Original Article

Formulation and Evaluation of Ibuprofen Tablets Using Gum of *Anacardium occidentale* as Binding Agent

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ABSTRACT

*Anacardium*gum derived from the edible seeds of *Anacardiumoccidantale*(family Anacardiaceae) was evaluated for its binding properties at a concentration of 5 % w/w and 10% w/w in Ibuprofen tablets with official starch as a control. A comparative analysis showed that the granules bound with *Anacardium*gum were relatively bigger and harder than the ones obtained with starch gum. The hardness, disintegration time and dissolution rate increased with increase in concentration of Anacardiumgum. Tablets containing 10% w/w of *Anacardium*gum had a binding capacity approximately twice that of starch with a dissolution rate of 58.5% after 30 min. The results obtained suggest that *Anacardium*gum possesses potential as a commercial binding agent.

Keywords: *Anacardium*gum, starch, disintegration, dissolution, hardness.

INTRODUCTION

Tablets

Tablets are solid preparations each containing a single dose of one or more active substances and usually obtained by compressing uniform volumes of particles.[1]

Excipients in tablet dosage forms

Binders & Adhesives

Binders are agents which hold the powder together to form granules. Binders are adhesives that are added to tablet formulation to provide the cohesiveness required for the bonding together of the granules under compaction to form tablets. Binders are either sugar or polymeric material.[1,2]

Natural polymer: acacia, tragacanth, gelatine etc.

Synthetic polymer: polyvinylpyrolidone, methyl & ethyl cellulose etc.

Diluents

Diluents are also synonymously known as fillers. Diluents are often added to tablet formulations for secondary reasons like to provide better tablet properties.[1]

 ISSN 2321 – 2748

Disintegrants

Disintegrants is the term applied to various agents added to tablet granulation for the purpose of causing the compressed tablet to break apart when placed in an aqueous environment.[1,2]

Lubricants

They are agent required to prevent adherence of the granules to the punch faces &dies. They also ensure smooth ejection of the tablet from the die.[1]

Glidants

Glidants are material that improves the flow characteristics of granulation by reducing interparticulate friction.[3]

Colour, Sweetner& Flavouring agents

The use of colour and dye in tablet making are disguising of coloured drugs. Product identification &production of more elegant product.Sweetners and flavouring agents are used to impart taste and flavour to make the product palatable.[1,2]

MATERIALS USED

- Ibuprofen tablet (Obtained as gift sample from IPCAC, Bangalore)
- Gum of *Anacardium occidentale* (Locally obtained)
- Diethyl ether (Medilise Chemicals, kannur)
- Starch (Yarrow chem. Product Mumbai-400037)
- Talc (Burgoyne Burbides&Co,Mumbai)
- Lactose (Spectrum reagents and chemicals Pvt. Ltd. Cochin)
- Magnesium stearate (Ozone international, Mumbai)
- Distilled water

All the reagents in this study were of A.R. grade.

INSTRUMENTS

1. Double beam UV-visible spectrophotometer [Systronics 2203]
2. Dissolution apparatus [Electro lab tablet dissolution tester model no.TDT-06T]
3. Disintegration apparatus [Dolphin]
4. Ostwald's viscometer
5. Monsanto hardness tester [ROLEX tablet hardness tester]
6. Roche friabilator [double drum] (Dolphin ^{TM})]
7. Electronic weighing balance [LCGC chromatography solutions Pvt.Ltd]
8. Tablet compression machine [Rolex Scientific Engineers]

METHODS

1. Preformulation studies of Anacardium-occidantale gum

Preformulation studies were performed on the Anacardium gum, which include purification and physic-chemical characterization of the gum.

