PHYSICOCHEMICAL PROPERTIES OF MONTMORILLONITE, KAOLINITE AND MAIZE-STARCH PREPARED BY DIRECT COMPRESSION WITH PARACETAMOL POWDER: (2) A COMPARATIVE STUDY

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Abstract: Clay minerals can accommodate polar organic compounds between their layers to form a variety of intercalated compounds; from which drugs release are potentially controllable, hence these new materials have great potential as a delivery host in the pharmaceutical field. The various powder hybrids were thoroughly mixed by wet granulation process, dried, sieved and the blends were compressed on a single punch machine. The tablets were subjected to various tests, uniformities were shown in diameters (12.45±0.01 mm), thicknesses (0.33±0.01 mm), and weights (not > 0.52±0.01 g); the varying results obtained were more pronounced in hardness, friability, disintegration, and dissolution tests. Maximum hardness measured are shown as follows: Na-MMT 8.90±0.33 KN, Kaolinite 10.60±0.33 KN and MS 8.74±0.33 KN; maximum friability reported were in the following order Na-MMT 0.40±0.01%, Kaolinite 0.20±0.01% and MS 0.46±0.01%. dissolution of tablets in 0.1M HCl and the UV absorbance at 242 nm showed varying PCM concentrations released as MS 1.17A, Na-MMT 0.71A and Kaolinite 0.40A The disintegrant physical properties of Maize-Starch were compared to Montmorillonite and Kaolinite, to ascertain the better disintegrant physical properties possessed by selected clay minerals that can be used as alternative to Maize-Starch. The objective of the present study was to formulate paracetamol (PCM) by direct compression method. The work also examines the advantageous effect of clay minerals as drug carrier for PCM, a derivative of aniline most widely used as analgesic and antipyretic drug.

Keywords: Montmorillonite, kaolinite, maize-starch, paracetamol, direct compression, disintegrant physical properties

Introduction

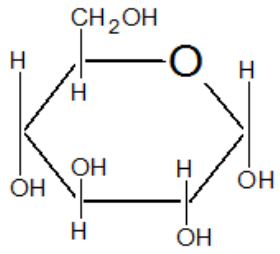
Disintegrants are group of expicients that are mixed with active pharmaceutical ingredients to form conventional tablets by direct compression (Bushra *et al.*, 2008). Maize-starch is a typical example of disintegrant being used. Disintegrants are prepared in powder mixture before wet granulation. Many tablet formulations containing both internal and external starch follow an intermediate pattern, firstly disintegrating into granules, which then disaggregated into fine particles (Alebiowu and Itiola, 2003; Pilpel *et al.*, 1978).

The effect of various ratios of disintegrants on the disintegrant properties of PCM tablets prepared with montmorillonite and Kaolinite were investigated. MS was used as a standard. Improved drug dissolution and bioavailability are always invariably followed by rapid disintegration of solid dosage forms (Iwuagwu and Okoli, 1992).

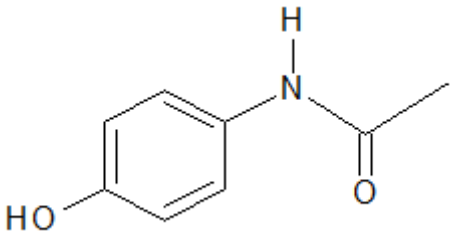
Materials and Method

Materials

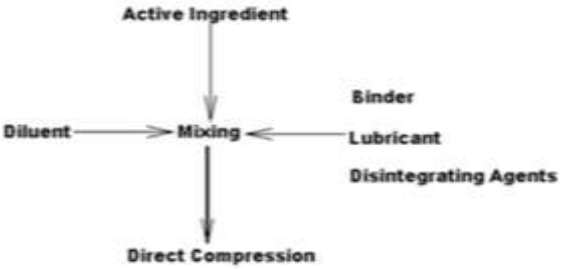
Sample clay contained predominant minerals (namely Montmorillonite and Kaolinite) were obtained from areas located in Okada Town and Usen Community, covering distance of about 28 and 32 km from Benin City, Edo State, Southwestern Nigeria respectively. Sodium-Montmorillonite contains sodium magnesium aluminum silicate hydroxide, Kaolinite contains aluminum silicate hydroxide as derived from X-ray diffractogram (XRD) analysis and X-ray Fluorescence (XRF) analysis in their powder preparations.



Source: Rowe *et al*. (2006)
Fig. 1: Structural formula of maize starch (dextrose) or glucose anhydrous



Source: wikipedia.org/wiki/file.paracetamol_skeletal.svg
Fig. 2: Chemical structure of paracetamol (acetaminophen $C_8H_9NO_2$) 4-hydroxyacetanilide



Source: Armstrong (2002)
Fig. 3: Direct compression process

Preparation of tablets

Paracetamol, 10% MS and excipients were mixed for 30 min, lubricants magnesium stearate and aerosil 200 were added to the mixture after passing through 180 µm sieve, stirring continued for 5 min., similar granulation process were made for 5, 10 and 15% clay minerals-paracetamol mixtures; and all powder mixtures were sieved through 500 µm sieve. Tablets of 530 mg in weight and 12 mm diameter were prepared by direct compression using a single punch tableting machine, Kilian SP 300 (Kilian and Co GmbH, Germany). Tablets were compressed with force of 7 kN and uniform weight and diameter of tablets were measured.

