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Research Article

STUDIES ON MUCILAGE FROM *HIBUSCUS ROSA-SINENSIS LINN* AS ORAL DISINTEGRANT

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ABSTRACT

Plant product serve as an alternative to synthetic products because of local accessibility, eco-friendly nature and lower prices compared to important synthetic products. Natural gums and mucilage have been widely explored as pharmaceutical excipients. The present study was undertaken to separate mucilage from leaves of *Hibusccus rosa-sinensis* and explore its use as tablet disintegrant. Mucilage extracted from the pods of *Hibusccus rosa-sinensis* were subjected to toxicity studies for its safety and preformulation studies for its suitability as a disintegrating agent. The mucilage extracted is devoid of toxicity. Dispersible tablets of Aceclofenac were prepared and compared with different concentrations viz; 2, 4, 6 and 8 %(w/w) of *Hibusccus rosa-sinensis* mucilage powder and Ac-Di-Sol®. Eight formulations were prepared and evaluated for physical parameters such as thickness, hardness, friability, weight variation, drug content, disintegration time and drug dissolution. The formulated tablets had good appearance and better drug release properties. The study revealed that *Hibusccus rosa-sinensis* mucilage powder was effective as disintegrant in low concentrations (4%). The mucilage was found to be a superior disintegrating agent than Ac-Di-Sol®.

Keywords: *Hibusccus rosa sinensis* mucilage, Disintegrating agent, Dispersible tablets.

INTRODUCTION

Mucilage is glutinous substance which mainly consists of polysaccharides, proteins and uranides. Dried up mucilage or the concentrated mucilage is called as Gum. The main difference between them is that mucilage do not dissolve in water whereas gum dissolves in water. Mucilage is formed in the normal growth of plant by mucilage secreting glands. Mucilage and gum are well known since ancient times for their medicinal use. In modern era they are widely used in Pharmaceutical industries as thickeners, water retention agents, suspending agents and disintegrants. Naturally the demand of these substances is increasing and new sources are tapped. India due to geographical and environmental positioning has traditionally been a good source for such products. *Hibiscus rosa-sinensis Linn* has not been explored as a pharmaceutical excipient. *Hibiscus rosa-sinensis Linn* of the *Malvaceae* family is also known as the shoe-flower plant, China rose, and Chinese hibiscus. The plant is available in India in large quantities, and the leaves contain mucilage [1,2]. The leaves are used in traditional medicines as emollients and aperients to treat burning sensations, skin disease, and constipation [3]. The plant contains cyclopropanoids, methyl sterculate, methyl-2-hydroxysterculate, 2-hydroxysterculate malvate, and β-rosasterol. Mucilage of *Hibiscus rosa-sinensis* contains L-rhamnose, D-galactose, D-galactouronic acid, and D-glucuronic acid [4]. The leaves contain carotene (7.34 mg/100 g of fresh material) and are used as cattle feed [5]. The leaves also contain moisture, protein, fat, carbohydrate, fibers, calcium, and phosphorus [6]. The objective of this study was to extract mucilage from the leaves of *Hibiscus rosa-sinensis Linn* and examine the various pharmaceutical properties of the dried mucilage to assess its functionality as an excipient

MATERIAL AND METHOD

Materials

Aceclofenac was received as a gift from Aristo Pharmaceuticals (Mumbai, India). The leaves of *Hibiscus rosa-sinensis Linn* were collected from the medicinal garden of the Sigma Institute of Pharmacy, (Baroda, India.) Ac-Di-Sol® and Microcrystalline cellulose were gifted from (Maple Biotech Pvt. Ltd., Pune, India), Aspartame (Ranbaxy, New Delhi, India). Talc and magnesium stearate were purchased from S.D. Fine Chem Ltd. Mumbai, India. All other solvents and chemicals were of analytical-reagent grade. Deionized double distilled water was used throughout the study.

Methods

Extraction of mucilage

The fresh leaves of *Hibiscus rosa-sinensis Linn* were collected, washed with water to remove dirt and debris, and dried. The powdered leaves were soaked in water for 5–6 h, boiled for 30 min, and kept aside for 1 h for complete release of the mucilage into water. The material was squeezed from an eight-fold muslin cloth bag to remove the marc from the solution. Acetone was added to the filtrate to precipitate the mucilage in a quantity of three times the volume of the total filtrate. The mucilage was separated, dried in an oven at a temperature < 50 °C, collected, dried-powdered, passed through a sieve (number 80), and stored for further use in desiccators [7].

