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Evaluation of a new tablet excipient from the leaves of *Mussaenda frondosa* Linn.

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ABSTRACT

Mussaenda frondosa Linn, family, Rubiacae, traditionally used in Indian folk medicine. Here an effort was made to investigate the efficacy of the mucilage obtained from the leaves of Mussaenda frondosa Linn as tablet excipient. The mucilage extracted from the leaves of Mussaenda frondosa Linn and studied for various physicochemical properties. Tablets were manufactured using extracted mucilage as the binding agent and comparison was made against the tablets prepared with starch paste as the standard binder on studying the standard parameters like diameter, thickness, weight variation, hardness, friability, disintegration and in-vitro dissolution study. Stability studies were conducted for 4 weeks periods.The mucilage shows good physicochemical properties that assessed as an excipient in formulation of tablets. The tablets prepared by using 5-10% mucilage shows the release rate in a sustained manner and that of 1% shows the drug release more than 90% within 4 h, which can be considered as the ideal concentration for preparation of tablets. At the end of 4th week appreciable changes was not observed for the stability study. Mussaenda frondosa mucilage could be used as a good binding agent at very low concentrations. This can be used for sustaining the drug release from tablets, since the prepared tablets produced a sticky film of hydration on the surface, which ultimately reduces drug release rate and hence it can be evaluated for its efficacy to sustain the drug release.

Key words: Mucilage, Pharmaceutical excepients, Tablets, Physicochemical characterization

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INTRODUCTION

Excipients are the additives used to convert active pharmaceutical ingredients into pharmaceutical dosage form suitable for administration to patients [1]. New and improved excipients continue to be developed to meet the needs of conventional drug delivery systems and to meet the needs of advanced tablet manufacturing. Mucilage and gums have been known since ancient times for their medicinal uses. In the modern era also they widely used in pharmaceutical industries as tablet binders, emulgents and thickners in cosmetics and suspensions as film-forming agents and traditional colloids [2, 3]. Hence the demand for these substances is increasing and new sources are getting tapped [4, 5]. 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 still being imported from the European countries to meet up the ever- increasing demand [6]. Mussaenda frondosa Linn, family Rubiaceae is a handsome erect shrub with grey bark, leaves simple, opposite, ovate and the flowers are yellowish green outside and orange green with in terminate cymes [7]. The plant has been used medicinally in treatment of various disorders like demulcent, used in leprosy, eye trouble, intestinal worms, astringent, expectorant, febrifuge and anti-inflammatory [8].

In the present study an effort was made to extract the mucilage from the leaves of Mussaenda frondosa Linn and investigate the pharmaceutical properties of the mucilage to assess its suitability as an excipient in the pharmaceutical formulation. Here the potential binding capacity of the mucilage has been evaluated with the standard starch paste as a tablet binder.

MATERIALS AND METHODS

Paracetamol was obtained as gift sample from Modern Pharmaceutical (Kerala, India). The leaves of *Mussaenda frondosa* were collected from the local area. The plant was authenticated at the Botanical Department of Calicut University in Calicut, India. Lactose IP, Starch, Purified talc and Magnesium stearate were procured from SD Fine Chemicals Ltd. All other reagents used were analytical grade.

Isolation of mucilage

The fresh leaves of Mussaenda frondosa Linn were collected, washed with water to remove dirt and debris and then dried. The powdered leaves were soaked in water for 5-6 hrs, boiled for 30 min and kept aside for 1 hr for complete release of the mucilage in to the 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 $<50^0$C, collected, dried, powdered and passed through a sieve NO: 80 and stored for further use in the desiccators.

Phytochemical examination

Preliminary tests were performed to confirm the nature of mucilage obtained. For the detection of presence of carbohydrates and mucilage, the standard tests Molisch's test and Ruthenium red [9] test were done.

Physicochemical characterization of mucilage

Dried-powdered mucilage was studied for solubility [10, 11], pH, weight loss on drying, swelling index, density and viscosity.

