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Isolation and Characterization of Mucilage from *Tinospora cordifolia* as Tablet Binder and Release Modifier

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ABSTRACT

Natural polymers play a very important role in various pharmaceutical formulations. They are effortlessly accessible, low cost, biodegradable, non-poisonous, non-irritating and may be considered as pharmaceutical excipients. Nowadays investigation is ongoing for finding natural gums and mucilage for diversity of reasons including use in pharmaceutical formulations. The present study is focused on the isolation of mucilage from *Tinospora cordifolia* and characterization for use as pharmaceutical binder and release modifier. The tablets were prepared by wet granulation process using four different compositions of mucilage (1%, 2.5%, 5%, 10% w/w) alone and in combination with potato starch (10% w/w). The tablets were characterized for pre and post pressure parameters, like, angle of repose, tapped density, bulk density, Carr's index, Hausner's ratio, friability and hardness, variation of weight, disintegration time, content uniformity and studies of *in vitro* drug release. It was found that release of drug from the tablet decreased (3 and 5 h) with increase in concentration of mucilage (5 and 10% w/w) and found sustained release of drug from the tablet for more than 6 hours at higher concentration of mucilage combined with starch (10% w/w). The result shows the potentials of *Tinospora cardifolia* mucilage for use as binder for the preparation of uncoated tablet and for sustained release drug formulation.

Keywords: *Tinospora cordifolia*, Mucilage, Tablet binder, Release modifier.

Introduction

Binders are pharmaceutical excipients that are consistently employed for formulation of tablet to impact cohesion on powder mix and improve the flow properties of the granules.[1] The working mechanism of binders in pharmaceutical formulation is to cause agglomeration of powder thereby forming granules by the process of granulation. The binder modifies the properties of the granules by promoting the formation of strong cohesive bonds between such particles.[2] A major investigation on natural excipients for drug delivery system utilizes proteins and polysaccharides, due to their ability to act in a broad range of materials and their properties of alterations of molecular structure.[3] Polysaccharide hydrocolloids including mucilage, gums and glucans are abundant in nature and consistently found in several higher plants. These polysaccharides are structurally different classes of biological macromolecules with broad range of applications in pharmaceutical and medical sciences.[4] Plant mucilage are pharmaceutically suitable polysaccharide with a wide range of applications, such as thickening, binding, disintegrating, emulsifying, stabilizing, suspending and gelling agents.[5]
They are also used as materials for sustained and controlled release of drug. These polymers are well known as natural gums. Mucilage are biocompatible, economical and easily available, they are best likened to semi-synthetic excipients because of their less toxicity, low cost, availability, emollient and non-irritant nature.[5,6] The synthetic polymers have certain disadvantages, such as high cost, toxicity, environmental pollution during synthesis, non-renewable sources, side effects, less patient compliance, etc.[7] *Tinospora cordifolia* (Figure 1) commonly called heart-leaved moonseed in English, Guduchi or Giloy in Hindi and Gulancha in Bengali belongs to the family Menispermaceae. It is a genetically disparate, large, deciduous climbing shrub with greenish yellow typical flowers, found at higher altitude.[8-10] Recently, the plant is of great interest to researchers across the world due to its medicinal properties like anti-diabetic, anti-inflammatory, anti-oxidant, anti-allergic, anti-malarial, anti-periodic, anti-spasmodic, anti-arthritic, anti-stress, immunomodulatory, hepatoprotective and anti-neoplastic activities.[11] In the present study, an extraction was made for mucilage from the stems of *T. cordifolia* and investigated for the possibility of use as binder and release modifying material in the formulation of drug in solid dosage forms. Diclofenac sodium, a Non-steroidal Anti-inflammatory Drug (NSAID) which is commonly used in the management of pain of various etiologies.[12]

Materials and Methods

Plant Material
The stems of *Tinospora cordifolia* were collected from Khagrachari district, the hill tract region at Chittagong division in Bangladesh and authenticated by Dr. Shaikh Bokhtear Uddin, Associate Professor, Department of Botany, University of Chittagong, Bangladesh. A voucher specimen was deposited (Accession No. 15327) at the herbarium in the Department of Botany, University of Chittagong, Bangladesh.

