Formulation Design and *in vitro-in vivo* Evaluation of Sustained Release Aspirin Microparticles Based on PEGylated Lipids

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Abstract: Background: PEGylation is a strategy that on therapeutic molecules such as drugs, proteins and macromolecules, in order to improve their delivery. It has this unique property of increasing the size and molecular weight of biomolecules that are conjugated in nature in order to improve water solubility, reduction in renal clearance and protects the drug from enzymatic degradation. Objectives: The objectives of this work was to formulate sustained release aspirin-loaded solid lipid microparticles based on PEGylated lipid matrix, to evaluate the *in-vitro* properties of the SLM and to study the anti-inflammatory and ulcerogenic properties of the SLM. Methods: Aspirin-loaded solid lipid microparticles (SLMs) were formulated by cold homogenization method. Furthermore, they were analyzed for the encapsulation efficiency, *in-vitro* release, particle size, anti-inflammatory and ulcer inhibition properties. Results: Particle size ranged from 9.36±2.63 to 16.77±5.80 µm for batches B_1 to D_1 SLMs loaded with 10% LM, 5% PEG 4000 and 0.25-1% aspirin respectively, while batches B_2 to D_2 formulated with 10% LM, 10% PEG and 0.25 -1% aspirin had particle size range of 9.09±4.03 to 15.71±10.09 µm. Batches D_1 containing 1% of aspirin had the highest encapsulation efficiency of 58%. Maximum *in-vitro* release of 29.20% and 15.85% were obtained at 6 h for batches D_1 and B_2 respectively. SLMs showed an average of 66.67 − 83.3% oedema inhibition, while the reference had 50%, and ulcer inhibition of 75% for batch D_1. Conclusion: Due to the good properties exhibited by the aspirin-loaded SLMS, they could be used for the treatment of inflammation.

Keywords: PEGylation, Solubility, Solid-lipid Microparticles, Aspirin, Cold Homogenization, Ulcer

1. Introduction

Over the years, a lot of strategies have been put in place in order to improve the delivery of pharmaceutical agents. Two major ways a drug delivery can be modified is either through a change in formulation or by a change in molecular structure. PEGylation is a new approach that is used to enhance drug properties which involves the chemical attachment of polyethylene (PEG) moieties to therapeutic compounds [1, 2]. PEGylation has been used to change the pharmacokinetic and pharmacodynamics of therapeutic molecules and liposomes [3, 4]. PEG moieties are normally produced by linking repeating units of ethylene oxide. These moieties are inert and are long-chain amphiphilic molecules. Chemical coupling of polymers to peptides and protein drugs usually lead to decreased clearance, retention of biological activity, stable linkage and enhanced water solubility. When they are achieved, it could lead to sustained plasma concentration, decreased adverse effects, improved patient compliance and also enhance the quality of life [5, 6]. Branched chain PEG conjugates have increased pH thermal stability and increased resistance to proteolytic digestion when compared to linear

PEG conjugates [7]. For PEG-induced pharmacological changes to be maintained, there must be a stable linkage between the PEG moiety and the drug [8]. Some of the physical and chemical changes that occur during pegylation include: increase in size and molecular weight, changes in the physio-chemical parents of the molecule such as changes in conformation, steric hindrance, electrostatic binding properties and hydrophobicity [5]. The systemic clearance is furthermore reduced by these changes via a number of mechanisms such as decrease in renal clearance, proteolysis and opsonisation [9]. The absorption half-life of a subcutaneous administered drug can be increased by pegylaton [10]. Small molecules require a PEG mass of 40 to 50 KD in order to retard their glomerular filtration [10]. This can be achieved by attaching a large PEG moiety at a single site or attaching several small PEG moieties at more than one site [10]. Some of the common PEGylation techniques employed in formulation include: molecular (PEG conjugation) and particle (PEG-coating) PEGylation [11]. Objectives of this work include to formulate sustained-release aspirin – loaded solid lipid microparticles based on PEGylated lipid matrix, to evaluate the *in vitro* properties of the SLM, to also study the anti – inflammatory and ulcerogenic properties of the SLM.

2. Materials and Methods

The following materials were used as procured: Aspirin (Evans pharmaceutical limited, England), sorbic acid (Sigma® chemical company, USA), Absolute ethanol (Sigma Aldrich, USA), Phospholipon® 90H (Phospholipid GmbH, koln, Germany) distilled water (pharmaceutical chemistry Department, UNN), Tween 80 (Merck, Darmstadt, Germany) Softisan® 154 (Schuppen, Condea Chemic GmbH, Harmburg Germany), PEG 4000 (Sigma Aldrich, USA), stearic acid (Sigma Aldrich, USA), potassium chloride, hydrogen chloride, monobasic potassium phosphate and sodium hydroxide (Merck, Darmstadt Germany). All other reagents and solvents were analytical grade and were used as supplied.

2.1. Preparation of Lipid Matrix

The lipid matrix was prepared by fusion method using Phospholipon® 90H, Softisan® 154 and stearic acid at a ratio of 0.5: 2: 3 respectively. The lipids were weighed and melted together in a beaker placed on the magnetic stirrer hot plate at 80 ℃, stirred with a glass stirrer until a transparent homogenous white melt was obtained. The homogenous lipid melt was stirred steadily until it solidified at room temperature [12].

