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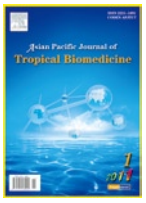

Document heading

Evaluation of *Trapa bispinosa* Roxb. starch as pharmaceutical binder in solid dosage form

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ABSTRACT

Objective: To evaluate binding efficiency of *Trapa bispinosa* Roxb. starch (TBS) in diclofenac sodium tablets. **Methods:** Diclofenac sodium tablets were prepared using wet granulation method. The starch paste in different concentrations (5%-15% w/w) was evaluated for optimized binder concentration. Preformulation study of the drug with TBS and different excipients were also analyzed using fourier transform infrared spectroscopy (FTIR) and isothermal stress testing (IST). **Results:** Preformulation study of the drug, water chestnut starch and different excipients showed no interaction or, drug degradation in FTIR and IST, respectively. The tablets were evaluated for hardness, friability, drug content, disintegration and dissolution studies, and all the parameters were found within the official specifications. **Conclusions:** The results reveal that this starch has potential to be used as binder at industrial scale in pharmaceutical solid dosage form development.

1. Introduction

Since last five decades ago many natural, semi-synthetic and synthetic compounds have been explored as excipients for pharmaceutical drug development. In all these compounds starches remain a strong choice because of its high availability, biocompatibility and multifunctional behaviour. Starches are one of the most used pharmaceutical excipient globally[1]. Although maize and potato starch is the most frequently used excipient in tableting, many researchers have tried to develop various botanical starches for use as tablet excipients[2-10]. Binders are substances which impart necessary cohesiveness between the granules for proper bonding during compression. Binders are added to tablet formulation to impart plasticity and thus increase the interparticulate bonding strength within the tablet granules and also increase the degree of consolidation or compactions while decreasing the brittle fracture tendency during tableting[11].

Water chestnut [*Trapa bispinosa* (*T. bispinosa*) Roxb.] is an aquatic angiosperm and found throughout Southeast Asian regions like India, Pakistan *etc*[12]. Starch is the major carbohydrate reserve in water chestnut. Despite in high carbohydrate content, mainly in the form of starch, water chestnut is not included among starches for industrial purpose, which is mainly obtained from potato, maize, tapioca and rice. Earlier some workers evaluated its disintegration ability in tablet dosage form[13]. Diclofenac was chosen as a model drug. It is mainly used as anti-inflammatory and analgesic agent in the treatment of arthritis and acute injury.

In the present study we aim to evaluate the binding efficiency of *T. bispinosa* in diclofenac sodium based tablets, and simultaneously comparative study was carried out with official starches.

2. Materials and methods

2.1. Material collection

Diclofenac sodium was purchased from Yarrow chem products, Mumbai, India. Potato starch, maize starch, talc and magnesium stearate were procured from Loba Chemie, India. Lactose monohydrate was kindly donated by Meggle Excipits Pvt. Ltd., Germany. Water chestnut was procured from the local market of Uttar Pradesh, India.

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2.2. Isolation of starch

The outer layer of water chestnut fruits was peeled off and the white part was washed and cut into pieces. The fruits were powdered in a blender and washed with distilled water. The washing steps were repeated until the supernatant was clear and the starch was free of color. The starch was then dried in an air oven at (45±2) ℃.

2.3. Preformulation study

2.3.1. Fourier transform infrared spectroscopy (FTIR) analysis

To study the drug-excipient interaction FTIR spectrum of pure drug, different excipients and final formulation were recorded immediately after mixing on an FTIR spectrophotometer (Bruker, Germany) in the range of 450-4 000 cm^{-1} using potassium bromide discs.

2.3.2. Isothermal stress testing (IST)

Binary blends of diclofenac sodium (100 mg) and binders were kept into inert glass vials and blended on a vortex mixer for 10 sec. The open glass vials were kept at 50 ℃ for 3 weeks and the drug content was determined. The binary blend of drug-excipients and pure drug were stored in closed glass vials in refrigerator at 4 ℃, and used as control[14].

