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COMPARATIVE STUDIES OF BINDING PROPERTY OF STARCH FROM VARIOUS NATURAL SOURCES ON METFORMIN TABLETS

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Abstract: The aim of the study was that comparing the binding effects of isolated starch from various natural sources like rice and potato. Mucilage's of the starches of varying concentrations of 2, 4 and 6%w/w were used to produce Metformin Hydrochloride granules by wet granulation method and compressed into tablets. For the evaluation of granular properties different tests were carried out like bulk and tapped densities, Carr's index, Hausner's ratio and angle of repose. The granules were compressed into tablets and evaluated for different parameters like weight uniformity, friability, disintegration time and dissolution rate. The study concluded that an increase in binder concentration led to an increase in crushing strength, decrease in friability and increase in disintegration time of the tablets. Rice starch produced the hardest tablets and also the least friable tablets, the longest disintegration time and dissolution time when compared to potato starches.

Keywords: Metformin Hydrochloride, binders, binding effect, Rice starch, Potato starch.

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INTRODUCTION

Starch is one of the most widely used excipients in the manufacture of solid dosage forms. Starches from different sources have been evaluated and used as excellent binders in either mucilage or the dry powdered form. Binders[1,2] are agents employed to impart cohesiveness to the granules. This ensures the tablet remains intact after compression as well as improving the flow qualities by the formulation of granules of derived hardness and size. The choice of a suitable binder for a tablet formulation requires extensive[3].

Extraction of Rice starch[4,5]: Broken pieces of rice were soaked in 0.4% aqueous solution of NaOH then insoluble protein, glutein dissolved and grains softened by the soaking, diluted suspension is centrifuged to separate starch by centrifuge apparatus and isolated starch was dried at 60^{o}C for 3 days.

Extraction of Potato starch[4,5]: Potato was thoroughly washed and all foreign materials were removed. The potato was peeled, weighed and washed. The washed potato was pulverized using a blender. Enough quantity of water was added to the pulp which then passed through a sieve. The filtrate was allowed to settle and 0.1N sodium hydroxide was added to separate the starch and proteinous materials as well as to neutralize the prevailing slight acidity. Excess sodium hydroxide was removed by washing several times with distilled water. The clear supernatant fluid was poured away while sedimented starch was collected on a tray and air-dried on a table at room temperature.

Formulation of Metformin Hcl granules and tablets [6]:

Metformin Hcl granules were prepared with rice starch and potato starch as binders in six different formulation of each starch which contains 2%, 4%, and 6% of starch, 2.5% PVP-K 15 is used as disintegrant 0.2% Talc is used as glidant and 0.2% Magnesium stearate as lubricants. The wet granulation method was employed in the formulation of the tablets. The required quantities of Metformin hcl and disintegrant were weighed and mixed with the binder mucilage. The resulting wet masses were screened by passing them manually through a mesh no.12 and dried for 20minutes at 40ºC in the oven and then screened through sieve.no.60 µm and then dried to constant weight in the oven. The granules were then mixed with the required quantities of lubricants and then compressed into tablets.

Table No. 1: Formulation Composition of Metformin Hcl Powder Blends

	F1	F2	F3	F4	F5	F6
Metformin Hcl	250	250	250	250	250	250
Lactose	73.25	66.25	59.75	73.25	66.25	59.75
Potato Starch	7	14	21	-	-	-
Rice Starch	-	-	-	7	14	21
PVP-K30	9.25	9.25	9.25	9.25	9.25	9.25
Saccharin	3.5	3.5	3.5	3.5	3.5	3.5
Mag. Stearate	3.5	3.5	3.5	3.5	3.5	3.5
Talc	3.5	3.5	3.5	3.5	3.5	3.5
Total Weight(mg)	350	350	350	350	350	350

PRECOMPRESSION PARAMETERS OF GRANULES[6]:

1. Angle of repose:

Fifty grams (50 g) of the granules was placed in a plugged glass funnel which had a distance of 10cm from the flat surface. The granules were then allowed to flow through the funnel orifice by removing the cotton plug from the funnel orifice. The height of the heap (*h*) formed as well as the radius of the heap (*r*) was noted. The angle of repose (*Q*) was calculated as:

$$Q = \tan^{-1}\frac{h}{r}$$

2. Bulk and Tapped densities:

Thirty grams (30 g) of the granules were carefully poured through a short stemmed glass funnel into a 100ml graduated cylinder. The volume occupied by the granules was read and the bulk density calculated in gm/ml. The cylinder containing the granules was tapped fifty times from a height of 2cm and the tapped density calculated in gm/ml.

