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Research Article

EXTRACTION OF POLYSACCHARIDE POLYMER FROM *DIOSCOREA TRIFIDA* AND EVALUATION AS A TABLET BINDER

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ABSTRACT

The objective of the present investigation was to extract starch from yam (*Dioscorea.trifida*) and to evaluate it as a binder for tablets in comparison with potato starch, corn starch, gelatin and acacia in the formulation of Ibuprofen based tablets. The micrometric properties of yam starch possessed bulk density of 0.51 g/cc with angle of repose 24^0 and average particle size of 33.5µm showing good flow properties and compressibility. The ibuprofen tablet formulations with increased binder concentration of yam starch 5-15% tablet weight showed positive influence on the hardness and disintegration time. The *in-vitro* dissolution studies showed that formulation F-2 (10w/w binder of tablet) showed similar drug release profile when compared with the conventional marketed product. The comparative binder efficiency of the yam starch with other natural binders corn starch, potato starch, acacia and gelatin were studied. It was observed that with 5% w/w of binder in the tablet, the gelatin possessed highest hardness with delayed disintegration time and drug dissolution when compared to other binders. The binder capacity of polymer could be depicted in the order Gelatin > Acacia> Potato starch > Yam starch > Corn starch. Thus, the extracted yam starch could be used as an effective and alternative polymer binder in the manufacture of tablets and its concentration can be optimized depending upon the physico-chemical, micrometric properties of the drug and other excipients.

Keywords: Yam starch, Ibuprofen, Binder, Tablets

INTRODUCTION

Polymers, also known as macromolecules, are very large molecules consisting of many repeating units and are formed by a process known as polymerization which links together small molecules known as monomers.

Starches are widely available, naturally occurring carbohydrate, found in almost all organs of plants, most especially in roots, rhizomes, fruits and seeds[1]. Starch has been used as multifunctional excipient in tablet formulations due to their relative inertness, abundance, low cost and suitable physico-chemical properties. Starch and their derivatives are used as diluents, glidants, binders and disintegrants etc.

Yams are the annual or perennial tuber-bearing and climbing plants belonging to the genus *Dioscorea*, a genus of over 600 species of flowering plants in the family *Dioscoreaceae*. In many parts of Africa and South East Asia, yam is a primary agricultural commodity, classified as the third most important tropical root crop after cassava and potatoes. The high starch content of yam tubers (70 to 80% dry weight) has made them a potential source of starch that could be explored commercially. Ibuprofen is a non-steroidal phenyl acetic acid derivative. Ibuprofen has been shown to have potent anti-inflammatory, analgesic and anti-pyretic properties. Its biological half life is 1.8-2.4 hrs[2, 3].

Thus in the present study, the compressional and tableting properties of starch obtained from species of yam namely *Dioscorea trifida* has been investigated in comparison with the official corn starch and potato starch using ibuprofen as the model drug .

MATERIALS AND METHODS

Materials

Ibuprofen was procured from Yarrow Chem. Products, Mumbai. The starches used were Yam starch extracted from Yam (Dioscorea.trifida) purchased from local market in Bangalore, Corn starch & Potato starch (Hi Media Laboratories Pvt. Ltd., Mumbai), Acacia (Ranbaxy Fine Chemicals Limited,New Delhi); Gelatin (S.D Fine-Chem Ltd., Mumbai.) All other ingredients used were of analytical grades.

Isolation of yam starch

Fresh tubers of yam were collected and washed with distilled water, peeled, washed again and then cut into small pieces. The pieces were then washed with 2% w/v sodium metabisulphite in distilled water to prevent darkening and then milled into a fine paste using a laboratory mill. The slurry was strained through a muslin cloth and the filtrate was left to settle. The supernatant was decanted at 12 h. intervals and the starch slurry re-suspended in distilled water. The starch cake was collected after 3 days and dried in a hot air oven at 60 ^{0}C for 12 h. The dried mass was pulverized using a laboratory sifter and then screened through a # 85 mesh sieve[4].

Evaluation of Yam Starch

Phyto-chemical Studies

Extracted starch was subjected to preliminary tests to confirm the nature of the obtained powder. The tests performed were to determine the presence of polysaccharides[5].

