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Comparative evaluation of modified starches in different tablet formulations as disintegrants

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ABSTRACT

New modified starches such as starch citrate and starch phosphate were prepared and evaluated as disintegrants in tablet formulations in comparison with sodium starch glycolate (SSG). Tablets of (i) Cetirizine (ii) Diclofenac sodium and (iii) Paracetamol were prepared by wet granulation method employing starch citrate and starch phosphate at 4% strength as disintegrant in the tablets. The formulated tablets were evaluated for various tableting properties, like hardness, thickness, friability, weight variation, disintegration time and dissolution rate. Comparative evaluation of the above-mentioned parameters established using sodium starch glycolate (SSG) as disintegrant at 4% strength in the tablets. Starch citrate and Starch phosphate exhibited good disintegrating properties like sodium starch glycolate.

Keywords: Modified starches, Starch citrate, Starch phosphate, Sodium starch glycolate, Disintegrant, Tablets, Cetirizine, Diclofenac sodium, Paracetamol.

INTRODUCTION

During the last two decades, pharmaceutical researches have tried different adjuvants to improve product performance. It is reported that the dissolution and bio-availability of a drug from solid dosage form depend much on its formulation additives and method of manufacture or processing variables [1-4].

A disintegrant is added to the tablet formulations to facilitate a break up or disintegration of tablet when it contacts GI Fluids. Tablet disintegration may be critical to the dissolution of the drug and to the attainment of satisfactory bioavailability. Starch USP and various starch derivatives are the most common disintegrants [5, 6]. Modified starches such as sodium starch glycolate (SSG), starch citrate, starch phosphate, pregelatinised starch and hypochlorite modified starch have been evaluated as effective disintegrants [7-12].

Starch phosphate is one of the modified starches produced by phosphorification of free hydroxyl groups of anhydroglucose units of starch molecule. They are (free OH^-) esterified with phosphate reagents generally orthophosphate salts [13, 14]. Starch citrate is a biodegradable product produced by the reaction of starch with citric acid. Wing [15] has reported reaction of starch with citric acid to yield starch citrate, a biodegradable product possessing high ion exchange capacity. Wepner et al [16] have described a process for the synthesis of citrate derivatives of starch. The objective of the present study is to compare and evaluate the novel disintegrants like starch citrate and starch phosphate with proven disintegrant SSG in Paracetamol, Diclofenac sodium and Cetirizine tablet formulations.

MATERIALS AND METHODS

Materials: Paracetamol, Diclofenac sodium, Cetirizine were gift samples from Balaji Drugs, Surat, Gujarat, India. Starch, Citric acid, Potassium di hydrogen ortho phosphate, Sodium Starch Glycolate, Talc, Magnesium Stearate,

Micro Crystalline Cellulose (Avicel-101), Hydroxy Propyl Methyl Cellulose (5cps) were procured from commercial sources. All other sources were of Pharmacopoeial grade.

Preparation of Starch Citrate

Starch Citrate was prepared based on the method of Klaushfer et al [17] with some modifications. Citric acid (20g) was dissolved in 20 ml of water, the pH of the solution was adjusted to 3.5 with 10 M Sodium Hydroxide and finally the volume was made up to 50 ml by adding water. This solution was mixed with 50g of potato Starch in a stainless steel tray and conditioned for 16 h at room temperature (28°C). The tray was then placed in hot air oven and dried at 60°C for 6 h. The mixture obtained was ground and further dried in a hot air oven at 130°C for 2 h. The dry mixture was repeatedly washed with water to remove unreacted Citric acid (yellow color). The washed starch citrate was further dried at 50°C to remove the water/moisture completely. The product obtained was ground and sized.

Preparation of Starch Phosphate

Starch phosphate was prepared based on the method of Choi et al [18] with some modifications. Potato starch (100 g) and potassium di hydrogen orthophosphate anhydrous (30 g) were suspended in 100 ml of water and continuously stirred for 20 min. This starch slurry was then filtered and the wet starch mixture was conditioned for 12 h at room temperature (28°C). To enhance phosphorylation, this mixture was heated in a hot air oven at 130°C for 3 h. The product obtained was ground and sized.