2.2. Formulation of SLMs

The cold homogenization technique was used to prepare the aspirin-loaded SLMs using the formula in Table 1. A 10% quantity of the lipid matrix was melted at 80 ℃ on a thermostatic magnetic stirrer. About 5% or 10% polyethylene glycol (PEG) 4000 was added to the molten lipid matrix (LM). An appropriate amount of the aspirin was dispersed in the molten LM- PEG melt, the mixture was allowed to solidify. The lipid matrix dispersion was ground using mortar and pestle. Appropriate amounts of tween 80 and sorbic acid were dispersed in ethanol and added to the ground dispersion inside a bottle. The mixture was homogenized immediately at 5000 rpm for 10 min and poured on a cellophane foil and allowed to dry under the fan. The formulations were stored in air-tight containers.

Table 1. SLM compositions.

Batch	*LM: PEG 4000	Aspirin (%)	Tween 80 (%)	Sorbic acid (%)
A1	2:1	-	1.5	0.1
B1	2:1	0.25	1.5	0.1
C1	2:1	0.5	1.5	0.1
D1	2:1	1	1.5	0.1
A2	1:1	-	1.5	0.1
B2	1:1	0.25	1.5	0.1
C2	1:1	0.5	1.5	0.1
D2	1:1	1	1.5	0.1

* LM is made up of Phospholipon® 90H, softisan® 154 and stearic acid at 0.5: 2: 3.

2.3. Determination of Percentage Yield

The percentage yield of the formulations was determined using the formula below: [13]

$$\text{Percentage yield} = \frac{W_1}{W_2 + W_3} \times \frac{100}{1} \qquad (1)$$

Where; W_1=weight of SLM (g), W_2=weight of loaded drug (g); W_3=weight of excipients (g)

2.4. Characterization of SLMs

2.4.1. Time-dependent pH Stability Studies

About 1 g of each of the batches was dispersed in 100 ml water and pH was studied for 7 days using pH meter (Hanna instrument, Padova, Italy).

2.4.2. Determination of Particle Size and Morphology

About 200 mg of the SLM from each batch was placed on a microscope slide and was dispersed in small amount of water. The slide was covered with a cover slip and imaged under a Hund® binocular microscope (Weltzlar, Germany) attached with a Motic image analyzer (Moticam, China), at a magnification of 400×.

2.4.3. Determination of Drug Content, Encapsulation Efficiency (EE) and Loading Capacity (LC)

About 5 ml of the unlyophilized SLMs from each of the batches were centrifuged at 4000 rpm for 15 min. The supernatant was diluted with water, filtered (Whatman no. 1) and analysed using spectrophotometer.

$$\text{ADC (mg)} = \text{theoretical drug content} - \text{amount of aspirin in the supernatant} \qquad (2)$$

Amount of aspirin in supernatant=$\frac{A}{K}$x D. F   (3)

Encapsulation efficiency; EE (%)=$\frac{ADC}{TDC}$ x 100   (4)

Where,

ADC=Actual drug content and TDC=theoretical drug content

The loading capacities (LC) of the batches of the formulated SLMs were determined using the formular:

$$LC=\frac{\text{Amount of drug encapsulated}}{\text{weight of lipid}} \text{ x 100}$$ (5)

2.4.4. In Vitro Drug Release Studies

Beer's plot of aspirin in simulated gastric fluid (SGF) (pH 1.2) was obtained at a concentration range of 0.001 – 0.01 mg/ml at a predetermined wavelength of 225 nm. The dissolution medium was 500 ml of freshly prepared SGF maintained at 37 $\pm$ 1 ℃. The polycarbonate dialysis membrane was pre-treated by soaking in the dissolution medium for 24hours prior to use. 0.1 g of aspirin-loaded SLMs of each formulation was placed in the polycarbonate dialysis membrane containing 2 ml of the dissolution medium, securely tied with thermo-resistant thread and placed in the basket. Speed of magnetic stirrer was maintained at 100 rpm. About 5 ml was withdrawn from the dissolution medium at different time intervals for 3 hours and analyzed spectrophotometrically. Equal volume of withdrawn dissolution medium was replaced with fresh medium at each time interval. The drug release at each time was determined with reference to standard beer's plot.

2.4.5. Fourier – Transform Infrared Spectroscopy (FTIR)

A 0.4 g of potassium bromide (KBr) was weighed and ground into powder. A 0.001 g of each sample was weighed into separate ground KBr, thoroughly mixed together and molded into a disc. The disc was inserted into the sample compartment of the instrument. The scan button was pressed and the infra-red spectrum was generated.

2.4.6. In Vivo Studies

Anti-inflammatory studies

Anti-inflammatory property of the aspirin-loaded SLMs was performed using the rat paw oedema model [14]. The inflammogen used was undiluted egg albumin. Wister rats (90-110 g) were divided into eight groups. Group A – F were made up 3 animals per group and G and H were 2 animals per group. The animals were fasted and dehydrated for 12 hours prior to the experiment. The aspirin-loaded SLMs, that is batches A1, A2, B1, B2, C1 and C2 were administered to the rats orally (A – F), at a dose equivalent to 200mg/kg body weight. The reference group, batch G was given 200mg/kg of pure aspirin while control group (H) received 10 ml/kg of water. After 30 minutes of administration, oedema was induced on the animal in the sub-plantar region of the rat's right hind paw.

The volumes of distilled water which was displaced by the hind paw were obtained by the plethysmometer before and at

30 minutes, 1, 1.5, 2, 3, 4, 5, 6, 7, 8 hours after the egg albumin injection.

Anti-inflammatory response was then obtained for each time interval as percentage inhibition of oedema:

% inhibition=$\frac{V_o - V_t}{V_o}$ x 100   (6)

V_t=volume of oedema at a given time

V_o=volume of oedema in control rats at same time [15].