Molisch test

It is a general method for the detection of carbohydrates. The strong H_2SO_4 hydrolyses carbohydrates (poly- and disaccharides) to liberate monosaccharides. The monosaccharides get dehydrated to form furfural (from pentoses) or hydroxyl methyl furfural (from hexoses) which condenses with α- napthol to form a violet coloured complex[6]. A violet coloured complex was obtained with the sample powder which confirms it as a carbohydrate.

Iodine test

Polysaccharides combine with iodine to form a coloured complex. Thus starch gives blue colour while dextrins red colour with iodine[6]. A blue colour was obtained after reaction with iodine , hence it was confirmed as starch

Solubility studies

The solubility studies of extracted yam starch ws conducted in selected polar and non-polar solvents. The extracted starch was insoluble in alcohol, chloroform, acetone, methyl chloride and it formed a gelly nature in hot water[7].

Micrometric studies of yam starch

Particle Size Analysis

The particle size of yam starch polymer was determined using optical microscope (Olympus LITE image). Small amount of polymer was taken on a slide and spread into a thin layer. A total of 100

particles were counted and their size determined. The average particle size in micrometers was reported.

Bulk density

The accurately weighed powder was introduced into a 100ml graduated cylinder and the volume was noted. The bulk density was calculated using the formula:

$$\text{Bulk density } (\rho) = \frac{\text{Mass of powder (w)}}{\text{Bulk volume } (V_b)}$$

Tap density

The accurately weighed powder was introduced into a 100ml graduated cylinder. The cylinder was fixed on to the Tap Density Apparatus ETD – 1020 (Electro lab) and the timer knob was set for 100 tappings. The volume occupied by the powder was noted. After 100 tapping's the final volume was noted. The tap density was calculated using the formula:

$$\text{Tap density} = \frac{\text{Mass of powder (w)}}{\text{Tap volume } (V_t)}$$

Angle of repose

A glass funnel was placed 2 cm above the horizontal plane using a clamp. The sample of 25 g was transferred into funnel keeping the orifice of the funnel blocked by the thumb. Then the thumb was removed and the powder was allowed to flow. When the powder was emptied from the funnel, the height (h) of the pile and radius (r) of the base was measured. The angle of repose was calculated using the formula:

$\theta = \tan^{-1} h/r$

Carr's index

The difference between the tapped and bulk density divided by the t apped density was calculated and ratio expressed as a percentage[8].

$$\text{Carr's Index} = \frac{\text{Tap density – Bulk density}}{\text{Tap density}} \times 100$$

Hausners ratio

It is the ratio of tapped density to Bulk density of the granules. The ratio gives as insight to the degree of densification of powders which could occur during tableting [9].

$$\text{Hausners ratio} = \frac{\text{Tap density}}{\text{Bulk density}}$$

Bulkiness

The bulkiness of the powder determination is very useful to select appropriate dies and punches for the compression of the tablets.

Bulkiness = 1/ Bulk Density

IR spectral analysis

FTIR spectra of yam starch, potato starch and corn starch were recorded in the scanning range of 400 – 4000 cm^{-1} using FTIR-8400 S (Shimadzu Corporation, Japan). The samples were prepared in KBr disks by means of a hydrostatic press at 6-8 tons pressure.

Swelling Power

Starch suspension (5% w/v) was prepared at room temperature with shaking for 5 min. and sedimentation volume was measured. The dispersion was allowed to stand for 24 h. and the swelling capacity was calculated as:

Swelling capacity = V_2/V_1

Where V_1 refers to the initial volume occupied by starch and V_2 refers to the final volume after 24 h.

Formulation of Ibuprofen tablets using isolated yam starch as a binder

The conventional tablets of ibuprofen were prepared by using isolated starch from yam (5-15%w/w of tablet) by aqueous wet granulation method as shown in Table-1. The tablets were also prepared using other established natural binders like corn starch, potato starch, acacia and gelatin for the comparative study.

