Scientia Africana, Vol. 10 (No. 2), December, 2011.pp 82 - 90
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EVALUATION OF THE DISINTEGRANT AND DISSOLUTION PROPERTIES OF POWDER AND CELLULOSE OBTAINED FROM COCOA POD HUSK ON PARACETAMOL TABLETS

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Received 27 – 10 – 10
Accepted 14 – 06 - 11

ABSTRACT

Extracted cellulose and powder from cocoa pod husk were characterized physicochemical, their distingrant efficacy determined and compared with standard disintegrants such as maize starch and micro crystalliro cellulose. To evaluate the disintegrant and dissolution efficacy of extracted cellulose and powder from cocoa pod husk on paracetamol tablet, the extracted cellulose and powder were obtained from dried and sized cocoa pod shell through a chemical process involving washing, filtration and bleaching at 40-60^{o}C using 3.5% w/w nitric acid, sodium hypochlorite sodium hydroxide whitened using hydrogen peroxide processed powders admixed for wet granulation technique of paracetamol tablet formulation. The formulation result show cocoa pod husk powder as a good tablet disintegrant at concentration of 2.5 – 7.5% w/w using wet granulation method since it caused paracetamol tablet to disintegrate within official time (British pharmacopeias) of 15 ± 5 minutes standard deviation while that formulated with the extracted cellulose which seem to be most useful as a direct compression excipient and in sustained release formulation could not disintegrate within the 15 ± 5 minutes time when incorporated in the wet granulation paracetamol tablet formulation method. The inability of the cellulose to cause disintegration at a concentration of 2.5 – 7.5% w/w could be due to the possible formation of a viscous gel when hydrated thereby retarding the breakdown of the moist granule and lowering the dissolution rate than microcrystalline cellulose used as reference standard. Also from physicochemical results the powder obtained at concentration of 2.5 – 7.5% w/w evidenced as a good disintegrant in wet granulation tablet formulation while the cellulose instead of enhancing disintegration, increased in its binding property in the presence of moisture hence likely useful as direct compression exicipient.

Key words: Cocoa pod husk powder and cellulose, disintegration, dissolution, micro crystalline cellulose (mcc), maize starch (ms).

INTRODUCTION

In view of the ever increasing demand of tablet as a dosage form and the limited financial resources available to developing countries, there is the need to explore new sources of excipients in tablet formulation. One of the abundant groups of materials which could be useful for such are agricultural waste. Cocoa pod husk is an abundant agricultural waste-material which has been observed to be richin cellulose and other components. (Okiemen F.E, 2006)

(Simpson, B.K, 1985), and this could make it useful in tabletting.

Cellulose is a major constituent of the cell wall of most plants and is one of the most abundant phytochemical compound on earth. The cellulose and its derivatives have been widely used in packaging paper and textile industries hence together with the derivatives it's use are no less significant pharmaceutically.

Tablets are solid preparation containing a unit dose of one or more medicaments and are obtained by compressing unit volume of particles. (British Pharmacopoiea, 1980). Tablet additives are added to the medicaments to help improve the tabletting properties of the drug. The excipients which must be inert and impact stability and aesthetic to the drug are classified according to the role they play such as diluents, binders, disintegrants, lubricants, glidants and so on (Sharma S. 2010).

Compression transforms a particulate system with a high surface area into a solid mass of low porosity causing inaccessibility of internal fluid to the drug. Disintegrants therefore help to prevent this and cause tablets to breakdown into small Fragments thereby increasing the surface area and allowing for the penetration of the dissolving fluid. Disintegrants opposes the efficiency of the tablet binder and the forces that act during compression to form tablets by providing a hydrophilic pathway within the tablet structure through a 'wicking' mechanism with subsequent rupture of inter particular bonds and also through a secondary mechanism termed as 'swelling' hence it was observed that an ideal disintegrant should improve both disintegration and dissolution of a tablet and should be effective in small concentrations (Aggnestad T. et al 2001).

