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A Comparat ve Study of Binding Propert es of Naturally Isolated Starch in Tablet Dosage Form

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Abstract

Starch is the most commonly used as excipient in pharmaceutical preparations. They are used as Diluents, fillers and disintegrant in tablets. The bioavailability of any drug in the formulation is affected by various excipient presents in it. In case of tablets formulation, binders plays very important role in dissolution as well as bioavailability of drug. In the present work a comparative study of the binding properties of naturally isolated pear and guava starch was done in tablet formulated by using famotidine drug. Starch was isolated from natural source and then it was used in 2% w/v, 4% w/v, 6% w/v and 8% w/v in formulations, as binding agent. Then formulated tablets were further evaluated for various parameters. The hardness and disintegration time of the formulated tablets was found to be increased with increase in starch concentration. Hardness of optimized formulation, in case of pear and guava starch was 6.5 ± 0.11kg and 6.0 ± 0.09 kg, disintegration time was 10.0 ± 0.28 and 8.0 ± 0.60 min and friability was 0.48 ± 0.15 and 0.76 ± 0.41 respectively. The cumulative drug release after one hour for tablets containing 4% w/v of pear and guava starch (optimized formulation) showed maximum drug release was about 80.69% and 83.54 ± 0.15 respectively. Then optimized formulation used for in vivo study. From the results, it was observed that, both pear and guava starch has significant binding characteristics. The percentage cumulative release of drug shows that guava starch has better binding properties then pear starch and both isolated starch was used as binding agents in pharmaceutical formulations for future aspects.

Key words: Binder; Tablets; *In-vitro* dissolution; Famotidine; Pear Starch; Guava Starch

Introduction

There are different types of excipients used in pharmaceutical industries. The physiochemical properties of any formulation are depends upon type of excipients used. Excipients also affect the solubility and dissolution behavior of any drugs [1]. The solubility parameters of any drug cause various problems in formulation developments and also affect the bioavailability of drug. In other words the bioavailability of drug is depends upon the solubility parameters. Excipients are used in the form of diluents, binders, disintegrant, antiadherent etc.

Binders plays very important role in the formulation of tablets especially in case of tablets formulation. Binders obtained from the natural source are more demanded due to its availability, cost, and compatibility and less side effects [2]. Due to these parameters starch obtained from natural source is choice of interest for the researchers. It is rational choice of a suitable binder in a formulation requires skill and extensive knowledge regarding the properties of a binders. The role of the binders in very important in case of direct compression is especially, when a high dose of a poorly compressible drug is used in the formulation [3].

There are different varieties of starch available in industry like corn starch, wheat starch, potato starch and maize starch are used as in the form of binder in pharmaceutical formulation [4]. The mechanism of action of binding agent is to enhance the cohesive forces between the particles as well as to maintain them in intact form in the formulations. They also help to improve the flow property of granules as well as powder drugs [5].

In the present study was done to improve the solubility and dissolution rate of a drug by using pear and guava starch and then compare to it. The starch was isolated from the natural sources of pear and guava. Then isolated starch was evaluated and used as binding agents in the tablet formulations. Wet granulation method was used for the preparation of tablets. The tablets were then evaluated for the various evaluation parameters [6].

Materials and Methods

The starch used in for study extracted from the natural sources. All sources were purchased from local market. Drug was obtained as gift sample from Sun Pharma, Jammu. Carboxy methyl cellulose, magnesium stearate, Talc (Central Drug House, New Delhi). All other chemicals were analytical grade.

Extraction of starch

Take the fresh fruit of pear and guava fruit and washed them properly. Then peeled it and chopped in to grinder. Mixed 0.5% w/v NaOH solution into it in a ratio of 1:3 and kept for 2 hr Filter

the mixture and washed with saline water for several times to remove all the soluble impurities [7] . Then treated with petroleum ether to remove any fatty material and then filtered it. Left for sedimentation overnight. Then starch was collected after washing with ethanol. Finally crushed the starch in to fine powder form and preserved for further use [8].

Characterization of Starch

Identification test

1 g of starch was boiled in 50 ml of water. After that the mucilage was cooled and 2 drops of 0.1 N iodine solutions were added in to 1 ml of the mucilage the color change was noted [9].

