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Gambir Extract Nanoemulgel Formulation Based on Maggot Oil as Oil Phase

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Abstract

Gambir extract is the extraction result of gambir plant (Uncaria gambir) which contains polyphenol compounds. The gambir extract encompasses catechins which act as antimicrobials and antioxidants. The nanoemulgel formulation in this study utilized 9% gambir extract (Uncaria gambir) as the active ingredient and 1% Black Soldier Fly (BSF) maggot oil as the oil phase in the manufacture of nanoemulsions. The emulsification method was administered by implementing a magnetic stirrer with a spontaneous mixing technique. Nanoemulsion characterization employed is the Particle Size Analyzer (PSA) encompassed particle size, polydispersity index, and zeta potential, hence, the results were in accordance with nano criteria, that were 382.27 ± 72.28 nm, 0.29 ± 0.14, and -0.57 ± 1.28 mV respectively. The physical evaluation of nanoemulgel incorporated organoleptic tests, homogeneity, pH with a value of 6.23 ± 0.31, spreadability with a value of 5.83 ± 0.15 g.cm/second, and adhesion with a value of 7.33 ± 0.90 seconds which fulfilled the criteria for nanoemulgel preparation.

Keywords*:* *Gambir extract; maggot oil; nanoemulgel*

I. INTRODUCTION

The free radicals may originate from vehicle fumes and cigarette smoke which contain CO^2 and heavy metals, high stress, the addition of chemicals to food and drinks consumed daily, and exposure to UV rays. Continuous exposure to free radicals is tremendously detrimental for the body as it causes skin damage, heart disease, stroke, and cancer. Therefore, to protect the skin from free radicals, antioxidants are required to inhibit the formation of free radicals.

Indonesia is rich in natural materials which possess antioxidant compounds, particularly those derived from plants, one of which is the gambir plant (*Uncaria gambir*). Gambir (*Uncaria gambir*) is a type of herbal plant which has been identified for a long time in Indonesia and other regions. Gambir is added to areca nut chews and as an additive in traditional Chinese medicine. Gambir owns traditionally been employed to cure diarrhea, sore throat, heal burns, anticancer drugs, immunomodulators, and others [1]. Gambir's primary content is catechins (up to 51%), tannins (22-50%), and many other alkaloids. There are nine derivatives of catechin compounds discovered in gambir plants such as (+)-catechin, (+)-epicatechin, gamlyin A1, gamlyin A2, gamlyin B2, epigallocatechin, catechin-(4α-8)-epicatechin, gambirflavan D1, and gambirflavan D2 [2]. The content of (+)-catechins is the highest level among the 9 types of catechins with a concentration of around 45.66% of the total catechins in gambir. Catechins are polyphenolic compounds which possess potential as antioxidants and antibacterial [3]. Based on this explanation, gambir is utilized to produce skincare preparations to prevent free radicals and is useful as an antibacterial to prevent acne. Furthermore, to maximize the penetration of active ingredients into the skin, it is necessary to develop a delivery system into nanoemulgel preparations. Nanoemulgel from gambir extract has not been extensively studied. Thus, further research is required regarding the nanoemulgel formulation.

Nanoemulgel is a gel-based nanoemulsion preparation. This preparation owns a small particle size so that it can increase the ability of the compound particles to penetrate the skin membrane and form a gel that has controlled release and good bioavailability [4]. The gel dosage form is a topical preparation which is easily applied to the skin and possesses interesting organoleptic characteristics compared to other topical preparations. It is because gel preparations contain water which can cool, moisturize, easy to use, and easily seep into the skin. Nanoemulgel encompasses gels and emulsions with an oil phase and a water phase, as well as the addition of surfactants and cosurfactants.

The oil phase conducted in the nanoemulgel formulation utilizes maggot oil. Maggot, which derives from the Black Soldier Fly (BSF) species, which has been considered as a decomposing organism, can be employed as an oil phase in nanoemulgel formulations as it possesses the appropriate characteristics as an oil phase. The implementation of maggot oil in this formulation is in accordance with the recycling factor. In cosmetic formulations, it generally employs Virgin Coconut Oil (VCO). Maggot oil also possesses several drawbacks such as changes in the concentration of VCO in cosmetic emulsions which possess a significant effect on the pH and viscosity of the emulsion. They will be smaller and droplet size is getting bigger. Thus, it was replaced with the implementation of maggot oil as the oil phase [5].

