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Isolation and Characterization of Mucilage from Hibiscus rosa sinensis as Tablet Binder and Release Modifier.

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1. 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 gives the information about Hibiscus rosa sinensis. Various plant gums had been used in the development of pharmaceutical formulations among them the gum obtained from the Hibiscus has its own identity in pharmaceutical and pharmacological world . Therefore, Diclofenac sodium tablets were formulated by employing Hibiscus rosa sinensis mucilage as a natural polymer to sustain the drug release from matrix system .The tablets were prepared by wet granulation process using different composition of mucilage with potato starch. The tablets were characterized for pre and post pressure parameters like, angle of response, tapped density, bulk density ,Carr's index , Hauser's ratio ,friability and hardness, variation of weight, disintegration time, content uniformity and study of in-vitro drug release .The result shows the potential of Hibiscus rosa sinensis mucilage for use as binder for the preparation of uncoated tablet and for sustained release of drug formulation.

Keywords : Hibiscus rosa sinensis, Mucilage, Disintegration, Macerate

2. Introduction

For health purpose more than three quarter of the world's population depends on plants. For the medicinal purpose more than 30% of total plant species are used. Leave, stems, bark, roots, flowers are the different organs of plant from which the drug is obtained. When plants are grown under the unfavorable condition or injured, then they produce gum and it is generally translucent and amorphous substance. These may be ionic and non-ionic polysaccharide and considered as plant hydrocolloids. The process from which the gum is produced is known as gummosis. Plant gums and mucilage's are widely used in pharmaceutical preparation by the formulation of granules of desired hardness, strength, and size. Hibiscus rosa sinensis mucilage is

also used as disintegrate and super disintegrate in pharmaceutical preparations. For the sustained release matrix tablets. Hibiscus rosa sinensis mucilage is good swelling, good flow rate and suitability for matrix formulation. This mucilage used as a binder in various pharmaceutical tablets. It has a glossy dark green leaves with medium texture. It is most suitable plant. It is easily available all over India. They perform various pharmacological action and used in many pharmaceutical dosage form.

In present study, an extraction was made for mucilage from the Hibiscus and investigated for the possibility of use as binder and release modifying material in the formulation of drug in solid dosage form. Diclofenac sodium, a Non-steroidal Anti-inflammatory drug (NSAID) which is commonly used in the management of pain of various etiology. These drug are used frequently and commonly in humans as well as animals to mange pain, fever and inflammation for the treatment of different clinical condition such as rheumatic disorders, musculoskeletal disorders, sports injuries, muscular cramps and other syndromes involving pain and inflammation. This is also used to treat chronic pain associated with cancer. Solid dosage form like as Tablet is the self-administration, compactness and easy manufacturing sometimes immediate onset of action. Diclofenac Sodium that is effective in the management of mild-to moderate postoperative pain. In present study it gives the information of utility of plant Hibiscus rosa sinensis as pharmaceutical excipients for the development of various dosage form. And also concentrating on the pharmacological application of plant in various disease.

3. Plant and Drug Profile:

Plant :Hibiscus rosa sinensis

Fig. No.01(a), (b) Hibiscus rosa senensis plant

Taxonomy Of Hibiscus rosa sinensis

- Kingdom : Plantae
- Class : Magnoliopsida
- Order : Malvales
- Family : Malvaceae
- Genus : Hibiscus
- Species : Rosa-sinensis

4. Material and Methods

8.1 Material

- **Plant Material:**

The leaves and stem of Hibiscus rosa sinensis were collected.

- **Drug and Chemicals**:

SR. No.	Chemicals	Make
1	Diclofenac Sodium	Loba
2	Potato Starch	Roquette
3	Lactose	Loba
4	Talc	Loba
5	Magnesium Stearate	Loba
6	Acetone	Loba
7	Sodium Starch Glycol ate	Loba
8	Distilled water	Loba
9	Alcoholic α-napthol	Loba
10	Con.H_2SO_4	Loba
11	Fehling's reagent A and B	Loba
12	Lead acetate	Loba
13	Ruthenium red	Loba

Table No.01 List of Chemical.

