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Evaluation of Disintegrant properties of Microcrystalline Cellulose obtained from *Luffa cylindrica* in Asprin-based Formulations

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This study aims at obtaining microcrystalline cellulose from the dried fruits of ***Luffa cylindrica*** and evaluating its potential as a tablet disintegrant. Alpha cellulose was obtained by soda process from the dried fruits of *L. cylindrica* plant. The microcrystalline cellulose, coded LC-MCC, was obtained from the alpha cellulose content of the plant by acid hydrolysis. Its disintegrant ability in comparison with corn starch BP and Avicel PH 101 was investigated in a directly compressed asprin tablet formulation. The tablet properties evaluated include crushing strength, friability, disintegration time and dissolution rate. The asprin tablets formed were good and acceptable as none had surface defects. The study showed that LC-MCC has disintegrant properties. LC-MCC produced tablets with longest disintegration time compared to tablets prepared with Avicel PH 101 and corn starch BP at all disintegrant concentrations investigated. The disintegrant properties of these agents were concentration dependent. The dissolution rate profiles of asprin tablet formulations mirrored the disintegration times. Microcrystalline cellulose alone (either as LC-MCC or Avicel PH 101) however, at the concentrations and compressional pressure used in this study is not an effective disintegrant in asprin tablet formulation.

Keywords:*Luffa cylindrica*, microcrystalline cellulose, disintegrant properties, asprin tablets.

INTRODUCTION

An excipient is defined as 'any component, other than the active substances, intentionally added to the formulation of a dosage form' (1). Excipients are widely applied in drug formulation and they modify a whole variety of physical, physico-chemical and physico-technical properties of the drug and these may lead to changes in the biopharmaceutical performance of the system (2). An example of simple and common dosage form is the tablet, which may comprise a drug that is frequently present in very low concentration, and other excipients (adjuvants) which might include diluents, binding agents, disintegrants, lubricants, colorants, plasticizers and surfactants (3). Microcrystalline cellulose, (MCC), is an example of commonly used excipient in tablet dosage formulations. MCC is a purified alpha cellulose, the amorphous fraction of which is removed by acid hydrolysis. It is reputed for having excellent dry binding and disintegration properties (4).

L. cylindrica (Cucurbitaceae) is an annual plant which is naturalized in most part of the world (rarely cultivated). It is commonly known as vegetable sponge and the fibre of the fruit is a possible paper material (5). As part of on-going efforts to develop local raw materials for pharmaceutical industry, we have in the present work, obtained microcrystalline cellulose from the dried fruit of *Luffa cylindrica* plant and compared it with corn starch BP and Avicel PH 101 as disintegrants in directly compressed asprin formulation.

MATERIALS AND METHODS

MATERIALS

Sodium hydroxide (BDH, England), sodium hypochlorite as 'Jik®' (Reckitt and Colman Ltd, Nigeria), hydrochloric acid (Fisons, UK), Avicel PH

101 (FMC corporation, USA), asprin (Vision pharmaceutical Co. Ltd., China) and corn starch BP (BDH Chemicals Ltd, Poole, UK). All other chemicals used were of analytical reagent grade and water was double distilled.

Mature dried fruits of *Luffa cylindrica* were collected from the premises of the National Institute for Pharmaceutical Research and Development, Abuja, Nigeria. The dried fruits were identified in the herbarium units of National institute for Pharmaceutical Research and Development, Abuja.

METHODS

Extraction of Alpha-Cellulose

The dried outer coat of the fruit was removed and the fibrous fruit manually sawed into four parts longitudinally, and the seeds removed. It was further chopped into small bits, which were oven dried at 60 °C until brittleness was achieved. This was milled into chips using a Kenwood Blender model BL 350 (Kenwood Ltd, UK). A 300 g quantity of this material was placed in a stainless steel container to which was added 4 L of 2% w/v sodium hydroxide and digestion was effected for 3 h at 80 °C in a water bath (FGL 1083 Karl Kolb Scientific). This step, also removes lignin in the form of soluble complexes. Following thorough washing and filtration, it was bleached (thrice) with 2.6 L of a 1:1 aqueous dilution of sodium hypochlorite for 30 min. at 100 °C. The washed and filtered material was then treated with 2.4 L of 17.5 % w/v sodium hydroxide at 80 °C for 1 h. The resulting alpha-cellulose was washed thoroughly with water. The extraction process was completed by whitening with a 1:1 aqueous dilution of sodium hypochlorite for 15 min. at 80 °C and washing with water until neutral. The cellulose material was filtered, pressed and manually reduced to small lumps, which were dried in a fluidized bed dryer (Copely, laboratory model) at an inlet air temperature of 57 – 60 °C for 60 min.