Ulcerogenicity

The rats as grouped above were sacrificed by ether anesthesia and the stomach (gastric mucosa) was examined for ulceration. The lesions were counted and divided into large (greater than 2 mm in diameter), small (1-2 mm), and punctiform (less than 1 mm).

Severity of mucosal damage was scored as follows:0, 1, 2, 3, or 4

Where; 0 – no lesions or one punctiform lesion; 1 – two to five punctiform lesions; 2 – one to five small ulcers; 3- more than five small ulcers or one large ulcer; 4 – more than one large ulcer [16].

2.4.7. Micromeritics of SLMs

Bulk and tapped densities

A 4g quantity of each batch of SLMs was weighed out and placed in 50 ml measuring cylinder which was in a tilted position. The volume of the powder was recorded as the bulk volume [17].

The bulk density was determined by the equation:

Bulk density=$\frac{\text{Mass of powder (g)}}{\text{Bulk voume (ml)}}$ (7)

The cylinder was then tapped on a wooden surface at 2 seconds interval until no change in volume was noticed and the volume was noted. Tapped density was obtained by the equation:

Tapped density=$\frac{\text{Mass of powder (g)}}{\text{Tapped voume (ml)}}$ (8)

Angle of repose

The static angle of repose was determined by the fixed height core method. 4g of each sample was placed in the funnel at fixed height of 5cm. the sample was released and a cone-shaped heap was formed. Height of the sample was noted and radius of the heap was obtained by dividing its diameter by two. Angle of repose (θ) was calculated using the formular:

θ=tan^{-1} (height/radius)   (9)

Compressibility index and Hausner's ratio

Carr's compressibility index (%) was obtained using the formular:

$\frac{\text{Tapped density}-\text{bulk density}}{\text{Bulk density}}$x 100   (10)

Hausner's ratio was obtained using the formular:

$$\frac{\text{Tapped density}}{\text{Bulk density}} \qquad (11)$$

3. Result and Discussion

From the results shown in Table 2 above, batch A1 which had no drug and batch C2 with 0.5% drug had the highest yield; 72.6% and 75.4% respectively. Batches D1 and D2 containing 1% aspirin each had yield of 69.1% and 62.9% respectively. They also showed the least recovery among all the batches. For the SLMs formulated with 5%. PEG 4000, batch A1 with 0% aspirin gave highest yield of 72.6% while D1 with 1% aspirin had least yield of 69.1%. For the SLMs formulated with 10% PEG 4000, batch C2 loaded with 0.5% aspirin had highest yield of 75.7% while batch D2 loaded with 1% aspirin showed least yield of 62.9%.

The results above showed that the SLMs loaded with 1% aspirin (D1 and D2) had the least percentage yield for batches formulated with 5% PEG 4000 (A1 – D1) and those formulated with 10% PEG 4000 (A2 – D2). The low yield recorded with these batches may be linked to the amount of aspirin incorporated into the formulations. Hence, their amounts may be adjusted.

3.1. Percentage Yield

Table 2. Percentage yield of SLMs.

Batch	Yield (%)
A1	72.60
B1	70.50
C1	72.40
D1	69.10
A2	65.70
B2	70.84
C2	75.70
D2	62.98

The results of particle size of aspirin-loaded and unloaded SLMs are shown in Table 3.

The particle size of aspirin-loaded SLMs ranged from 9.36 – 16.77μm for batches B1 – D1 containing 10% LM, 5% PEG 4000 and loaded with 0.25, 0.5 and 1% aspirin respectively. Also the particle size batches of B2 – D2 containing 10% LM, 10%, PEG 4000 and loaded with 0.25, 0.5 and 1% aspirin ranged from 9.09 – 15.71μm. The results showed that there was no direct relationship between particle size and drug loading [18]. Particle size, however, increased with encapsulation efficiencies of the aspirin-loaded SLM formulations. Also batches D1 and D2 containing 1% aspirin each had highest particle size than other batches. The same was reported by [18]. The unloaded SLMs (batch A1) containing 10%LM and 5% PEG had highest particle size than all other batches. This is due to drug entrapment causing bending of the hydrocarbon chains of the lipid matrix which then leads to size reduction shown by loaded SLMs [19]. The photomicrographs of the SLM formulations showed that the SLMs were spherical and smooth. Although the spherical shape of particle may be attributed to high shear force of the homogenizer [19].
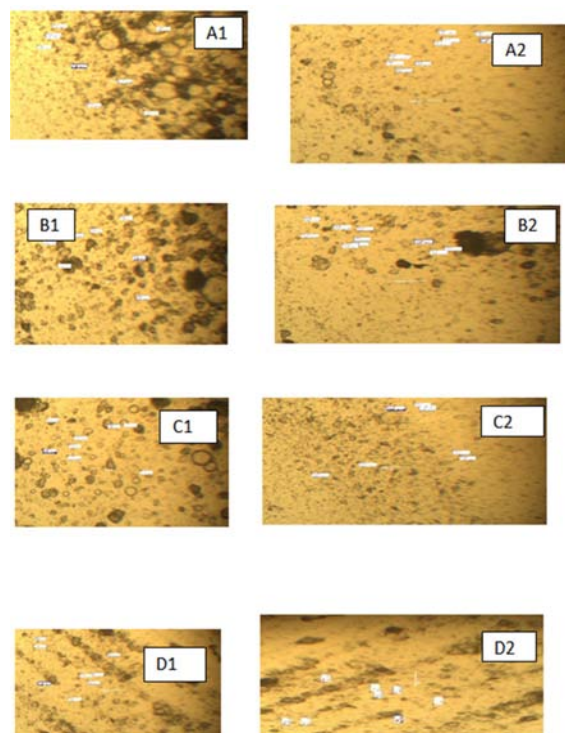

Figure 1. Photomicrographs of aspirin loaded and unloaded SLMs. Batches B1-D1 were formulated with 10% LM, 5% PEG 4000 and 0.25, 0.5 and 1% aspirin respectively while batches B2-D2 were formulated with 10% LM, 10% PEG 4000 and 0.25, 0.5 and 1% aspirin respectively, while unloaded batch A1 contains 10% LM and 5% PEG.

