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Physicochemical Characterization of *Sus scrofa domesticus* Fat and a Preliminary Evaluation of its Potential as a Matrix Former in Ibuprofen Granules

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of article.

Abstract

Background: There is an increasing interest and search for local and natural sources as active pharmaceutical excipients.
Purpose: The study aimed at investigating the physicochemical characteristics of *Sus scrofa domesticus* (SSD) fat and its potential as a matrix former in ibuprofen granule formulations.
Methods: SSD fat was extracted from the domestic pig by wet rendering and purified. The fat was characterized for its organoleptic and physicochemical properties and used in the formulation of batches of ibuprofen granules by melt granulation using varying concentrations (5.0-15%w/w). Conventional granules were formed with maize starch (15%w/w) for control. Formulated granules were evaluated for flow properties, encapsulated in hard gelatin capsules and subjected to *in-vitro* drug release studies.
Results: SSD fat was snow white in colour. Soluble in organic solvents but insoluble in water. pH of the fat was 7.4, viscosity (147.4 millipascal), peroxide value (11.0 meq/kg), acid value (3.4) and saponification value (196.3). Granules formulated with SSD fat exhibited poor flowability and their dissolution profiles showed retardation in ibuprofen release with increase in fat concentrations. Granules formulated with 5.0 and 10%w/w of the fat exhibited 43 and 27% ibuprofen release within 4 h while the conventional granules showed a drug release of 98% within 1.0 h.
Conclusion: The physicochemical properties of SSD fat was found to possess favourable potential properties relevant in the formulation of a drug delivery system. The retardation of ibuprofen release from the granules showed that SSD fat has a potential application as a matrix former in controlled release formulation.

Keywords: *Sus scrofa domesticus*, ibuprofen, matrix granules, dissolution profiles

INTRODUCTION

Substances used in drug formulation are either employed as active drugs or excipients and they are often obtained from various sources such as natural or synthetic processes. The natural sources range from plants, animal or minerals (Dias *et al*., 2012). In order to get a clear understanding of new drug compound or excipients, an extensive evaluation and characterization is often carried out of the physical and chemical properties and its overall behaviour in relation with other substances. Information gathered from physicochemical characterization of a new drug molecule or excipients will justify its choice as well as its useful application as good or bad candidate in the final product (Moreton, 1996 and Okafor *et al*., 2002).

Fats are semisolid or solid at ambient temperature, containing a wide range of compounds whose basis is in long chain organic acids called fatty acids. Fats on the other hand are esters of such organic acid formed with the alcohol glycerol. Basically, in chemistry, fats is simply referred to as triglycerides, composed of free fatty acids and the distribution of fatty acids vary from oil to oil (Ockerman and Basu, 2006). Fats when highly purified and refined to pharmaceutical grade have found wide applications as fillers, binders, lubricants, solubilizers, emulsifiers and emollients in a variety of dosage delivery forms including tablets, capsules, suppositories, emulsions and semi-solid cosmetic preparations (Grassa 2000).

Some natural fats and waxes that have been investigated as excipients in drug delivery includes dika fat in the formulation of sustained release theophylline tablets and capsules (Umekoli *et al*., 2009), goat fat in the preparation of sustained release ibuprofen tablets (Eichie *et al*., 2010) and carnauba wax in the formulation of matrix tablets of metronidazole (Arhewoh *et al*., 2015). In some of these studies, low drug entrapment efficiency and influx of fluid to the core of tablet thereby necessitating the inclusion of surfactants in the formulation to facilitate dissolution, were some of the drawbacks encountered by the researchers.

Sus scrofa domesticus fat is the fat obtained as a bye-product from the adipose tissues of the domestic edible pig, a specie of the wide pig family (Suidae), genus (Sus) and specie (Sus scrofa). This fat is used commonly in many western cuisines as cooking fat or shortening similar to butter, (Ockerman and Basu 2006 and Alfred 2002).