2. Purification of Gum

The gum was cleaned by removing the bark and other extraneous material by hand; dried in a hot air oven at 50^0c for about 8 hours until it become sufficiently brittle. The dried gum was manually sorted into light coloured and dark coloured grades. The light coloured grades selected by further processing by milling in a domestic blender into the powder and designated as crude cashew gum (CCG). 100 g CCG was dissolved in 200 ml distilled water and allow standing for 24 hours with intermittent stirring. The gum mucilage was strained with muslin cloth to remove any insoluble debris or impurities and precipitated with 350 ml of 96%ethanol. The precipitated gum was refiltered and washed with diethyl ether and dry in hot air oven at 50^0c for 8hrs. The dried purified gum was milled and screened

through 180 mm sieve. This is purified cashew gum (PCG).[4]

3. Physico-chemical characterization of the gum (See table no. 1)

A). Solubility test

The separated gum was evaluated for solubility in water, acetone, chloroform and ethanol in accordance with the B.P specifications.[4,5]

B). Loss on drying

The method adopted was that of B.P 2004 for acacia. 1.0g of the sample was transferred into each of several petri dishes and then dried in an oven at 105^0C until a constant weight was obtained. The moisture content was then determined as the ratio of weight of moisture loss to weight of sample expressed as a percentage.[4,5]

C). Ash values

Ash values such as total ash, acid insoluble ash and water soluble ash were determined according to I.P.[5]

D). Hausner's ratio

This was calculated as the ratio of tapped density to bulk density of samples.[5]

$$H.R = Dt / Db$$

Dt–tapped density

Db – bulk density

E). Compressibility index (C %)

This was calculated using the equation

$$\% \text{ Compressibility} = \frac{Dt-Db}{Dt} * 100$$

4. Preparation of Standard Graph

100mg of ibuprofen was weighed and transfer into a 100 ml volumetric flask and was dissolved in phosphate buffer of pH 7.2 & make up to100 ml. This was the standard stock solution containing 1mg/ml of ibuprofen. From this stock solution 10ml was taken and made up to 100 ml with phosphate buffer pH 7.2. This was the second standard stock solution (100µg/ml). From this solution dilutions of 20µg/ml, 40µg/ml, 60µg/ml, 80µg/ml, 100µg/ml were made and absorbance was measured at 221 nm using double beam UV-Visible Spectrophotometer. Phosphate buffer pH7.2 was taken as blank. The standard plot was drawn using the data obtained.[6] (See table no. 2)

5. Preparation of Granules

The granule comprising of ibuprofen, lactose, starch powder, talc and magnesium stearate were prepared using wet granulation technique. The powder excluding talc and magnesium stearate were mixed for 5 minute and massed with appropriate amount of binder solution of PCG (5%w/v, 10%w/v) and starch paste to prepare 3 categories of ibuprofen tablet. The damp mass was screened through sieve no.12 and dried at 60^0C for 1 hr in a hot air oven. The dried granules are passed through sieve no.16& 44. The manufacturing additives like magnesium stearate and talc were added and punched into tablet using tablet punching machine.[7] (See table no. 3)

Pre-compression evaluation

1. Determination of Bulk Density

10g of tablets granules placed in the measuring cylinder (100ml) and volume was noted. Adjust for 50 tapping and volume of the powder was noted, the procedure was repeated until two volumes were same. Bulk density can be calculated by using equation[8,9]

$$\text{Bulk density} = \frac{\text{weight of the granule}}{\text{Bulk volume}}$$

2. Determination of Angle of Repose

A funnel was fixed at a particular height 'h' on a stand. A white bond paper was placed below the funnel on the table. The

 ISSN 2321 – 2748

granules whose angle of repose was to be determined is passing slowly through the funnel until it form a pile. Further addition of the granules were stopped when the granules touches the tip of the funnel. Circumference of the pile of the granule was drawn. The radius of the pile was noted in cm. The angle of repose of the granule was calculated by using the following formula:-[8,9]

$\theta = \tan^{-1}(h/r)$ Θ-Angle of repose
h-Height of the pile in cm
r-Radius of the pile in cm

3. Density related properties

The carr's index of the granules was calculated from the difference between tapped and bulk densities divided by the tapped density.[8]

% compressibility = Dt-Db/Dt * 100

The Hausner ratio was calculated by dividing the tapped density by bulk density of the granules.

H.R = Dt / Db

CHARACTERISATION OF TABLETS

Thickness

Thickness of tablets was determined using screw guage.5tablets from each batch were used, and average value was calculated.[10,11]

Weight Variation Test

To study weight variation, 20 tablets of each formulation were weighed using analytical balance, and the test was performed according to the official method given in IP.[12,13]

Hardness

For each formulation, the hardness of 5 tablets was determined using Monsanto hardness tester. After compression the tablets were stored in amber coloured bottle (closed). Tablet hardness was tested for randomly selected 5 tablets. Hardness testing was done using Monsanto hardness tester. The tablet was held alone its oblong axis in between the two jaws of the test. At this point reading should be zero kg/cm^2. Then constant force was applied by rotating the knob until the tablets fractured. The value at this point was noted in kg/cm^2.[2,12,14].

