Journal of Natural Product Research and Applications (JNPRA)

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Extraction characterization and investigation of breadfruit seed oil for possible pharmaceutical application

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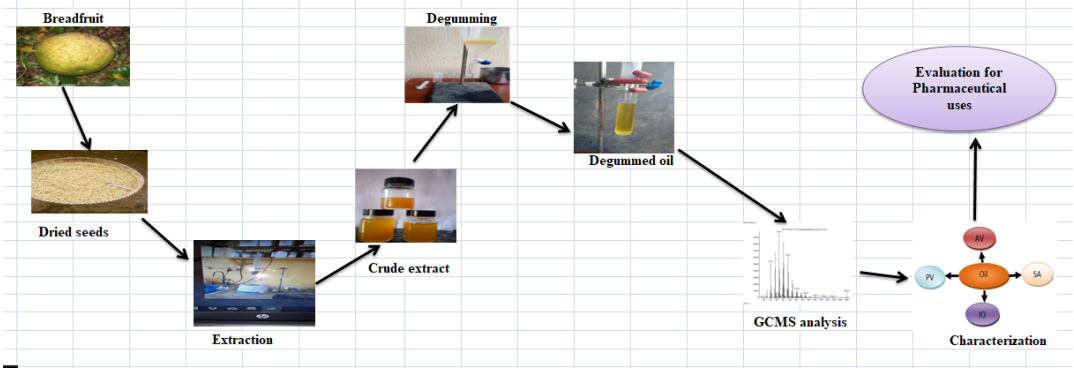
Highlights

- Extraction of oil from breadfruit seeds by a cold maceration and by soxhlet methods resulted in oil yields of 13.69 % and 23.54 % respectively.
- Fatty acid determination showed that the oil contained predominantly poly unsaturated long chain fatty acids.
- Values obtained for most of the determined physicochemical parameters were suggestive of the oil's suitability for edible uses and pharmaceutical application.
- The hydrolyzed form of the oil exhibited higher solubility for selected poorly water soluble drugs than the crude form.

Graphical abstract



Abstract
This work aimed at extracting, characterizing and evaluating breadfruit seed oil for potential pharmaceutical applications. The breadfruit oil was purified by degumming, bleaching, neutralization and enzyme hydrolysis. The oil was characterized for the yield, pH value, iodine, acid, peroxide and saponification values and fatty acid composition. Results obtained were interpreted with respect to their relevance in pharmaceutical formulations.The percentage yields of the oil from the soxhlet procedure was 23.54 % while the yield from the cold maceration extraction method was 13.69 %. The iodine, acid, peroxide and saponification values were, 17.50 ± 0.05, 3.40 ± 0.33, 7.20 ± 0.08, and 236.46 ± 0.02 respectively. Gas chromatographic- infrared studies identified five polyunsaturated long chain fatty acids. The breadfruit oil has good edible properties by virtue of its moderate acid and peroxide values. Its high iodine and low saponification values may necessitate the addition of antioxidants in pharmaceutical formulations containing breadfruit oil. The results obtained in this work suggest that breadfruit oil has good potential for pharmaceutical applications.

Keywords: extraction; polyunsaturated; chromatography; degumming; hydrolysis; pharmaceutical.

1. Introduction

Plant oils have become an attractive component of many foods, pharmaceutical and cosmetics formulations ostensibly due to their biocompatibility, biodegradability, biosafety and relative non-immunogenicity (Fallah et al., 2022), They also have available sources in many plant parts which in themselves, are widely distributed in many different vegetations and cultures. Plant oils are also in the group of materials described as "Generally Recognized as Save (GRAS)" by the United States Food and Drugs Administration (eCFR 2018).