In recent time, there has been increasing interest and search for natural pharmaceutical ingredients either as active pharmaceutical ingredients or excipients used in the formulation of drugs. Natural substances are characterised by low toxicity, high stability, environmentally friendly and biodegradability which make them quite appealing as pharmaceutical excipients, (Ahad *et al*., 2011). Hence, this study sets out with the aim to convert the bye-product fat obtained from *Sus scrofa domesticus* (edible pig) into useful pharmaceutical grade excipients in the formulation of a drug dosage form. The objective is to extract and characterize the physicochemical properties of *Sus scrofa domesticus* fat and carry out a preliminary evaluation of its pharmaceutical excipient potential as a matrix former in ibuprofen granule formulations. Ibuprofen was used a model drug because of its short biological half-life of 1.8-2.0 hours and administered orally every four to six hours daily. This dosing frequency makes it an ideal drug candidate for modified or sustained release preparation.

METHODOLOGY

Materials

Ibuprofen was a kind gift from Emzor Pharmaceutical Ltd, Lagos, Nigeria. Ethanol and hydrochloric acid (Sigma Aldrich, U.K). All other chemicals including acetone, chloroform, petroleum ether, benzene, heptane, hexane, distilled water, sodium thiosulphate, potassium hydroxide, starch (indicator) and phenolphthalein solution were of analytical grade. *Sus scrofa domesticus* fat was extracted from a mixture of adipose tissues from the back, belly and kidney of a local domestic pig obtained from an abattoir in Benin City, Edo State, Nigeria.

Methods

Extraction of *Sus scrofa domesticus* fat

A standard method for rendering fat was adopted. About 6.0 kg weight of adipose tissues from the back, belly and kidney of a pig were washed thoroughly to remove all extraneous materials and then cut into smaller pieces. The chopped pieces was heated in a stainless steel cooking pot with 1.0 L of water for 1.0 h. The liquid content of the pot containing the melted fat and water was decanted and thereafter, the molten fat was separated from the aqueous phase by filtration. The weight of the molten fat was taken and used to calculate the percentage yield of the extraction process before been stored in a freezer for subsequent purification.

Purification of extracted *Sus scrofa domesticus* fat

The fat was purified using a previously described method (Eichie *et al.,* 2010). A 650 g of the extracted fat was heated with 20 g of activated charcoal over a hot water bath for 1.0 h with occasional stirring. The molten mixture was filtered while hot with a Buckner funnel under vacuum. The molten fat filtrate obtained was allowed to cool and then stored in a freezer prior to evaluation.

Physicochemical characterization of the *Sus scrofa domesticus* fat

Organoleptic properties

Some organoleptic parameters such as odour, colour, taste and texture of the purified fat was determined by three different assessors. Judgements were taken from the consensus decision of two assessors.

Solubility

The method of Mahmud *et al*. (2008) was adopted with slight modifications. The solubility of the fat was determined at room temperature in various solvents such as distilled water, acetone, chloroform, ethanol, petroleum ether, benzene, heptane and hexane. A 5.0 mg sample of the fat was dispersed in 100 ml of the test solvent inside test tubes and left overnight (24 h). The supernatant liquid was carefully transferred to a pre-weighed evaporating dish and heated to dryness over a water bath. The weight of the dried residue with reference to the weight of the fat sample was used to calculate the solubility of the fat in the solvent using Equation 1. The solubility was determined in triplicates and mean values recorded.

$$\text{Solubility} = \frac{\text{weight of residue}}{\text{weight of sample}} \times \frac{100}{1} \qquad (1)$$

pH

The pH of 100 ml of the melted fat was determined directly using digital pH meter (Jenway 3510, UK). The pH meter was immersed in the melted fat until the meter indicated a steady pH of the sample. The experiment was carried out in triplicates and the mean and standard deviation values reported.

Iodine value

The Wijs method of Association of Analytical Chemists was adopted (A.O.A.C., 1984). A quantity of the fat (0.5 g) was dispersed in 15 ml of chloroform in a 250 ml volume stoppered bottle, then, 25 ml of Wijs solution was added. The mixture was allowed to stand for 30 min in a dark cupboard. A volume of 20 ml 15 % iodide solution was added into the bottle and titrated with 0.1 N sodium thiosulphate solution until the yellow colour disappeared. A volume of 2 ml of 1.0 % starch indicator was added and the titration continued until a blue colour disappeared. A blank titration was run with equal volume of Wijs solution. This was done in triplicates and mean value determined. The iodine value was calculated from Equation 2.

$$\text{Iodine value} = \frac{(B-S)\times N\times 1.269}{\text{weight of sample}} \qquad (2)$$

Where B = volume in millilitres of standard sodium thiosulphate required for the blank.

