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Comparative Tableting Properties of Three Local Potato Starches III: The Disintegrant Properties

J. Muazu[1*], H. Musa[2], A. B. Isah[2], P. G. Bhatia[2]

1. University of Maiduguri, Nigeria

2. Ahmadu Bello University, Zaria, Nigeria

ABSTRACT

This study aimed at comparing the disintegrant properties of three potato starches with Maize starch BP as well as effect of method of incorporation of disintegrant on release of paracetamol tablet formulation. The disintegrant property was assessed by both disintegration and dissolution times of the formulation. The results showed that tablets produced with potato starch were similar in disintegration and dissolution times with those formulated with Maize starch BP. Disintegrants employed extra-granularly showed better disintegration than intra-granular or intra-extra-granular. Therefore the potato starches can be used as a disintegrant in paracetamol tablets formulation

Keywords: disintegrants, potato starch, formulation, dissolution time, incorporation

*Corresponding Author Email: jmuazu@gmail.com

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INTRODUCTION

Disintegrants are substances added to tablet formulation for purpose of fragmentation of tablet when placed in aqueous environment. Tablets are expected to break up within specified period when in contact with body fluids, the break-up of tablet increases the surface area of the tablet fragments so that dissolution can take place and ultimately for a drug to elicit therapeutic effect. Therefore, the rate of release of medicament from a disintegrated tablet is greater than that of intact tablet. The "breaking up" is aided by a disintegrant e.g. starches, celluloses, algins, gums, etc. The disintegrants have a major function to oppose the efficiency of the tablets binder and the physical forces that act under compression to form tablet, the stronger the binder, the more effective must be the disintegrating agents in order for the tablets to release its medication[1].

The use of disintegrant depends on the tablet. The desired concentration of disintegrant normally varies from 5% -20 %. Incorporation of disintegrant in tableting is achieved by either addition of total amount of disintegrant to powder before granulation (intra granular disintegrants) or addition of total amount of disintegrant to granules just before compression(extra granular disintegrants). However, 50% disintegrant may be added before granulation and 50 % after granulation (intra-extra granular disintegrants).

Mechanism of action of disintegrants

The mode of action of disintegrants is a subject of controversy, disintegrants especially starch has high affinity for water and swells when moistened, thus facilitating the rupture of tablet matrix. However, others suggested that its disintegrating action in tablets is due to capillary action rather than swelling[2].

Swelling

Although not all effective disintegrants swell when in contact with water, swelling is believed to be a mechanism in which certain disintegrating agents (such as starch) impart the disintegrating effect. Starch swells on contact with water; the adhesiveness of other ingredients in a tablet is overcome causing the tablet to fall apart[3].

Wicking (Porosity and Capillary Action)

Effective disintegrants that do not swell are believed to impart their disintegrating action through porosity and capillary action. Tablet porosity provides pathways for the penetration of fluid into tablets. The disintegrant particles (with low cohesiveness and compressibility) themselves act to enhance porosity and provide these pathways into the tablet. Liquid is drawn up or "wicked" into these pathways through capillary action and rupture the inter particulate bonds causing the tablet

to break apart. The spherical shape of the starch grains increases the porosity of the tablets, thus promoting capillary action

Deformation

Starch grains are generally thought to be "elastic" in nature meaning that grains that are deformed under pressure will return to their original shape when that pressure is removed. But, with the compression forces involved in tableting, these grains are believed to be deformed more permanently and are said to be "energy rich" with this energy being released upon exposure to water. In other words, the ability for starch to swell is higher in "energy rich" starch grains than it is for starch grains that have not been deformed under pressure[4].

Disintegration due to disintegrating particle/particle repulsive forces

This mechanism of disintegration attempts to explain the swelling of tablet made with 'non-swellable' disintegrants. Guyot-Hermann[5] has proposed a particle repulsion theory based on the observation that non-swelling particle also cause disintegration of tablets. The electric repulsive forces between particles are the mechanism of disintegration and water is required for it. Researchers found that repulsion is secondary to wicking[6,7].

It is believed that no single mechanism is responsible for the action of most disintegrants. But rather, it is more likely the result of inter-relationships between these major mechanisms.