Plant oils and fats belong to the class of biological substances known as lipids. They are generally edible and widely consumed as part of a daily meals in almost all cultures. Chemically, oils and fats belong to the ester group of organic compounds and are made up of three fatty acids units joined to a glycerol unit (trihydroxy alcohol). They are described by features relating to the number of carbon atoms in the chain, the nature of the carbon - carbon linking bonds (saturated or unsaturated) as well as the position(s) of the unsaturated bond (if any). On these bases, fatty acids are classified as saturated fatty acid (SFA) for the types having no double bond, monounsaturated fatty acid (MUFA) for types with only one double bond and polyunsaturated fatty acid (PUFA) for fatty acids with more than one unsaturated bonds. Orsavova et al. (2015). Fatty acids that have 4 – 6 carbon atoms in their structure are referred to as short chain fatty acids (SCFAs) while the types possessing 6 – 12 carbons are medium chain fatty acids (MCFAs). Long chain fatty acids (LCFAs) have 14 – 20 carbon atoms in the carbon chain (Saxena et al., 2013; Gurram et al., 2014).

Compared to mineral oils and animal fats, plant oils find wider uses in the food and pharmaceutical industries because of their greater safety profiles, higher gastrointestinal digestibility and minimal associated health hazards (Fallah et al., 2022). Due to such potentials, plant oils have become subject of many research endeavors not only the chemistry but also in the pharmaceutical sciences fields (Rueda et al., 2015). A few Nigerian plant oils have been successfully extracted, characterized and investigated for varied applications. Orsavova et al. (2015) characterized the fatty acid contents of 14 plant oils in an attempt to ascertain the dependence of cardiovascular mortality on the dietary intake of fatty acids. Obite et al. (2008) utilized the duo of palm kernel (*Elaeis guineensis*) oil (PKO) and palm oil (PO) for the formulation of self-emulsifying drug delivery system (SEDDS) to improve the

solubility and in vitro release of metronidazole - a poorly water soluble drug. The formulation exhibited improved drug performance and product stability. Similarly, Obite et al. (2011) successfully formulated a self-nanoemulsifying drug delivery system (SNEDDS) based on melon (*Cucumis melo*) oil and admixture of cow (*Bos taurus*) fat for the oral delivery of indomethacin. A few challenges have been associated with the use of plant oils in pharmaceutical product formulation. In their natural state, most plant oils are very unstable, subject to oxidative degradation, rancidity and deterioration in aesthetic and organoleptic qualities (Prajapati et al., 2011). The high viscosity of some plant oils and the tendency of some to solidify at room temperature limit their utilization in the formulation of liquid pharmaceutical products. Moreso, some plant oils posses natural colours, odour and tastes that make them unattractive for pharmaceutical uses.

.African breadfruit (*Treculia africana*) is a large, slow-growing, evergreen tree with a dense, spreading crown; usually growing 15 - 50 m tall (Ajiwe et al., 1995). The plant belongs to the family Moraceae which are widely cultivated in the tropics. The tree is, however, reported to be native to East Indies but grow in many tropical countries including Nigeria, Senegal, Ghana and Sudan (TPD, 1995). The tree produces spherical bulky fruits which bear large quantity of seeds per fruit head. The seeds are consumed locally as snacks in fried form or cooked as porridge. Ethnomedicinaly, the seed and stem back extracts of the tree are used as antimicrobial, anti tussive, wound healing and antidiabetic remedies (Ojimelukwe and Ugwuona, 2021)). The flavonoid constituents of (*T.africana*) extracts is also reported to possess scavenging properties against free radicals in the body (Cathrine, 2020). Similarly, the anti aging and cell protective properties of both seed and leaf extracts of breadfruit-loaded creams has been reported (Naz et al., 2016). From th industrial use oerspective, Ajiwe et al., (1995) reported that breadfruit oil was predominantly unsaturated and semi-drying with high saponification and acid values and could be used for making soaps, hair shampoos and alkyd resins. Our literature search did not; however find any work that investigated the suitability of breadfruit (*T. africana*) oil for pharmaceutical formulations.

2. Materials and methods

Fresh and matured African breadfruit (*T. africana*) heads were purchased from a local market, Afor Obollo in Udenu Local Government Area of Enugu State, South East Nigeria The samples were identified by Mr. Patrick Obi a taxonomist in the Department of Pharmacognosy, Enugu State University of Science and Technology, Enugu State who also issued a registration number, PCG/001/002 and deposited a voucher specimen at the faculty herbarium. All other reagents and chemicals were of analytical grades and were used as purchased except otherwise specified by the manufacturer.

