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Research Article

Investigating extraction methods of coconut oil in Metronidazole-Loaded topical microsized-emulsions for management of Rosacea

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Abstract

Emulsions for topical application are promising for the delivery and stability of poorly water-soluble drugs and those with challenging oral delivery. Coconut oil (oil from Cocos nucifera Linne, CNO) is used for cosmetic purposes, but there is limited published literature on its use in the delivery of drug-loaded preparations for topical or transdermal applications. The aim of this study was to formulate and evaluate metronidazole-loaded topical emulsions using CNO obtained from three different extraction methods. CNO was obtained using maceration in warm water and n-Hexane of the coconut meat to obtain hot method extract- HME, cold method extract- COE, and the chemical method extract- CME, respectively. The HME, COE, and CME were used to formulate corresponding metronidazole-loaded microsized emulsions (HMEE, COEE, and CMEE, respectively) at a predetermined oil-to-surfactant ratio of 1.5:1 using a homogenizer. The surfactant mix was composed of triethanolamine to stearic acid in the ratio of 1:10. The formulated drug-loaded emulsions were evaluated for physicochemical properties, stability, and antimicrobial activity. The chemical extraction method produced the highest CNO yield (72%), while the cold extraction method produced the lowest (32%). Drug-loaded emulsion COEE had the lowest viscosity of 4.29 Pas when compared with CMEE (4.82 Pas) and HMEE (4.6 Pas), had the least stability as reflected in its largest globule size of 28.46 µm, whereas globule size for CMEE and HMEE were 9.78 and 25.95 µm, respectively. Overall, metronidazole-loaded emulsions reduced the drug activity against the test organisms as determined by the measured zones of inhibition. These findings highlight the potential of a coconut oil-based emulsion for the topical delivery of drugs (e.g., metronidazole); however, for biocompatibility and to achieve the intended therapeutic outcome, careful selection of the drug of choice incorporated into the formulation for the target organism is needed. Also, while the chemical method of extraction for coconut oil would be a good choice to achieve a higher yield, the emulsion prepared from CNO using the hot extraction method showed adequate stability.

Keywords: Topical formulations, Coconut oil extraction, microsized emulsions, metronidazoles cream,

Introduction

Drug delivery to and through the skin offers an alternative but attractive route of drug administration. Being non-invasive and convenient, and bypassing hepatic first-pass metabolism and gastrointestinal degradation, topical delivery to the skin and the transdermal route have an edge over parenteral and oral delivery routes [1]. Furthermore, as the largest organ of the body, the skin offers a wide range of sites for drug application, especially for targeting pathological points of interest. Emulsions, and more recently micro- and nanoemulsions, have been in the arsenal of formulation strategies for the delivery of potent therapeutic agents topically and for transdermal applications. It is well known that a greater proportion of commercially available emulsions for therapeutic indications are applied topically [2].

Several drug actives have been formulated for topical use in pyodermas and related conditions, including anti-infectives such as clotrimazole, mupirocin, clindamycin, azelaic acid, and gentamicin [3];

antiallergics such as mepyramine, diphenhydramine, and doxepin; and steroidal components, e.g., betamethasone, beclometasone, and hydrocortisone.

Metronidazole, a nitroimidazole antibiotic, is widely used orally and parenterally to treat anaerobic bacterial and protozoan infections. Despite its oral bioavailability of over 95% and an average peak plasma concentration of about 2 h after dosing, metronidazole is associated with gastrointestinal side effects (e.g., metallic after taste, nausea, vomiting, diarrhoea, furry tongue, etc.), making it a good candidate for consideration in topical delivery [4]. Metronidazole has been used in conventional gels to manage rosacea (adult acne) [3]. However, it has been observed that topical use of metronidazole can cause dryness, burning, and irritation; hence, as an adjunct to overcome these undesirable effects when treating rosacea, the addition of moisturizers is vital [3,5]. Formulating metronidazole as an emulsion (cream) to provide not only antimicrobial activity but also a moisturizing effect could meet that need.