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Figure 1: *Tinospora cardifolia*

Drug and Chemicals
Diclofenac sodium was obtained from Incepta Pharmaceutical Limited, Dhaka, Bangladesh as gift sample. All the other materials, such as Potato Starch, Lactose, Microcrystalline Cellulose (MCC), Talc and Magnesium stearate were of pharmaceutical grade and were purchased from Taj Chemical Store, Chittagong, Bangladesh.

Separation of Mucilage
An established method previously described by Malviya, 2011[13] was followed for the isolation of mucilage from the stems of *Tinospora cordifolia* with minor modifications as described below.

Step 1: Extraction of Mucilage
The collected stems of *Tinospora cordifolia* were washed with tap water to remove adhering dirt and sun-dried. The dried stems were crushed using a mechanical grinder. The powdered stem (100 g) was macerated in warm (~50˚C) distilled water (300 mL) for 4 h, boiled for 2 h and allowed to stand for another 2 h to release the mucilage into water. The macerate was transferred into a muslin bag and filtered to obtain 150 mL of the filtrate.

Step 2: Isolation of Mucilage
Acetone (450 mL) was added to the filtrate (150 mL) that was collected from the previous step. Due to insolubility of mucilage in acetone, the mucilage was separated by precipitation from the solution. The precipitated mucilage was filtered and dried in an oven at 40°C.

The dried mucilage was grounded and passed through an 80-meshsieve. The sieved mucilage (9.85 g) was stored in a desiccator until further use.

Physicochemical Characterization of Isolated Mucilage
Chemical Characterization: Aqueous solution of the isolated mucilage was used for chemical characterization. Carbohydrates, proteins, mucilage, gums, alkaloids, fats and tannins were tested according to standard procedure.[14]

Solubility: Solubility of the dried mucilage was determined by shaking in different solvents.[14]

Organoleptic Evaluation: The isolated mucilage was assessed for organoleptic properties like, colour, odour, taste and texture.[14]

pH: The pH of the mucilage (1% w/v solution in water) was determined using a pH meter (microprocessor pH meter, model 211).[14]

Swelling Index: The swelling index is the volume in milliliter occupied by 1 g of a test material in an aqueous liquid under specific condition. The swelling index of the mucilage was determined by accurately weighing 1 g of mucilage into a 25 mL glass-stoppered measuring cylinder. Distilled water (25 mL) was added into the cylinder and shaken thoroughly every 10 minutes for 1 h. Then it was allowed to stand for 3h at room temperature. The increased volume of water which was occupied by the swelled mucilage was measured. The procedure was repeated another twice and the mean value calculated.[14]

Evaluation of Binding Properties of Mucilage
Preparation and Evaluation of Granules
The properties of granules and binding in tablets formed using mucilage isolated from *T. cordifolia* stem were evaluated using diclofenac sodium as the test drug. Granules were prepared using different concentrations of mucilage (1%, 2.5%, 5% and 10% w/w) alone and in combination with potato starch (10% w/w) by the wet granulation technique (Table 1).[15] The granules were evaluated for tapped density, bulk density, Hausner's ratio, Carr's index and Angle of Repose.[15]

Fabrication and Evaluation of Tablets
The dried granules were compressed by using single punch machine. The prepared tablets were evaluated for different parameters including average weight variation, hardness, friability, drug content, disintegration time and *in vitro* drug release.[16]

Table 1: Formulation compositions of *Tinospora cordifolia* mucilage tablets.

Ingredient	Formulation (mg)								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Diclofenac sodium	50	50	50	50	50	50	50	50	50
Mucilage	2.5 (1%)	6.75 (2.5%)	12.5 (5%)	25 (10%)	2.5 (1%)	6.75 (2.5%)	12.5 (5%)	25 (10%)	-
Starch	-	-	-	-	25 (10%)	25 (10%)	25 (10%)	25 (10%)	25 (10%)
Lactose	167.5	163.25	157.5	145	142.5	138.25	132.5	120	145
Na-starch glycolate	25	25	25	25	25	25	25	25	25
Talc	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Mg-sterate	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Tablet wt.	250	250	250	250	250	250	250	250	250