2.1. Recovery of breadfruit seeds from fruit heads

A three kilograms (3 kg) weight of breadfruit seeds were recovered from the ripe and soft fruit heads by manual pressing and picking. The seeds were, parboiled at 100 ^{o}C for 15 min and drained to remove excess water. The parboiled seeds were threshed using commercial attrition mill to free the seeds from the pericarps. The clean seeds were weighed, sun-dried for 75 h and thereafter milled to obtain fine powder using a domestic grinder (Zetech Machines D4, Aba) following the method of Nwabueze and Nwafor (2014). The powder was weighed and stored at room temperature in tightly sealed polyethylene plastic container

2.2. Extraction of breadfruit oil from seeds

Oil was extracted from African breadfruit seeds using two extraction techniques, namely; soxhlet extraction and cold maceration. Soxhlet extractor (ST 243 Soxtectm Denmark) was

used for the extraction in accordance with the Association of Official Analytical Chemists AOAC, (995) procedure.. In brief, a 250 mL of n-hexane was used as the solvent to extract oil from 200g of dry bread fruit seed powder. The oil was recovered from the solvent using a rotary evaporator, (Hei-Vap Core, Heidolph Instruments, GMB Germany) as described by Azwanida (2015).

Oil extraction by cold maceration was carried out using the modified process reported by Abubakar et al. (2014). Herein, a 3 kg of the powdered seed was placed in a 2.5 L capacity amber colored glass bottle containing 600 mL of n-hexane. The bottle was tightly screwed to prevent solvent evaporation, and was allowed to stand for 7 days with intermittent shaking after which the liquid was strained through a piece of cotton wool tightly stacked into the discharge pipe of a plastic funnel.

2.3. Determination of the oil yield

The yields of oils from the two different extraction techniques were calculated using the equation:

$$Yeild = \frac{wo}{ws} \times 100 \text{ ----------Eqn 1.}$$

Where: *W*o = weight of the extracted oil and Ws = weight of the seed flour. The extraction and calculation of yields were done in triplicate processes and the yield values reported were calculated as mean ± standard deviation (SD).

2.4. Purification of extracted oil

The breadfruit oil was treated to improve the quality, reduce viscosity, and enhance the clarity and to remove associated impurities. In this case, four stages of purification were carried out namely: degumming, neutralization, bleaching and deodorization.

2.4.1. Degumming of oil

A modified version of the method reported by Mounts (1978) was employed in degumming the oils. In brief, a 50 % w/w (based on oil weight) quantity of hot water (previously heated to 100 ^{o}C) was added to the oil and the mixture was agitated in a flask shaker (Flask shaker-FS,1 Stuart^{R} Germany) for 50 min. The hot mixture was placed in a separatory funnel and allowed to stand for 3 h. The water layer was carefully removed while the oil portion was recovered.

2.4.2. Neutralization of oil

The oil neutralization method reported by Jahani et al. (2008) was adopted with slight modification. Briefly, a 30 g of the degummed oil was poured into a beaker and heated to 80 °C. A 40 ml of 0.1 M NaOH was added and the mixture stirred to obtain a uniform solution. To this solution, sodium chloride equivalent to 10 % of the weight of the oil was added and stirred. The mixture was then transferred into a separatory funnel and allowed to stand for 1h so that the soap formed was separated from the oil. Two portions of 100 ml hot water were separately added to the oil solution to remove any remaining soap. The neutralized oil was then drawn off into a beaker and used for the next process of purification.

2.4.3. Bleaching and deodorization of oil

The oil was bleached and deodorized using activated charcoal as reported by Obite et al. (2000). A 2 %w/w suspension of activated charcoal in oil was heated in a beaker at 90 °C for 1 h. Thereafter the suspension was vacuum-filtered using Burkner's funnel.

2.5. Modification of oil

The extracted oil was further subjected to the enzyme catalyzed hydrolysis with view to converting some long chain fatty acids to medium and short chain types. This was expected to be achieved by breaking some bonds of the long chain fatty acids.