Drug-excipient compatibility study

The FT-IR spectrum of the drug-excipient sample was recorded in an IR spectrometer (Shimadzu FTIR 8400S, USA), using potassium bromide (KBr) discs prepared from powdered samples mixed with dry KBr in the ratio 1 : 200. Triplicate measurements were made, and the spectrum with the clearest identifiable peaks was chosen.

Preparation of granules

Lactose and starch powder were passed through sieve No: 40. Paracetamol IP was mixed with lactose and starch powder and were homogeneously dry-mixed. The granules prepared by wet granulation method using Mussaenda and starch binders in concentration of 1%, 2%, 5%, 8% and 10%w/w. the moistened friable mass was passed through sieve No: 16 and granules were dried at 50^0cfor 30 min. the dried granules were re-sieved through sieve No: 20.

Preparation of tablets

Magnesium stearate and talc were mixed with prepared granules. This uniformly mixed blend was compressed into 450 mg tablets using flat face round tooling on a Rimek-I rotary tablet machine. The tablets were stored in tightly closed glass container and evaluated for following parameters.

Evaluation of prepared tablets

Compressed tablets were then evaluated for shape, diameter and thickness, weight variation, disintegration, hardness, friability study. Diameter and thickness were measured by using Vernier Caliper. Hardness was measured by Monsanto type hardness tester. Friability was determined in friabilator (Electrolab EF-2, USP). For disintegration test, one tablet was placed in each tube of disintegration apparatus (Electrolab ED-2L, USP) and the test was carried out using distilled water as a disintegrating media.

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In-vitro dissolution study

In vitro dissolution studies of prepared tablets were performed using USP apparatus type II (Electrolab TDT-08L) at 50rpm in pH 7.8 phosphate buffer (900ml) medium at the temperature $37^0C \pm 0.5^0C$. At specified intervals, 5ml of samples were withdrawn and filtered through Whatmann filter paper No.41. From this filtrate 1ml was withdrawn in to 10 ml volumetric flask and the volume was made up to the mark. After removal of each sample, 5 ml of fresh dissolution medium was added to the vessel to maintain the constant volume. The samples were then analyzed at 249 nm by UV-visible spectrophotometer (Shimadzu UV 1700). The amount of drug released was determined by reference to a calibration curve constructed in the three sets of same dissolution media. The mean of three determinations was used for the data analysis.

Stability studies

The stability of the formulated tablets of Mussaenda mucilage was tested according to International Conference on Harmonization guidelines. It was carried out, on the storage of formulated mucilage tablets at room temperature, 40^0 and 5^0 for 4 weeks. Tablets were withdrawn at the end of 4 weeks and evaluated for change in hardness, disintegration and in-vitro drug release.

RESULTS

Phytochemical analysis

The presence of carbohydrate and mucilage was substantiated with the positive result upon the treatment with Molisch's Test (formation of purple color) and Ruthenium red test (formation of pink color on powdered particles), respectively.

Physicochemical properties

Table-1 shows some physicochemical parameters of the extracted mucilage. The extracted mucilage is slightly soluble in water and a dispersion of it yielded a brown, slimy solution and it was practically insoluble in ethanol, acetone and chloroform. A 1% w/v suspension of mussaenda mucilage in water gave a pH of 6.9; the near neutral pH of mucilage implies that when used in uncoated tablets, it may be less irritating to GIT. The weight loss on drying indicates the amount of moisture present in the material available to interact with other material. For the dried mucilage, the loss on drying was 5.68%. The swelling index of ratio of mucilage, determined in distilled water, was 35. The density and viscosity was found to be $1.27 gm/cm^3$ and 9.1 mPa respectively.

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Drug-excipient compatibility study

The FTIR spectra of the mixture of drug and mucilage revealed that there was no major physical and chemical interaction between the drug and mucilage.

Formulation and evaluation of tablets

After studying the chemical-chemical interaction the mucilage was selected as tablet binder in the formulation of Paracetamol tablets, and the tablets were formulated with various percentages of this mucilage. The standard binder starch paste was also used for the comparison study (Table-2).

