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Research Article

EVALUATION OF NATIVE AND CARBOXYMETHYLATED *AMARANTHUS PENICULATUS* (RAJGIRA) STARCH AS A TABLET DISINTEGRANT

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Abstract

Native rajgira starch and carboxymethyl rajgira starch (CMS) were evaluated as tablet disintegrants in comparison with rice starch. Tablets were prepared with wet granulation method and dibasic calcium phosphate was used as filler, each starch at various concentrations between 3-12% w/w as a disintegrant and magnesium stearate as a lubricant. Paracetamol (PCM) was used as a model drug for drug dissolution testing. Tablet properties including hardness, friability, disintegration and dissolution were evaluated. The results showed that tablet hardness increased with the amount of starch in the tablets. Tablets containing rajgira starch and rice starch showed higher tablet hardness while the tablets containing CMS showed obvious superior hardness to that of the other starches. The disintegration of tablets containing native rajgira starch was faster than that of tablets with rice starch. With increasing native starch concentrations, the disintegration of the tablets was found to be faster. Tablets with CMS disintegrated in a similar manner to those with native rajgira starch when the concentrations were up to 9% by weight. The disintegration was delayed with higher concentrations. The PCM tablet with rajgira starch as a disintegrant gave faster initial dissolution than the others. It can be concluded that native rajgira starch and its carboxymethyl derivative can be used as superior disintegrants in tablet formulation.

Key-words: Rajgira starch; Carboxymethyl Rajgira starch; Disintegrant; *Amaranthus Peniculatus.*

Introduction

A disintegrant is a substance added into a tablet blend to facilitate the breakup of the tablet contents into smaller particles. This will promote a more rapid release and subsequent absorption of the active drug. A good disintegrant must be effective at low concentrations to avoid or reduce the influence on the tablet properties such as hardness, friability or compressibility. Starches i.e. rice, potato etc were the first disintegrating agents used in tablets [1-2]. Moreover, native starches have been modified to obtain various desired properties. Carboxymethyl starch is a starch derivative in which the hydroxyl groups in anhydroglucose unit were etherified with carboxymethyl groups. The degree of substitution (DS), the average number of carboxymethyl groups per anhydroglucose unit, markedly affects the properties of the starch [3]. The CMS made from potato starch has been used for pharmaceutical preparations, as a super disintegrant [4].

Amaranthus paniculatus Linn (Family Amaranthaceae) is commonly known as `Rajgira', `Rajagiri' The Amaranthaceae family consists of hardy, weedy, herbaceous, fast growing, cereal-like plants, with a seed yield of up to 3 tons/hectare.

Amaranth belongs to the so-called improper cereals (pseudo-cereals) and called the third millennium crop-plant due to its high nutritional value and modest demands at growing.

For its features amaranth is important as prevention for people of all ages. Lysine has a unique meaning for small children (it supports the production of brain cells) and minerals, vitamins, unsaturated fatty acids, quality protein for sportsmen, which support the growth of muscular matter. Amaranth recovers cells and influences metabolism significantly.

This study was designed to evaluate the efficacy of rajgira starch (***A. paniculatus***) and its carboxymethyl derivative as tablet disintegrants compared with other commercial native starch.

Materials and Methods

Materials

Paracetamol (PCM; Nutan Gujrat industrial estate, Vadodara), dibasic calcium phosphate (New India Chemical Enterprises, Kochi) and magnesium stearate (G. S. Chemical Testing Laband Allied Industries Bombay,

India) were used as the active drug, filler and lubricant, respectively. Disintegrants in this study was rice starch (S.D. fine chem. Ltd. Mumbai, India), rajgira starch (*A. peniculatus*), was purchased from a local market in Bareilly and carboxymethylated rajgira starch.