The use of oils such as olive oil, castor oil, and coconut oil, as well as similar plant-based lipids, as bases in topical formulations has been documented [6,7]. Since oils are an important ingredient in creams and topical formulations, the type of oil, extraction method, and formulation technique can affect the quality and stability of the preparations. This is because the extraction method can affect the physicochemical and biological properties of the extracted oils [8]. Oil from the *Cocos nucifera* plant (Coconut oil) is a natural lipid rich in medium-chain triglycerides and has lauric acid as the predominant fatty acid [9]. For its biocompatibility and availability, coconut oil was selected as the oil base for this work. Previous researches have documented that the method of extraction produced CNO of varying yield, quality, constituents, and usefulness [10,11]. CNO obtained by hot extraction has been reported to possess health-related antioxidant benefits - decrease in low-density lipoprotein (LDL) cholesterol but higher high-density lipoprotein (HDL) cholesterol- compared to that extracted by the cold method [12,13]. Also, coconut oil derived by solvent extraction has been reported to contain more polyphenols than that obtained by the cold method, and this constituent is suggested to be responsible for the high resistance of such CNO to oxidation [14]. This research work, therefore, aimed to evaluate coconut oil derived from three extraction methods (hot, cold, and solvent) with regard to physicochemical properties and to assess the quality of their metronidazole-loaded topical emulsions.

Materials and methods

Collection and extraction of coconut oil

The fresh coconut fruits were harvested from Obot Akara Local Government Area of Akwa Ibom State, a South-South region of Nigeria, and authenticated at the herbarium of the Department of Pharmacognosy and Natural Medicine, Faculty of Pharmacy, University of Uyo, Nigeria. The coconut fruit endosperm was manually dishelmed from the shell, the brown bark part of the meat was scraped off, and the endosperm was washed to remove any extraneous matter. The weight of the washed endosperm was then determined using an electronic balance (OHAUS Galaxy, UK).

About (3770 gm) of the obtained clean endosperm was grated (using a domestic grater made of tin) and divided into 2 unequal portions (a 1/3 portion and a remaining 2/3 part). A portion (the one-third part, 1223 gm) was oven-dried (TT-9053 Technology & Techmel USA) at 80 °C for about 5 h and kept for use in the chemical extraction method. The other portion (the two-thirds part, 2447 gm) was macerated with about 4.9 litres distilled water (maintained at 70 °C) for 12 h. The marc was filtered using a muslin cloth. To achieve thorough extraction, the maceration was repeated, and the filtrate was allowed to stand overnight until the milky lipid layer separated, floating on the water. The milky lipid phase was collected by decanting and then divided into two equal portions for use in the hot and cold extraction methods, respectively.

Hot method extraction

This method, as reported by Oseni and coworkers (2017) [15], was employed with slight modification. About 700 ml of the collected milky lipid phase was emptied into a clean stainless steel heating pan and heated to boiling for 20 min to remove all traces of water by evaporation. The oil was left to cool, then collected into a clean container for storage.

Cold method extraction

As described by Oseni and colleagues (2017) [15], with slight modification, the other half of the coconut milk/lipid layer obtained during maceration was subjected to a freeze-thaw cycle followed by centrifugation. This second part of the coconut milk (700 ml) was placed in a refrigerator set at 0 °C to freeze for 12 h, then removed and allowed to thaw at room temperature to obtain the oil. This cycle was maintained for 48 h. The freeze-thawed milky liquid was put in a centrifuge (table-top laboratory centrifuge model 80-2, Wincom, China) set at 4000 rpm for 30 min to separate the milk into three distinct liquid layers of different densities: water (below), cream (middle layer), and oil (upper layer). The oil was carefully decanted and stored for evaluation and use.

Chemical extraction method

The method, as reported by Okene and Evbuomwan, was employed with some modifications to the solvent. The oven-dried, grated coconut was placed in a Soxhlet apparatus (Eie-213ep, India) maintained at 70 °C and the oil was extracted using n-hexane as solvent. The oil-solvent mixture was then separated using a distillation apparatus (Rubbertron, India) to recover each liquid in the mixture [16].

