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Utilization of *Lawsonia Inermis* Mucilage as a Novel Binder in Conventional Tablet Dosage Form

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ABSTRACT

The study was involved to formulate oral tablet dosage form of diclofenac sodium using mucilage extracted from the *Lawsonia inermis* as a binder. Purified extracted mucilage was subjected to physicochemical characterization and four formulations each containing 100mg of Diclofenac sodium were prepared by wet granulation method using different mucilage concentrations viz. 2.5, 5, 7.5 & 10 % w/w. Lactose was used as diluent while magnesium stearate and talc were employed as lubricant and glidant respectively. The prepared formulations were evaluated for pre-compression parameters like angle of repose, bulk density, tapped density, hausner's index and carr's index for granules while tablets were evaluated for various post-compression parameters like tablet thickness, hardness, weight variation, friability, content uniformity, disintegration time, and in-vitro drug release study. Pre-compression and post-compression evaluation showed that parameters evaluated were all found to be within the pharmacopoeial limits. Among all the formulations, L-3 and L-4 showed an optimum drug release of 94.16 % and 91.90 % over the period of 60 min respectively and thereby exhibited satisfactory drug release phenomenon for conventional oral tablets of Diclofenac sodium.

Keywords: Diclofenac sodium, *Lawsonia inermis*, Mucilage, Binder, Conventional

1. INTRODUCTION

India is gifted with great abundant variety of flora and fauna. Today, the whole world is increasingly interested in natural drugs and excipients. Natural materials have advantages over synthetic materials because they are non-toxic, less expensive and freely available. Various gums like gelatin, acacia, alginic acid, guar gum, maize starch, and potato starch have been used as binder in pharmaceutical formulations. Finding novel binder however still is useful in the pharmaceutical industry for manufacture of tablets[1]. Binders are agents used to impart cohesive qualities to the powdered material during the production of tablets. Most commonly used binders are natural and synthetic gums. A number of plant gums or mucilage's have been used as binding agents in tablet formulations. Gums are non-toxic and there wide availability has made them of continuing interest. They impart cohesiveness to the tablet formulation, which ensures that the tablet remains intact after compression as well as improving the free flowing quality. Binders have been used as solutions and in dry form, depending on the other ingredients in the formulations and the method of preparation[1-3]. Oral route of drug administration is the most appealing, convenient, significant and popular route for the delivery of drugs owing to ease of swallowing, self medication, and most economic. Tablets are the most popular and preferred oral formulation available in the market because of its ease of manufacturing, convenience in administration, accurate dosing, stability compared with oral liquids and because it is more tamperproof than capsules [4-7].

Natural polymers are growing rapidly and it continues to remain and important in the new formulation development. In addition Natural polymers are much safer than synthetic. They provide many applications in the formulation development of dosage form, such as binder, disintegrator, diluents and release modifier. Therefore, it is a novel approach to enhance the use of natural polymers in the formulation development of dosage form, because of the ease availability at an affordable price, high safety margin and higher productivity. *Lawsonia inermis* mucilage is obtained from the freshly collected leaves of plant belongs to family Lythraceae. The study was undertaken to evaluate the binding potential of mucilage extracted from the *Lawsonia inermis* in the formulation of Diclofenac sodium oral tablet dosage form.

2. MATERIALS AND METHODS

2.1 Materials

Diclofenac sodium was purchased from Yarrow Chem Products, Mumbai, India. *Lawsonia inermis* leaves were collected from nearby locality and plant sample was authenticated from Botanical Survey of India, Dehradun, Uttarakhand (India). All the other chemicals used were of analytical grade and were also purchased from Central Drug House, New Delhi, India.

2.2 Extraction and Purification of *Lawsonia inermis* mucilage[8-10]

Extraction of mucilage from the leaves of *Lawsonia inermis* was carried out by a hot maceration process. The crushed leaves were soaked in warm water for 4 hours, boiled for 2 hours and kept aside for 2 hours for release of mucilage into water (Figure 1). The material was squeezed in a muslin bag to remove the mark from the filtrate. Equal volume of ethyl alcohol was added to filtrate to precipitate the mucilage; the mucilage was separated, dried in oven at 45^0 C. The powdered mucilage was stored in tight closed container until further use (Figure 2).

