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Research Article

Formulation development and mosquito repellence testing of pharmaceutical gels containing *Lantana camara* flower extract

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ABSTRACT

Purpose: Plant based alternative medicines are gaining popularity due to their numerous beneficial effects over synthetic medicines. The flower extract of the *Lantana camara* is scientifically proven to possess potent mosquito repellent properties. Therefore, this study was focused on formulation development and mosquito repellence testing of *L. camara* flower extract based pharmaceutical gel formulations.

Method: The gel formulations were prepared using *L. camara* flower extract, polyethylene glycol 4000, Carbopol 940 and *Aloe vera* at five different ratios. The colour, odour, spreadability and pH of the gels were determined to evaluate their physical and chemical properties. Physical stability was evaluated for 90 days at room temperature (28±5ºC) subjecting the formulations to centrifugation and cycling tests. The most stable formulations were subjected to *in vitro* lethal toxicity assay and mosquito repellence testing.

Results: All formulations had a prominent lavender smell, smooth and non-gritty texture with light-yellow colour on day one. Only two formulations maintained unchanged organoleptic properties until the end of the 90-day stability testing period. All formulations had a pH between pH 4.0-7.0 and a spreadability range of 9.5-16.6 g.cm/s. Only one formulation underwent creaming after centrifugation. The lavender smell was reduced in two formulations after the cycling test. Out of the five formulations, two formulations were proven stable for 90 days while the other formulations were unstable due to creaming and fluidity. *In vitro* toxicity assay indicated that the stable formulations were non-toxic. The two stable formulations (1g) maintained 100% repellence activity for 6 hours.

Conclusion: Two stable pharmaceutical gel formulations containing *L. camara* flower extract were developed with acceptable quality and stability.

Key words: *Lantana camara* flower extract, pharmaceutical formulation, repellence

INTRODUCTION

Various pathogens causing diseases such as dengue, malaria, and yellow fever are carried by mosquito species of the *Anopheles*, *Culex*, and *Aedes* genera. (1) When mosquitoes feed on the host's blood, their saliva triggers an immune response by binding the Immunoglobulin G (IgG) and Immunoglobulin E (IgE) antibodies to antigens. These immune reactions frequently result in discomfort, itching, redness, and bumps. Additionally, mosquito bites can provoke substantial skin irritation due to allergic responses to the mosquito's saliva upon contact. (2) At present, the primary method for managing mosquito-borne diseases is the control of mosquitoes and protection of individuals against mosquito bites. This can be accomplished through the application of mosquito repellents. (3)

The purpose of applying mosquito repellents on the skin and other surfaces is to prevent the landing of mosquitoes thereby, decreasing the contact between humans and mosquitoes. The olfactory senses of mosquitoes may be blocked due to the active ingredients in such formulations facilitating the repellent action. Mosquito-borne diseases such as dengue and malaria may be prevented or limited due to the use of mosquito repellents. (4) Since synthetic mosquito repellents are not widely accepted by the public due to their drawbacks such as irreversible environmental damage, being non-degradable in nature, and high price, plant-based repellents may be preferred as they are associated with being less toxic, with low potential of generating side-effects and their lower cost. (3-5)

Lantana camara plant is commonly known as "*Gandapana*," in the Sinhala language. It is a weed that can be seen in tropical, subtropical, and temperate areas of the world. (6) The flowers of *L. camara* are available in orange, white, and red colours which may differ with age. (6) As *L. camara* is known to contain phytochemicals including triterpenoids, flavonoids, alkaloids, steroids, saponins, coumarins, tannins, and carbohydrates, it is regarded as a plant with many medical benefits. (6-8) Many medicinal benefits of this plant have been reported including antipyretic, antimicrobial, anti-mutagenic, fungicidal, insecticidal, and nematocidal effects. In addition, its flower extracts are used to treat various disease conditions such as cancers, asthma, tumours, bilious fevers, chickenpox, eczema, measles, ulcers, and swelling. (9-11) The flower extract of *L. camara* in coconut oil was proven to be protective against *Aedes* mosquitoes and provided a protection of 94.5% from *Aedes albopictus* and *Aedes aegypti* mosquitoes. The protective action was observed to be higher for the *L. camara* flower extract as compared to its leaf extract. (7)

Pharmaceutical gel formulations were developed in this study to overcome the disadvantages of the commonly used topical pharmaceutical formulations including creams, ointments, and lotions such as stickiness and poor spreading coefficient. (13,14) Evaluation of chemical and physical properties of the pharmaceutical formulations is mandatory as they affect the stability of prepared pharmaceutical formulations. Hence, the developed pharmaceutical formulations were evaluated for organoleptic properties, spreadability, and pH. (15) Further, the physical stability of the gel formulations was observed at room temperature (28±5ºC) during a period of 90 days by subjecting selected formulations to centrifugation and cycling tests. (16, 17)

Therefore, this study focused on the formulation, development, and repellence testing of *L. camara* flower extract based pharmaceutical formulations with the aim of enhancing the use of plant-based mosquito repellents.