Disintegrant action can be evaluated by measuring the liquid contact angle on the tablet and the hydration and swelling capacity of the disintegrant (British Pharmacopoiea, 1980) (Huang Y, 2003). They may be incorporatet into tablet formulations intragranularly, extraganularly or by a combination of both. The disintegration time of the tablet may be influenced by the complex interaction of such factors as the rate at which liquid penetrates the tablet, the nature and method of incorporation of lubricant, the degree of composition and the reduction in inter particulate bond strength in the presence of water (Umuwangho M 2005)(Adebayo A. S, 2003).

In tablet production however, the ultimate aim is for it to carry out its therapeutic function. In most cases this occurs after the drug has dissolved in the fluids of the gastro intestinal tract to increase its surface area and enhance absorption. Several factors affecting disintegration time includes tablet hardness, shape, size, amount of lubricant, blending time, nature and concentration of active ingredient, method of incorporation of binder and disintegrant, speed, force of compression and age of the finished product (Paradkar W.A, 2002) (Rasak M., 2008).

Dissolution rate, regarded as the ultimate quality assurance test for tablets if conducted under appropriate physiological condition, correlates with in-vivo dissolution rate. However it is opined that dissolution cannot indicate the extent of absorption because of various in-vivo factors such as stomach emptying time, pH of gastro intestinal fluids, location of the specific sites of drug release and mechanism of absorption (Kitamori, N 1976).

The aim of this work is to determine the usefulness of the test samples (CPHC and CPHP) as tablet excipients which can go a long way in diversifying local sourcing of pharmaceutical raw materials and lowering cost of drug production.

MATERIALS AND METHODS

Extracted cocoa pod husk powder and cellulose (Pharm Research Lab. University of Lagos), Paracetamol powder, microcrystalline cellulose, Poly Vinyl Pyrollidone (PVP), Talc, Maize starch, lactose and Magnesium stearate

Scientia Africana, Vol. 10 (No. 2), December, 2011.pp 82 - 90
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(Purchased at Open Market, Idumota, Lagos),Phosphoric buffer of pH 6.8 (M & B Nig. Limited.)

The wet granulation method of tablet formulation was used for this evaluation and the granules were formed according to the formulae in Table 1.

The method involve the mixture of the drug (500mg paracetamol powder) with the filler and disintegrant (CPHP, MS) and blending in a mortar for 10 minutes. After which binding solution (warm water) was added to the powder mix and with continuous stirring, the mucilage (PVP) was added.

The mixing was continued for another 10 minute before the moist mass formed was passed through a 1μmsieve aperture and dried in an oven at $40^{o}C$ for 4 hours.

The dried granules formed were then passed through a 1μm sieve again, and stored in a tightly closed container from where they are collected for phsysicochemical analysis, compression after blending with Talc/Magnesium stearate into tablet which was then subjected to disintegration and dissolution test.

Table 1: Formulation of Tablets Using the Test Sample and Standard as Disintegrants (50%Intragrannular 50%Extragranular and 100% intragranular)

pcm(mg)	lactose (mg)	pvp % w/w	talc/mg.st 1:1% w/w	cphc % w/w	mcc % w/w	cphp% w/w	ms % w/w
		XY	*XY*	*XY*	*XY*	*XY*	*XY*
500	60	3 3	1 1	2.5 2.5	- -	- -	- -
500	45	3 3	1 1	5.0 5.0	- -	- -	- -
500	30	3 3	1 1	7.57.5	- -	- -	- -
500	75	3 3	1 1	- -	- -	- -	- -
500	60	3 3	1 1	- -	2.5 2.5	- -	- -
500	45	3 3	1 1	- -	5.0 5.0	- -	- -
500	30	3 3	1 1	- -	7.5 7.5	- -	- -
500	60	3 3	1 1	- -	- -	2.5 2.5	- -
500	45	3 3	1 1	- -	- -	5.0 5.0	- -
500	30	3 3	1 1	- -	- -	7.5 7.5	- -
500	60	3 3	1 1	- -	- -	- -	2.5 2.5
500	45	3 3	1 1	- -	- -	- -	5.0 5.0
500	30	3 3	1 1	- -	- -	- -	7.5 7.5

- *X* – Test sample and standard 50% intra and 50%. Extragranular
- *Y* – Test sample and standard 100%. Intragranular

Compression to Tablets: The granules where necessary, were mixed with the exodisintegrants. The required amount of lubricant and glidantwas added and blended for 5 minutes. The granules were then transferred into a single punch tabletting machine set at a pressure of 0.3mmHg to produce flat-faced tablets of 12.55mm diameter, 4.65mm width and weight targeted at 495 to 505mg.