Therefore, research on nanoemulgel formulations was performed by utilizing gambir plant extract (*Uncaria gambir*) and maggot oil as the oil phase to obtain stable nanoemulgel formulations by characterizing nanoemulsions and examining the physical properties of the nanoemulgel preparations.

II. METHOD

2.1 Gambir Extract Nanoemulsion Formulation

The nanoemulsion formulation can be perceived in Table 1.

Table l. Gambir Extract Nanoemulsion Formulation

Ingredient	Concentration (%b/v)	Function
Gambir extract	9%	Active substance
Maggot oil	1%	Oil phase
Span 80	0.5%	Surfactant
Tweens 80	4.5%	Surfactant
PEG 400	3.4%	Kosurfactant
Aquadest	Ad 100%	Solvent

The preparation of nanoemulsion requires gambir extract (active substance), maggot oil (oil phase), span 80 and tween 80 (surfactant), PEG 400 (cosurfactant), and distilled water as a solvent. In the preparation of nanoemulsion, the oil phase and the water phase are heated on a hotplate with a magnetic stirrer to a temperature of 70°C. The oil phase encompasses span 80 which is heated with maggot oil at 70°C. The first water phase was prepared by heating tween 80, a portion of PEG 400, and aquadest to 70°C. The second aqueous phase was prepared by dissolving the gambir extract powder in distilled water and filtered to obtain a liquid extract, then added the remaining PEG 400. The oil phase was applied to the aqueous phase, stirred employing a magnetic stirrer at 400 rpm for 30 minutes until a nanoemulsion was generated [6].

2.2 Characterization of Gambir Extract Nanoemulsion

Particle size measurements were performed using a Particle Size Analyzer (PSA) with dynamic light scattering. Samples of up to 10 mL were obtained and placed in a previously cleaned cuvette. PSA examines the cuvette once it is placed in the sample holder [7].

2.3 Gambir Extract Nanoemulgel Formulation

Nanoemulgel begins with the preparation of a gel base, carbomer is dispersed in 25 ml of hot distilled water (70˚C) per gram, and developed for 15 minutes. Stirring was administered until it was perfectly dispersed employing a homogenizer at 9600 rpm for 5 minutes. TEA was applied to the carbomer dispersion to neutralize the pH of the carbomer and stirred until homogeneous for 15 minutes. Furthermore, for HPMC gel base, it was dissolved in 20 times the weight of HPMC, developed for 15 minutes, then homogenized utilizing a stamper mortar. Then, the carbomer and HPMC were mixed together.

The nanoemulgel formula is demonstrated in Table 2.

Table 2. Gambir Extract Nanoemulgel Formulation

Ingredient	Concentration (%b/v)	Function
Carbomer	1%	Gel base
HPMC	0.25%	Gel base
TEA	1%	pH stabilizer
Glycerin	5%	Humectants
BHT	0.03%	Antioxidant
Methyl paraben	0.18%	Preservative
Propyl paraben	0.02%	Preservative
Aquadest	Ad 100%	Solvent

Methyl paraben and propyl paraben were dissolved in hot distilled water (70°C), administered BHT and glycerin little by little, homogenized with a gel base. The final step, the previously formed nanoemulsion, was dispersed into the gel phase with a homogenizer at a speed of 9600 rpm for 15 minutes to form a homogeneous nanoemulgel [7].

2.4 The Physical Properties of the Preparation Test

Evaluation of the physical preparation of gambir extract nanoemulgel in accordance with maggot oil incorporates organoleptic tests, homogeneity tests, pH tests, spreadability tests, and adhesion tests.

1. Organoleptic Test

The organoleptic test was employed by visually observing the nanoemulgel preparation which encompasses color, odor, and dosage form [8].