2.4. Tablet formulation

To evaluate binding property of water chestnut starch, diclofenac tablets were prepared using wet granulation method. All the ingredients were weighed accurately and mixed thoroughly except magnesium stearate, composition shown in Table 1. The starch paste prepared in different concentrations was used as binding agent. The wet mass was then passed through 16/20 mesh and finally lubricated with magnesium stearate and purified talc. The tablets were compressed on ten station rotary tablet machine (Shakti Engineering, Ahmedabad, India). The tablets were round and flat with an average diameter of 6 mm.

2.5. Evaluation of granules

The granules were evaluated for micromeritic properties like bulk density, tapped density, angle of repose, hausner ratio and compressibility index which were measured by the method described elsewhere[15].

2.6. Tablet characterization

2.6.1. Hardness

Hardness is the force required to break a tablet in a diametric compression. It was measured using Monsanto hardness tester expressed in kg/cm^2.

2.6.2. Friability

Friability of the tablet was determined using Roche friabilator (Campbell electronics, Mumbai, India). Pre-weighed sample of tablets was placed in the friabilator and subjected to 100 revolutions at 25 rpm/min.

2.6.3. Drug content

The prepared tablets were powdered and the blend equivalent to 100 mg of diclofenac sodium was weighed and dissolved in suitable quantity of phosphate buffer pH 6.8 solutions and the drug content was analyzed spectrophotometrically at 278 nm. Each sample was analysed in triplicate.

2.6.4. Weight variation

Twenty tablets were selected randomly from the batch and weighed individually to check for % weight deviation as per specification of Indian pharmacopoeia.

2.6.5. Disintegration and dissolution study

The disintegration time (DT) of the prepared tablets was carried out using distilled water as medium at (37.0±0.5) ℃ using USP disintegration test apparatus (Tab Machine, Mumbai, India). The *in vitro* dissolution study was carried out in USP dissolution apparatus Type-II (Model No- TDT-08L, Electrolab, Mumbai, India). The dissolution medium used in the study was phosphate buffer (pH 6.8), and all the spectrophotometric study was carried out at 276 nm[16] using UV-Vis spectrophotometer (Hitachi, Japan).

2.7. Statistical analysis

Statistical analysis was carried out using the analysis of variance (ANOVA) on computer software GraphPad Prism 5 (GraphPad software Inc., San Diego, USA).

3. Results

The yield of starch from the fruits of *T. bispinosa* Roxb. (water chestnut) was found to be 33.8% w/w on dry weight basis. In the preformulation study, the FTIR spectra of pure drug and different excipients were scanned at room temperature (Figure 1). The IST study was done to reconfirm drug-excipient interaction at physicochemical level. After 3 weeks of stressed condition, the assay of drug was carried out by UV method at 276 nm (Table 2). The granules after drying in the oven were examined for powder properties (Table 3). The bulk density and tapped density of the granules are in the range of 0.51-0.53 and 0.66-0.68 g/mL, respectively. The granules were free flowing in nature, which is exhibited from its angle of repose (21-23 θ) and hausner ratio (≤1.33). The tablets prepared in different concentration showed good hardness, but its value slight increases as the concentration of starch increased in tablets. All the tablets passed the friability, weight variation and drug content tests and their limits were within the official range. The disintegration behavior of the tablet was shown in Table 4, disintegration behaviors of all the starches decreased as the concentration of binder increased in the formulation (F3, F6 and F9). The dissolution behavior of all the formulations was presented in Figure 2. From the dissolution data it could be concluded that the amount of dug release solely depends upon the binder concentration.

Table 1
Formulation compositions of diclofenac sodium tablets.

