



# Evaluating Coconut Oil and Coconut Water-Loaded Gels for the Alleviation of Chloroquine-Induced Pruritus

Emmanuel Uronnachi<sup>1\*</sup>, Onyinye Okpalaku<sup>1</sup>, Ebere Okoye<sup>1</sup>

<sup>1</sup>Department of Pharmaceutics and Pharmaceutical Technology, Nnamdi Azikiwe University, Awka, Anambra State, Nigeria.

## ABSTRACT

Coconut water and coconut oil were extracted from mature coconuts and their gels were formulated and characterized. Their anti-pruritic effect was evaluated. Seven batches of 1 % hydrogels were formulated from carbopol, and carboxymethylcellulose (CMC), singly and in combination. The formulations were administered to rats with Eurax<sup>®</sup> cream as the positive control. Pruritus was induced by subcutaneous injection of Chloroquine phosphate on 27 Wistar rats at a dose of 20 mg/kg subcutaneously, and an oral dose of 158 mg/kg. Itching bouts were counted. The formulations were mildly alkaline with pH ranging from (7.0 - 9.5). Viscosity values ranged from (201 mPas - 1890 mPas). The gels were more stable at 25 ± 2 °C. Anti-pruritic evaluations showed that the animals treated with CMC + Carbopol gel containing coconut oil exhibited the least frequency of itching bouts, with sustained anti-pruritic activity. ANOVA showed statistically significant differences (p < 0.05) in results between Eurax<sup>®</sup> and the CMC + Carbopol gel containing coconut oil. There was no significant difference in anti-pruritic effects between the CMC + Carbopol gel containing either coconut oil or water. Coconut oil gels may easily be applied as a therapy in the management of itching resulting from drug-induced allergy.

**Key Words:** Coconut oil, Pruritis, Coconut water, Gels, Chloroquine

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## INTRODUCTION

Pruritus manifests as an unpleasant sensation urging one to scratch. As one of the most common clinical manifestations in medicine, it is divided into acute and chronic stages, based on the duration of the clinical manifestation. Furthermore, it may manifest clinically as an adverse reaction to an administered drug. Its pathogenesis may involve several cytokines and inflammatory neuro-mediators and usually involves the central and peripheral nervous system [1].

Drugs may cause itching as a concomitant symptom of drug-induced skin reactions or in the form of pruritus without skin lesions [2]. Chloroquine-induced pruritus has been reported as being more predominant in black-skinned people and people of negroid descent while administration

of the drug to whites rarely elicits itching, thus suggesting a genetic pre-disposition to the symptom [3]. Furthermore, *in vitro* skin cell studies showed that chloroquine preferentially binds to melanocytes as opposed to keratinocytes [4]. The non-histaminergic nature of CQ itch makes it a good model for probing the mechanisms of chronic itch.

There are striking similarities between CQ itching pathways and other forms of chronic itch. These include the shared roles of skin, kappa opiate receptor, nitric oxide, serotonin via 5HT1B/D receptors, neural and spinal  $\mu$  opiate receptors, cytokines (especially interleukins), and tumor necrosis factor [5].

Two varieties of coconut oil exist: virgin and refined oil. Virgin coconut oil (VCO) is made by cold-pressing the liquid from the fresh part of coconut meat. It has a milky

**Corresponding author:** Emmanuel Uronnachi

**Address:** Department of Pharmaceutics and Pharmaceutical Technology, Nnamdi Azikiwe University, Awka, Anambra State, Nigeria.

**E-mail:** ✉ em.uronnachi@unizik.edu.ng

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appearance. This method of oil extraction preserves the contents of vitamin E, pro-vitamin A, and polyphenols. Various properties of this oil have been reported as anti-inflammatory, analgesic, and anti-cancer [6]. Natural plant oils, due to their easy availability, accessibility, and low cost are most commonly used globally for treating various skin ailments [7, 8]. Coconut oil contains compounds that exhibit antimicrobial, anti-inflammatory, antioxidant, and anti-pruritic actions making it an important, cost-effective, alternative, and complementary medicine to target various xerotic and inflammatory skin diseases in which the skin barrier is disrupted [9, 10].

CQ-induced pruritus has been an obstacle leading to poor compliance in patients [11]. Regardless of the route of administration, CQ is a major inducer of a very discomforting, generalized body itch within about 2 hours of administration. Chloroquine-induced itch is mostly independent of the route of administration as many patients are forced to stop further drug ingestion. This has led to poor patient compliance, CQ-induced resistance, increased cases of relapse, and an overall poor prognosis. Chloroquine-induced itching is often regarded as a characteristic 'histamine-independent' itch signaling pathway [12].

Several remedies for itching exist with varying degrees of efficacy [13]. Unfortunately, antihistamines are only effective if the itching (pruritus) is caused by histamine (as in urticaria). They only benefit non-histamine-mediated itch through their sedating tranquilizing properties [14].

Several substances have been shown to reduce the itching associated with chloroquine [15-18] while some other mechanisms have been discovered to ameliorate the itching associated with chloroquine use [19-21].