Extraction of rajgira starch

The grains of *Amaranthus paniculatus* were thoroughly washed with water to remove any dirt or adherent material. The grains ware then dried and coarsely ground in a mixer grinder and passed through 22-mesh sieve. These coarsely ground grains were extracted repeatedly with 0.25% sodium hydroxide in a ratio of 1:5, until seeds became free from proteins(tested with Biuret reagent). The protein free grains were washed continuously for 2 hrs with distilled water till free from sodium hydroxide and proteins. The residue was transferred to the grinder and ground with water to obtain a white paste of starch and fiber. Filtration was done through bolting cloth of 200-mesh size. Filtrate was collected and kept for sedimentation. The sediment obtained was subjected to centrifugation at 6000 rpm for 15 min. The upper brownish layer was scraped and remaining white layer was transferred in the tray dryers and dried at 45^0 C for 5hrs. The dry starch obtained was passed through 60 mesh.

Carboxymethylation of rajgira starch

Sodium carboxy methyl starch (CMS) is prepared by the reaction of starch with sodium monochloroacetate in presence of sodium hydroxide and in presence of organic solvent (isopropyl alcohol) based on Williamson Ether synthesis. And mechanics is essentially SN_2 (Substitution nucleophilic bimolecular).

Starch – OH +Cl CH_2 COONa +NaOH → Starch - OCH_2 COONa +Nacl +H_2O

Starch Sodium monochloro acetate → Carboxy methyl starch

Multistage carboxymethylation of the starch:

The second stage carboxymethylation was done of the sodium CMS obtained from first stage as under the same conditions (requirements) as were in first stage. Similarly third stage carboxymethylation was carried out using starch obtained after second stage as a raw material but in the third stage, starch was getting gelatinized there for only double modification was done[6].

Modified starch also complies with all the pharmacopoeial specifications except pH and residue on ignition.

Morphology

The shape and surface structure of native rajgira starch was studied using scanning electron microscopy. The starch sample was attached on a stub and coated with gold to increase its conductance. The sample was viewed and photographed.

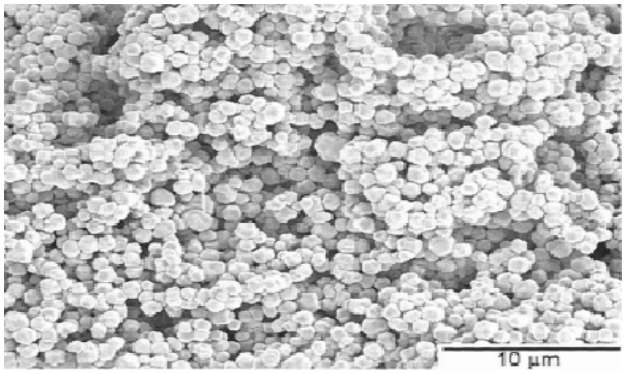


Fig-1: SEM of Native Rajgira Starch.

Swelling power

The swelling power (by weight) of starches was measured using the following method.Starch (0.5 g) was dispersed in water (10 ml). The suspension was heated at 85 °C in a water bath for 30 minutes with vigorous shaking every 5 minutes. The starch gel was then centrifuged at 2,200 rpm for 15 minutes. The weight of sediment was used for calculation of the swelling power. The determination was run in triplicate[5].

Amylose content

The amylose content of the starch was determined using chemical reaction between amylose and iodine. Starch (0.5 g) was dispersed in water (100 ml). The suspension was heated at 85 °C in a water bath for 30 minutes with vigorous shaking every 5 minutes. The slurry was then filtered. Iodine solution 0.1 mL was added to 0.5 ml of the filtrate and purified water was used to adjusted volume to 10 ml. After mixing, absorbance was read at 590 nm using a UV/Visible spectrophotometer.

Tablet preparation

The efficiency of rajgira starch as a tablet disintegrant was evaluated and compared with rice starch and

carboxymethyl rajgira starch. Dibasic calcium phosphate and magnesium stearate were used as filler and lubricant, respectively. PCM was used as a model drug in drug release evaluation. The formulations are shown in Table 1. Tablets were prepared by wet granulation method .The tablets of 200 batch size each were punched using single punch machine (Cadmach, U.K). The weight variation, test for hardness, friability, disintegration time, uniformity of content and *In–vitro* release pattern tests were performed according to pharmacopoeial specifications. The tablet weight was 250 mg.

Tablet hardness

The tablet hardness was determined on an electronic digital hardness tester (Erweka, Germany). Ten tablets were measured individually. The mean values and standard deviation were calculated.