METHODS

Main materials

The main materials used to formulate the gels were *L. camara* flowers, *Aloe vera* leaves, citric acid, Carbopol 940, distilled water, polyethylene glycol 4000, potassium sorbate, triethanolamine, and lavender oil. *L. camara* plant was authenticated by the National Herbarium located in the premises of the Royal Botanical Gardens, Peradeniya, Sri Lanka. *L. camara* flowers and *Aloe vera* leaves were obtained from the home gardens at Nittabuwa, Sri Lanka.

Preparation of the *L. camara* flower extract

The preparation of the *L. camara* flower extract was carried out according to the method described by Dua *et al.* (7) Initially, *L. camara* flowers (25 g) were crushed in a mortar with distilled water (25 mL) to make a thick slurry. Methanol (50 mL) was added to the slurry, followed by coconut oil (50 mL). This was then mixed for 4 hours in an orbital mixer. The upper layer was then separated by a separating funnel and kept in a water bath at 60^{o}C for approximately 1 hour to remove methanol. Subsequently, Tween 80 (12.5 mL) was added with distilled water (25 mL) to the separated layer and mixed well.

Preparation of the *Aloe vera* gel

Aloe vera gels were prepared according to the method described by Sameer *et al.* (17) First, washed, and air-dried *Aloe vera* leaves were cut in the middle lengthwise and the gel was obtained gently to avoid contamination with the sap of the leaf skin. Then the gel was subjected to grinding at room temperature (28±5°C) for 10 minutes to avoid browning followed by, filtration through a muslin cloth. The pH of the gel was adjusted to a value between pH 3.0 to 3.5 by adding citric acid**.**

Preparation of the *L. camara* flower extract based pharmaceutical formulation

An emulsion was prepared according to the following ratio *i.e.* 4 Coconut oil: 2 Distilled water: 1 Tween 80. Then, 5 mL from the prepared emulsion was taken to prepare each pharmaceutical gel formulation. This was carried out by slightly modifying the method described by Jamadar *et al*.. (18) First, accurately weighed Carbopol 940 was taken into a beaker and dispersed in 50 mL of distilled water. The beaker was kept aside for 30 minutes and then stirred for 30 minutes. Then the required amount of polyethylene glycol 4000 was taken into a beaker and potassium sorbate was added to it and stirred. After the dispersion of all the Carbopol 940, the mixture of polyethylene glycol 4000, potassium sorbate, and the calculated amount of *L. camara* flower extract (5%) was added to the latter with constant stirring. The volume was made up to 100 mL by adding *Aloe vera* gel and triethanolamine followed by drop-wise addition of lavender oil. Finally, the mixture was poured into a wide-mouth plastic container and the formulation was allowed to set. The five different formulations (100 g) were prepared with different ratios according to this method. *L. camara* flower extract, triethanolamine, potassium sorbate, distilled water, and lavender oil were incorporated in fixed volumes. The *Aloe vera* gel, Carbopol 940, polyethylene glycol 4000 volumes were changed as shown in Table 1.

Evaluation of physical and chemical properties

The changes in colour, odour, and texture of the pharmaceutical formulations were determined at room temperature (28±5 °C) during the stability evaluation period of 90 days.

Spreadability of each gel was assessed by applying excess pharmaceutical formulation

Table 1. Composition of five pharmaceutical gel formulations

Ingredients	Formulation 1	Formulation 2	Formulation 3	Formulation 4	Formulation 5
Carbopol 940	1.0%	1.5%	2.0%	2.5%	3.0%
Distilled water	50%	50%	50%	50%	50%
Polyethylene glycol	5.0%	7.5%	10.0%	12.5%	15.0%
Potassium sorbate	1.0%	1.0%	1.0%	1.0%	1.0%
Aloe vera gel	35.8%	32.8%	29.8%	26.8%	23.8%
Triethanolamine	2.2%	2.2%	2.2%	2.2%	2.2%
Lavender oil (drops)	2	2	2	2	2

(1g) between two glass slides followed by compression to obtain a uniform thickness by placing a 500 g weight for 5 minutes on the upper glass slide. Spreadability (S) was determined by measuring the spread diameter of the sample using the following equation. (19). Where M is the weight tied to the upper slide, L is the distance travelled by the gel on the surface of the glass and T is the time taken.

