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DEVELOPMENT AND CHARACTERIZATION OF SUSTAINED-RELEASE ARTEMETHER-LOADED SOLID LIPID MICROPARTICLES BASED ON MIXED LIPID CORE AND A POLAR HETEROLIPID

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ABSTRACT

The objective of this study was to formulate and evaluate artemether-loaded solid lipid microparticles SLMs from templated captex 300® and *Capra hircus* (goat fat) homolipid for sustained delivery in the treatment of malaria. Various ratios of captex 300®, goat fat and Phospholipon® 90G were used to prepare the templated lipid matrices and characterized by differential scanning calorimetry (DSC). The templated lipid matrices were employed to formulate SLMs containing various concentrations (1.0, 3.0 and 5.0 $\%^{w}/_{v}$) of artemether by melt-emulsification technique. Physicochemical characterizations were performed on the SLMs with respect to mean particle size, morphology, encapsulation efficiency, compatibility, time-dependent pH stability and drug release in phosphate buffered saline (PBS, pH 7.4) compared with artemether injection (control). The DSC results showed that the formulated lipid matrices were suitable for the development of the SLMs. Stable spherical artemether-loaded SLMs with encapsulation efficiency and mean particle size that ranged from 20.49 ± 1.15 % to 87.02 ± 3.13 % and 1.60 ± 0.05 µm to 21.30 ± 0.50 µm, respectively, were developed. Among the formulations, SLMs based on Captex 300® and goat fat (1:1) at 1.0 and 3.0% artemether concentrations (batches A_1 and A_2) as well as SLMs based on Captex 300® and goat fat at (2:1) at 1.0% artemether concentration (batch C_1) gave significantly ($p<0.05$) greater *in vitro* drug release in PBS than artemether injection. This study has shown that artemether-loaded SLMs based on Captex 300® and goat fat templated with Phospholipon® 90G could be employed as an alternative sustained-release formulation than artemether injection for enhanced malaria treatment.

KEYWORDS: **Artemether-loaded solid lipid microparticles (SLMs); sustained release; *Capra hircus* (goat fat); captex 300®; Phospholipon® 90G.**

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INTRODUCTION

Malaria remains a disease of global importance and despite the gains made in the decline in incidence and mortality rates between 2010 and 2019, the Covid-19 pandemic contributed to the 14 million more malaria cases and 47 000 more deaths in 2020 compared to the numbers estimated in 2019 [1]. As with the previous years, the African region still has the highest figures of the global malaria burden, with a higher proportion of deaths occurring in children less than 5 years [1, 2]. The pilot introduction of the RTS,S malaria vaccine in Ghana, Kenya and Malawi is a great development in the fight against malaria as it has led to the official recommendation of the vaccine by the World Health Organization (WHO), for use in the prevention of *Plamodium falciparum* malaria in children living in areas with moderate to high transmission [1]. This notwithstanding, the challenges of slow decision making, supply chain management, increased immunization visits, and vaccine misconceptions which are associated with the introduction of new vaccines in low and middle-income countries might prevent the effective use of malaria vaccines [3]. This indicates the need for continuous availability of anti-malarial medications to effectively meet the Global technical strategy for malaria targets of 90% reduction in incidence and mortality rates by 2030 [1].

The artemisinin-based combination therapies ACTs are still the first line of treatment for uncomplicated malaria caused by *P. falciparum.* Artemether is a classic example of artemisinin and its use in combination with lumefantrine is to enable a longer lasting effect of the co-formulated drug [4]. Artemether is rapidly absorbed following oral administration, attains a peak plasma concentration within two hours after a dose, and has a short half-life (1.5-3/5h) which points to the need for frequent dosing and possible increase in side effects [4-6]. Furthermore, Artemether class II status based on the Biopharmaceutical Classification System (BCS) infers a problem of poor aqueous solubility [7], but its lack of cross resistance to other drugs and ability to rapidly decrease parasitemia is ideal for its continuous use as an antimalarial agent [2]. A sustained release formulation of Artemether will therefore help to solve the above problems while avoiding the associated issues of extra active ingredients.

Lipids have been employed as vehicles for drug delivery because of their physiological compatibility and biodegradability [8]. In addition, the solid nature of lipid matrices is known to improve bioavailability, prolong drug release, mask taste and protect drugs from degradation [8]. Solid lipid microparticles (SLMs) are a major type of lipid-based drug delivery systems and also possess the beneficial properties listed above as well as aiding a longer shelf-life and sustained release profile [2]. SLMs are of the micro-scale dimension and usually have a matrix obtained from glyceride, fatty alcohol, solid alcohol and fatty acids with high melting points [9]. *Capra hircus* (goat fat) has been well studied as a single lipid core in the formulation of solid lipid microparticles for aspirin, chloroquine phosphate and gentamicin with good results [9-11]. In addition, we have previously reported a study in which a mixed lipid core of goat fat and Compritol 880® was employed in the formulation of artemether-entrapped SLM. The results showed good compatibility between artemether and formulation excipients, improved bioavailability and a higher drug release in alcoholic buffer. [2]. Captex 300® is a medium-chain triglyceride obtained from natural sources or commonly prepared from vegetable oil fatty acids and glycerol. It finds great application in the cosmetic industries where it is used in foams, creams, ointments, and lotion formulations [12]. Different types of Captex® have been used as an excipient in pharmaceutical formulations, especially in the development of self-nanoemulsifying drug delivery systems (SNEDDS) with favourable outcomes [13,14].

To the best of our knowledge, there are no reports of a study combining goat fat and Captex 300® as a lipid matrix in the delivery of artemether. Hence, our aim was to formulate artemether SLM to yield a sustained release delivery profile using the melt-emulsification technique. Furthermore, our objectives were to explore goat fat (natural fat) and Captex 300 as favourable excipients in this formulation and to evaluate the *in vitro* characteristics of the dosage form.

MATERIALS AND METHODS

Materials

The materials used in the study include artemether powder [JUHEL Pharmaceuticals Limited, Enugu State, Nigeria], ethanol, activated charcoal, betonite, monobasic potassium phosphate, sodium hydroxide pellets and disodium hydrogen phosphate (BDH Chemicals Limited, Pooles, England), concentrated hydrocholoric acid (Sigma-Aldrich, Germany), sorbitol, sorbic acid, goat fat, Captex 300® (Gattefossé, USA), Phospholipon® 90G (Phospholipid Köln, Germany).

Extraction and purification of goat fat (*Capra hircus*)

The lipid was extracted from goat fat by wet rendering method [10, 15, 16]. Extraneous materials were physically removed from the adipose tissue and the tissue was cut into smaller pieces. The tissue was subjected to moist heat boiling in water on a water bath for 45 minutes. The molten fat was separated from the aqueous phase by filtering with a muslin cloth. The product was further purified by heating the fat with bentonite and activated charcoal in an oven after which it was filtered using a fluted filter and stored for further studies.

Preparation of the lipid matrices

Appropriate quantities of goat fat and Captex 300® were measured at ratios 1:1, 1:2, and 2:1 and were melted in a thermos-regulated water bath at 80 °C after which they were mixed with a predetermined quantity of Phopholipon® 90G and allowed to solidify. The formed matrices were stored in airtight containers until used.

Characterization of the lipid matrices and solid lipid microparticles

The prepared lipid matrices and the individual lipids (Phospolipon® 90G, goat fat and captex 300®) were characterized by differential scanning calorimetry (DSC) to study their thermal properties using a differential scanning calorimeter (DSC 204 F1 Netzch, Germany). This DSC analysis was extended to the drug and the solid lipid microparticles (SLMs). Briefly, the thermal properties (melting transitions and change in heat capacity) of the pure artemether powder, the pure lipids, the unloaded SLMS and loaded SLMS were determined by performing the DSC analysis at a heating rate of 10 °C/min from 35 °C to 190 °C temperature range for non-drug loaded samples and from 35 °C to 400 °C temperature range for the drug loaded SLMs, under an inert nitrogen atmosphere with a flow rate of 20 ml/min.