2. Homogeneity Test

The homogeneity test was conducted by weighing 1 gram of nanoemulgel, then smeared on a glass slide, covered with another glass slide, and perceived how homogeneous the preparation was. A good preparation is if there are no visible coarse grains [9].

3. pH Measurement

In the pH measurement, the first step is to rinse the electrode and temperature probe with aquadest, turn on the pH meter, then dip the electrode in the sample, wait until the reading on the screen stabilizes and the autolock indicator appears on the screen, then record the number printed on the pH meter [9]. The pH value requirements for topical preparations must be close to normal skin pH, which is in the range of 4.5-7.0 [10].

4. Spreadability

The spreadability was performed by depositing 0.5 gram of nanoemulgel on a transparent glass covered with graph paper and allowing it to spread to a predetermined diameter. Then, it was coated with transparent glass and loaded (50 g, 100 g, 150 g, 200 g and 250 g). The area increase was then measured when the weight was applied [11]. The results of a good distribution of nanoemulgel preparations ranged from 5-7 cm [12].

5. Adhesion

An adhesive strength test was used to perform the adhesion test. The nanoemulgel sample was distributed on a glass slide, then covered with another glass slide for 5 minutes while 250 grams of weight was placed on it. The weight is then lifted, and the two attached glass objects are freed, and the time is recorded until the two object glasses are free of each other. The time starts when the load is released and ends when the object glass is withdrawn [11]. The range of adhesion of topical preparations is at least more than 1 second [13].

III. RESULTS AND DISCUSSION

3.1 Gambir Extract Nanoemulsion Formulation

Nanoemulsion is a form of drug delivery system encompassing water-oil dispersions with a particle size of 20-500 nm stabilized in the presence of surfactants. The nanoemulsion's small droplet size makes it kinetically stable, eliminating sedimentation and creaming during storage [14]. Surfactants, cosurfactants, and oils are constituents of nanoemulsion, and their concentrations influence the properties of the final nanoemulsion. The surfactant component helps to reduce the tension of the interfacial film layer, making the produced nanoemulsion more stable. Cosurfactants, on the other hand, are surfactant auxiliary materials that work to reduce surface tension between the oil and water phases, reduce the amount of energy required to destroy globules, and produce smaller globule sizes. While the oil component acts as a lipophilic carrier to breakdown lipophilic drugs [15].

A preliminary experiment was performed in this research to generate a nanoemulsion formulation for gambir extract with an oil: surfactant: cosurfactant phase ratio of 1: 5: 3.4. The concentration of maggot oil utilized is not excessively high, thus it does not cause nanoemulsion instability or issues when creating nanoemulsions. Tween 80 and Span 80 are employed as surfactants because they provide an excellent consistency and enhance the stability of oil-in-water emulsions. PEG 400 is a cosurfactant in the recipe that helps surfactants reduce interfacial tension and increase non-polar group solubility, resulting in a transparent and stable emulsion with no separation [16].

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Emulsification is performed with a magnetic stirrer and a spontaneous mixing approach, which can aid in the formation of smaller droplets but does not require any special equipment, is energy efficient, and simple to perform. Because the spontaneous mixing approach is a low energy emulsification method, it is dependent on environmental factors such as composition, temperature, and stirring to produce metastable conditions. The oil phase employed will influence droplet size and the stability of the generated nanoemulsion. More Tween 80 in the composition will further reduce the interfacial tension of the two liquids that do not mix, and this will be aided by the addition of PEG 400, which will further lower the interfacial tension by increasing interfacial fluidity and so increasing the entropy of the system. The increase in fluidity and entropy contributes to the production of thermodynamically stable nanoemulsions [17]. When preparing nanoemulsions, the oil phase should not be mixed too quickly or too slowly with the stirrer. Turbulence will occur if it is too rapid, causing the size of the dispersed globules to become uneven and resulting in a bigger particle size. Meanwhile, excessively sluggish stirring will make it impossible for the elements to become homogenous [18].