Particle size determination

A small amount of starch was mixed was taken, put few drop of glycerol and then observed under the microscope with the aid of a calibrated eyepiece. The particle size of each sample dispersed in glycerol was determined [10].

Paste clarity

Aqueous suspension (1%) of isolated starch was taken and heated in a boiling water bath for about 30 minutes with intermittent shaking. Then after cooling measured the clarity (transmittance% at 650nm) of starch against blank **(Figure1-3)** [11].

Moisture content

3 g weight each of starch was taken in moisture analyzer and the reading was recorded as mean value[12]. The moisture content calculated as –

M.C. (%) = W1 - W_2/ W_1 X 100

W_1 = Weight of wet sample (grams), and W_2 = Weight of dry sample (grams)

Figure 1: Moisture content from starch.

Swelling capacity

Weight 10g of starch (Vd) and measured the tapped volume. Then the powder was dispersed in 85 ml of distilled water and make up the final volume up to 100 ml. After 18 hrs, the volume of the sediment (Vw) was estimated and swelling capacity [13] was determined as

Swelling capacity = Vw – Vd/Vd %

Where, Vw= Volume of the sediment, Vd = Tapped volume

Figure 2: Swelling capacity of starch.

Ash value of starch

Total 2 g quantity of starch was weighed into a silica crucible and incinerated [14]. Determination of ash value was done by measurement of the residue left after complete combustion in a muffle furnace at 350° C.

% Total ash value = Wt. of total ash / Wt. of crude drug taken X 100

Figure 3: Ash value of starch.

Flow Properties of Starch

Angle of Repose

The angle of repose was determined by allowing the powder to free flow through a funnel on to the surface. Further addition of powder was stopped as the pile touched the tip of the funnel [15]. The rough circle was drawn around the pile without disturbing it. The height and diameter of resulting cone/pile was measured. The same procedure was repeated three times to get average value [16].

Bulk Density

About 100 gm of powder was taken into a dry 250 ml of measuring cylinder. Than level of powder was adjusted without compacting and the apparent volume (Vo) was noted [17].

Tapped Density

Accurately weighed quantity of powder was introduced into a measuring cylinder [18]. The cylinder was tapped 500 times and the tapped volume (Va) was measured.

Identi ication of Starch

The I.R. structure of both the starches was obtained on FTIR spectrometer from 4000 cm^{-1} to 400 cm^{-1} using KBr pellets method. Then compared with spectra of reference starch. IR spectrum of starches shows all characteristic peaks as in references starch.

Formulation of Famotidine Tablets

Four batches of the tablet containing 20 mg famotidine were prepared. The batches contained pear and guava starch as binders respectively in concentrations of 2, 4, 6, and 8% w/w. Carboxy methyl cellulose used as the disintegrant in 7.5% with 0.5% magnesium stearate as lubricant.

Wet Granulation and Compression

Wet granulation method was used for the preparation of tablets. About 50 tablets were prepared for the study for each batch. Take calculated amount of drug, lactose and sodium carboxymethyl cellulose and mixed in a mortar. Then passed the mixture through sieve 44. Then calculated amount of starch mucilage of various concentrations (2, 4, 6 and 8% w/w) was mixed to get wet mass. Pass the damp mass with sieve no. 22 and dried at 50 C in an oven for 6 hrs. The dried granular mass was passed again through sieve no. 44 to obtain uniform sized granules. After that disintegrant were mixed and compressed the granules under single punch machine to formulate tablets.

Evaluation of Tablets

Hardness test

Hardness testing was carried out by using Monsanto hardness tester as per procedure given in I.P. Five tablets were selected at random from each batch to measure the hardness. Then the mean hardness was calculated for each batch. The value of hardness was expressed in kg/cm2.

Weight uniformity test

Twenty tablets from each batch were selected randomly and weight individually using an analytical balance. Then their mean weights were calculated.

Friability test

Friability testing was carried out by using Roche friabilator as per procedure given in I.P. 10 tablets were taken and the weight was determined. Then they were placed in the friabilator and allowed to make 100 revolutions at 25 rpm. The tablets were then dusted and reweighed. The percentage weight loss was calculated.

Disintegration Test

It was performed as per official method prescribed in I.P. for uncoated tablets. 0.1 N HCl of 900 volumes was used as disintegrating medium used. The temperature of media was maintaining about 37ºC throughout the experiment. 5 tablets elected from each batch of formulation and put in the disintegration tube. The time taken to break up into small particles was recorded and calculates the mean disintegration time.