It has been reported that chlorpheniramine or hydroxyzine hydrochloride provided symptomatic relief [22].

Nwonu *et al.* [23] investigated the possibility of interaction upon concomitant administration of coconut fruit water and chloroquine sulfate in adult male rabbits. The results of the study demonstrated a strong interaction between coconut fruit water and chloroquine sulfate thus reducing its bio-availability. This oral administration is helpful for the management of drug toxicity. However, it can interfere with certain pharmacokinetic properties such as its volume of distribution, and plasma half-life in the process. There is a need for a dosage form that is less interfering with the drug's pharmacokinetics. Choi *et al.* [12] reported that crotamiton inhibits both histamine- and chloroquine-dependent itch pathways and suppresses scratching behavior induced by both compounds in mice.

Coconut water and oil are already known to the population in their natural state as an age-long itch relief. There is a need for a natural pharmaceutical formulation that possesses: water solubility in external body fluids, cutaneous penetrability, cosmetic appeal (hair and skin),

little or no pharmacokinetic interference, little or no adverse effects, ease of administration, sustained actions, safety, and physical stability.

Hydrogels have the ability to form three-dimensional polymer networks that are hydrophilic in nature and can absorb water to expand without dissolving. This makes them an attractive choice in drug delivery. Particularly, carboxymethyl cellulose hydrogels have attracted considerable research attention for the development of safe drug delivery carriers because of their non-toxicity, good biodegradability, good bio-compatibility, and low immunogenicity [24].

This study aims to formulate, characterize, and evaluate coconut water- and oil-loaded gels for their anti-pruritic activities on female Wistar rats using the chloroquine-induced pruritus model in rats.

## MATERIALS AND METHODS

### Materials

#### Plant materials

Mature coconuts (*Cocos nucifera*) used in this study were harvested in March, from a local herbalist farm in an open market in Awka, Anambra State, Nigeria. The plant samples were identified by a taxonomist and deposited at the Pharmacognosy and Traditional Medicine Department, Faculty of Pharmaceutical Sciences, Agulu, Nnamdi Azikiwe University, Awka, Anambra State, Nigeria.

#### Reagents

Ethanol (absolute), triethanolamine (JHD, Guangdong Guanghua Sci-Tech Co., China); chloroquine phosphate injection 40mg/ml (Labquin), Eurax cream (Novartis Corporation, Malaysia), Carbopol (Carbomer 934), carboxymethyl cellulose (CMC), potassium sorbate (Nantong Alchemy Biotech Development Co., China), Veet® hair removal cream (Reckitt Benckiser Co., UK).

### Methods

#### Extraction of *cocos nucifera* water

Coconuts were randomly selected for each experiment [25]. The coconuts were de-husked to obtain coconut water which was poured into clean plastic bottles and refrigerated until needed.

#### Aqueous extraction of coconut milk

Coconut milk preparation, filtration, and separation was carried out according to Jasman *et al.* [26]. The coconut meats were grated, weighed, and blended using an electric blender (Molgold, United Kingdom). The blended meat was soaked in warm water (50 °C) at a ratio of 1:2 (coconut meat: water). The mixture was kneaded, wrapped in a muslin cloth, and then squeezed to obtain coconut milk.

The extracted coconut milk was poured into a clean beaker and allowed to stand.

*Centrifugation of VCO (virgin coconut oil)*

This was done using a Centrifuge (80-2B, China) at a speed of 1000 rpm for 20 min. The obtained oil was passed filtered through a Whatman no 1 filter paper. The volume of oil was determined.

*Pilot study of anti-pruritic effects of coconut water and coconut oil*

This section of the pilot study aimed to determine the best route of administration of the pruritogen.

A total of 18 female albino rats ranging from 3-6 months old and weighing between 150-200 g were obtained from the Animal laboratory facility of the Department of Veterinary Physiology and Pharmacology, University of Nigeria, Nsukka. Animals were kept in clean cages and had free access to food and water. The rats were fed with pelletized feed (Vital Feeds, Nigeria). Also, they had 12-hour light and dark cycles. They were kept for one week to acclimatize to their new environment. The rats were divided into six (6) groups.

A pair of scissors was used to shave the napes off its fur to a diameter of about 1.5 cm. A small quantity of Veet® hair removal cream (Reckitt Benckiser Co., UK) was applied to the shaved portions and left for a minute, after which, a water-whetted cotton wool was used to rub off the area till fur-less skin was seen. The shaved rats were used for the study on the next day to allow for acclimatization, as they had a tendency to scratch the shaved portions after shaving.

The next day, the rats were given coconut fluids by oral gavage using a stainless-steel feeding needle (Harvard Apparatus, USA) inserted into a 1 ml syringe (BD, USA). The dose volume of the coconut milk, water, and oil was 20 ml/kg weight of the rat. A time interval of 15 min elapsed and then a 20 mg/kg dose of chloroquine was injected into rats through selected parenteral routes of drug administration, but the rats grouped in the oral route were given 158 mg/kg of chloroquine. Evaluation of pruritus was done by video recording of the animals, followed by visualization and counting of scratching bouts. The number of scratching bouts and distance run for each animal were registered over 30 min after the CQ challenge and the results were analyzed [27].