Formulation of the solid lipid microparticles

The solid lipid microparticles were prepared adopting the melt emulsification technique [10]. A weighed quantity of the lipid matrix was melted at 80 °C and appropriate quantity of artemether (1, 3 and 5%) was dissolved in absolute ethanol and added to the lipid melt. The alcohol was allowed to evaporate out of the solution. The aqueous phase was prepared by heating distilled water at 80 °C with appropriate quantities of Tween® 80, sorbitol (surfactant) and sorbic acid (preservative). The aqueous phase was poured into the lipid melt both being at equivalent temperatures and the mixture homogenized with a homogenizer (Ultra-Turrax, Germany) at 12,000 rpm for 5 minutes. The resultant SLMs were poured into pre washed amber coloured bottles. The procedure was repeated using different ratios of the lipid matrix. Twelve (12) batches of the SLMs were produced nine of which were loaded with the drug (artemether) and three were unloaded SLMs of ratio 1:1, 1:2, and 2:1. The three ratios (1:1, 1:2, 2:1) of lipid melt each contained at 1, 3 and 5 % of artemether. The formulation compositions of the developed SLMs are shown in Table 1.

Characterization of the solid lipid microparticles (SLMs)

Morphology and particle size analysis

The SLM formulations were smeared on the microscope slides and covered with cover slips. The slides were placed under the light microscope, adjusted for a clear view and viewed at a magnification of X100. The particles were snapped using a digital camera and the particles sizes determined.

Drug encapsulation efficiency

Approximately 6 ml of the artemether-loaded SLMs were added into a microconcentrator (5,000 MWCO 8,000, Germany). They were then centrifuged at 15,000 revolutions for 120 min. The supernatants were collected and appropriately analyzed by UV/VIS spectrophotometer at a maximum wavelength of 300 nm, using absolute ethanol as the blank. The amount of drug encapsulated was calculated with reference to a standard Beer's plot of artemether in absolute ethanol to obtain the % encapsulation efficiency using the formula shown below.

$$Entrapment\ efficiency = \frac{total\ drug\ loaded - drug\ in\ supernatant}{total\ drug\ loaded}\ x100$$

In vitro drug release studies

In *vitro* drug release apparatus with a receiver compartment volume of 10 ml and effective diffusion area of 2.8 cm^2 was used in the *in vitro* release studies. A millipore membrane filter (0.22 µm) was used. The receptor phase (phosphate buffer pH 7.4) was continually stirred with a magnetic stirrer and kept at a temperature of 37 ± 0.5 °C throughout the experiment. A 5 ml volume of the drug-loaded SLMs were placed in the donor compartment. At various time intervals 5 ml of the sample was withdrawn from the receiver compartment and replaced with 5 ml of the medium to maintain a sink condition. This study was done for 12 hours and was performed for all the samples as well as the commercial artemether

injection for comparison. The samples collected were analyzed using the spectrophotometer at a wavelength of 300 nm and the concentration determined from a standard Beer's plot of artemether in phosphate buffer.

Time dependent pH stability study

The pH of dispersions of the SLMs were determined over time (at 24 h, 1 week and 1 month), using a pH meter (pH ep® Hanna instrument, Padova, Italy).

Statistical analysis

All experiments were performed in replicates (at least n=3) for validity of statistical analysis. Results were expressed as mean ± SD. ANOVA and student t-tests were performed on the data sets generated using SPSS. Differences were considered significant for P values < 0.05.

RESULTS

Thermal characterization of lipid matrices and SLMs

The DSC thermogram of goat fat showed an endothermic peak at 53.7^{o}C while that of Captex 300 showed endothermic peaks at100.9 ^{o}C (fig 1a, 1b). Figures 1c-1e shows the DSC thermograms of binary mixtures of Captex 300 and goat fat matrices. The thermogram showed sharp endothermic melting peaks at 50.5, 50.6 and 50.7 ^{o}C for the ratios of 1:1, 1:2 & 2:1 lipid matrices, with corresponding enthalpies of -30.55, -21.55 and -10.85 Mw/mg respectively. The DSC thermogram of phospolipon 90G (P90G) (Fig.2a) showed a sharp endothermic single peak corresponding to a melting at 232^{o}C, and crystallizes partially at 327.9^{o}C. Figures 2b-2d shows the DSC thermograms of mixtures of P90G / Captex300 / goat fat lipid matrices.

The DSC thermogram (Figure 3a) of pure drug (artemether) showed two adjacent endothermic peaks at 88.8^{o}C and 183.2^{o}C respectively. It equally showed enthalpies of -21.01 and -16.05 mW/mg for the drug due to the decomposition it underwent during melting, which subsequently gave the pseudo melting peak (183.2^{o}C). The DSC thermogram of drug-free SLM formulations are shown in figure 3b-3d, whereas the DSC thermograms of SLM formulations containing 1 %, 3 %, 5 % artemether are shown in figures 4, 5 and 6 respectively.

The DSC thermogram of SLM without artemether formulated with P90G-structured Captex300-goat fat matrix (1:1) showed two endothermic transitions with enthalpies of -83.65 and -185.7 mW/mg and melting points of 85.4^{o}C and 118.0^{o}C, respectively. Similarly, the DSC thermogram of SLMs containing 3 % artemether formulated with P90G-dtructured Captex-goat fat matrix (1:1) show two endothermic transitions with enthalpies of -103 and -127 Mw/mg and melting points of 76.5^{o}C and 110.0^{o}C, respectively.

Drug encapsulation efficiency

The encapsulation efficiency ranged from 20.496 to 87.02 % (Table 2). According to the results shown in the table, formulations containing 1% artemether at 1% had the lowest encapsulation efficiency while those containing 5% artemether had the highest percentages of drug loading. It is also seen that SLM with lipid ratio of 1:2 and 5% artemether showed the highest encapsulation efficiency (87.07 %) while SLM formulated with lipid ratio 1:1 and 1% artemether showed the lowest percentage of loading (20.50 %).

Morphology and particle size analysis

Mean particle sizes of the SLMs are shown in Table 3 while the morphological features of representative batches of the formulated SLMs are depicted in Figure 7. From the results, it can be seen that the drug unloaded SLM with particle lipid ratio 1:2 which had a particle size of 21.3µm had the largest particle size. The SLM with the lowest particle size was the 5 % loaded SLM with lipid ratio 1:2 (B_3).

In vitro drug release studies

The *in vitro* release rates of the formulated SLMs were compared with the commercial artemether oily injection and the results are shown in Figures 8 to 10. The result shows that the commercial sample had peak release at the sixth hour after which no increase was observed throughout the 12-hour release study period. Batch SLM-1:2 (3%) showed the least maximum percentage release with peak release 1 % at 10 hours. All the formulated SLMs showed maximum release between the 10th to 12th hour periods whereas the commercial oil injection showed peak release (4.5 %) at the 6th hour.

Time dependent pH stability studies

Table 4 shows the time-dependent pH stability test results performed on the formulations. The pH of all batches of the preparations ranged from 3.80 to 4.47 for the entire period of study.

DISCUSSION

This melting point value was similar to that found in literature [9, 15]. Captex 300 showed the tendency of undergoing rapid crystallization with increased heat. The binary mixtures of goat fat and Captex 300

Table 1: Formulation compositions of the SLMs

Batch	Ratio of Captex® to goat fat	Artemether (g)	Sorbitol (g)	Sorbic acid (g)	Tween® 80 (ml)	Distilled water to (ml)
A_0	1:1	0	2.0	0.05	0.75	50
A_1	1:1	0.5	2.0	0.05	0.75	50
A_2	1:1	1.5	2	0.05	0.75	50
A_3	1:1	2.5	2	0.05	0.75	50
B_0	1:2	0	2	0.05	0.75	50
B_1	1:2	0.5	2	0.05	0.75	50
B_2	1:2	1.5	2	0.05	0.75	50
B_3	1:2	2.5	2	0.05	0.75	50
C_0	2:1	0	2	0.05	0.75	50
C_1	2:1	0.5	2	0.05	0.75	50
C_2	2:1	1.5	2	0.05	0.75	50
C_3	2:1	2.5	2	0.05	0.75	50

Key: A_0-A_3, B_0-B_3 and C_0-C_3 are SLM formulations containing 1:1, 1:2 and 2:1 ratio of captex and goat fat, respectively; A_0-C_0 are unloaded SLMs; A_1-C_1, A_2-C_2 and A_3-C_3 contain 1.0, 3.0 and 5.0% of artemether, respectively.