S = M.L / T

Changes in the pH of the prepared gel formulations was determined throughout the 90 days of stability evaluation period. The pH was determined at room temperature using a pre-calibrated digital pH meter (Milwaukee, SE-220, Romania).

Evaluation of physical stability

All gel formulations were kept at room temperature for 90 days where each formulation was subjected to centrifugation and cycling tests. Each formulation was kept without centrifugation and cycling to compare formulation instability due to creaming, fluidity, sedimentation, flocculation, and phase separation.

During the centrifugation test, the gel formulations were centrifuged at 4000 rpm for 5 minutes (Gemmy Industrial Corp., PLC-025, Taiwan) and kept for 28 days at room temperature.

Each formulation was subjected to 6 cycles of low to high temperature fluctuations for the cycling test. Each cycle consisted of storing a sample of gel at low temperature (8°C) for 1 hour and then at high temperature (40°C) for 1 hour followed by observation for instability.

***In vitro* lethal toxicity assay**

A brine shrimp lethality bioassay was conducted on *L. camara* flower extract and for the formulated pharmaceutical gels. For the bioassay artificial sea water (1 L) was prepared at the laboratory and the pH was adjusted to pH 8.0. Then the artificial sea water was aerated using an air pump. Brine shrimp eggs were added to the surface of the medium and kept for 24 hours with

illuminated light (60-Watt bulb). The hatched nauplii were collected after 24 hours. Then, ten nauplii were transferred to test tubes containing 5 mL of the prepared pharmaceutical formulations (0.1 g/ mL, 0.05 g/ mL, 0.025 g/ mL, 0.0125 g/ mL, 0.00625 g/ mL, 0.003125 g/ mL) and for the negative control (artificial sea water). The number of surviving nauplii was counted after 24 hours and the percentage lethality was calculated for each gel concentration using the following equation. (20)

$$\text{Lethality \%} = \frac{\text{Number of dead nauplii} * 100}{10}$$

Repellence testing

Ethical approval was granted from the Ethics Review Committee at CINEC Campus, Malabe, Sri Lanka, before performing the repellence testing (ERC Reference number: ERC/CINEC/2022/024, 29th June 2023).

Aedes Albopictus strains used in this experiment originated from eggs separately collected from the indoor insectary, Molecular Medicine Unit, Faculty of Medicine, University of Kelaniya. The collected mosquito eggs were transferred to 1 L plastic trays. Hatched larvae were counted and transferred to a properly labelled plastic tray (40 cm x 30 cm x 5 cm) containing 2 L of distilled water. For experimental quality control and for the maintenance of uniform-sized larvae; a density of 1,000 larvae per tray was maintained.

Adults were held in a properly labelled cage (30 cm x 30 cm x 30 cm). About seven hundred adult mosquitoes were reared in one cage having a 1:1 male: female ratio. Adult mosquitoes were fed with a 10% sucrose solution. Mosquitoes were reared in an environment with a temperature of 26°C–27°C and 78%-80% RH having a 12-hour light and 12-hour dark cycle. (21) Blood feeding was carried out according to the standard guidelines. Standardized mosquito rearing and laboratory testing conditions were maintained to ensure the reliability and reproducibility of data.

Estimation of complete protection time ($ED_{99.9}$)

The volunteers who were free of skin diseases like skin irritation, erythema, and allergies to the formulation gel were selected by performing a patch test. In preparation for the laboratory studies, the test area of the volunteer's skin was initially washed with unscented soap and rinsed with water, then rinsed with a solution of 70% ethanol or isopropyl alcohol in water and dried with a towel.

A mosquito cage measuring 35-40 cm per side was utilized. It had a solid bottom and top, with a screen or netting on the back, a clear acrylic sheet on the right and left sides for viewing, and two fabric sleeves on the front for access. For the test, 50-100 non-blood fed female mosquitos from colony-maintaining population cages were used 7 – 10 days post-emergence. A sleeve was used for testing the candidate repellents. Before applying the formulation below the wrist, the hand of the volunteers was protected by gloves made of material through which the mosquitoes could not bite while the volunteer avoided movement of the arm.