Table 1: Formulation of Ibuprofen tablets

Ingredients - mg/tablet	F1	F2	F3	F4	F5	F6	F7
Ibuprofen (drug)	200	200	200	200	200	200	200
Yam starch (binder)	15	30	45	-	-	-	-
Potato starch (binder)	-	-	-	15	-	-	-
Corn starch (binder)	-	-	-	-	15	-	-
Gelatin (binder)	-	-	-	-	-	15	-
Acacia (binder)	-	-	-	-	-	-	15
Aerosil (disintegrant)	8	8	8	8	8	8	8
Magnesium stearate (glidant)	4	4	4	4	4	4	4
Talc (lubricant)	8	8	8	8	8	8	8
Dicalcium phosphate (diluent) q.s.	300	300	300	300	300	300	300

Evaluation of formulations

Drug polymer compatibility studies: The compatibility studies of drug, polymer and the physical mixture (1:1) of both drug and polymer were carried out by KBr disc method in the scanning range of 400-4000cm^{-1} using Fourier Transform Infrared Spectrophotometer (Shimadzu FT-IR 8400-S)

Pre-compression studies

Various granular properties of the formulation like bulk density, tap density, angle of repose, Hausner's ratio, Carr's index, and bulkiness were determined according to the procedure discussed earlier.

Post compression analysis

Weight variation test

Randomly sampled 20 tablets were accurately weighed, the average weight was calculated and the tablets were weighed individually using the digital weighting balance (Shimadzu, Japan) [10].

Hardness test

Monsanto hardness tester was used for the test. The tablet was held between the edges of the fixed and movable part of the instrument. The scale was adjusted by sliding so that the zero on the scale coincides with the pointer. The adjustable knob was moved slowly till the tablet breaks[12]. The hardness was measured in kg/cm^2.

Friability

Accurately 20 tablets were carefully dedusted and weighed. The tablets were placed in a Roche friability test apparatus and rotated 100 times at 25 ± 1 rpm. Then the tablets were removed, dedusted and weighed.

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

Drug content

Randomly ten tablets were weighed and crushed to form powder with mortar and pestle. The powder triturate equivalent to average

weight of tablet was taken in a 100ml volumetric flask, Ibuprofen dissolved and diluted by using phosphate buffer pH7.2. The resultant 5ml of sample was withdrawn and diluted suitably to desired concentration using phosphate buffer pH 7.2 and the drug content was estimated using U.V-spectrometer (UV-1700, Shimadzu) at 222nm.

***In-vitro* disintegration time**

A tablet was placed in each of the six tubes of the disintegration test apparatus (Electro Lab, Mumbai, India). The assembly was suspended in water maintained at a temperature of $37^0C \pm 2^0C$ and operated simultaneously.

The time taken for the tablets to disintegrate completely was noted by using stop watch[11].

***In-vitro* drug release studies**

Drug release study was carried out using dissolution rate test apparatus USP XXIII (Type II) (Electro Lab, Mumbai, India). The dissolution medium used was 900ml of phosphate buffer pH 7.2 and the study conducted at 37^0C with 50 rpm. The sample was withdrawn at different time intervals and replaced with fresh medium in order to maintain sink condition. The withdrawn samples were diluted suitably and drug content was estimated using U.V-spectrophotometer at 222nm.

RESULTS AND DISCUSSION

The isolation of starch from yam of the genus *Dioscorea.trifida* was successfully established. The identity of starch product was confined and had good bulk density of 0.5125g/cc. with average particle size of 33.5µm.

Evaluation of yam starch

Table 2: Micrometric studies of Yam starch

Parameters*	Bulk density (g/cc)	Tap density (g/cc)	Angle of repose (θ)	Carr's index	Hausner's ratio	Bulkiness	Particle size analysis (µm)	Swelling power
Yam Starch	0.5125 + 0.12	0.683 + 0.08	24^0 + 2	24.96 + 1.16	1.83 + 0.19	1.15 + 0.011	33.5 + 1.3	1.36+0.005

* Mean value of three determinations + S.D

Fourier transforms infrared (FTIR) spectroscopy analysis

FTIR spectra of yam starch, potato starch and corn starch were performed by FTIR Shimadzu FT-IR 8400-S. The comparative results of the spectral interpretation (Fig. 1-3) confirmed the identity of the yam starch. Drug-polymer compatibility studies are done to evaluate interaction between drug and polymer. The IR spectra of Ibuprofen, yam starch and mixture of both drug and polymer are indicated in the Figures (3-5). The IR spectra of Ibuprofen has shown characteristic peaks at 3093.61 cm^{-1} indicating C-H aromatic stretch, 1460.01 cm^{-1} indicating C=C stretch, 779.19 cm^{-1} indicating C(out of plane), 2867.95 cm^{-1} indicating C-H aliphatic stretch. The physical mixture also showed the characteristic peaks of pure drug indicating that there was no interaction between the drug and yam starch.