Table 2: Drug encapsulation efficiencies of the SLMs

Formulations	Ratio of Captex 300: Goat fat: drug (%)	Drug encapsulation efficiency (%)
A_1	1: 1 (1 %)	20.49 ±1.15
A_2	1:1 (3 %)	80.31 ±2.66
A_3	1:1 (5 %)	84.25 ±1.79
B_1	1: 2 (1 %)	41.65 ±3.01
B_2	1: 2 (3 %)	83.12 ±2.34
B_3	1:2 (5 %)	87.02 ±3.13
C_1	2:1 (1 %)	46.03 ±2.88
C_2	2:1 (3 %)	77.88 ±3.47
C_3	2:1 (5 %)	86.66 ±4.10

Key: A_0-A_3, B_0-B_3 and C_0-C_3 are SLM formulations containing 1:1, 1:2 and 2:1 ratio of captex and goat fat, respectively; A_0-C_0 are unloaded SLMs; A_1-C_1, A_2-C_2 and A_3-C_3 contain 1.0, 3.0 and 5.0% of artemether, respectively.

Table 3: Mean particle size of the SLM formulations

Formulation code	Ratio of Captex300®-Goat fat	Mean particle size (µm)
A_0	1:1	4.80 ± 0.01
A_1	1:1	2.40 ± 0.50
A_2	1:1	4.80 ± 0.05
A_3	1:1	5.98 ± 0.50
B_0	1:2	21.30 ± 0.50
B_1	1:2	4.80 ± 0.01
B_2	1:2	3.62 ± 0.30
B_3	1:2	1.60 ± 0.05
C_0	2:1	2.40 ± 0.50
C_1	2:1	3.60 ± 0.10
C_2	2:1	4.80 ± 0.50
C_3	2:1	9.60 ± 0.01

Key: A_0-A_3, B_0-B_3 and C_0-C_3 are SLM formulations containing 1:1, 1:2 and 2:1 ratio of captex and goat fat, respectively; A_0-C_0 are unloaded SLMs; A_1-C_1, A_2-C_2 and A_3-C_3 contain 1.0, 3.0 and 5.0% of artemether, respectively.

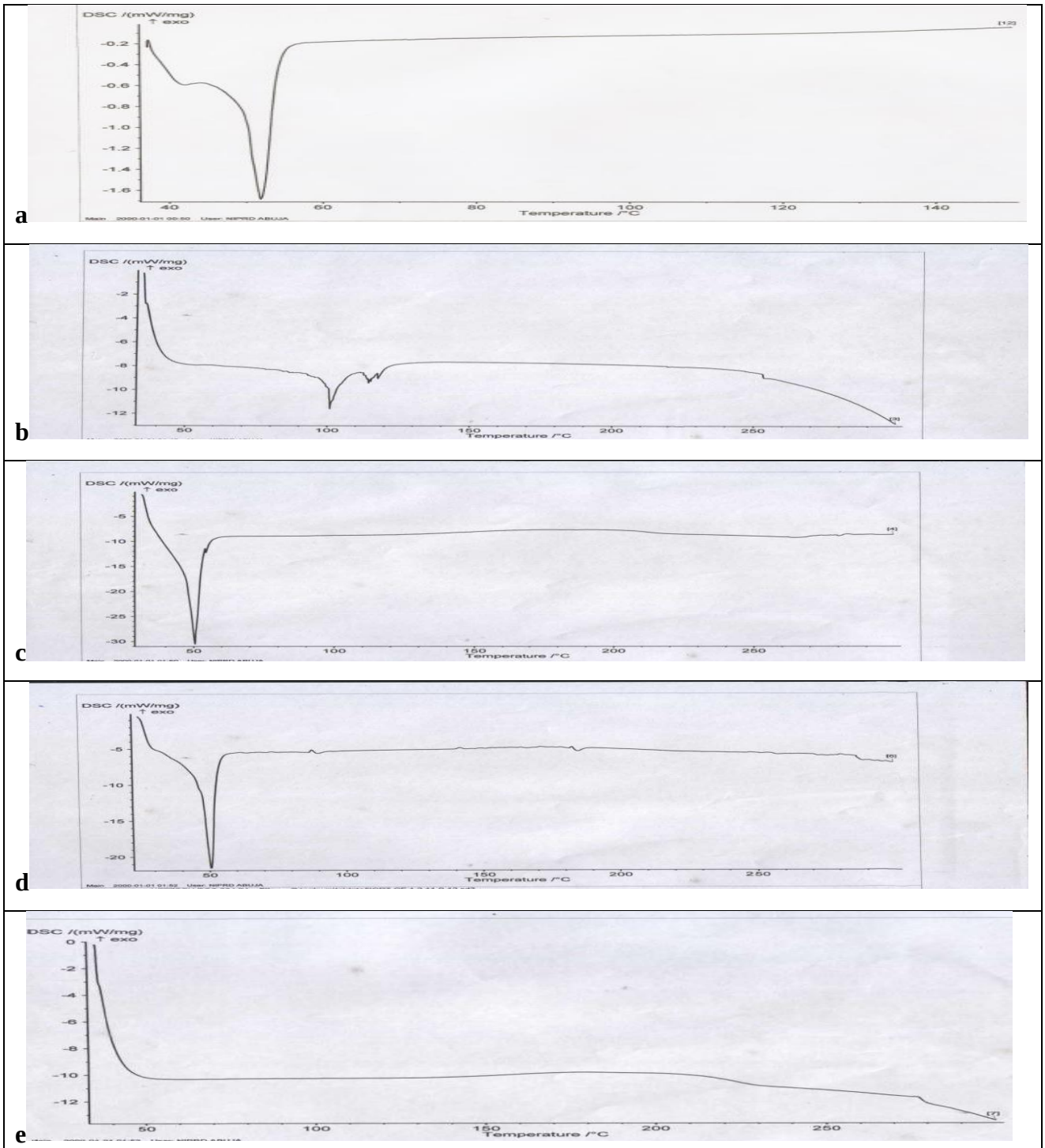

Fig. 1: DSC thermograph of (a) goat fat, (b) Captex 300® (c) Captex300 / goat fat matrix (1:1) (d) Captex300 / goat fat matrix (1:2) (e) Captex 300® / goat fat matrix (2:1).