Initially, the readiness of mosquitoes to land or probe was assessed by inserting an untreated (alcohol or diluent treated) arm into a cage for 30 seconds. The procedure was repeated with the other arm in the second cage. If landing or probing was not achieved in either cage, the experiment was discarded. Before testing commenced, 1 g of the

prepared candidate repellent was applied to one arm, and the other arm was not treated with the repellent. After 30 minutes, the repellent-treated arm was inserted into the appropriate cage and exposed for 3 minutes to determine landing or probing activity. Next, the other arm was exposed to determine landing or probing activity. This procedure was repeated at 30-minute intervals and was used consistently throughout the experiment. The occurrence of one landing or probing in a 3-minute test interval concluded the test for each repellent dose. Complete protection time was calculated as the number of minutes elapsed between the time of repellent application and the first mosquito landing or probing. Most repellent studies were completed in 8 hours or less. This procedure was conducted for a stable formulation with lavender oil and for a stable formulation without lavender oil to check the repellence of the lavender oil. Protection (p) is expressed as a proportion of the number of mosquito landings or probing on the treated arm (T) in relation to the number of landings or probing on the control arm (C) of the same individual (the diluent-applied test arm before repellent treatment and the other arm at the end of the experiment). (22, 23)

$$p = 1 - (T / C) = (C - T) / C$$

Independent sample t-test was performed to compare the repellence of the stable formulations the control and to compare the formulation without lavender oil with the stable formulations with lavender oil.

RESULTS

Physical and chemical properties

The tested organoleptic properties remained unchanged in only two formulations at the end of the 90-day stability testing period (Table 2) All five pharmaceutical gel formulations had an acceptable spreadability ranging 9.5-16.6 g.cm/s (Table 2). (24)

The pH values of four pharmaceutical gel formulations did not change drastically, but a prominent decrease of pH from 7.0-4.0 was seen in one formulation (Table 2)**.**

Stability evaluation

Out of the five pharmaceutical gel formulations, three formulations were unstable at room temperature during the 90-day stability evaluation period. Instability due to creaming and fluidity were mainly observed. Two formulations demonstrated acceptable stability throughout the 90-day stability evaluation period (Table 2).

Only two pharmaceutical formulations were unstable during 28 days after centrifugation. Creaming and fluidity were observed as the main types of instability. Three formulations demonstrated acceptable stability throughout the 28 days of stability evaluation after centrifugation (Table 2).

During all 6 cycles of temperature fluctuation, no changes were observed in the three stable pharmaceutical gel formulations. However, the absence of lavender smell was observed in two formulations following the fourth cycle at high temperature conditions. (Table 2).

In vitro lethal toxicity assay

Only the formulation with a concentration of 0.1 g/ mL of L. *camara* flower extract was observed with 20% lethality. All other formulations were not lethal.

Mosquito repellent activity

The two stable pharmaceutical formulations showed 100% repellence for the first 7 hours,

Table 2. Physical, chemical properties and stability evaluation of the pharmaceutical gel formulations

Gel formulation		1	2	3	4	5
Organoleptic properties on day 1		Light yellow colour with smooth texture	Light yellow colour with smooth texture	Light yellow colour with smooth texture	Light yellow colour with smooth texture	Light yellow colour with smooth texture
Organoleptic properties on day 90		Different to day 1	Different to day 1	Different to day 1	Unchanged	Unchanged
Spreadability (g.cm/s)		16.5	12.16	10.16	9.6	9.6
pH	Day 1	7.0	4.9	4.7	4.2	4.0
	Day 15	6.6	4.7	4.7	4.2	4.0
	Day 29	6.0	4.5	4.0	4.2	4.0
	Day 43	5.8	4.3	4.2	4.0	4.0
	Day 57	5.0	4.3	4.2	4.0	4.0
	Day 71	4.8	4.2	4.2	4.0	4.0
	Day 85	4.7	4.1	4.1	4.0	4.0
Centrifugation test (28 days)		Unstable (creaming, fluidity)	Unstable	Stable	Stable	Stable
Cycling test (6 cycles)		No lavender smell from cycle 4-6 at high temperature	No lavender smell from cycle 4-6 at high temperature	Unchanged	Unchanged	Unchanged

Table 3. Mosquito repellence test results of the tested pharmaceutical gel formulations