Production of Microcrystalline Cellulose (LC-MCC)

A 50 g quantity of the alpha cellulose obtained was placed in a glass container and hydrolyzed with 1.2 L of 2.5N hydrochloric acid at 100 °C for 30 min. The hot acid mixture was poured into cold water which was followed by vigorous stirring with a glass rod. The microcrystalline cellulose obtained by this process was washed with water until neutral, pressed and dried in a fluid bed dryer at an inlet air temperature of 57 – 60 °C for 60 min. Following further milling and sieving the fraction passing through 0.710 mm sieve was used for this investigation.

Preparation of Asprin Compact and Effects of Disintegrant Type

Compacts of asprin powder (a practically insoluble hydrophobic direct compression drug) alone and tablets of asprin containing cellulose or corn starch were prepared. The compositions of these formulations are shown in Table 1.

Table 1: Formula for asprin/cellulose or corn starch compacts

	Formulations			
Ingredient (wt. %)	A	B	C	D
Asprin	300 mg	300 mg	300 mg	300 mg
Avicel PH 101	-	30 mg	-	-
LC-MCC	-	-	30 mg	-
Corn starch	-	-	-	30 mg
Weight of compact	300 mg	330 mg	330 mg	330 mg

Enough material was weighed to yield 40 tablets per formulation. The asprin powder was mixed geometrically with the other ingredient in the formulation. The powder mixture was compressed at a fixed compressional force of 0.8 tons using the Carver hydraulic hand press (Model C, Carver, Inc, USA) with a dwell time of 1 min. at maximum pressure.

Before each compression, the die (10.5 mm diameter) and the flat-faced punches were lubricated with a 2 % w/v dispersion of magnesium stearate in ethanol-ether (1:1).

Effects of Disintegrant Concentrations on Asprin Tablet Properties

Twelve batches of Asprin tablets were produced by the direct compression technique. The formula used for the production of the tablets is as shown in Table 2.

Table 2: Formula for asprin/cellulose/starch tablets

Ingredients	Amount required for 40 tablets (g)			
	A	B	C	D
Asprin crystals	12	12	12	12
LC-MCC/Avicel PH 101	0.6	0.9	1.2	2.4
/Corn starch	(5% w/w)	(7.5% w/w)	(10% w/w)	(20% w/w)
Weight of each tablet (mg)	315	322	330	360

Corn starch, LCC-MCC and Avicel PH 101 (as disintegrants) were dried at 60 °C for 4 h in an electric drying cabinet. Batches of tablets containing 5%, 7.5%, 10% and 20% concentrations of agent were prepared using asprin powder as an active ingredient. The mixture of each of the disintegrants with active ingredient were effected geometrically in a mortar for 5 min. Appropriate quantities (as shown in Table 2) of the mixture were individually weighed and compressed in a Carver hydraulic hand press (Carver Inc, USA) at a fixed compressional force of 0.8 tons using flat-faced punches (10.5 mm diameter) with a dwell time of 1 min. at maximum pressure.

EVALUATION OF TABLET PROPERTIES

In order to allow for equilibration of compacts and/tablets, all tests were initiated 72 h after compression.

Friability

A sample of twenty tablets was selected from each batch and de-dusted by directing a stream of air unto the tablets. The weighed sample of tablets was placed in the drum of a friabilator (Roche Fribilator) programmed to revolve for 4 min. at 25 r.p.m after which the tablets were dedusted. The weights before and after the test were used to calculate the percent friability.

Crushing Strength

The crushing strengths of six tablets obtained at the compression force setting were determined using a tablet crushing strength tester (Karl Kolb, West Germany). The mean crushing strength was determined in each case.

