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Research Article

Adsorptive property of kaolin in some drug formulations

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Abstract

Purpose: *Kaolin is a known adsorbent, has lubricant property in powders and is therefore proposed as a lubricant in tablet formulations. This study was carried out to evaluate whether kaolin can adsorb some active drugs when mixed with them in tablet formulations even at very low concentrations.*

Method: *Chloroquine and chlorpheniramine tablets were formulated with powder mixtures containing various concentrations of kaolin. The effect of kaolin on the physical properties of the tablets were examined and compared with those of standard lubricants like magnesium stearate and talc. Chloroquine and chlorpheniramine tablets and powders of amoxicillin/clavulanic acid oral powder and ampicillin/cloxacillin injection were also mixed with and without various concentrations of kaolin in water. Chemical assay of the drugs in the solutions were determined over time.*

Results: *Kaolin significantly reduced the amount of each of the drugs in the solutions containing kaolin.*

Conclusion: *Kaolin reduces the amount of some drugs when incorporated in drug formulations. Therefore, its inclusion in such drug formulations should not be encouraged.*

Keywords: *Adsorption, ampicillin/cloxacillin, amoxicillin/clavulanic acid, chloroquine, chlorpheniramine, drug formulation, kaolin.*

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Introduction

Many studies[1-7] in Nigeria have demonstrated the usefulness of many local raw materials in the formulation of pharmaceutical products. For example, kaolin has been shown to have superior lubricant property to talc and stearic acid at the concentration range of 0.2%-1.0%. Edible-clay also demonstrated such similar property[8]. Oladimeji *et al*'s[9] assumption that kaolin, at such low concentrations, would not exert any appreciable adsorptive properties on drugs was not proven scientifically. However, it has been pointed out[10, 11] that the pressing need for local raw materials does not imply that their undesirable properties should be ignored.

Kaolin has long been employed to adsorb toxic substances from the alimentary canal and in the treatment of diarrhoea associated with food poisoning[12]. Although it has excellent lubricant properties in tableting, at low concentrations, its adsorptive nature may militate against its use even at such low concentrations. This work, therefore, aims at examining this assumption.

Materials and Methods

Pharmaceutical grade powders of kaolin, talc, lactose and maize starch (BDH, England), magnesium stearate (Hopkins & Williams, England), chloroquine sulfate (May & Baker, Nigeria), and chlorpheniramine maleate (Glaxo, Nigeria) were used. Also amoxycillin/clavulanic acid oral powder and ampicillin/cloxacillin injection powder, chloroquine and chlorpheniramine tablets were purchased from a local pharmacy.

Tablet Preparation

Granules containing either chloroquine sulfate or chlorpheniramine maleate, as active ingredients, were prepared using the wet granulation method[11]. Kaolin, talc, or magnesium stearate (0 - 2% w/w) were separately added extra-granularly as lubricant/glidant to dried 50 g batches of free flowing granules of each drug formulation and mixed intimately for 10 min. The mixed granules were compressed using a single-punch tableting machine, type KS (The Kilian and Co. GMBH, KOLN-NIEHL) into flat faced tablets (12.5 mm diameter and 300 mg in weight for chloroquine and 7.0 mm diameter and 80 mg in weight for chlorpheniramine formulations).

Dissolution studies

The chloroquine and chlorpheniramine tablets with or without kaolin were stored at ambient temperature for 1 month. Dissolution studies were then carried out on the tablets prepared in our laboratory and on those purchased locally, amoxycillin/ clavulanic acid, and ampicillin/cloxacillin powder combinations (also purchased locally) using Erweka Dissolution Apparatus[13]. For the drug samples purchased locally, the dissolution media were 500 ml of 0.5% w/w and 1% w/w kaolin in distilled water at 37±0.5 ^{o}C.

Assay of active ingredients in solution

Chloroquine and chlorpheniramine were assayed using the British Pharmacopoea (B.P.) titrimetric method for chloroquine sulfate tablet and B.P. spectrophotometric method for chlorpheniramine maleate tablet[14]. For the formed tablets, dissolution test was conducted after one month' s storage.

For the study on amoxycillin/clavulanic acid oral powder, an amount of the powder equivalent to 0.1 g of the drug in the mixture was dissolved in sufficient distilled water to produce 100 ml. The solution (2 ml) was diluted to 100 ml with buffered copper sulfate solution, pH 5.2, and 10 ml was transferred to a test tube (covered with a stopper). The tube was heated on a water bath at 75 ^{o}C for 30 min, cooled rapidly to room temperature, and the volume was adjusted to 10 ml with distilled water. The extinction of a 1cm layer of solution at a maximum of about 320 nm was measured using the unheated buffered

solution of the drug as blank (Smart A., 1991; unpublished article).

Ampicillin and cloxacillin content in ampicillin/cloxacillin injection power were determined as earlier described[14-15].

Each assay was carried out in five replicates and the mean drug content was recorded for each drug.

