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Full Length Research Paper

Some *in vitro* and pharmacodynamic evaluation of indomethacin solid lipid microparticles

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The purpose of this study was to investigate some *in vitro* and pharmacodynamic properties of indomethacin-loaded solid lipid microparticles (SLMs). A blend of homolipid from *Capra hircus* and Phospholipon® 90G comprised of the lipid matrix. The SLMs were prepared by the hot homogenisation technique. The effects of Carbosil® and sodium chloride on the release profile and particle size of the SLMs were investigated. The anti-inflammatory and gastro-protective characteristics of the SLMs were also studied. The particle size ranged from 5.0 to 20 µm. The encapsulation efficiency ranged from 46 to 72%; with sodium chloride-containing batches recording highest values. Maximum drug release was within 80 min. Significant (P < 0.05) anti-inflammatory effect was exerted by the SLM. Relative high ulcer index associated with unformulated indomethacin powder and the absence of gastric lesions in rats that received oral administration of SLM affirmed the gastro-protective potential of the SLM. In conclusion, improved anti-inflammatory and gastro-protective effects were achieved with indomethacin-loaded SMLs.

Key words: Anti-inflammatory, gastro-protective, solid lipid microparticles (SLMs).

INTRODUCTION

The oral delivery of lipophilic drugs presents a major challenge, because of their low aqueous solubility and possible unpredictable bioavailability. Although, lipophilicity is a prerequisite for most drug permeation and absorption through the lipid-rich biological membranes, the feasibility of absorption is contingent upon aqueous solubility, without which absorption may be impaired (Arun et al., 2008).

Unionized species as postulated by Henderson-Hasselback are characteristically lipidic in nature. It then follows that an enabled dosage form capable of enhancing the solubility of poorly soluble drugs in the gastrointestinal tract (GIT) may produce soluble unionized species with chemical suitability for absorption, especially when nonionic excipients are utilized.

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Lipid-based formulations are typically reputed to improve the solubility and bioavailability of per orally-administered poorly soluble drugs (Hou et al., 2003; Pouton, 2000). Fundamentally these formulation techniques promote wetting or solubilization of drug and enhance permeability or further undergo intraluminal processing to solubilize the drug (Fricker et al., 2010). Intraluminal processing is facilitated by bile secretion which creates a pool of cholesterol/phospholipid/bile salt complex with surfactant property which facilitates dissolution of poorly soluble drugs and lipophilic drug formulations. Examples of lipid formulations include emulsions, micellar solutions, liposomes, lipid nanoparticles, structured lipid carriers, self-emulsifying oil formulations, solid dispersions, solid-lipid compacts, and drug lipid conjugates.

Apart from synthetic forms, plant-based lipids have also been explored as potential excipients in lipid-based formulations. Although, chemical specificity and purity may not be optimal plant lipids, may be superior to

synthetic forms as regards toxicity and biocompatibility. Solid lipid microparticles (SLMs) are a simple lipid-based delivery system comprising of drug dispersion in a solid lipid matrix.

They are emulsion systems, differing from conventional emulsions by their particulate nature, and can be lyophilized into discrete microparticles (Jasper et al., 2007). If the post-homogenization product yields particles of spherical micrometric dimensions ranging from 1 to 250 µm and having a hydrophobic solid drug core in a phospholipid matrix, they are called lipospheres (Domb and Maniar, 2007). The formulation principle is similar to oil-in-water (O/W) emulsions. Instead of using a liquid lipid, a solid lipid whose solid state is maintained at both room and body temperature is used for this case. Several authors have adopted the melt dispersion cum homogenization technique to prepare lipospheres as an alternative method of microencapsulation to avoid the use of toxic organic solvents and monomers associated with polymeric microparticles (El-Gibaly and Abdel-Ghaffer, 2005; Tewes et al., 2006). In addition to biocompatibility, other advantages include large-scalability, flexible dosage form applicability, controlled drug release, taste-masking, and solubility-enhancement of poorly soluble drugs (EL-Kamel et al., 2007; Shivakumar et al., 2007).

Indomethacin, a weak acidic drug with a PK_a of 4.5 belongs to a class of drugs called non-steroidal anti-inflammatory drugs (NSAIDs) and class 11 biopharmaceutic classification system (De Filippis et al., 1991; Tirkkonen and Paronen, 1992; Yuce and Canefe, 2008). NSAIDs (non-selective) are drugs with analgesic, antipyretic and anti-inflammatory properties (Domb and Maniar, 1996; Martindale, 2009) which inhibit cyclo-oxygenase (COX) enzyme and consequently inhibit the synthesis of prostaglandins and thromboxanes from arachidonic acid. They therapeutically inhibit COX-2, the inflammatory agent at inflamed tissues and also COX-1 with attendant toxicities, such as gastrointestinal problems (Bhupinderjit et al., 1999; Martindale, 2009).

