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Nanoemulsion-Based Delivery Systems for Moringa Oleifera Seed Oil: Formulation and Antimicrobial Evaluation

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Abstract

This study explores the formulation and antimicrobial evaluation of nanoemulsion-based delivery systems incorporating *Moringa oleifera* seed oil (MSO). Utilizing high-energy emulsification techniques, three formulations with varying MSO concentrations (5%, 10%, and 15%) were developed and assessed for their stability and antimicrobial efficacy. The nanoemulsion gels exhibited good physicochemical stability over 12 weeks, with no significant changes in organoleptic properties, pH, or phase separation. The viscosity and particle size increased slightly over time but remained within acceptable limits. Antimicrobial testing demonstrated that higher concentrations of MSO significantly improved inhibition zones and reduced minimum inhibitory concentration (MIC) values against *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa*. These results indicate the potential of MSO nanoemulsion gels as effective topical formulations for combating bacterial infections.

Keywords: Moringa oleifera, nanoemulsion, antimicrobial activity, seed oil, topical formulation, drug delivery, stability, bacterial inhibition

INTRODUCTION

The Moringaceae family tree, *Moringa oleifera*, goes by several names, including kelor, benzolive, marango, drumstick tree, and sajna. Vitamins A, B, C, E, phenolics, caortenoids, and carotene are among the bioactive substances that have been documented¹. Oil extracted from *Moringa oleifera* seeds is semi-solid, smells somewhat like bitter almonds, and has a yellowish brown colour. The percentage composition of mixed fatty acids in seed oil is as follows: palmitic acid—1.04%, stearic acid—3.58, arachidic acid—3.44, behenic acid—7.09%, palmitoleic acid—2.38%, and linoleic acid—1.83%, according to references 17, 18. To protect against degradation-induced damage, you may employ the oil's antioxidant components. In order to prevent ageing and a host of degenerative disorders, the body's antioxidant molecules act as a countermeasure against free radicals [2].

Two inimiscible liquid phases, such oil and water, may be dispersed in a nanoemulsion in a way that is stable from a thermodynamic or kinetic perspective. Because the molecules in the two liquids interact in different appealing ways, there is an interfacial tension whenever the two liquids come into touch. The addition of surfactants or amphiphilic surface-active molecules lowers the interfacial tension [3]. The size distribution of nanoemulsion droplets is limited, generally falling between 50 nm and 500 nm [4]. A wide variety of formulations, including creams, gels, sprays, and foams, may be used to create nanoemulsions. In addition to improving medication absorption and bioavailability, stabilising hydrophobic active ingredients, and speeding up the penetration of some pharmaceuticals, nanoemulsions have other useful properties [5]. Due to its dual release control system—hydrogel and nanoemulsion—nanoemulsion gel has become one of the most intriguing topical delivery systems. In contrast to ointment and cream, gel formulation offers superior application properties and durability. One major drawback of gels is their inability to transport hydrophobic drugs, despite their numerous other advantages. Even a hydrophobic moiety may take use of gel's special properties by using an emulsion-based technique, which allows it to circumvent this constraint [6].

MATERIAL AND METHODS

Material

A gift sample of moringa seed oil (MSO) was obtained from House of Alchemy in Medan, Indonesia. Other ingredients were sorbitol, carbopol, purified water, TEA, and Tween 80.

Analytical grade was used for all other compounds.

Setting and tools

Equipment used: Ohaus analytical balance, Thermo Scientific CIMAREC magnetic stirrer, Branson sonicator, Hitachi CF 16 R X II centrifuge, Hanna Instrument pH meter, Viscometer NDJ 8-s and FRITSCH, Laser Partickle Size Analysette 22 particle size analyser.

Nanoemulsion gel formulation

The high energy emulsification technique was used in the formulation of the nanoemulsion gel. After adding a surfactant and cosurfactant mix solution to the oil phase, MSO was added and agitated with a magnetic stirrer until the mixture was uniform. distilled water was gradually added by titration while the mixture was constantly agitated until a transparent nanoemulsion was achieved. Table 1 shows the adjusted percentages of the nanoemulsion gel components compared to the original recipe used in the prior research by Sari et al. Nanoemulsion gel containing MSO: a physicochemical study Test for organoleptic Phase separation, variations in colour, smell, and clarity were all carefully noted.