2.3 Physicochemical Properties of *Lawsonia inermis* mucilage[9-12]

Macroscopic properties of the mucilage were evaluated by observation of the colour, taste and odour of the powdered mucilage. The isolated and purified mucilage was evaluated for solubility in water, ethanol, acetone and chloroform. Other physicochemical properties were also determined like loss on drying, pH, angle of repose, bulk density, tapped density, hauser's index and carr's index.

2.4 Preformulation studies of Diclofenac sodium [8, 12]

Pre-formulation studies were performed on the diclofenac sodium, which included determination of solubility, melting point, λmax, calibration curve and compatibility studies. Solubility was determined in ethanol, acetone, ether and distilled water. Melting point was determined by capillary method and the temperature at which powder gets melted was noticed. A solution of diclofenac sodium was scanned in the range of 200-400 nm using UV/ Visible double beam spectrophotometer to determine its λmax value. Standard calibration curve was prepared by plotting absorbance values of standard solutions of diclofenac sodium against their respective concentrations. Compatibility study was performed using fourier transform infrared (FTIR) spectral analysis of diclofenac sodium, *Lawsonia inermis* mucilage and combined mixture of both.

Fig 1: *Lawsonia inermis* leaves extract

Fig 2: *Lawsonia inermis* mucilage powder

2.5 Preparation of Diclofenac Sodium Tablets[10, 13]

Tablets each containing 100 mg of Diclofenac sodium were prepared by wet granulation method using different binder concentrations viz. 2.5, 5, 7.5 & 10 % w/w in various formulations. Binder level was adjusted by lowering the level of lactose in the formula. All ingredients were dry mixed manually in mortar and water is used as granulating fluid. The wet mass was granulated by passing them manually through a number 12 mesh sieve. The granules were dried at 50ºC for 1to 2 hrs in tray dryer. The dried granules were passed through sieve.no.22, after blending with lubricants and were compressed by using hydraulic press with flat faced punches. The tablet formulation was developed for 250 mg tablet weight. The compressed tablets were stored in a tight closed container.

2.6 Pre-compression evaluation [10, 12, 13]

2.6.1 Angle of Repose

$$\tan \theta = h/ r \qquad \text{or} \qquad \theta = \tan^{-1} (h/ r)$$

Where; θ = angle of repose, h = height of the cone, and r = radius of the cone base

2.6.2 *Bulk Density*

$$D_b = W/ V_b$$

Where; D_b = Bulk density, W = weight of granules, and V_b = volume (V_b) of granules before tapping.

2.6.3 Tapped Density

$$D_t = W/ V_t$$

Where; D_t = Tapped density, W = weight of granules, and V_b = volume (V_b) of granules after tapping.

2.6.4 Hausner's Index

$$\text{Hausner's index} = D_t / D_b$$

Where, D_t is the tapped density and D_b is the bulk density

2.6.5 Carr's Index

$$\text{Carr's Index (\%compressibility)} = [(D_t - D_b) \div D_t] \times 100$$

Where, D_t is the tapped density and D_b is the bulk density.

2.7 Post-compression evaluation [11, 12]

2.7.1 Tablet Thickness

The thickness of the tablets was determined by using vernier caliper.

2.7.2 *Hardness*

The hardness of the tablets was determined using Monsanto hardness tester. It is expressed in kg/cm^2.

2.7.3 *Weight Variation*

To study weight variation, tablets were weighed using a digital balance and the test was performed according to the official method.

2.7.4 *Friability*

The friability of tablets was determined using Roche Friabilator. It is expressed in percentage (%).

$$\% \text{ Friability} = [(\text{Initial Weight} - \text{Final Weight}) \div \text{Initial Weight}] \times 100$$

% Friability of tablets less than 1% are considered acceptable.

2.7.5 Content Uniformity

Drug content was determined measuring the absorbance at 276 nm using Elico SL210 UV-Visible double beam spectrophotometer. The drug content was estimated from the standard curve of diclofenac sodium.

2.7.6 Disintegration Time

Disintegration time test was carried out according to USP specification.