S = volume in millilitres of standard sodium thiosulphate required for the sample.

N = Normality of standard sodium thiosulphate solution.

1.269 = concentration conversion coefficient

Acid value

The method of British Pharmacopoeia (2010) was adopted. Ten grams of pure fat was dissolved in 50 ml of a mixture of equal volume of ethanol (96 %) and petroleum ether previously neutralised with 0.1 mole potassium hydroxide using 0.5 ml phenolphthalein as

indicator. The mixture was heated in a water bath to a temperature of 90 °C to completely dissolve the fat. The resulting solution was titrated with 0.1 M potassium hydroxide until a pink colour persisted for about 15 sec. The volume titre (η millilitres) was noted. The temperature was maintained at 90 °C during titration which was done in triplicates and the mean value determined. The acid value was calculated using Equation 3. (Chen, 2013).

$$I_A = \frac{5.610\eta}{m} \qquad (3)$$

Where I_A = Acid value

η = volume of the titrant

m = Weight or quantity of pig fat used for the titration

5.610 = concentration conversion coefficient i.e. 0.1 mole KOH.

Specific gravity (Relative density)

The official method used in British Pharmacopoeia (1988) was adopted, using fluid displacement which involve the use of pycnometer (specific gravity bottle), with water as a non-solvent for the fat. The empty pycometer (50 ml capacity) was weighed, then filled with water and the weight determined. The bottle was filled with molten fat, and the weight noted, and the weight difference used to compute the value. Triplicate determinations were carried out and mean values determined. The relative density (specific gravity) was then calculated using Equation 4.

$$\text{Specific gravity} = \frac{\text{weight of Xml of oil}}{\text{weight of Xml of water}} \qquad (4)$$

Saponification value

The BP (2010) method was employed. A 2.0 g sample of fat was weighed into a conical flask and 25 ml 0.5 N alcoholic potassium hydroxide was added. This was attached to a reflux condenser and the flask heated in boiling water for 1 h with frequent shaking. Phenolphthalein 1.0 % solution (1 ml) was added, the excess alkali was titrated hot with 0.5 ml hydrochloric acid. The titre was noted (a ml). A blank titration was done without the fat and the titre (b ml) was noted. Triplicate titrations were done for both the blank and fat sample and mean values computed. The saponification value was then calculated using Equation 5.

$$\text{Saponification value} = \frac{\text{(b-a)ml} \times 28.05}{\text{weight of sample}} \qquad (5)$$

Unsaponifiable matter

The neutralized liquid from the saponification value exercise was made alkaline with 1.0 ml of aqueous 3.0 M potassium hydroxide. This was transferred to a separator and washed with 50 ml of water. The solution was extracted three times while warm with 50 ml quantities of diethyl ether. Each was poured into another separator containing 20 ml of water. The third extract was then added and all shaken properly with 20 ml of water purified water. The ether extract was washed with 20 ml of aqueous 0.5 M potassium hydroxide solution and twice with 20 ml quantity of water until the wash was no longer alkaline to phenolphthalien. The ether extract was poured into a conical flask and the weight noted. The solvent was evaporated and the residue recovered in oily form. The flask was reweighed to get the weight of residue plus the flask. The difference between the weight of the empty flask and the weight of the residue and the flask gives the weight of the residue. The experiment was carried out in triplicates and mean value determined. The unsaponified matter was determined using Equation 6. (AOAC, 1980; Ockerman, 1991).

$$\text{Unsaponifiable matter} = \frac{\text{weight of residues}}{\text{weight of sample}} \times \frac{100}{1} \qquad (6)$$

Peroxide value

Pig fat sample (5.0 g) was weighed into a 250 ml stoppered conical flask and 30 ml acetic acid chloroform mixture (3:2) was added to the flask and swirled to dissolve, 0.5 ml saturated potassium iodide was added and the mixture allowed to stand for 1 minute with occasional shaking. Then, 30 ml of water was added. The liberated iodine was then titrated with 0.1 N sodium thiosulphate solution until the yellow colour disappeared, 0.5 ml starch solution was added as indicator and titration continued until the blue colour disappeared. The volume of titre ($\eta_1$mls) was noted. Blank determination without fat was conducted

and volume of titre noted ($\eta_2$mls). Determinations were made in triplicates. The peroxide value was then calculated using Equation 7. (Ockerman, 1991 and Ronald *et al*., 1991).

$$\text{Peroxide value} = \frac{\text{titre x N x 100}}{\text{weight of sample}} \qquad (7)$$

Where titre = No of millilitres of sodium thiosulphate used (Blank corrected).