Evaluation of Tablets: The tablets produced were evaluated on the basis of the following parameters: hardness, uniformity of weight, friability, disintegration time and dissolution rate.

Hardness (Crushing Strength): The Copley Schleuniger 28 model tablet hardness tester was used to determine the breaking strength of the tablets. The hardness of five tablets selected at random from each batch were recorded. The mean of four determinations was calculated.

Uniformity of Weight: Twenty tablets drawn randomly from each batch were weighed individually and then weighed together. The mean, standard deviation and coefficient of variation were calculated.

Friability: Ten tablets were selected randomly, weighed individually and placed in a friabilatorto tumble for 4 minutes at 25 revolution per minute. The tablets were reweighed after carefully brushing off the dust from the surface while the % loss in weight of the ten tablets is taken as % friability.

Disintegration Time: The British Pharmacopoiea (BP) method was adopted. A disintegration apparatus (Type T.4 ErwekaApparatus W. Germany) was used. The disintegration apparatus consisted of distilled water maintained at 37±0.5^{o}C. One tablet was placed in each of the six glass tubes having at the lower end a mesh 10 sieve. The apparatus was switched on and the time it took all the six tablets to disintegrate was determined using a stop watch. The disintegration time of each batch was the mean of four replicate determinations.

Dissolution Rate Test: This was carried out in accordance with the United States Pharmacopoiea (USP) (1990) using SOTAX.AT 7 dissolution apparatus. The paddle method was adopted at 75rpm with a dissolution medium consisting of phosphate buffer maintained at 37±0.5^{0}C.

The standard solution was prepared by weighing 65.5mg of paracetamol powder and dissolving in the buffer solution then making up to 100ml with same buffer solution. 1ml of the prepared sample was withdrawn using a pipette and diluted to 100ml with same buffer solution and analysedspectrophotometrically upon serial dilution.

For the dissolution, one tablet was placed in each of the six tubes in a suitable vessels containing the dissolution medium placed in a 900ml buffer solution (water bath) maintained at 37^{o}± 0.5^{o}C. The rotating paddle was switched on at a speed of 75 *rpm*. The stirring motor of the paddle is placed through the centre hole of the vessel cover and was centred to permit smooth rotation and prevent wobbling. 10ml of the sample was withdrawn at intervals of 5, 15, 25, 30 and 45 minutes and quickly replaced with equal volume of the buffer. The sample was filtered and 1ml of the filtrate diluted to 100ml with buffer of pH 6.8 and used for the assay along with the standard using a properly cleaned cuvette placed in the UV/visible spectrophotometer type spectronic 21 by Milton Roy Co. England, at a wavelength of 249nm. The quantity of paracetamol dissolved was calculated, using the relation: $\frac{a}{b} \times \frac{100}{1}$ where a is absorbance of sample b is absorbance of standard solution.

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RESULTS

Table 2: Paracetamol Tablets Made Using the Test Sample and standard as Disintegrants (50% Intra; 50% Extra Granular)

	Concn %w/w	Crushing Strength Kg/cm^2	Friability (%)	Disintegration Time (mins)	% Dissolution T_{45mins}
CPHC	2.5	7.82±0.5	0.65	49±0.6	28.35±0.8
	5.0	7.56±0.4	0.88	46±0.5	26.38± 1.1
	7.5	6.88±0.5	0.8	43±0.5	27.17±0.9
CPHP	2.5	9.26±0.3	0.59	3±0.2	95.98±1.3
	5.0	8.8±0.4	0.53	9.1±0.2	92.24±2.6
	7.5	9.24±0.4	0.56	11±0.4	88.73±2.3
MCC	2.5	7.46±0.6	0.8	2.2±0.2	97±1.4
	5.0	7.6±0.5	0.84	1.7±0.2	97±1.2
	7.5	7.26±0.5	0.784	1.5±0.1	98±0.9
MS	2.5	7.46±0.3	1.1	1.2±0.1	99±0.7
	5.0	8.48±0.4	0.73	1.5±0.1	98±1.3
	7.5	7.88±0.3	0.885	1.1±0.07	98±1.2
*		6.94±0.4	1.2	14.5±0.3	80±1.6