3.2 Nanoemulsion Characterization

Based on the experiments, a maggot oil-based gambir extract nanoemulsion is obtained, as demonstrated in Figure 1, which depicts the stages of making gambir extract nanoemulsion incorporating gambir extract with a clear dark brown color (Figure 1A), nanoemulsion with a mixture of maggot oil, tween 80, span 80, PEG 400, and aquadest (Figure 1B), and homogeneous gambir extract nanoemulsion (Figure 1C). The gambir extract nanoemulsion produced was yellowish white in hue, slightly hazy, and had no precipitation. The smaller the particle size, the clearer the solution. If the particle size decreases, the preparation can provide high absorption efficiency in a variety of administration routes [17]. Several factors can influence the color and clarity of the resulting nanoemulsion, incorporating the addition of the water/aquadest phase, which affects the gel phase to disappear and a clear nanoemulsion to generate. It could possibly be due to smix (Tween 80 and Span 80) failing to reduce interfacial tension [19]. Furthermore, the concentration of the surfactant used influences the clarity of the nanoemulsion; the bigger the composition of the surfactant, the larger the emulsion droplet size, and the smaller the resultant size, the clearer the resulting nanoemulsion [20]. Likewise, the speed of stirring affects the formation of particle size

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[18]. The diameter properties of the nanoemulsion droplet particles are also affected by the type of oil. In this situation, virgin coconut oil (VCO) is a popular oil for the production of nanoemulsions as it includes triglycerides with dominant medium chain fatty acids, specifically 5.21% capric, 48.66% lauric, and 17.82% myristic, which are stable at low and high temperatures [20]. Based on research, maggot oil encompasses triglycerides with fatty acids such as 24.6% lauric acid, 24.5% oleic acid, 19.3% linoleic acid, 18.4% palmitic acid, 8% stearic acid, and 3.3% myristic acid [21].

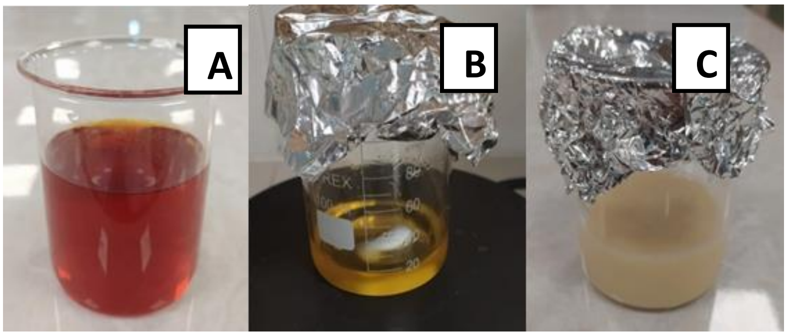

Figure 1. (A) Gambir Liquid Extract; (B) No-Extract Nanoemulsion; (C) Gambir Extract Nanoemulsion

Table 3. PSA Measurement Results

Sample	Particle Size (nm)	Polydispersity Index	Zeta Potential (mV)
Gambir Extract Nanoemulsion	382.27 ± 72.28	0.29 ± 0.14	-0.57 ± 1.28

*) Data are presented as mean ± SD (n=3)

Nanoemulsion characterization was measured employing a Particle Size Analyzer (PSA) to determine particle size, polydispersity index (PDI), and zeta potential. The PSA results are illustrated in Table 3, indicating that nanoemulsion of gambir extract made from maggot oil owns an average particle size of 382.27 ± 72.28 nm. These results incorporate the particle size in the nanoemulsion system which ranges from 20-500 nm [14]. The smaller particle size of the active ingredient in the nanoemulsion technology allows the active ingredient to penetrate the tissue more easily and quickly reach the target [22]. Particle or droplet size is an essential chemical feature of nanoemulsions, with the benefit of increasing solubility, drug release, and bioavailability. The smaller the particle size, the greater the area available for skin penetration [23].

The polydispersity index (PDI) value owns an average of 0.29 ± 0.14. PDI demonstrates the uniformity of the distribution of a particle where the PDI value ranges from 0.05-0.7. The experimental PDI values satisfied the criterion for being in a monodisperse system, indicating that the particle size had a uniform shape and a limited particle distribution. The polydispersity index value is critical as it affects the size uniformity of the nanoemulsion; a low polydispersity index value suggests higher size uniformity [17].