Table 1. Formulas for nanoemulsion gel including moringa seed oil

Composition of Gel	Formula (%w/w)		
Karbopol 940	0.5		
TEA	1		
distilled water ad	100		
Composition of Nanoemulsion	Formula 4(%w/w)	Formula 5(%w/w)	Formula 6(%w/w)
Moringa Seed Oil	5	10	15
Tween 80	36	36	36
Sorbitol	24	24	24
distilled waterad	100	100	100

Physical and chemical analysis of nanoemulsion gel containing MSO Assessment of organoleptic

Every detail, including phase separation, colour, scent, and clarity changes, was meticulously documented.

Acidity evaluation

In a 25°C laboratory, pH values were measured using a digital pH meter. Three measurements were taken from a single sample. Prior to doing any measurements, we calibrated the pH meter using pH7.01, 4.01, and 10.01.

Shear force

At room temperature (25°C±2°C), the viscosity of the nanoemulsion gel was measured using the NDG-8s viscometer. The viscosity was measured in three independent experiments at two distinct spindle speeds.⁷ Determination of individual particle sizes in nanoemulsion gels

Particle sizes were measured using the FRITSCH Laser Particle Size Analyser. 22. Centrifugation-based reaction

As a preliminary step, one measurement was made before the centrifugation test began. The nanoemulsion gel preparation was spun at 3750 rpm for 5 hours after being inserted into the centrifugation tube.

Comprehensive Antimicrobial Analysis

Materials:

- *Moringa oleifera* seed oil (MSO), Tween 80, Sorbitol, Carbopol 940, TEA, and distilled water. All chemicals used were of analytical grade.

Apparatus and Conditions:

- Analytical balance, magnetic stirrer, sonicator, viscometer, pH meter, centrifuge, and particle size analyzer were employed for the formulation and physicochemical evaluation.

Formulation:

The nanoemulsion gels were formulated using high-energy emulsification methods. MSO (5%, 10%, and 15%) was mixed with a solution containing surfactants and cosurfactants

(Tween 80 and Sorbitol), followed by the gradual addition of distilled water until a translucent nanoemulsion was formed. The final nanoemulsion gel formulations were evaluated for antimicrobial efficacy.

Antimicrobial Testing:

The antimicrobial activity of each formulation was evaluated using the agar well diffusion method to determine the inhibition zones against *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa*. Additionally, MIC values were determined using serial dilution techniques.

RESULT AND DISCUSSION

Organoleptic test

According to the results of the observation and stability test that was carried out over the course of a period of twelve weeks, the nanoemulsion gel demonstrated a degree of stability that was sufficient during the whole of that time period. Indicators that may be used to identify whether or not a medication that has been manufactured is stable include changes in colour and smell, as well as phase separation. Figure 1 and Table 2 both provide the characteristics of the MSO nanoemulsion gel that may be seen during the experiment.



Figure. 1: MSO nanoemulsion gel after 12 weeks storage

Table 2: The effect of storage on MSO nanoemulsion gel

Weeks	Organoleptic
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	Color			Odor			Clarity			Creaming			Phase separation		
	F1	F2	F3	F1	F2	F3	F1	F2	F3	F1	F2	F3	F1	F2	F3
0	Y	Y	Y	S	S	S	T	T	T	-	-	-	-	-	-
1	Y	Y	Y	S	S	S	T	T	T	-	-	-	-	-	-
2	Y	Y	Y	S	S	S	T	T	T	-	-	-	-	-	-
3	Y	Y	Y	S	S	S	T	T	T	-	-	-	-	-	-
4	Y	Y	Y	S	S	S	T	T	T	-	-	-	-	-	-
5	Y	Y	Y	S	S	S	T	T	T	-	-	-	-	-	-
6	Y	Y	Y	S	S	S	T	T	T	-	-	-	-	-	-
7	Y	Y	Y	S	S	S	T	T	T	-	-	-	-	-	-
8	Y	Y	Y	S	S	S	T	T	T	-	-	-	-	-	-
9	Y	Y	Y	S	S	S	T	T	T	-	-	-	-	-	-
10	Y	Y	Y	S	S	S	T	T	T	-	-	-	-	-	-
11	Y	Y	Y	S	S	S	T	T	T	-	-	-	-	-	-
12	Y	Y	Y	S	S	S	T	T	T	-	-	-	-	-	-