*Determination of the anti-pruritic effects of coconut oil and water on CQ-induced itch*

This was done to determine the anti-pruritic efficacy of the coconut extracts, upon topical administration. The dorsal views of the neck region of the rats were shaved as previously described. The next day, eight female Wistar rats were placed in two groups of four animals. Afterward, 0.5 ml each of coconut oil and coconut water was topically administered to the rats on the shaved portions, according to their respective groups. The rats were left for a 15-minute interval and then administered 2 mg (50 µl of 40 mg/ml) chloroquine, injected subcutaneously into the shaved portions. Evaluation of pruritus was done by video recording of the animals, followed by visualization and counting of scratching bouts as previously described [27].

**Table 1.** Formula for different polymer-based gels

Ingredients	Polymer-based gel formulations						
	A	B	C	D	E	F	G
Coconut water (ml)	5	5	5	---	---	---	---
Coconut oil (ml)	---	---	---	5	5	5	---
CMC (g)	0.1	---	0.05	0.1	---	0.05	0.05
Carbopol (g)	---	0.1	0.05	---	0.1	0.05	0.05
Glycerol (g)	7.2	7.2	7.2	7.2	7.2	7.2	7.2
Potassium Sorbate (%)	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Ethanol (%)	2.4	2.4	2.4	2.4	2.4	2.4	2.4
Triethanolamine (qs)	qs	qs	qs	qs	qs	qs	qs
Distilled Water (ml)	5.2	5.2	5.2	5.2	5.2	5.2	10.2

**Key**

A-Coconut water gel (CMC- based); B-Coconut water gel (Carbopol-based); C-Coconut water gel (CMC + Carbopol-based); D-Coconut oil gel (CMC-based); E-Coconut oil gel (Carbopol-based); F-Coconut oil gel (CMC + Carbopol-based); G-Plain gel

*Preparation of polymer-based gels of coconut water and coconut oil*

Twenty grams of seven gel formulations were prepared, (labeled A-G) according to the formula presented in **Table 1**. Briefly, the required quantities of CMC, glycerol, ethanol, and potassium sorbate were weighed out and

placed in a mortar. Water was added and the mixture was stirred gently until the CMC dissolved. Then two drops of triethanolamine were added to enhance the gelation process of the CMC. Gentle stirring continued till a uniform mixture was obtained. The mixture was transferred to a clean and dry container and made up to the



required weight. The entire procedure was repeated using carbopol and then CMC/carbopol co-polymers and also with coconut oil in place of coconut water, while a plain gel was formed without the addition of the coconut oil or water.

*Characterization and stability evaluation of formulated gels*

The gels formed were characterized accordingly at intervals of 7, 30, and 90 days post formulation to evaluate their stability at a temperature of (25 ± 1°C).

*Organoleptic characterization*

The gels were physically observed for color, appearance, clarity, consistency, and phase separation.

*Determination of pH*

The Digital pH meter (AVI-65, India) was used. Calibration was done using buffer solutions (pH 4 and 7). Triplicate readings were taken.

*Determination of viscosity*

The viscosity of the gel formulations was measured with a rotational viscometer (IIDJ-1B, China) using spindle no 5.

*Comparative evaluation of the anti-pruritic activity of the formulated gels*

The animals (27 Wister rats) were shaved as previously described. Subsequently, the rats were divided into nine groups of three rats per group (Groups A-I).

The rats in groups A-H were administered with the formulations above and after 15 min, 2 mg (50 ul of 40 mg/ml) of chloroquine injection was injected subcutaneously to all rats in each group. Evaluation of pruritus was done as previously described [27].

*Statistical analysis*

The recorded data were subjected to paired t-tests to check for statistical differences in the mean number of scratching bouts across different groups. Analysis of variance (ANOVA) was carried out to assess the relationship between the anti-pruritic reductions in the different treatment classes being tested. All the statistical analyses were computed with IBM SPSS statistics software version 23. A P value < 0.05 was considered the statistically significant cut-off.

**RESULTS AND DISCUSSION**

*Yield of coconut oil*

The percentage (extraction) yield of coconut oil was 15.5 % v/w.

*Pilot study on the anti-pruritic effects of coconut extracts*

The results of the administration of the various extracts to animals were recorded in **Table 2**.