Preparation of tablets

Tablets of (i) Diclofenac sodium (170 mg) and (ii) Paracetamol (170 mg) (iii) Cetirizine (90mg) were prepared by conventional wet granulation method employing HPMC (5%) as a binder, Micro crystalline cellulose (Avicel-101) as diluent, Talc (2%) Magnesium stearate (2%) as lubricants and water as granulating fluid. Starch phosphate and starch citrate were included in the formulations as disintegrants at 4 % strength in each case. For comparison tablets were also prepared employing sodium starch glycolate (established disintegrant) as disintegrant at 4% strength in the tablets. 9 batches of tablets were made using the 3 drugs and 3 disintegrants. The granules were compressed into tablets on a tablet punching machine (M/s Clit Jemkay Engineers Pvt. Ltd) to a hardness of 5 kg/cm^2 using 6 mm round and 8 mm flat punches. In each case 50 tablets were compressed.

Table 1: Formulation design

INGREDIENTS	F1	F2	F3	F4	F5	F6	F7	F8	F9
PARACETAMOL	125	125	125	---	---	---	---	---	---
DICLOFENAC SODIUM	---	---	---	50	50	50	---	---	---
CETRIZINE	---	---	---	---	---	---	5	5	5
STARCH CITRATE	3.4	---	---	2	---	---	1.8	---	---
STARCH PHOSPHATE	---	3.4	---	---	2	---	---	1.8	---
SODIUM STARCH GLYCOLATE	---	---	3.4	---	---	2	---	---	1.8
AVICEL(MCC-101)	29.6	29.6	29.6	104.7	104.7	104.7	76.9	76.9	76.9
HPMC (5cps)	8.5	8.5	8.5	8.5	8.5	8.5	4.5	4.5	4.5
MAGNESIUM STEARATE	3.4	3.4	3.4	3.4	3.4	3.4	1.8	1.8	1.8
TOTAL TABLET WEIGHT	170	170	170	170	170	170	90	90	90

Evaluation of Tablets

Weight variation test was performed, Hardness of tablets was tested using Monsanto Hardness tester. Friability of the tablets was determined in a Roche friabilator. Disintegration time was determined in a Thermonic tablet disintegration apparatus using water as test fluid.

Estimation of Drug Content in the Tablets

From each batch of tablets prepared, five tablets were accurately weighed and powdered. Tablet powder equivalent to 20 mg of drug was taken for assay into a 100 ml conical flask and extracted with 3 X10 ml quantities of methanol. The methanolic extracts were filtered and collected into a 50 ml volumetric flask and the volume was made up to 50 ml with methanol. The solution was then suitably diluted with 0.1N hydrochloric acid in the case of Cetirizine, with phosphate buffer of pH 7.8 in the case of Paracetamol and with phosphate buffer of pH 6.8 in the case of Diclofenac sodium. The absorbance of the solutions was measured at 231 nm for Cetirizine, at 249 nm for Paracetamol and at 276 nm for Diclofenac sodium. Drug content of the tablets was calculated using the standard calibration curve in each case.

Table 2: Evaluation of tablets

Formulation	Drug Content (%)	Hardness (Kg/cm^2)	Friability (% weight loss)	Disintegration Time (min-sec)	Weight Variation (maximum % deviation)
F1	99.54	5.2	0.77	1.30	1.5
F2	98.05	4.6	0.64	1.13	2.0
F3	100.56	4.8	0.79	1.09	1.3
F4	98.84	5.4	0.78	1.38	1.4
F5	99.04	5.4	0.78	1.33	1.7
F6	98.83	5.8	0.82	1.16	2.5
F7	99.52	3.2	0.86	0.58	1.5
F8	100.09	3.2	0.84	0.55	1.6
F9	100.47	3.4	0.79	0.37	1.5