Tablet physical properties

Uniformity of diameter, thickness, mass, tablet hardness and friability

The diameter and thickness were determined with micrometer screw gauge. The average tablet weight was determined by weighing 20 tablets individually using an analytical balance. Hardness was determined using Morsantus manually operated tablet hardness tester; and 10 tablets of each formulation were tested (Ph. Eur. Method 2.9.8) (British Pharmacopeia, 2003a; Murkesh *et al.,* 2007). Friability was determined by placing 10 tablets of each formulation in a Friability test machine (Erweka T.A., LOSCHEN, W. Germany) operating the drum for 4 min at 25 rpm (Ph. Eur. Method 2.9.7) (British Pharmacopeia, 2003b). Friability was determined using the formula stated below (Wu *et al.*, 2007; Biljana *et al.*, 2011):

Friability = [(Initial weight × Final weight) ÷ (Initial weight) × 100] (%).

Water retention capacity

The tablet is placed on a piece of tissue paper (12 x 10.75 cm) folded twice with one side right angle immersed in a small dish containing deionised water; then the wetted tablet was weighed at interval of 10 min until the time for complete wetting is measured at 25^{o}C. Water uptake ratio R was determined by applying the equation below (Iwuagwu and Okoli, 1992; Oyi *et al.,* 2009; Biljana *et al.,* 2011):

$R = [W_b - W_a] \div W_a$.

Where W_b and W_a are the weight before and after adsorption respectively.

Disintegration time

Disintegration time was measured with Manesty apparatus Type MK4, (England). Tests were carried out in 800 ml of 0.1M HCl solution at 37±2^{o}C. The entire tests were run using 6 tablets of each formulation (Ph. Eur method 2.9.3) (British Pharmacopeia, 2003c).

Dissolution study

Dissolution test was carried out using the paddle method at the speed of 100 rpm (described in Ph. Eur. Method 2.9.3) (British Pharmacopeia, 2003c). Filtered Samples of 10 ml pipette were withdrawn from dissolution medium at every 10 min time intervals. 6 experimental readings of each sample solutions taken were serially diluted by factor of 10 in 100 ml and 1 in 10 ml in a fresh dilution medium. The absorbance was measured by a spectrophotometer (UV-Visible Spectrometer 8643, Agilent, France) at 242 nm (Iwuagwu and Okoli, 1992; Biljana *et al.,* 2011).

Results and Discussion

The results of the experimental determination of tablet physical properties of the maize-starch, Na-MMT and Kaolinite carried out are shown in Table 1.

Table 1: Tablets physical properties (TPP) for Na-MMT, kaolinite and MS

S/N	Tablet Properties	MS	5% Na-MMT	5% KAO	10% Na-MMT	10% KAO	15% Na-MMT	15% KAO
1	Diameter (mm) X±SD, n = 10	12.45(±0.01)	12.43(±0.02)	12.31 (±0.02)	12.43(±0.04)	12.32(±0.01)	12.43(±0.02)	12.31(±0.01)
2	Thickness (mm) X±SD, n = 10	0.33(±0.01)	0.33(±0.00)	0.31 (±0.00)	0.33(±0.00)	0.31(±0.00)	0.33(±0.00)	0.31(±0.00)
3	Mean Weight (g) X±SD, n = 10	0.52(±0.01)	0.52(±0.01)	0.51(±0.01)	0.52(±0.01)	0.51(±0.01)	0.52(±0.01)	0.51(±0.01)
4	Hardness (KN) X±SD, n = 10	8.74(±0.05)	8.50(±0.33)	8.40(±0.33)	8.70(±0.33)	9.50(±0.33)	8.90(±0.33)	10.60(±0.33)
5	Friability (%) X±SD, n = 10	0.44(±0.01)	0.39(±0.01)	0.56(±0.01)	0.40(±0.01)	0.57(±0.01)	0.40(±0.01)	0.58(±0.01)
6	Water Up Take (g) X±SD, n=10	0.25(±0.08)	0.13(±0.00)	0.03(±0.00)	0.18(±0.18)	0.04(±0.01)	0.21(±0.01)	0.09(±0.05)
7	DT (min)	1.52 min	>15 min	>15 min	>15 min	>15 min	2.43 min	11.27 min
8	Absorbance (A)	1.17	0.23	0.21	0.54	0.30	0.71	0.40

MS=Maize Starch, Na-MMT=Sodium Montmorillonite, KAO=Kaolinite, DT=Disintegration Time

Diameter, thickness and weight of the solid dosage

The measured diameters 12.45±0.01 mm for MS tablets show the same close values as for those of 5 - 15% Na-MMT. Whereas, 12.31±0.01 mm diameters of 5 to 15% Kaolinites were slightly different from MS diameters recorded, indicating that the Kaolinites tablets capped after compression (Wu *et al.,* 2007). The same relative constant thickness 0.33 (±0.01) mm and 0.52 (±0.01) g weights were recorded for MS and Na-MMT dosage forms; whereas slightly different thickness 0.31 (±0.00) mm and weights 0.51 (±0.01) g were recorded for 5 to 15% Kaolinites.