**Table 2.** Pilot study on coconut extracts

Routes of drug administration	Scratching bouts over 30 min					
	5	10	15	20	25	30
A <sub>1</sub> milk (SC)		**	*			
A <sub>2</sub> water (SC)						
A <sub>3</sub> oil (SC)						
B <sub>1</sub> milk (IM)						*
B <sub>2</sub> water (IM)		*				
B <sub>3</sub> oil (IM)						
C <sub>1</sub> milk (IP)			*	*		
C <sub>2</sub> water (IP)						
C <sub>3</sub> oil (IP)						
D <sub>1</sub> milk (oral)						
D <sub>2</sub> water (oral)						
D <sub>3</sub> oil (oral)						
E <sub>1</sub> milk (IV)						
E <sub>2</sub> water (IV)						
E <sub>3</sub> oil (IV)						
F <sub>1</sub>	*	*				
F <sub>2</sub>	*	*				
F <sub>3</sub>						

**Key**

One scratch is indicated with asterisks (\*).

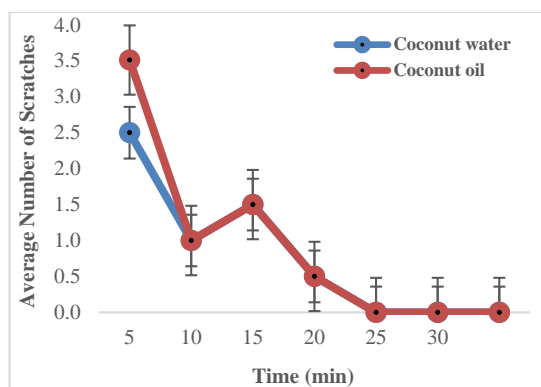
A - SC (Subcutaneous); B - IM (Intramuscular); C - IP (Intraperitoneal); D - O (Oral); E - IV (Intramuscular); F - Control

*Evaluation of anti-pruritic effects of coconut extracts*

**Figure 1** shows the anti-pruritic effects of topically-

administered coconut water, and coconut oil against chloroquine-induced itching over a 30-min period.





**Figure 1.** Anti-pruritic effects of coconut water and coconut oil

*Physical properties of coconut gel formulations*

**Table 3** shows the physical properties of the formulated gels. From the results, the formulations were emollient, non-greasiness, and ease removed.

**Table 3.** Organoleptic evaluation

S/No	Property	A	B	C	D	E	F	G
1.	Color	Colorless	White	White	Creamy	Creamy	Creamy	Colorless
2.	Appearance	Transparent	Translucent	Translucent	opaque	opaque	opaque	Transparent
3.	Odor	Nutty	nutty	nutty	nutty	nutty	nutty	bland
4.	After-feel	Emollient	Emollient	Emollient	Emol-lient	Emollient	Emollient	Emollient
5.	Removal	Easy	Easy	Easy	Easy	Easy	Easy	Easy
6.	Phase Separation	Yes	No	no	yes	No	No	No
7.	Consistency	+	+++	++	+	++	++	++

**Key**

A-Coconut water gel (CMC- based); B-Coconut water gel (Carbopol-based); C-Coconut water gel (CMC + Carbopol-based); D-Coconut oil gel (CMC-based); E-Coconut oil gel (Carbopol-based); F-Coconut oil gel (CMC + Carbopol-based); G-Plain gel; H-Eurax.

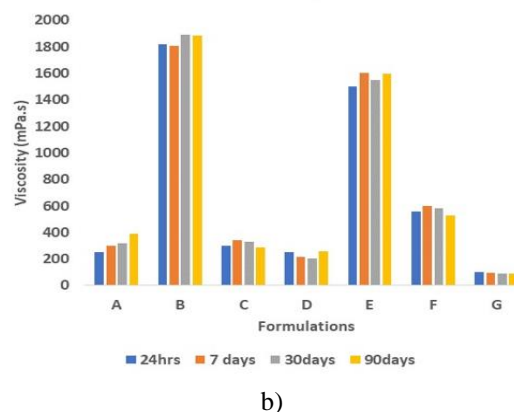
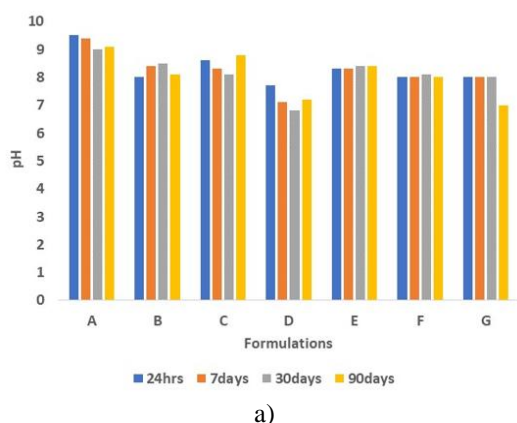
*Characterization of gels*

*pH*

The mean pH readings of the coconut-based gels over 90 days are presented in **Figure 2a**. The pH values obtained ranged from  $(7.00 \pm 0.49)$  to  $(9.5 \pm 0.03)$ .

*Mean viscosity*

The mean viscosity values of the coconut-based gels over 90 days are presented in **Figure 2b**. The values obtained ranged from  $(201 \pm 19.56)$  mPaS to  $(1890 \pm 56.3)$  mPaS. The values of the formulations were constant, with a slight increase between days 1 and 7.



