothermic peak at 161.21^{o} corresponding to its melting point, The DSC thermograms of drug mixture showed identical peaks corresponding to pure drug indicated the absence of well defined chemical interaction between the drug and the mucilage

TABLE 2 PHYSICOCHEMICAL PROPERTIES OF *CAESALPINIA PULCHERRIM*

s.no.	Parameters	*Caesalpinia pulcherrim*
1	Solubility	Soluble, forming viscous solution
2	Swelling index%	8.3
3	pH	5.7
4	Loss on drying %w/w	8.3
5	Viscosity cp	3.51
6	Microbial load (no of CFU/g of mucilage)	170

TABLE 3: BODY WEIGHT OF THE RATS IN ACUTE TOXICITY OF THE AQUEOUS EXTRACT FROM SEEDS OF *CAESALPINIA PULCHERRIM*

	Body weight (g)		
	Day 0	Day 7	Day 14
Control	222±1.4	230±1.9	242±1.6
Group I	214±1.5	228±1.7	249±2.1
Group II	223±1.6	234±1.9	247±1.2
Group III	219±1.1	236±2.1	251±1.1
Group IV	218±1.7	231±1.4	246±1.4

Values are expressed as mean ±S.D. (n = 3)
A significant difference from control, $p < 0.05$

Fig.1

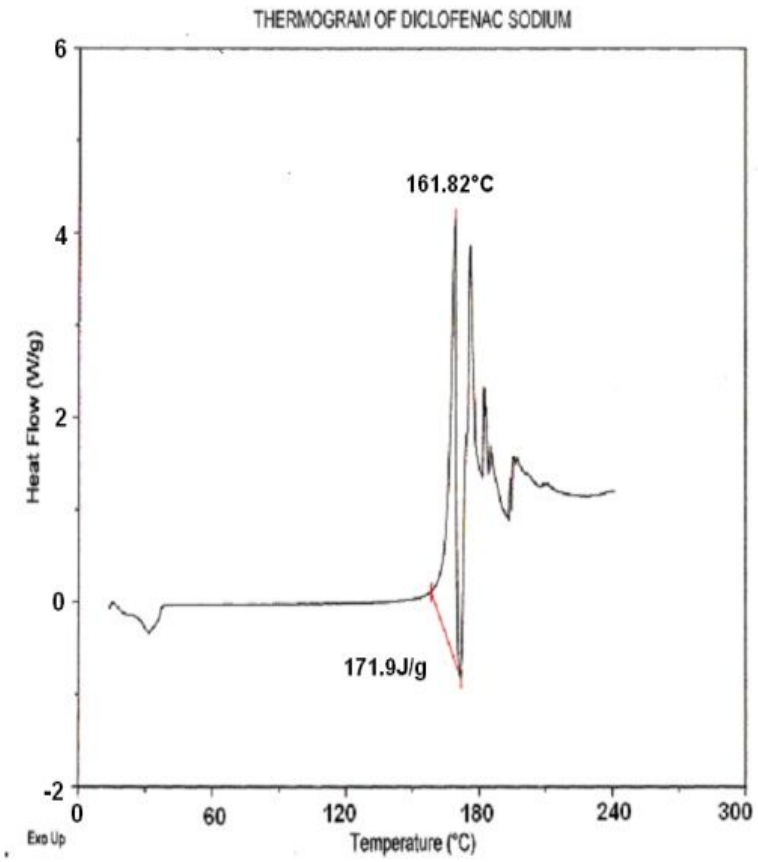
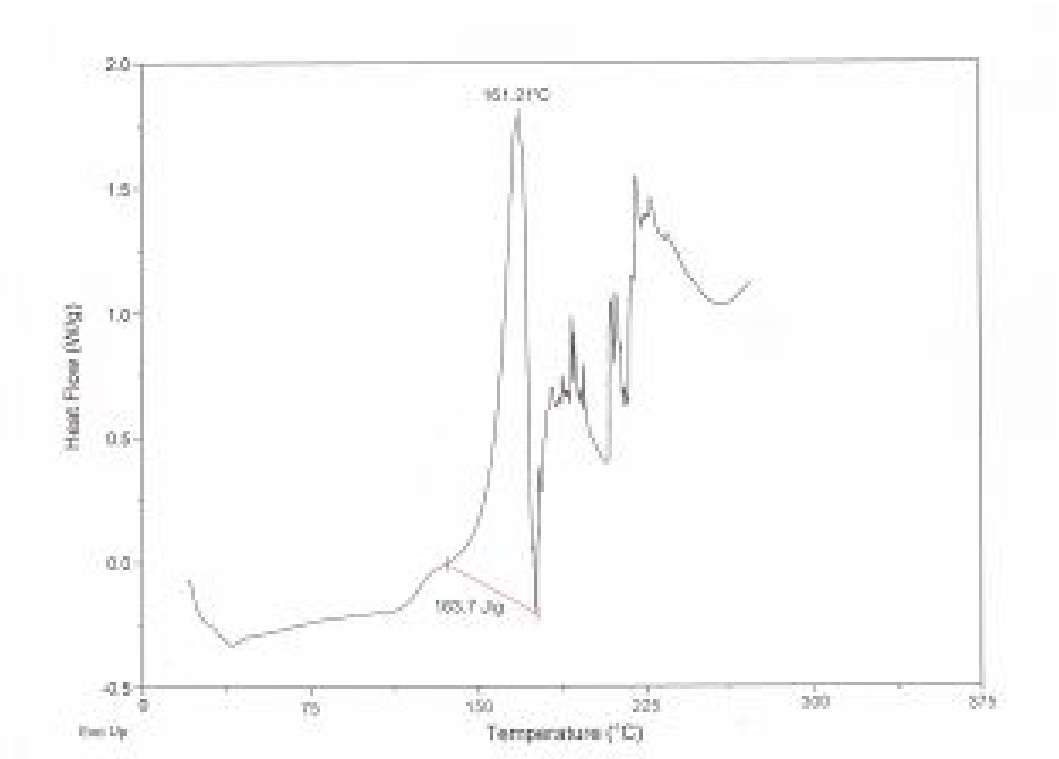