The poor solubility and GIT irritation effect of indomethacin are core limitations to its oral use. A formulation strategy therefore that is capable of addressing these two concerns will be highly beneficial. In this work, therefore, the objective was to formulate indomethacin-loaded SLMs using a matrix blend of synthetic and animal-based fat, and to follow up *in vitro* evaluation with pharmacodynamic (anti-inflammatory and ulcerogenic) studies. The potential usefulness of this formulation strategy to improve the poor solubility and reduce or prevent the gastric irritation effect of indomethacin is being evaluated in this work.

MATERIALS AND METHODS

The following materials were used as procured from their local suppliers without further purification: hydrochloric acid, sodium hydroxide, potassium dihydrogen phosphate, Tween 80 (Sigma Aldrich, Seelze, Germany), sorbitol, indomethacin (Merck, Germany), Phospholipon® 90G (GmbH, Köln, Germany), activated charcoal (Bio–Lab. UK ltd, London), and thiomersal (Synochem, Germany). Goat *(Capra hircus)* fat was obtained from a batch processed in our laboratory. All other reagents and solvents were of analytical grade.

Extraction and purification of fat from *C. hircus*

The fat was extracted by grating the adipose tissue prior to boiling with half its weight of water on a water bath for 45 min. Molten fat was separated from the aqueous phase using a muslin cloth. Further purification was carried out by heating a 2% w/w suspension of a 1:9 ratio blend of activated charcoal and bentonite in the lipid at 80 to 90°C for 1 h. Thereafter, the suspension was vacuum-filtered using buchner funnel.

Preparation of lipid matrix (LM)

Hot melt (80°C) of Phospholipon® 90G and *C. hircus* fat were mixed together at a ratio of 30:70. The mixture was continuously stirred with a stirrer until it attained homogeneity and cooled into a solid mass.

Preparation of SLMs

The method of previous workers (Jaspert et al., 2007; Cortesi et al., 2003) was adopted with modification, using the hot homogenization technique. Indomethacin and Carbosil® were consecutively dispersed in a hot melt (80°C) of lipid matrix and were stirred to constitute the lipid phase. The latter was then introduced into a hot (70°C) aqueous solution of sorbitol, Tween 80, thiomersal, with or without sodium chloride and were homogenized (Ultra-turrax, T25 Basic digital, Ika/Staufen, Germany) for 10 min at 5000 rpm. The final volume of the emulsion was maintained at 100 ml. Table 1 shows the formulation excipients and their w/v % concentrations.

Particle size determination (microscopy)

The particle size of the SLMs was determined by introducing few drops of aqueous dispersion of the SLM on a slide and was imaged under a Hund® binocular microscope (Weltzlar, Germany) with a Motic image analyser (Multicam, China) at X100 magnification.

Encapsulation/Loading efficiency

SLMs from each batch were centrifuged at 3000 rpm for 30 min and 0.5 g quantity was triturated with 20 ml of phosphate buffer prior to subsequent transference to a 100 ml volumetric flask. The flask was made up to volume, stirred, and filtered (Whatman No. 1 filter paper). Indomethacin content of appropriate dilutions were spectrophotometrically (Model SP6 - 450 UV/Vis Pye Unicam) determined at 278 nm. Duplicate determinations were made for all the batches.

The encapsulation efficiency (EE) (the percentage fraction of the theoretical quantity of drug entrapped in the lipid matrix post-homogenization) was therefore calculated from the following equation:

$$EE = \frac{\text{Final quantity of drug encapsulated}}{\text{Initial quantity of drug incorporated}} \times 100 \quad (1)$$

Table 1. Formulae for different batches of SLMs.

Batch	LM (w/v %)	Indomethacin (w/v %)	Tween 80 (w/v %)	Sorbitol (w/v %)	Thiomersal (w/v %)	Sodium chloride (w/v %)	Carbosil® (w/v %)
X1	5.0	0.50	2.5	4.0	0.0025	-	0.1
X2	5.0	0.75	2.5	4.0	0.0025	-	0.2
X3	5.0	1.00	2.5	4.0	0.0025	-	0.5
X4	5.0	1.50	2.5	4.0	0.0025	-	1.0
Y1	5.0	0.50	2.5	4.0	0.0025	0.9	0.1
Y2	5.0	0.75	2.5	4.0	0.0025	1.2	0.2
Y3	5.0	1.00	2.5	4.0	0.0025	1.5	0.5
Y4	5.0	1.50	2.5	4.0	0.0025	2.0	1.0
Z1	5.0	-	2.5	4.0	0.0025	-	0.1
Z2	5.0	-	2.5	4.0	0.0025	0.9	0.1

X and Y: various formulation codes of indomethacin-loaded SLMs; Z: control; LM: lipid matrix.