Evaluation of the *Cocos nucifera* oil

The coconut oil obtained from each of the three methods was evaluated for physicochemical properties, including pH, viscosity, acid value, density, and saponification value, using standard methods reported in the literature [15-17]. Specifically, to determine the pH, about 50 ml of CNO extracted via the hot method was placed in a 100 ml beaker, and the pH electrode (model 3305 Jenway, USA) was immersed in the oil and allowed to equilibrate before the displayed pH value was recorded. This was determined in triplicate. The same procedure was used to determine the CNO obtained by the cold and the chemical methods. For the viscosity, 50 ml of the CNO in a 100 ml beaker was taken, to which the spindle code 2 of the Viscometer (Brookfield, NDJ-55, India) was immersed and maintained at 60 rpm to determine the oil's resistance to flow. The displayed value was then noted. The determination was in triplicate for the different oils.

Table 1. Composition of metronidazole microsized emulsion formulation.

Ingredients	Composition (%w/w)
Metronidazole	2
Stearic acid	14.5
Coconut oil	25
Glycerin	1
Triethanolamine	1.5
Methyl paraben	0.07
Propyl paraben	0.03
Water	55.9

Formulation of metronidazole emulsion

The metronidazole emulsion (cream) was prepared as described by Saptarini and Hadisoebroto [18] with some modifications. The lipophilic ingredients (e.g., metronidazole, stearic acid, coconut oil, and propyl paraben) in quantities determined by the formula (Table 1) were placed in a 250 ml beaker (beaker A). In another 250 ml beaker (beaker B), the hydrophilic components glycerin, triethanolamine, methyl paraben, and water were mixed. Both beakers were heated to 700 °C on a water bath (model DKZ, England) with constant stirring. The contents in beaker B were gradually incorporated into beaker

A at that temperature with continuous stirring using a Silverson homogenizer (L4R, USA) until cool. This was repeated for the preparations of the oils obtained by the different methods.

Evaluation of the metronidazole microsized emulsion

The organoleptic properties, homogeneity, pH, and viscosity of the formulated emulsions were determined using published methods as previously described [15-18].

Photomicrography

A thin smear of the formulated emulsion was made on a glass slide, covered with a slip, and mounted on a microscope (Olympus CX 21 USA), which was connected to an armscope (MD500) and viewed at ×10 magnification. Snapshots of the globule sizes were taken, and the mean size of 20 globules was determined. This was repeated for all the formulations.

Stability studies

Two studies were conducted to assess the stability of the emulsions: accelerated stability studies and real-time studies. In each case, a 20 ml quantity of the formulation was put in a measuring cylinder and covered with aluminium foil to prevent water loss by evaporation. For accelerated stability studies, the measuring cylinders were then allowed to stand at four different temperatures, 20, 25, 40, and 55 °C for 24 h. For real-time stability, the formulations in the cylinders were kept at room temperature for a month, with weekly observations. In both cases, observations for various physico-chemical parameters such as phase separation, colour, odour, homogeneity of the cream, and changes in the pH of 1% aqueous dispersion of each emulsion were noted [19].

Antibacterial evaluation

The antibacterial activities of the prepared emulsions (COEE, CMEE, and HMEE) were investigated by screening them against four standard test bacteria organisms (*B. subtilis, P. aeruginosa, E. coli and S. aureus*) using the agar well diffusion method and employing two techniques of media inoculation- the pour and the spread plate techniques. Exactly 20 ml of freshly prepared sterile molten agar culture media was poured into an 8.5 cm-wide disposable petri dish and allowed to set (solidify). Using the spread technique of media inoculation, 0.05 ml of each standard test organism was dropped on the solidified agar surface and spread using a glass spreader. With a sterile cork borer, wells of 8 mm were bored into the agar mat and few drops (about 100 µl) of corresponding metronidazole solution (equivalent of 2 mg/ml concentration) and the emulsion (a 100 mg/ml dispersion in distilled water, equivalent to 2 mg/ml of metronidazole concentration) were introduced to the wells and left on the bench to stand for sometime to ensure diffusion. For the pour plate inoculation technique, 0.05 ml of overnight broth cultures of each of the standard test organisms was introduced into appropriately labeled petri dishes. Then 20 ml of sterile molten agar was poured into each plate and allowed to set (solidify), after which a sterile cork borer was used to create wells in the solid agar mat. Into each well, drops (equivalent of 100 µl) of corresponding emulsion formulations (100 mg/ml dispersion in distilled water to give 2 mg/ml of metronidazole concentration) and metronidazole solution (equivalent of 2 mg/ml concentration) were introduced and left on the laboratory bench for a while to equilibrate. After equilibration and diffusion, all the plates were packed and incubated at 37 ± 0.2 °C for 24 h. The plates were then examined for growth of the respective organisms or any zone of clearance around the wells. The diameters of these zones of microbial growth clearance (zones of microbial inhibition) were measured and used as an assessment of antimicrobial activity. These tests were performed in duplicates.