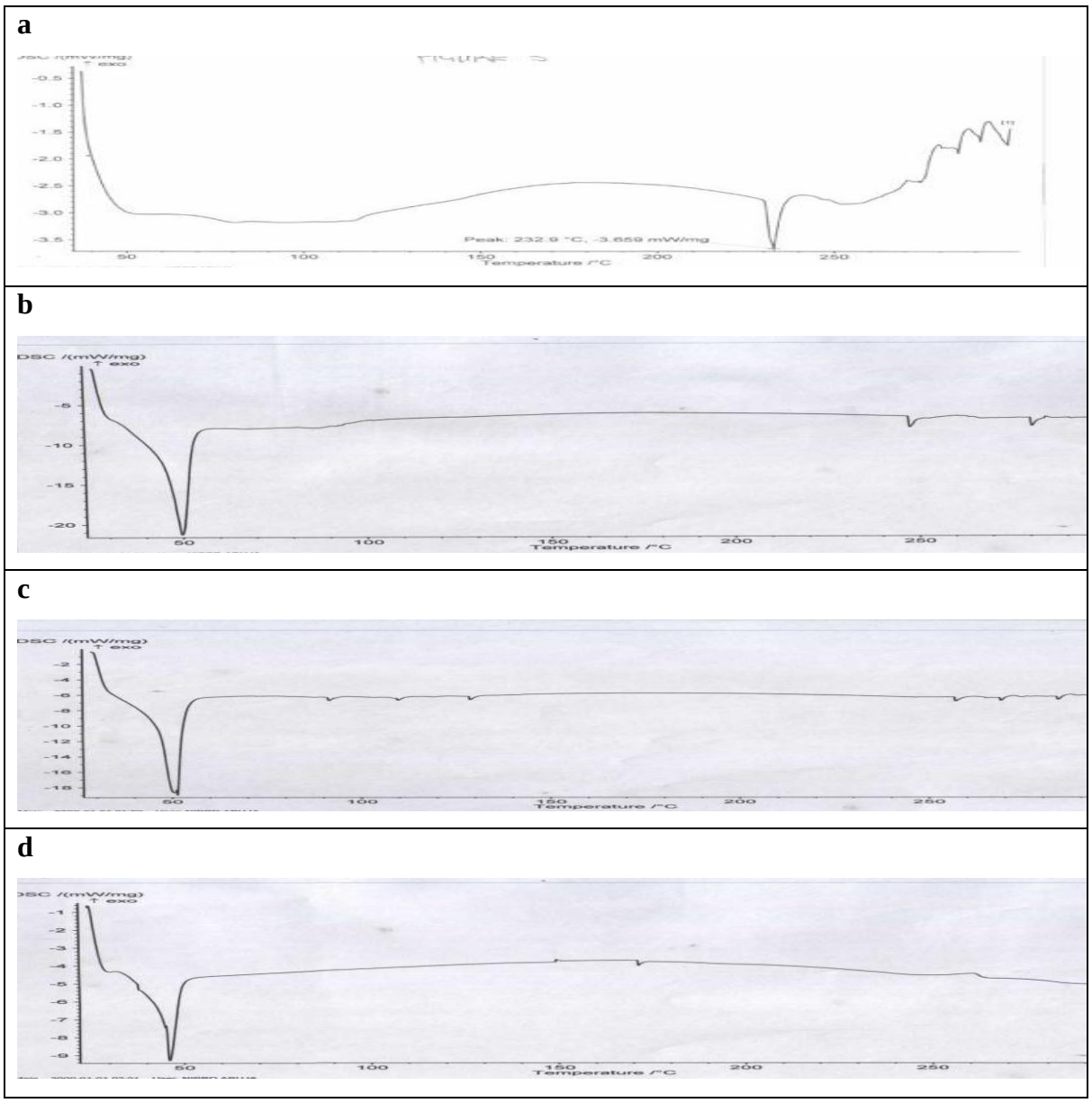

Fig. 2: DSC thermograph of (a) Phospholipon 90 G (P90G) (b) P90G-structured Captex300 / goat fat matrix (1:1) (c) P90G-structured Captex300 / goat fat matrix (1:2) (d) P90G-structured Captex300 / goat fat matrix (2:1).

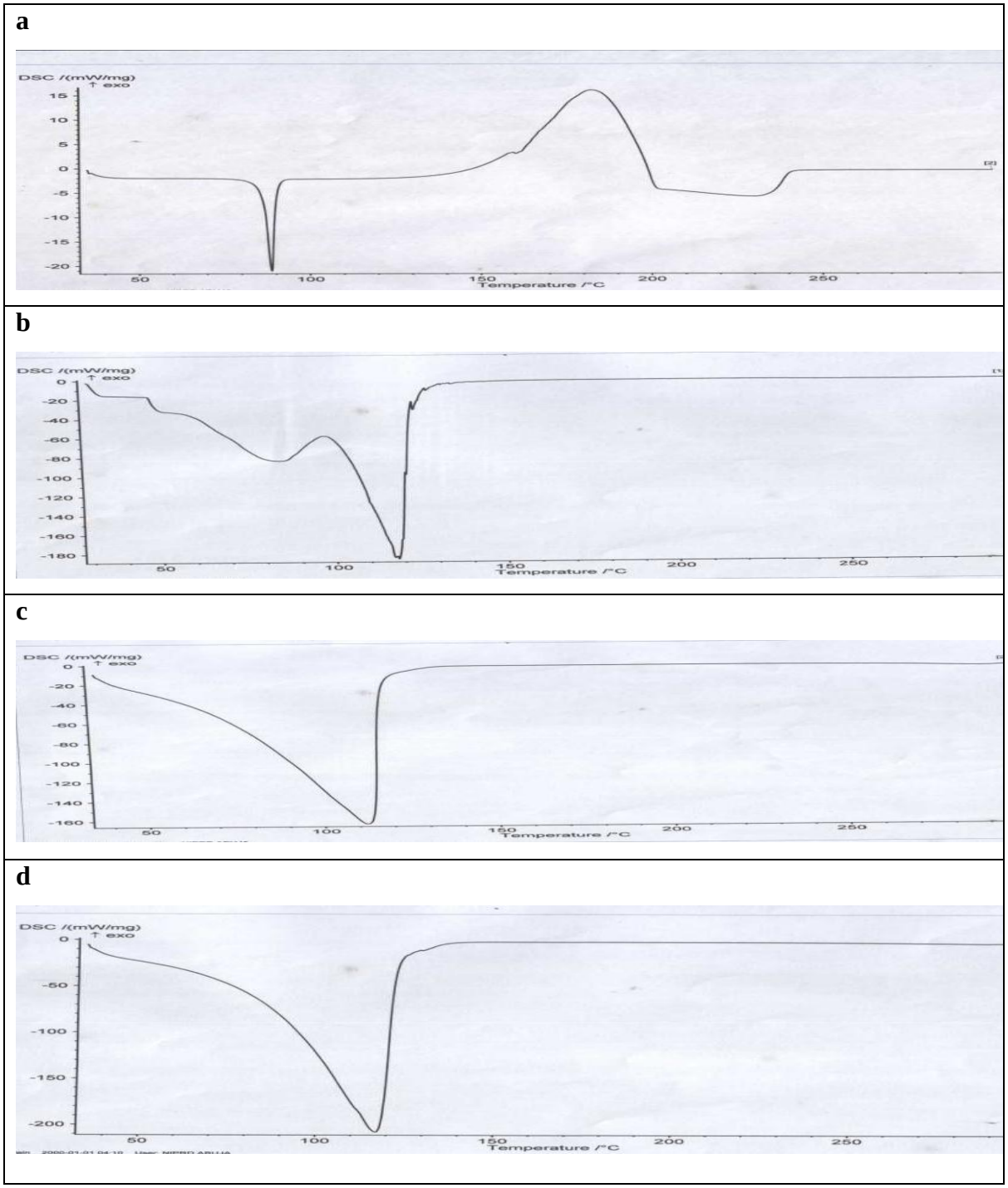

Fig. 3: DSC thermograph of (a) Pure artemether (b) drug-free SLM formulation (1:1) (c) drug-free SLM formulation (1:2) (d) drug-free SLM formulation (2:1).