The study is aimed at evaluating the disintegrant properties of three local potato starches

MATERIALS AND METHODS

Paracetamol powder: May and Baker LTD Dagenham England, Maize starch: May and Baker LTD Dagenham England, Talc: BDH Chem. LTD Poole England, Magnesium stearate: BDH Chem. LTD Poole England, Lactose (East Anglia Chemicals), Hydrochloric acid (Merck, Germany), Kaffir potato: Barikin Ladi, market, Jos, Nigeria, Sweet potato: Gamboru Market, Maiduguri, Nigeria, Irish potato: Gamboru Market, Maiduguri, Nigeria

Working formula for the assessment of potato starches starch as disintegrants in paracetamol tablets is given in Table 1. The wet granulation method of massing and screening was used in preparing all the batches of paracetamol granules. The paracetamol powder and the intra-disintegrant maize starch or potato starches of concentration between 2.5 to 10%w/w depending on the batch were dry-mixed for 5 minutes. An appropriate quantity of freshly prepared starch mucilage of concentration 5% W/V was added to each of the batch to produce granules. The wet mass were passed through a 1.6mm (1600μm) Sieve mesh screen the wet granules were dried at

40°C to constant weight in a Gallen Kamp hot air oven and then later dried screened through sieve mesh 1.4mm (1400µm).

Table 1: The working formula for studying the disintegrant properties of potato starches compared to Maize starch B.P in paracetamol tablets

Excipients	Percentages of each excipient (%w/w)	Actual contents of excipients per tablet (mg)	Actual content of Excipient Per 500 Tablets (g)
Paracetamol	77	500	250
Disintegrant: Kaffir,	2.5	16.25	8.13
Sweet, Irish or	5	32.50	16.25
Maize starch	7.5	48.75	24.38
	10	65.00	32.50
Binder: Maize starch mucilage	5	QS	QS
Glidant/Lubricant Magnesium stearate	0.2	1.3	0.65
Talc	2	13	6.5
	Total weight	**650**	**325**

Granules were also prepared with 50% and without disintegrant. For batches prepared with 50% disintegrants, additional 50 % was added after granulation. While whole quantities of disintegrants were added to batches without disintegrants. The granules were then mixed with the Extra-granular excipients, namely 0.2%w/w magnesium stearate and 2%w/w Talc in a Tumble mixer for 5 minutes. The granules were compressed at 5.5 metric tones using 12.5mm bi-convex faced punches on a single punch tableting machine.

Statistical analysis

SPSS a statistical software program version 16 was used to compare means and the analysis of variance. $P<0.05$ was considered significant.

RESULTS AND DISCUSSION

The effect of varying concentration of disintegrant on crushing strength is illustrated in Figure 1, it was observed that as the concentration of disintegrant is increased the crushing strength of Paracetamol tablet slightly increased up to the maximum value (7.5 % w/v) after which almost a steady state or a decline was observed. The initial increase in crushing strength has been explained earlier[8]. It was as a result of small proportion of the starch added as disintegrant been wetted in the process of granulation thereby acting as a binder. A steady state or decline can be as a result of saturation, that is, no more wetting agents available to wet the excess starch.

The friability of Paracetamol tablets formulated with various starches is shown in Figure 2. Friability was observed to slightly decrease with increase in disintegrant concentration from 2.5-7.5 % w/w, this might be attributed to the fact that part of the disintegrant were wetted by binder (vehicle used) as a result it also acts as a binder i.e. additional bonds are formed apart from the bonds formed by the original binder in the formulation. This additional binder confers resistance to the tablet abrasion.