Friability

For each formulation the friability of 10 tablets was determined using the Roche friabilator. This test tablets subjected to the combined effect of shock abrasion by utilising a plastic chamber which resolves at a speed of 25 rpm, dropping the tablets at a distance of 6 inches in each revolution. Samples of reweighed 10 tablets were placed in a Roche friabilator which was then operated for 100 revolutions for 4 min. The tablets were than dusted and reweighed. %friability (%F) was calculated as follows[12, 14]

$$\%F = \frac{\text{loss in weight}}{\text{Initial weight}} \times 100$$

Assay of formulated Ibuprofen tablets

Weigh accurately about 10 tablets and calculated average weight of one tablets. Powder the tablets and weigh the powder a quantity equivalent to 0.25g Ibuprofen and extract with 10 mi of chloroform .Filter and wash the residue with 3 quantities of 5 ml of chloroform. Collect the precipitate and evaporate by gentle heating on a heating mantle .Dissolve residue in 50 ml of methanol and titrated against 0.1N sodium hydroxide solution by using phenolphthalein as indicator.[15]

In-vitro dissolution rate studies

In-vitro release rate of ibuprofen tablet was determined using single station USP dissolution test apparatus. A single tablet was placed in a 900 ml of dissolution medium (phosphate buffer with pH7.2). The sink

condition was maintained at temperature 37^0C and speed was fixed at 100 rpm for 30 min. withdraw a suitable volume of the medium (5ml) and filtered through what Mann filter paper, rejecting the first 1ml of the filtrate. Dilute a suitable volume of the filtrate with the same solvent. Measure the absorbance of the resulting solution at a maximum about 221 nm by a UV-Spectrophotometer. The concentration of the drug released at different time interval was determined from standard graph. From this cumulative % drug release was calculated and this was plotted against function of time to find out the pattern of drug release. The rates of drug released were determined.[12,14]

RESULT AND DISCUSSION

Thickness

The thickness of formulated tablets was found to be in the range of 8-10mm which was acceptable. The results obtained are as given in Table no.4**.**

Weight Variation test

Percentage deviation of formulated tablets was found to be within the specification limits of ±5%.The results obtained are as given in Table no.5.

Hardness test

Hardness of formulated tablets was found to be in the range of 4-6 kg/cm^2, which is specified within the limit as given in the IP. The results are as given in Table no.6.

Determination of Angle of repose

The angle of repose of granules was found to be satisfactory as per I.P specifications. The results are as given in Table no.7.

Determination of Bulk density

The bulk density values are as given in Table no.8.

Friability test

The friability of formulated tablets ranges between 0.55-0.82percent which complies with friability test, because the percentage friability does not exceed 1%. The values are as given in Table no.9.

Disintegration test

The disintegration time for the given tablet was found to be 4 minute which complies with the limit for uncoated tablets (within 5 mints.)

Determination of drug content

The formulation with 10% PCG was found to contain higher drug content and percentage yield. The results are as given in Table no. 10.

In-vitro dissolution rate studies

The graph shows that, the drug releasing property of F2 was similar to that of F3. And F1 has slow releasing property compared to other two tablets. From this study it was found that 10%PCG has good binding property and drug releasing property similar to that of starch paste. The results obtained are as given in TABLE NO.11, 12 & 13.

CONCLUSION

Ibuprofen tablets were prepared by using cashew gum of *Anacardium occidentale* as binding agent (5%, 10%) by a process of wet granulation. These tablets were compared with tablets prepared from starch paste (10%) as binding agent.

From the quality control tests of ibuprofen tablets prepared using different binders (10% PCG, 5% PCG, Starch paste) it was found that 10% purified crude cashew gum has good binding property and it can be used in tablet formulation. Further tablet evaluation studies suggest that F2 has good drug releasing and pharmacokinetic property.