Fig.2



EVALUATION OF GRANULES

The granules prepared were evaluated for mean particle size (µm), tapped bulk density, loose bulk density, flow rate, Carr index (%), Hausner ratio and angle of repose. Flow properties of the granules were determined as good flow ability is prerequisite for the preparation of the tablets with an acceptable weight variation for all the formulations the flow rate of the granules between 6 – 9 g/s. All the formulations tested had a Carr index ranging between 11.7 and 12.9% while their Haugner ratio was below 1.25. The mean particle size was found to be satisfactory for preparation of tablets. The angle of repose was found to be between 20-26^{o}. Hence, all granules exhibited good flow property (Table-4).

EVALUATION OF TABLETS

Six batches of tablets were prepared using mucilage at 5 different concentration of isolated mucilage and Starch mucilage (10% concentration) was used as standard binder for comparison. The prepared tablets were evaluated for weight variation, Hardness, friability, Disintegration time and in-vitro dissolution profiles. The results are shown in table 5.

All the formulations had coefficient of variation values of less than 3% release to their mean weight. The hardness of the tablet varies between 3 – 7 kg/cm^2. The hardness of the tablets increased with increase in percentage of binding agent. The tablets prepared with 10% of starch mucilage (ST I) showed equal hardness when compared to formulation PJ IV and PJ V but the formulation PJ I, PJ II and PJ III have less hardness as compared to formulations (ST I) have enough hardness to withstand the mechanical shocks of handling in manufacturing by packing.

The friability values were decrease with increase binder concentration of isolated *Caesalpinia pulcherrim* seed mucilage. But overall friability values were less than specified limits. This demonstrated the effectiveness of the gum to use as binder. The disintegration time of the tablet varied between 2 – 5 minutes. The disintegration time increase the concentration of binder, but all the values were within the pharmacopeial limits. At 8% and 10% concentration, the disintegration time was higher for tablets prepared with 2%, 4% and 6% mucilage and equal to standard formulations as 10% starch mucilage used as a binder.

TABLE 4: EVALUATION OF THE GRANULES

Properties	CP I	CP II	CP III	CP IV	CP V	ST I
Mean particle size (µm)	359.5	356.81	362.56	360.21	355.67	380.74
Tapped bulk density	0.655 g / cm^3±0.01	0.634 g / cm^3±0.01	0.648 g / cm^3±0.04	0.639 g / cm^3±0.02	0.639 g / cm^3±0.02	0.631g/cm^3± 0.02
Loose bulk density	0.596 g / cm^3±0.02	0.583 g / cm^3±0.02	0.590g / cm^3±0.01	0.581 g / cm^3±0.03	0.581 g / cm^3±0.01	0.526g/cm^3± 0.01
Flow rate (g/s)	8.2	7.6	6.8	7.2	7.6	6.4
Carr index (%)	12.2	11.5	8.8	10.7	11.7	11.9
Hausner ratio	1.06	1.15	1.13	1.17	1.06	1.08
Angle of repose	23°02’	23°74’	24°93’	25°96’	25°59’	22°24’

TABLE- 5 EVALUATIONS OF TABLETS

Formulations	Hardness	Friability (%)	Weight variation (%)	Disintegration time (min)
CP I	3.29±0.13	0.6238±0.03	220.45±2.68	2min, 55sec
CP II	4.13±0.16	0.4530±0.05	217.85±2.01	3min, 13sec
CP III	5.18±0.17	0.3269±0.04	218.95±2.39	3min, 43sec
CP IV	6.23±0.13	0.2397±0.02	219.56±2.57	4min, 41sec
CP V	6.63±0.56	0.2141±0.07	219.10±2.29	4min, 55sec
ST I	6.57±0.14	0.2092±0.03	220.37±2.42	4min, 14sec

Conclusion

As per pharmacopeia, disintegration time of uncoated tablets should be < 15 min[8].It was found that the tablets prepared using 8-10% concentration of isolated *Caesalpinia pulcherrim* seeds mucilage Exihibited disintegration time and Hardness within the standard limit. Formulations of 2, 4, 6% mucilage exihibited less hardness and disintegration time, when compared with 10% starch binder formulation, but the formulations have enough hardness to withstand the mechanical shocks of handling in manufacturing and packing. Taking all theabove parameters into consideration, the study has revealed a good potential of *Caesalpinia pulcherrim* mucilage as a binder for conventional tablet formulations.

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