Disintegration Time

The B.P. (1993) method was adopted. The Manesty disintegration time testing unit (Erweka) was used and the medium consisted of 0.1 N hydrochloric acid which was maintained at 37°C. A tablet was placed in each of the six glass tubes carrying a 10 mesh sieve. Using a stopwatch, the time it took each of the six tablets to disintegrate was determined for each batch of tablets. Six replicate determinations were made and the mean and deviation calculated for each batch.

Dissolution Profile Studies

Dissolution rate test was performed with an apparatus meeting the requirements of the United States Pharmacopoeia (Erweka Dissolution Rate Testing Unit, Type DT). The paddle method was used. The dissolution medium used was 0.05 M acetate buffer of pH 4.5 (600 ml). The temperature of the bath for all determinations was kept constant at 37° ± 0.5 °C and the paddle rotation speed of 50 r.p.m was maintained (for every determination). In order to follow the dissolution rate, only one tablet was dropped at a time into the medium. Samples (5 ml) were withdrawn at regular intervals with the aid of syringe fitted with cotton wool from the dissolution medium. The withdrawn samples were replaced with equal volume of the medium in each case.

Sample Assay

Concentrations of asprin in the withdrawn samples were determined spectrophotometrically using an aliquot suitably diluted (1:10) with 0.05M acetate buffer in a Millon spectronic 1001 plus model spectrophotometer at 265 nm wavelength. Calibration curve (or Beer's Plot) of the active drug was prepared.

RESULTS AND DISCUSSION

The yield of alpha-cellulose was approximately 44 percent w/w of the original material while that of microcrystalline cellulose, LC-MCC, obtained from the alpha-cellulose was 65 percent w/w. Consequently, the yield of LC-MCC was approximately 29 percent w/w of the starting material.

Asprin Compact Characteristics and the Effect of Types of Disintegrant

The characteristics of asprin compact and the effect of types of disintegrant are shown in Table 3. Generally, the incorporation of as low as 30 mg (approximately 9.1% w/w) of disintegrants in the asprin compact affected the compact properties significantly. The extents of the effect exerted on these properties were dependent on the disintegrant types. The effect on the compact properties investigated was greatest with the compact prepared with corn starch as disintegrant.

Table 3: Effect of disintegrant types on asprin compact characteristics

Formulations	Crushing Strength (kgf)	Friability (%)	Dist. Time (min)
A. (Asprin alone)	26.0 (0.46)	0.0	180
B (Asprin + Avicel)	22.6(0.66)	0.54	46.5
C. (Asprin + LC-MCC)	23.4(0.51)	0.42	72.25
D (Asprin + Corn starch)	21.2(0.58)	0.92	10.25

Values in the bracket show the standard deviation.

The crushing strength of asprin compacts reduced with the incorporation of the disintegrants. The order of reduction in crushing strength is as follows: corn starch > Avicel > LC-MCC. The effect of disintegrant types on crushing strength will be more appreciated when compared with the crushing strength values of asprin compact without disintegrant which was 26.0 kgf. Thus, it seems that the cohesive force between asprin crystals is stronger than adhesive forces between Asprin and disintegrant particles. An alternative explanation could be that the disintegrant served as a surface contaminant of asprin crystals and consequently reduced the bonding ability between crystals and hence the overall bonding strength of the compacts. Asker *et al* (6) have indicated that the strongest bonds are formed between clean surface, so that addition of disintegrant to the asprin crystals for compression might be expected to weaken the cohesive bonds between the particles of asprin due to the presence of a physical barrier (or contaminant) of disintegrant between the particles of asprin.

The percent friability of all asprin compacts was very satisfactory as all compacts had less than 1% friability. However, the most friable compacts were those made from asprin and corn starch which has 0.92%. The percent friability was a reflection of crushing strength. The lower the crushing strength of the compacts, the more friable the compacts.

The disintegration time of all compacts showed the disintegration power of the three disintegrants investigated. Except for compacts made from asprin/starch blend, all compacts did not disintegrate within the official limit of 15 min. Thus, LC-MCC and /Avicel PH 101 would not be considered as an effective disintegrant like corn starch. This is in agreement with literature report (7) where it has been stated that at equivalent concentrations, microcrystalline cellulose is not as effective a disintegrant as starch. Comparatively, the disintegrant power of Avicel PH 101 used in this investigation was more than that of LC-MCC. The reason for this observation could be due to expected low degree of crystallinity of Avicel (as compared to LC-MCC) as well as its increased surface area sequel to smaller particle size.