REFERENCES

1. Leonlachmann,Herbert.A.liberman,Joseph.L. Kanig. The Theory and Practice of Industrial Pharmacy, 3rd edition, Page No: 293-44
2. M.Aulton, Pharmaceutics- The Science of Dosage form design, 2nd edition, page no: 457
3. *International Journals of Drug Discovery and Herbal Research*, July-September, page no: 128-33
4. Scholars research library per Pharmacia letter, 2011
5. *International Journals of pharmacy and Pharmaceutical Sciences*, volume I, Issue4, 2010.
6. *International Journals of pharmacy and Pharmaceutical Sciences*, volume II, issue 3, July 2009, page no: 693-04
7. *Journal of food engineering*, march 2009
8. Agro food industry Hi-tech, volume 19, Nov-Dec 2008.
9. Science alert (An open access publisher) *Journal of biological sciences* 2008, page no; 288-99
10. NISCAIR online periodical repository (NOPR) Research journals of scientific and industrial research (JSIR), July 2007
11. Biotechnology & Applied biochemistry, Feb-2002
12. Indian Pharmacopeia, 2007, volume II, page no 1217-18.
13. Indian drugs June-2008 page no; 461-68
14. Physical pharmacy by Alfred Martin, 4th edition, page no. 447.
15. Pharmaceutical analysis, volume I, by P C Kamboj, page no. 334
16. Indian Pharmacopoeia 1996, page no.387-88.
17. Laboratory manual of Physical Pharmaceutics by C V S Subrahmanyam, page,no;46-51.

Table 1. Physicochemical properties of Anacardium gum

Some physicochemical properties of Anacardium gum	
Parameters	Result
Solubility	It is sparingly soluble in water forms viscoussolution, insoluble in ethanol, methanol, acetone and ether.
Loss on drying	8%
Total ash	2%
Acid insoluble ash	0.5%
True density	1.5g/dl
pH	5.65
Compressibility index	20%
Hausner's ratio	0.9

Table 2. Formula for the preparation of Ibuprofen tablets

Formulation	Ibuprofen	Lactose	Starch powder	Magnesium stearate	Talc	Binding agent	Starch paste
F1	200 mg	31.9%w/w	4.1%w/w	0.15%w/w	1%w/w	5%PCG	_
F2	200 mg	31.9%w/w	4.1%w/w	0.15%w/w	1%w/w	10%PCG	_
F3	200 mg	31.9%w/w	4.1%w/w	0.15%w/w	1%w/w	_	10%W/W

Table 3. Standard graph for Ibuprofen

Concentration (µg/ml)	Absorbance 221 nm	Standard deviation
0	0	0
20	0.135	0.751
40	0.249	0.777
60	0.359	0.806
80	0.496	0.834
100	0.623	0.857

 ISSN 2321 – 2748

Table 4. Thickness variation

Sl. No.	F1 (mm), SD	F2(mm),SD	F3 (mm),SD
1	8.1±0.63	9.2±0.15	10±0.20
2	9.0±0.30	9.5±0.20	9.6±0.30
3	9.0±0.58	8.3±0.55	9.9±0.32
4	8.4±0.49	8.1±0.62	9.3±0.37
5	10 ±0.58	8.0±0.66	8.5±0.61
6	8.3±0.90	9.1±0.62	8.1±0.65
7	8.7±0.68	8.6±0.70	9.8±0.79
8	9.2±0.46	8.2±0.75	9.4±0.91
9	9.1±0.95	10±0.78	9.3±0.95
10	8.2±0.75	8.2±0.94	8.1±0.97

