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Research Article

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Some physical characteristics of artemether and piroxicam solid lipid microparticles prepared with dika fat

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ABSTRACT

Dika fat was applied in the formulation of artemether and piroxicam solid lipid microparticles. Hot homogenization method was used in the preparation of the microparticles with varying labrasol® surfactant concentration (0.5%, 1.0% and 1.5%w/w) and dika fat/ phospholipon®90G ratios (1:0, 4:1 and 9:1). The microparticles were evaluated for particle size and drug encapsulation efficiency (EE%) while the pH of the unloaded microparticle dispersions was examined. Optimum particle sizes were observed at 1.5%w/w labrasol level and pH of the dispersions were slightly acidic. Drug encapsulation or entrapment efficiency of the microparticles decreased with the addition of phospholipon®90G. Artemether and piroxicam can be loaded in dika fat based solid lipid microparticles.

Keywords: Solid lipid microparticles, hot homogenization, encapsulation efficiency, dika fat, phospholipon®90G, labrasol®.

INTRODUCTION

Combinatorial chemistry and high-throughput screening used in drug discovery have resulted in an increase of poorly water-soluble drug candidates [1]. Many new chemical entities have bioavailability problems after oral administration [2]. Solid lipid nanoparticles is one of the different approaches used to solve these problems. Improved bioavailability and protection of sensitive drug molecules from the environment have been observed [3]. Dika fat is a lipid obtained from *Irvingia gabonensis var excelsa* while phospholipon®90G (phosphatidylcholine) is a phospholipid with special amphiphilic character. Artemether and piroxicam used for this research are drugs under the biopharmaceutics classification system II (BCS II).

EXPERIMENTAL SECTION

Materials

The following materials were utilized as supplied by the manufacturers; piroxicam, artemether (gift from pauco pharmaceuticals, Nigeria), labrasol®-caprylocaproylmacrogol glyceride (Gattefosse, france), phospholipon®90G (lipoid, Germany). Dika nuts were obtained from Nsukka farm, Nigeria.

Extraction of dika fat

Dika fat was extracted from the nut of *Irvingia gabonensis var. excelsa* with petroleum ether (40 – 60°C) using soxhlet apparatus and a rotary evaporator.

Formulation of unloaded solid lipid microparticles

Solid lipid microparticles were formulated using hot homogenization method. Dika fat (5%w/w) was melted at 60°C while aqueous labrasol surfactant solution (0.5%, 1.0%, and 1.5%w/w) was maintained at the same temperature in an electronic thermostat water bath for 5 min. The surfactant solution was then added to the molten dika fat with gentle stirring. The mixture was homogenized at 5,000 rev/min for 5 min with an Ultra-turrax® mixer while

submerged in the water bath. Afterwards, the dispersion was allowed to cool and kept in a refrigerator (4^0C) for 10 min. Further precipitation of lipid particles was stimulated by the addition of cold water to the dispersion. The procedure was repeated using dika fat/phospholipion® 90G lipid matrix at 4:1 and 9:1 mixtures.

Comparative evaluation of particles sizes of unloaded solid lipid particles and pH of the dispersions
The particles size of the solid lipid particles was comparatively evaluated using a digital light microscope mounted with a moticam camera for image capturing. The pH of the different dispersions was ascertained using pH meter.

Formulation of artemether and piroxicam loaded solid lipid microparticles
Optimized solid lipid microparticles were separately loaded with 1g of artemether and 500mg of piroxicam using hot homogenization method as describe above.