To investigate the cohesive property of yam starch as a binder, Ibuprofen conventional tablets were prepared using different concentration of yam as a binder (5-15% of tablet weight) and also it was compared with other widely used natural binders like corn starch, potato starch, gelatin and acacia. The tablets of different formulations were subjected to pre and post compression evaluation tests (Table 3 & 4). The pre-compression results depicted that all the formulations possessed good granular flow properties & bulk density. The results of weight variation and drug content indicated that all the batches of tablets were uniform with low standard deviation values. The hardness of the tablets increased with the increase in the binder concentration of yam starch. The comparative hardness values with the other binders showed that tablets with gelatin and acacia recorded an increased value of $5kg/cm^2$ as compared to starch binders and this further reflected in the disintegration and dissolution tests also. The disintegration time for binder (5% w/w of tablet) yam starch and gelatin were 4'28" & 8'14" minutes respectively.

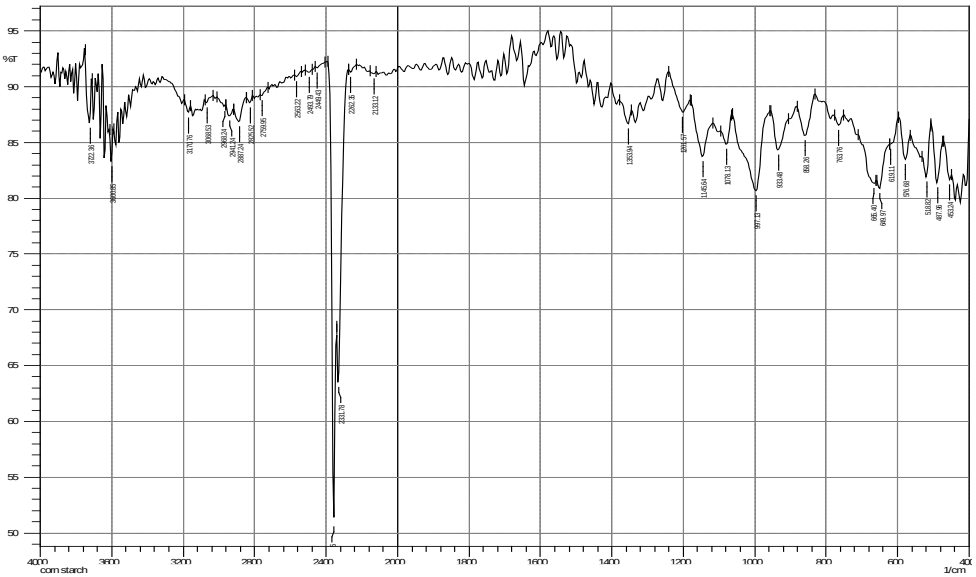

Fig. 1: IR spectrum of corn starch

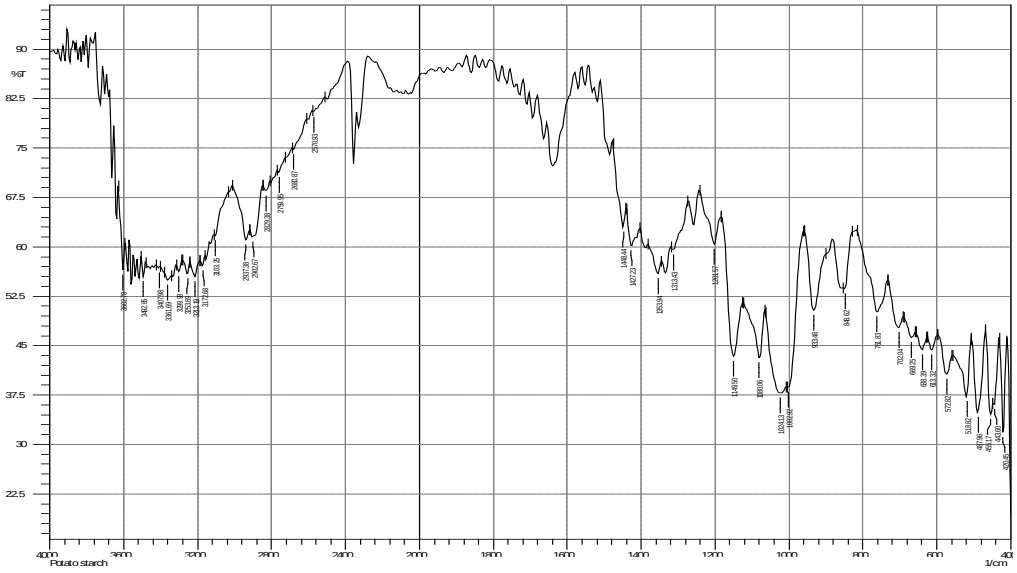

Fig. 2: IR spectrum of potato starch

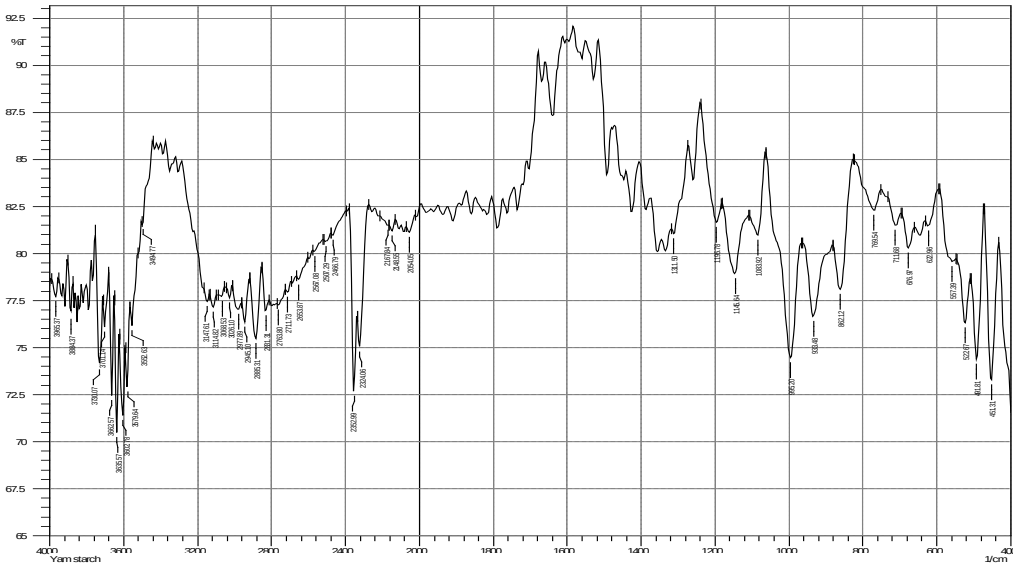

Fig. 3: IR spectrum of yam starch

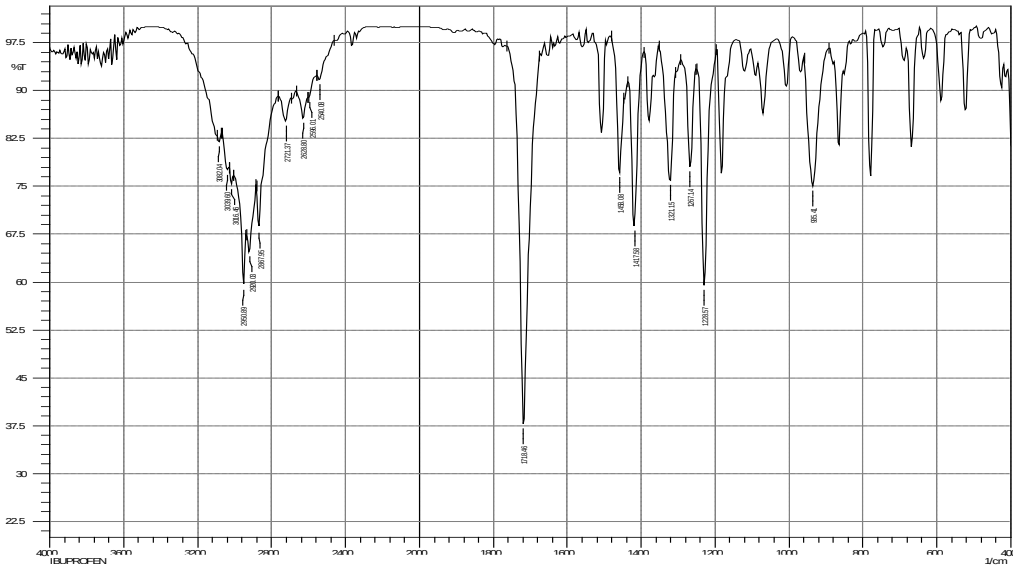

Fig. 4: IR spectrum of Ibuprofen

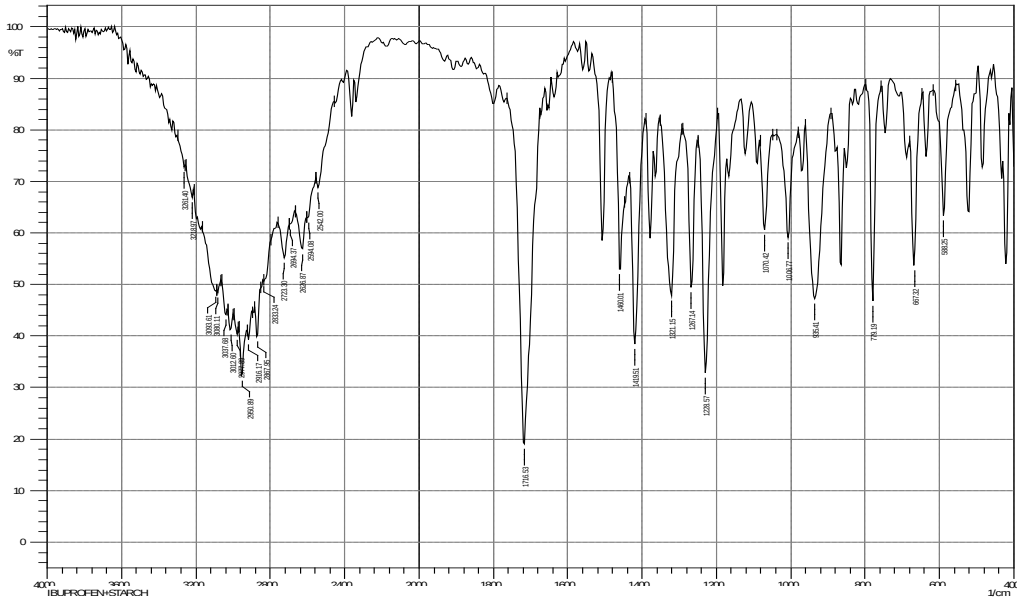

Fig. 5: IR spectrum of Ibuprofen and yam starch

Table 3: Results of Pre-compression studies of formulation blend

Parameters*	F1	F2	F3	F4	F5	F6	F7
Bulk density (g/cc)	0.637+0.004	0.635+0.004	0.564+0.005	0.625+0.006	0.606+0.002	0.426+0.002	0.440+0.003
Tap density (g/cc)	0.775+0.003	0.773+0.004	0.711+0.004	0.80+0.002	0.80+0.003	0.488+0.003	0.510+0.002