Instruments:

Sr No.	Instruments / Equipments	Source
1.	Electronic Balance	Tapson
2.	Bath sonicator	Bio techniques India
3.	Magnetic Stirrer	Remi Equipment Pvt. Ltd.
4.	UV-Visible Spectrophotometer	UV-1900 Shimadzu, Japan.
5.	FTIR	Aglient
6.	Dissolution Test Apparatus	LABINDIA DS8000
7.	Friabilator	India Mart

8.	Monsanto hardness tester	Vinsyst VMT 1
9.	Vernier Caliper	Labpro

Table No.02 List of Instruments used in research.

8.2 Maceration

This is an extraction procedure in which coarsely powered drug material, either leaves or stem, bark or root bark, is placed inside a container the menstruum is poured on top until completely covered the drug material. The container is then closed and kept for at least three days.

Fig No.05 (a),(b),(c),(d) Maceration process

a) Separation of Mucilage :

The isolation of mucilage from the Hibiscus rosa sinensis using acetone was collected.

Step 1 : Extraction of Mucilage

1. The collected leaves of Hibiscus rosa sinensis were washed with tapped water to remove adhering dirt and sun-dried.
2. The dried leaves were crushed using a mechanical grinder.
3. The powdered leaves(500gm) was macerated in warm (~50˚) distilled water for 20 hours, boiled for 10 hours and allowed to stand for another 10 hours to release the mucilage into water.
4. The macerate was transferred into a muslin bag and filtrate to obtain.

Step 2: Isolation of Mucilage

1. Acetone is added to the filtrate that was collected from the previous step.
2. Due to insolubility of mucilage in acetone the mucilage was separated by precipitation from the solution.
3. The precipitated mucilage was filtered and dried in an oven at 40˚c.
4. The dried mucilage was grounded and passed through an 80 meshsieve.
5. The sieved mucilage was stored in a desiccators for further use.

Fig. No.06(a), (b) Isolation of plant Mucilage.

8.3 Physiochemical Characterization of Isolated Mucilage :

1. **Solubility** :

   Solubility of the dried mucilage was determined by shaking in different solvents.

2. **Organoleptic Evaluation** :

   The isolated mucilage was assessed for organoleptic properties like colour, odour,

   and texture.

3. **pH :** The pH of the Mucilage (1%w/v solution in water)was determined using a pH meter.
4. **Swelling Index :** Weigh accurately 1g of mucilage into 25ml glass –stoppered measuring cylinder. Distilled water (25ml) was added into the cylinder and shaken thoroughly every 10min for 1 hr.Then it was allowed to stand 3 hr. at room temperature.

Formula :

$$\text{Swelling Index} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

5. **Flow Properties :**

   The dried Hibicus rosa sinensis leaves mucilage was evaluated for the flow properties which includes :

i. Angle of repose :

The angle of repose is determined by the funnel method. The granules allowed to flow through the freely on to the surface. The diameter of the granules is measured and angle of repose is calculated using the following eqution:

$$\tan \theta = h/r \text{ or } \tan1(h/r)$$

ii. **Bulk density** :Bulk density (Db) is determined through measuring the volume (Vb) of known weighed quantity (W) of granules using bulk density apparatus.

$$D_b = W / V_b$$

iii. **Tapped density** : Tapped density (D_t) is calculated by measuring the volume (Vt) of known weighted quantity (W) of granules using bulk density apparatus and using the formula:

$$Dt = W / Vt$$

iv. **Hausner's index** :Is calculated by dividing the tapped density by the bulk density of granules.

$$\text{Hausner's index} = Dt / Db$$

v. **Carr's index**: That determine % of compressibility of the granules can be measured from the difference between the tapped and bulk densities divided by the tapped density and the ratio expressed as a percentage.

$$\text{Carr's Index} = (D_t - D_b)/Dt \times 100$$

8.4 Method of preparation of Hibiscus rosa sinensis tablet:

- **Dry granulation method**:

a. Using dry granulation method tablet will be formed.

b. The properties of granules and binding in tablets formed using mucilage isolated from Hibiscus rosa sinensis leaves evaluated using diclofenac sodium as the test drug.

c. The granules were prepared using different concentration of mucilage (2.5%,10%,1%,5%).

d. The mucilage combine with potato starch (10%w/w) by dry granulation technique .

e. The prepared powder was passed through sieve no.22 to from a granules.

f. The granules were compressed by using single punch machine.