Tablet friability

The friability was conducted on twenty tablets using a friability tester (Erweka, Germany). The drum was rotated at 25 rpm for 4 minutes. Loss of tablet weight with respect to the initial value was then calculated as percent friability.

Disintegration time

The disintegration time was determined according to the disintegration test for uncoated tablets of The Indian Pharmacopoeia (IP-1996). Six tablets were tested. One tablet was placed in each of the six tubes of the basket and operated of the apparatus. Distilled water was maintained at 37±2 $^{\circ}$C as the immersion fluid. The average disintegration time and standard deviation of six tablets were determined.

Dissolution test

The dissolution test of Paracetamol tablet followed the monograph of PCM tablets in the USP XXII. In- vitro release pattern in phosphate buffer (pH 7.4) were determined by using apparatus 1 according to USP XXII and procedure followed as described in USP XXII. Values of cumulative percent drug dissolved at various time intervals were also found out and plotted against time. Values of t_{50} (time for 50% dissolution) and t_{70} (time for 70% dissolution) and t_{90} (time for 90% dissolution) were determined from this plot.

Results and Discussions

Extraction of rajgira starch and preparation of carboxymethyl rajgira starch

Wet rajgira grains contained about 10% starch. The properties of obtained rajgira starch were met the requirements of starch specified in The United States Pharmacopoeia (USP XXII). Carboxymethylation of rajgira starch in organic solvent medium at room temperature for 1 hour yielded CMS with a degree of substitution of 0.14.

Properties of rajgira starch and CMS

Scanning electron microphotographs of rajgira starch and CMS shown in Figure 1 indicated that the rajgira starch granules were polygonal with particle size of 2-10 μm.

Swelling power

The swelling power of the starches is presented in **Table 2**. The decreasing order of the swelling power was CMS > rajgira starch > rice starch. Tester et al., (2004) suggested that swelling power of starch was attributed to amylopectin, the swelling power has a negative correlation with amylose[7]. According to the amylose content of rajgira, rice starch shown in Table 2, rice starch (cereal seed starch) has higher amylose than rajgira starch. For CMS, the swelling power was much higher than that of the native rajgira starch. More water can penetrate into the starch granules due to the hydrophilicity of the carboxymethyl groups resulted in swelling of the starch granule and dissolution in water[8]. The amylose content of CMS was decreased as a result of the destruction of the helical structure during carboxymethylation. Therefore, the concentration of amylose-Iodine complex was lower, resulted in the amylose content.

Tablet evaluation

Hardness:

The effect of concentration of the rajgira starch compared with rice starch on tablet hardness is shown in Figure 2. The hardness increased with the concentration of starch in all formulations. The hardness of a tablet is a parameter that describes the amount and the strength of bonding in the tablet. From this study, the tablet containing CMS showed a superlative degree of hardness. Since CMS is more polarity than native starch, the particles were

bound with more amount and stronger hydrogen bonds. Such the CMS that has polar surface, at equilibrium under normal conditions, it had a water sorption layer which might possibly interact over a high concentration of hydrogen bonds. The two particles have a joint water sorption layer resulting in a strong interparticular attraction[9]. Thus, the boding strength of tablet containing CMS was higher than the native starch. Rajgira starch, which has polygonal shape, gave higher tablet hardness than rice starch (which has nearly round shape [4]. The polygonal shape of rajgira possessed higher degree of particle inter-locking during rearrangement phase of compression that enhanced particle consolidation during compression.

Friability

The tablet friability decreased with increasing amount of starch in the tablet. The higher the tablet hardness, the lower tablet friability was observed, because the interparticulate cohesiveness increased with increasing starch concentration. The increasing order of tablet friability was CMS < rajgira starch < rice starch respectively.