Angle of repose (θ)	20.31+0.5	19.65+0.7	19.82+0.8	19.65+1.0	21.76+1.2	20.81+1.0	19.65+1.0
Carr's index	17.8+1.2	17.8+0.8	20.6+0.8	21.87+0.7	24.25+0.9	12.70+1.2	13.7+1.2
Hausner's ratio	1.216+0.4	1.217+0.4	1.26+0.5	1.28+0.6	1.32+0.7	1.068+0.6	1.15+0.4
Bulkiness	1.56+0.8	1.57+0.9	1.77+1.2	1.6+1.0	1.65+1.2	2.34+0.8	2.27+0.7

* Mean value of three determinations + S.D

Table 4: Post compression evaluation of formulated tablets

Batch	Hardness* (kg/cm²)	Weight Variation* (mg)	Friability* (%)	Drug content %*	Disintegration time* (min.)
F1	3.5+0.05	297±4	0.67+0.04	98.6+1.2	4'28" +0.2
F2	4.2+0.02	296±4	0.52+0.04	99.12+2.09	5'46" +0.4
F3	4.5+0.06	298±7	0.41+0.06	97.32+1.2	6'12" +0.6
F4	4.5+0.02	294±6	0.32+0.08	100.4+2.02	4'52" +0.4
F5	4.5+0.03	301±4	0.36+0.07	98.32+0.09	5'32" +0.2
F6	5.0+0.04	297±5	0.24+0.02	99.16+0.08	8'14" +0.3
F7	5.0+0.02	296±6	0.27+0.02	99.46+1.06	7'32" +0.5