Formulation :

Formulation in mg						
Sr.No.	**Ingredient**	**F1**	**F2**	**F3**	**F4**	**F5**
1	Diclofenac sodium	50	50	50	50	50
2	Mucilage	6.75(2.5%)	25(10%)	2.5(1%)	12.5(5%)	_
3	Starch	_	_	25(10%)	25(10%)	25(10%)
4	Lactose	163.25	145	142.5	132.5	145
5	Na –Starch glycolate	25	25	25	25	25
6	Talc	2.5	2.5	2.5	2.5	2.5
7	Mg-sterate	2.5	2.5	2.5	2.5	2.5
8	Tablet weight	250	250	250	250	250

Table No.03 Formulation composition of Hibiscus rosa sinensis mucilage tablets.

Hibiscus rosa sinensis

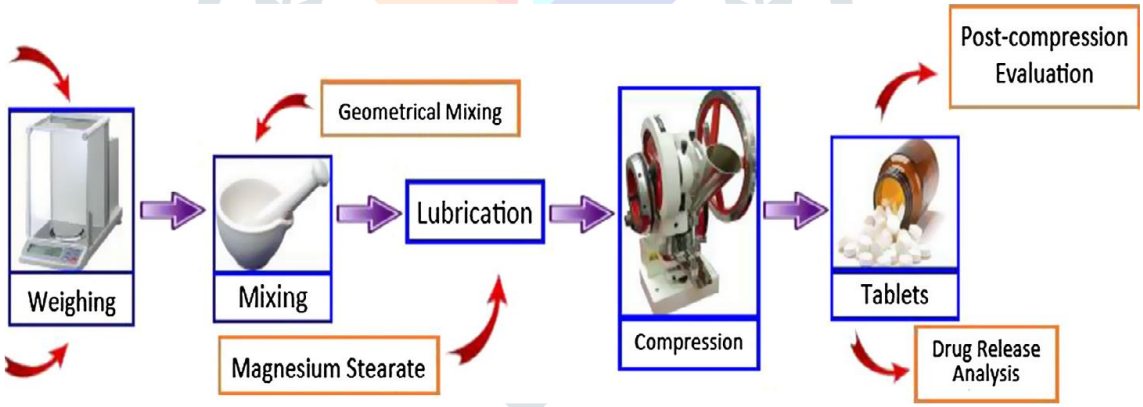

Fig.No.07 Preparation of Diclofenac sodium tablet.

Fig. No. 8 Diclofenac sodium tablet using Hibiscus Mucilage.

8.5 Evaluation of optimized Hibiscus tablet:

Physical appearance:

The tablets are visually observed for capping, chipping, lamination and changes in colour.

Tablet Thickness:

The thickness of the tablets can be determined by using vernier caliper. Five tablet are required, and average values are calculated.

Hardness:

The hardness of tablet is determined by using Monsanto hardness tester. It is expressed in kg/cm^2.

Weight variation:

Select randomly 20 tablets and weighted individually to check for weight variation.

Friability:

The friability of tablet is determined by using Roche Friabilator for 100 revolutions. The friabilator is operated at 25 rpm for4 min.The tablets are subject to combine effect of abrasion and shock in plastic chamber and dropping a tablet at height of 6 inch in each revolution.

$$\%Friability \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} 100$$

9.Result and Discussion

9.1 Physicochemical Characterization:

The phytochemicals investigation of isolated mucilage from Hibiscus rosa senensis leaves showed positive test with Ruthenium red and Molischs test which indicated the presence of mucilage and carbohydrate while tannin, alkaloids, glycoside,and flavonoids are absent.

Sr.No.	Test	Inference
1.	Carbohydrates	Present
2.	Tannins	Absent
3.	Alkaloids	Absent
4.	Glycosides	Absent
5.	Flavonoids	Absent
6.	Reducing sugar	Absent
7.	Mucilage	Present

Table No.04 Phytochemical screening of isolated Mucilage.

The isolated mucilage was soluble in NaoH and slightly soluble in water. Otherwise it was insoluble in other solvent like Methanol, Ethanol and Acetone.

Sr. No	Solvents	Solubility
1.	Water	Slightly Soluble
2.	NaoH	Soluble
3.	Methanol	Insoluble
4.	Ethanol	Insoluble
5.	Acetone	Insoluble

Table No.05 Solubility profile of Isolated Mucilage

Sr.no.	Parameters	Result
1.	Appearance	Brownish powder
2.	Odour	Characteristics
3.	Texture	Irregular
4.	Solubility	NaoH, Progressive Soluble in water forming viscous solution
5.	Yield	46.85g
6.	pH	6.90
7.	Swelling Index	66.17 -0.462%

Table No.06 Organoleptic and other properties of Isolated Mucilage.