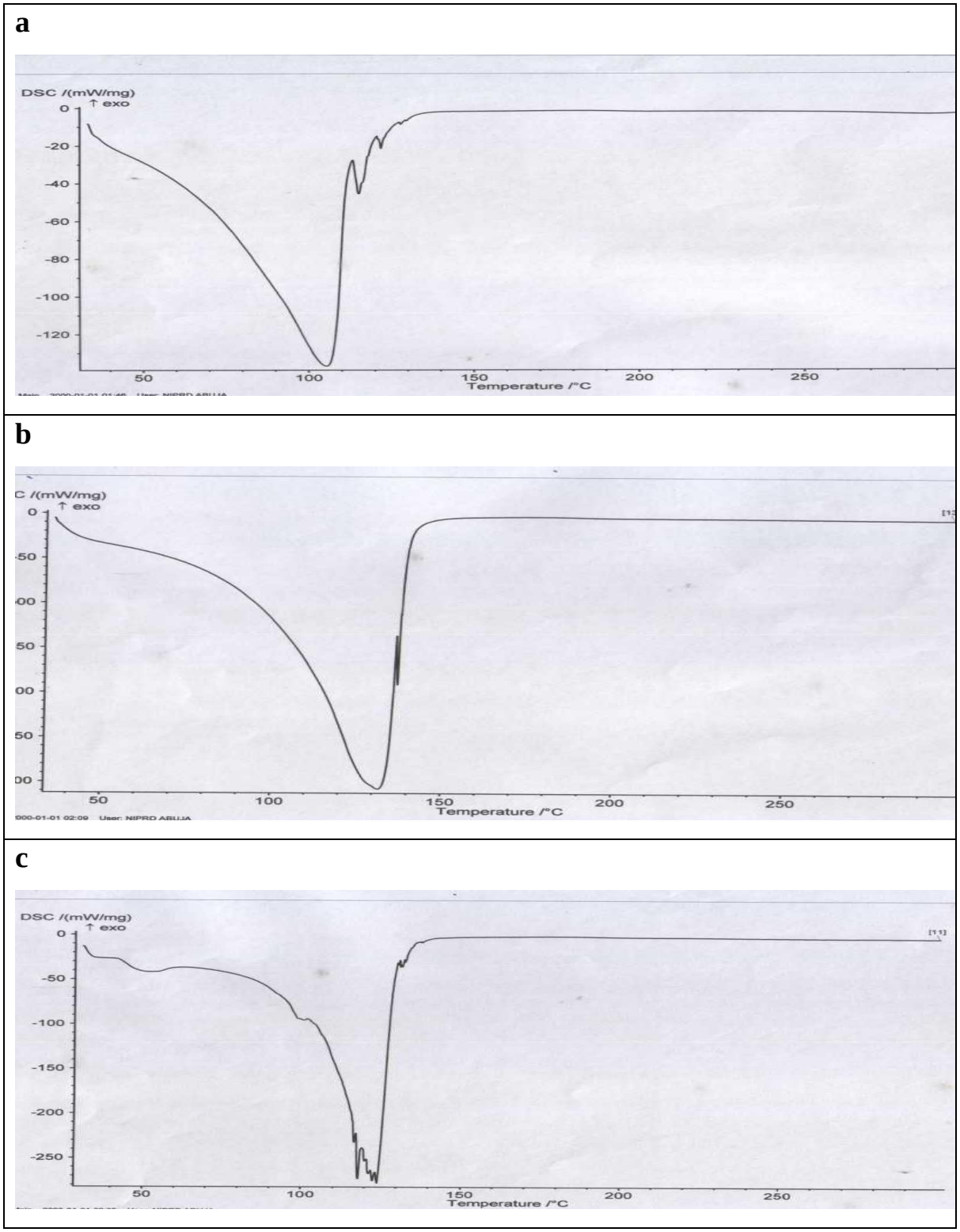

Fig. 4: DSC thermograph of (a) 1 % artemether SLM formulation (1:1) (b) 1 % artemether SLM formulation (1:2) (c) 1 % artemether SLM formulation (2:1).

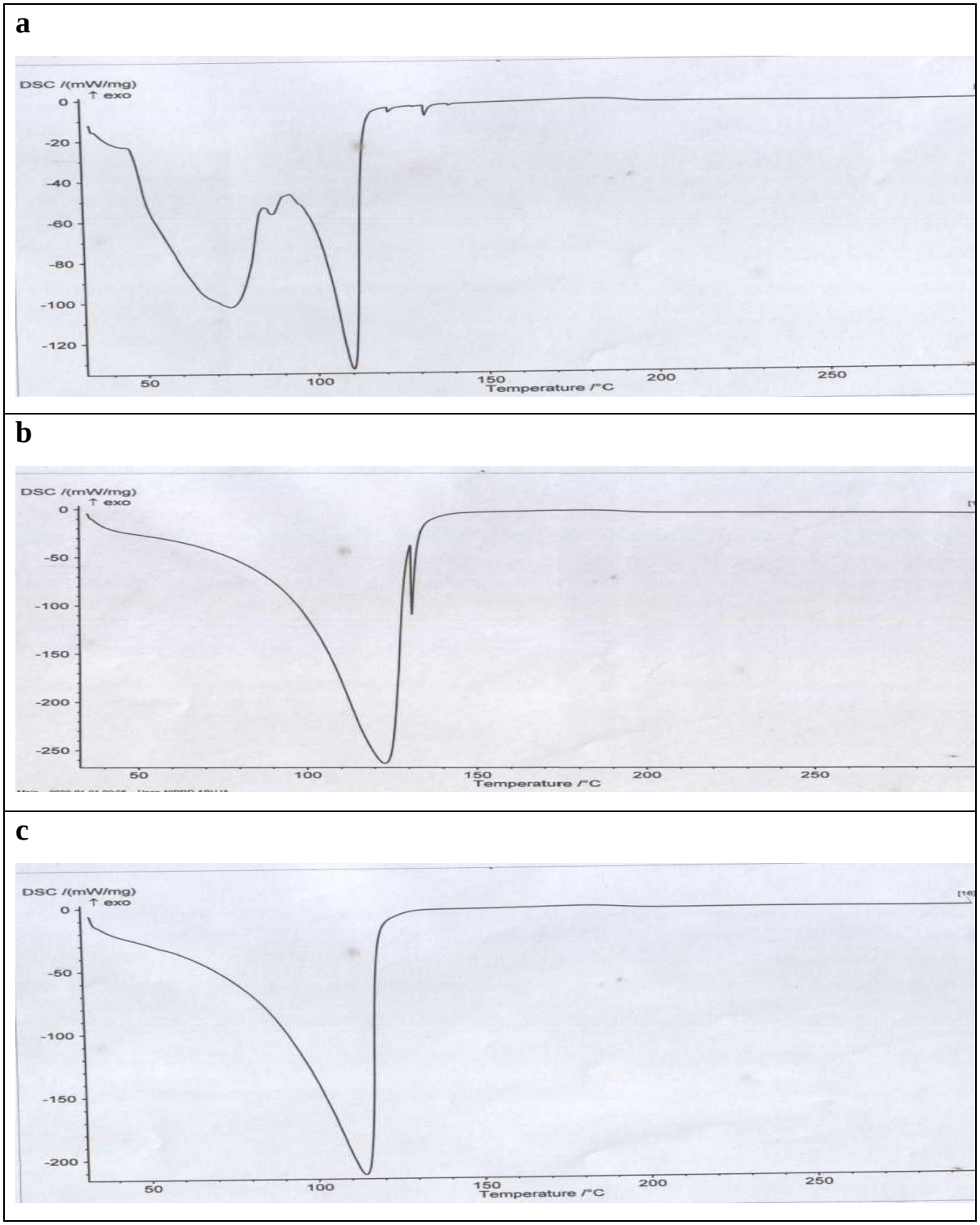

Fig. 5: DSC thermograph of (a) 3 % artemether SLM formulation (1:1) (b) 3 % artemether SLM formulation (1:2) (c) 3 % artemether SLM formulation (2:1).