Drug encapsulation efficiency
The content of artemether and piroxicam in the microparticles were determined using UV Spectroscopic method. The dispersions were centrifuged and the supernatant assayed at 254nm (artemether) and 333nm (piroxicam). The supernatant of artemether dispersions was treated with 1N HCl for derivatization, prior to absorbance reading. The drug encapsulation efficiency of the loaded microparticles was calculated using eqn. 1 and 2.

$$\text{Drug encapsulation efficiency (\%) (EE\%)} = \frac{\text{Real drug loading}}{\text{theoretical drug loading}} \times \frac{100}{1} \quad \text{----------1}$$

$$EE\% = \frac{W_{total} - W_{free}}{W_{total}} \times \frac{100}{1} \quad \text{---------- 2}$$

Where W_{total} = weight of drug added to the system.
W_{free} = weight of free drug dissolved in medium/supernatant

RESULTS AND DISCUSSION

Rapid creaming and excessive caking at the top of the dispersions were observed for formulations containing dika fat alone as lipid and prepared with 0.5% and 1.0%w/w labrasol. This phenomenom was not observed with dika fat dispersions produced with 1.5%w/w labrasol. Dispersions containing phospholipon®90G (P90G) did not exhibit this rapid surface particle size growth and caking. However a slight caking was observed as a ring at the contact point between the surface of all the dispersions and the walls of the containers. P90G, not only inhibited the caking (+ve effect) but also suppressed the precipitation of the solid dika fat particles after formulation (-ve effect) through reduced surface migration and particle size growth. These effects are facilitated by the low melting point of dika fat (39-40°C). The lower surfactant concentrations might not have effectively provided stabilization through steric hindrance. Therefore only optimized formulations were evaluated for particle size.

Particle size analysis
The images of the unloaded solid lipid particles were captured in fig 1,2,3,4 and 5 while particle size was presented in table 1.

Table 1: Particles size of unloaded solid lipid microparticles

Code	Dika fat (g)	Phospholipon 90 G (g)	Labrasol %w/w	Average particle size (μm)
A	4	_	1.5	733
B	4	1	0.5	611
C	4	1	1.0	568
D	4	1	1.5	342
E	4.5	0.5	1.5	330