In the current work, hydrolysis of the breadfruit oil was performed to increase its drug solubilising capacity. The enzyme catalyzed hydrolysis technique using *C. rugosa* lipase as adopted by Serri et al. (2008) was used. Briefly described, a 3 g weight of the oil and 30 ml of iso-octane were placed in a 250 ml capacity stoppered conical flask. Thereafter, 30 ml of phosphate buffer pH 7.5 was introduced into the flask to give an oil to buffer solution ratio of 1:1. Two separate layers were obtained. The enzymatic reactions were induced by introducing 0.3 g of lipase (*C. rugosa*) into the flask. The mixture was then agitated in an orbital shaker (Certomat, B. Braun) at 45 ^{o}C and at a speed of 200 rpm for 1h, after which the oil phase was removed for further uses.

2.6. Characterization of the breadfruit oil

Various standard methods as reported by Kyari (2008) were used to characterize the oil for saponification, iodine, acid and peroxide values. The oil was also evaluated for pH and viscosity. Quantitative results obtained were also calculated as mean ± SD with n = 3.

2.6.1. Determination of the acid values of breadfruit oil

Acid value refers to the number of milligrams of potassium hydroxide (KOH) required to neutralize 1 gram of an oil without induced acidity (Manzoor et al., 2007). The acid value was determined using the following AOCS (1995) method. A10 g quantity of the sample was placed in a 250 mL capacity conical flask. Exactly 100 mL of neutral ethyl alcohol was then added and the mixture heated to boiling. The resulting solution was titrated with 0.1N KOH using 2 drops of phenolphthalein as indicator. The flask was shaken continuously until persistent pink color that lasted for at least 1 min was obtained. The acid values (AV) were calculated using the formula:

$$AV = 0.56 \times V \quad \text{---------- Eqn 2}$$

Where: V is the volume of 0.1N KOH in mL.

2.6.2. Determination of the saponification values of bread fruit oil

The saponification value (SV) was determined using the America Oil Chemist's Society, AOCS (1995) method. The process involved complete saponification of the oil with excess of alkali (KOH) and then determination of the excess using back titration. Herein, a 2.0 g quantity of the oil was placed in a conical flask containing 30 mL of ethanolic KOH and was heated gently (reflux condenser) for 30 min at which saponification was completed indicated by the absence of oil matter and appearance of clear solution. After sample has cooled, 1.0 mL of phenolphthalein indicator was added and solution titrated with 0.1 M HCl until a pink color appeared. The above procedure was carried out for a blank solution using same quantity of KOH solution but without the oil. The tests and blank titrations were each done in triplicate and the average titres for each calculated. The saponification value was calculated using the formula:

$$\text{Saponification Value} = \frac{(Vo - Vi)}{M} \times 56.1 \times N \quad \text{----------} \qquad \text{Eqn. 3}$$

Where: V_O = volume of solution used for blank titration, V_I = volume of solution used for test titration, N = actual Normality of the HCl used and M = mass of sample

2.6.3. Determination of iodine value of extracted oil

The ISO 3961 method was adopted for the iodine value determination. Briefly, 0.4g of the oil sample was weighed into a conical flask containing 20 mL of carbon tetra chloride as solvent. Twenty-five mL volume of Dam's reagent was added to the flask using a safety pipette in a fume chamber. A stopper was then inserted and the content of the flask vigorously swirled. The flask was placed in the dark cupboard for 2.5 h. At the end of this period, 20 mL of a 10 % aqueous potassium iodide and 125 mL of distilled water were added using a measuring cylinder. The mixture was titrated with 0.1M sodium thiosulphate solution until the existing yellow colour disappeared. Few drops of 1 % starch indicator was added and the titration continued by adding the sodium thiosulphate drop wise until blue coloration disappeared following vigorous shaking. This procedure was repeated for the blank titration. The iodine value (IV) was calculated using equation: 4.

$$IV = \frac{12.69C(V1-V2)12.69C}{M} \text{ ---------- Eqn. 4}$$

Where: C = molar concentration of sodium thiosulphate used, V_1 = volume of sodium thiosulphate used for blank. V_2 = volume of sodium thiosulphate used for determination and M = mass of oil sample in grams.