**Figure 2.** pH (a) and Viscosity (b) of formulations  
**Key:**A-Coconut water gel (CMC-based); B-Coconut water gel (Carbopol-based); C-Coconut water gel (CMC+ Carbopol)-based; D-Coconut oil gel (CMC-based); E-Coconut oil gel (Carbopol-based); F-Coconut oil gel (CMC + Carbopol)-based; G-Plain gel

*Stability studies of gels*

The stability evaluation of the gels is presented in **Table 4**. From the results of the stability test, degradation of the gel formulations occurred as changes in coloration, loss of pleasant coconut aroma (Coconut water and oil gel), and separation of the oil from the formulation (Coconut oil gel). Degradation occurred in all of the gel formulations





except in the coconut oil gel containing CMC and Carbopol alongside the plain gel formulations.

**Table 4.** Stability studies of gels

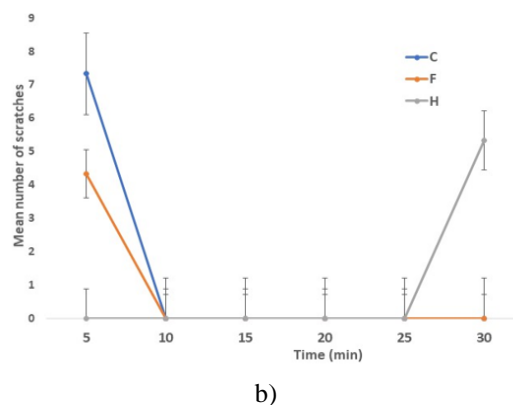
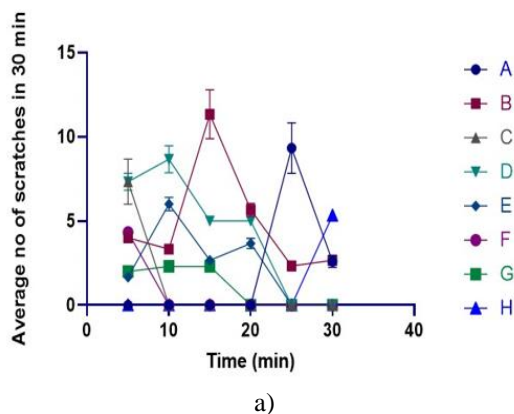
S/No	Property	A	B	C	D	E	F	G
<b>Appearance</b>								
1.	Day 1	Colorless	White	white	creamy	Transparent	creamy	Colorless
	Day 7	Colorless	White	white	creamy	Transparent	creamy	Colorless
	Day 30	Colorless	Pale white	white	creamy	Transparent	creamy	Colorless
	Day 90	Colorless	Pale white	white	creamy	Transparent	creamy	Colorless
<b>pH</b>								
2.	Day 1	9.5	8.0	8.6	7.7	8.3	8.0	8.0
	Day 7	9.5	8.0	8.6	7.7	8.3	8.0	8.0
	Day 30	9.0	8.5	8.1	6.8	8.4	8.1	8.0
	Day 90	9.1	8.1	8.8	7.2	8.4	8.0	7.4
<b>Consistency</b>								
3.	(24hrs)	+	+++	++	++	+++	++	++
	Day 7	+	+++	++	++	+++	++	++
	Day 30	++	++	++	+	+++	++	+
	Day 90	++	++	+	+	++	++	+
<b>Phase Separation</b>								
6.	Day 1	No	No	No	No	No	No	No
	Day 7	No	No	No	Yes	No	No	No
	Day 30	Yes	No	No	Yes	No	No	No
	Day 90	Yes	No	Yes	Yes	No	No	No

**Key:** +++ = Good ++ = moderate + = poor

A-Coconut water gel (CMC-based); B-Coconut water gel (Carbopol-based); C-Coconut water gel (CMC+ Carbopol)-based; D-Coconut oil gel (CMC-based); E-Coconut oil gel (Carbopol-based); F-Coconut oil gel (CMC + Carbopol)-based; G-Plain gel

*Anti-pruritic effects of coconut gels*

**Figure 3a** shows the average number of scratches of different coconut gel formulations, plus their controls, against chloroquine-induced itching over a 30-minute period.



**Figure 3.** Anti-pruritic effects of gel formulations against chloroquine-induced itching  
**Key:** A-Coconut water gel (CMC-based); B-Coconut water gel (Carbopol-based); C-Coconut water gel (CMC+ Carbopol)-based; D-Coconut oil gel (CMC-based); E-Coconut oil gel (Carbopol-based); F-Coconut oil gel (CMC + Carbopol)-based; G-Plain gel; H-Eurax cream

### Comparison of coconut gels with Eurax<sup>®</sup> cream

**Figure 3b** shows the anti-pruritic comparisons between the co-polymer-based gels and the positive control, at 5-minute intervals over a 30-min period of observation.