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Results and Discussion

Physicochemical Characterization

Phytochemical investigations of the isolated mucilage from *T. cordifolia* stem showed positive test with Ruthenium red and Molisch's test which indicated the presence of mucilage and carbohydrate while gum, tannin, alkaloids, glycoside and flavonoids were absent (Table 2). The solubility experiment showed neutral colloidal solution when dissolved in water at room temperature, a thick solution when dissolved in warm water, and was practically insoluble in all the organic solvents used (Table 3). The morphological and physical evaluation studies showed an odourless brownish powder with characteristic taste and had irregular texture and luster in nature. The pH of the mucilage was 6.3, swelling index 15.6%, moisture content 8.76% and yield 9.85% (Table 4). Due to the near neutrality of the pH value, it may be less irritating in gastrointestinal tract and hence suitable for uncoated tablets.[17,18]

Pre-compression Evaluation

The prepared granules were evaluated for various pre-compession parameters which include bulk density, tapped density, Carr's index, Hausner's ratio and Angle of repose. Results of the pre-compression parameters performed are shown in Table 5. The bulk density and tapped density for all formulations was found in the range of 0.29 ± 0.01 to 0.54 ± 0.01 g/cm^3 and 0.31 ± 0.01 to 0.63 ± 0.01 g/cm^3, respectively. Carr's index lies within the range of 8.50 ± 1.78 to 15.28±2.89 and Hausner's ratio was noted to be in the range of 1.05 ± 0.10 to 1.18±0.04 which indicate good flow ability of all the formulations.[3] The value of the angle of repose lies within the range of 25.23°± 0.25 to 30.00°± 0.20. Almost all the formulations showed angle of repose below 30° which is an indication of a good flow property of the granules.[17,19]

Post-compression Evaluations

The physical attributes of the tablets were found to be satisfactory. Typical tablets defects, such as capping, chipping and picking were not observed. All the diclofenac tablet formulations were tested for their physical parameters, like, weight variation, hardness, friability, content uniformity and disintegration time. Results for the post-compression parameters were found within acceptable ranges (Table 6).[19] Average weight variation for all formulations was from 244.8 mg to 259.00 mg. Hardness was found to be from 2.50±0.50 (F1) to 7.00 ± 0.50 (F8). The friability values of the prepared tablets were from 0.12 ± 0.02 (F8) to 0.70 ± 0.02 (F1). The friability value which was below 1% for all formulation is indicative of good mechanical resistance of the tablets.[17,19] Disintegration time for all formulations ranges from 2.20 ± 0.10 (F1) to 13.30 ± 1.20 (F8) minutes. The results of the present study showed that tablets formulated with mucilage (5% and 10% w/w) had increased hardness and disintegration time and decreased friability of tablets with increased mucilage concentration (5 and 10% w/w) alone or with starch (10% w/w). All the tablets in each batch exhibited uniformity in drug content with good disintegration time.

Table 2: Phytochemical screening of isolated mucilage.

Tests	Inference
Carbohydrates	+
Tannins	-
Alkaloids	-
Glycosides	-
Flavonoids	-
Reducing sugar	-
Protein	-
Mucilage	+

Note: '+' sign indicates Present and '–' sign indicates absent

Table 3: Solubility profile of isolated mucilage.

Solvents	Solubility
Water	Soluble (Colloidal solution)
Hot water	Soluble (Thicky solution)
Methanol	Insoluble
Ethanol	Insoluble
Acetone	Insoluble
n-Hexan	Insoluble

Table 4: Organoleptic and other properties of isolated mucilage.

Parameters	Result
Colour	Brownish
Odour	Odourless
Taste	Characteristic
Texture	Irregular
Yield	9.85%
pH	6.3
Swelling Index	15.6
Moisture content	8.76

Table 5: Pre-compression parameters of designed batches (F1-F9).