Results

The yields of CNO from the different methods, as shown in Table 2, reveal that the chemical method yielded the highest (72%), while the least was obtained with cold extraction (33%). Other physicochemical and organoleptic properties of the coconut oil obtained from the different methods are presented in Table 2, whereas the properties for the formulated emulsion and mean globule size for the

prepared emulsions HMEE, COEE, and CMEE were 25.95 μm, 28.46 μm, and 9.78 μm, respectively, as shown in Table 3.

Table 2. Properties of extracted oils from *Cocos nucifera Linne*.

Properties	Cold Method extracted Coconut Oil (COE)	Hot method extracted Coconut Oil (HME)	Chemical extracted coconut Oil (CME)
Solubility at room temperature	Insoluble in water	Insoluble in water	Insoluble in water
Density(g/mL)	0.92 ± 0.00	0.92 ± 0.00	0.92 ± 0.00
Oil yield (%)	33.26	69.56	72
pH	6.64 ± 0.00	6.12 ± 0.00	6.4 ± 0.00
Viscosity (mPas)	35.75 ± 0.05	35.55 ± 0.05	35.66 ± 0.05
Specific gravity	0.92	0.92	0.92
Saponification value (mg of KOH per g of oil)	169.14	164.37	164.37
Free fatty acid (mg KOH/g of oil)	0.52	0.40	0.30
Colour	colourless	Pale yellow	Pale yellow
Smell	characteristic	characteristic	Indistinct coconut/n-Hexane smell

Table 3. Properties of metronidazole micro-sized emulsions made from extracted the coconut oil.

Properties	Emulsion of COE	Emulsion of HME	Emulsion of CME
Colour	White	White	White
Smell	Coconut smell	Coconut smell	Indistinct (coconut/n-Hexane)
Homogeneity	Uniform	Uniform	Uniform
Viscosity (mPas)	4292 ± 5.60	4658 ±1.00	4815 ± 3.54
pH	7.94± 0.05	7.82 ± 0.07	7.79 ± 0.02
Globule (droplet) size (μm)	28.46 ± 5.97	25.95 ± 5.58	9.78 ± 4.48

Figures 1a-c show the photomicrographs of the emulsions formed from coconut oils obtained from the different methods, their size, and their distribution within the formulation. The findings from the stability studies of the formulated metronidazole-loaded emulsion over a 4-week duration are presented in Table 4, whereas the physicochemical observations noted on subjecting the formulated emulsions to accelerated stability studies at different temperatures are indicated in Table 5.

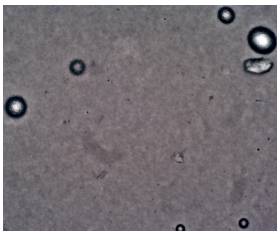

Figure 1a. Metronidazole loaded emulsion of coconut oil from cold extraction ×10 magnification.

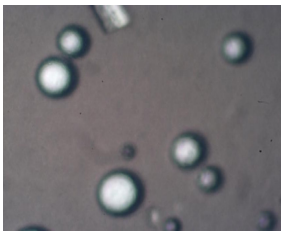

Figure 1b. Metronidazole loaded emulsion of coconut oil from hot extraction ×10 Magnification.

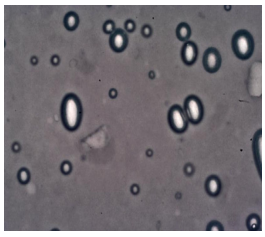

Figure 1c. Metronidazole loaded emulsion of coconut oil from solvent extraction ×10 magnification.

Table 4. Stability studies of the metronidazole micronized-emulsion formulations.