Physicochemical properties of dried powdered mucilage

Dried- powdered mucilage was studied for percentage yield, particle size, mass loss on drying, swelling index, bulk density, angle of repose, and compressibility.

Evaluation of toxicity

A toxicity study was carried out according to Knudsen and Curtis. The animals used in toxicity studies were sanctioned by the Institute Animal Ethical Committee (approved by CPCSEA). Albino rats of either sex were fasted for 24h and used. In the acute toxicity studies a dose of 250mg/kg of mucilage was administered orally to six rats with additional three kept as control. Then they were observed for motor reflexes for 48h. Since no mortality was observed and behavioral pattern was unaffected, further studies were carried out using different set of animals (6 tests and 3 controls) where dose of 500mg/kg of mucilage was administered and the animals were observed for 72h. In the second phase of chronic toxicity studies, 12 animals were used, divided into two groups, 4 as control and 8 as test animals. In the test group a dose of 250mg/kg was administered daily for a period of 30days. Body weights were recorded for both the groups at an interval of 10days. At the end, hematological parameters were studied in both the groups [8,9].

Drug excipient compatibility study

Preformulation studies were carried out according to official monographs and drug excipient compatibility studies were done by using FTIR. Results revealed that there was no compatibility related problems between the drug and excipients used in the formulation.

Formulation of mouth dissolving tablets

Dispersible tablets of aceclofenac were prepared by the conventional direct compression technique using *Hibiscus rosa-sinensis Linn* mucilage powder and Ac-Di-Sol® at concentrations of 2, 4, 6, 8% w/w. All the required ingredients as per the formulation table were weighed and passed through Size 40# sieve. The Mixture was then blended in a double cone blender for 15 mins. The blend was then compressed on a Cadmach single-stroke punch machine. The composition of each formulation is given in formulation table. [10, 11]

Table 1: Formulation table

Ingredients(mg)	T 1	T 2	T 3	T 4	T 5	T 6	T 7	T 8
Aceclofenac	100	100	100	100	100	100	100	100
Hibusccus mucilage	4	8	12	16	--	--	--	--
Ac-Di-Sol®	--	--	--	--	4	8	12	16
Magnesium stearate	9	9	9	9	9	9	9	9
Talc	9	9	9	9	9	9	9	9
Aspartame	12	12	12	12	12	12	12	12
Microcrystalline cellulose	66	62	58	54	66	62	58	54
Total weight	200mg							

Evaluation of dispersible tablets

Tablets were evaluated for appearance, texture, taste, mouth feel, weight variation, hardness, friability, thickness, disintegration time, wetting time and stability. In weight variation test, twenty tablets were selected at random and average weight was determined using an electronic balance (Shimadzu, AX200, Japan). Tablets were weighed individually and compared with average weight. The Pfizer hardness tester and the Roche friabilator were used to test hardness and friability loss respectively. Thickness of tablet was determined by using dial caliper (Mitutoya, Model CD-6 CS, Japan). To measure wetting time of tablet, a piece of tissue paper was folded twice and placed in a small Petri dish containing sufficient water. A tablet was kept on the paper and the time for complete wetting of tablet was measured. Disintegration time was determined using USP tablet disintegration test apparatus (ED2L, Electrolab, India) using 900 ml of distilled water at 37°C. [12,13,14]

Disintegration and wetting time studies

The disintegration time and wetting time of the tablets was determined using USP phosphate buffer solution, pH 7.4 at 37±0.5°C.

Dissolution Study

In vitro release of aceclofenac from tablets was monitored by using 900 ml of SIF (USP phosphate buffer solution, pH 7.4) at 37±0.5°C and 75 rpm using programmable dissolution tester [Paddle type, model TDT-08L, Electrolab, (USP), India]. Aliquots were withdrawn at one minute time intervals and were replenished immediately with the same volume of fresh buffer medium. Aliquots, following suitable dilutions, were assayed spectrophotometrically (UV-1700, Shimadzu, Japan) at 274 nm. [14]

Stability studies

The stability of selected formulations was tested according to International Conference on Harmonization guidelines for zone III and IV. The formulations were stored at accelerated (40± 2 °C/75±5% RH) test conditions in stability chamber for six months. At the end of three months, tablets were tested for disintegration time, hardness, friability and drug content.