Dissolution studies

The release of indomethacin from the SLMs was studied using the USP paddle method. The dissolution medium consisted of 900 ml of freshly prepared phosphate buffer (pH 7.4) maintained at 37 ± 0.5°C. Appropriate amount of SLM in 2 ml of the buffer solution was introduced into a polycarbonate dialysis membrane (previously macerated in the medium for 24 h) and securely tied with a non-reactive thermo-resistant thread. It was immersed and firmly suspended in the dissolution medium. The equipment was operated at an agitation speed of 50 rpm, while 5 ml sampling at predetermined time intervals was followed by fresh equivalent volume replacement. Samples were filtered and spectrophotometrically assayed for indomethacin content as described earlier (under encapsulation efficiency).

Anti-inflammatory studies

Egg albumin-induced rat paw oedema method was adopted in this study. All experimental protocols were in compliance with and approved by the animal ethics committee of the University of Nigeria, Nsukka and in compliance with the Federation of European Laboratory Animal Science Association and the European Community Council Directive of November, 1986 (86/609/EEC). Acute inflammation induced by sub plantar injection of egg-albumin was measured in terms of change in the volume of the rat hind paw (Ekpendu et al., 1994). Wistar rats (150 to 200 g) of both sexes were divided into 5 rats per group. The rats were fasted for 6 h with no access to water during the experiment. Water deprivation was to ascertain uniform hydration and to reduce unwanted differences in oedematous response (Winter et al., 1963). Dose of SLM (Y1) equivalent to 1 mg/kg of indomethacin was administered orally to the rats. The control group received normal saline (P2), while the reference group received pure sample of 1 mg/kg amount of indomethacin (P1). After 30 min post-treatment, oedema was induced by injecting 0.1 ml of fresh undiluted egg albumin into the sub planter region of the right hind paw of the rats. Subsequently, the volume of distilled water displaced by the paw was measured with the aid of a plethysmometer before and at 1, 2, 3, 4, and 5 h post induction of oedema. The anti-inflammatory activity was calculated at each time as percent inhibition of oedema using the following equation:

$$\text{Inhibition (\%)} = \frac{Vo - Vt}{Vo} \times 100 \quad (2)$$

where Vt is the volume of oedema in reference group at time t and Vo is the volume of oedema in control rats at the same time (Perez, 1996).

Ulcerogenic properties of SLMs

The method described by some workers (Cashin et al., 1979) was employed in this study. Experimental protocols were in compliance with and approved by the University of Nigeria, Nsukka animal ethics committee and compliant with the Federation of European Laboratory Animal Science Association and the European Community Council Directive. Healthy Wistar rats of both sexes (150 to 215 g) of five rats per group were fasted for 12 h. SLM (Y1) equivalent to 10 mg/kg of indomethacin was administered orally to the rats. The control group received normal saline (P2), while the reference group received indomethacin powder (P1) sample (10 mg/kg). After 5 h post treatment, the animals were sacrificed by ether anesthesia. Gastric mucosa was removed, cut along the lesser curvature and opened up to expose the mucosal surface (Ajali and Okoye, 2009). The mucosa was washed with normal saline and observed with an X10 magnifying glass. The number of observed ulcers was counted and the ulcer index determined as described previously (Main and Whittle, 1975).

Statistics

All statistical analysis was carried out using Statistical Packages for Social Sciences (SPSS) version 13 at $P < 0.05$.

RESULTS

Figures 1 to 4 show the photomicrographs of a few indomethacin-loaded SLMs. Student t-test showed that X1 and X2 without sodium chloride (NaCl) significantly ($P < 0.05$) had higher particle sizes than Y1. In most cases, the two control batches (Z1 and Z2), without entrapped drug, significantly ($P < 0.05$) recorded higher particle sizes than the drug-loaded batches. Furthermore, the control (Z1, without NaCl) indicated significantly higher particle size than the NaCl-containing batch (Z2). Apparently, drug entrapment and the inclusion of NaCl in

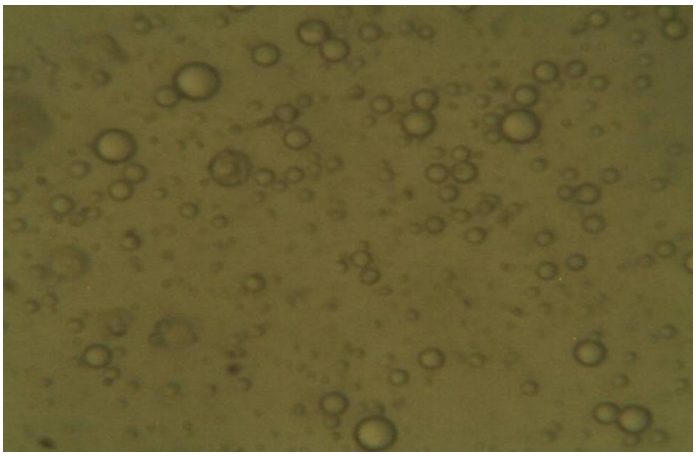

Figure 1. Photomicrograph of batch X1 indomethacin-loaded SLM: X1 contains 0.5% drug without NaCl.