2.6.4. Determination of peroxide value

The procedure used by Kyari (2008) was employed in the current determination with a slight modification. To a 1.0 g weight of the oil placed in a 250 mL capacity round bottomed flask was added 1g of potassium iodide. A 20 mL volume of 2:1 ratio mixture of glacial acetic acid and chloroform was also added and the mixture boiled for 1 min. The hot solution was then poured into a flask containing 20 mL of 5 % potassium iodide. Three drops of starch solution was also added to the solution which was then shaken gently. The solution was titrated with 0.024 N sodium thiosulphate solution and the peroxide value calculated using equation 5.

$$PV = \frac{Sx\ Nx103}{W} \text{ ----------Eqn. 5}$$

Where: S = volume of Sodium thiosulphate (mL), N = normality of Sodium thiosulphate solution and W= weight of oil in grams.

2.6.5. Profiling of breadfruit oil for fatty acid composition

The fatty acid composition of the oil was studied using a hyphenated gas chromatography/mass spectrometer equipment (Agilent Technologies-7890A GC and 5977B MSD) with experimental conditions of GC system as follows: Hp 5 MS capillary standard non-polar column, dimension: 30M. ID: 0.25mm. film thickness : 0.25 µm. and flow rate of mobile phase (carrier gas: HE) set at 1.0 mL/min. In the mass spectroscopy part, temperature program (oven temperature) was 40 ^{o} C raised to 250 ^{o} C at 5 ^{o}C/min and injection volume of 1 µL. Sample dissolved in methanol was run full scan at a range of 40.650 m/z and the results compared using Nist mass spectral library search program.

2.6.6. Drug solubility screening in crude and hydrolysed breadfruit oil

Three known poorly water soluble drugs namely, aceclofenac, ibuprofen and lumefantrin were screened to determine their relative solubility in the crude and hydrolyzed breadfruit oils. For each determination, an excess amount of the drug sample (500 mg) was put in a 5 mL vial containing 2 mL of the oil. The vials were securely covered and the contents mixed for 10 min using a vortex mixer. The mixtures were kept at 25±1.0 ^{o}C (ambient temperature) for 72 h to equilibrate. The samples were then removed from the shaker and centrifuged at

3000 rpm for 15 min. The supernatants were separately taken and filtered through a 0.45 µm whattman filter paper. The concentrations of the drugs in the various supernatants were determined by uv spectrophotometry after a 10-fold dilution with methanol and at the appropriate wavelengths for each drug.

3. Results and discussion

3.1. Oil yield

Table 1 contains information and data on the two extraction processes and their oil yields.

Table 1. Oil extraction and yield data for breadfruit seeds.

Parameters	Soxhlet extraction (SE)	Cold Maceration (CM)
Total volume of n-hexane	250 mL	600 mL
Extraction period (batch process)	10 h	168 h
Extraction temperature (^{o} C)	70	Ambient
Weight of dry powder per extraction batch	200.00 g	3.00 kg
Total weight of oil from all batches (g)	114.34	129.00
Oil yield (%)	23.54	13.69

Fig. 1. Crude breadfruit oil

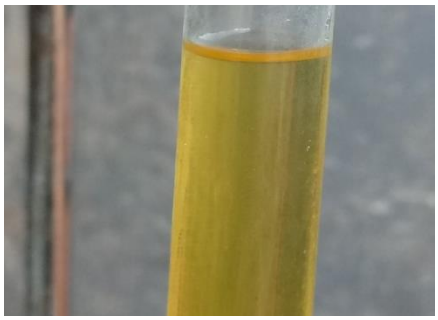


Fig 2. Purified breadfruit oil

The yield of oil from the breadfruit seeds obtained through soxhlet extraction and cold maceration methods were 23.54 and 13.69 %, respectively. These results suggest that the SE method is the more efficient technique. Interestingly, the results of yield obtained in our evaluation using the SE method is much higher when compared to the values of 15.58 – 19.30 % reported by Nwabueze and Nwafor (2014). This improved yield may be attributed to the quality of fruits used and the improved extraction strategies and procedure. The earlier researchers conducted each extraction run for a period of 40 min while ours lasted for 1 hr. Selection of well matured and healthy fruits may have equally improved the yield of oil. Manzoor et al. (2007) reported the impact of environmental, geological and seasonal differences on oil yields of plant materials. The yields from the *T. africana* fruits were, however, comparable to the values reported for cotton-seed (15.0 – 24.0%) and soybean (17.0 – 21.0%) (Pritchard, 1991).