3.2. Particle Size and Morphology

Table 3. The particle size of the SLMs.

Batches	Particle size (μm+ SD)
A1	29.64 + 29.74
B1	12.69 + 4.94
C1	9.36 + 2.63
D1	16.77 + 5.80
A2	15.84±7.86
B2	9.09 + 4.03
C2	15.71 + 10.09
D2	10.50 + 2.71

From Table 4 for SLMs with 5% PEG, batch D1 had highest EE of 58% with1% aspirin. For those with 10% PEG, batch B2 with 0.25% aspirin had a highest EE of 42%. These batches also showed highest loading capacities of 11.54 g/100g lipid and 7.19 g/100g lipid respectively.

However, batch B1 with 5% PEG and 0.25% aspirin and batch C2 with 10% PEG and 0.5% aspirin had least EE and LC of 12% and 0.58 g/100 g lipid and 13%and 1.32 g/100 g lipid respectively. According to Gugu *et al;* [18], they reported that encapsulation efficiency varied directly with the particle size and inversely with drug loading. Increase in drug loading decreased significantly the EE of the SLMs. This could be as a result of the saturation of the lipid matrix with increased drug content [18]. Encapsulation efficiency could be affected by concentration of polymer in dispersed phase, drug to polymer ratio and solubility of the polymer and organic solvent [20].

3.3. Drug Content, Encapsulation Efficiency (EE) and Loading Capacity (LC)

Table 4. Actual drug content (ADC), encapsulation efficiency, EE (%) and loading capacity (LC).

Batch	TDC (%)	ADC (%)	EE (%)	LC (g/100g lipid)
A1	-	-	-	-
B1	0.25	0.29	12.00	0.58
C1	0.5	1.90	39.00	3.80
D1	1	5.77	58.00	11.54
A2	-	-	-	-
B2	0.25	1.05	42.00	2.10
C2	0.5	0.66	13.00	1.32
D2	1	3.59	36.00	7.18

3.4. Time-dependent pH Stability Studies

Table 5. pH values.

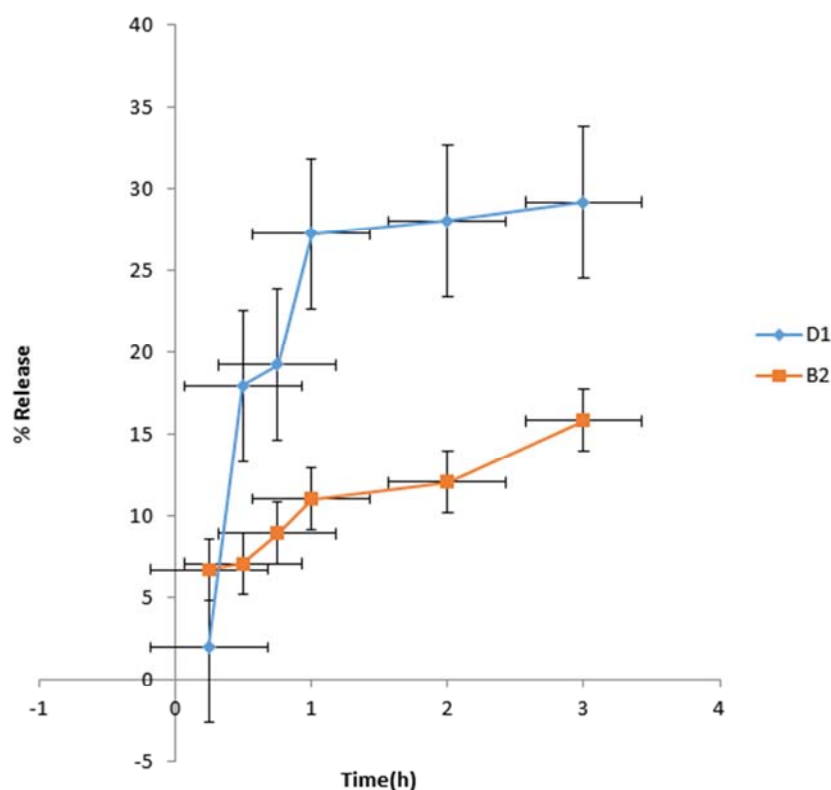| Batch	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
A1	4.5±0.00	4.9±0.07	5.0±0.00	5.1±0.00	5.2±0.00	5.5±0.00	5.2±0.00
B1	3.9±0.07	4.5±0.00	4.5±0.07	4.5±0.00	4.7±0.00	4.9±0.00	4.6±0.07
C1	4.0±0.00	4.2±0.07	4.3±0.07	4.4±0.07	4.6±0.00	4.8±0.07	4.7±0.00
D1	3.7±0.07	3.4±0.07	3.4±0.07	3.5±0.00	3.9±0.00	4.3±0.00	4.4±0.00
A2	4.8±0.07	4.7±0.07	4.6±0.00	4.7±0.00	4.8±0.07	5.0±0.07	4.8±0.07
B2	4.2±0.00	4.3±0.07	4.5±0.07	4.6±0.00	4.8±0.07	4.9±0.07	4.8±0.00
C2	4.1±0.07	4.0±0.00	4.5±0.00	4.6±0.07	4.6±0.00	4.7±0.07	4.9±0.07
D2	4.3±0.07	3.8±0.07	4.0±0.00	4.1±0.00	4.2±0.00	4.4±0.07	4.5±0.00

Figure 2. In-vitro drug release profile of aspirin loaded SLMs for batches D1 and B2 in SGF.