Figure.1: Dissolution of Cetirizine tablets

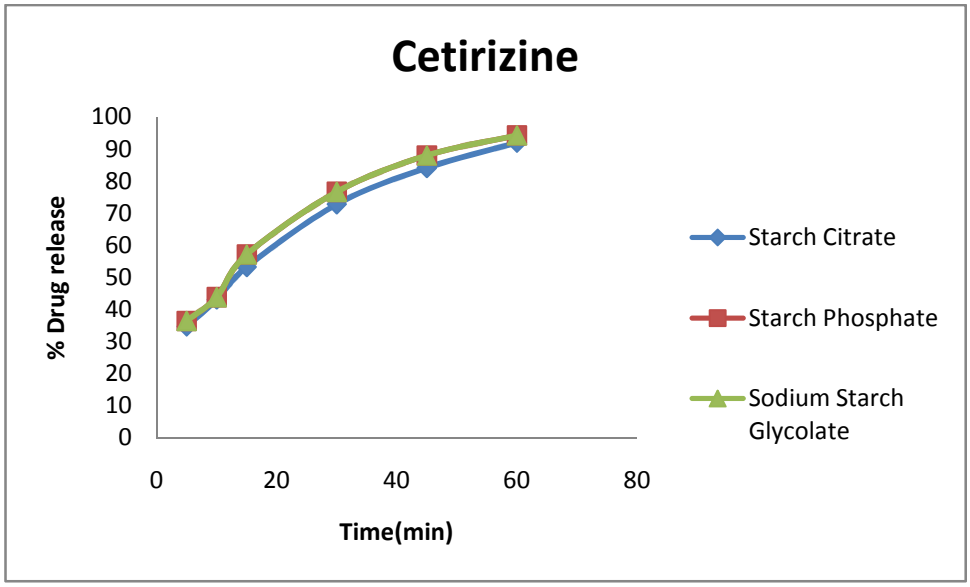


Figure.2: Dissolution of Diclofenac sodium tablets

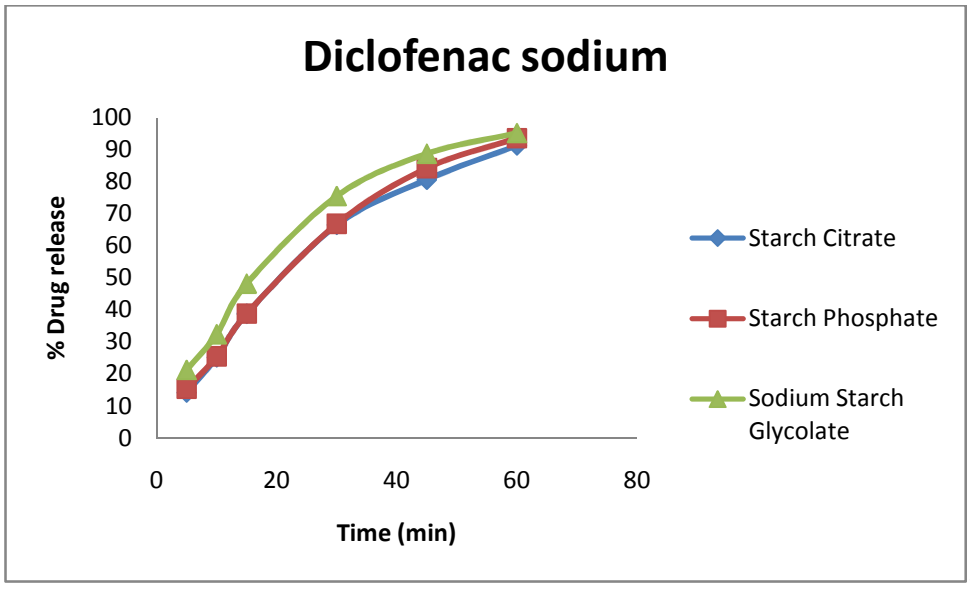
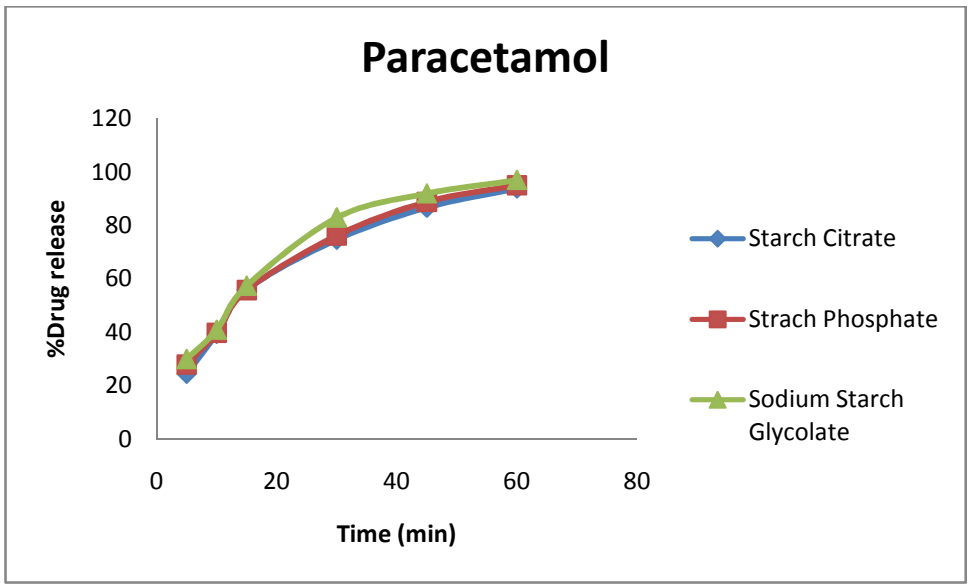