Properties	COE microsized-Emulsion (COEE)		HME microsized-emulsion (HMEE)		CME microsized-emulsion (CMEE)	
	Duration		Duration		Duration	
	Week 1	Week 4	Week 1	Week 4	Week 1	Week 4
Colour	white	white	white	white	white	white
Smell	Same as coconut oil	unchanged	same as coconut oil	unchanged	indistinct	unchanged
Homogeneity	+	+	+	+	+	+
Texture	Smooth	Smooth	Smooth	Smooth	Smooth	Smooth
pH	7.94 ± 0.05	7.94 ± 0.05	7.82 ± 0.07	7.89 ± 0.07	7.79 ± 0.02	7.77 ± 0.02
Viscosity (mPas)	4292 ± 5.60	4300 ± 5.61	4658 ± 1.00	4660 ± 1.00	4815 ± 3.54	4820 ± 3.55

Table 5. Physicochemical properties of the formulated microsized emulsions subjected to Accelerated Stability studies at varying temperatures.

Properties	COE microsized-Emulsion (COEE)				HME microsized- emulsion (HMEE)				CME microsized-emulsion (CMEE)			
	Temperatures °C				Temperatures °C				Temperatures °C			
	20	25	40	55	20	25	40	55	20	25	40	55
Colour	§	§	§	&	§	§	§	§	§	§	§	§
Smell	#	#	#	#	#	#	#	#	@	@	@	@
Homogeniety	+	+	-	-	+	+	+	+	+	+	+	-
Phase separation (cracking)	-	-	-	+	-	-	-	-	-	-	-	+
pH	7.42	7.78	8.62	7.25	7.09	7.89	8.71	6.23	6.61	7.01	9.08	7.38

§= white; # = Characteristic; @= indistinct; &= Colourless

Figure 2 a and 2 b show the pH changes in the emulsions over the course of four weeks at different temperatures, respectively.

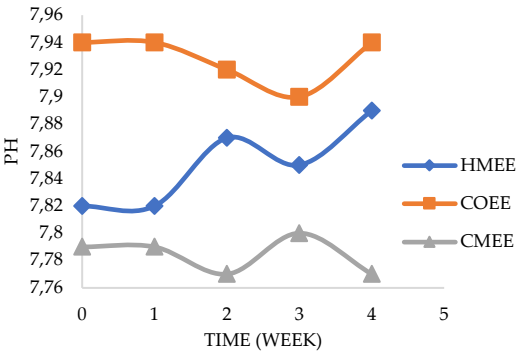

Figure 2a. pH changes in the formulated emulsion during a 4 weeks stability studies

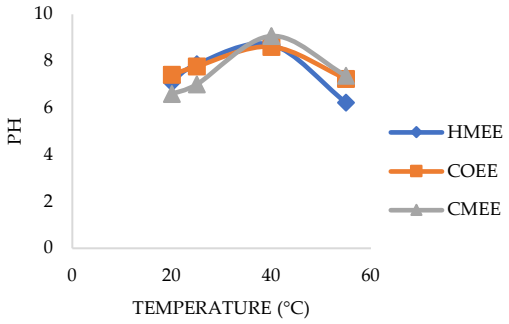

Figure 2b. Effect of accelerated stability studies on pH of the formulated emulsions

The results of antimicrobial activities of the formulated coconut emulsion against the test organisms are presented in Table 6.

Table 6. Antibacterial activities of formulated emulsion loaded with metronidazole.

Organisms	Zone of inhibition by Metronidazole (mm)		Zone of inhibition by HMEE formulation (mm)		Zone of inhibition by COEE formulation (mm)		Zone of inhibition by CMEE formulation (mm)	
	Pour plate	Spread plate	Pour plate	Spread plate	Pour plate	Spread plate	Pour plate	Spread plate
Bacillus subtilis	30.00 ± 0.00	15.00 ± 0.00	15.00 ± 0.00	-	12.50 ± 2.50	-	12.50 ± 2.50	-
Staphylococcus aureus	15.00 ± 0.00	15.00 ± 0.00	12.50 ± 2.50	11.50 ± 3.50	-	-	-	8.00 ± 0.00
Pseudomonas aeruginosa	15.00 ± 0.00	22.50 ± 2.50	-	15.00 ± 0.00	-	20.00 ± 0.00	-	20.00 ± 5.00
Escherichia coli	10.00 ± 0.00	9.00 ± 1.00	10.00 ± 0.00	-	-	-	12.00 ± 0.00	-