From the results as shown in table 5 above, the pH of the aspirin-loaded SLMs generally increased from 3.4 to 4.9. The pH of the unloaded SLMs also increased from 4.5 to 5.5. This is in agreement with the works by Gugu *et al*; [18] were they reported that the results of the pH of the aspirin loaded SLMs showed an increase pH over time. The same result of increase in pH was obtained for the unloaded SLMs. The pH of the formulations however remained in the acidic region throughout the study. The increased pH as shown by the formulations was due to the release of free fatty acids from the lipids [21].

3.5. In Vitro Drug Release Studies

The results of the *in vitro* drug release for batches DI and B2 in SGF is shown in Figure 2. At 0.75 h, and 3 h, about 19.25% and 29.20% of aspirin were respectively released from batch D1 containing 10% LM, 1% aspirin and 5% PEG 4000. For batch B2 containing 10% LM, 0.25% aspirin and 10% PFG 4000, about 8.95% and 15.85% of aspirin were released at 0.75 h and 3 h respectively.

The results of in vitro release for batches D1 and B2 in SIF are shown in Figure 3. At 0.75 h, 3h and 6 h, about 12.05%, 28.45% and 30.95% of aspirin were respectively released from batch D1 containing 10% LM, 1% aspirin and 5% PEG 4000. Also for batch B2 containing 10% LM, 0.25% aspirin and 10% PEG 4000, about 9.25%, 13.80% and 19.80%

aspirin were released at 0.75 h, 3 h and 6 h respectively. The aspirin-loaded SLMs showed sustained release properties both in SGF and SIF. The maximum release of the aspirin in SGF at 3 h for batches D1 and B2 were 29.20 and 15.85% respectively. Also max release for batches D1 and B2 at 6 h for batches D1 and B2 in SIF were 30.95% and 19.80%. From the result obtained in Figures 2 and 3, it could be deduced that the formulation had very drug release within the first 0.5 to 1 hour due to the effect of burst release. This is often encountered in lyophilized SLMs probably due to the presence of unencapsulated and loosely bound drug in the outer region of the SLMs. In aspirin formulation, this is advantageous especially since it serves as an analgesic, antipyretic and anti-inflammatory agent. This results were in agreement with the work done by [18, 19].
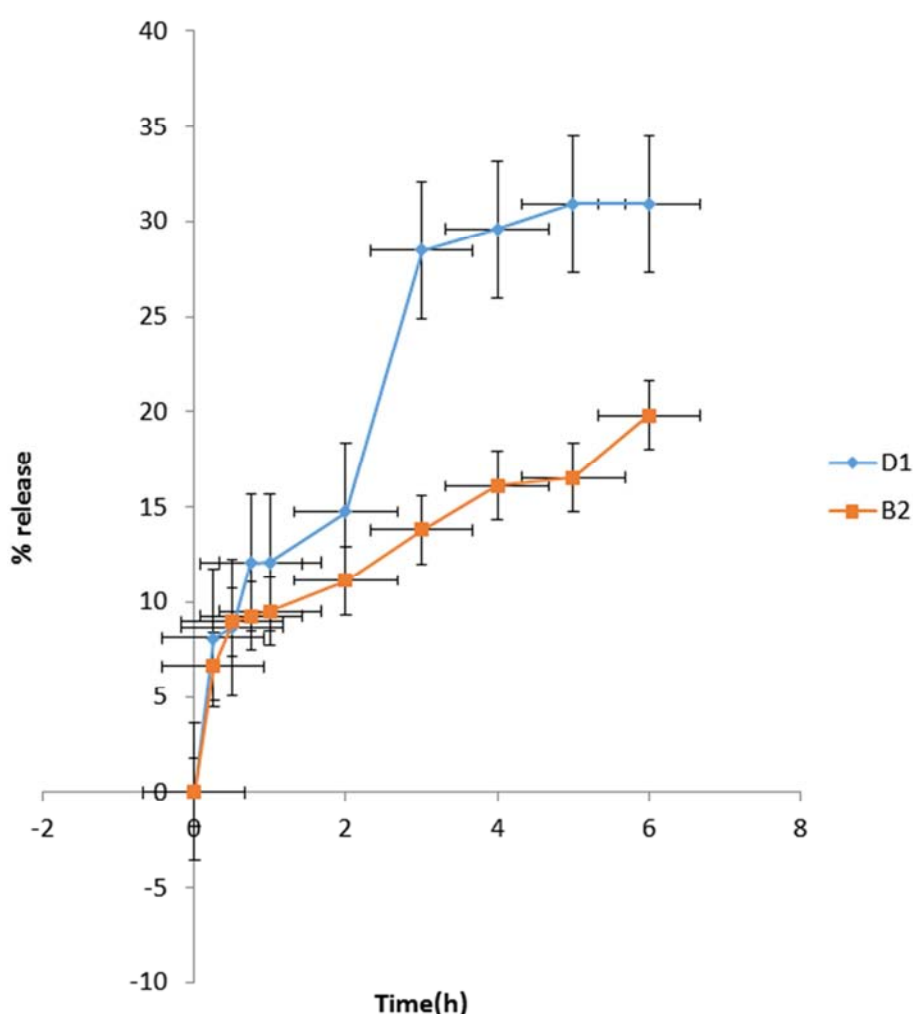

