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Proceedings

In vitro interaction between artemether-lumefantrine and some antacids and edible clay

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Abstract

Purpose: The study investigated the in vitro interactions between artemether-lumefantrine and some antacids and edible clay.
Methods: Adsorption studies using three antacids; magnesium trisilicate (MT), aluminium hydroxide (AH), magnesium hydroxide (MH) as well as edible clay (EC) were carried out. A tablet brand was evaluated for tablet properties and used to determine the effects of the adsorbents on tablet disintegration time and dissolution.
Results: Adsorption followed the rank order; MT(79.98%) > MH(74.21%) > AH(70.90%) > EC(37.10%) and AH(99.90%) > MH(76.20%) > MT(73.21%) > EC(47.11%) for artemether and lumefantrine respectively. The adsorbents had no effect on tablets disintegration times. There was retardation of drug dissolution and the order was: Emtrisil®(49.58%) > MT(52.20%) > MH(58.92%) > AH(62.67%) > EC(67.42%) and Emtrisil®(59.50%) > AH(62.76%) > MH(70.20%) > MT(72.80%) > EC(80.92%) as against 93.80% as against 93.86% in 0.1N HCl for artemether and lumefantrine respectively.
Conclusion: The co-administration of these antacids with artemether/lumefantrine tablets should be strongly discouraged.

Keywords: adsorption, antacids, artemether-lumefantrine, dissolution, edible clay,

Indexing: Index Copernicus, African Index Medicus

Background

Artemether in combination with lumefantrine is an artemisinin combination therapy (ACT) recommended by the World Health Organization for uncomplicated falciparum malaria [1]. It is one of the safest and effective anti-malarial combination in the treatment of chloroquine resistant *Plasmodium falciparum* infection [2,3].

Aim/Objectives

The study investigated the *in-vitro* interactions between artemether-lumefantrine and some adsorptive antacids and edible clay.

Materials and Methods

Adsorption studies using three antacids namely, magnesium trisilicate (MT), aluminium hydroxide (AH), magnesium hydroxide (MH) as well as edible clay (EC) were carried out to determine extent of adsorption of artemether and lumefantrine onto the adsorptive materials. A commercial artemether-lumefantrine tablet brand was evaluated for some tablet properties such as weight variation, hardness, friability and content of active following official protocols and then used to determine the effects of the adsorptive materials on tablet disintegration time and dissolution.

Results

The adsorption of both artemether and lumefantrine onto the adsorptive materials increased as their concentration was increased. Adsorption of artemether by the adsorbents followed the rank order; MT (79.98%) > MH (74.21%) > AH (70.90%) > EC (37.10%) while lumefantrine followed the rank order: AH (99.90 %) > MH (76.20 %) > MT (73.21 %) > EC (47.11 %) as shown in Figure 1.

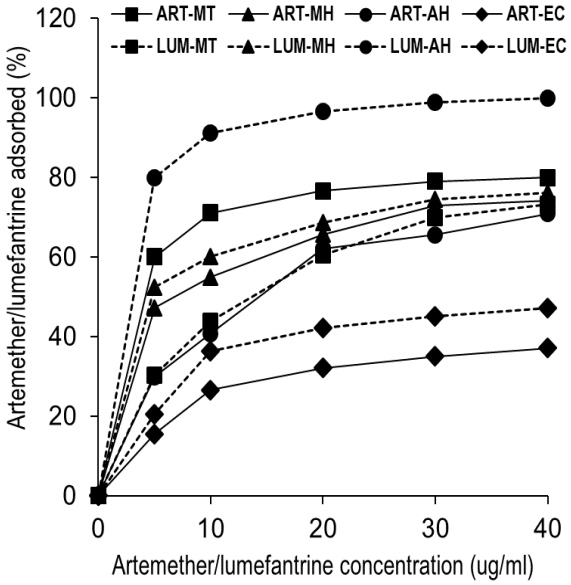

Figure 1: Adsorption of artemether (ART) and lumefantrine (LUM) onto magnesium trisilicate (MT), magnesium hydroxide (MH), aluminium hydroxide (AH) and edible clay (EC)

This disparity in the antacids' adsorptive capacities in the case is artemether may be due to the nature of the drug having a greater affinity for the available adsorption sites on magnesium trisilicate particle surfaces [4] while this is coupled with the large surface area of aluminium hydroxide in the case of lumefantrine [5]. The tablet parameters (weight, hardness, friability and content of active) of the commercial tablets met official BP specifications [6]. There was no significant increase in the disintegration times of the tablets in the presence of the antacids, edible clay and the commercial antacid suspension Emtrisil® (Table 1).

There was retardation of drug dissolution in the presence of the adsorptive materials. The percentage amount of artemether dissolved in 60 min and the order of dissolution retardation was as follows: Emtrisil® (49.58%) > magnesium trisilicate (52.20%) > magnesium hydroxide (58.92%) > aluminium hydroxide (62.67%) > edible clay (67.42%) (Figure 2a) while that of lumefantrine was Emtrisil® (59.50 %) > aluminium hydroxide (62.76 %) > magnesium hydroxide (70.20 %) > magnesium trisilicate (72.80 %) > edible clay (80.92 %) as against 93.80 % as against 93.86% in 0.1 N HCl (Figure 2b).