N = Normality of sodium thiosulphate

Viscosity

This was determined according to the official method in BP (1988). A suspended level viscometer (Size 2, Pyrex, England) was used for this determination. A sample of 20 g of the fat was melted and filled through the tube at 30 °C. The time taken by the fat to flow from top edge of the upper neck of the bulb to the top edge of the lower neck of the bulb was noted in seconds. The dynamic viscosity (η) in Pascal seconds (Pa s) was determined using Equation 8. This was done in triplicates and mean value employed.

$$\eta = k\rho t \qquad (8)$$

Where k = 0.1 mmS (Nominal viscometer constant obtained from table of values, BP 1988)

ρ = Mass/volume obtained by multiplying the relative density of the fluid being examined by 0.998203 (density of water at same temperature of 30 °C)

t = time in seconds for the meniscus to fall from upper neck to bottom neck of the bulb

Slip melting point

A melting point capillary tube with one end previously sealed was half filled with the sample of frozen fat. This was heated in a melting point apparatus (Gallenkamp, UK). The temperature at which the sample become sufficiently fluid was taken as the slip melting point. This was done in triplicates and mean values determined.

Solidification point

The thermistor cryoscope method described by Association of Analytical Chemists (A.O.A.C) was adopted. A sample 5.0 g of the frozen fat was heated in a beaker over a hot water bath maintained at a temperature of 80 °C until the fat completely melted. A thermometer (digital) was immersed into the beaker and the sample allowed to cool. The temperature at which the oil solidifies was noted as the solidification point (constant temperature), observed after crystals were formed (A.O.A.C, 1984 and Paquot, 1979). This was repeated in triplicates and mean values reported.

Smoke point

The Cleveland open cup method recommended by American Oil Chemist Society (A.O.C.S) was adopted with slight modifications. A sample of one hundred millilitres of the melted fat was poured into a beaker and placed over a Bunsen burner which was turned on. The temperature at which a bluish smoke started coming out was noted using a digital meat pocket thermometer of capacity - 40 to 230 °C which beeped at the smoke point. The temperature at which the smoke stopped was also noted. This experiment was repeated in triplicates and mean values determined (A.O.C.S, 2011).

Flash point

A sample of 10 ml volume of the melted fat was poured into an evaporating dish. A thermometer of capacity - 40 - 230 °C was suspended at the centre of the dish so that the bulb just dipped inside the oil without touching the bottom of the dish. This was placed on an electric stove and the temperature of the oil raised gradually. The temperature at which the oil started flashing (when flame was applied) without supporting combustion was noted as flash point. Determination was done in triplicates and mean values reported (Detwiter and Markley, 1990).

Gas chromatography-Mass spectroscopy (GC-MS)

GC-MS analysis of the fat was done using GCMS QP2010 Plus (Shimadzu Japan) system comprising an AOC-20i auto-sampler. The system was equipped with mass selective detector with an ion source having temperature 200 °C and interface temperature 250 °C. Capillary column used for MS analysis was Elite-1 fused silica capillary column with 30 mm × 0.25 mm (length × diameter) and 0.25 μm of film thickness. The temperature of the injector was adjusted to 250 °C, possessing a split injection mode at a pressure of 116.9 kPa. The initial temperature applied was 70 °C (3 min), which was further programmed to increase to 250 °C at a ramp rate of 10 °C/min. Helium (>

99.99%) was used as carrier gas with 49.2 cm/sec of linear velocity. The total flow programed was 40.8 ml/min with column flow of 1.80 ml/min. The MS program starting time was 3.00 min which ended at 24.00 min, with event time of 0.50 sec, scan speed of 666 µl sec^{-1} and scan range of 30-350 m/z.

A sample (5 mg) solution was injected into the GC inlet where it vaporized and swept into chromatographic column by a carrier gas. The solution flowed through the column and the mixtures were separated by virtue of their relative interaction with the coating of the column (stationary phase) and the carrier gas. The spectrometer broke the molecules into ionized fragments which were detected by mass to charge ratio. The spectrum of the sample solution was compared with the NIST library database and the compounds present identified (NIST, 2010).