Figure 3. *In-vitro release profile of aspirin-loaded SLM for batches D1 and B2 in SIF.*

Table 6. *Ulcer inhibitory properties of aspirin-loaded SLMs.*

Batches	Ulcer Score	Ulcer inhibition (%)	Ulcer diameter (mm)
D1	1.0±0.00	75	Lesion <1
B2	1.0±0.00	75	Lesion <1
Aspirin	4.0±0.00	0	Lesion <1

D1 was formulated with 10% LM, 5% PEG 4000 and contains 1% aspirin while B2 has 10% LM, 5% PEG 4000and 0.5% aspirin.

3.6. In Vivo Drug Studies

3.6.1. Ulcerogenicity

The results of ulcerogenic properties of the SLMs were shown in Table 6. Batch D1 formulated with 10% LM, 1% aspirin and 5% PEG 4000 achieved 75% ulcer inhibition with ulcer lesion of less than 1mm in diameter. Batch B2 containing 10% LM, 0.25% aspirin and 10% PEG 4000 also had 75% ulcer inhibition and ulcer lesion of less than 1mm in diameter. However, the pure aspirin sample had zero ulcer inhibitory effect. This results were in agreement with the work done by [19, 21] who individually discovered that there was inhibition of ulcer potential of NSAIDs by the SLM.

Table 7. Percentage inhibition of oedema.

Batch	0.5h	1h	2h	3h	4h	5h	6h	7h	8h
D1	16.67±0.0	16.67±2.3	33.3±2.3	33.3±2.3	50.0±0.0	50.0±0.0	83.3±0.0	83.3±0.0	83.3±0.0
B2	6.67±2.8	6.67±2.6	20.83±2.6	33.3±0.0	48.3±0.0	50.0±0.0	66.7±0.0	66.7±0.0	66.7±0.0
Pure Aspirin	6.67±0.0	8.33±2.3	33.3±2.3	33.3±3.3	41.67±0.0	41.67±0.0	41.67±0.0	50.0±0.0	50.0±0.0

*D1 was formulated with 10% LM, 5% PEG 4000 and contains 1% aspirin. B2 was formulated with 10% LM. 10% PEG 4000 and contains 0.25% aspirin.

3.6.2. Anti-inflammatory

The results of anti-inflammatory properties of batches D1 and B2 are shown in Table 7. At 0.5 h, aspirin-loaded SLMs had oedema inhibition of 6.67-16.67%. At 4h, the oedema inhibition of the SLM formulations was 48.33 – 50%. Also at 5, 6, and 7 h, about 50%, 66.67-83.33% and 66.67-83.33% inhibition of oedema respectively was achieved by the SLM formulation. Also at 8 h, aspirin-loaded SLM formulations had oedema inhibition of 66.67 – 83.3% compared to pure sample which achieved 50% oedema inhibition at same time. This results is a pointer that the formulation exhibited significant higher ant-inflammatory properties than the aspirin pure drug ($P< 0.05$). This could be due to the phospholipid component present in the SLM that thus improved its anti-inflammatory activity. This is in agreement with the work done by [19].

Table 8. Micromeritic properties of SLMs.

Batch	ρ_B (g/ml)	ρ_T (g/ml)	H. R	C. I (%)	A. R
A1	0.40±0.00	0.50±0.07	1.25	20.00	23.96±0.03
B1	0.40±0.00	0.50±0.00	1.25	20.00	30.02±0.7
C1	0.38±0.01	0.50±0.00	1.32	24.00	24.78±0.2
D1	0.36±0.01	0.44±0.07	1.22	18.18	23.58±0.01
A2	0.44±0.03	0.50±0.01	1.14	20.00	26.57±0.01
B2	0.40±0.00	0.50±0.01	1.25	20.00	21.31±0.01
C2	0.40±0.00	0.53±0.02	1.33	24.53	26.57±0.01
D2	0.40±0.00	0.50±0.02	1.25	20.00	26.10±0.00

B1, C1, D1, B2, C2and D2 are aspirin-loaded SLMs. B1, C1, D1, B2, C2and D2 had 5% PEG and 10% PEG respectively. ρ_B=Bulk density; ρt=tapped density; H. R=Hausner's ratio; C. I=Carr's compressibility index: A. R=Angle of repose.

3.7. Micromeritic Properties

The bulk densities of the SLM formulations ranged from 0.38 – 0.44 g/ml, while the tapped densities ranged from 0.44 – 0.53 g/ml. Flowable granules or powders are usually less dense than those that are less flowable [17]. The SLM formulation also had angles of repose ranging from 21.31 – 30.02%. Powders with angles of repose greater than 50 show poor flow properties whereas those with angles of repose close to 25° have very good flow properties [17]. Hausner's ratios of the SLM formulation ranged from 1.14 – 1.33. It is known that powders with less interparticulate friction have Hausner's ratio of approximately 1.2 while those that are more cohesive and less free-flowing have ratios greater than 1.6 [17]. Also, the compressibility index of the SLM formulations ranged from 18.18 – 24.5%. This shows that the formulation had good and passable flow characteristics. The results generated above showed that the SLM formulations had good flow properties. Therefore, they can be compressed as tablets, capsules or may be used as powdered formulation.