In comparing the co-polymer-based formulations, a trend of prolonged anti-pruritic actions was observed. The combined effects of both polymers aided drug release at a sustained rate. In addition, incorporating the coconut extracts into a gel dosage form enhanced its anti-pruritic potential, in contrast to using the coconut extracts alone (**Figure 1**).

The results of the pilot study showed that the SC proved to be the ideal route for the administration of the pruritogen, as it resulted in a greater number of scratches. Furthermore, The SC route allows for a faster onset of action to allow for recording the incidence of itching. Coconut milk had the least anti-pruritic activity of the three coconut fluids. Pruritus in the “F” group (chloroquine alone) was seen immediately after administration. Itching was not observed in the “D” group (oral). This may be due to the relatively longer time at which chloroquine attains plasma concentration to elicit the itching effect. This agrees with Tarrasón *et al.* [27], concluding that oral CQ does not induce pruritus due to insufficient skin levels. Also, in agreement with previous reports, there was an absence of pruritus at higher doses of up to 100 mg/kg [28].

Tarrasón *et al.* [27] reported that CQ at doses ranging from 8 to 32 mg/kg induced an increased scratching response after subcutaneous administration in mice. Our report validates this claim, as the animals used in this study were treated similarly, at a dose of (20 mg/kg).

The coconut water extracted was used immediately for the assessment because of instabilities previously reported [29].

Itching bouts were observed from the onset of the injection of the pruritogen. For both coconut water and oil, itching bouts peaked at 5 min. However, the frequency of scratches in rats treated with coconut water was slightly below that observed in rats treated with coconut oil. Interestingly, both extracts exhibited similar effects from the 10<sup>th</sup> minute. During this time, there was a steep decrease in their anti-pruritic actions till the 25<sup>th</sup> minute when pruritus ceased abruptly and remained so until the 30<sup>th</sup> minute. Both extracts can be said to elicit full anti-pruritic actions, 25 minutes after the administration of chloroquine. In comparing coconut water to coconut oil, the number of scratches was higher in coconut oil. This may have been due to the presence of large-weight decanoic (capric) acid derivatives of coconut oil phytoconstituents [30]. This contradicts Krishna *et al.* [31] who reported that lauric acid (a constituent of coconut oil) significantly penetrates the skin and actually can accumulate in the stratum corneum. The fact that it accumulates on the skin is beneficial and may imply non-interference in the pharmacokinetics of the

drug. From this study, coconut water exhibited more anti-pruritic action than coconut oil.

Fresh coconut water has a pH range of 4.2 to 6.0 and is colorless, naturally flavored, and mildly acidic. However, when aseptically extracted from the mature fruit, it has an average pH of 6.33 [32]. Formulation B was more acidic than A and C, possibly due to the influence of the carbomer as the gel former. There were variations in pH values for other treatment groups over the 90 days. Carbomers have been reported to be compatible with many active ingredients and this allows the achievement of the required pH value [33-35]. Formulation D was the most acidic of all. Although variable skin pH values are being reported in the literature, all are in the acidic range but with a broad range from pH 4.0 to 7.0 [36].

From the results of the viscosity tests, formulations B and D (Carbopol-based) had the highest viscosity values. The globules of carbomer molecules unfold into a bulk network, creating a structure formation that increases the viscosity of the system [33, 37]. The CMC-based gels had the least viscosity, while the Carbopol-based gels had the highest viscosity with good non-drip properties. The gelling agent (Carbomer 934) is highly effective in thick formulations such as viscous gels. Also, the relatively higher viscosities of the carbopol gels can be explained by the addition of triethanolamine. It was observed that the viscosity values slightly varied from day 1 to day 90. However, the least viscous formulation (D) had almost the consistency of water on day 90. This is a clear case of instability. This could also explain why formulation D had the lowest pH value (**Figure 2**). The use of CMC in formulating gels has been limited due to its low mechanical strength [24].

A majority of the gels exhibited pseudoplasticity. Ease of spread, sufficient skin residence time, and ease of application and collection are clinically important characteristics.

The rheological and mucoadhesive properties of a gel may give rise to a long residence time, but this is only advantageous if the drug remains in the formulation and is released throughout the complete period [38]. Also, the use of polymers will prevent the event of rancidity, especially in coconut water. In this study, formulation F was stable, effective, and sustained in action throughout observation. The effect of the dosage form is another consideration. Creams have lesser residence time on the skin, compared to gels, being largely aqueous. However, the hydrogel matrix, combined with coconut oil actives, presents a physicochemical advantage for transdermal drug delivery, in terms of skin permeability, balanced partition coefficient, and negligible skin barriers, whilst providing a soothing, non-greasy, but emollient feel. This has implications for patient compliance.

## CONCLUSION

This study has established the effectiveness of coconut oil and water formulated as gels, in managing chloroquine-induced pruritus in animal models. The result thus presents an argument for experimenting with its potent usage in humans for treating pruritis. The (Carbopol + CMC) gel matrix containing coconut oil was the most stable of all synthesized gels. This may have been due to the combined properties of both polymers and the coconut oil.