Disintegration time

The effect of starch concentration on the disintegration time of the tablets is showed in Table 3. The tablets without starch were not disintegrated in the tested time of 20 minutes, but tablet containing 3% of rice starch, rajgira starch and CMS disintegrated at 7, 3.5 and 4 minutes, respectively. Tablet containing a native starch that has higher swelling power disintegrated faster. At increasing amount of all native starches, a decrease in the disintegration time was seen. This result indicated that the increasing in swelling force by increasing amount of starch had more pronounce effect on the disintegration time than did the increased tablet hardness. Swelling is a predominant one of the disintegration mechanism[10]. The tablet formulated with CMS disintegrated more slowly than the tablet with native starches, especially in high concentrations of 10% and 12% by weight. This result was related to the swelling characteristic of CMS. Viscous or gel mass was observed when CMS was suspended in water at high concentrations. The viscous gel mass formation could impede the penetration of water in to the tablets and retarded the disintegration. The use of CMS as a tablet disintegrant in this study seemed to have the optimum concentration at 9% by weight.

Dissolution

The dissolution profiles of PCM tablets are shown in Figure 5. It can be seen that the dissolution corresponded to the disintegration property of the tablets. The faster tablet disintegration resulted in a faster drug release. However, all formulations were released more than 80% in 35 minutes, and a complete dissolution was obtained in 50 minutes.

Conclusions

Rajgira starch and CMS were evaluated for theirs efficacy as tablet disintegrant in comparison with rice starch. The results revealed that the shape of rajgira starch granules were polygonal with a size range of 2-20 μm. Its polygonal shape played a major role in increasing tablet hardness. Moreover, the tablet containing rajgira starch showed the fastest disintegration time, especially at low concentrations. The highest swelling power of rajgira starch has a marked effect on the tablet disintegration. CMS showed higher swelling power and more viscous gel. It could also be used as a tablet disintegrant. However, at high concentrations, the tablet disintegration and dissolution were retarded due to formation of gel mass (fig.1). With this special property, CMS had a potential to be used in drug controlled release dosage forms.

Table- 1: Tablet formulations.

Ingredient	Blank tablet (%w/w)	PCM tablet (%w/w)
Starch as disintegrant	0,3,6,9,10,12	9
PCM	-	76
Magnesium stearate	0.25	0.25
Emcompress® q.s. to	100	100

Table-2: Swelling power and Amylose content of different starch.

Starch	Swelling power, Times (SD)	Amylose content, % (SD)
Rice starch	9.32 (0.12)	27.22 (0.24)
Rajgira starch	17.04 (0.74)	12.24 (0.30)
CMS	63.34 (0.81)	2.32 (0.02)

Table-3: *In vitro* evaluation of various tablets using different starches as disintegrant.

Formulation	Uniformity of weight		Assay(percent of labeled amount)	Hardness (kg/cm^2)± SD	Friability %±SD	Disintegration time (s)
	Average wt.(mg)	Maximum %deviation				
CMS_1	598.3± 3.5 [a]	3.6± 0.03 [a]	102.6 ± 7.9 [a]	4.8±0.09 [a]	0.12±0.01 [a]	389± 5.0 [a]
CMS_2	596.5± 17.8 [a]	3.8± 0.2 [a]	101.33± 6.2 [a]	4.6±0.06 [b]	0.15±0.03 [b]	211± 4.8 [b]
CMS_3	597.3± 24.9 [a]	4.1± 0.3 [b]	98.6± 4.9 [a]	4.3±0.05 [a]	0.2±0.01 [b]	234± 3.2 [b]
RAS_1	593.4± 25.2 [b]	4.2± 0.4 [a]	101.33± 2.1 [b]	4.5±0.02 [s]	0.4±0.04 [a]	183± 7.0 [a]
RAS_2	596.3± 13.4 [b]	4.2± 0.3 [a]	104.0± 3.8 [b]	4.3±0.02 [a]	0.5±0.03 [a]	198± 3.3 [b]
RAS_3	595.5± 23.9 [b]	4.5± 0.5 [a]	98.6± 3.9 [a]	4.1±0.02 [a]	0.61±0.02 [b]	221± 4.2 [a]
CS_1	583.6± 17.9 [a]	3.7± 0.2 [a]	102.6 ± 3.2 [a]	4.6±0.06 [b]	0.41±0.00 [a]	285± 6.1 [a]
CS_2	586.7± 23.4 [b]	3.9± 0.4 [a]	97.81± 3.4 [b]	4.1±0.08 [b]	0.52±0.03 [b]	320 ± 3.9 [b]
CS_3	579.5± 19.9 [b]	4.0± 0.5 [a]	102.8 ± 3.4 [a]	3.8±0.05 [a]	0.7±0.01 [b]	395± 4.1 [a]

* Mean ± S.E.M , n=6. [a] Significantly different from control ($P < 0.01$).