Key: (-) signifies no activity observed

Discussion

The extraction method affected oil yield, colour, and fatty acid value, but had no effect on oil density or pH (Table 2). These findings on oil yield resonate with those reported by Rohman and coworkers [20]. A possible reason for this is that solvent extraction, as an effective technique in vegetable oil extraction, leaves no residual oils in the coconut meat or cake, thereby resulting in a greater yield [21]. Moreover, during oil recovery by centrifugation in the cold extraction method, some quantity was likely lost to the cream formed in the middle layer, thereby reducing the overall yield. Also, the extraction

method likely affected the proportions of constituents (e.g., polyphenols and cholesterol) in the obtained oil, as reported by other researchers, which could be reflected in the variation in their colour [10-13]. The oils had similarities in density and pH. Importantly, the densities (0.908-0.921 g/ml) were in line with standard values reported for coconut oil [22]. The free fatty acids in vegetable oils are indicated by their acid value. From our findings (Table 2), the fatty acid content falls below the maximum amount of 4 mg KOH per gm of oil recommended by the CODEX (2015) [22]. The age and storage conditions of the oil can affect the acid value [23]. Using free fatty acid value, the oils could be ranked as COE > HME > CME.

The formulated emulsions were characterized by pH, globule size, and viscosity. The globule size of each metronidazole emulsions was in the micrometer size range 9.78-28.46 μm (Table 3). Emulsions, from literature, can be categorized as macro (1-20 mm), micro or nano emulsions (1-100*nm*) depending on the globule size ranges and stability status [24]. Based on globule size, the topical emulsion formed is not in the range of microemulsion or nanoemulsion, but can be ranked as COEE > HMEE > CMEE. While COEE showed sparse globule distribution per area of slide view, CMEE was densely distributed, and HMEE was between the two extremes. Globule size and distribution are good predictors not only of appearance and stability but also of drug release and the therapeutic effect of the incorporated drug (metronidazole) on the skin [25-27]. The appearance of larger globules, especially over time during storage, could indicate instability, likely due to Oswald ripening or gradual coalescence. The globule size in COEE could explain its phase separation at elevated temperature during the accelerated stability studies, compared with the other emulsions (Table 5). The emulsions formed were slightly alkaline, with pH values ranging from 7.79 to 7.94 (Table 3). This is within the acceptable range approved for creams and lotions [28]. Although skin care products have pH range between 4 to 8 in order to maintain the acid mantle and the skin has the capacity to maintain homoeostasis, some skin conditions such as rosacea favour the use of products with alkaline pH to prevent damage to skin barriers and give a good foundation for the application of moisturizers to address the skin dryness, sensation and stinging that characterise rosacea [28,29]. Since the oil was slightly acidic, the presence of triethanolamine in the formulation likely adjusted the emulsion's pH and served as a buffer [18].

Viscosity of creams (emulsions) has been reported to be as low as 290–480 mPas or as high as 48,950 mPas [30,31]. The emulsions formed can be ranked by viscosity as COEE < HMEE < CMEE. It must be noted, however, that the viscosity of emulsions/creams affect its pourability/extrusion from their container of storage. The stability studies at room temperature showed that over four week period, the formulations stored at room temperature were stable (Table 4). Colour, homogeneity, smell, pH, and viscosity are parameters that can be used to assess emulsion stability. The stability profile of a product is important for determining its shelf life, storage conditions, and labelling instructions. While there were very slight increase in the viscosities on storage, these differences were not significant to make the formulation unstable. Generally, the pH did not change appreciably, although there was a slight increase in HMEE and CMEE, and a decrease in CMEE (Figure 2).

However, at higher temperatures, the COEE and CMEE showed the absence of homogeneity (for COEE starting at 40 °C and for CMEE at 55 °C) as shown in Table 5. Also, phase separation (cracking) was observed in both COEE and CMEE emulsions at 55 °C. It must be noted that, across all formulations, the pH increased significantly at 40 °C but returned to near initial values at 55 °C (Figure 3). In the formulations, HMEE remained stable at all tested temperatures throughout the accelerated stability studies. This may be related to the phenolic constituents reported to be present in CNO obtained by the hot method [14,12]. The stability of the formulation at different temperatures, as seen in stability findings give basis for industrial application for commercial use, and the formulations can be ranked as HMEE>CMEE>COEE.