* -No Disintegrant

Table 3: Paracetamol Tablets Made Using the Test Samples and standard as Disintegrants (100% Intra Granular)

	Concn %w/w	Crushing Strength Kg/cm^2	Friability (%)	Disintegration Time (mins)	% Dissolution T_{45mins}
CPHC	2.5	8.66±0.7	0.78	59±1.3	23±0.3
	5.0	9.32±0.7	0.73	63±1.8	22±0.3
	7.5	8.14±0.5	0.81	56±1.4	25±0.4
CPHP	2.5	7.3±0.5	0.86	5.2±0.2	84±1.3
	5.0	7.6±0.4	0.84	9.0±0.6	79±1.4
	7.5	6.8±0.4	0.93	7.0±0.6	87±1.3
MCC	2.5	7.8±0.4	0.83	13.1±0.8	93±1.9
	5.0	9.2±0.5	0.75	8.7±0.2	96±1.4
	7.5	10.8±0.8	0.63	0.4±0.3	97±1.8
MS	2.5	8.8±0.4	0.7	10.8±0.4	98±1.1
	5.0	7.44±0.3	0.88	7.0±0.3	98±1.2
	7.5	7.0±0.3	0.91	2.1±0.2	99±0.4
*		6.94±0.4	1.2	12.5±0.3	89±1.6

***** = No disintegrant

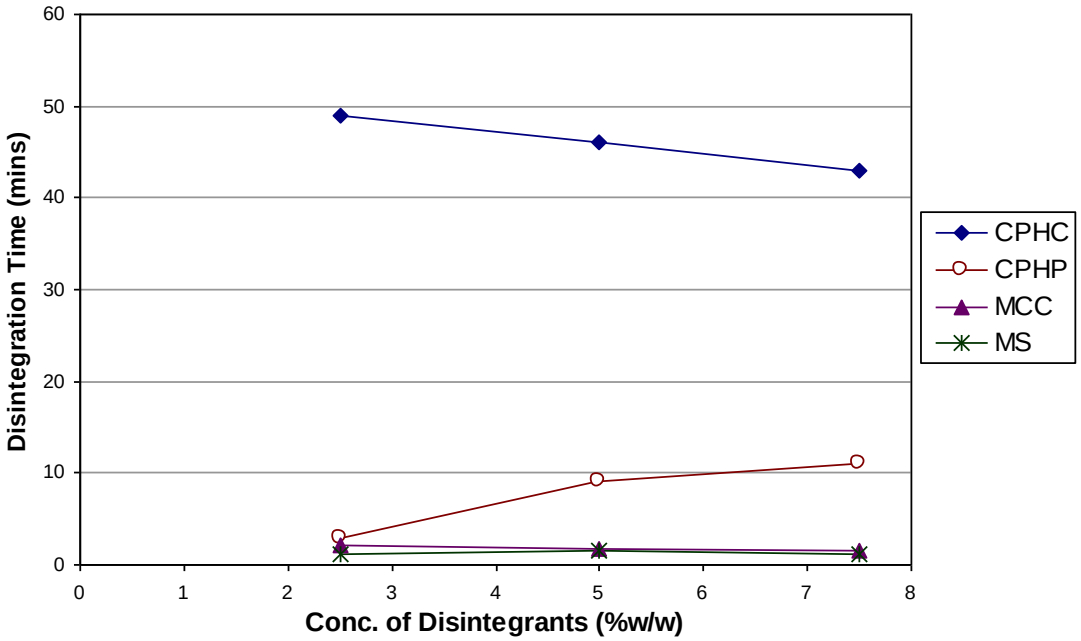

Fig. 1: Disintegration time against concentration of disintegrants (50% intra and 50% extragranular).