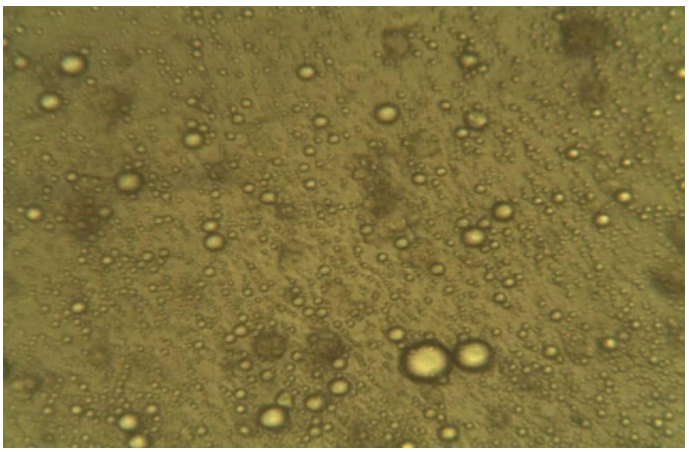

Figure 2. Photomicrograph of indomethacin-loaded batch Y1 SLM: Y1 contains 0.5% of drug and 0.1% NaCl.

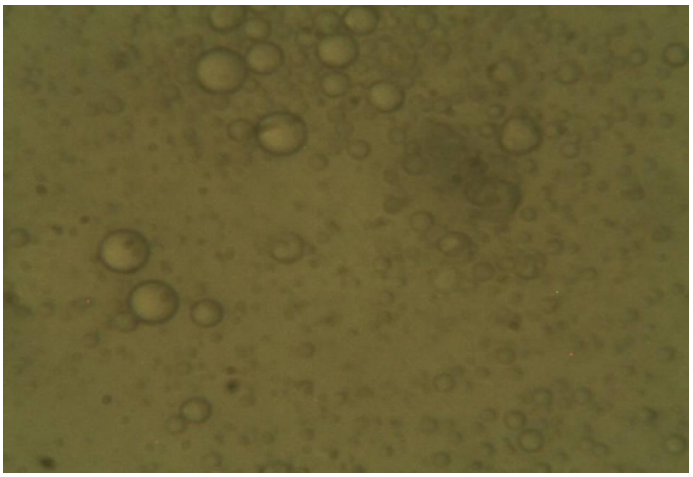

Figure 3. Photomicrograph of batch X2 indomethacin-loaded SLM: X2 contains 0.75% of drug, without NaCl.

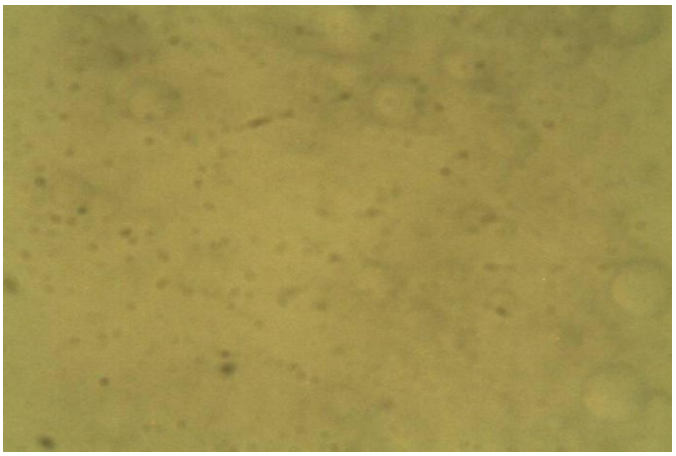

Figure 4. Photomicrograph of batch Z2 indomethacin-loaded SLM: Z2 contains 0.9% NaCl and no drug.

the continuous aqueous phase contributed to reduced particle size in some cases.

The EE was derived as percent fraction of the incorporated drug that was ultimately encapsulated. Student t-test ($P < 0.05$) evaluation indicated that NaCl significantly ($P < 0.05$) promoted higher EE in most cases. Drug load inversely affected EE significantly ($P < 0.05$) (Figure 5). Theoretical drug:Carbosil® (DC) ratio calculated from Table 1, for X1 to X4 or Y1 to Y4 was 5, 3.75, 2.0, and 1.5 respectively. X1 and Y1 with DC value of 5 recorded highest EE, thus projecting them as optimum formulations.

The drug release profile in Figure 6 indicates a biphasic pattern, while Figure 7 shows the T50 and T85 values of the various batches, with maximum drug release taking place between 45 and 75 min. X1 to X4 batches witnessed an initial slow release for about 40 min prior to a faster release phase. On the other hand, the initial release phase for Y1 to Y4 was between 10 to 30 min. Generally, batches containing NaCl witnessed minimal but distinct faster drug release than those without it, with the curves of the later (X1 to X4) having a cluster effect, and similar T50 or T85 values (Figures 6 and 7).