Table 5. Weight variation test

SL. NO.	WEIGHT VARIATION F1, SD (%)	WEIGHT VARIATION F2,SD (%)	WEIGHT VARIATION F3,SD (%)
1	0.93 ±1.13	-1.06±0.38	1.22±0.47
2	0.70±1.52	0.70±1.98	-1.57±1.07
3	-1.58±1.07	-1.94±1.50	-1.40±0.53
4	-2.99±1.57	0.35±0.78	-2.45±0.79
5	-0.88±1.21	-0.17±1.6	-2.10±1.58
6	0.93±0.86	1.23±0.43	-1.92±1.25
7	-0.35±1.46	-2.47±0.79	1.05±0.42
8	1.94±1.38	1.47±0.53	1.40±1.52
9	-0.70±2.53	0±0.44	0.17±1.28
10	-1.76±2.65	-0.53±0.48	1.22±1.81
11	-2.29±0.65	0.88±0.53	1.57±1.43
12	-1.41±1.66	1.94±1.5	1.40±0.42
13	1.05±0.41	0±0.12	0.17±0.63
14	-2.11±1.44	-1.94±1.5	0.52±1.63
15	2.22±1.09	0±0.3	1.2±1.52
16	1.41±0.63	-1.5±1.4	1.57±1.33
17	3.17±0.86	1.41±0.79	-1.92±1.42
18	3.52±1.44	0.17±0.85	1.22±1.28
19	1.05±0.66	0.88±1.98	0.17±0.58
20	1.58±0.72	1.59±0.53	-1.92±0.88

Table 6. Hardness test

Sl no.	F1 (kg/cm^2), SD	F2 (kg/cm^2)	F3 (kg/cm^2)
1	4	5	6
2	5.5	5.5	5
3	5	4	5.5
4	6	5.5	4
5	6	6	5

Table 7. Angle of repose test

Binder	Height Of pile h (cm)	Radius of pile r (cm)	Angle of repose $\Theta=\tan^{-1}(h/r)$	Average ' θ ' in degree
F1	2	3.83	30.59	30.72^0
	2	3.33	30.83	
	2	3.26	31.48	
F2	2	3.25	31.6	30.76^0
	2	3.43	30.24	
	2	3.4	30.46	
F3	2	3.25	31.60	30.72^0
	2	3.43	30.22	
	2	3.41	30.34	

Table 8. Bulk density

Formulations	Bulk density (g/cm)
F1	0.625
F2	0.555
F3	0.625

Table 9. Friability test

Formulations	%Friability
F1	0.55%
F2	0.78%
F3	0.82%

Table 10. Drug content test

Formulations	Drug content	% yield
F1	193 mg	96.5% w/w
F2	185 mg	92.5%w/w
F3	190 mg	95.1 %w/w

Table 11. Dissolution rate studies for ibuprofen tablets using 5% PCG (F1)

Time (min)	Concentration (µg/ml)	%drug dissolved
0	-	-
5	0.8	7.2
10	1.6	14.4
15	2	18
20	4.8	43.2
25	4.9	44.1
30	5.9	53.1

Table 12. Dissolution rate studies for Ibuprofen tablets using 10% PCG (F2)

Time (min)	Concentration (µg/ml)	%drug dissolved
0	-	-
5	1.5	13.5
10	2.7	24.3
15	4.3	38.7
20	4.9	44.1
25	6.1	54.9
30	6.5	58.5

Table 13. Dissolution rate studies for ibuprofen tablets using starch paste (F3)

Time (min)	Concentration (µg/ml)	%drug dissolved
0	-	-
5	1.2	10.8
10	2.1	18.9
15	4.5	40.5
20	5	45
25	5.3	47.7
30	6.4	57.6