Results and Discussion

Kaolin enhanced the production of good quality tablets but it adversely affected the dissolution and release of the active drug in contact with it even at low concentrations. Table 1 shows that the presence of kaolin in the tablets caused a reduction in the amount of chloroquine and chlorpheniramine available in solution. The amount found in the solution decreased as the concentration of kaolin in the tablets increased. There was approximately 42% decrease in chloroquine concentration (from 82.4% to 41.1%) and 64% decrease in chlorpheniramine concentration (from 79.7% to 16.0%) when kaolin concentration in the tablets was 1%. The pure drug substances that were briefly exposed to kaolin were also affected. Table 2 shows that chloroquine and chlorpheniramine samples progressively lost their drug content in 1% kaolin suspension over a period of 40 min. Chloroquine lost about 50% in less than 8 min while chlorpheniramine lost the same amount in about 10 min. Probably, this is due to adsorption of the drugs by kaolin. Saturation of the adsorptive sites by chloroquine was within 20 min while chlorpheniramine achieved that in about 25 min. Also, the drugs purchased locally namely, chloroquine and chlorpheniramine tablets, amoxycillin/clavulanic acid and ampicillin/cloxacillin powder combinations were similarly affected. Within 60 min the amount of amoxycillin/clavulanic acid and ampicillin/cloxacillin powder combinations reduced from 100% to 89.5±0.8% and

Table 1: Content of chloroquine and chlorpheniramine in the tablets formulated with kaolin after 1 month storage

Kaolin concentration (%w/w)	% Amount of chloroquine	% Amount of chlorpheniramine
0.0	82.4 ± 1.3	79.7 ± 0.9
0.5	79.4 ± 0.8	62.5 ± 1.2
0.75	47.6 ± 1.6	16.5 ± 1.3
1.0	41.1 ± 1.0	16.0 ±1.2

Table 2: Effect of exposure of pure drugs (chloroquine & chlorpheniramine) to 0% and 1% kaolin

Time (min)	% Amount of chloroquine dissolved in solution in presence of kaolin		% Amount of chlorpheniramine dissolved in solution in presence of kaolin	
	0.0% kaolin	1.0% kaolin	0.0% kaolin	1.0% kaolin
0	100±0.6	100 ±0.6	100±0.6	100±0.6
1	100±0.6	65.5±1.2	100±0.6	78.6±1.1
3	100±0.6	63.5±0.8	100±0.6	75.7±1.2
4	100±0.6	62.6±0.9	100±0.6	75.6±0.9
5	100±0.6	61.0±0.8	100±0.6	75.1±0.9
6	100±0.6	51.8±1.0	100±0.6	68.3±1.2
7	100±0.6	51.4±0.9	100±0.6	64.5±0.8
8	100±0.6	43.5±0.7	100±0.6	61.2±1.0
9	100±0.6	43.2±0.8	100±0.6	50.2±1.2
10	100±0.6	42.8±1.2	100±0.6	49.2±0.9
20	100±0.6	40.0±0.9	100±0.6	49.0±0.7
25	100±0.6	38.4±1.1	100±0.6	48.3±1.0
30	100±0.9	38.4±0.6	100±0.6	48.3±0.9
40	100±0.6	38.4±0.8	100±0.6	48.3±1.2

Table 3: Effect of exposure of antibiotic powder combinations to 1% $w/_w$ kaolin (k) in dissolution medium

Time (min)	Amox/Clav* in 0% kaolin	Amox/Clav in 1% kaolin	Amp/Clox** in 0% kaolin	Amp/Clox in 1% kaolin
0	0 ± 0	0 ± 0	0 ± 0	0 ± 0
5	58.2±0.8	47.6±0.8	68.0±0.8	56.1±1.1
10	88.6±0.6	62.6±0.9	96.2±0.9	94.2± 1.1
15	96.2±0.5	86.4± 0.8	100±0.6	93.8±0.8
20	100±0.8	89.3±0.6	100±0.9	93.8±0.8
40	100±0.6	89.5±1.1	100±0.7	93.8±0.6
60	100 ± 0.5	89.5±0.8	100 ± 1.1	93.8 ± 0.9

*Amoxicillin/clavulanic acid powder; **ampicillin/cloxacillin

93.8±0.9%, respectively, in the presence of 1% kaolin (Table 3). These can be attributed to the adsorption of the drugs by the kaolin in the dissolution medium.

Kaolin is essentially a hydrated aluminium silicate[16], the silica moiety being responsible for the absorptive activity of kaolin[17]. Interaction studies[17, 18] between silica and some hydrophobic molecules showed that the positive charges on the molecules promote adsorption of the molecules on the silica. All the drugs studied here (chloroquine, chlorpheniramine, amoxycillin, clavulanic acid, ampicillin and cloxacillin) have nitrogen (N_2) atoms in their structure and these provide the binding sites for the silica in kaolin. The degree of the adsorption depends on the number of binding sites and how free these binding sites are[18, 19]. Chloroquine and chlorpheniramine have three and two N_2 atoms, respectively. Both also have tertiary N_2 atoms and another N_2 atom in a conjugated ring system. The antibiotics, amoxycillin, clavulanic acid, ampicillin and cloxacillin, all have N_2 atoms enclosed in ring systems. It is therefore not surprising that chloroquine and chlorphniramine were highly adsorbed (approximately 61% and 51%, respectively, in 40 min) unlike the antibiotics (amoxycillin/clavulanic acid, ampicillin/ cloxacillin) with N_2 atoms in the ring system (approximately 10% and 6%, respectively, in 60 min). Chloroquine tablets lost more drug than chlorpheniramine tablets for the same time period because it has three N_2 atoms (two of them are tertiary) unlike chlorpheniramine with two N_2 atoms.

Statistical comparison of the amount of drugs in solution in the presence or absence of kaolin, using a Student *T*-test at 95% confidence interval showed a 2-tailed p-value of less than or equal to 0.01 indicating a significant adsorption of the drugs by kaolin.

Conclusion

The incorporation of kaolin in the formulation of chloroquine and chlorpheniramine tablets, and in amoxycillin/clavulanic acid and ampicillin/cloxacillin powder combinations significantly reduces the amount of the active drugs released into the dissolution medium from the formulations. Therefore, its inclusion in such drug formulations should not be encouraged. Kaolin, no doubt, has glidant properties.

Although the adsorptive ability of kaolin has been demonstrated for four drugs in this study, it is possible that kaolin may also adsorb other drugs. It is therefore not advisable to use kaolin as a lubricant in a tablet formulation.

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