Treatment stability testing times	0	1 hr	2 hrs	3 hrs	4 hrs	5 hrs	6 hrs	7 hrs	8 hrs
Repellence of formulation 4	100%	100%	100%	100%	100%	100%	100%	98.7%	98.0%
Repellence of formulation 5	100%	100%	100%	100%	100%	100%	100%	99.5%	98.0%
Repellence of the formulation without lavender	100%	100%	100%	100%	100%	100%	98.0%	96.0%	95.4%

but repellence decreased to 98.7% and 99.5% at 8 hours, respectively. The lavender smell-free formulation had repellence rates, dropping from 98.0% at 6 hours to 96.0% at 7 hours and 95.4% by the end of the test. (Table 3). Hence the t-test proved that the stable formulations had a significant repellent activity compared to the control ($p < 0.05$; $6.133*10^{-6}$) and the formulation without the lavender oil did not show a significantly different repellent activity with the stable formulations with lavender oil ($p > 0.05$; 0.079).

DISCUSSION

Five different pharmaceutical formulations were prepared using the flower extract of the plant *L. camara*. All pharmaceutical formulations were subjected to evaluation of physical stability with respect to physical properties such as organoleptic properties and spreadability as well as chemical properties such as pH measurements along with centrifugation and cycling tests.

Initially all formulations were light yellow in colour with a prominent a lavender smell and a smooth, non-gritty texture along with cool feeling on application. At the end of the observation period, there was no change in the colour and odour of two pharmaceutical formulations observed out of the five formulations prepared.

Spreadability is the ability of a formulation to spread consistently over a skin surface, which is an important factor in determining the efficacy of the formulation and ease of application. (24) The correlation between spreadability and rheology of a formulation is essential in determining the behaviour and characteristics of the product. Generally, a formulation with high spreadability often has low viscosity and exhibits fluid-like behaviour that allows it to be easily applied and spread uniformly over a surface with less effort. A formulation with less spreadability generally has high viscosity, resists spreading and needs a greater effort to disperse it uniformly. Poor spreadability of gel a formulation may result in decreased effectiveness, unequal distribution, and difficulty in application, whereas good spreadability can lead to a lack of control, wastage, run-off, or leaking and reduced performance of the formulation. (24,25) Maintaining an ideal balance in spreadability is essential to ensure the effectiveness and efficacy of a formulation. In this study, all pharmaceutical formulations were within the accepted spreadability range of 9.5 - 16.6 g.cm/s. (24-26)

The pH was determined to ensure that the developed formulations were within the desired pH range for application onto the skin. A pH value of 4.7 is considered the average pH of the skin. (27) Maintaining an optimum pH in topical gel formulations is essential for preserving the stability of active ingredients, ensuring skin compatibility, facilitating skin absorption, controlling microbial growth, achieving the appropriate consistency and rheological properties. Formulations that contain pH-sensitive compounds may experience pH fluctuations over time. This may take place because of chemical reactions or interactions among formulation components, leading to destabilization of the formulation structure. Changes in pH may impact the solubility and stability of active substances, which may result in decreased effect of the active ingredient. (28) In this study, the pH of the formulations was within the pH range (pH 4.0-7.0) throughout the study.

Furthermore, pharmaceutical gel formulations can be affected by creaming, fluidity, sedimentation, flocculation, phase separation, changes in pH and the growth of microorganisms. (29) Creaming takes place when the dispersed phase of the gel rises or settles due to density differences. This can lead to unequal distribution of active ingredients and inconsistent product texture. Gel compositions must retain their desired consistency and viscosity. Changes in fluidity can make application and dosing difficult, reducing the product's effectiveness. Solid particles settle at the bottom of the gel formulation with time, causing sedimentation. This can change the texture and appearance of the product and lead to unequal distribution of components. The clumping of particles in the gel is known as flocculation. It can form visible aggregates, impacting the product's appearance and stability. Phase separation is an irreversible mechanism that occurs when the components of a formulation split into different phases, and the texture and appearance of the formulation become inconsistent. As a result, the required homogeneity of the formulation is disturbed, which might result in an ineffective or visually unpleasant product. (30) Unstable formulations could threaten shelf-life, product efficiency and consumer satisfaction. Therefore, stability evaluation is essential to assess the quality and effectiveness of a product, ensure its safety and prevent degradation under various environmental conditions such as temperature, humidity, and light exposure. (29, 30) During the 90 days of physical stability evaluation, only two pharmaceutical gel formulations were stable at room temperature, while other formulations were subjected to creaming and fluidity with a bad odour.