[b] Significant different from starch ($P < 0.01$).

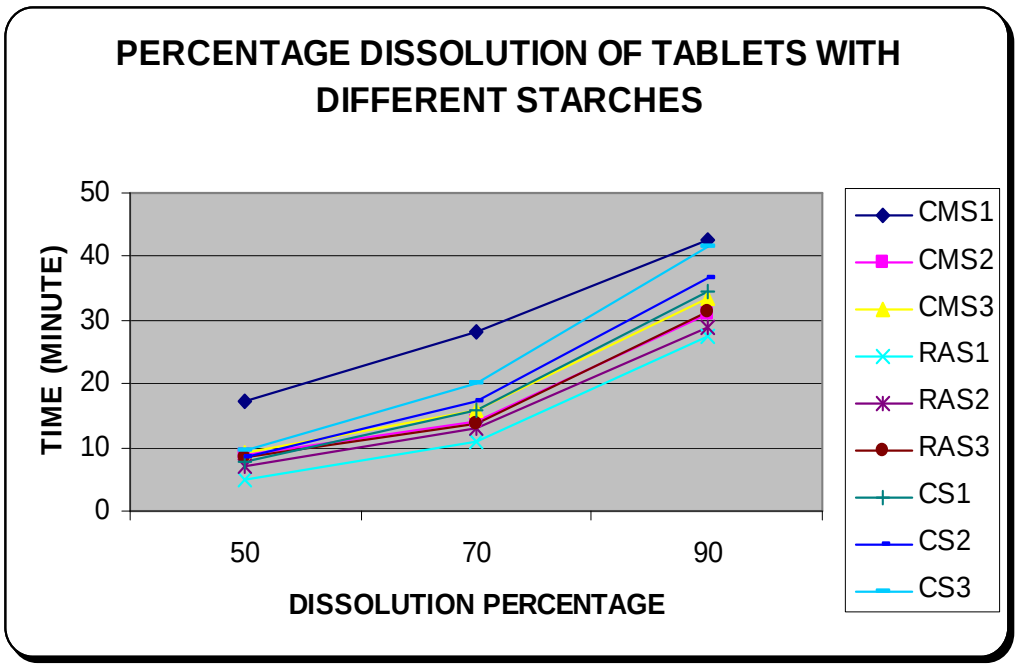
Table-4: Dissolution parameter of Paracetamol tablets containing different starches as disintegrant.

Formulation	t_{50}(min)	t_{70}(min)	t_{90}(min)
CMS_1	17.3± 0.2 [a]	28.1± 0.4 [b]	42.7± 0.7 [b]
CMS_2	8.7± 0.5 [a]	14.0± 0.8 [b]	31.0± 0.6 [a]
CMS_3	9.0± 0.4 [a]	15.9± 0.5 [b]	33.5± 0.5 [b]
RAS_1	5.0± 0.7 [a]	10.9± 0.8 [a]	27.5± 0.6 [a]
RAS_2	7.0± 0.5 [a]	12.9± 0.4 [a]	28.9± 0.7 [b]
RAS_3	8.3± 0.2 [a]	13.8± 0.6 [a]	31.5± 0.9 [a]
CS_1	7.9± 0.4 [b]	15.9± 0.5 [a]	34.4± 0.4 [a]
CS_2	8.6± 0.3 [b]	17.3± 0.6 [a]	36.5± 0.5 [a]
CS_3	9.6± 0.4 [b]	20.0± 0.8 [a]	41.6± 0.5 [a]

* Mean ± S.E.M, n=6. [a] Significantly different from control ($P < 0.01$).

[b] Significant different from starch ($P < 0.01$).

Fig-1: Dissolution of tablets with different starches.



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