 ISSN 2321 – 2748

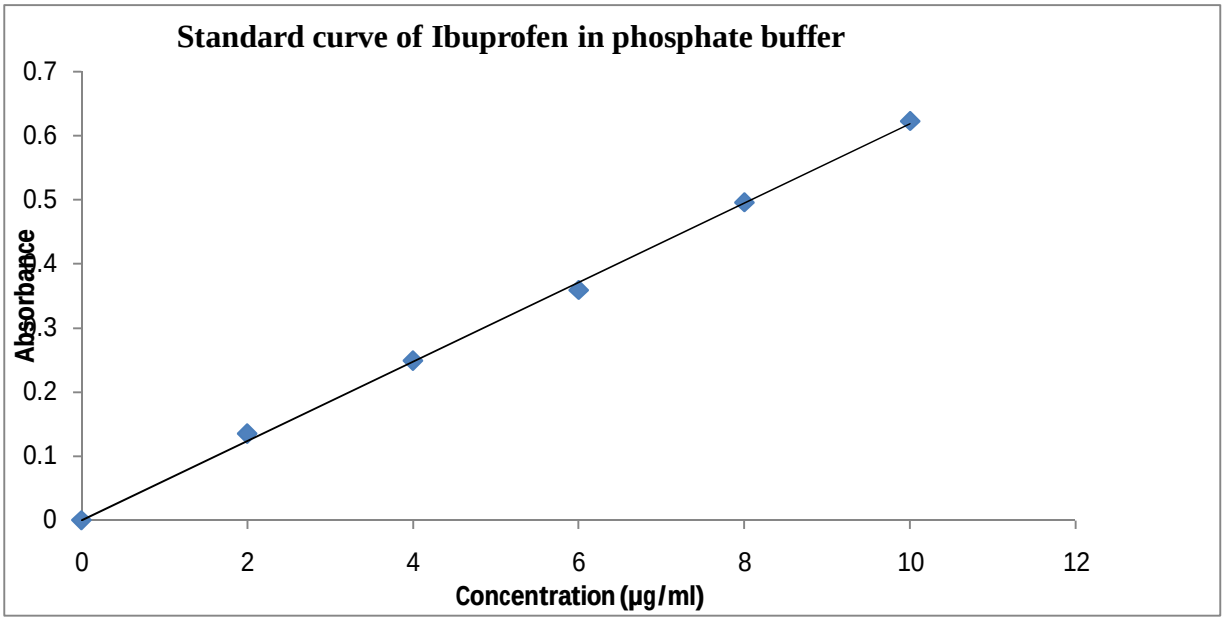

Figure 1. Standard graph of Ibuprofen

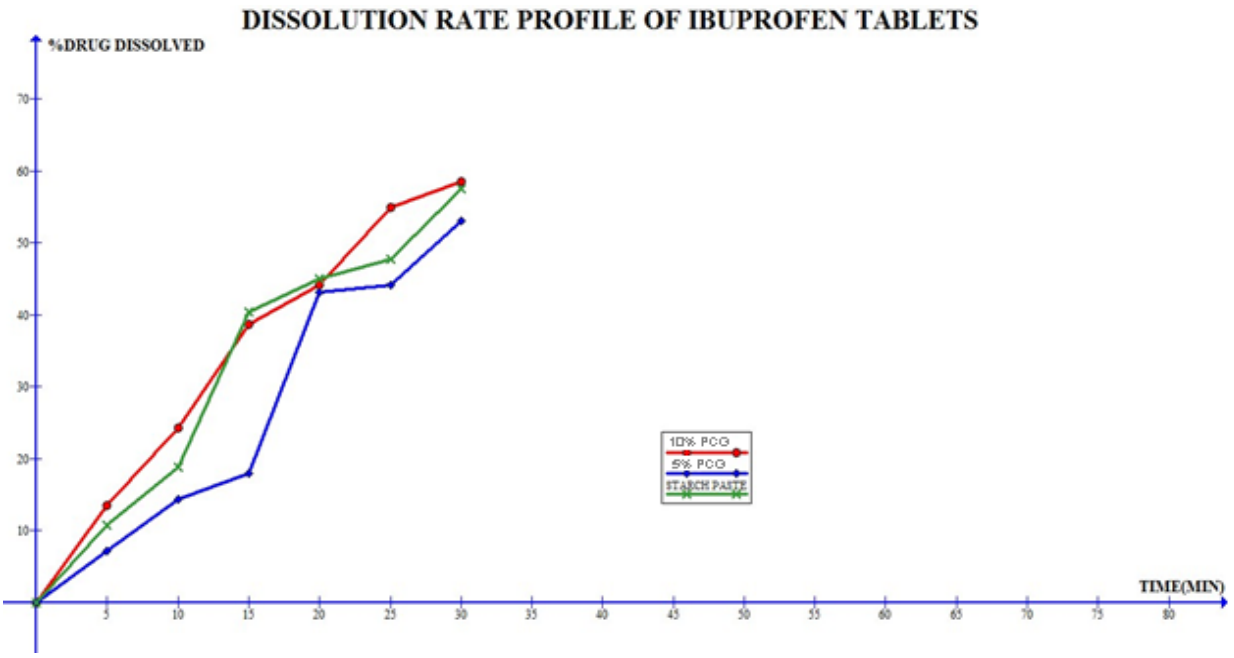

Figure 2. Dissolution rate profile of F1, F2, F3