Centrifugation tests are used to assess the stability of formulations, particularly those containing suspended particles or emulsions. The formulation is subjected to centrifugal forces resembling stress and acceleration conditions that may occur during storage or transportation. (31) This test evaluates the tendency for phase separation or sedimentation of a gel formulation. Throughout the centrifugation test, three pharmaceutical formulations were stable at room temperature, while one pharmaceutical formulation was subjected to creaming followed by fluidity in other formulation along with a bad odour. This indicates the possibility of microbial contamination, and it is recommended to perform microbial testing for further evaluation of the developed formulations. The two pharmaceutical formulations which did not undergo any changes during the centrifugation tests were also unstable during the evaluation of organoleptic properties at the end of 90 days.

The basis of performing a cycling test is to evaluate the stability, durability, reliability and efficiency of a product or material under recurrent or cyclic stress or harsh conditions in the environment. This test consists of subjecting the test product through a series of stress cycles that resemble the desired or expected usage conditions over a particular period ensuring the products fulfil the intended standards, and consumer expectations throughout their shelf-life. (32) During the cycling test, significant changes in any of the formulations were not observed. Only a faint lavender smell was noticed in two pharmaceutical formulations (Table 2).

The *in vitro* lethal toxicity assay is a simple and inexpensive bioassay that is performed to test the toxicity of the prepared formulations.

However, insufficient information about the mechanism of action, limited biological complexity, challenges in standardized experimental conditions, difficulty in predicting long-term effects, lack of specificity and limited sensitivity are limitations of this study. Considering the pharmaceutical formulations, only the formulation with 0.1 g/mL concentration produced 20% lethality.

The efficacy of mosquito repellent gels in disease prevention is essential for public health efforts and can contribute to overall mosquito-borne disease control and management. The mosquito *Aedes albopictus* was used to examine the effect of repellent activities in the prepared two stable pharmaceutical formulations. The number of mosquitoes landing on the treated arm and the number of mosquitoes landing on the control arm of the same individual were counted every half an hour for 8 hours. The two stable pharmaceutical formulations demonstrated 100% repellence for 6 hours and 98.0% at 8 hours. These results indicated that those two formulations had > 90% repellence for more than 8 hours, with a complete protection time of 6 hours. Several studies have suggested that lavender oil has mosquito repellent properties. The high volatility of lavender oil contributed to poor longevity, and this was resolved by incorporating it into the mosquito repellent formulation. (32) The repellence test for pharmaceutical formulation without lavender oil exhibited 100% repellence for 5 hours and 95.4% at 8 hours. This observation demonstrated that the two stable pharmaceutical formulations containing *L. camara* flower extract exhibited significant mosquito repellent efficacy, showcasing a statistically significant change in mosquito attraction compared to the control group and the addition of lavender oil elevated the protection time of the prepared pharmaceutical gel formulations. Moreover, these physically stable two pharmaceutical formulations could be recommended as mosquito repellent formulations and appropriate substitutes for chemical mosquito repellents such as N, N-diethyl-3-methyl benzamide (DEET) due to their effectiveness, non-toxicity, affordability, and environmental friendliness. Synthetic mosquito repellents cause irreversible damage to the ecology, and the compounds are non-biodegradable in nature. The negative effects of DEET include unpleasant odour, sub-chronic toxicity, mutagenicity, reproductive and neurological damage. (33)

CONCLUSION

The two pharmaceutical formulations comprising 26.8% *Aloe vera*, 12.5% polyethylene glycol 4000, 2.5% Carbopol 940 and 23.8% *Aloe vera*, 15% polyethylene glycol 4000, 3% Carbopol 940 respectively, were observed as the non-toxic, most stable pharmaceutical formulations. These were within the spreadability range of 9.5–16.6 g.cm/s with a light-yellow colour, good lavender smell, smooth, non-gritty texture, and prominent mosquito repellence.

Therefore, these two stable pharmaceutical gel formulations will be further recommended for microbial testing, preclinical testing, and clinical testing prior to obtaining relevant market authorization for commercialization as natural mosquito repellents.

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AUTHOR'S DECLARATION:

The authors declare that all persons listed as authors have read and given approval for the submission of this manuscript.

COMPETING INTERSTS:

The authors declare that they have no conflict of interests.

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