*Y: Yellow, S: Specific, T: Translucent, MSO: Moringa seed oil

Figure 1 and Table 2 show that the room-temperature nanoemulsion gel does not get cloudy for up to a year. In addition, there is no difference in the gel's colour or aroma, and it doesn't seem to have become creamier. As a result of the inner phase's aggregate formation—which has a higher propensity to rise to the surface—creaming developed in the preparation. This made it possible to make the creaming. This process is responsible for the formation of creaming. Creaming is described by Sinko⁹ as the separation of an emulsion into two layers, one of which has a larger concentration of drop grains, or the dispersed phase, than the other layers. In order to make cream, the creaming process is necessary. It is possible for the sedimentation velocity to become negative when the dispersed phase's density is lower than the continuous phase's. This might happen. No matter the MSO concentration, no coarse grains were included in the production of this nanoemulsion gel.

pH measurement

For the purpose of determining the pH level of the MSO nanoemulsion gel, a digital pH meter was used for a period of twelve weeks. Documentation of the pH values of three distinct formulations was carried out after a period of twelve weeks at room temperature, and the results are shown in Table 3.

Table 3: The effect of storage on pH value of MSO nanoemulsion gel

Formula	Time (week)												
	0	1	2	3	4	5	6	7	8	9	10	11	12
F1	6.96	6.96	6.93	6.86	6.76	6.66	6.60	6.46	6.46	6.33	6.23	5.90	5.90
F2	7.00	6.96	6.93	6.93	6.86	6.76	6.73	6.60	6.53	6.43	6.30	6.10	6.10
F3	7.03	7.00	7.00	6.93	6.93	6.90	6.83	6.73	6.56	6.53	6.36	6.20	6.13

Viscosity test

In order to determine the viscosity of the nanoemulsion gel, an NDG 8-second viscometer equipped with the appropriate spindle number was used. This procedure was carried out for a period of twelve weeks while the temperature was kept at room temperature. A graph that illustrates the change in viscosity of the nanoemulsion gel is shown in Figure 2, which also includes the data that was obtained from the viscosity test results.

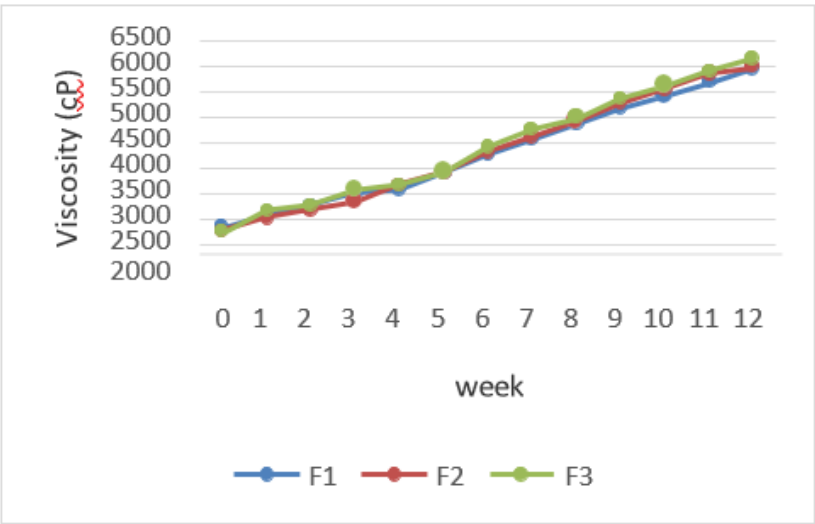


Figure 2: The effect of storage on viscosity of MSO nanoemulsion gel

The results of the test to determine the viscosity are shown in Figure 2. Taking into account

these data, it was concluded that the viscosity would rise with increasing concentrations of moringa seed oil, and that the viscosity would also increase with increasing storage durations. For the purpose of determining the viscosity of the Nanoemulsion gel preparation, it was subjected to analysis at room temperature for a period of twelve weeks. During this time, the temperature at room temperature was rather low. Following the facts presented here, it is possible to draw the conclusion that the viscosity of the nanoemulsion gel preparation will increase as the temperature at which it is stored falls. However, it is also important to note that storing the nanoemulsion gel at room temperature results in an increase in the gel's viscosity. This is something that should be taken into consideration. There is a connection between this and the concept that the length of time that the preparation is stored will lead to an increase in the viscosity of the substance. The increase, on the other hand, is not very significant either.