In Vitro Dissolution studies

Dissolution studies were performed as per procedure given in I.P. The test is performed by using USP-II dissolution apparatus. 900 ml of 0.1N HCl, pH 1.2 was used as dissolution medium. The temperature of medium was 37 ± 2oC throughout the experiments. The speed of rotation was 100 rpm. The samples were withdrawn at 10, 20, 30, 40, 50 and 60 min. by replacing equal amount of fresh dissolution medium. Then sample were analysed using UV Spectrophotometer and % cumulative drug release was calculated.

In-Vivo Study

The In-Vivo study was carried out for optimized formulation. Formulation having 4 % Pear and guava starch shows maximum drug release used for further study. The experimental protocol for animal studies was carried by Deshpandey Laboratories Pvt. Ltd., M.P. Bhopal, India, With Report Generation no. 031218 and CPCSEA / IAEC approval no. DL/IAEC/02/2018. Healthy Wistar rats of 3 to 4 months old, in the weight range of 150–250 g were used the study. Wistar Rats were housed in PP cages with free access to sterile food water and bedding material. Animals were housed in light controlled 12-12h and noise controlled rooms with 25°C temp and controlled humidity. Animals were fasted overnight prior to drug administrations. The calculated dose was given through oral route. Then blood samples were withdrawn from animals at different time intervals and plasma samples were measured for OD on a UV. Spec.

Stability Study

Stability study of optimized formulation was carried out as per the ICH guidelines. All the physiochemical parameters and dissolution rate of tablets were observed. The results revealed that there was no significant difference between the initial and stored tablets.

Results and Discussion

The starch was isolated from natural fruit was evaluated and the results shows that all the characteristics properties of starch are near about match with reference starch as shown in **(Table 1)**. The IR spectrum of isolated starch was also shows the entire characteristic peaks as in reference starch peak. Hence it confirms isolated compound was pure starch without containing any impurities (**Table 2)**. The formulation table was represented by (**Table 3)**. The drug calculations were made for 50 tablets for each batch. Starch mucilage used was in 2, 4, 6 and 8% w/w for tablet prepared by using wet granulation method. Tablets were prepared by using pear and guava starch as binding agent and then evaluated for different factors such as hardness, weight variation, friability, disintegration time and in- vitro dissolution study as shown in (**Tables 4 and 5)** The average weight variation of the tablets was found to be with the I.P. limits. The hardness values of the tablets were increased with the increase in the conc. of binding agents. The value of friability was decreased with increase in the conc. of binder. The tablet containing 4% starch friability was 0.72 ± 0.23 for pear and 1.08 ± 0.28 for guava starch. The disintegration time, were found to be increased with the increasing concentration of starch. The tablets with 4% binder conc. shows maximum drug release 80.69 ± 0.12 for pear and 83.54 ± 0.15 for guava starch after 1 hr as shown in (**Tables 6 and 7)** . The in-vivo study of optimized formulations was shown in (**Tables 8 and 9)** From the results, it was observed that, both pear and guava starch has improved dissolution rate and bioavailability. The improved in the bioavailability of drug was due swelling properties of starch.Guava starch has better binding properties then pear starch as shown in results. Stability study of optimized formulation shown in **(Tables 10 and 11)**. The results revealed that all the formulations are physically and chemically stable and there were no significant difference found in between the initial and stored tablets. All the results were within the limits, which show that all the formulations are chemically stable. From the fallowing study it was concluded the pear starch showed significant binding properties. The results from various evaluations show that pear starch had significant binding characteristics. Hence it can be used as tablet binder in pharmaceutical formulations and serve as best source for the production of industrial products **(Figures 4 and 5)**

S no	Properties	Pear starch	Guava starch
1	Identification test (Color with I2)	Black	Black
2	Starch color	Yellow	Cream to brown
3	Particle size (µ)	2270	868 ± 012
4	% Yield	57	53 ± 004
5	Paste clarity (%)	825	504 ± 014
6	Moisture content (%)	201	256 ± 011
7	Swelling capacity (%)	23	41 ± 006
8	Ash value (% w/w)	42	026 ± 016
9	Bulk density (g/ml)	119	0775 ± 008
10	Tapped density (g/ml)	138	089 ± 015
11	Carr's index (%)	1376	125 ± 014
12	Hausner's ratio	115	114 ± 021
13	Angle of repose	2112	1144 ± 021

14	Flow properties	Excellent	Excellent

Table 1: Characterization of Starch.