3. Percentage compressibility (Carr's index) and Hausner's ratio:

The percentage compressibility (*CI*) was calculated from the difference between the tapped densities (*Dt*) and the bulk densities (*Bt*) divided by the tapped densities. The Hausner's ratio (*HR*) is the ratio between the tapped and bulk density.

$$CI = \frac{Dt - Bt}{Dt} \times 100$$

$$HR = \frac{Dt}{Bt}$$

POSTCOMPRESSION EVALUATION OF TABLETS[7,8]:

Weight variation Test: Twenty tablets from each formulation were selected randomly and average weight was determined. Individual tablets were then weighed and compared with average weight.

Hardness test: The force required to break a tablet in a diametric compression was determined by using Pfizer tablet hardness tester.

Friability: The weight of twenty tablets was noted and placed in the friabilator and then subjected to100 revolutions at 25 rpm. Tablets were dedusted using a soft muslin cloth and reweighed.

Percent friability = [initial weight – final weight **/** initial weight] × 100

Thickness Test: By using Screwguage can identify the thickness of the tablets.

Drug content uniformity: The drug content uniformity was determined by taking the powder equivalent to 10mg, and then it was dissolved in P^H6.8 phosphate. Required dilution (10µg/ml) was prepared and absorbance was taken against the blank at 232nm.

In vitro disintegration time:

Six (6) tablets were placed in each compartment of the Erweka disintegration apparatus, with water thermo stated at 37 ± 2^{O}C and pH6.8 Phosphate buffer as the medium. The tablets were considered to have passed the test after the six (6) tablets passed through the mesh of the apparatus in 15 minutes.

In vitro Dissolution studies:

Dissolution rate of Metformin Hcl from all formulations was performed using ELIGHT SCIENTIFIC LABORATORIES an eight stage dissolution rate testing apparatus with paddle. The dissolution fluid was 900 ml of P^H6.8 phosphate buffer with a speed of 50 rpm and temperature of 37±0.5˚C were used in each test. 5 ml of sample was withdrawn at different time intervals (5, 10, 15, 20, 30, 40 and 45 mins) and fresh medium was replaced to maintain sink conditions. The samples were analyzed by using UV- Visible spectrophotometer at λ_{max} 232 nm. Dissolution studies were performed in triplicate.

RESULTS AND DISCUSSION:

Bulk and tapped density of the granules was significantly increased with increasing concentration of starch and the good correlation was observed between the concentration of binder and the density. The bulk and tapped densities exhibited by rice starch granules lower as

compare to that of potato starch granules. A Carr's Index of less than 15% indicates an adequate flow of granules and stable packing while values of more than 25% are characteristic of poor flow property all formulations shows Carr's Index more than 15% which shows poor flow property. Hausner ratio may be related to the compressibility of powder and value of more than 1.2 are indicative of passable compressibility here all formulation shows Hausner ratio more than 1.2 which shows poor compressibility. Angle of repose gives a qualitative assessment of internal and cohesive friction forces. An angle less than 30^{o} indicate good flow potential. All starches of granules showed an angle of repose less 30^{o} and were therefore classified as material with good flow potential.

Table.No.2: Evaluation of tablet blend of formulations

Formulation	Bulk Density (g/cc)	Tapped Density(g/cc)	Hausner ratio	Compressibility index (%)	Angle of repose
F1	0.464	0.574	1.23	19.1	29.47
F2	0.423	0.501	1.16	15.5	27.63
F3	0.456	0.542	1.22	15.8	25.54
F4	0.467	0.559	1.25	16.4	26.23
F5	0.485	0.593	1.10	18.2	27.21
F6	0.460	0.556	1.21	17.2	30.38

Tablet thickness is varying with compressional force and density of granules. The tablet thickness of all the formulation is found which may be attributed to their similar bulk and tapped densities and same compressional force used. Tablet hardness is observed higher (2.5-3.8 kg/cm^2) with rice starch at all the concentration employed compared with the potato starch which may be due to higher compaction power and good binding potency of these starches. The weight variation found in the range (2-4%) in case of all the formulation. All the batches prepared passed the weight variation test as per reported in USP.