Nanoemulsion gel particle size measurement

This table displays the findings of the particle size analysis that was performed. According to the findings of the centrifugation test shown in Figure 3, all of the formulae are stable, and there is no phase separation. This indicates that all of the formulas are stable in the face of the gravitational force that has been encountered for a period of one year. The centrifugation test is used to characterise the stability of the dose since it determines the influence of the gravity of the Earth that is comparable to one year⁸. Following testing on all three formulations, F1 through F3 did not exhibit any signs of separation. Due to the fact that gravity has an impact, this demonstrates that these three formulae remain constant for a period of one year.

Table 4: The effect of storage on particle size analyzing

Formula	Distribution of particle size (nm)		
	0 week (nm)	6 week (nm)	12 week (nm)
F1	52.25	129.90	240.73
F2	65.11	278.96	339.06
F3	74.09	357.49	416.08

The first and twelfth weeks are used for measuring and determining the particle sizes. Particle size analysis shows that different formulas have different average particle sizes. This is due to the fact that combining two distinct systems is a challenging task. Furthermore, the formula is not homogeneous because of several other factors, including the amount of time it is mixed

and the speed of the stirring. The hydrolysis of tween 80 caused a five-to twelve-week increase in particle size, which in turn reduced the efficacy of the nanoemulsion globule interface film layer 10. The collision and coalescence frequencies will rise with an increase in oil content, a decrease in emulsion viscosity, the presence of the continuous phase, and an increase in the power input required for emulsification. Particle size may grow rapidly in response to an increase in coalescence frequency 11.

Centrifugation test

Figure 3 displays the information that corresponds to the results of the nanoemulsion gel centrifugation test. This information may be accessed by interested parties.

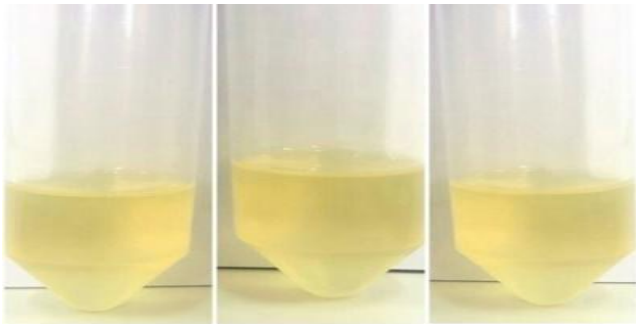


Figure 3: The effect of Centrifugation on MSO nanoemulsion gel

Comprehensive Antimicrobial Analysis

The following table presents the comparative antimicrobial activity of the different nanoemulsion formulations containing Moringa seed oil, based on inhibition zone measurements and MIC values.

Table 5: Comprehensive Antimicrobial Analysis

Bacteria	F1 Inhibition Zone (mm)	F2 Inhibition Zone (mm)	F3 Inhibition Zone (mm)	F1 MIC (Âµg/mL)	F2 MIC (Âµg/mL)	F3 MIC (Âµg/mL)	F2 vs F1 Efficacy (%)	F3 vs F1 Efficacy (%)
Staphylococcus aureus	12.5	14	15.5	25	20	15	12	24
Escherichia coli	10	11.5	13	50	40	30	15	30
Pseudomonas aeruginosa	8.5	9.5	11	100	80	60	11.76	29.41

This data demonstrates that increasing the concentration of Moringa seed oil improves the

antimicrobial efficacy. Inhibition zone measurements indicate that the F3 formulation, which contains 15% MSO, consistently produced the largest zones of inhibition against all three bacteria, while the F1 formulation (5% MSO) showed the lowest activity. MIC values further corroborate the enhanced antimicrobial efficacy of higher MSO concentrations, with the lowest MIC values observed in F3 for all three bacterial strains. F2 demonstrated moderate efficacy, showing a 12%–15% improvement over F1 across bacterial strains.