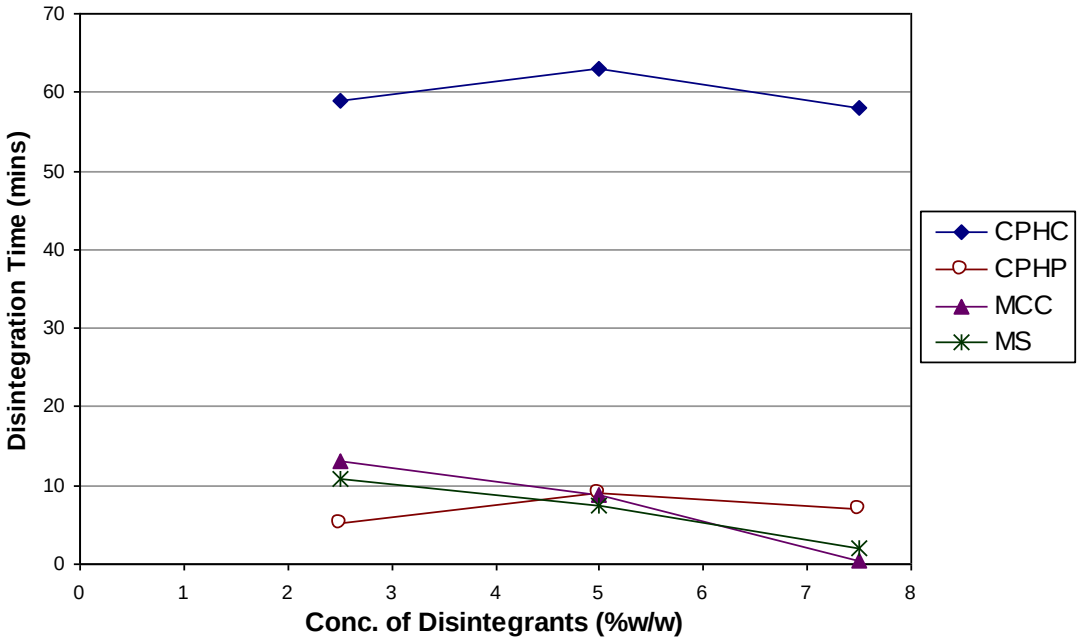

Fig. 2: Disintegration time against concentration of disintegrants (100% intragranular).

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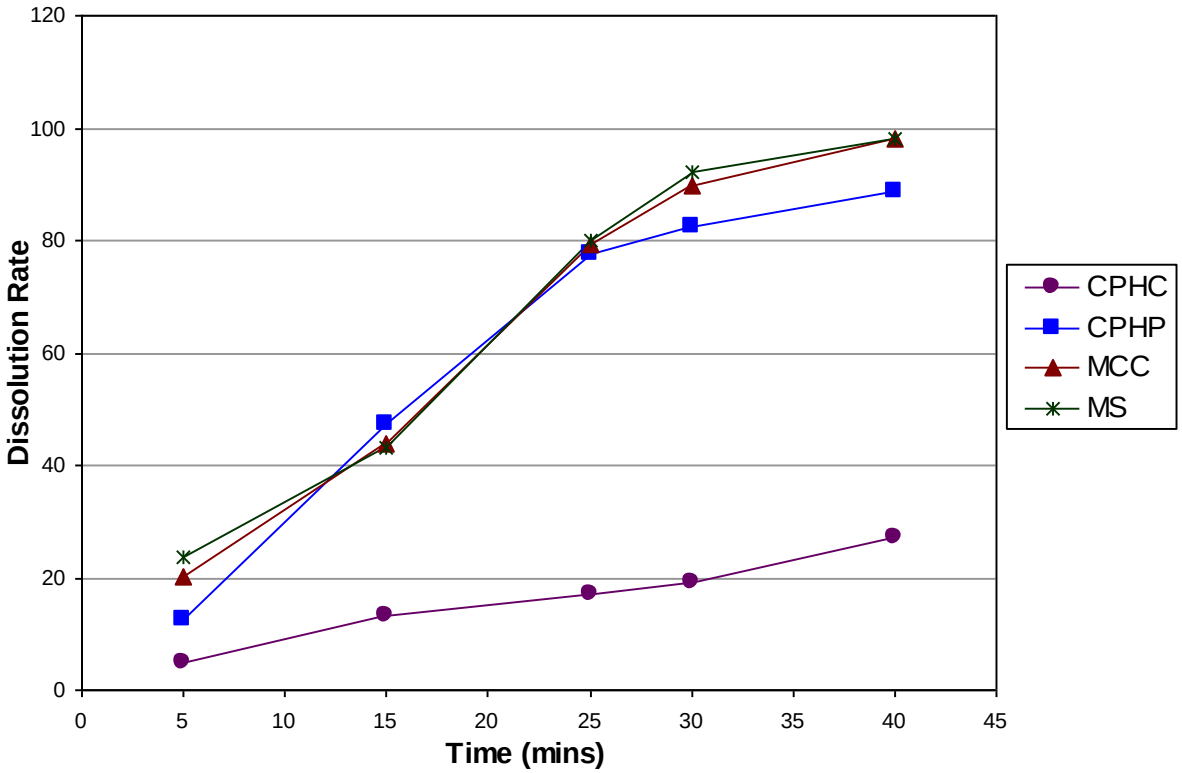