The physical tests for all the formulated tablets were shown in Table-3. All the batches of tablets exhibited the diameter and thickness, uniformity in weight, hardness and friability values were within the pharmacopoeial limits. The mucilage had given increase in disintegration time with increase in concentration. At 10% concentration of Mussaenda mucilage, the disintegration time was higher for the tablets prepared by using 10% starch.

In-vitro release study

The in-vitro dissolution profile of with different concentrations of Mussaenda mucilage and Starch paste is shown in Figure 1&2. It was found that, the rate of release from the tablets prepared using Mussaenda mucilage at 1% concentration was more than 90% in 4 h. The mucilage had given a decreased release rate with increase in concentration. The % cumulative release of the formulated tablets is shown in Table-4.

Stability studies

In order to determine any change on storage, stability of the formulated tablets was carried out at room temperature, 40^0 and 5^0 for 4 weeks. Tablets were withdrawn at the end of 4^{th} week and evaluated for change in hardness, disintegration and in-vitro drug release study. An appreciable change in the hardness, friability and in-vitro drug release from the formulated tablets was not observed after the stability study.

DISCUSSIONS

The natural mucilage from the plant *Mussaenda frondosa* were extracted by maceration using water followed by precipitation method. The phyto-chemical analysis of the extracted mucilage was confirmed for the presence of carbohydrates and mucilages from the Molisch's test and Ruthenium red test respectively. The various physicochemical properties of extracted mucilages were carried out such as the weight loss on drying, solubility, pH, swelling index, density and viscosity and found out that the mucilage shows the physicochemical properties with in the Pharmacopoeial limits. The drug excipient compatibility study was carried out to determine the possible chemical interactions between the active ingredient and the carrier. It

was done with the aid of FTIR spectroscopic methods. It was confirmed that there is an absence of chemical interaction between the selected drug and extracted excipient.

The tablets were formulated by wet granulation technique. The prepared tablets were evaluated for weight variation, hardness, friability, disintegration and in-vitro dissolution tests to determine effect of concentrations of the extracted mucilage. From these studies it was determined the effect of suitable concentration of the mucilages, and are compared to the tablets formulated by the standard binder. The in-vitro dissolution studies shows the effect of concentration levels of Mussaenda and it was shown the optimum release rate at low concentration level itself than compared to standard binder. Overall, the formulation M5 containing 1% w/w of Mussaenda mucilage was found to be promising and has shown the drug release rate from the tablets was more than 90% in 4 h. It was observed that, the mucilage may be used as binding agent in tablet formulations and the mucilage 1% w/w can be used for the preparation of uncoated tablets. This mucilage can be used for sustaining the drug release from tablets by increasing the concentration level, since the prepared tablets produced a sticky film of hydration on the surface, which ultimately reduces drug release rate. An appreciable change in hardness, friability and in-vitro release study was not observed after the stability study.

Finally, it can be concluded that the mucilage of *Mussaenda frondosa* can be used in low concentration as a binder in comparison with standard binder. The results suggested that Mussaenda mucilage could be a potential binder in low concentration level and can be revealed for further studies in the efficacy to formulate sustain release systems.

CONCLUSION

From the present investigation, it can be concluded that the mucilage of Mussaenda mucilage can be used in low concentration as a binder in comparison with standard binder. The results suggested that Mussaenda mucilage could be a potential binder in low concentration level and can be revealed for further studies in the efficacy to formulate sustain release systems.

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Table: 1 – Results of Physicochemical characterization of mucilage of Mussaenda:

Sl. No	Parameter	Observation
1	Solubility	Slightly soluble in water, practically insoluble in alcohol, chloroform and acetone. It forms a thick gel in water.
2	pH	6.9
3	Swelling index	35
4	Loss on drying	5.68%
5	Density	1.27gm/cm^3
6	Viscosity	9.1 mPa

Table: 2- Paracetamol tablet formulations containing Mussaenda mucilage used the as binder