3.2. Purification of the extracted oil

The purifications of the oil involved water-based degumming and heat-bleaching using activated charcoal. The resulting oil showed observable reduction in viscosity, exhibited light golden yellow color and transparent appearance, as against the viscous, deep yellow and opaque appearance of the crude sample. The lighter viscosity of the degummed oil may have

been due to the solubilization and removal of the natural phospholipid components of the oil during the degumming process. Similarly, the activated charcoal, under high temperature, adsorbed part of the natural oil coloring pigment and the characteristic odor of breadfruit oil. The implication is that degummed oil is likely to produce pharmaceutical products having better aesthetic appearance and more attractive organoleptic characteristics especially for liquid pharmaceutical formulations.

3.3. Characterization of breadfruit oil

The purified breadfruit oil was characterized for some physicochemical parameters as shown in Table 2.

Table 2. Summary and pharmaceutical implications of the physicochemical characteristics of breadfruit oil

Parameter	Value obtained	Desirable for use	Implication for pharmaceutical use	Ref.
Yield (%)	23.54 ± 14.13	High yield	Process improvement required	
Colour	Yellow	Colourless	Decolourization necessary	Nurhan (2016)
Odour	Characteristic	Odourless	Deodourization required	Nurhan (2016
State at room temp.	Liquid	Liquid	Good for purpose	
Acid value	3.40 ± 0.33	High	Low acid value desirable for pharmaceutical formulation. Neutralization required	WHO/FAO (1999)
Peroxide value	4.20 ± 0.08	>10 meqO_2/kg	Value within standard specification	WHO/FAO (1999)
Iodine value	127.50 ± 0.05	High	Antioxidant necessary in formulation. Amber coloured, air-tight packaging required.	WHO/FAO (2000)
Saponification value	75.46 ± 0.02	Low	Valur suggests presence of large molecular weight, long chan fatty acids. Hydrolysis necessary	CODEX-STAN 210 (1999)
Viscosity ($_C$P)	29.67 ± 0.07	Moderate	Moderate viscosity required for liquid formulations	

3.4. Iodine value

Iodine value is a measure of the relative degree of insaturation of the oil fatty acids.. It is an indicator of oil stability and resistance to oxidative degradation (Qin and Zhong, 2016). High iodine values may, however be a desirable edible properties (Eromosele et al., 1997).The determined iodine value of our sample is 127.50 ± 0.05. This value is relatively high suggesting the predominance of unsaturated fatty acids in the oil and greater tendency for oxidative degradation and rancidity (Siddeeg and Xia, 2015). Pharmaceutical products formulated with this oil will require the inclusion of an antioxidant and such product should be packaged in an amber colored air tight container with patient instructions to store products in cool and dry places away from direct sunlight.

3.5. Peroxide value of extracted oil

The peroxide value (PV) obtained for the oil sample was 4.20 ± 0.08 meq O_2/kg. Peroxide value is a measure of the quantity of active oxygen contained in one (1) gram of the oil

(Pandurangan et al., 2014). The value indicates to what extent the oil has undergone oxidative degradation and rancidity during processing or storage and as such can be used for quality control of oils. The 4.20 ± 0.08 value obtained for the sample oil fell within the acceptable range for good oil suitable for food and pharmaceutical application. Generally, it is recommended that fresh oils should have a peroxide value less than 10 meq O_2/kg. as values higher than 30 meq O_2/kg are associated with rancid taste (Ekwu and Nwagu, 2004; Siddeeg and Xia, 2015).