The result of anti-inflammatory effect (AIE) of the SLMs in Table 2 is indicative that indomethacin-loaded SLMs demonstrated significantly ($P < 0.05$) better AIE than the unformulated indomethacin. The time (T50) for 50% AIE to be achieved was 2 h for Y1, while dissolution studies profiled 42 min as its dissolution T50. It is interesting to note that sharpest AIE rise (30 to 45.5%) occurred between 0.5 and 1 h (30 to 60 min). Subsequent increments were rather gradual. This seemed to approximate the dissolution T50 of 42 min.

Furthermore, drug release profile in Figure 3 evidenced a biphasic release that delineated T50 as part of the second and sharp phase. Remarkable absence of mucosal lesions in the GIT depicted in the indomethacin SLM-treated animals (Table3) was indicative of gastro-

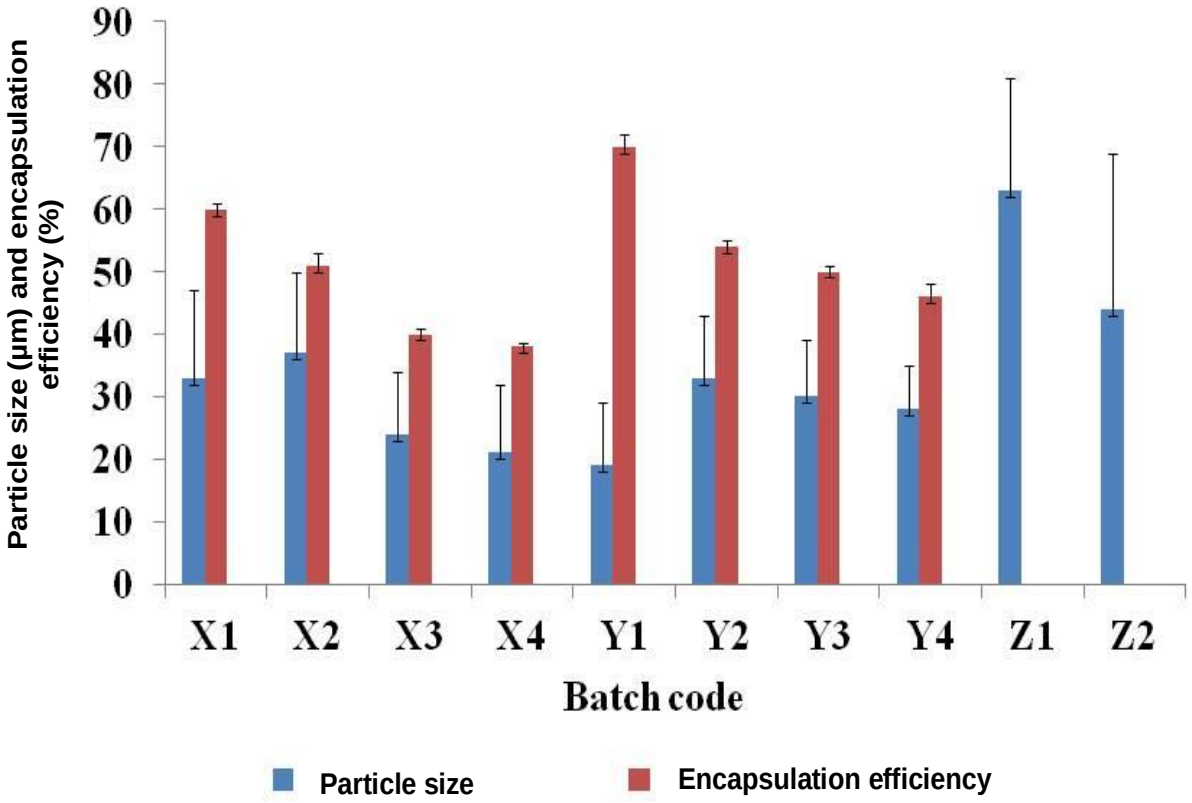

Figure 5. Chart representation of the mean particle size and encapsulation efficiency values of the SLMs. X – Y: various formulations of indomethacin-loaded SLMs; X1 – X4: 0.5 to 1.5% indomethacin and 0.1 to 1% carbosil® without sodium chloride; Y1 – Y4: 0.5 to 1.5% indomethacin, 0.1 to 1% carbosil® and 0.9 to 2% sodium chloride; Z1 – Z2: contain no drug.