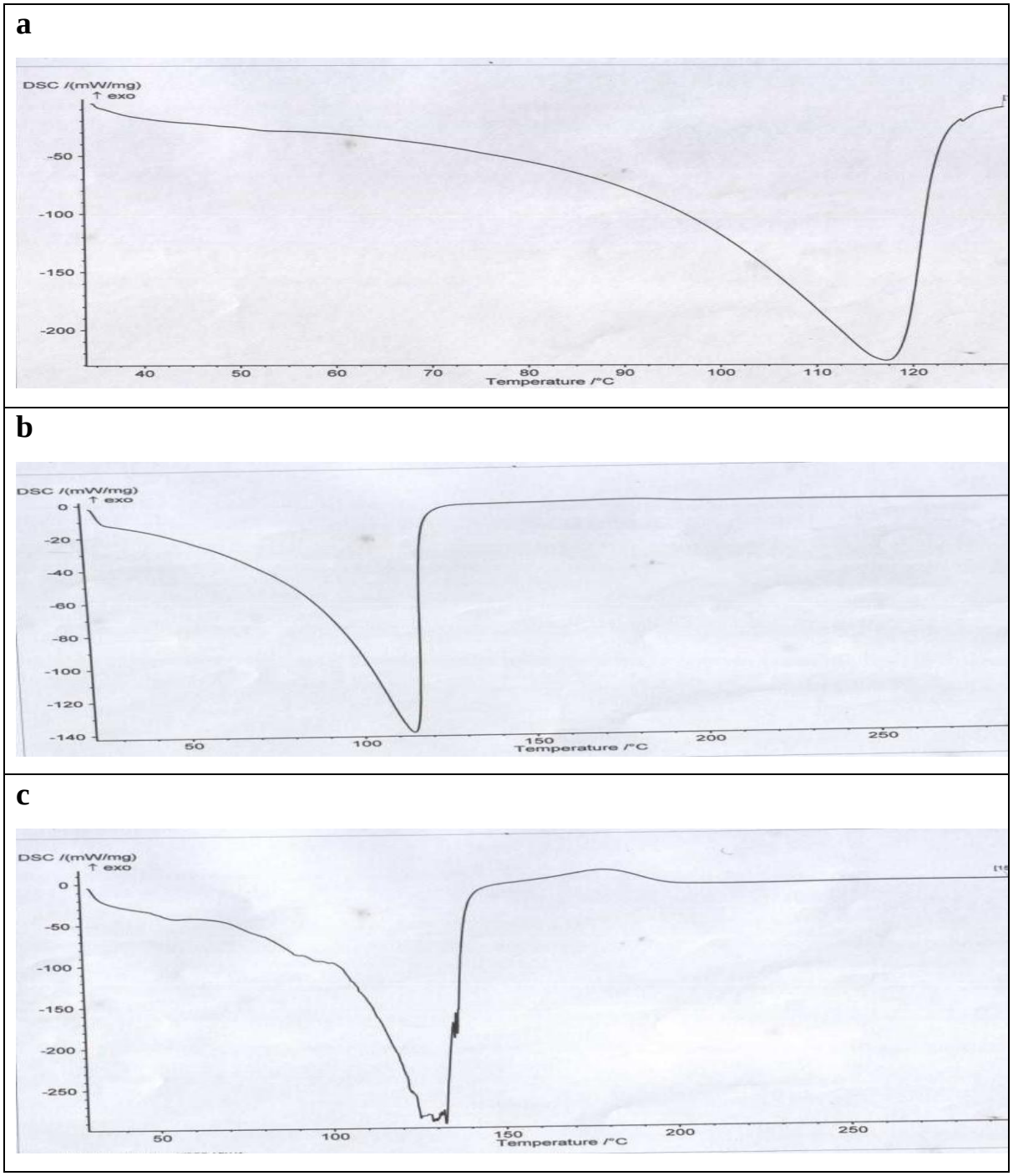

Fig. 6: DSC thermograph of (a) 5 % artemether SLM formulation (1:1) (b) 5 % artemether SLM formulations (1:2) (c) 5 % artemether SLM formulation (2:1).

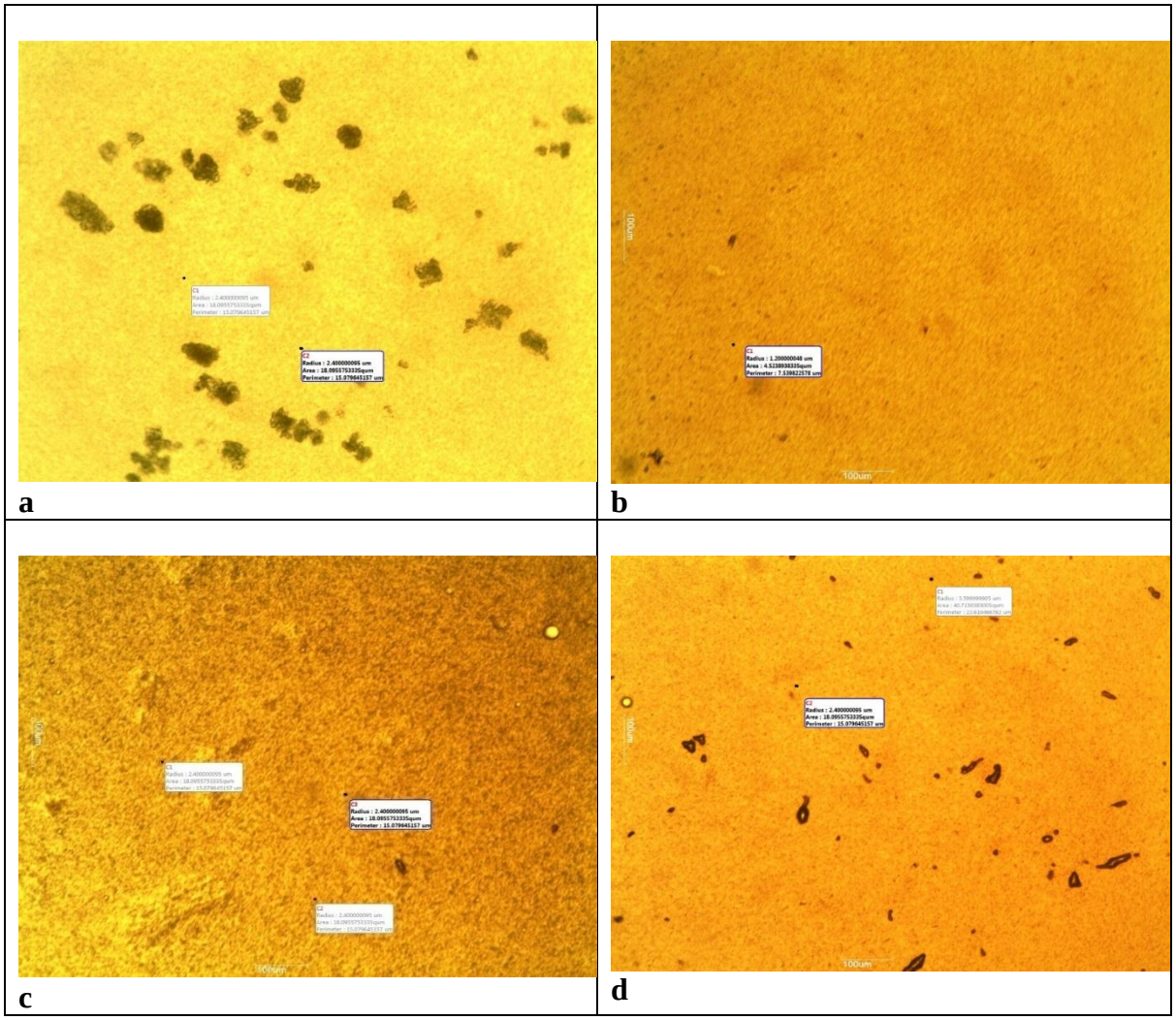

Fig. 7: Photomicrograph of representative batches of (a) Drug free SLM (captex300:goat fat) 1:1 (b) Drug loaded SLM (captex300:goat fat 1:1) 1% (c) Drug loaded SLM (captex300:goat fat 1:1) 3% (d) Drug loaded SLM (captex300:goat fat 1:1) 5%.