9.2 Pre-compression Evaluation:

a) Flow Properties:

Dried Hibiscus rosa-sinensis leaves mucilage powder has an excellent flow properties based on Angle of repose ,Bulk density and Tapped density . Carr's index and Hausner's ratio values was excellent range of flowability. The mucilage now regarded very suitable to be used in tablet manufacturing.

Sr.No.	Flow properties	Observation
1.	Angle of repose (ɵ)	25.37±0.434
2.	Bulk density (g/cm^3)	0.75±0.014
3.	Tapped density (g/cm^3)	0.83±0.017
4.	Carr's index (%)	9.44±0.178
5.	Hausner's ratio	1.10±0.002

Table No.07 Mucilage flow properties.

b) UV-vis spectra analysis:

The UV spectrum of Hibiscus rosa sinensis shows weak absorption bands at 340nm and 325nm is due to aromatic nature of compound, α-β unsaturated ketones and aldehyde.

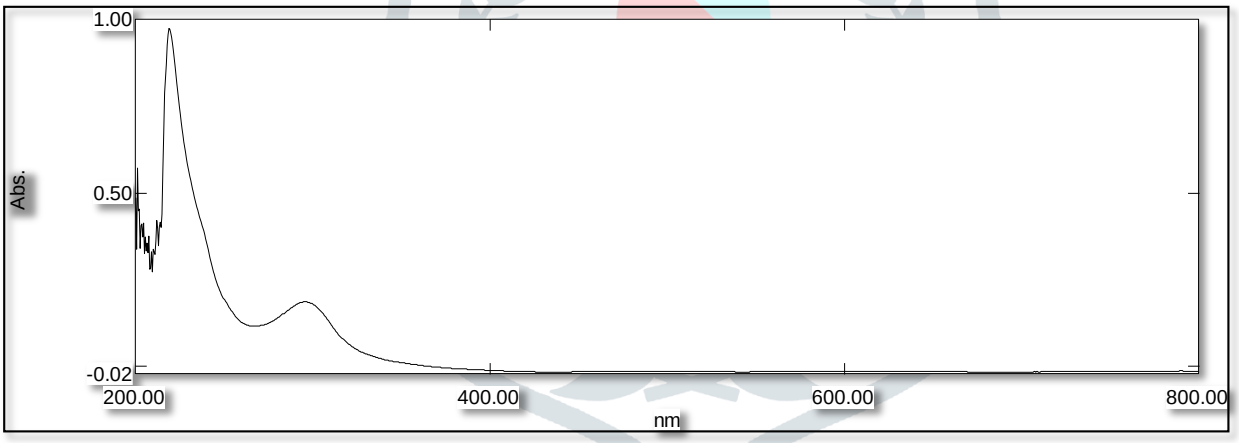

Fig. No.09 Determination of λ_{max} of Hibiscus rosa sinensis.

c) Fourier Tansform Infrared (FT-IR) spectral studies:

FTIR spectroscopy was used to characterize the functional groups in Hibiscus mucilage.