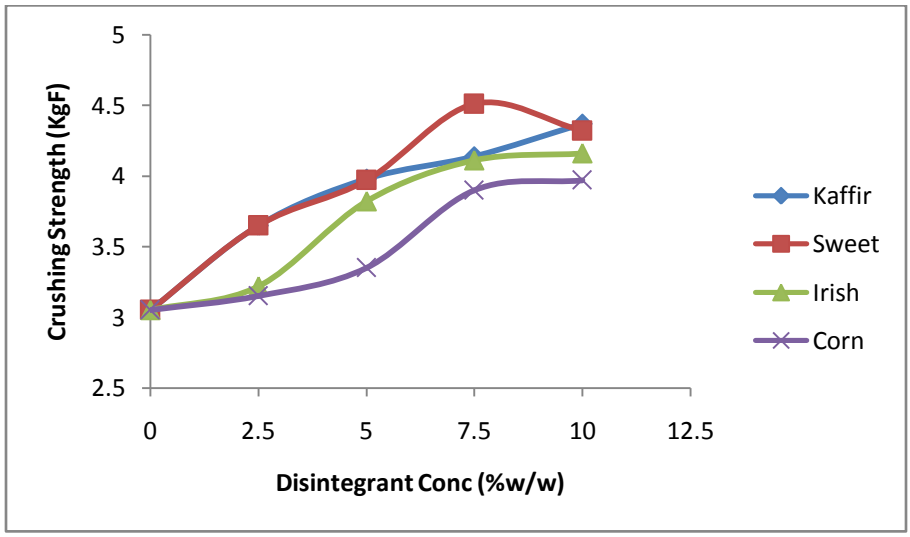

Figure 1: Plots of Hardness (KgF) against Disintegrant Concentration (%w/v) in Paracetamol tablets produced from Kaffir, Sweet, Irish and Maize starches as disintegrant

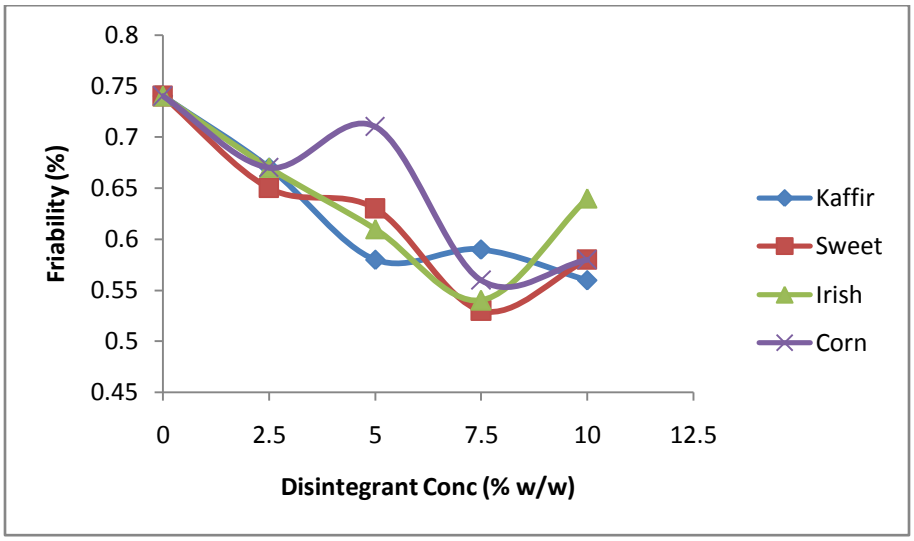

Figure 2: Plots of Friability (%) against Disintegrant Concentration (%w/w) in paracetamol tablets produced from Kaffir, Sweet, Irish and Maize starches as disintegrant.

However, there was no significant difference ($p>0.05$) between the starches. The friability of all the formulation at all disintegrant concentration has passed the BP 2002 specification of less than 1%.

Despite increasing interest in controlled release drug delivery systems, the most common tablets that are intended to be swallowed whole and to disintegrate and release their medicament rapidly in the gastrointestinal tract still remains the dosage form of choice[9]. For many solid dosage forms, disintegration precedes dissolution; therefore, the proper choice of disintegrant and its consistency of performance are of critical importance to the formulation development of that tablet[7,10]. Out of the three potato starches studied, tablets formulated with Irish potato starch disintegrate more rapidly than the other formulations. This could be attributed to the relatively lower hardness of the tablets.