Preparation of Ibuprofen granules

Using the formula in Table 1, melt granulation was employed in preparing batches of matrix granules with SSD fat while wet granulation was used for a batch of conventional granules with maize starch mucilage. The required quantities of ibuprofen powder and the molten SSD fat or maize starch mucilage were sufficiently triturated in a mortar with a pestle to form a homogeneous mixture. The mixture was force-screened through a size 1.7 mm sieve and granules obtained were passed through a sieve of smaller size (700 µm). Resulting granules were stored in airtight bottles in a desiccator with activated silica gel before their evaluations.

Evaluation of granules

The following micromeritic properties of the formulated granules were evaluated;

Bulk and tapped densities

Granules (5.0 g) was loosely poured into the measuring cylinder and the volume occupied was noted. The cylinder was subjected to 100 taps and the final tapped volume noted. The bulk and tapped densities were calculated using the volumes occupied by the granules.

Carr's index

The difference between the tapped densities and bulk densities was divided by the tapped density and result expressed as percentage.

Hausner's ratio

The ratio was determined by dividing the tapped density with the bulk density of the granules.

Angle of repose

The fixed funnel method was used. A funnel was clamped with the tip about 3 cm above a graph paper placed on a flat surface. Exactly 5.0 g of the granules were carefully poured through the funnel forming a cone heap of granules on the graph paper. The radius or mean diameter of the base of the cone was determined and the angle of repose calculated using Equation 9.

$$\theta = \tan^{-1}(h/r) \qquad (9)$$

Where θ = angle of repose, h = height of the heap of granules and r = radius of the base of the heap of granules.

Filling of granules into capsules

Samples of the granules equivalent to 200 mg ibuprofen were manually filled into hard gelatin capsules shells of 250 mg capacity. The capsules were stored in air tight containers containing activated silica gel as a desiccant before their use in the *in vitro* dissolution studies.

***In vitro* dissolution studies**

The USP (2004) paddle method was used. A dissolution apparatus (Caleva ST7, UK) containing 900 ml of phosphate buffer (pH 7.2) maintained at 37 ± 0.5 °C and a paddle revolution of 50 rpm was used. Two capsules from each batch was introduced into the dissolution and a 5 ml sample was withdrawn from the leaching fluid at predetermined intervals for 4 h with a pipette fitted with a cotton wool plug. The withdrawn sample was replaced with equal amount of fresh dissolution medium kept at the sample temperature. The samples withdrawn were filtered, diluted twice and their absorbance determined with a UV visible spectrophotometer at a wavelength (λ max) of 221 nm (T70, PG Instruments Ltd, USA). The determinations were carried out in triplicates and mean values reported. The corresponding amount of ibuprofen released at any time was extrapolated from the equation (y = 0.052x) obtained from the standard curve of pure ibuprofen previously obtained.

Table 1: Formula for the preparation of ibuprofen granules

Ingredients	Batches					
	A	**B**	**C**	**D**	**E**	**F**
Ibuprofen (mg)	200	200	200	200	200	200
Sus scrofa domesticus purified fat (mg)	10	15	20	25	30	-
Maize starch mucilage (15 %w/w)	-	-	-	-	-	qs

RESULTS

Percentage yield

The percentage yield from the wet rendering process of extraction of the fat from the adipose tissues of the domestic pig was 85 %.

Organoleptic properties of purified SSD fat

Results of organoleptic properties of SSD fat are shown in Table 2. The fat was odourless and bland in taste, off white (solid form) and slight yellowish in liquid form with a smooth texture.

Table 2: Organoleptic properties of the purified SSD fat

Parameters evaluated	Characteristic feature
Odour	Odourless
Taste	Bland
Colour	Off white (solid), slight yellowish (liquid)
Texture	Smooth

Physicochemical properties of purified SSD fat

Results of physicochemical properties of the purified extracted SSD fat are shown in Table 3. The SSD fat was soluble in organic solvents, insoluble in water and has a pH of 7.4 ± 0.5. The iodine value was 48.22 ± 2.3 while the acid value was 3.4 ± 0.10. The saponification value was 196.35 ± 0.7 and the unsaponifiable matter value was 0.9 ± 0.15 %. The melting point range was 30 - 32 °C while the peroxide value and viscosity were 11 ± 0.76 meq/kg and 147.40 ± 1.02 millipascal respectively. Other properties of the fat were solidification point (28 °C ± 0.10), smoke point (121 °C ± 0.10), flash point (202 °C ± 0.10) and specific gravity (0.915 ± 0.002).