3.6. Saponification value of the oil

Kalepu et al. (2013) reported an inverse relationship between saponification value and the mean molecular weight and the average fatty acid chain lengths. High SV may suggests the dominance of medium chain fatty acid over long chain types in an oil and vice versa. The investigated breadfruit oil has a saponification value of 75.46 ± 0.02, a value considered as relatively low suggesting that the oil has predominance of long chain high molecular weight fatty acids. Interestingly, high SV portends tendency for foaming that may be a challenge for liquid pharmaceutical preparations (Rowe et al., 2006). On the contrary, the low foaming propensity of the oil (as suggested by low SV) may limit its use for pharmaceutical soap formulation due to likely poor soap effects (Siddeeg and Xia, 2015; Alyas et al., 2006).

3.7. Acid value of the oil

Acid value (AV) is a common parameter in the standard specification of fats and oils. It is the weight of potassium hydroxide (KOH) in mg needed to neutralize the organic acids present in 1g of fat or oil. This parameter is useful in the determination of the level of lipase and other physical factor-induced decomposition of glycerides (Demian et al., 1990). It equally reflects the quantity of the free fatty acids (FFA) present in the oil. Low free acid content is desirable for edible oils Kardash and Turyan (2005) and Jahani (2008). The current breadfruit oil with acid value of 3.4 ± 0.33% may be adjudged as good for pharmaceutical uses. The value compares well with that of melon (*Cucumis melo*) seed oil (a widely consumed oil) which has been reported by Obite et al. (2011) to be 4.30 ± 0.86.

3.8. Fatty acid profiles of breadfruit seed oil

A hyphenated gas chromatography/mass spectrophotometer equipment (GC/MSD - Agilent technologies, USA) was used to study the fatty acid profile of the breadfruit oil. Eighty seven (87) molecular entities were identified among which were six fatty acids. Table 3 shows the major fatty acids while Table 4 contains the GC/MS fragmentation ions of the various fatty acids.

Table 3. Fatty acid composition of breadfruit oil.

Compound	Molecular structure	Double bond	Chain length
n- hexadecanoic acid	CH3(CH2)14COOH)	nil	long
Cis-13-octadecanoic acid	$C_{18}H_{34}O_2$	2	long
9-12-octadecanoic acid	$C_{18}H_{32}O_2$	2	long
Cis-11eicosenoic acid	$CH_3(CH_2)_7CH=CH(CH_2)_9CO_2H$	1	long
9-octadecenoic acid		1	long
(linoleic acid)	$C_{18}H_{32}O$		
Oleic acid	$CH_3(CH_2)_7CH=CH(CH_2)_7CO_2H$,	1	long

Table 4. GCMS fragmentation ion of some breadfruit oil fatty acids.

Name of compounds	Molecular formula	Molecular mass (m/z)	Fragment ions (m/z)
n- hexadecanoic acid	$C_{16}H_{32}O_2$	256	43,73,87,129,187,105, 213, 230, 256
Cis-13-octadecanoic acid	$C_{18}H_{34}O_2$	284	29,55,83,111,137,166,193,222,264,284
9-12-octadecanoic acid	$C_{18}H_{32}O_2$	290	15,41,67,95,123,160,182,209,236,280
Cis- 11-eicosenoic acid	$C_{20}H_{38}O_2$	310	29, 55, 83, 111, 138, 165, 188, 208, 229, 250, 292, 310
9-octadecenoic acid	$C_{18}H_{34}O_2$	283	29, 55, 83, 111, 130, 161, 180, 199, 222, 264, 283
Oleic acid	$C_{18}H_{34}O_2$	282	41, 55, 69, 83, 97, 111, 125, 137, 180, 222, 264, 282

Of the seven fatty acids identified, one was saturated, three were mono unsaturated while two were poly unsaturated. The predominance of long chain unsaturated fatty acids would have constituted a major challenge for the use of this oil as pharmaceutical solvent for the reason of poor drug solubility and tendency for oxidative degradation of unsaturated long chain fatty acids. Cannon (2011) reported that medium chain fatty acids (MCFA) exhibit higher solubility for drugs and are less susceptible to oxidative degradation. The report also noted that MCFAs are less hydrophobic, possess higher mobility in the lipid-water interface and are more easily hydrolysed than the LCFAs. Shukla (2015), similarly reported that when long chain triglyceride (LCT) was used in their work, a higher proportion of surfactant (Cremorphor RH40) was required to form pharmaceutical microemulsions whereas the opposite was the case when a medium chain triglyceride (MCT) was used. To enhance the drug solubility, they hydrolyzed the oil.