2.8 *In vitro* Drug Release Profile Studies [11, 12]

The release rate of Diclofenac sodium from tablets was determined using the United States Pharmacopoeia (USP) XXIV dissolution testing apparatus II (paddle method). The dissolution test was performed using 900 ml of 0.1 N HCl, at 37 ± 0.5°C and 50 rpm. A sample (10 ml) of the solution was withdrawn from the dissolution apparatus, and the samples were replaced with fresh dissolution medium. The samples diluted to a suitable concentration with 0.1N HCl. Absorbance of these solutions was measured at 275 nm using a UV-Vis double beam spectrophotometer. Cumulative percentage of drug release was calculated using the equation obtained from a standard curve.

3. RESULTS AND DISCUSSION

Preformulation studies of *Lawsonia inermis* mucilage was performed for determining the macroscopic properties, solubility, loss on drying, pH and flow properties while solubility, melting point and λmax were estimated as preformulation parameters for Diclofenac sodium. Macroscopic properties showed that *Lawsonia inermis* mucilage, obtained after extraction from the fresh leaves of plant, was a free flowing brown colour powder with bland taste and no odour. The mucilage was found to be soluble in water and gave viscous solution on standing but insoluble in ethanol, acetone and chloroform. It has pH around 6.0 to 6.5 with acceptable limit loss on drying (5.12 %). Flow properties of mucilage was determined in terms of angle of repose (28.80º), bulk density (0.48 g/ml), tapped density (0.58 g/ml), hausner's index (1.21) and carr's index (17.24%). All these physicochemical properties were tabulated in Table 1.

Preformulation studies of Diclofenac sodium were performed for determining the solubility, melting point and λmax. The results showed that the drug was found to freely soluble in ethanol and acetone, sparingly soluble in distilled water while practically insoluble in ether. Melting point of Diclofenac sodium was found to be 168°C approx. The λmax of Diclofenac sodium was found to be 275 nm (Figure 3) and standard calibration curve of Diclofenac sodium was prepared as showed in Figure 4. Compatibility studies were performed using Fourier transform infrared (FTIR) spectroscopy. FTIR spectra of the Diclofenac sodium, *Lawsonia inermis* mucilage and combined mixture of both

were obtained (Figure 5, Figure 6 and Figure 7). Spectral analysis showed that there were no signs of incompatibilities between drug and mucilage.

Table 1: Physicochemical Properties of *Lawsonia Inermis* Mucilage

Parameters		Results
Macroscopic Property	Colour	Brown
	Taste	Bland
	Odour	Odourless
Solubility	Water	Soluble
	Ethanol	Insoluble
	Acetone	Insoluble
	Chloroform	Insoluble
Loss on Drying (%)		5.12
pH		6.0-6.5
Angle of Repose (º)		28.80^0
Bulk Density (g/ml)		0.48
Tapped Density (g/ml)		0.58
Hausner's Ratio		1.21
Carr's Index (%)		17.24

Wet granulation method was used to prepare granules of Diclofenac sodium as per the formula given in the Table 2. The granules of different formulations were evaluated for angle of repose, bulk density, tapped density, hausner's index and carr's index as pre-compression parameters and results were shown in Table 3. Angle of repose values ranged from 32.98°-34.16º indicates good flow property of granules. The bulk density and tapped density ranged from 0.449-0.632 g/ml and 0.511-0.720 g/ml respectively were found to be within the limits as per standards. The free flowing properties of granules were then calculated by determining hausner's index and carr's index (%). The hausner's index values were ranged from 1.12-1.14 and carr's index values were ranged from 11.14-12.22%.

The post-compression evaluation of tablet formulations were based on quality control parameters which include thickness, hardness, weight variation, friability, content uniformity and disintegration time. All the results relative to post-compression evaluation were tabulated in Table 4. Thickness of tablets in all formulations was found to be ranged from 3.60-3.66 mm. All the formulations showed reasonably good hardness values ranged from 5.84-5.92 kg/cm^2. The weight variation of 20 tablets from the average was remained within ±0.1% and thus revealed that the tablets were within the range of pharmacopoeial limit. The % friability of tablets was ranged between 0.39-0.44 % and found to be within the pharmacopoeial limit. Content uniformity of all tablets was within the range of 89.99 to 98.88 % indicating good uniformity among different formulations of the tablets. The disintegration time was found to be ranged from 12-16 min for all the formulations and could be a contributing factor in considering the role of this mucilage as a release modifier.