S No	Peak (cm^{-1})	Interpretation	Reference starch	Guava starch	Pear starch
1	3200-3500	-OH stretching	3366	3431	3431
2	2700-3000	-C-H stretching	2930	2927	2925
3	1640-1650	-O-H bending	1649	1638	1642
4	1300-1400	-C-H stretching	1458	1456	1458
5	1300-1350	-C-C-H Stretching	1340	1342	1370
6	1100-1300	-C-O stretching	1241	1053	1156

Table 2: Interpretation of FTIR spectra of Guava starch.

S No	Ingredient	Category	Amount mg/tab
1	Famotidine	Active	20
2	Lactose	Diluents	Variable (153-140)
3	Sodium carboxyl methyl cellulose (75%)	Disintegrant	15
4	Pear Starch (2-8%)	Binder	Variable (4-16)
5	Talc (25%)	Glidant	50
6	Magnesium stearate (15%)	Lubricant	30
7	Total Wt		200

Table 3: Formulation of Famotidine Tablet.

S No	Parameter	Binder concentration			
		2%	4%	6%	8%
1	Hardness (kg/cm2)	44 ± 05	56 ± 012	60 ± 06	65 ± 011
2	Weight variation (g)	198 ± 043	201 ± 046	195 ± 054	204 ± 024
3	Friability (%)	102 ± 021	072 ± 023	063 ± 042	048 ± 015
4	Thickness (mm)	455 ± 025	446 ± 031	450 ± 027	458 ± 017
5	Disintegration time (min)	45 ± 010	58 ± 000	70 ± 020	100 ± 028

Table 4: Evaluation of Famotidine Tablets with Pear Starch Results have been expressed as mean ± SD (n = 3).

S No	Parameter	Binder concentration			
		2%	4%	6%	8%
1	Hardness (kg/cm2)	43 ± 011	45 ± 008	58 ± 006	60 ± 009
2	Weight variation (gm)	198 ± 055	205 ± 066	207 ± 024	202 ± 034
3	Friability (%)	14 ± 025	108 ± 028	084 ± 054	076 ± 041
4	Thickness (mm)	458 ± 028	457 ± 045	448 ± 034	459 ± 026
5	Disintegration time (min)	35 ± 022	40 ± 080	65 ± 090	80 ± 060

Table 5: Evaluation of famotidine tablets with Guava starch Results have been expressed as mean ± SD (n = 3).

S No	Time (min)	Percentage cumulative drug release			
		2%	4%	6%	8%
1	00	00	00	00	00
2	10	1019 ± 019	1302 ± 010	911 ± 005	754 ± 021
3	20	1761 ± 014	2092 ± 015	1508 ± 024	1020 ± 014
4	30	2803 ± 015	3907 ± 009	2199 ± 026	1826 ± 027
6	40	4154 ± 034	5615 ± 014	3848 ± 021	2541 ± 025
7	50	5325 ± 014	6834 ± 011	4922 ± 026	4129 ± 022
8	60	6923 ± 012	8069 ± 012	7147 ± 025	6505 ± 021

Table 6: In- Vitro Dissolution Studies of famotidine tablets with Pear Starch Results have been expressed as mean ± SD (n = 3).

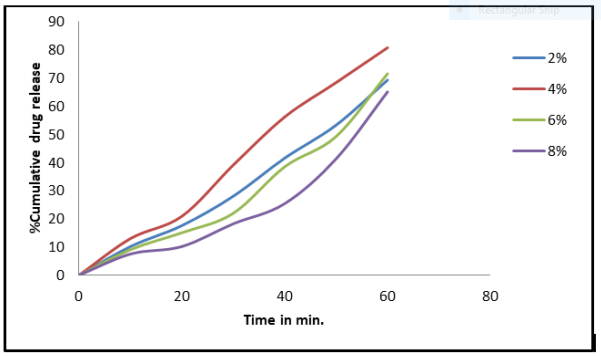

Figure 4: In vitro drug release of famotidine tablets with pear starch.