3.9. Drug solubility studies

Figure 3 is the chart showing the relative solubility of three known poorly water soluble drugs, namely; aceclofenac, ibuprofen and lumefantrin in the crude and hydrolyzed breadfruit oils.

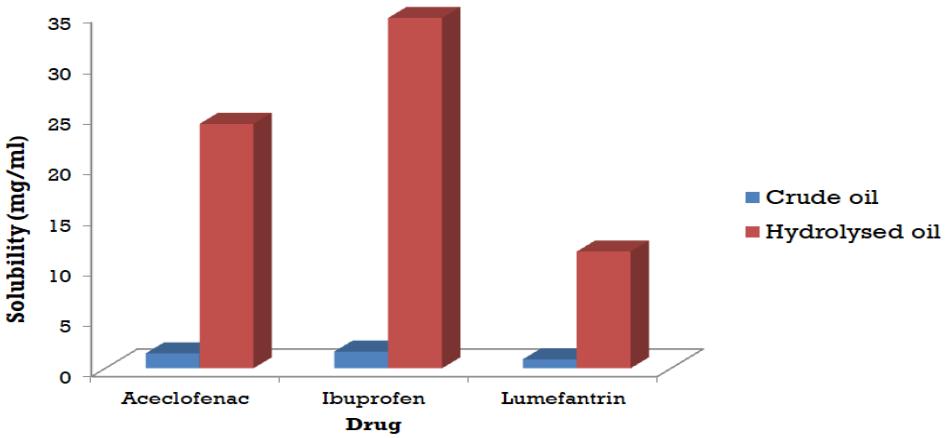


Figure 3. Relative solubility of aceclofenac, ibuprofen and lumefantrin in breadfruit oil.

It can be inferred from the chart that each of the three drugs exhibited higher solubility in the hydrolyzed oil than in the crude sample. The solubility of aceclofenac, ibuprofen and lumefantrin in the crude oil were 1.47 ± 0.34, 1.65 ± 0.75 and 0.89 ± 0.82 mg/mL respectively. Conversely, the solubilities in the hydrolyzed oil for the three drugs were 24.17 ± 0.53, 34.65 ± 0.37 and 11.55 ± 0.18 mg/mL respectively. The higher solubilizing capacity of the hydrolyzed oil for the three drugs is justified by the knowledge that long chain fatty acids generally have lower solvent capacity for poorly water-soluble drugs (Shukla, 2015). The hydrolytic process broke down the long chain polyunsaturated fatty acids to the medium chain structures that exhibited higher solvent capacity for the drugs.

4. Conclusion

Breadfruit oil has good potentials for use as oil based excipient in pharmaceutical formulations given its relatively good drug solvent capacity, edible nature and wide availability. Apart from its nutritional and ethnomedicinal importance, the current study revealed the possibility of use of the oil as excipient in pharmaceutical emulsions, creams and as tablet lubricant. Purification and hydrolysis of the oil to promote its organoleptic properties, storage stability and aesthetic appearance enhances its usefulness. Although the low extractive yield of the oil may pose a challenge to its industrial utilization, such can be overcome by process optimization. Future works on breadfruit extract may explore its applicability in the formulation of other pharmaceutical dosage forms as well as full structural elucidation of its phytocomponents and in silico screening for potential bioactive therapeutic molecules.

Acknowledgments

The authors wish to acknowledge the technical assistance of Mallam Isah Yakubu and Mrs Sabina Omeh for working additional hours when we were doing the laboratory experiments.

Author contribution statement

Conceptualization, design and structuring of the work (RO), Literature review and introduction (RO, AAO), extraction, purification and characterization of oil (IJA, OJ, CA and AAO, interpretation of results (RO, LU and JO) preparation of manuscript (RO AAO) proofreading and review of manuscript (RO, JO,LU). All authors gave the final approval for the submission of the manuscript for publication.

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