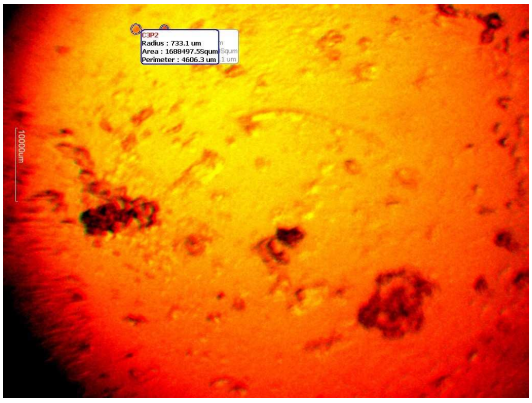

Fig 1 : microparticle image of A

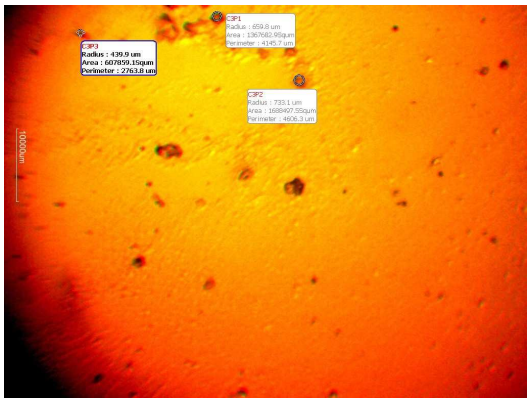

Fig 2 : microparticle image of B

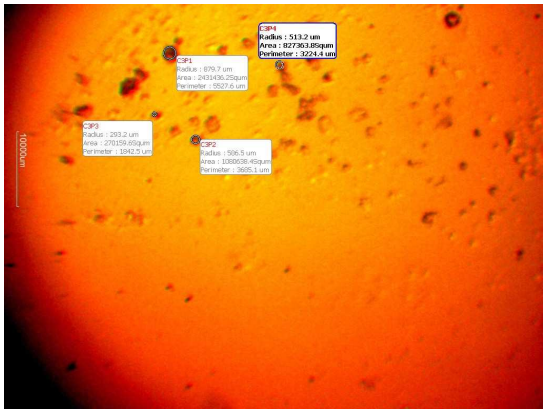

Fig 3 : microparticle image of C

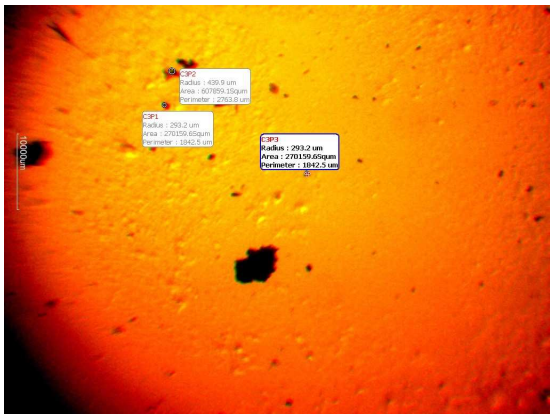

Fig 4 : microparticle image of D

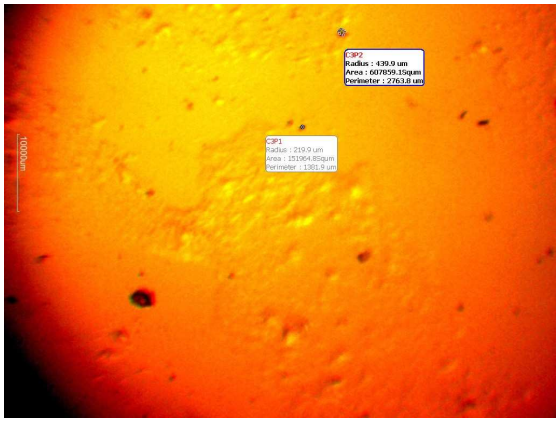

Fig 5 : microparticle image of E

The result of the particle size analysis showed that particle size of the solid lipid microparticles reduced as surfactant (labrasol) concentration increased and in the presence of phospholipon 90G. 1.5%w/w of the surfactant may have effectively reduced the interfacial tension between molten lipid matrices and water while also providing effective steric hindrance to prevent particle size growth. Higher concentrations of the surfactant would cause excessive foaming during preparation. The particles size analysis was used to select formulations prepared with 1.5%w/w labrasol due to the small particle size obtained. The pH of these selected formulations A, D and E are 6.23, 5.79 and 5.81. The pH values were all within slightly acidic range.

Artemether and piroxicam loaded solid lipid microparticles

Artemether and piroxicam loaded solid lipid microparticles were prepared for the selected formulations. However, formulations containing 4:1 dika fat/P90G mixture were difficult to precipitate, therefore encapsulation efficiency was obtained for the other preparations only. Table 2 shows the encapsulation efficiency (EE%) of the selected formulations. The result showed marked reduction in EE% of the dika fat in the presence of phospholipon 90G for

both artemether and piroxicam microparticles. The P90G might have reduced and delayed the solidification of dika fat. This would likely facilitate drug diffusion to the external phase of the medium [4].

Table 2: Drug encapsulation efficiency of selected solid lipid microparticles

Formulation	W_{total} (mg)	W_{free} (mg)	Drug encapsulation efficiency (%)
Artemether + dika fat + labrasol	1000	183.3	81.67
Artemether + dika fat + P90G + labrasol (9:1 lipid mixture)	1000	733.3	26.67
Piroxicam + dika fat + labrasol	500	70.7	85.86
Piroxicam + dika fat + P90G + labrasol (9:1 lipid mixture)	500	399.9	20.02

Although the encapsulation/entrapment efficiency of dika fat based piroxicam microparticles was high, the piroxicam seem to be trapped more in its crystalline form since it is only slightly soluble in dika fat.

CONCLUSION

Dika fat could be utilized effectively in the formulation of solid lipid microparticles using 1.5%w/w labrasol. A reduction in particles size and improve physical stability can be achieved with the addition of phospholipon 90G, although this may cause a reduction in drug entrapment. Artemether and piroxicam can be loaded in dika fat based solid lipid microparticles.

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