Effect of Disintegrant Concentrations on Asprin Tablet Properties

Table 4 shows the results of the effect of disintegrant concentrations on asprin tablet properties. Generally, as disintegrant concentration increases from 5% to 20%, crushing strength and disintegration time decrease while percent friability increases.

Table 4: Effect of disintegrant concentrations on asprin tablet properties

Formulation (% Disintegrant)	Crushing Strength (kgf)	Friability (%)	Disintegration time (min)
Asprin + LC-MCC 5.0%	22.6 (0.92)	0.21	88.8
7.5%	23.93 (1.67)	0.26	76.3
10%	21.67 (0.99)	0.60	60.0
20%	19.9 (1.55)	1.0	56.5
Asprin + Corn-starch 5.0%	23.5 (1.51)	0.73	32.0
7.5%	21.27 (1.19)	0.84	12.5
10%	18.73 (1.83)	0.96	10.0
20%	14.73 (2.50)	1.56	2.6
Asprin + Avicel PH 101 5.0%	25. 13 (1.53)	0.29	51
7.5%	23.17 (1.67)	0.29	35.8
10%	21. 37 (1.11)	0.56	31.0
20%	17.6 (1.52)	0.44	12.25

Values in bracket show the standard deviation.

The results showed that at all concentrations asprin tablet prepared using LC-MCC as the disintegrant had comparable crushing strength with those made from asprin/Avicel blend; with the crushing strength of asprin/LC-MCC tablet insignificantly higher. However, at corresponding concentrations of corn starch as disintegrant, the crushing strength of asprin tablets were lower when compared to those made from the microcrystalline cellulose materials. This could be due to the fact that starches are less compressible than microcrystalline cellulose. Again, high concentrations of disintegrants (especially with corn starch) reduced the crushing strength of the tablet significantly. For example, using corn starch as disintegrant, the tablet crushing strength was reduced from 23.5 kgf at 5% concentration to 14.73 kgf at 20% concentration. This could be attributed to decreased asprin particle contacts due to increased concentration of disintegrants which resulted in weak bond formation.

The percent friability at all concentrations of disintegrants, except at 20% concentration for corn starch was within the 1% acceptable limit. However, tablets containing corn starch were more friable. This observation is in close agreement with earlier explanation – starches are less compressible as microcrystalline cellulose. Correlation was also found between crushing strength and friability of tablet. As the crushing strength of tablets decreased the material loss from tablet (i.e. percent friability) increased.

Also shown in Table 4 is the effect of disintegrant concentrations on the disintegration time of asprin tablet. The results, again, showed corn starch as the most effective disintegrant. Except for 5% concentration of corn starch, tablets made at higher concentrations disintegrated within the official limit of 15 min. At all concentrations of LC-MCC disintegrant however, the disintegration times were far beyond the 15 min. official limit. The same trend was observed for tablets prepared with Avicel at all concentrations, except at 20% which disintegrated in 12.25 min. Though microcrystalline cellulose has been reported to produce very hard tablets yet disintegrate quickly (7), our results indicate the converse. However, microcrystalline cellulose is known to perform excellently as disintegrant at concentration above 20% (7). The difference in disintegration time between LC-MCC and Avicel at all corresponding concentrations could possibly be due to differences in inherent material and particle properties of the celluloses. Such properties would include degree of crystallinity and particle size (hence particle surface area). Overall, at all concentrations of disintegrant used in this investigation, microcrystalline cellulose alone, either as LC-MCC or Avicel, would not be an effective disintegrant in asprin tablet formulation.

The dissolution rate profiles of the tested asprin tablets are shown in Figure 1 (a) and (b). Values T 50% and T 70% (representing the time taken for 50% and 70% respectively of the total drug content of the tablets to be released) as well as the maximum dissolution percent at the end of 30 and 60 min. are recorded in Table 5. The results show large variations in the dissolution rate profiles of asprin tablet both with respect to types and concentrations of disintegrants. In general, the dissolution rate profiles somewhat mirrored the disintegration time properties of these formulations (Table 4).