Gas chromatography-mass spectroscopy (GCMS)

The result from the GCMS analysis of the SSD fat extract is shown in Figure 1. The major components identified were oleic acid (peak 9, 31.62 %), stearic (peak 8, 18.17 %) and palmitic (peak 10, 13.94 %) acids. Trace components included linolenic acid (peak 11), esters of palmitic acid (peaks 5 and 6) and capric acid (peak 2).

Micromeritic properties

The results of the micromeritic properties of the ibuprofen granules prepared with *Sus scrofa domesticus* fat and starch mucilage are presented in Table 4.

The angle of repose values of the granules ranged from 24.5 – 46.3° with those batches formulated with SSD showing increasing value with increasing concentration of the fat. The Carr's indices and Hausner's ratios of the granules which ranged from 29.0 - 40.0 % and 1.11-1.71 respectively, also exhibited increasing values with increasing concentrations of the SSD fat. On the other hand, the flow rates of the granules which was between 0.10-1.43 g/sec showed a decreasing flow with increasing concentrations of the SSD fat.

Table 3: Physicochemical properties of the purified SSD fat

Parameter		Characteristic feature
Solubility:	Water	Insoluble
	Phosphate buffer	Soluble
	Acetone	Soluble
	Chloroform	Soluble
	Ethanol	Soluble
	Petroleum ether	Soluble
	Benzene	Soluble
	Heptane	Soluble
	Hexane	Soluble
pH		7.4 ± 0.5
Iodine value		48.22 ± 2.3
Acid value		3.4 ± 0.10
Saponification value		196.35 ± 0.70
Unsaponificable matter		0.9 % ± 0.15
Peroxide value		11 ± 0.76 meq/kg
Viscosity		147.40 ± 1.02 millipascal
Melting point		30 - 32 °C
Solidification point		28 °C ± 0.10
Smoke point		121°C ± 0.10
Flash point		202 °C ± 0.10
Specific gravity		0.915 ± 0.002