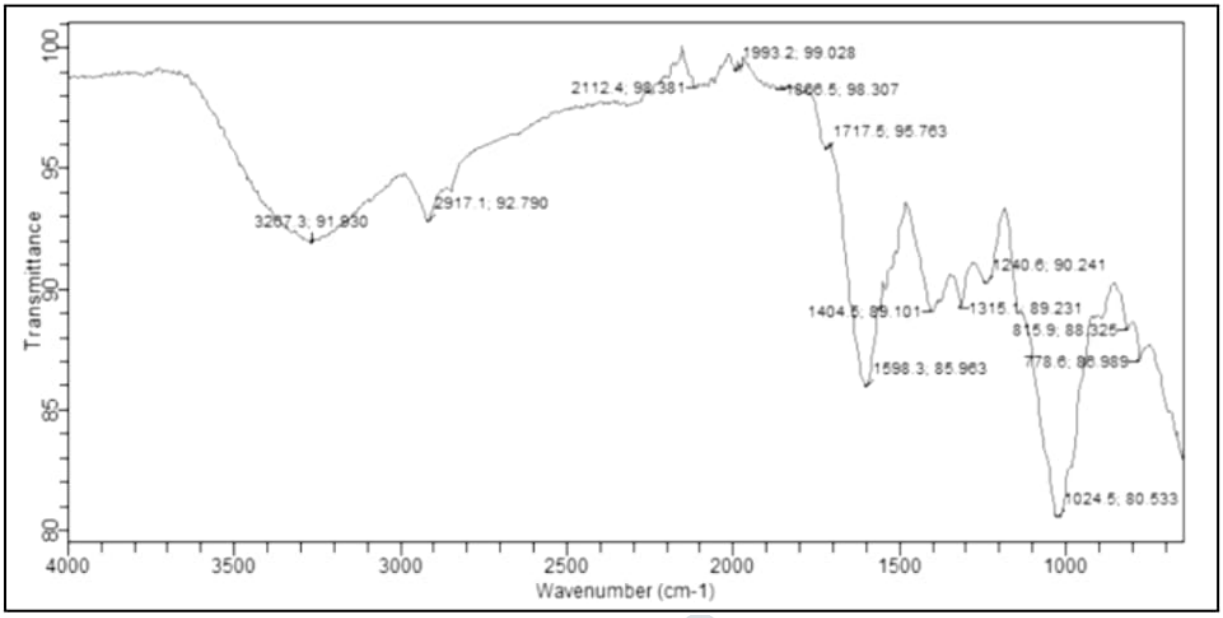

Fig. No.10 FTIR spectra of the isolated Hibiscus rosa sinensis Mucilage.

Sr. No.	Peak(frequency) cm^{-1}	Functional group
1.	3267.3	Alcohol O-H stretch
2.	2917.1	Alkyl C-H stretch
3.	2319.3	C-H stretch
4.	2112.4	Alkynyl C=C stretch
5.	1598.3	Aromatic C=C bending
6.	1404.5	C-H bend
7.	1315.1	C-H rock
8.	1240.6	C-O bend, aromatic
9.	1024.5	C-O stretch

Table No.08 Functional groups Present in Hibiscus Mucilage .

9.3 Post-compression Evaluations:

The physical attribute of the tablets was found to be satisfactory. All the Diclofenac tablet formulations was tested for their physical parameters, like weight variation, hardness, friability, thickness and disintegration time.

FC	Average weight(mg)	Hardness(kg/cm^2)	Thickness(mm)	Friability (%)	DT (min.)
F1	493.80±2.50	4.2±0.30	4.88±0.03	0.70±0.02	3.23±0.25
F2	498.40±1.64	5.00±0.20	4.84±0.06	0.25±0.02	4.83±0.29
F3	495.5±2.66	4.2±0.29	4.80±0.04	0.53±0.03	3.59±0.76

F4	498.2±1.23	4.00±0.50	4.85±0.02	0.23±0.02	9.57±0.77
F5	496.54±3.22	3.20±0.32	4.79±0.04	0.55±0.02	4.08±0.50

Table No.0 9 Post-compression parameters of designed batches.

a)In vitro drug release study:

The in vitro drug release study was indicated that 100% drug release was observed from the tablets prepared using low concentration of mucilage(1 and 2.5%w/w) within 1 to 2 h. The mucilage showed a decreased release rate with increased concentration of mucilage. Release of 100% at higher mucilage concentration (5and 10%w/w) for 4 to 5 h, respectively. It was also found that higher concentration of mucilage (5%w/w) in combination with starch (10%w/w) sustained release of drug from the tablet more than 5 h.

Time(min)	**Formulation**			
	F1	**F2**	**F3**	**F4**
15	11.48	9.55	7.9	12.75
30	40.50	30.54	18.93	31.12
60	69.20	45.23	31.22	75
120	100	66.85	49.56	100
180		81.50	67.54	
240		91.63	84.15	
300		100	91.20	
360			97.6	

Table No.10 In Vitro percentage of drug release study.

10. Conclusion:

The mucilage of Hibiscus rosa sinensis used in present study. It shows a good binder and drug release modifier. Due to the non-irritating nature of mucilage, and it is ability to form a sticky film of hydration of tablet surface. Its also used for the preparation of uncoated tablet and for sustained drug release tablet.

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