Potential zeta values have an average of -0.57 ± 1.28 mV. The zeta potential value of -30 mV to +30 mV is sufficient to maintain the stability of the nanoemulsion dispersion system. The zeta potential is useful in determining the stability of systems with scattered particles since it determines the degree of repulsion between dispersed particles that are equally charged and close together [17].

3.3 Gambir Extract Nanoemulgel Formulation

After integrating the nanoemulsion into a gel foundation, the nanoemulgel formulation was established. The gambir extract nanoemulgel formulation based on maggot oil involves numerous components, including a gelling agent derived from a 4:1 mixture of carbomer and HPMC. The gel basis was made up of 1% carbomer and 0.25% HPMC. This concentration seems to have the look of an optimum gel basis, with an excellent semisolid gel texture, that is not too dense or liquid, which is stable. The nanoemulgel formulation utilizing carbomer gel basis at 1% concentration possesses colorless, transparent, odorless, emollient, simple to remove, non-greasy, and decent consistency [24].

Triethanolamine (TEA) is another excipient administered in the preparation as a pH stabilizer. TEA was selected as it can create an alkaline environment to the carbomer, causing the resultant gel to thicken and clarify. The TEA concentration utilized is 1% because the more TEA added, the higher the pH of the mixture, because the pH of TEA as an alkalizing agent is 10.5 [25]. Carbomer will establish hydrogen bonds with water when mixed and will be diffused in water; however, an agent is required to neutralize the carbomer in order to create a gel mass. When TEA ionizes the carbomer, electrostatic repulsion occurs, resulting in the formation of a three-dimensional structure and a solid gel mass. Furthermore, the use of glycerin as a humectant attracts water molecules from the outside, which helps to bind moisture to the skin. Humectants also assist in preventing water loss from the preparation, making it more stable. Based on the research, the pH and viscosity of the nanoemulgel were relatively stable with the use of 5% glycerin which could

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be observed in the stability test parameters incorporating the freeze thaw test and centrifugation as well as tests at room temperature during 28 days of storage [26]. Because of the presence of oil, which can destabilize and produce rancidity, BHT is an antioxidant. Bacterial contamination caused by the gel's high-water content can be avoided by combining 0.18% methyl paraben and 0.02% propyl paraben. The combination of the two is the most popular since it can create a synergistic impact to enhance its activity, resulting in more effective results [27].

3.4 Physical Properties of Gambir Extract Nanoemulgel

The result of the physical properties test of maggot oil-based gambir extract nanoemulgel preparations in this study is demonstrated in Table 4 below.

Table 4. Physical Properties Test Results

Test Type	Result
Organoleptic	Semisolid, pale yellow, smells typical of maggot oil
Homogeneity	Homogeneous
pH	6.23 ± 0.31
Spreadability (g.cm/sec)	5.83 ± 0.15
Adhesion (seconds)	7.33 ± 0.90

*) Data are presented as mean ± SD (n=3)

1. Organoleptic

The produced nanoemulgels possessed the characteristics displayed in Figure 2 based on the organoleptic test of the nanoemulgel preparations, which was performed by evaluating the shape, smell, and color. The dosage forms received were semisolid, had a strong maggot oil odor, and were pale yellow in color. The emulgel formulation did not change shape, smell, or color after 6 weeks of storage at room temperature. These findings demonstrate that an oil-based gambir extract nanoemulgel can retain its stability and the active components in the formulation.

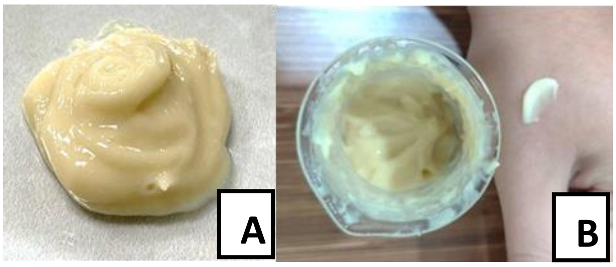

Figure 2. (A) Gambir Extract Nanoemulgel; (B) Gambir Extract Nanoemulgel After 6 Weeks Storage

2. Homogeneity

The homogeneity test determines whether or not the gambir extract nanoemulgel generated from maggot oil is homogeneous. Figure 3 illustrates that there are no coarse grains on the transparent glass, indicating that the nanoemulgel is homogeneous, and it is expected that this nanoemulgel would have a favorable therapeutic impact.