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**Conflict of interest:** None

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**Ethics statement:** All animal experiments were carried out under the guidelines of the Animal Ethics Committee of the Faculty of Pharmaceutical Sciences, Nnamdi Azikiwe University, Awka, Nigeria, and EU directive 2010/63/EU for animal experiments.

## REFERENCES

- [1] Welz-Kubiak K, Reszke R, Szepietowski JC. Pruritus as a sign of systemic disease. *Clin Dermatol.* 2019;37(6):644-56. doi:10.1016/j.clindermatol.2019.07.031
- [2] Szepietowski JC, Weisshaar E (eds). *Itch - Management in Clinical Practice.* Curr Probl Dermatol. Basel, Karger. 2016;50:1-8. doi:10.1159/000446006
- [3] Cukras C, Huynh N, Vitale S, Wong WT, Ferris FL, Sieving PA. Subjective and objective screening tests for hydroxychloroquine toxicity. *Ophthalmology.* 2015;122(2):356-66.
- [4] Silva PUJ, Oliveira MB, Vieira W, Cardoso SV, Blumenberg C, Franco A, et al. Oral pigmentation as an adverse effect of chloroquine and hydroxychloroquine use: A scoping review. *Medicine (Baltimore).* 2022;101(11):e29044. doi:10.1097/MD.00000000000029044
- [5] Ajayi AAL. Itching, chloroquine, and malaria: a review of recent molecular and neuroscience advances and their contribution to mechanistic understanding and therapeutics of chronic non-histaminergic pruritus. *Int J Derm.* 2019;58(8):880-91. doi:10.1111/ijd.14252
- [6] Umate N, Kuchewar V, Parwe S. A narrative review on use of virgin coconut oil in dermatology. *J Indian Sys Med.* 2022;10:86-9. doi:10.4103/jism.jism\_34\_22
- [7] Pham LJ. Coconut (cocos nucifera). In *Industrial oil crops 2016* Jan 1 (pp. 231-242). AOCS Press. doi:10.1016/B978-1-893997-98-1.00009-9
- [8] Kappally S, Shirwaikar A, Shirwaikar A. Coconut oil – a review of potential applications. *Hygeia: J Drugs Med.* 2015;7:34-41. doi:10.15254/H.J.D.Med.7.2015.149
- [9] Vaughn AR, Clark AK, Sivamani RK, Shi VY. Natural Oils for Skin-Barrier Repair: Ancient Compounds Now Backed by Modern Science. *Am J Clin Derm.* 2018;19(1):103-17.
- [10] Edris AE. Pharmaceutical and therapeutic potentials of essential oils and their individual volatile constituents: a review. *Phytother Res.* 2007;21(4):308-23. doi:10.1002/ptr.2072
- [11] Ryu K, Heo Y, Lee Y, Jeon H, Namkung W. Berbamine reduces chloroquine-induced itch in mice through inhibition of MrgprX1. *Int J Mol Sci.* 2022;23(22):14321.
- [12] Choi D, Ji Y, Jang Y, Lee WJ, Shim WS. Crotamiton, an Anti-Scabies Agent, Suppresses Histamine- and Chloroquine-Induced Itch Pathways in Sensory Neurons and Alleviates Scratching in Mice. *Biomol Ther.* 2020;28:569-75. doi:10.4062/biomolther.2020.063
- [13] Bonchak JG, Lio PA. Nonpharmacologic interventions for chronic pruritus. *Itch.* 2020;5(1):e31. doi:10.1097/itx.0000000000000031
- [14] Callen JP, Jorizzo JL, Bologna JL, Piette WW, Zone JJ (eds). *Dermatological Signs of Internal Disease (Fourth Edition)*, W.B. Saunders; 2009. pp. i-iii.
- [15] Yang YY, Du LX, Zhu JY, Yi T, Yang YC, Qiao Z, et al. Antipruritic effects of geraniol on acute and chronic itch via modulating spinal GABA/GRPR signaling. *Phytomedicine.* 2023;119:154969. doi:10.1016/j.phymed.2023.154969
- [16] Miyahara Y, Funahashi H, Haruta-Tsukamoto A, Kogoh Y, Kanemaru-Kawazoe A, Hirano Y, et al. Differential Contribution of 5-HT4, 5-HT5, and 5-HT6 Receptors to Acute Pruriceptive Processing Induced by Chloroquine and Histamine in Mice. *Biol Pharm Bull.* 2023;46(11):1601-8. doi:10.1248/bpb.b23-00445
- [17] Lee WJ, Shim WS. Rg3-enriched Korean red ginseng alleviates chloroquine-induced itch and dry skin pruritus in an MrgprA3-dependent manner in mice. *Integr Med Res.* 2023;12(1):100916. doi:10.1016/j.imr.2022.100916
- [18] Aman N, Rauf K, Khan SA, Tokhi A, Rehman NU, Yameen MA. Effect of commercial and green synthesized ZnO NPs in murine model of