* Mean value of three determinations + S.D

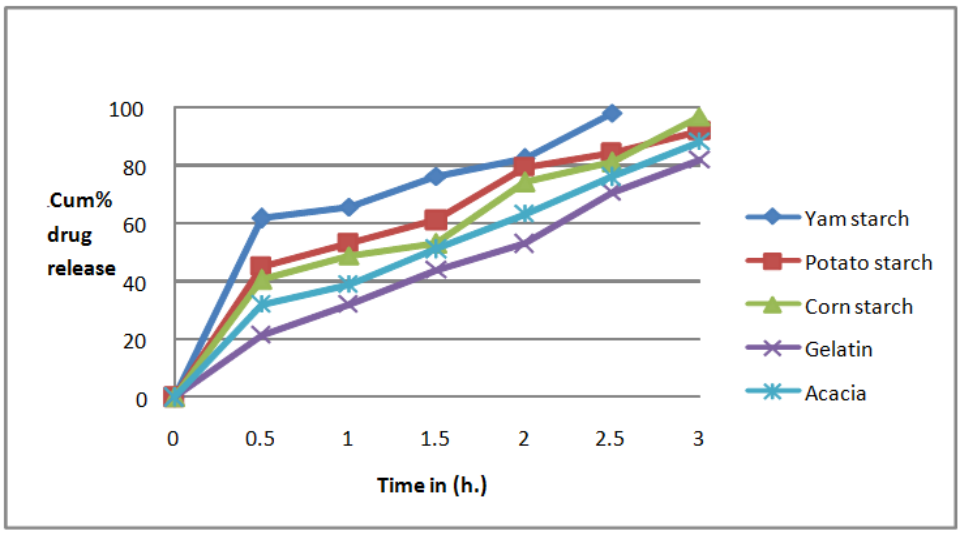

Fig. 6: *In-vitro* Ibuprofen dissolution studies using different binder concentration with 5% w/w of tablet

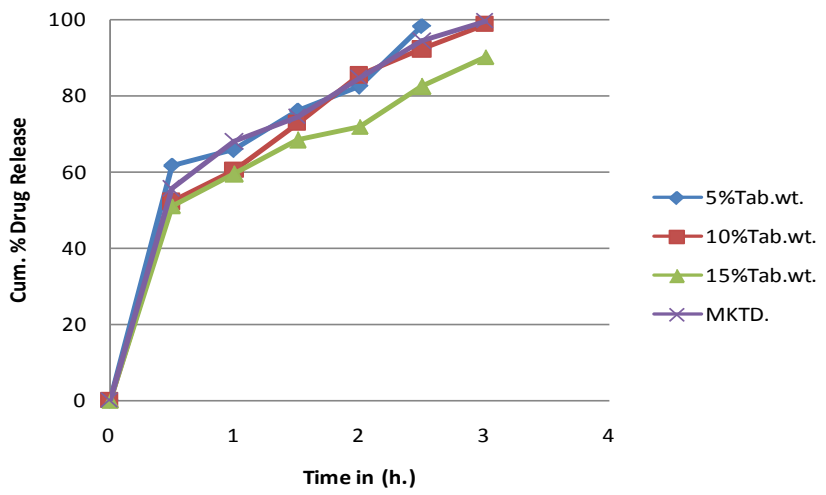

Fig. 7: Comparative *in-vitro* ibuprofen release from tablet formulation using varied concentration of yam starch binder with the marketed product

The comparative drug release profile of the formulations using different binders (5%w/w of tablet) showed that the drug release was complete within 2.5h. and 3h. with yam starch and corn starch whereas for other formulations at the end of 3h. the drug release was 90% with potato starch, 85% and 80% using acacia and gelatin. The effect of different binder concentration of yam starch (Figure 7) revealed that there was an increase in the cohesiveness, hardness and disintegration time with decreased drug release profile in the tablets and the dissolution profile of formulation F-2 was comparable with that of the marketed product

CONCLUSION

The tablet binder property of yam starch was investigated and reported to be a good granulating agent for the formulation of tablets. The binder concentration had an increased effect on the mechanical properties of the tablets whereas it had a decreased effect on the drug release kinetics. Thus depending upon the tablet strength and suitability of drug release requirement, the concentration of yam starch as a binder can be optimized for the manufacture of various tablet dosage form.

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