Figure 3: UV absorption spectra of Diclofenac sodium

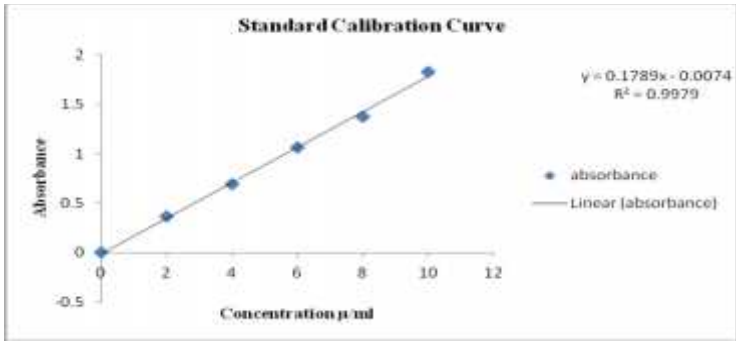

Figure 4: Standard calibration curve of Diclofenac sodium

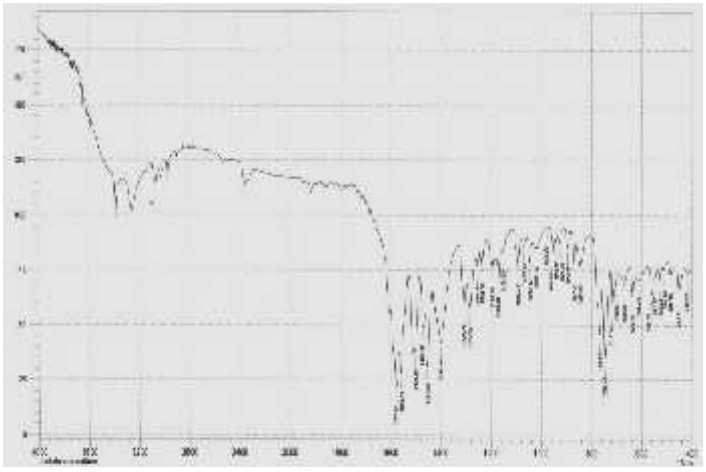

Figure 5: FTIR spectra of Diclofenac sodium

Table 2: Formulation of Diclofenac Sodium Tablets

Ingredients	Formulations (mg/tablet)			
	L-1 (2.5%)	L-2 (5%)	L-3 (7.5%)	L-4 (10%)
Diclofenac Sodium	100	100	100	100
Lawsonia inermis mucilage	6.25	12.5	18.75	25
Lactose	136.25	130	123.75	117.5
Magnesium Stearate	5	5	5	5
Talc	2.5	2.5	2.5	2.5
Total	250	250	250	250

* L- *Lawsonia inermis* mucilage

Table 3: Pre-Compression Evaluation of Diclofenac Sodium Granules

Parameters	Formulations			
	L-1	L-2	L-3	L-4
Angle of Repose (º)	34.16±0.04	33.77±0.08	32.98±0.23	33.69±0.14
Bulk Density (g/ml)	0.449±0.07	0.576±0.17	0.632±0.25	0.550±0.01
Tapped Density (g/ml)	0.511±0.01	0.652±0.03	0.720±0.12	0.619±0.07
Hausner's Index	1.13	1.13	1.14	1.12
Carr's Index (%)	12.13	11.65	12.22	11.14

*Values are in mean±s.d. (n=3) (s.d.= standard deviation)

Table 4: Post-Compression Evaluation of Diclofenac Sodium Tablets

Parameters	Formulations			
	L-1	L-2	L-3	L-4
Tablet Thickness (mm)	3.60±0.01	3.64±0.16	3.66±0.21	3.62±0.15
Hardness (Kg/cm^2)	5.84±0.15	5.86±0.08	5.92±0.12	5.90±0.23
Weight Variation (mg)	256±0.05	250±0.01	252±0.11	250±0.15
Friability (%)	0.39±0.02	0.42±0.09	0.42±0.16	0.44±0.24
Content Uniformity (%)	89.99	94.88	95.55	98.88
Disintegration Time (min)	12	13	15	16