Fourier transform infra-red spectroscopy (FTIR)

The FTIR spectra of pure aspirin, batch B2, stearic acid and batch D1 are shown in Figures 4, 5, 6 and 7 respectively. The infrared spectrum of pure aspirin revealed the absorption of C=C (aromatic), C=0 (acid) and C=O (ester) functional groups at 1597.80cm^{-1}, 1748.34cm^{-1} and 1875.72cm^{-1} respectively. Also, the infrared spectrum of batches D1 and B2 each showed the absorption of C=C (aromatic), C=O (acid) and C=O (ester) at 1593.94cm^{-1}, 1744.48cm^{-1} and 1844.84cm^{-1}. The spectrum of the drug showed that its functionalities were not significantly altered by the excipients, hence, the drug was compatible with the excipients. The standard band frequencies of aspirin showed that the major principal peaks at or around the requisite wave numbers were present thus there was no interaction between the drug and polymer.
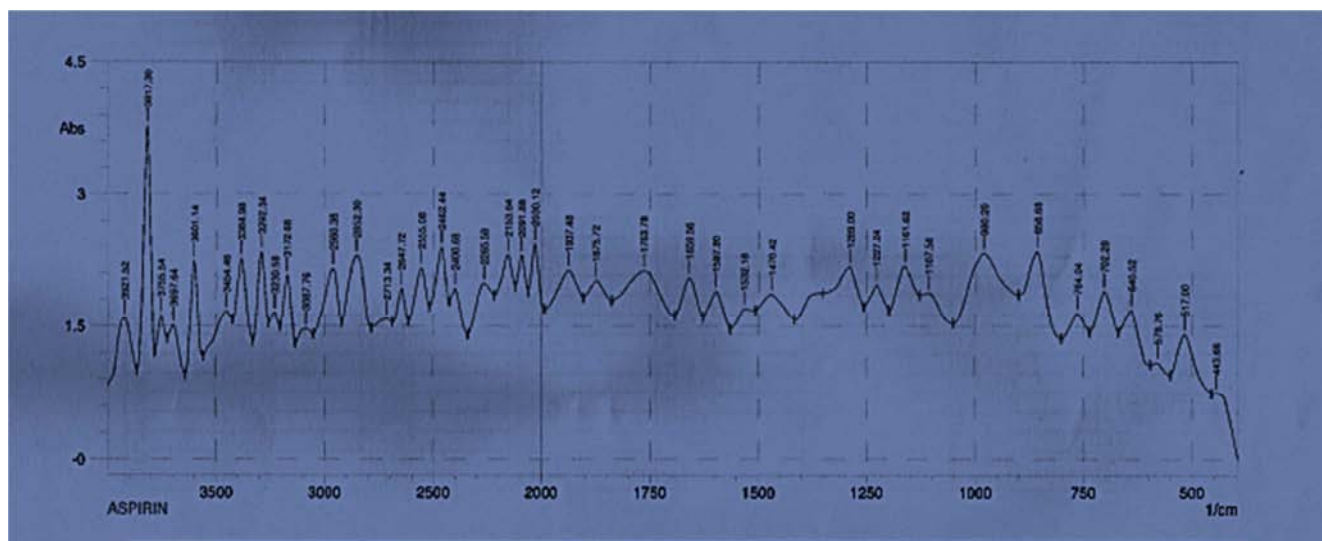
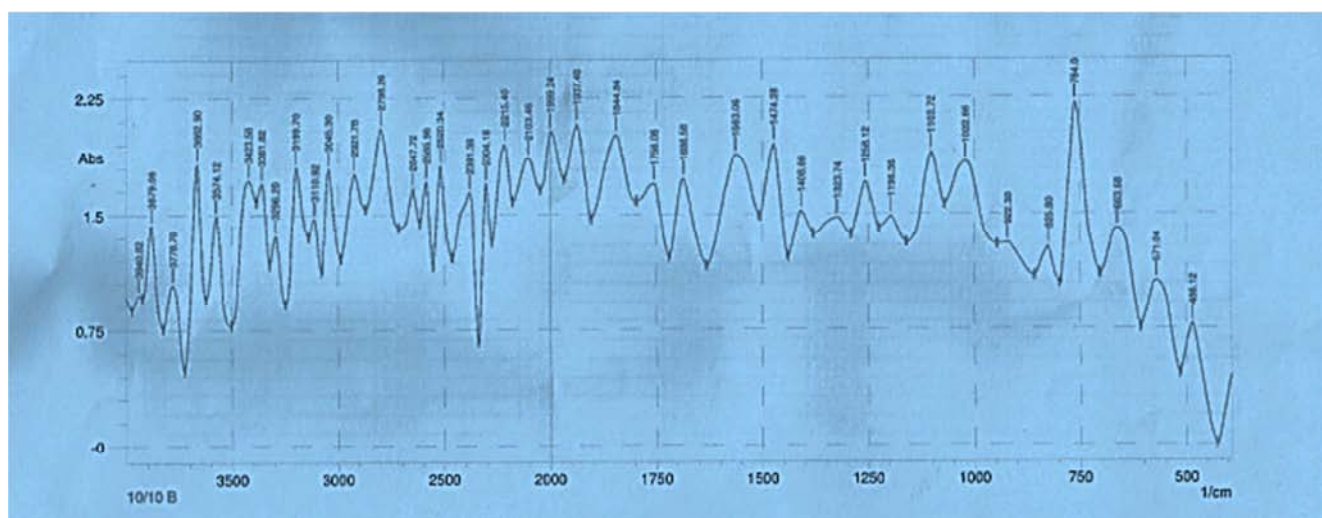*Figure 4. FTIR spectrum of aspirin.*
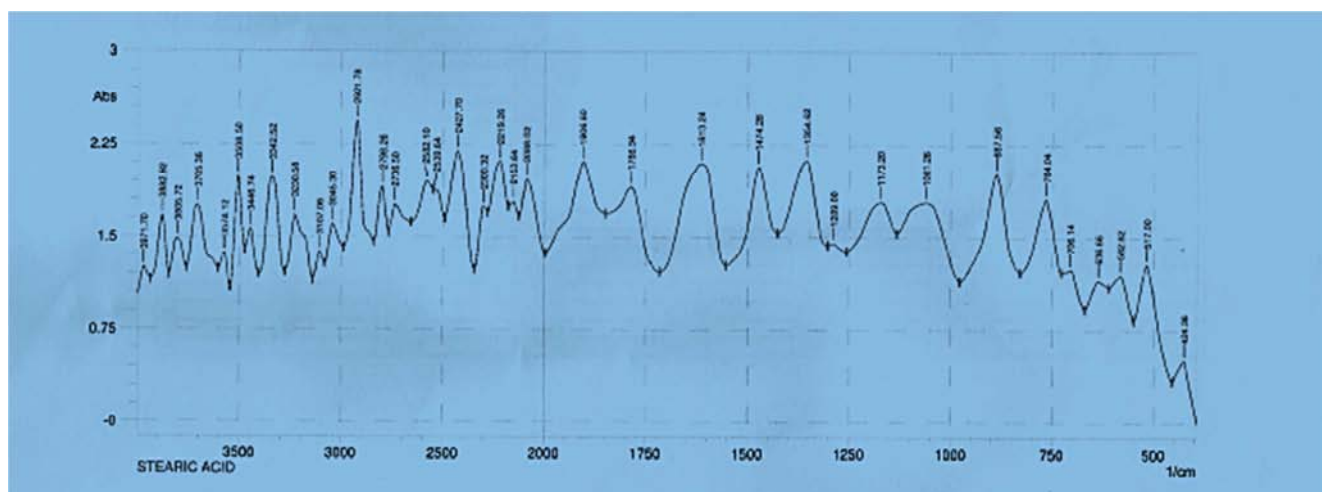