SL No	Ingredients	PRODUCT CODE				
		M1 10%	**M2 8%**	**M3 5%**	**M4 2%**	**M5 1%**
1	Paracetamol IP	250 mg	250 mg	250 mg	250 mg	250 mg
2	Mussaenda mucilage	45.0 mg	36.0 mg	22.5 mg	9.0 mg	4.5 mg
3	Lactose	98.5 mg	107.5 mg	12.0 mg	134.5 mg	139.0 mg
4	Starch (8%)	36.5 mg	36.5 mg	36.5 mg	36.5 mg	36.5 mg
5	Talc	10 mg	10 mg	10 mg	10 mg	10 mg
6	Magnesium stearate	10 mg	10 mg	10 mg	10 mg	10 mg
	Total weight of tablet	450mg	450mg	450mg	450mg	450mg

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Table: 3- Paracetamol tablet formulations containing Standard binder (Starch paste) used the as binder

SL No	Ingredients	PRODUCT CODE				
		S1 10%	S2 8%	S3 5%	S4 2%	S5 1%
1	Paracetamol IP	250 mg	250 mg	250 mg	250 mg	250 mg
2	Starch paste	45.0 mg	36.0 mg	22.5 mg	9.0 mg	4.5 mg
3	Lactose	98.5 mg	107.5 mg	12.0 mg	134.5 mg	139.0 mg
4	Starch (8%)	36.5 mg	36.5 mg	36.5 mg	36.5 mg	36.5 mg
5	Talc	10 mg	10 mg	10 mg	10 mg	10 mg
6	Magnesium stearate	10 mg	10 mg	10 mg	10 mg	10 mg
	Total weight of tablet	450mg	450mg	450mg	450mg	450mg

Table: 4 – Comparison of evaluation of formulated Paracetamol tablets using Mussaenda and starch binders (SD)

Formulations	Diameter (mm)	Thickness (mm)	Weight variation (mg)	Disintegration time (min)	Hardness (Kg/Cm^2)	Friability %± SD
M1	9±0.1132	4±0.1842	451.1±0.0173	40	4±3128	0.4±0.09
M2	9±0.1459	4±0.1739	453.5±0.0161	43	5±0.2750	0.2±0.27
M3	9±0.1382	4±0.0986	448.4±0.1831	35	4±0.1381	0.9±0.07
M4	9±0.1092	4±0.1582	452.1±0.0160	25	4±0.1792	0.1±0.51
M5	9±0.1473	4±0.1321	451.6±0.0151	30	3.5±0.2817	0.72±0.02

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S1	9±0.1528	4.1±0.1523	453.8±0.0173	19	5±0.0950	1.9±0.09
S2	9±0.0872	4.2±0.1655	452.1±0.0182	10	5±0.5110	1.3±0.08
S3	8±0.0890	4.1±0.1063	450.7±0.0154	15	4±0.5069	0.91±0.12
S4	8±0.1101	4.0±0.2921	449.8±0.0162	10	2±0.2615	0.5±0.05
S5	9±0.1213	4.1±0.1810	445.1±0.0131	10	2±0.3810	0.42±0.01

Table: 5– Comparative effects of different concentration levels of Mussaenda mucilage used as the binding agents on the release rate of Paracetamol tablets

Time in hours	M5 (1%)	M4 (2%)	M3 (5%)	M2 (8%)	M1 (10%)
1	68.04	40.536	23.184	16.416	8.712
2	79.776	53.280	34.416	18.36	15.192
3	85.176	64.728	50.328	21.024	21.384
4	94.248	76.896	61.488	21.528	23.976

Table: 6 – Comparative effects of different concentration levels of Standard binder used as the binding agents on the release rate of Paracetamol tablets

Time in hours	S5 (1%)	S4 (2%)	S3 (5%)	S2 (8%)	S1 (10%)
1	67.536	73.224	73.44	58.752	75.312
2	78.912	90.936	90.504	74.016	80.136
3	88.2	92.952	91.296	82.944	88.632
4	90.792	88.392	92.088	89.856	91.8

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Fig 1: Dissolution profile of Paracetamol tablets made with different concentrations of Mussaenda mucilage