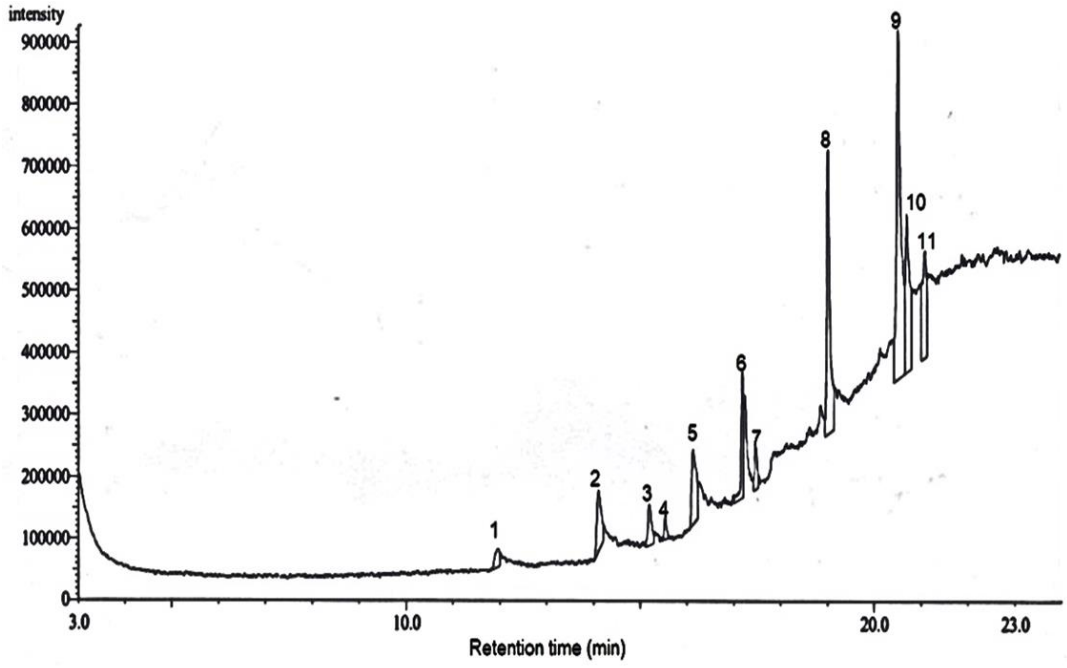

Figure 1: GCMS spectrum of the purified Sus scrofa domesticus fat

Table 4: Micromeritic properties of the formulated ibuprofen granules

Batch	Fat conc. (% w/w)	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Angle of repose (°)	Carr index (%)	Hausner's ratio	Flow rate g/sec
A	5.0	0.40 ± 0.01	0.58 ± 0.03	39.0 ± 1.00	29 ± 0.02	1.41 ± 0.02	0.35
B	7.5	0.41 ± 0.03	0.58 ± 0.04	40.0 ± 1.25	31 ± 0.02	1.45 ± 0.21	0.26
C	10	0.34 ± 0.02	0.55 ± 0.03	40.4 ± 2.10	38 ± 0.01	1.61 ± 0.12	0.15
D	12.5	0.40 ± 0.02	0.51 ± 0.42	42.2 ± 0.21	39 ± 0.02	1.70 ± 0.33	0.10
E	15	0.41 ± 0.02	0.50 ± 0.43	46.3 ± 1.20	40 ± 0.02	1.72 ± 0.12	0.10
F	0	0.30 ± 0.02	0.52 ± 0.03	24.5 ± 0.12	36.2 ± 1.2	1.11 ± 0.22	1.43

***In vitro* drug release**

The result of the dissolution profiles of ibuprofen matrix granules packed in gelatin capsules are shown in Figure 2. The results show that the drug release pattern varied as concentration of the SSD fat was increased. The higher the concentration of the fat, the lower the release of ibuprofen from the granules. The drug release pattern from all the batches showed a burst release within the first 5 min followed by retarded release which increased with increase in the SSD fat. Batches D and E containing 12.5 and 15 % of the fat did not release their drug content within the 4 h of testing while batch F, prepared with the starch mucilage achieve a 100 % release within 1.0 h.

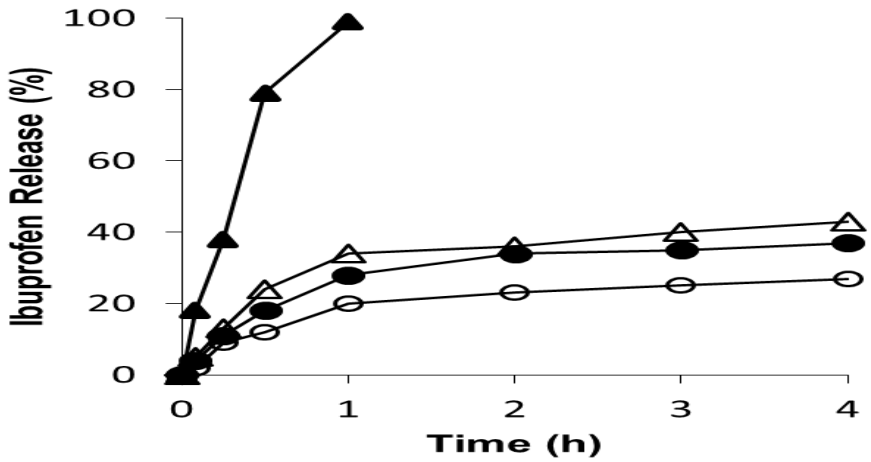

Figure 2: Dissolution profile of the formulated ibuprofen granules using varying amounts (w/w) of SSD fat and maize starch mucilage. SSD fat: 5 % (△), 7.5 % (●), 10 % (O); Maize starch mucilage: 15 % (▲)

DISCUSSION

This study evaluated the physicochemical characteristics of *Sus scrofa domesticus* fat (SSD fat) and the possibility of its utilization as a matrix former in the formulation of ibuprofen matrix granules. The percentage yield of 85 % from the fat extraction process is considered high especially as a natural product. The fat solubility profile and pH of 7.4 makes the extracted SSD fat a source that can be explored in the pharmaceutical industry in the formulation of emulsions and creams. The fat's other physicochemical parameters such as the iodine value which measures the number of grams of iodine absorbed by 100 grams of oil indicating the amount of unsaturation or double bond present in the fat shows that the SSD fat is an oil containing fatty acids with reasonable unsaturation when compared with the values of some oils such as coconut oil (6-9), palm oil (51-54), castor oil (82-88) or olive oil (75-94) and comparable to some other animal fat such as bone oil (52-55) or lard (58-65) (Karleskind, 1992).