Fig. 3: Dissolution rate of tablets using test samples and standard (50% w/w intra and 50% w/w extragranular.

DISCUSSION

Various batches of paracetamol tablets were formulated using each of the powders at concentration and mode of incorporation shown in Table 1. Following the prescribed limit of 15 minutes disintegration time, (British pharmacopoeia 1980), the tablets formulated using Cocoa pod husk powder, Micro crystalline Cellulose and Maize starch all disintegrated within the specified time limit of 15 ± 5 minutes while paracetamol tablet prepared with cocoa pod husk cellulose failed to disintegrate within 15 ± 5 minutes. This could be attributed to the possible formation of viscous gel by the Cellulose when hydrated thereby retarding the breakdown of the tablets. The results also shows that the disintegration efficiency is more when the disintegrants are added 50% intragranularly and 50% extragranularly than when the disintegrants are incorporated 100% intragranularly hence disintegration ability of the powder affected by process of incorporation (Harry, Z. 2008). This can also be attributed to a faster "wicking" action in tablets containing extragranulardisintegrant because when disintegrants are added extragranularly, they distribute on the surface of the tablet more than when added intragranularly. Also extragranulardisintegrants have a high tendency to absorb water from surrounding fluid through a rapid "wicking" mechanism.

It is however worth noting that disintegrant efficiency depends primarily also on the physico chemical nature of the disintegrants and other tabletting parameters such as compaction pressure hence affected by the

porosity of the tablet matrix(Shotton E., 1976)(Miller R.A 1980) (Thema, K, 1978).

The results of the studies on disintegration time are also shown in figures 1 and 2 while the effects on dissolution are shown in figure 3. The resulting graph shows that the disinstegration and dissolution time of tablets prepared with the Cocoa pod husk cellulose (CPHC) was longer than that of similar tablets prepared using the Cocoa pod husk powder (CPHP) and the standard (MCC and MS) as disintegrant depicting increased binding or cohesive properties of the extracted CPHC.

CONCLUSION

The formed tablet using the test samples (CPHP and CPHC) upon physiocochemical analysis showed relative deviation in property but comparism with standard (MCC and MS), the CPHP showed similarity in disintegrant and dissolution profile. This depicts that the CPHP possess similar disintegrant property while CPHC with wide deviation lacks such disintegrant activity especially when used in wet granulation of paracetamol tablet formulation.

This CPHC though ineffective as a disintegrant in such technique (wet granulation),is suspected to be very useful an excipient in direct compression and hence in sustained release tablet formulation.

With this result therefore and in the search for new tablet excipient to reduce the ever increasing burden of imported pharmaceutical raw materials especially in developing countries, agricultural waste material such as Cocoa pod husk should be sourced while the powder and cellulose be extracted and utilized for such economic purpose as a possible disintegrant and excipient in pharmaceutical research, for tablet formulation and also in other allied industries.

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