Ingrediants (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Diclofenac sodium	100	100	100	100	100	100	100	100	100
Lactose (q.s.)	300	300	300	300	300	300	300	300	300
Binder*	15	30	45	15	30	45	15	30	45
Disintegrant	15	15	15	15	15	15	15	15	15
Magnesium stearate	03	03	03	03	03	03	03	03	03
Talc	03	03	03	03	03	03	03	03	03

*: Binder type F1–F3 contains water chestnut starch, F4–F6 contains potato starch and F7–F9 contains maize starch.

Table 2
Results of analysis of IST samples after 3 weeks of storage.

Sample	Ratio (Dug: excipient)	% Drug release	
		Control sample	Stressed sample
Drug–Diclofenac sodium)	–	102.12	99.34
Drug–WCS starch	1:1	101.45	100.10
Drug–Lactose	1:1	100.32	99.98
Drug–Mag. stearte	1:1	100.45	99.01
Drug–Talc	1:1	100.98	99.27

WCS: water chestnut.

Table 3
Evaluation of the granules utilizing different starches (mean±SD) (n=3).

Formulation code	Bulk density (g/mL)	Tapped density (g/mL)	Hausner ratio	Carr's compressibility (%)	Angle of repose (θ)
F1	0.52±0.12	0.67±0.88	1.28±1.40	22.38±1.10	21.23±1.10
F2	0.52±0.23	0.67±0.65	1.28±1.50	22.38±1.60	22.03±1.40
F3	0.53±0.13	0.68±1.40	1.28±1.80	22.05±1.80	22.14±0.50
F4	0.51±1.50	0.68±0.11	1.33±1.30	25.00±1.30	22.09±2.10
F5	0.52±0.60	0.68±2.60	1.30±2.20	23.52±2.40	21.19±0.40
F6	0.53±2.40	0.67±2.40	1.26±2.30	20.89±2.10	20.45±1.90
F7	0.51±1.90	0.68±1.10	1.33±3.30	25.00±1.44	23.12±1.40
F8	0.51±3.30	0.66±2.20	1.29±1.70	22.72±0.83	21.11±1.20
F9	0.52±0.30	0.66±2.10	1.26±1.10	21.21±0.33	22.08±1.90

Table 4
Physical parameters of diclofenac sodium tablets prepared with different starches (mean±SD) (n=3).

Formulation code	Hardness (kg/cm^2)	Friability (%)	Drug content (%)	Weight deviation (%)	Disintegration time (min)
F1	5.60±0.20	0.95±0.26	97.35±0.30	2.30±0.18	1.24±0.05
F2	5.80±0.35	0.63±0.15	98.26±0.20	1.60±0.28	8.34±0.12
F3	6.10±0.20	0.44±0.21	98.13±0.21	2.70±0.20	16.24±0.10
F4	5.80±0.30	0.63±0.40	97.33±0.26	2.90±0.15	2.12±0.05
F5	6.10±0.25	0.34±0.35	98.43±0.23	1.40±0.35	7.36±0.09
F6	6.10±0.22	0.22±0.25	96.32±0.20	2.30±0.14	12.44±0.15
F7	6.00±0.30	0.69±0.16	97.48±0.30	1.50±0.20	3.46±0.20
F8	6.00±0.10	0.46±0.24	98.98±0.34	1.70±0.12	6.34±0.14
F9	6.20±0.15	0.30±0.24	97.98±0.34	2.70±0.12	14.34±0.23