The saponification value and unsaponifiable matter of the SSD fat which is the number of the milligrams of potassium hydroxide required to neutralize the fatty

acids resulting from hydrolysis and the material left behind after saponification which remains non-volatile respectively also compares favourably with bone oil (192-200) or lard (192-197) (Karleskind, 1992). A viscosity value of 147.40 millipascal shows that the SSD fat was of a stiffer consistency than other animal fats and oils with lower values. Also, the high values of the fat's smoke and flash point indicates that the fat or oil can be useful for deep frying (British Pharmacopoeia, 2010). Similar high values have been reported by the United States Department of Agriculture (USDA) and American Oil Chemists Society (A.O.C.S, 2011).

The viscosity, melting point, solidification point and specific gravity of the fat are relevant in granule formation with the fat. These properties mean that the fat is stiff, melts at a low temperature and solidifies quickly over a short temperature range. While the high viscosity of the fat will hinder easy spread of the fat over drug powder particles, the low melting and solidification points will ensure granule preparation at low temperatures and quick solidification of drug particle matrix coatings. Temperatures as high as 80 and 62 °C are needed for granule preparation with carnauba and bees waxes respectively (Tinto *et al*., 2017).

The GCMS spectrum of the extracted SSD fat confirms the fatty acids composition of the fat.

The purified fat from SSD contains mostly fatty acids such as oleic acid, palmitic acid, stearic acid, linolenic acids (Omega 3 fatty acids), gamma linolenic acids (Omega-6-fatty acids) and their esters. The palmitic and stearic acids are saturated while the oleic, gamma linolenic and linolenic acids are unsaturated (Ajayi, 2009, Omeje *et al*., 2018). The omega 6 and omega 3 fatty acids contained in the pure fat are useful antioxidants. Previous studies on the composition of pig fat indicated the abundance of three major fatty acids - linolenic, stearic and palmitic acids. The amounts of these fatty acids in the fat has been traced to the diets and variety of the pig from which the fat is gotten (McEvoy *et al*., 2000; Zamora-Rojas *et al.*, 2013; Ajayi *et al*., 2014).

Granules formulated with the purified SSD fat exhibited varied micromeritic properties. The differences in their bulk and tapped densities which reflects the packing fraction and compressibility property of the granules was observed to decrease with increasing concentration of the fat. This decrease can also be seen in all the other properties of the granules, from their angles of repose through their Carr's indices, Hausner's ratios and flow rate. The implication is that there is a reduction in the flow properties of the granules as the fat concentration was increased in the granules formulation and good flow properties are very essential in establishing weight and content uniformity during capsule filling and tableting. Another implication is the compressibility of the granules. This property also decreased as the concentration of the fat was increased. Generally, all the batches of granules produced with the purified SSD fat had poor flow properties and poor compressibility. Only the conventional granules exhibited satisfactory flow properties with low angle of repose and a high flow rate.

The *in-vitro* release profile for the ibuprofen encapsulated granules formulated with the purified SSD fat at concentrations 5.0 - 10% w/w showed retarded release of the drug with initial prompt release within the first 5 min while the 12.5 and 15 % w/w did not release their drug content. This can be taken that ibuprofen release from the granules was concentration-dependent; the higher the concentration of the SSD fat, the lower the percentage amount of drug released. These results suggest that SSD fat is a release retardant with potentials for sustained release and it could be applied in the formulation of sustained release dosage forms, particularly for drugs with short biologic half-life in order to enhance patient acceptance and compliance while reducing the frequency of dosing

CONCLUSION

The physicochemical properties of SSD fat was evaluated and found to possess favourable potential properties that will be relevant in the design and formulation of drug delivery system. The fat was successfully employed in the formulation of ibuprofen granules. Dissolution profiles of the formulated ibuprofen granules showed increasing drug release retardation with increasing concentrations of the fat. Hence the SSD fat has a potential application as a matrix former and may find application in sustained release drug delivery particularly for drugs with short biological half-life that require frequent dosing.

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