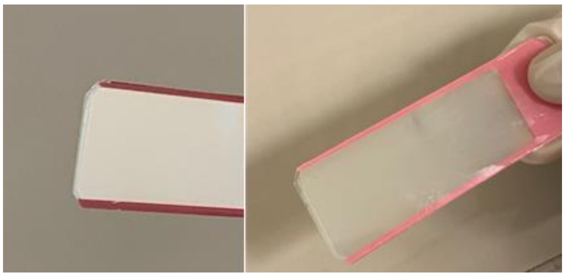

Figure 3. Result of Gambir Extract Nanoemulgel Homogeneity Test

3. pH Value

The pH of gambir extract nanoemulgel based on maggot oil was measured to be 6.23 ± 0.31, indicating that it is safe to use on the skin because the pH of the nanoemulgel matches to the pH of human skin, which is between 4.5 and 7.0 [9]. A pH value which is too low or too high may affect a change in the pH of the skin and cause damage to the skin coat. Damage to the skin's mantle layer may cause the skin to lose its acidity, be more easily irritated, and damaged [28].

4. Spreadability

The spreading power test is designed to determine the preparation's spreading power when applied to the skin. The nanoemulgel preparation is expected to spread easily when applied to the skin of the desired body part, increasing the surface area in contact with the drug and optimizing drug absorption on the skin that is implemented. The spreadability of gambir extract nanoemulgel based on maggot oil was 5.83 ± 0.15 g.cm/second. The formula meets the necessary spreadability value of 5-7 cm based on testing results [12].

5. Adhesion Test

The objective of the adhesiveness test is to determine the intrinsic capacity of an oil-based gambir extract nanoemulgel to adhere to the skin when applied. The nanoemulgel exhibits excellent adhesion, lasting more than one second [13]. The longer the preparation is adhered to the skin, the more of the medicine is absorbed into the skin, enhancing the treatment's efficacy. The adhesion test using gambir extract nanoemulgel based on maggot oil took 7.33 ± 0.90 seconds.

CONCLUSION

From the experiments that have been carried out, a maggot oil-based gambir extract nanoemulgel formulation has been successfully synthesized. The results of the particle size, polydispersity index, and zeta potential values were incorporated in the nano criteria, which were 382.27 ± 72.28 nm, 0.29 ± 0.14, and -0.57 ± 1.28 mV, respectively. Testing the physical properties of nanoemulgel obtained semisolid results, yellowish white color, distinctive odor of maggot oil, homogeneity, pH value 6.23 ± 0.31, spreadability with a value of 5.83 ± 0.15 g.cm/second, and adhesion with a value of 7.33 ± 0.90 seconds.

REFERENCE

[1] M. Y. Musdja, M. A. Hapsari, and A. Agusta, “Comparison of activity and inhibitory mechanism between (+)-catechin and water extract of gambier (uncaria gambir roxb.) against some bacteria,” *Sci. J. PPI - UKM*, vol. 4, no. 2, pp. 55–60, 2017, doi: 10.27512/sjppi-ukm/se/a29012018.

[2] M. Y. Musdja, H. A. Rahman, and D. Hasan, “Antioxidant Activity of Catechins Isolate of Uncaria Gambier Roxb in Male Rats,” *LIFE Int. J. Heal. Life-Sciences*, vol. 4, no. 2, pp. 34–46, 2018, doi: 10.20319/lijhls.2018.42.3446.

[3] H. Arakawa, M. Maeda, S. Okubo, and T. Shimamura, “Role of hydrogen peroxide in bactericidal action of catechin,” *Biol. Pharm. Bull.*, vol. 27, no. 3, pp. 277–281, 2004.