Table 4: Time-dependent pH results for all batches of the SLM formulations

Formulation code	24 hours	1 week	1 month
A_0	4.10±1.05	4.06±1.15	3.80±1.05
A_1	4.18±1.01	4.16±1.02	4.04±1.11
A2	4.40±1.10	4.36±1.10	4.28±1.15
A_3	4.21±0.05	4.21±0.05	4.06±0.08
B_0	4.18±1.05	4.16±1.12	4.08±0.15
B_1	4.15±1.10	4.15±1.12	4.08±1.12
B_2	4.22±1.00	4.23±1.05	4.32±1.15
B_3	4.19±1.05	4.19±1.07	4.13±0.05
C_0	4.22±O.05	4.22±0.05	4.22±0.05
C_1	4.34±1.01	4.34±1.05	4.30±1.03
C_2	4.33±0.15	4.27±1.05	4.20±1.18
C_3	4.49±1.05	4.47±1.15	4.46±1.05

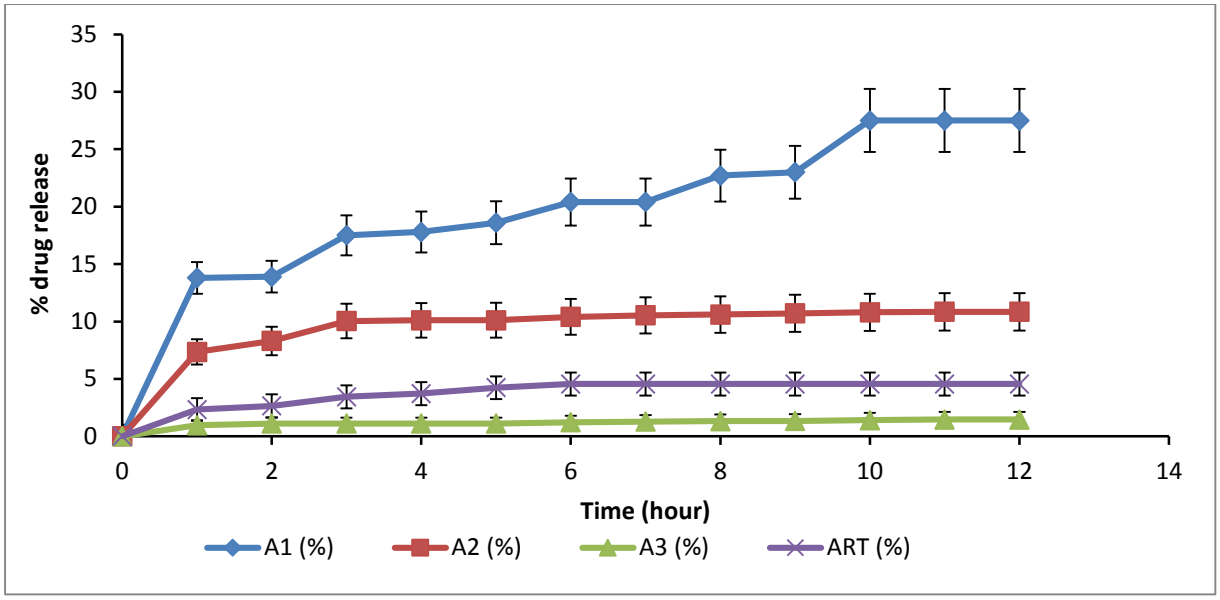

Fig. 8: Percentage drug release against time for SLMs based on 1:1 ratio of captex and goat.
Key: A_1, A_2 and A_3 are SLM formulations containing 1.0, 3.0 and 5.0% artemether, respectively, and 1:1 ratio of captex and goat fat, while AR is the market artemether formulation (artemether injection).

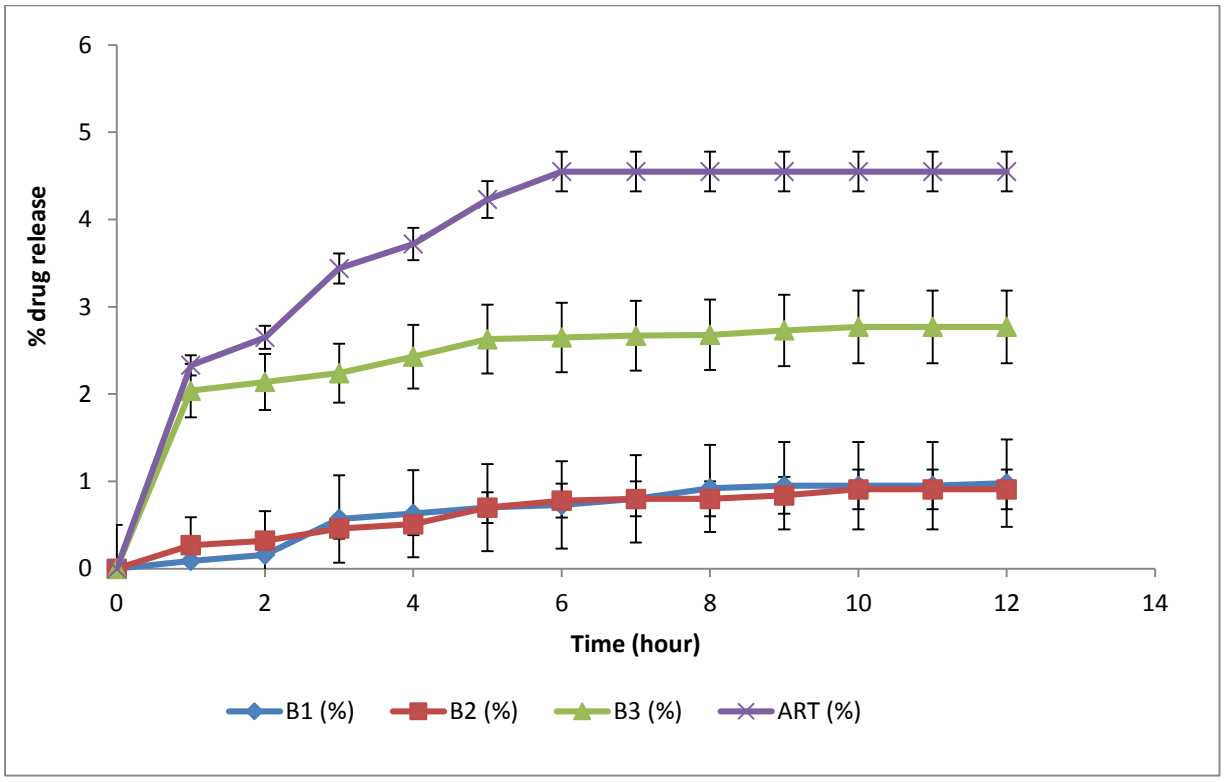

Fig. 9: Percentage drug release against time for SLMs based on 1:2 ratio of captex and goat.
Key: B_1, B_2 and B_3 are SLM formulations containing 1.0, 3.0 and 5.0% artemether, respectively, and 1:2 ratio of captex and goat fat, while AR is the market artemether formulation (artemether injection).