S No	Time (min)	Percentage cumulative drug release			
		2%	4%	6%	8%
1	00	00	00	00	00
2	10	1123 ± 009	1512 ± 011	1011 ± 002	854 ± 011
3	20	2121 ± 004	2802 ± 045	1818 ± 004	1590 ± 003
4	30	3213 ± 045	3927 ± 039	2709 ± 011	2656 ± 021
6	40	4204 ± 019	5515 ± 044	3938 ± 021	3321 ± 007
7	50	6105 ± 014	7504 ± 023	5772 ± 013	4889 ± 025
8	60	7303 ± 012	8354 ± 015	6947 ± 001	6265 ± 033

Table 7: In- Vitro dissolution studies of famotidine tablets with guava starch Values are mean ± SD (n = 3) significant at p< 005

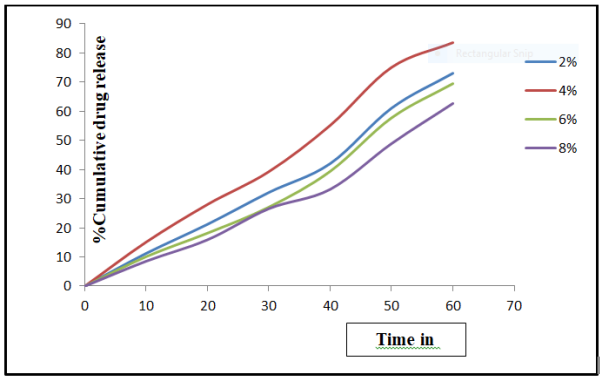

Figure 5: In vitro drug release of famotidine tablets with guava starch.

S No	Time (hr)	Optimized Formulation of Pear Starch	Optimized Formulation of Guava Starch
		Conc	Conc
1	05	014 ± 001	028 ± 002
2	05	066 ± 003	057 ± 015
3	10	066 ± 003	028 ± 013

Table 8: Release rate of drug in formulations

S No	Parameters calculated	Optimized Formulation of Pear Starch	Optimized Formulation of Guava Starch
1	C max	065 ± 011	055 ± 004
2	T max	5 ± 021	5 ± 006
3	T1/2	114 ± 006	117 ± 005
4	Ka(hr-1)	06045 ± 010	05895 ± 008
5	KE(hr-1)	02351 ± 009	01667 ± 011
6	Vd (L)	1138 ± 005	1345 ± 003
7	CL (L/hr)	065 ± 011	224 ± 006
8	AUC (µg/ml hr)	68 ± 008	65 ± 005

Table 9: Pharmacokinetic Parameters of In vivo release study.

Parameters	Time (in days)					
	00	15	30	60	90	180
Physical appearance	White	White	White	White	White	White
Hardness (gm/cm3)	45 ± 008	45 ± 018	44 ± 008	44 ± 008	43 ± 002	42 ± 005
Friability (%)	099 ± 028	099 ± 028	099 ± 028	099 ± 038	098 ± 031	098 ± 033
Disintegration time (min)	40 ± 080	40 ± 080	40 ± 081	39 ± 010	38 ± 050	39 ± 080
In-vitro drug release	8184 ± 015	8184 ± 015	8134 ± 015	8160 ± 015	8084 ± 011	8194 ± 010

Table 10: Accelerated Stability Studies of Pear at temperature (40 ± 2°C) Values are mean ± SD (n = 3) significant at p< 005.

Parameters	Time (in days)					
	00	15	30	60	90	180
Physical appearance	White	White	White	White	White	White
Hardness (gm/cm3)	56 ± 012	56 ± 012	56 ± 0012	55 ± 012	55 ± 014	55 ± 022
Friability (%)	072 ± 023	072 ± 023	072 ± 043	071 ± 021	071 ± 013	072 ± 003
Disintegration time (min)	58 ± 008	58 ± 001	58 ± 010	58 ± 000	56 ± 002	56 ± 003
In-vitro drug release	8069 ± 012	8064 ± 012	8169 ± 012	8009 ± 012	8019 ± 012	8065 ± 012

Table 11: Accelerated Stability Studies of Guava at temperature (40 ± 2°C)

Values are mean ± SD (n = 3) significant at p< 005.

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