Table.No.3: Post Compressional Evaluation of formulations

Formulation	Hardness (kg/cm^2)	Friability (%)	Weight Variation (mg)
F1	2.5±0.24	0.27	348±0.67
F2	3.0±0.62	0.29	348±0.77
F3	3.8±0.16	0.24	350±0.86
F4	3.2±0.22	0.32	351±0.74
F5	3.6±0.15	0.24	349±0.88
F6	3.8±0.16	0.28	350±0.56

Table.No.4: Post Compressional Evaluation of formulations

Formulation	Disintegration time (mins)	Drug content (%)	Thickness (mm)
F1	10±0.54	97.2±0.62	3.8±0.15
F2	12±0.63	97.72±0.23	3.9±0.03
F3	15±0.48	98.4±0.34	4.2±0.01
F4	12±0.57	97±0.56	3.9±0.06
F5	15±0.72	99.44±0.49	4.0±0.10
F6	16±0.41	99.8±0.27	4.2±0.03

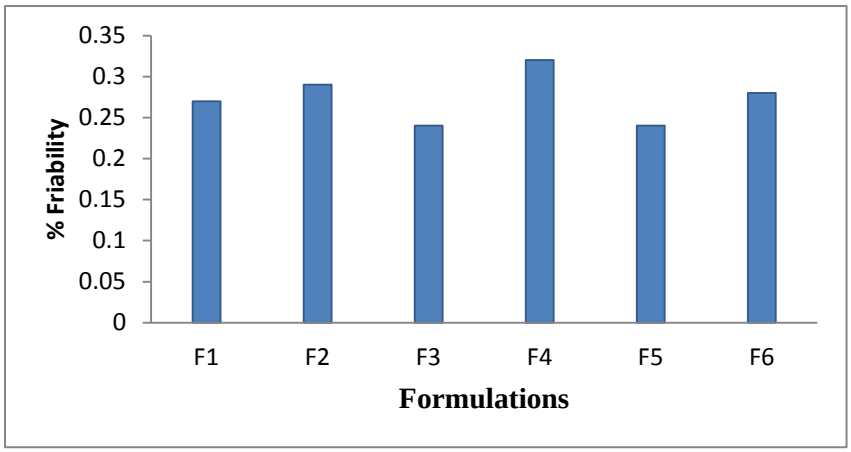


Fig.No.1: Bar graph comparison friability of formulations

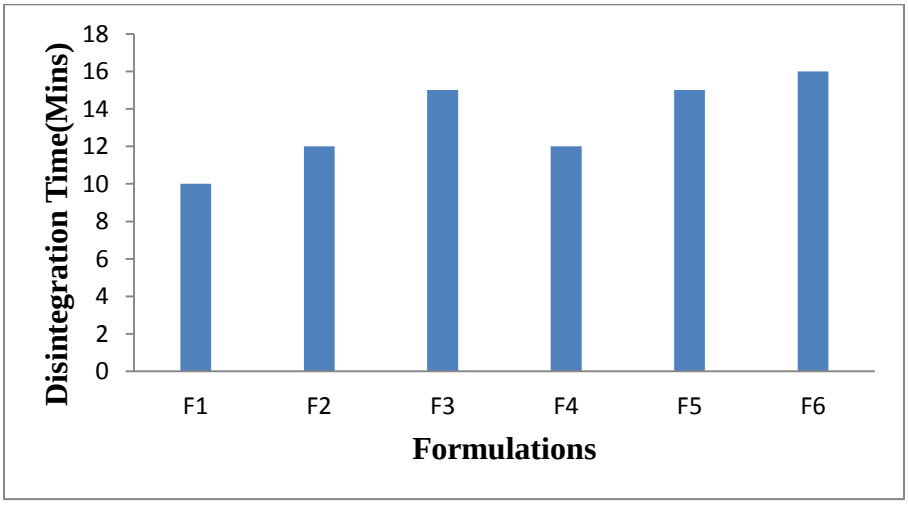


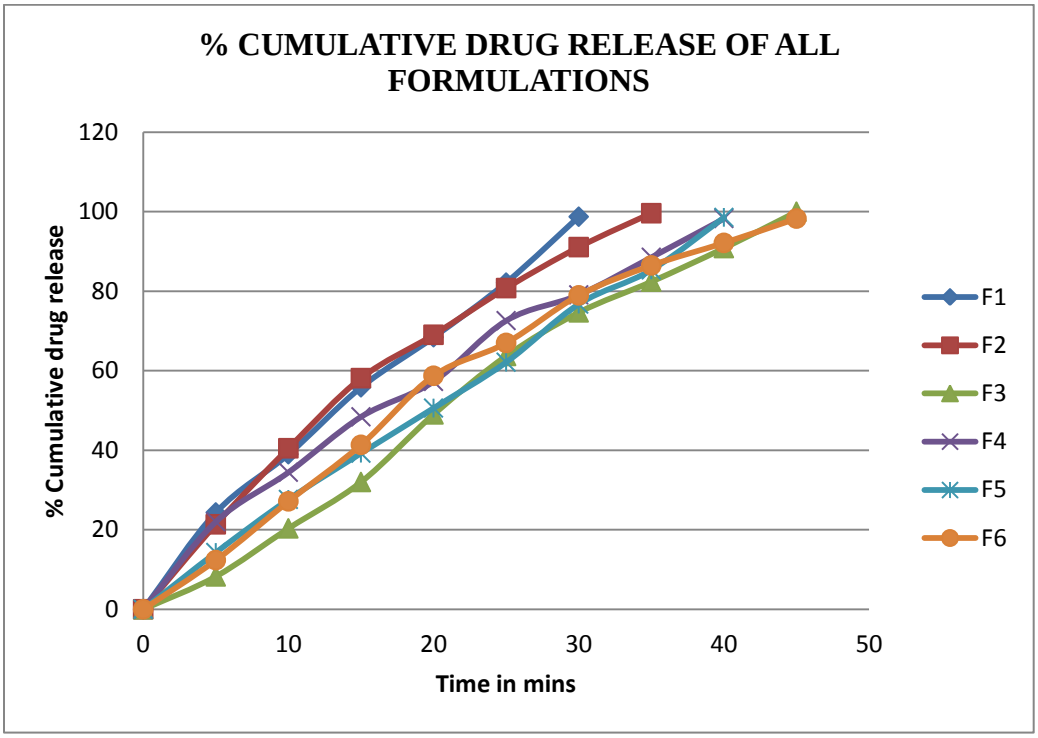
Fig.No.2: Bar graph comparison between Disintegration time for formulations

Friability is another mechanical property of a tablet with compendia l (USP 1995) specification not more than 1%. It was observed that Metformin Hcl tablets prepared with potato and rice starches pass the friability test. Disintegration time (10-15 min) is observed to be higher with rice starch at all the concentration employed compared with the potato starch which may be due to higher compaction power and good binding potency of the starch. The concentration of the drug in all the formulations with superdisintegants was found to be 97±0.56– 99.8±0.27. It was within the IP limits.

Table. No. 5: Cumulative % drug release of formulations

Time(min)	F1	F2	F3	F4	F5	F6
5	24.34±0.89	21.36±0.32	8.26±0.65	22.02±0.76	14.28±0.56	12.36±0.98
10	38.98±0.22	40.48±0.26	20.34±0.86	34.44±0.464	27.62±0.24	27.14±0.78
15	55.81±0.89	58.11±0.98	32±0.44	48.4±0.53	39.24±0.68	41.34±.62
20	68.4±0.32	69.01±0.27	49±0.32	57.28±1.0	50.59±0.55	58.71±0.65