[4] M. N. Jivani, C. P. Patel, and B. G. Prajapati, “Nanoemulgel Innovative Approach for Topical Gel Based Formulation,” *Res Rev Heal. Care Open Acc J*, vol. 1, no. 2, pp. 1–5, 2018.

[5] I. Mu’awanah, B. Setiaji, and A. Syoufian, “Pengaruh konsentrasi virgin coconut oil (vco) terhadap stabilitas emulsi kosmetik dan nilai sun protection factor (spf),” *Bimipa*, vol. 24, no. 1, pp. 1–11, 2014.

[6] Fahleni, N. Safira, and N. Salsabilla, “Formulasi dan uji aktivitas antioksidan emulgel ekstrak kulit buah kakao (theobroma cacao l.),” *J. Ilm. Farm. Bahari*, vol. 12, no. 2, pp. 117–121, 2021.

[7] S. H. Yuliani, M. Hartini, B. Pudyastuti, and E. Perdana Istyastono, “Comparison of physical stability properties of pomegranate seed oil nanoemulsion dosage forms with long-chain triglyceride and medium-chain triglyceride as the oil phase,” *Tradit. Med. J.*, vol. 21, no. 2, pp. 93–98, 2016.

[8] C. M. Ardika Sari, D. Andriani, and D. Wahyudi, “Optimasi kombinasi hpmc dan carbopol dalam formula sediaan gel hand sanitizer ekstrak etanol biji pepaya (carica papaya l.) serta uji aktivitas antibakteri terhadap escherichia coli,” *J. Insa. Farm. Indones.*, vol. 3, no. 2, pp. 241–252, 2020, doi: 10.36387/jifi.v3i2.563.

[9] Y. E. Christian, D. Rahmat, and Y. Farida, “Formulasi nanoemulgel ekstrak daun cantigi (vaccinium varingiaefolium miq.) sebagai antioksidan,” *Maj. Farmasetika*, vol. 7, no. 5, pp. 478–493, 2022.

[10] F. R. Nurasyfa, S. E. Priani, and G. C. E. Darma, “Formulasi sediaan emulgel mengandung minyak atsiri rosemary (rosmarinus officinalis l.) serta uji aktivitasnya sebagai antijerawat terhadap bakteri propionibacterium acnes,” *Pros. Farm.*, vol. 5, no. 2, pp. 706–716, 2019.

[11] R. Riski, A. H. Umar, and Rismadani, “Formulasi emulgel antiinflamasi dari ekstrak temulawak (curcuma xanthorrhiza Roxb),” *J. Pharm. Med. Sci.*, vol. 1, no. 2, pp. 1–4, 2016.

[12] A. Indalifiany, M. H. Malaka, Sahidin, A. Fristiohady, and R. Andriani, “Formulasi dan uji stabilitas fisik nanoemulgel ekstrak etanol spons petrosia sp.,” *J. Farm. Sains dan Prakt.*, vol. 7, no. 3, pp. 321–331, 2021.

[13] T. Imanto, R. Prasetiawan, and E. R. Wikantyasning, “Formulation and characterization of nanoemulgel containing aloe vera l. powder,” *J. Farm. Indones.*, vol. 16, no.

1, pp. 28–37, 2019, [Online]. Available: http://journals.ums.ac.id/index.php/pharmacon

[14] E. Zulfa, D. Novianto, and D. Setiawan, "Formulasi nanoemulsi natrium diklofenak dengan variasi kombinasi tween 80 dan span 80: kajian karakteristik fisik sediaan," *Media Farm. Indones.*, vol. 14, no. 1, pp. 1471–1477, 2019.

[15] Rahmadevi, B. Hartesi, and K. Wulandari, "Formulasi sediaan nanoemulsi dari minyak ikan (oleum iecoris) menggunakan metode sonikasi," *J. Healthc. Technol. Med.*, vol. 6, no. 1, pp. 248–258, 2020.