Table 1: Disintegration times of Lumartem® tablets in various media at 37 ± 0.5 °C

Disintegration medium	Adsorbent Conc. (%w/v)	Disintegration time (min)
Water	0	0.20 ± 0.02
0.1 N HCl	0	0.26 ± 0.02
Magnesium trisilicate	0.2	0.39 ± 0.01
	0.5	1.67 ± 0.03
	1.0	2.45 ± 0.04
Magnesium hydroxide	0.2	0.36 ± 0.07
	0.5	1.61 ± 0.02
	1.0	2.30 ± 0.04
Aluminium hydroxide	0.2	0.31 ± 0.03
	0.5	1.50 ± 0.05
	1.0	1.95 ± 0.02
Edible clay	0.2	0.21 ± 0.02
	0.5	0.51 ± 0.02
	1.0	1.20 ± 0.06
*Emtrisil®	0.2	0.72 ± 0.03
	0.5	1.89 ± 0.02
	1.0	2.82 ± 0.04

± Standard deviation

*Each ml of Emtrisil® contains 50 mg of magnesium trisilicate, 50 mg of magnesium carbonate and 50 mg of sodium bicarbonate.

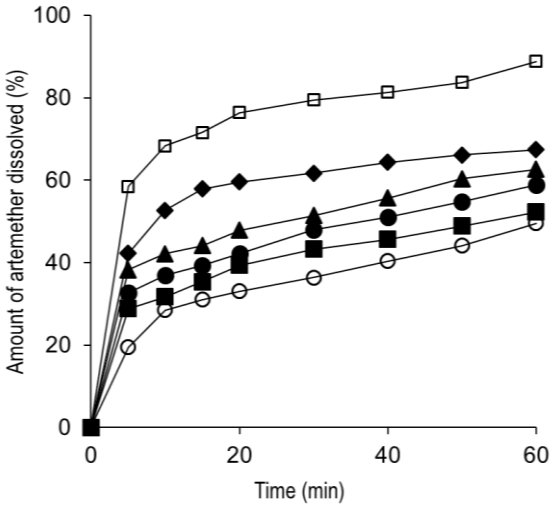

Figure 2a: Dissolution profiles of artemether from Lumartem® tablets in magnesium trisilicate (■), magnesium hydroxide (●) aluminium hydroxide (▲), edible clay (◆), Emtrisil® (○) and 0.1 N HCl (□)

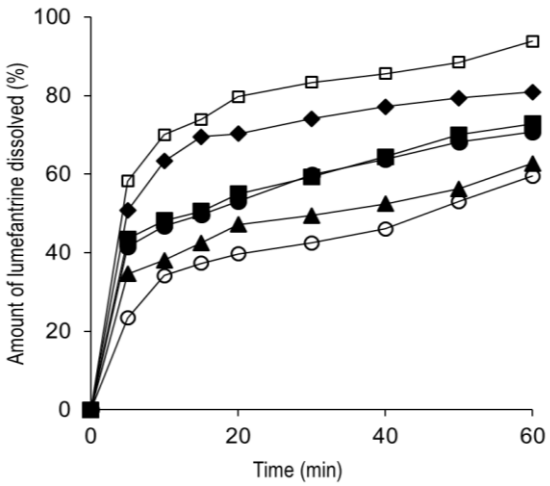

Figure 2b: Dissolution profiles of lumenfantrine from Lumartem® tablets in magnesium trisilicate (■), magnesium hydroxide (●) aluminium hydroxide (▲), edible clay (◆), Emtrisil® (○) and 0.1 N HCl (□)

Also, the concentration of adsorbent affected the amount of artemether and lumefantrine dissolved. At higher antacid concentration, the inhibitory effect on drug dissolution was more pronounced (Figure 3).

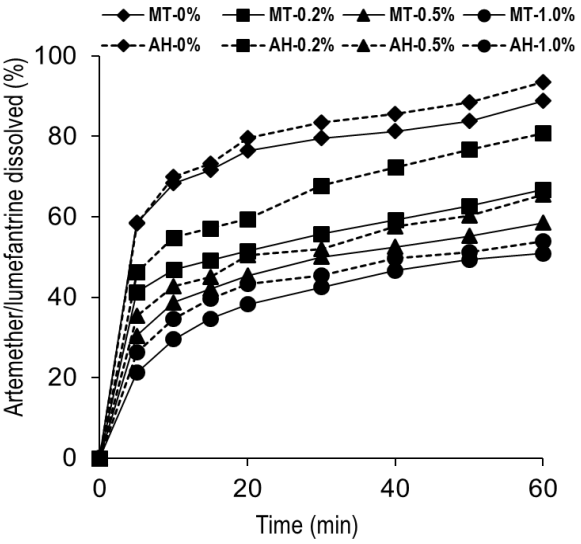

Figure 3: Dissolution profiles of artemether and lumefantrine from Lumartem® tablets in various suspension concentrations of MT and AH respectively ((0 (◆), 0.2 (■), 0.5 (▲), 1.0 (●) %w/v) in 0.1 N HCl)

Conclusion

The study has shown that a significant adsorption of artemether and lumefantrine onto the antacids and edible clay exist which could lead to a reduction of the amount of the drug available for absorption in the gastrointestinal tract. This may in turn reduce the bioavailability of the drug with subsequent drug resistance by micro-organisms and treatment failure. Therefore, the co-administration of these antacids with artemether should be strongly discouraged.

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