*Values are in mean±s.d. (n=3) (s.d. = standard deviation)

Table 5: *In vitro* Release Data of Diclofenac Sodium Tablets

Time (min)	Cumulative % of drug release			
	L-1	L-2	L-3	L-4
5	40.12	35.19	28.63	24.87
10	64.98	56.27	35.28	31.98
20	78.67	69.18	49.52	44.65
30	89.34	83.17	63.78	61.43
40	92.65	94.71	81.78	79.90
50	-	-	91.56	87.78
60	-	-	94.16	91.90

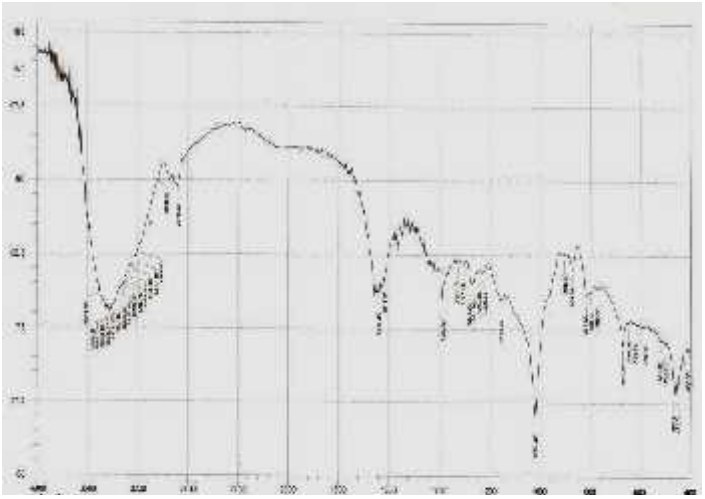

Figure 6: FTIR spectra of *Lawsonia inermis* mucilage

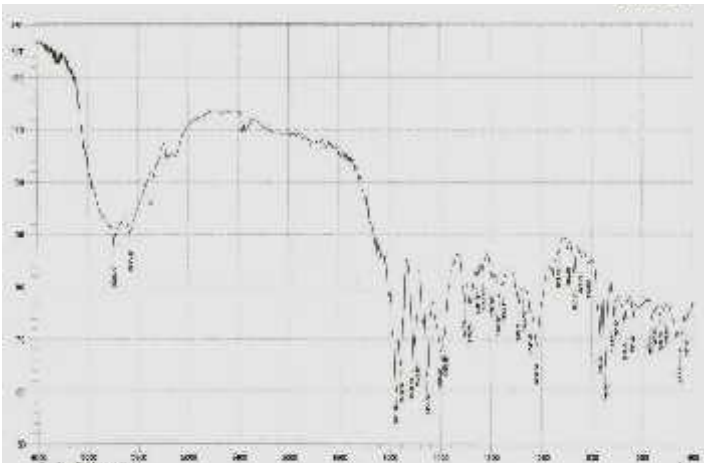

Figure 7: FTIR spectra of mixture of Diclofenac sodium with *Lawsonia inermis* mucilage

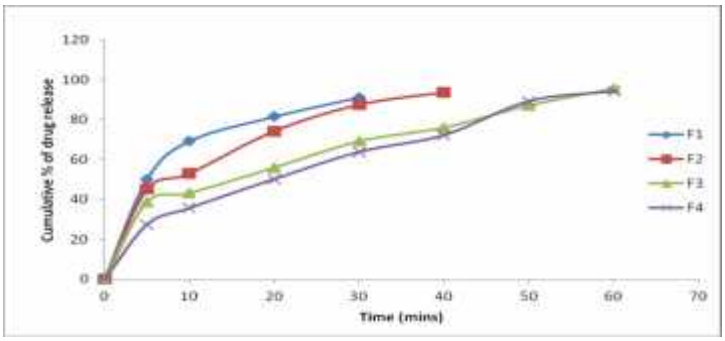

Figure 8: *In vitro* release profile of Diclofenac sodium tablets

Among all the formulations, L-3 and L-4 showed a desired drug release of 94.16 % and 91.90 %, respectively, over the period of 60 minutes. It has been observed that the cumulative percent drug release decreases with increasing concentration of mucilage.

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