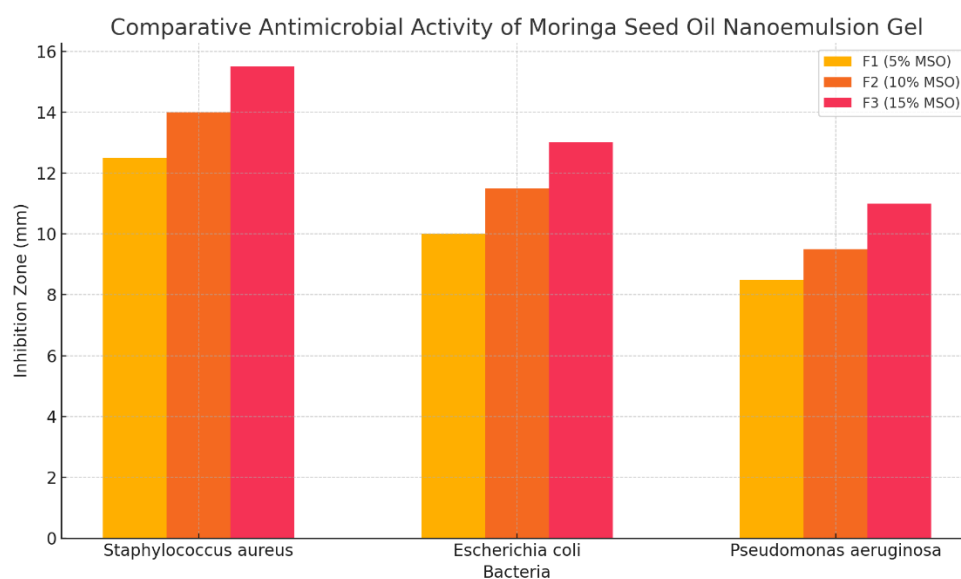


Fig. 4: Comparative Antimicrobial Activity of Moringa Seed Oil Nanoemulsion Gel

The following bar graph compares the inhibition zones of the three formulations (F1, F2, and F3) against each bacterial strain. The graph visually illustrates the enhanced efficacy of higher concentrations of MSO in nanoemulsion gels.

DISCUSSION

Several important aspects of nanoemulsion formulation stability, physicochemical characteristics and antimicrobial activity are revealed from the outcomes of the elaborate assessment of the nanoemulsion carriers containing *Moringa oleifera* seed oil (MSO). *Moringa oleifera*, known for its bioactive constituents like vitamins, phenolic and antioxidants, is now being investigated for its role in pharmaceutical applications especially the antimicrobial property in topical application [1]. This work focused on the development of stable nanoemulsions gels and the evaluation of the antimicrobial activity against key microbes such *S. aureus*, *E. coli* and, *P. aeruginosa*.

The organoleptic characteristics of the gel containing the MSO nanoemulsion did not show any change in colour, odour and clarity up to the end of the fourth week of storage and up to the twelfth week of storage, although the gel matrix was soft and friable. Lack of phase separation or creaming suggested that the sample formulations could not undergo phase separation or creaming under the storage conditions that were employed. This is in concordance with stability of emulsions where equal ratio of oil, surfactant and water does not allow for phase separation [11, 25]. The observed transparency and uniformity of the nanoemulsions also indicate that the above high-energy emulsification technique was efficient in producing a stable system with small droplet sizes and which is very essential in counteracting phase inversion, aggregation and coalescence [1, 17].

The pH results showed a progressive decline of pH in all the three formulations over the 12 weeks period but the pH values were still within the range of the acceptable skin surface pH of 5.5 to 7 [12, 26]. As expected, the samples with higher concentration of Moringa seed oil has a greater change in pH, which the researchers assumed was due to the liberation of free fatty acids when stored. The shift in the pH is the key element in determining skin compatibility while at the same time helps in maintaining stability of the active ingredients in the product formulation [2]. The pH of the final rinse should also be at 5~7 to avoid getting either an acidic or basic pH that may interfere with the effectiveness of the product and cause skin irritation and or the product to easily wash off the skin.