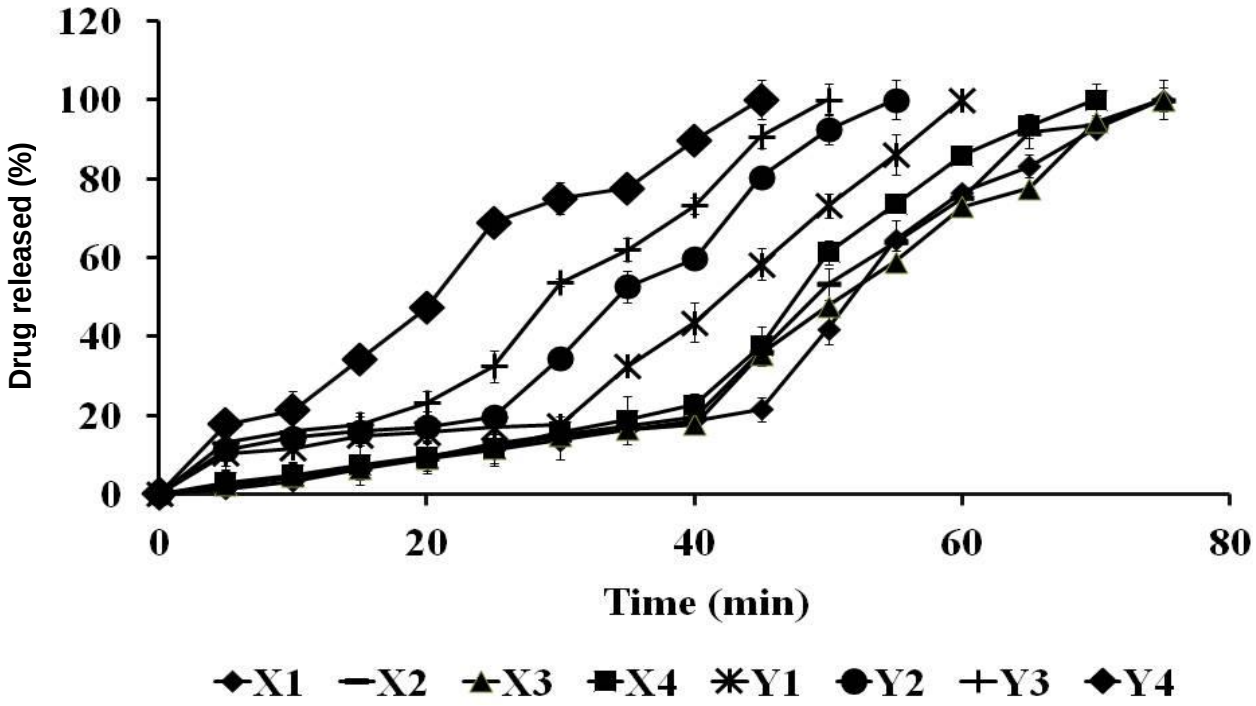

Figure 6. The release profile of indomethacin SLMs in phosphate buffer, pH 7.4.

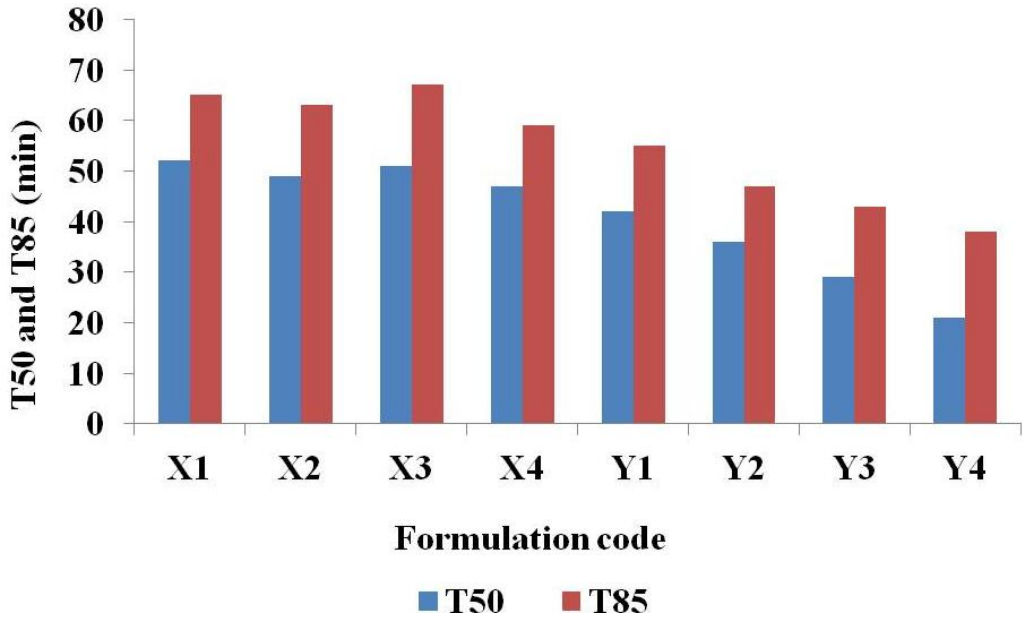

Figure 7. Chart representation of the T50 and T85 values of indomethacin SLMs.

protective potential of the lipid formulation. In contrast, the unformulated indomethacin powder induced multiple ulcers in the animals' gastric mucosa, to the index tune of 14.