Figure.3: Dissolution of Paracetamol tablets



Dissolution Rate Studies:

Dissolution rate of the tablets prepared was studied using 8 station dissolution rate apparatus (M/s Lab India Disso 2000) employing a paddle stirrer at 50 rpm and at 37 ºC. Hydrochloric acid 0.2 M (900 ml) was used as dissolution fluid for Cetirizine and 6.8P^H phosphate buffer solution (900 ml) was used as dissolution fluid for Diclofenac sodium tablets. Phosphate buffer of pH 7.8 (900 ml) was used as dissolution fluid in the case of Paracetamol tablets. Samples of dissolution fluid, 5 ml each, were withdrawn at 5, 10, 15, 20, 25, 30, 40, 50, 60 min through a filter (0.45 µ). The samples were suitably diluted with the corresponding dissolution fluid and assayed for Paracetamol at 249 nm, Diclofenac sodium at 276 nm and Cetirizine at 231 nm using the corresponding dissolution fluid as blank. Each sample withdrawn was replaced with an equal amount of drug free dissolution fluid. All dissolution experiments were conducted in triplicate.

RESULTS AND DISCUSSION

Starch citrate was prepared by reacting starch with citric acid at elevated temperatures. When citric acid is heated, it will dehydrate to yield an anhydride. The citric anhydride can then react with starch to from starch citrate. Starch citrate passed through mesh no.120 was collected and used in the formulation.

Starch phosphate was prepared by reacting starch with potassium hydrogen orthophosphate anhydrous at elevated temperatures. Powder which passes through mesh no. 80 and retained on mesh no. 120 was collected for use in formulation.

Tablets of (i) Diclofenac sodium (170 mg) and (ii) Paracetamol (170 mg) (iii) Cetirizine (90mg) were prepared by conventional wet granulation method employing starch citrate, starch phosphate and SSG as disintegrant at 4% concentration. 9 batches of tablets with 3 drugs and 3 disintegrants were prepared.

All the tablets were evaluated for weight variation, drug content, hardness, friability, and disintegration time and dissolution efficiency.

In the test for uniformity of weight the percentage deviation was less than 2.5% in all the cases. Drug content was within 100±3% of the labelled claim in each case. Hardness of the formulated tablets was in the range 3-6 kg/cm^2. Weight loss in the friability test was less than 0.78%.

As such, all tablets formulated employing starch citrate and starch phosphate were of good quality with regard to weight variation, hardness, friability, and drug content and disintegration time. The dissolution profiles were represented in graphs. All the dissolution parameters indicated very rapid and higher dissolution of the drug from tablets formulated employing starch citrate and starch phosphate as disintegrants. The drug dissolution from the tablets formulated employing starch citrate and starch phosphate were much higher than the official specification in all cases. All the formulated tablets of newly modified starches gave nearly similar dissolution as of the established disintegrant SSG.

CONCLUSION

In present study the disintegrating properties of sodium citrate and sodium phosphate had been studied in comparison with commercially available sodium starch glycolate. Comparative evaluation studies proved that the modified starches exhibit similar disintegration and dissolution properties like sodium starch glycolate. Hence starch citrate and starch phosphate are economical and better choice for commercial use.

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