Table 5: Dissolution time (T_{50}% and T_{70}%) of asprin tablets in 0.05 M acetate buffer

		Dissolution times (min)		Maximum dissolution (%) at:	
		T 50 %	T 70 %	30 min	60 min
10	LC-MCC	*	*	21.92	34.94
	Avicel	56	*	33.56	52.74
	Corn starch	49	*	39.72	56.16
20	LC-MCC	52	*	37.66	57.54
	Avicel	25	*	58.22	65.06
	Corn starch	23	44	65.76	79.46

* 50% or 70% dissolution did not occur at the end of the period.

Fig. 1a: Dissolution rate of aspirin tablets formulated with 10% of disintegrant

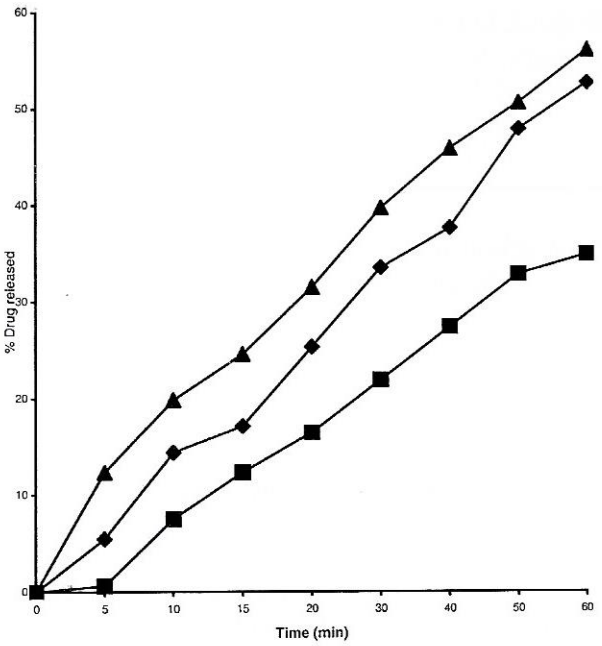

Figure 1a: Dissolution rate profile of aspirin tablets (Asprin formulation with 10% conc. of disintegrant); (■) – LC-MCC, (▲) – Corn starch, (♦) – Avicel PH 101

Fig. 1b: Dissolution rate profile of aspirin tablets formulated with 20% of disintegrants

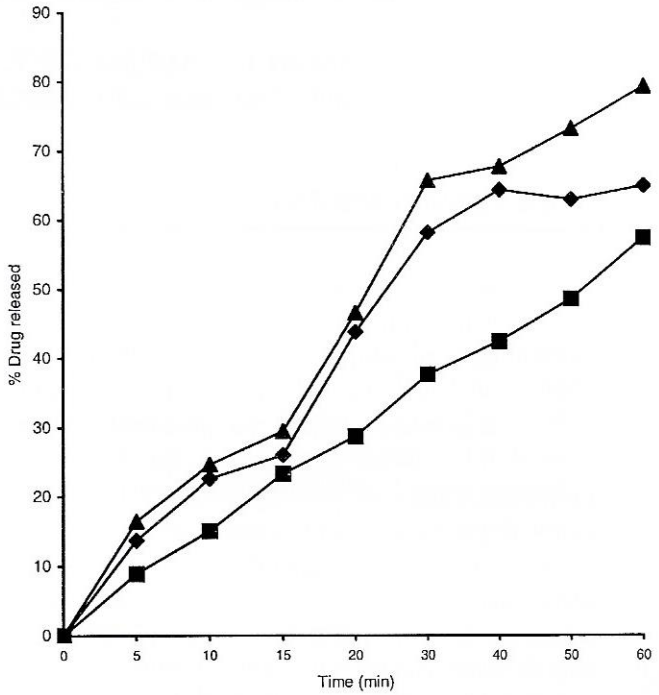

Figure 1b: Dissolution rate profile of aspirin tablet (Aspirin formulation with 20% conc. of disintegrants); (■) – LC-MCC, (▲) – Corn starch, (♦) – Avicel PH 101

CONCLUSION

The finding of this study clearly showed that LC-MCC has disintegrant properties. Its disintegrant ability is however not comparable to that of Avicel PH 101 and Corn starch B.P. The study also revealed that microcrystalline cellulose alone either as a LC-MCC or Avicel PH 101) at the concentrations and compression pressure used in this study is not an effective disintegrant in asprin tablet formulation.

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