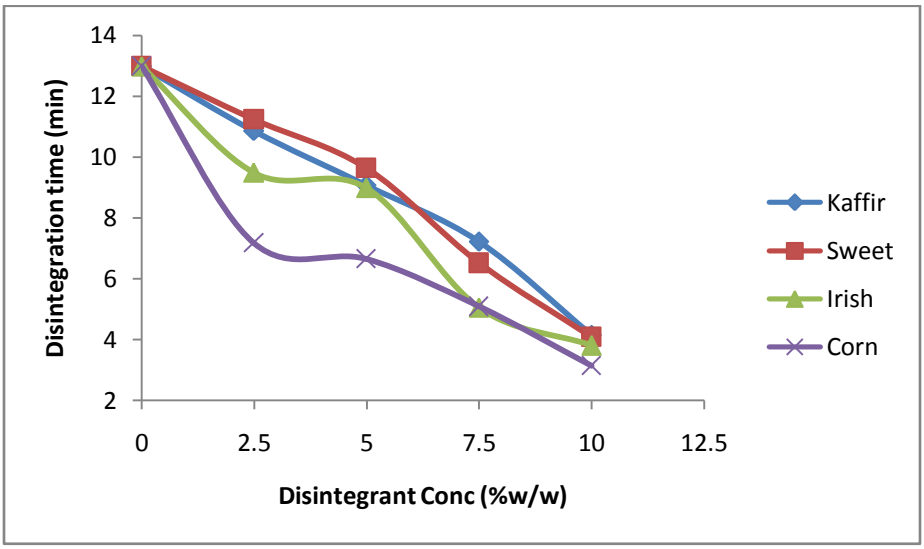

Figure 3: Plots of Disintegration Time (min) against Disintegrant Concentration (%w/w) in Paracetamol tablet formulated from Kaffir, Sweet, Irish and Maize starch as disintegrant.

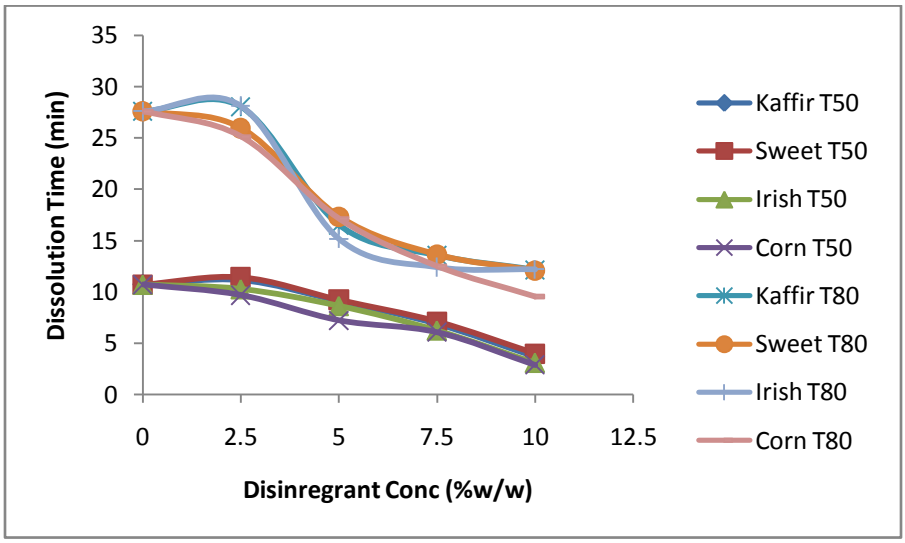

Figure 4: Plots of Dissolution Time (min) against Disintegrant Concentration (%w/w) in Paracetamol tablet formulated from Kaffir, Sweet, Irish and Maize starches as disintegrant.

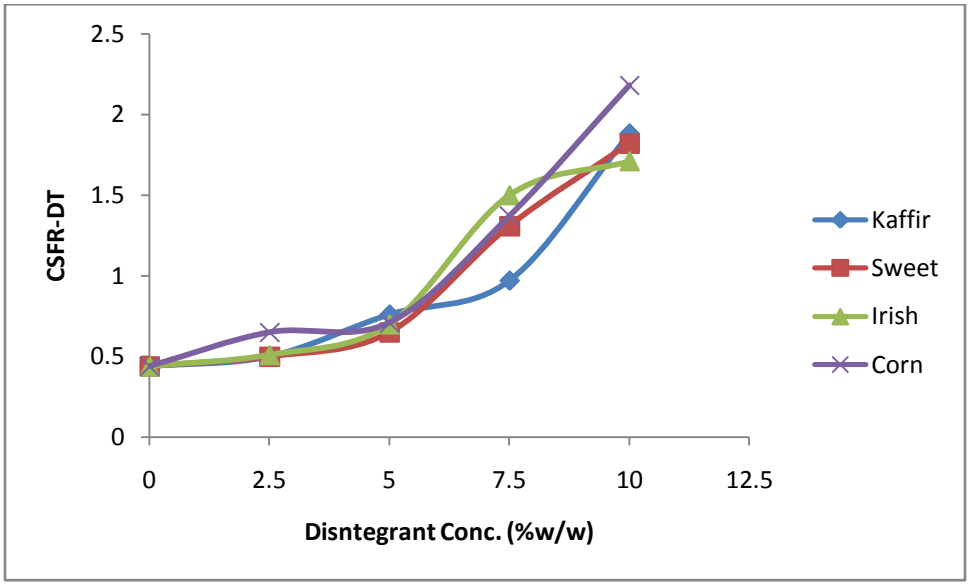

Figure 5: Plots of Crushing Strength Friability – Disintegration Time against Disintegrant Concentration (%w/w) in Paracetamol tablet formulated from Kaffir, Sweet, Irish and Maize starches as disintegrant.