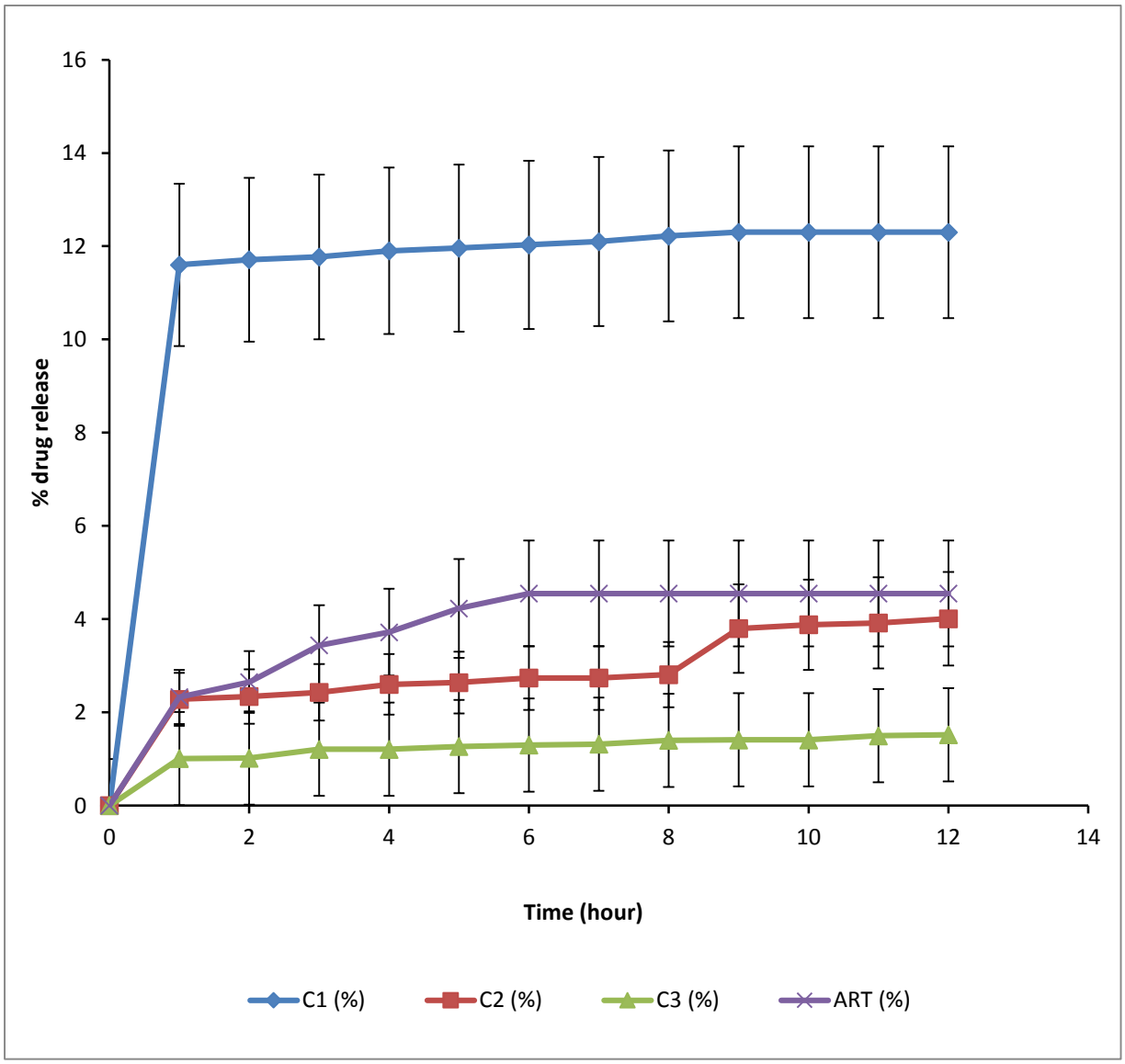

Fig. 10: Percentage drug release against time for SLMs based on 2:1 ratio of captex and goat.
Key: C_1, C_2 and C_3 are SLM formulations containing 1.0, 3.0 and 5.0% artemether, respectively, and 2:1 ratio of captex and goat fat, while AR is the market artemether formulation (artemether injection).

formed very stable matrix when blended together with lower endothermic melting points when compared to the individual lipids. The different ratio blends didn't seem to have any effect on the mixtures. Reduction in enthalpy generally suggests less crystallinity of the lipid matrices. Therefore, it may be more facile for drug encapsulation to take place. The DSC thermogram of PG90 confirms the purity of P90G and that its melting is instantaneous at a high heat capacity. It also shows that the P90G has the tendency of undergoing rapid crystallization with increased heat. The DSC thermograms of the lipid matrices generally showed lower melting endotherms as well as enthalpies. The phospholipid bilayer structure formed around the lipid core may increase the drug loading capacity, as biologically important molecules can be anchored on the colloidal particle surface and surface-modification also enables stabilization of colloidal particles especially when generation of the microparticles is carried out in aqueous medium [17]. The phospholipid 90 G consists of linoleic, oleic, stearic, and palmitic acids, which are fatty acids with different chain lengths and degrees of saturation. The interaction of these fatty acids with that present in goat fat and Captex300 may have resulted in the partially amorphous nature of the lipid matrix, consistent with earlier studies [18].

The DSC thermogram of artemether-loaded SLMs showed that the melting endotherms as well as the enthalpies depend on the lipid content and concentrations of the drug in the formulation [10]. The artemether single peaks obtained from the drug-loaded SLMs suggest that the drug exists in an amorphous form in the microparticles. Also the close enthalpy values for the batches indicates that the microparticles were properly encapsulated in the microparticles. It also shows that the method of preparation used is very reliable. The artemether-loaded SLMs generally had lower melting endotherms as well as enthalpies as compared to the zero-drug counterparts. This implies that the drug loadings resulted in a shift of the melting endotherm towards the lower temperature ranges. This suggests that the artemether loadings in the SLMs formulated with P90G-structured Captex300-goat fat matrices generally produced less-ordered crystals or amorphous state, such that the melting of the substance required less energy than the perfect crystalline substance (blank SLM), which needs to overcome lattice forces. However, the decrease in melting point is associated with numerous lattice defects and the formation of amorphous regions in which the drug is located. In other words, the less crystalline matrices generated enhanced the solubilisation and entrapment of artemether in the core of the microparticles. The long term benefit is suggestive of a prolonged release-carrier system with improved bioavailability performance.

Overall, the DSC results showed that there was no incompatibility between the drug and the excipients. The results revealed the compatibility of the artemether and the lipids as well as the stability of the drug in the lipid matrices. This is because the formulations gave lower melting endotherms as well as enthalpies than the artemether pure drug, implying that the artemether exists in amorphous state in the formulations and is also properly solubilized in the matrix systems.

Results showed that the encapsulation efficiency (%) increased as the concentration of drug added increased. The drug encapsulation efficiency gives an insight to the drug loading capacity of the formulation and it is an important tool to evaluate the drug carrier system [19]. Microparticles should contain high drug content in order to decrease the amount of the drug administered at a time. Good loading capacity shows that the drug has high solubility in the lipid melt, and if the SLM is shown to hold the drug it means all the components of the system worked properly.

The SLMs were well formed, smooth and non-porous. Generally, it is seen that as the drug concentration increased in the drug loaded formulations, the particle sizes also increased. However, drug-loaded formulations containing lipid ratio 1:2 showed an opposite trend, such that the particle sizes decreased as the drug concentrations increased. Particle size is important in drug formulation as it influences the physicochemical performance of dosage forms [20-31].

It could be seen from the release profiles that the SLMs 1:1 (1%), 1:1 (3%) and 2:1 (1%) had higher release rates than the commercially available oily injection, whereas the other drug-loaded batches did not show improved drug release when compared with the commercial sample. The SLM- 1:1 (1%) continued to increase in its percentage release, achieving a maximum percentage release (27 %) at the 10 hours, which shows a relatively good sustained release in line with earlier studies [9, 11, 20]. This could allow for once-daily dosing with the developed SLM formulations. However, it should be kept in mind that dose dumping could occur and this should be avoided as it can result to unwanted side effects as was observed by earlier researchers [2, 8].

The pH test of formulated samples is important as it gives an idea of the stability of the drug over a period of time [5, 6]. From the results obtained it can be seen that pH of the samples did not vary extensively

on storage. This showed the samples were relatively stable on storage.

CONCLUSION

Artemether-loaded solid lipid microparticles (SLMs) were successfully formulated via melt-emulsification from Phospholipon® 90G template lipids consisting of rational blends of Captex 300® (glyceryl tricaprylate) and goat fat. Formulations based on Captex 300® and goat fat (1:1) at 1.0 and 3.0% artemether concentrations (batches A_1 and A_2) as well as SLMs based on Captex 300® and goat fat at (2:1) at 1.0% artemether concentration (batch C_1) gave significantly ($p<0.05$) greater *in vitro* drug release in PBS than artemether injection. This gave insight that artemether-loaded SLMs based on Captex 300® and goat fat templated with Phospholipon® 90G could be employed as an alternative sustained-release formulation than artemether injection for enhanced malaria treatment, thus encouraging further development of the optimized formulations.

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