25	82.13±0.72	80.75±0.65	63.69±0.52	72.58±0.54	62.12±0.54	66.97±0.56
30	98.7±0.93	91.06±0.98	74.65±0.58	79.06±0.67	76.74±0.63	78.92±0.77
35	-	99.58±0.57	82.38±0.46	88.51±0.75	85.33±0.89	86.45±0.83
40	-	-	90.82±0.58	98.24±0.32	98.54±0.84	92.12±0.63
	-	-	99.96±0.54	-	99.34±0.26	98.24±0.98

The result of in vitro drug release study shows that for F1 and F2 tablet formulated with potato starch shows faster drug release profile in comparison to other starch tablet. While in case of formulation F3 to F_6 the slower drug release was observed with potato starch tablet and rice starch tablet. In all the formulation, the drug release rate decreased when the proportion of binder increased which may be due to increase in compaction force and greater degree of binding. In all the formulation, the drug release rate decreased when the proportion of binder increased. It was reasoned that, as the amount of binder in the compact increased, there would be a greater degree of binding.



SUMMARY AND CONCLUSION

It has been concluded from the results in this study that the tablet formulated with rice starch will have good effects on the friability, hardness, disintegration time and percentage of drug release from the tablets produced. Tablet formulated with rice starch are less friabable, harder, shows longer time for disintegration and good drug release profile in comparison to tablets formulated with potato starch. The percentage of drug release shows that the rice starch had a great influence on binding strength of the tablet. If this could be proved in a large scale, then it is very much beneficial to the tablet manufacturing industry as it is cheap and abundantly available.

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