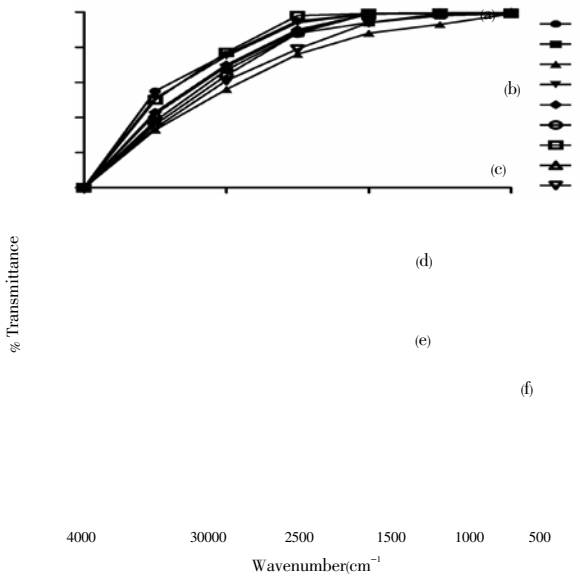

Figure 1. FTIR spectrum of diclofenac (a), talc (b), magnesium stearate (c), water chestnut starch (d), lactose (e) and final formulation (f).

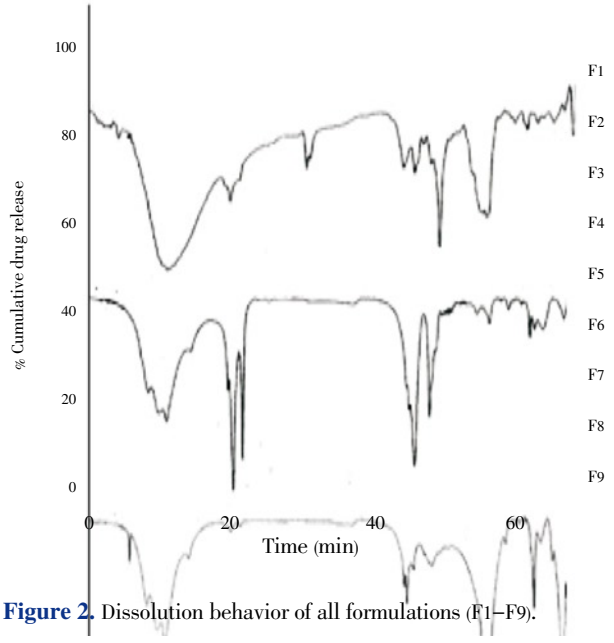

Figure 2. Dissolution behavior of all formulations (F1–F9).

4. Discussions

The FTIR spectrum of diclofenac sodium contains major peaks at 3 382 cm^{-1} due to NH stretching of secondary amine, 1 571.72 cm^{-1} because of -C=O stretching of the carboxylic group and at 745.12 cm^{-1} owing to C-Cl stretching, which is also present in final formulation, revealing no drug-excipient interaction. In IST study, no physical change was appeared and the drug contents were within the limit, showing no drug degradation during the stress condition. On the basis of above results, it was concluded that there is no physicochemical interaction between drug and used excipients. The binding efficiency of tablets prepared with high concentration (10%-15% w/w) of starch showed increased hardness that might be due to stronger cohesive bond formation between the granules. All other physical parameters were found within the official specification. The disintegration time of the diclofenac tablets, prepared with high concentration (15% w/w) of starch showed an increase in DT value that might be due to less penetration of solvent in the tablet pores due to formation of stronger bonding between the granules. The dissolution of drug in gastric environments also indirectly depends upon disintegration time of the formulation. From the dissolution study it can be concluded that drug is rapidly dissolves at low concentration of starch, while at higher concentration the native starch forms a viscous mass that makes barrier in movement of dissolution medium into the pores of dosage form. In all the above formulations, F2, F5 and F7 showed very promising results in all the parameters. In case of TBS as binder, the optimized concentration of starch could be 10% w/w to formulate diclofenac sodium tablet. From the foregoing results, it can be concluded that starch from *T. bispinosa* Roxb possesses excellent quality to be used as natural binder in pharmaceutical formulations.

This study showed the binder property of water chestnut (*T. bispinosa* Roxb) starch in diclofenac sodium based tablets. The diclofenac sodium tablets prepared with this starch showed promising and comparable characteristics like hardness, friability, drug content, weight variation, disintegration and dissolution with the official starch binders. All the results imply that water chestnut starch can be used as an alternative source of tablet binder at industrial scale.

Conflict of interest statement

We declare that we have no conflict of interest.

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