RESULTS AND DISCUSSION

The extracted and purified mucilage was cream colored and odorless. The average yield of dried mucilage obtained was 17%. To determine the safety level of extracted mucilage, toxicity studies were carried out. The studies showed no manifestations of toxic syndromes. Acute toxicity studies were performed to assess the suitability of extracted mucilage for oral delivery.

Table 2: Physicochemical characterization of mucilage

Sr. No.	Physicochemical parameter	Results
1	Percentage yield	17%
2	Average particle size	165 µm
3	Loss on drying	10%
4	Swelling ratio	9
5	Bulk density	0.65 g/cc
6	Angle of repose	26.5°
7	Compressibility Index	16%

Evaluation of toxicity

To determine the safety level of the extracted mucilage, acute as well as chronic toxicity studies were carried out. In both the studies no manifestation of the toxic syndromes were observed. To assess the suitability of gum for the oral delivery the body weight profile of the animals were recorded at regular interval of 10days for chronic studies. It was found that the weight of test and control and the rate of increase in weight of test and control were comparable. Hence it can be inferred that chronic administration of mucilage might not influence either the food intake or growth. Hematological parameters that were determined at the end of 30days continuous administration of mucilage were also comparable to that of control group (Table III). The effective concentration of the disintegrant in the conventional dosage form does not normally exceed beyond 10% of the formulation, which is approximately 15-20 mg/kg of the dose. Hence it can be concluded that the mucilage is not likely to exert any toxic effect on the body.

Table 3: Effect of mucilage on various Hematological parameters*

Hematological parameters	Mucilage treated group[1]	Control group[1]
Bleeding time in minutes	4.25 ± 0.12	4.19 ± 0.07
Clotting time in minutes	38.17 ± 0.22	37.37 ± 0.15
Total count of RBC/mm^3	9.55x10^6 ± 0.19	9.28x10^6 ± 0.25
Total count of WBC/mm^3	4125 ± 0.20	4130 ± 0.27
Hemoglobin Content	14.0 ± 0.07	14.3 ± 0.03

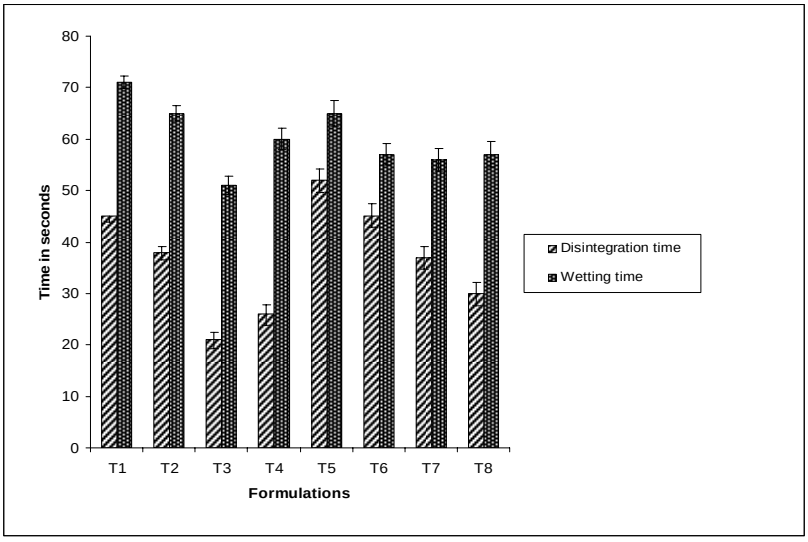
* Data was recorded after 30days of chronic oral administration of mucilage. 1. Data represents SD of six readings.