DISCUSSION

The incorporation of materials into lipid matrices constitutes external stress on the membrane which imposes elastic deformation that varies with the properties of the material. Three elastic modes of membranes that have been identified include, bending (curvature), stretching and tilting deformations (May et al., 2004). Bending has been reported as prominent during self-emulsification of self-emulsifying drug delivery system (SEDDS)/self-microemulsifying drug delivery system (SMEDDS) (Bagwe et al., 2001). Tilting, on the other hand, involves hydrophobic (hydrocarbon chain) tail tilting with respect to the monolayer plane. Drug entrapment which significantly reduced particle size, in comparison to drug-free SLMs, may have predisposed the phospholipid membranes to tilting and bending since the hydrophobic characteristic of indomethacin warranted concentration and entrapment within the hydrocarbon tail of the amphiphile already consolidated by the animal lipid constituent. Since Z1 and Z2 were not drug-loaded, obvious absence of significant external stress would be anticipated within their particles. This was probably responsible for the observed larger particle sizes. On the other hand, particle size reduction in some of the batches containing NaCl may be attributed to a possible interaction between the hydrophilic polar heads of the phospholipid and the sodium chloride. Increased membrane potential and permeability by NaCl (Nwafor and Coakley, 2003) probably facilitated more aqueous diffusion, thus making the lipid particles of Y1 and Z2 (amidst NaCl) relatively more susceptible to particle disruption than X1 and Z1, and consequently, yielding comparatively smaller particles.

In a previous unpublished research work, we reported higher encapsulation efficiency (89 to 91%) at 0.5% drug load, for a Carbosil® containing lipid matrix as compared to a control without Carbosil®. This actually motivated the incorporation of Carbosil® in all the batches in our present investigation. Carbosil® forms a colloidal dispersion in water, but a smooth viscous dispersion in oil. Its inclusion was intended to generally enhance drug entrapment efficiency. However, there was an interplay between drug load and Carbosil® content as interpreted by drug:carbosil® ratio. This interplay was most significant in X1 and Y1 at a value of 5, followed by X2 and Y2. High value was indicative of higher drug concentration relative to Carbosil®. Below this value palpability waned or was lost, as depicted in the EE values in Figure 5. Furthermore, the hydrophilicity of Carbosil® is attributed to the presence of silanol (Si-OH) group on its surface which potentially interacts with non-polar moieties via hydrogen bonding that exists between the silanol group and other Carbosil® particles to form a three dimensional gel structure (Obitte et al., 2009, 2010; Patil et al., 2004). It may be that the three dimensional gel structures promoted drug entrapment within them. The presence of NaCl in some of the formulations also had effect on the EE. Batch Y1 that contained NaCl entrapped 72% of the drug, whereas X1 without it entrapped 60%. The

Table 2. Anti-inflammatory property of indomethacin SLM.

Batch	Paw volume oedema (ml ± SD)[a] and percent inhibition of oedema (%)					
	0.5 h	1 h	2 h	3 h	4 h	5 h
Y1	0.70 ± 0.18(30.0)	0.60 ± 0.34(45.5)	0.50 ± 0.27*(50.0)	0.45 ± 0.19*(55.0)	0.40 ± 0.27*(57.9)	0.30 ± 0.37*(68.4)
P1 (Reference)	0.80 ± 0.17(20.0)	0.85 ± 0.11(22.7)	0.70 ± 0.23*(30.0)	0.60 ± 0.12*(40.0)	0.55 ± 0.22*(42.0)	0.40 ± 0.29*(1.5)
P2 (Control)	1.00 ± 0.13	1.10 ± 0.16	1.00 ± 0.19	1.00 ± 0.11	0.95 ± 0.16	0.95 ± 0.12

*Reduction in oedema significant at $P < 0.05$ compared to control. Values of oedema shown are mean ± SD, [a]n = 5; values in parenthesis are percent inhibition of oedema calculated relative to control; Y1: indomethacin-loaded SLM; P2: normal saline; P1: unformulated indomethacin powder.

presence of the electrolyte in the aqueous phase may have provided an ionized aqueous milieu that interacted strongly with the polar groups through pore development caused by membrane potential increase (Nwafor and Coakley, 2003), thus minimizing escape of entrapped drugs. Pore-opening may have additionally impelled re-entrapment of drug lost to the aqueous phase during agitation.