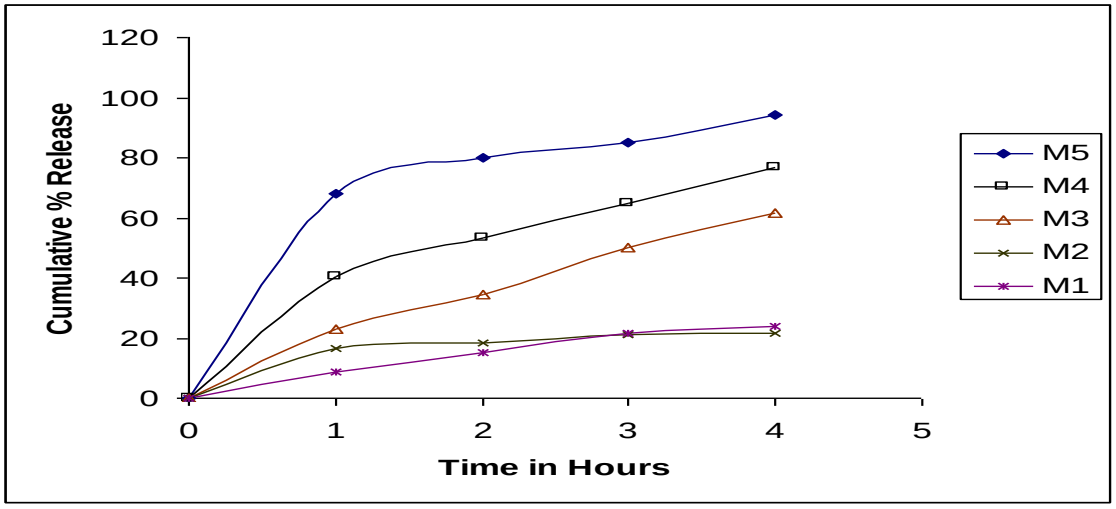
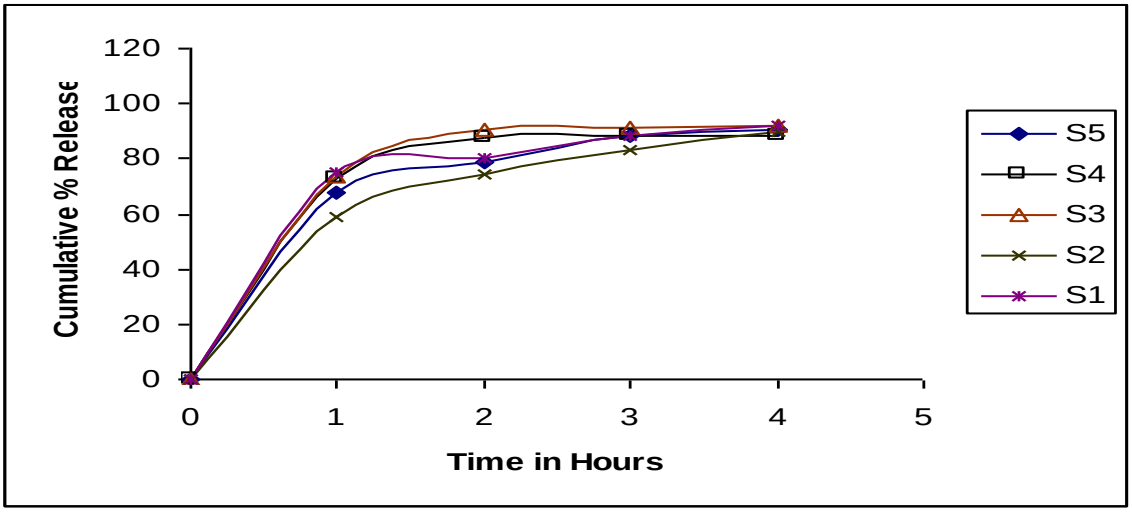


Fig 2: Dissolution profile of Paracetamol tablets made with different concentrations of Starch paste



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