Influence of method of incorporation of disintegrant on quality of tablets

Table 2: Quality control parameters of tablets produced with different methods of incorporation of disintegrant.

Disinte-grant	Method of Incorpo-ration	Weight (mg)	Diameter (mm)	Thickness (mm)	Crushing Strength (KgF)	Friability (%)	Disintegration Time (min)
		622.33±1.94	12.52±0.01	5.12±0.02	3.05±0.07	0.53±0.23	12.98±0.75
Kaffir	IG	631.67±2.83	12.54±0.01	5.17±0.04	3.98±0.61	0.58±0.05	9.07±0.04
	EG	634.67±1.15	12.54±0.02	5.16±0.01	4.61±0.08	0.65±0.07	7.65±0.47
	IEG	633.33±2.52	12.54±0.01	5.16±0.01	4.39±0.08	0.82±0.16	8.23±0.24
Sweet	IG	633.00±1.00	12.55±0.02	5.16±0.02	3.97±0.60	0.63±0.18	9.64±0.07
	EG	631.33±1.53	12.55±0.01	5.16±0.01	4.64±0.24	0.67±0.04	7.08±0.22
	IEG	633.00±1.00	12.55±0.02	5.16±0.02	4.39±0.20	0.72±0.04	7.18±0.24
Irish	IG	632.67±3.06	12.55±0.01	5.16±0.01	3.82±0.04	0.61±0.06	8.99±0.34
	EG	633.00±1.00	12.54±0.02	5.16±0.02	4.24±0.27	0.63±0.11	7.41±0.20
	IEG	630.67±1.15	12.55±0.02	5.15±0.01	4.46±0.25	0.67±0.04	8.05±0.09
Maize	IG	634.67±1.15	12.54±0.02	5.16±0.01	3.35±0.60	0.71±0.18	6.66±0.07
	EG	633.67±0.58	12.53±0.02	5.16±0.01	4.19±0.09	0.80±0.07	3.63±0.30
	IEG	634.33±1.53	12.54±0.02	5.15±0.03	3.72±0.21	0.88±0.16	4.65±0.34

Key: IG = Intra granular, EG = Extra granular, IEG = intra-extra granular

The effect of the concentration of starch disintegrant on the disintegration time is shown in figure 3. Increase in concentration led to a decrease in the disintegration time. This could be due to the increase in swelling, which is associated with the increase in starch concentration[11]. significant

difference ($p<0.05$) was observed by increasing the concentration of all the starches from 0 to 5%w/w, at concentration 5% w/w tablet disintegrate in less than 15 minutes. And there was no more significant difference seen by increasing the disintegrant concentration from 7.5 to 10% w/w. The order of disintegration time was Maize>Irish> kaffir > sweet. The disintegration time of potato starches were higher than that of maize starch BP, this might be attributed to their respecting swelling power which the proponents of disintegration by swelling and rupture put forward.

Relationship between dissolution time and disintegrant concentration was illustrated in Figure 4. At 5% w/w concentration, 80% of all the starches dissolved, which complied with standards (70% to dissolve in 30 minutes). The result also showed that increase in disintegrant concentration might not be necessary as the 5% w/w was sufficient to give the required dissolution. The order of dissolution follows that of disintegration.

The effects of disintegrant concentration on CSFR-DT values of paracetamol tablets is shown in figure 5, increase in disintegrant concentration was observed to increase the CSFR-DT value with Maize starch showing higher value.

The results of method of incorporation of disintegrant on disintegration time are presented in table 2. The rank order of disintegration time for the mode of addition was observed to be external < internal – external < internal for all the starches. This order could be due to the initial amount of starch disintegrant exposed to the disintegrating medium. For external disintegrants, a larger amount of starch disintegrant was initially exposed to the disintegrating fluid, which led to the absorption of large quantities of water and subsequent generation of higher swelling force. This force activated the active mechanism of disintegration at a faster rate than for internal-external and internal modes of disintegrant addition[4,12].

CONCLUSION

From the tests conducted, it can be conclude that the potato starches compared well with standard Maize starch BP in disintegration. Extra-granular method of disintegration was a better method than intra-granular for all the starches.

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