The antibacterial activities of the formulations against the tested bacterial organisms showed that, generally, the control (metronidazole solution) had higher activity than the respective emulsion formulations, as indicated by the zone of inhibition (Table 6). A possible reason could be the partitioning of metronidazole between the oil and water phases of the emulsion, thereby affecting its release and its ability to exert activity against the bacteria tested. Adetunji *et al.* (2020) had reported in their work that coconut oil showed significant antibacterial activity against *Staphylococus aureus* and *Pseudomonas aeruginosa* than its microemulsion formulation although no drug was incorporated [25]. Also, the findings generally indicate that the emulsions showed activity against three of the tested organisms, depending on the inoculation technique. The pour plate technique showed greater antibacterial activity (e.g., against B. *subtilis*). The exception was observed in the case of the *Pseudomonas aeruginosa* test organism, where the effectiveness of the technique was reversed.

Conclusion

The extraction method influenced the properties of the coconut oil obtained, and these, in turn, can affect its potential use and applications. The micro-sized emulsion made from CNO obtained by hot extraction maintained stability throughout the study and at higher temperatures in accelerated stability studies, demonstrating its potential for industrial applications. The CNO extracted by the chemical method gave the highest yield, and the emulsion prepared from it showed the best activity against B. *subtilis,* even better than the control (pure metronidazole solution). Thus, it can be appreciated that the extraction method to be used for CNO should be guided by the purpose of the intended product and the desired yield, to achieve a quality grade suitable for topical emulsions.

Competing interests

The authors declare that they have no competing interests.

References

1. Gelmetti C. Local antibiotics in dermatology. Dermatol Ther. 2008;21(3):187-95.
2. Lu GW and Gao P. Emulsions and microemulsions for topical and transdermal drug delivery in Handbook of non-invasive drug delivery systems. 2010;59-94.
3. Bandyopadhyay D. Topical Antibacterials in dermatology. Indian J Dermatol. 2021;66(2): 117-25.
4. Lee LL, Rowland J, Y Ling CH, Fiakos E. Quantitty survey of intravenous administration of metronidazole in its different forms in a tertiary teaching hospital. Intern Med J. 2010;40(8):592-6.
5. Tirnaksiz F, Kayiş A, Çelebi N, Adişen E, Erel A. Preparation and evaluation of topical microemulsion system containing metronidazole for remission in rosacea. Chem Pharm Bull. 2012;60(5):583-92.
6. Nunes A, Goncalves L, Marto, J, Martins AM, Silva AN, Pinto P, et al. Investigations of Olive oil industry by-products extracts with potential skin benefits in topical formulations. Pharmaceutics. 2021;13(4):465.
7. Atmanto D. Effectiveness of utilizing VCO oil and Castor oil on natural creams for dry skin treatment due to environmental factors. J Phys: Conf Series. 2019;1402(2):022093.
8. Abdul Aziz ZA, Ahmad A, Mohd Setapar SH, Karakucuk A, Azim MM, Lokhat D, et al. Essential oils: Extraction techniques, Pharmaceutical and Therapeutic potential-A review. Curr Drug Metab.2018;19(13):1100-1110.
9. Shasidhar Y, Vishwakarma MK, Pandey MK, Janila P, Variath MT, Manohar SS, et al. Molecular mapping of oil content and fatty acids using dense genetic maps in groundnut (Arachis hypogaea L.). Front Plant Sci. 2017;8:794.
10. Ibrahim AI, Nurjanah S, Kramadibrata AM, Naufalin R, Erminawati, Dwiyanti H. Influence of the different extraction methods on the physicochemical characteristics and chemical composition of coconut oil (Cocos nucifera L.) IOP Conf Ser: Earth Environ Sci. 2019;250(1):012102.
11. Mansor TST, Che Man YB, Shuhaimi M, Abdul Afiq MJ, Ku Nurul FKM. Physicochemical properties of virgin coconut oil extracted from different processing methods. International Food Research Journal. 2012;19(3):837-45.
12. Seneviratne KN, Hapuarachchi CD, Ekanayake S. Comparison of the phenolic-dependent antioxidant properties of coconut oil extracted under cold and hot conditions. Food Chemistry. 2009;114(4):1444-9.