FC	Bulk Density (g/cm^3)	Tapped Density (g/cm^3)	Carr's Index (%)	Hausner's Ratio	Angle of Repose (°)
F1	0.29 ± 0.01	0.31 ± 0.01	8.50 ± 1.78	1.05 ± 0.10	26.63 ± 0.23
F2	0.33 ± 0.02	0.37 ± 0.015	9.88 ± 1.16	1.09 ± 0.03	25.23 ± 0.25
F3	0.36 ± 0.01	0.41 ± 0.015	12.24 ± 1.86	1.14 ± 0.02	28.43 ± 0.45
F4	0.43 ± 0.02	0.50 ± 0.02	14.69 ± 1.48	1.17 ± 0.02	26.30 ± 0.20
F5	0.37 ± 0.0	0.44 ± 0.015	15.19 ± 1.70	1.18 ± 0.03	29.30 ± 0.26
F6	0.43 ± 0.01	0.50 ± 0.01	14.58 ± 1.24	1.17 ± 0.02	28.40 ± 0.10
F7	0.45 ± 0.02	0.51 ± 0.015	14.04 ± 1.45	1.14 ± 0.05	29.57 ± 0.31
F8	0.54 ± 0.01	0.63 ± 0.01	13.22 ± 0.74	1.15 ± 0.01	30.10 ± 0.2
F9	0.37 ± 0.02	0.44 ± 0.01	15.28 ± 0.2.89	1.18 ± 0.04	27.10 ± 0.2

Note: All data represent Mean ± SD.

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Table 6: Post-compression parameters of designed batches (F1-F9).

FC	Average Weight (mg)	Hardness (kg/cm^2)	Friability (%)	Content uniformity (%)	DT (min.)
F1	244.80 ± 2.58	2.50 ± 0.50	0.70 ± 0.02	94.44 ± 0.81	2.20 ± 0.10
F2	253.40 ± 2.67	3.00 ± 0.50	0.65 ± 0.02	95.24 ± 0.88	3.23 ± 0.25
F3	251.55 ± 1.64	4.33 ± 0.29	0.47 ± 0.03	97.88 ± 1.65	4.10 ± 0.53
F4	258.5 ± 2.04	5.33 ± 0.58	0.25 ± 0.02	95.65 ± 0.65	4.83 ± 0.29
F5	241.40 ± 2.09	3.67 ± 0.29	0.53 ± 0.02	93.69 ± 1.21	3.77 ± 0.59
F6	245.50 ± 4.05	4.00 ± 0.50	0.33 ± 0.02	97.79 ± 0.75	6.83 ± 0.74
F7	253.80 ± 3.26	6.33 ± 0.29	0.21 ± 0.01	96.11 ± 0.51	9.57 ± 0.76
F8	259.00 ± 3.26	7.00 ± 0.50	0.12 ± 0.02	97.80 ± 1.20	13.30 ± 1.20
F9	239.30 ± 3.26	3.17 ± 0.29	0.55 ± 0.02	96.55 ± 1.26	4.03 ± 0.50

Note: All data represent Mean ± SD

Table 7: *In vitro* percentage of drug release study.

Time (min.)	Formulation								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
15	12.67	10.48	10.91	8.54	8.98	6.83	6.3	4.15	17.72
30	48.01	38.39	33.57	26.54	31.37	14.25	16.93	12.23	31.32
60	100	67.77	48.01	43.25	52.54	26.54	30.94	21.24	74
120		100	74.35	63.38	80.94	43.4	48.89	33.61	100
180			100	80.93	100	60.74	66.45	43.18	
240				91.25		75.76	83.13	62.06	
300				100		100	92.35	76.55	
360							98.5	89.15	

In vitro drug release study

The i*n vitro* drug release is shown in Table 7. This indicated that 100% drug release was observed from the tablets prepared using low concentration of mucilage (1 and 2.5% w/w) within 1 and 2 h. The mucilage showed a decreased release rate with increased concentration of mucilage. Release of drug was 100% at higher mucilage concentration (5 and 10% w/w) for 3 and 5 h, respectively. It was also found that at higher concentration of mucilage (5 and 10% w/w) in combination with starch (10% w/w) exhibited sustained release of drug from the tablets for more than 6 h. These tablets have shown less diffusion of drug by producing hydrated sticky film on the surface of tablets. This may be the reason for the reduced dissolution with increased mucilage concentration.

Conclusion

The mucilage of *Tinospora cordifolia* stem used in the present study has been shown to be a good binder and drug release modifier combined with potato starch. Due to the non-irritating nature of the mucilage, and its ability to form a sticky film of hydration on tablet surface, it could also be used for the preparation of uncoated tablets and for sustained drug release tablets.

Conflict of interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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