Figure 5. FTIR spectrum of batch B2.

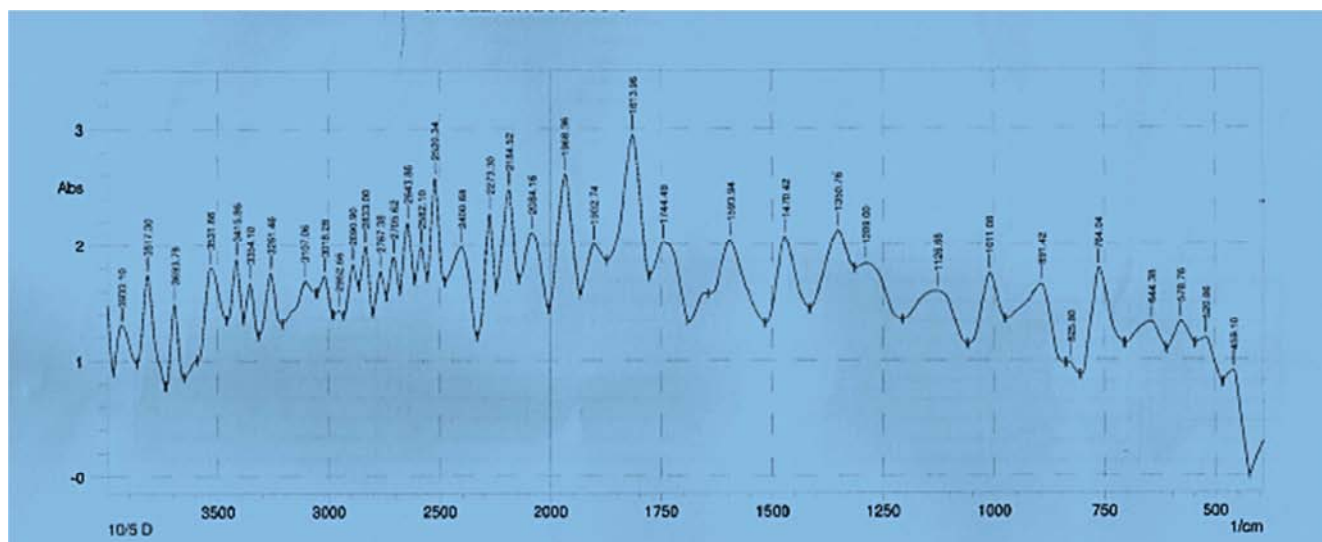*Figure 6. FTIR spectrum of stearic acid.*

Figure 7. *FTIR spectrum of batch D1.*

4. Conclusion

Aspirin could be formulated as SLMs, but there is need for a new delivery system of aspirin to be in place. The SLM formulations was shown to enhance absorption, inhibit ulcers in patent on long term therapy, better disease management and the use of safety excipients. This study has to be enhanced in order to enable patients lay hold of its numerous benefits.

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