Some workers reported faster drug release caused by 0.9% NaCl in the dissolution medium (Yue et al., 2008). Others also attributed increased dissolution rate to the osmotically induced microcapsule pore-opening occasioned by NaCl (Tirrkonnen et al., 1995) probably due to the membrane potential-increasing ability of sodium chloride (Nwafor and Koakley, 2003). Although, in this work, NaCl was only incorporated into the aqueous phase and not the lipid matrix; however, during the homogenization process, some interaction may have taken place between the SLM and aqueous-borne NaCl, especially at such a high agitation speed. This may have promoted pore-opening of the matrix; consequently, enhancing drug release during dissolution studies. Another factor that had across-the-board effect on dissolution rate was the alkaline dissolution medium that enhanced the release of the acidic drug, indomethacin.

Drug absorption enhancement was the basis for the observed anti-inflammatory activity. Phosphatidylcholine has been reported to enhance the lymphatic transport of some drugs(Koo and Noh, 2001; Trevaskis et al., 2006). Hydrolyses of endogenous and formulation-based phospholipids by phospholipase A2 and the stimulation of the release of bile salts, phospholipid, and cholesterol by exogenous lipid, probably associated to produce mixed micelles which ultimately provided a solubilizing platform for the poorly soluble drug (Fricker et al., 2010; Porter et al., 2007; Carey et al.,1983; Tirkkonen et al., 1995).

The aforementioned mechanisms may have been responsible for the superior anti-inflammatory effect of indomethacin SLMs as compared to the unformulated indomethacin, ultimately occasioning absorption-enhancement and possible consistent bioavailability. NSAIDS associated with phosphatidylcholine have previously been reported to improve therapeutic effect of the NSAIDS relative to the NSAID alone (Bhupinderjit et al., 1999).

It should be recalled that indomethacin belongs to class 11 biopharmaceutics classification system, characterized by low aqueous solubility and high permeability. High and consistent permeability can only be guaranteed if solubility, which is the rate-limiting step is improved. In this work, the lipid formulation carrier has demonstrated the capacity to enhance drug absorption by pharmacodynamically providing significantly ($P < 0.05$) higher anti-inflammatory activity over unformulated indomethacin. NSAIDs pharmacologically inhibit COX-2, the inflammation promoting agent at inflamed tissues and also COX-1 with attendant toxicities, such as gastrointestinal problems (Bhupinderjit et al., 1999; Martindale, 2009). The assiduous search for selective NSAIDs gave birth to such hope-raising drug alternatives as celecoxib, rofecoxib, and valdecoxib. Unfortunately, cardiovascular risks truncated the fate of rofecoxib and valdecoxib. Hitherto, in some countries, the acceptability and continued use of celecoxib is contingent upon label warnings of potential cardiovascular risks. In the light of this, recourse to traditional non-selective, inexpensive NSAIDs (indomethacin, acetylsalicylic acid, etc) with pharmaceutically enabled functional capability to mitigate or preclude gastrointestinal disorders without compromising therapeutic efficacy would be a welcome development. This is the reason for our choice of a lipid- based delivery system for the delivery of indomethacin. The application of phospholipids in the oral delivery of NSAIDs is premised upon the gastroprotective potential of both the endogenous and exogenous forms (Fricker et al., 2010; Parnham and Leyek, 1988). Phospholipid (phosphatidylcholine) maintains the

Table 3. Ulcerogenic property of Indomethacin SLM.

Batch	Ulcer index (Mean ± SD)[a]
Y1	0.00 ± 0.00
P1 (Reference)	14.00 ± 1.12
P2 (Control)	0.00 ± 0.00

[a]n = 5; Y1: indomethacin-loaded SLM; P1: unformulated indomethacin powder; P2: normal saline.

hydrophobic integrity of the mucosal surface of the GIT which NSAIDs may erode (Katare et al., 1991). Gastric surface mucus produces surfactant-like phospholipid which is subsequently mobilized to the luminal interface of the mucus gel layer to institute hydrophobicity (Bhupinderjit et al., 1999; Lichtenberger, 1985; Kao and Lichtenberger, 1991). Phospholipids stimulate COX-1 to synthesize prostaglandin, whereas some NSAIDs including indomethacin inhibit COX-1. Synthesis of prostaglandin by the phospholipid appeared to have superseded its inhibition by indomethacin, hence, the observed gastro protection. It is pertinent to mention that *C. hircus* lipid which constituted 70% of the entire lipid matrix could be sourced at a very little cost. Therefore, the economic and pharmaceutical significance of a blend of Phospholipon 90 G and the animal lipid was underscored by obvious synergism provided by the retention of the unique biological function of the phospholipid and the impartation of firm structural discreteness by the animal lipid.

Conclusion

In this study, particle size, encapsulation efficiency, and drug release were affected by sodium chloride, drug load, and the lipid matrix. Secondly, the formulation strategy employed in this work provided barrier fortification against gastric ulceration without compromising the anti-inflammatory activity of indomethacin. We therefore conclude that lipid microparticles involving a phospholipid and lipid derived from *C. hircus* were robustly effective in ensuring acceptable pharmacodynamic characteristics.

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