Evaluation of dispersible tablets

Tablets were obtained of uniform weight due to uniform die fill, with acceptable weight variation as per pharmacopoeial specification. Hardness of the all the formulations were measured in kg/cm2. The hardness of all formulations was found to be 3-4 kg/cm2. Drug content of all the formulations were found to be in the range of 96-99%, which is within acceptable limits. Friability values of all the formulations were within the limit i.e. is less than 1.0% indicated that tablets had a good mechanical resistance. Results of Post compression parameters are shown in Table 4. Wetting time was used as a parameter to correlate with disintegration time in oral cavity. This is an important criterion for understanding the capacity of disintegrants to swell in presence of little amount of water. Since the dissolution process of a tablet depends upon the wetting followed by disintegration of the tablet, the measurement of wetting time may be used as another confirmative test for the evaluation of dispersible tablets. The wetting time of formulated tablets was found in the range of 35- 87s. The disintegration times of all the formulations were within official requirements that are less than 180s. Comparison between disintegration time in oral cavity, wetting time and disintegration time (*Invitro*) for mucilage powder formulations are shown in Figure 1. Disintegration time in oral cavity was found between 34-78 s for mucilage powder. This showed good correlation between disintegration time in oral cavity and wetting time for all formulations. All designed formulations using mucilage powder and Ac-Di-Sol® showed rapid dissolution and percent cumulative drug release (%CDR) at the end of 12 min was between 79-99%.

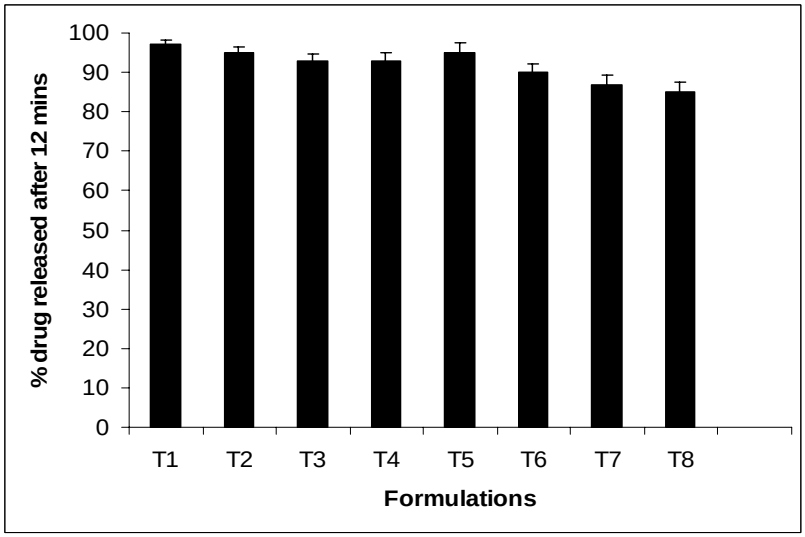
Table 4: Post compression parameters of various formulations

Parameters	T 1	T 2	T 3	T 4	T 5	T 6	T 7	T 8
Hardness (Kg/cm^2)	3.4	3.6	3.4	4.0	3.6	3.7	3.7	3.9
Friability (%)	0.54	0.65	0.45	0.53	0.32	0.55	0.34	0.47
Thickness (mm)	2.5	2.4	2.5	2.7	2.6	2.5	2.7	2.7
Drug Content (%)	97.23	96.25	96.56	97.54	98.89	99.12	97.23	96.12



(T1-Mucilage 4mg, T2-Mucilage 8mg, T3-Mucilage 12mg, T4-Mucilage 16mg, T5- Ac-Di-Sol® 4mg, T6- Ac-Di-Sol® 8mg, T7- Ac-Di-Sol® 12mg, T8- Ac-Di-Sol®16mg)

Fig. 1: Comparison of *In Vitro* wetting time and disintegration time of various formulations.



(T1-Mucilage 4mg, T2-Mucilage 8mg, T3-Mucilage 12mg, T4-Mucilage 16mg, T5- Ac-Di-Sol® 4mg, T6- Ac-Di-Sol® 8mg, T7- Ac-Di-Sol® 12mg, T8- Ac-Di-Sol®16mg)

Fig. 2: Comparison of *In Vitro* release profile of various formulations.

CONCLUSION

From the present study, it can be concluded that natural super disintegrants like *Hibiscus rosa-sinensis Linn* mucilage powder showed better disintegrating property than the most widely used synthetic super disintegrants like Ac-di-sol® in the formulations of FDTs and may be used as disintegrant at the level of 6%w/w in tablet formulations. As primary ingredients are cheap, biocompatible, biodegradable and easy to manufacture. They can be used as superdisintegrants in place of currently marketed synthetic superdisintegrating agents.

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