13. Jer Ng Y, En Tham P, Khoo KS, Cheng CK, Chew KW, Show PL. A comprehensive review on the techniques for coconut oil extraction and its application. Bioprocess Biosyst Eng. 2021;44(9):1807-1818.
14. Gutfinger T. Polyphenols in Olive oil. Journal of the American oil Chemist Society. 1981;58:966-8.
15. Oseni NT, Fernando W, Coorey R, Gold I, Jayasena V. Effect of extraction techniques on the quality of coconut oil. African Journal of Food Science. 2017;11(3):58-66.
16. Okene EO, Evbuomwan BO. Solvent extraction and characterization of oil from coconut seed using alternative solvents. Intern J Engr Tech Res. 2014;2(12):135-138.
17. Rohman A, Irnawati, Erwanto Y, Lukitaningsih E, Rafi M, Fadzilah NA, et al. Virgin coconut oil: Extraction, physicochemical properties, Biological activities and its authentication Analysis. Food Reviews International. 2019;37(1):1-21.
18. Saptarini NM, Hadisoebroto G. Formulation and evaluation of lotion and cream of nanosized chitosan-mangosteen (garcinia mangostana l.) pericarp extract. Rasayan J. Chem. 2020;13(2):789-95.
19. Bhagwat GB, Kadam SS, Hivarale M, Porwal A. Stability study and evaluation of ayurvedic formulation – anoac cream. Anveshana Ayurveda Medical Journal. 2017;3(6):1596-9.
20. Rohman A, Irnawati YE, Lukitaningsih E, Rati M, Fadzilah NA, et al. Virgin Coconut oil: Extraction, Physicochemical Properties, Biological Activities and its authentication analysis. Food Reviews International. 2019;37(1):46-66.
21. Tayde S, Patnaik M, Bhagt, SL, Renge VC. Epoxidation of vegetable oils. A review. International Journal of Advanced Engineering Technology. 2011;2(4):491-501.
22. CODEX (2015). Codex Alimentarius Commission /FAO/WHO, Food Standards. Standard for named Vegetable oils. CODEX-STAN 210, (amended) Ed. FAO-UN/WHO. [cited 2022 Jan 12].
23. Jauro A, Oshieke KC, Adamu HM. Extraction and characterisation of Pentaclethra macrophyllas seed oil. Journal of Chemical Society of Nigeria. 2001;36(1):180-4.
24. Kale SN, Swore SL. Emulsion Micro Emulsion And Nano Emulsion- A Review. Sys Rev Pharm. 2017;8(1):39-47.
25. Adetunji OA, Adesanwo B, Odeniyi MA. Characterization of microemulsions formulated from naturally and chemically extracted oils from Cocos nucifera Linne. Nigerian Journal of Pharmaceutical Research. 2020;16 (1):39-48.
26. Pandey S, Das U, Patel A. Formulation and exvivo evaluation of metronidazole microemulsion loaded hydrogel for preventing of peridonitis. Journal of Pharmaceutical Investigation. 2014;44:225-36.
27. Cevikelli T, Guven UM, Ozturk AA. Metronidazole loaded novel microemulsion formulation for topical delivery and characterization with validated new UPLC method. Fabad Journal of Pharmaceutical sciences. 2024;49(1):111-128.
28. Nieradko-Iwanicka B, Chrobok K, Skolarczyk J, Pekar J. What is the pH, Fe, and Cl2 content of cosmetics one use? A pilot study on safety of skin care products. Pol J Public Health. 2017;127(2):78-81.
29. Palval-Santos A, Goncalves T, Peixoto D, Pires PC, Velsenker K, Jha NK, et al. Rosacea topical treatment and care: from traditional to new drug delivery system. Mol Pharm 2023;20(8):3804-28.
30. Chen MX, Alexander KS, Baki G. Formulation and evaluation of antibacterial creams and gels containing metal ions for topical application. Journal Pharm. 2016;2016:5754349.
31. Okafo SE, Anie CO, Alalor CA, Uchenna L. Evaluation of physicochemical and antimicrobial properties of creams formulated using Pterocarpus santalinoides seeds methanol extract. JAPS. 2023;13(5):126-135.

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