- chloroquine-induced pruritus. *Int J Nanomedicine*. 2019;14:3103-10. doi:10.2147/IJN.S202256
- [19] Zhang Q, Li T, Niu J, Xiao J, Zhang M, Zhang R, et al. Inhibitory effects of antibiotic-induced gut microbiota depletion on acute itch behavior in mice. *Brain Res Bull*. 2022;190:50-61. doi:10.1016/j.brainresbull.2022.09.014
- [20] Gadotti VM, Kreitinger JM, Wageling NB, Budke D, Diaz P, Zamponi GW. Cav3.2 T-type calcium channels control acute itch in mice. *Mol Brain*. 2020;13(1):119. doi:10.1186/s13041-020-00663-9
- [21] Miyahara Y, Funahashi H, Haruta-Tsukamoto A, Kogoh Y, Kanemaru-Kawazoe A, Hirano Y, et al. Differential Contribution of 5-HT<sub>4</sub>, 5-HT<sub>5</sub>, and 5-HT<sub>6</sub> Receptors to Acute Pruriceptive Processing Induced by Chloroquine and Histamine in Mice. *Biol Pharm Bull*. 2023;46(11):1601-8. doi:10.1248/bpb.b23-00445
- [22] Bussaratid V, Walsh D, Wilairatana P, Krudsood S, Silachamroon U, Looareesuwan S. Frequency of pruritus in plasmodium vivax malaria patients treated with chloroquine in Thailand. *Trop Doct*. 2010;30(4):211-2.
- [23] Nwonu PC, Obidike RO, Nwonu CNS. Interaction between chloroquine sulphate and coconut fruit water in adult male rabbits. *Int J Adv Res*. 2017;5:1972-6.
- [24] Zhang W, Liu Y, Xuan Y, Zhang S. Synthesis and applications of carboxymethyl cellulose hydrogels. *Gels*. 2022;8(9):529.
- [25] Bosco S. Optimization of Aqueous Extraction of Virgin Coconut Oil Using Response Surface Methodology. *CORD*. 2013;29(1):11. doi:10.37833/cord.v29i1.96
- [26] Jasman J, Sudirman S, Erlin L. Evaluation of yield and quality of virgin coconut oil produced using repeated batch fermentation with baker's yeast. *Agric Nat Resour*. 2021;55(1):51-6.
- [27] Tarrasón G, Carcasona C, Eichhorn P, Pérez B, Gavaldà A, Godessart N. Characterization of the chloroquine-induced mouse model of pruritus using an automated behavioural system. *Exp Dermatol*. 2017;26(11):1105-11. doi:10.1111/exd.13392
- [28] Inan S, Cowan A. Kappa opioid agonists suppress chloroquine-induced scratching in mice. *Eur J Pharmacol*. 2004;502(3):233-7. doi:10.1016/j.ejphar.2004.09.010
- [29] Burns DT, Johnston E, Walker MJ. Authenticity and the Potability of Coconut Water - a Critical Review. *J AOAC Int*. 2020;103(3):800-6.
- [30] Oganezi NC, Onyejekwe AF. Identification of fatty acids and other compounds in coconut oil extracted by different methods using gas chromatography – mass spectrometry. *Asian Basic Appl Res J*. 2023;5(1):41-8.
- [31] Krishna G, Raj GD, Bhatnagar AS, Chandrashekar P. Coconut Oil: Chemistry, Production and Its Applications- A Review. *Indian Coconut J*. 2010;53(3):15-27.
- [32] Awua AK, Doe ED, Agyare R. Exploring the influence of sterilization and storage on some physicochemical properties of coconut (*Cocos nucifera* L.) water. *BMC Res Notes*. 2011;4(1):451. doi:10.1186/1756-0500-4-451
- [33] Islam MT, Rodriguez HN, Ciotti S, Ackermann C. Rheological characterization of topical carbomer gels neutralized to different pH. *Pharm Res*. 2004;21(7):1192-9. doi:10.1023/B:Pham.0000033006.11619.07
- [34] Rabisková M, Sedláková M, Vitková M, Kuna M. Carbomers and their use in pharmaceutical technology *Ceská Slov Farm*. 2004;53(6):300-3.
- [35] Panzade P, Puranik PK. Carbopol Polymers: A Versatile Polymer for Pharmaceutical Applications. *Res J Pharm Technol*. 2010;3(3):672-5.
- [36] Lambers H, Piessens S, Bloem A, Pronk H, Finkel P. Natural skin surface pH is on average below 5, which is beneficial for its resident flora. *Int J Cosmet Sci*. 2006;28(5):359-70.
- [37] Varges PR, Costa CM, Fonseca BS, Naccache MF, de Souza Mendes PR. Rheological characterization of Carbopol® dispersions in water and in water/glycerol solutions. *Fluids*. 2019;4(1):3. doi:10.3390/fluids4010003
- [38] Paulsson M, Edsman K. Controlled drug release from gels using surfactant aggregates: I. Effect of lipophilic interactions for a series of uncharged substances. *J Pharm Sci*. 2001;90(9):1216-25.