Hardness and friability

Hardness: As the selected clay minerals increases in % w/w ratio the hardness increases (Eiche and Kudohinbu, 2009). Hardness test of 15% Na-MMT measured is 8.90 (±0.03) KN which is higher than that of 10% Na-MMT 8.70 (±0.03) KN, 5% NaMMT exhibits very low hardness of 8.50 (±0.03) KN. 15, 10 and 5% Kaolinite show similar trends of hardness and the values are 10.60 (±0.03) KN, 9.50 (±0.03) KN, and 8.40 (±0.03) KN, respectively and MS 8.74 (±0.05) KN. The decreasing order of hardness is generally shown as Kaolinite > Na-MMT > MS. Na-MMT and MS have relatively the same hardness properties. The larger granules with smaller surface area and higher percentage of void inside of such tablets with weaker inter-particulate bonding requiring the lower crushing strength for diameter fracture (Eiche and Kudohinbu, 2009).

Friability: Kaolinite show relatively high friability values but not greater than 0.58 (±0.01)% compared to Na-MMT with low friability values that are relatively constant but not greater than 0.40 (±0.01); MS friability is 0.44 (±0.01). Increasing order of friability is shown as Kaolinite > MS > Na-MMT. Thus Kaolinite is easily capped and friable implying that it has more weight loss compared to Na-MMT. Generally Na-MMT and MS are less friable than Kaolinite because they do not have void space but better adhesive properties. When pharmaceutical powders are compressed into tablets, elastic recovery is responsible for capping, lamination or chipping tendencies, such as entrapment of air, elastic characteristics of materials, radial relaxation of tablets and non-uniform density distribution (Wu *et al.,* 2007).

Water uptake

MS shows good water uptake value 0.25 (±0.08)g which is better than those obtained for clay minerals. Water uptake obtained for Na-MMT and Kaolinites increased as their % W/W ratios increases. The ascending order of water uptake in 5, 10 and 15% Na-MMT are 0.13 (±0.00)g, 0.18 (±0.18)g and 0.21 (±0.01)g, respectively. 5, 10 and 15% Kaolinites show similar ascending order of water uptake as 0.03 (±0.00)g, 0.04 (±0.01)g, and 0.09 (±0.05)g respectively. In the presence of water Na-MMT show better water uptake (indicating better capillary actions) and ability to swell than Kaolinite. Hence Na-MMT can function as a good tablet disintegrant. This result is in correlation with the small porosity of tablet and longer wetting and disintegration time (Murkesh *et al.,* 2007).

Disintegration time

The disintegration time of MS was ≤ 1.52 min, the disintegration time of 15% Na-MMT was 2.43 min, disintegration time of 15% Kaolinites was 11.27 min; the rest 5% and 10% Na-MMT and Kaolinite disintegrated above 15 min, this result shows that low swelling exist between particle-particle bonding which give rise to longer disintegration time (Oyi *et al.,* 2009). MS and 15% Na-MMT exhibited better disintegrant property than that shown by 15% Kaolinite.

Dissolution and absorbance

The active ingredients (PCM) released into 0.1M HCl at time interval of 10 min for 6 dilutions were determined by UV Spectrometer Absorbance readings. 15% Na-MMT, Kaolinite and MS absorbance values were recorded as 0.71A, 0.40A and 1.17A, respectively, MS and 15% Na-MMT released more PCM solutes into the acid medium than 15% Kaolinite. The Absorbance values of 0.23A and 0.54A were recorded for 5 and 10% Na-MMT respectively which showed better amount of PCM released into the medium than 0.21A and 0.30A observed for 5 and 10% Kaolinite,s respectively.

Conclusion

The hardness increases as %W/W ratio of the disintegrant increases. Na-MMT and MS is less friable than Kaolinite. The average disintegration time of MS was ≤ 1.52 min which was considered to be slightly better than that of Na-MMT, and the latter disintegrate at time interval not greater than 2.43 min whereas 15% Kaolinite disintegrated at 11.27 min. Moreover disintegration time of 5 and 10% Na-MMT and Kaolinite in 0.1M HCl were >15 min. Therefore results obtained for dissolution tests show that MS had superiority over Na-MMT, and Na-MMT had values that were more better than those of Kaolinites. It can be generalized that the Na-MMT show stronger prospects than Kaolinite as alternative disintegrant to MS in the formulation of certain solid pharmaceutical dosage; whereas Kaolinite being acidic in nature exhibited poor dissolution property. In addition the results of some tablets physical properties (TPP) show that Na-MMT and MS had better properties than Kaolinite, hence Na-MMT can function as a good tablet disintegrant. It can be generalized that the Na-MMT has great prospects of being used as alternative disintegrant to MS in the formulation of certain solid pharmaceutical dosages.

Conflict of Interest

Authors declare that there is no conflict of interest.

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