Regarding **viscosity**, the study observed a positive correlation between the concentration of Moringa seed oil and the viscosity of the nanoemulsion gels. Higher oil content, as seen in Formula 3 (15% MSO), resulted in increased viscosity over time. This is in line with previous studies that suggest oil concentration and surfactant levels play pivotal roles in determining the viscosity of nanoemulsion gels [15]. Furthermore, the rise in viscosity over time suggests that long-term storage at room temperature promotes the aggregation of oil droplets or a gradual restructuring of the gel network. Although this increase in viscosity was not drastic, it is crucial to monitor as changes in texture can influence product application and patient compliance [24-75].

The molecule size appropriation was one more basic boundary contemplated, as more modest particles improve the strength and infiltration of the plan. From week 1 to week 12, the

study's particle sizes increased across all formulations, with larger increases observed in formulations with higher oil concentrations. The dissolution of surfactant layers over time, which permits droplets to coalesce and increase the overall droplet size [10, 28], is probably to blame for the increase in particle size. This molecule size increment highlights the significance of choosing suitable emulsification methods and settling specialists, particularly for long haul item capacity. Maintaining nanoemulsion formulations' efficacy and consistency necessitates a stable distribution of particle sizes [18].

The antimicrobial assessment gave unquestionable proof of the adequacy of Moringa seed oil in fighting normal bacterial strains. The outcomes from the restraint zone tests exhibited that rising the convergence of MSO in the plans upgraded their antimicrobial movement, with the F3 definition (15% MSO) showing the biggest zones of hindrance. The MIC esteems additionally affirmed this pattern, as lower MIC values were seen with expanding oil fixations. These discoveries line up with past exploration that has recognized the bioactive mixtures in Moringa oil, like isothiocyanates, as key supporters of its antimicrobial properties [5, 29]. By protecting the skin and creating an unfavorable environment for bacterial proliferation, the oil's antioxidant components, which assist in neutralizing free radicals, may also enhance the gel's capacity to inhibit microbial growth.

Pseudomonas aeruginosa outperformed *Staphylococcus aureus* in terms of resistance to MSO formulations, according to a comparison of inhibition zones and MIC values. This is steady with the writing, where gram-negative microbes like *Pseudomonas* are frequently less vulnerable to plant-based antimicrobial specialists because of their cell wall structure [3, 30]. Regardless, the F3 plan exhibited a 24% improvement in viability against *Staphylococcus aureus* and a 29% improvement against *Pseudomonas aeruginosa* contrasted with the F1 detailing, displaying the capability of MSO to be figured out in higher fixations for better antimicrobial results.

The discoveries of this study feature the adaptability of Moringa seed oil in nanoemulsion-based conveyance frameworks. The study demonstrates that MSO can be used to create stable nanoemulsions with effective antimicrobial properties. These details show promising solidness and physicochemical properties as well as have potential for clinical use in battling microbial contaminations, particularly when higher groupings of Moringa seed oil are utilized. Further exploration could investigate the enhancement of the surfactant-to-oil proportion and assess the nanoemulsion gels' exhibition in vivo models, giving a more

complete comprehension of their remedial potential [6, 23].

CONCLUSIONS

The study demonstrates that stable formulations with significant antimicrobial activity can be produced by effectively incorporating *Moringa oleifera* seed oil (MSO) into nanoemulsion-based delivery systems. The nanoemulsion gels showed great physicochemical strength more than 12 weeks, with no significant changes in variety, smell, or stage detachment. According to the analysis of the viscosity and particle size, higher concentrations of MSO resulted in an increase in viscosity and a gradual increase in particle size over time, but these changes had no effect on the stability as a whole. Antimicrobial testing revealed that formulations with higher MSO concentrations, particularly the 15% formulation (F3), were more effective against bacterial strains like *Pseudomonas aeruginosa*, *Escherichia coli*, and *Staphylococcus aureus*. The increased antimicrobial potential of higher MSO concentrations is further supported by the decreased MIC values and the expanded inhibition zones. These discoveries feature the promising capability of MSO nanoemulsion gels as compelling effective specialists for battling bacterial contaminations, making ready for future exploration on improving plans and investigating their clinical applications.

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