[16] D. Saryanti, I. Setiawan, and H. H. Dayanto, "Use of cmc na as gelling agent in nanoemulgel formulation of methanol extract of sappan wood (caesalpinia sappan l)," *J. Trop. Pharm. Chem.*, vol. 6, no. 1, pp. 21–29, 2022, doi: 10.25026/jtpc.v6i1.276.

[17] F. S. Handayani, B. H. Nugroho, and S. Z. Munawiroh, "Optimasi formulasi nanoemulsi minyak biji anggur energi rendah dengan d-optimal mixture design (dmd)," *J. Ilm. Farm.*, vol. 14, no. 1, pp. 17–34, 2018, [Online]. Available: http://journal.uii.ac.id/index.php/JIF

[18] N. M. D. Listyorini, N. L. P. D. Wijayanti, and K. W. Astuti, "Optimasi pembuatan nanoemulsi virgin coconut oil," *J. Kim.*, vol. 12, no. 1, pp. 8–12, 2018.

[19] P. H. Ratnapuri *et al.*, "Formulasi dan evaluasi nanoemulsi dari ekstrak herba kelakai," in *Prosiding Seminar Nasional Lingkungan Lahan Basah*, 2022, vol. 7, no. 2, pp. 262–268.

[20] S. Ariviani, W. Atmaka, and S. Raharjo, "Karakterisasi dan uji stabilitas digestif nanoemulsi beta karoten yang dibuat dengan metode emulsifikasi spontan," *Agritech*, vol. 38, no. 1, pp. 30–38, 2018, doi: 10.37311/ijpe.v1i3.11400.

[21] M. Y. Abduh, M. Jamilah, P. Istiandari, and R. Manurung, "Bioconversion of rubber seeds to produce protein and oil-rich biomass using black soldier fly larva assisted by microbes," *J. Entomol. Zool. Stud.*, vol. 5, no. 4, pp. 591–597, 2017.

[22] R. Noveriza, M. Mariana, and S. Yuliani, "Keefektifan formula nanoemulsi minyak serai wangi terhadap potyvirus penyebab penyakit mosaik pada tanaman nilam," *Bul. Penelit. Tanam. Rempah dan Obat*, vol. 28, no. 1, pp. 47–56, 2017, doi: 10.21082/bullittro.v28n1.2017.47-56.

[23] A. N. Bestari, T. . S. Sulaiman, and D. A. Purnamasari, "Pengaruh pengecilan ukuran partikel pada kasus pembuatan pulveres dari tablet terhadap kecepatan dan profil disolusi serta stabilitasnya," *Maj. Farm.*, vol. 13, no. 1, pp. 45–55, 2017, [Online]. Available: https://jurnal.ugm.ac.id/majalahfarmaseutik/article/download/38468/21987

[24] G. Kaur, B. PMS, and J. K. Narang, "Topical nanoemulgel: a novel pathway for investigating alopecia," *J. Nanomed. Nanotechnol.*, vol. 08, no. 06, pp. 6–10, 2017, doi: 10.4172/2157-7439.1000472.

[25] R. Andaryekti, M. Mufrod, and S. Munisih, "Pengaruh basis gel sediaan masker ekstrak

daun teh hijau (camellia sinensis linn.) pada karakteristik fisik dan aktivitas bakteri staphylococcus aureus," *Maj. Farm.*, vol. 11, no. 2, pp. 294–299, 2017.

[26] H. Damayanti, S. Wikarsa, and G. Jafar, "Formulasi nanoemulgel ekstrak kulit manggis (garcinia mangostana l.)," *J. Ris. Kefarmasian Indones.*, vol. 1, no. 3, pp. 166–176, 2019, doi: 10.33759/jrki.v1i3.53.

[27] N. H. Base, R. Arief, and S. R. Hardiyanti, "Evaluasi mutu fisik dan uji aktivitas antibakteri sediaan gel minyak nilam (pogostemon cablin, benth) terhadap staphylococcus aureus," *J. Pengabdi. Masy. Yamasi*, vol. 13, no. 3, pp. 1576–1580, 2019.

[28] N. Jusnita and K. Nasution, "Formulasi nanoemulsi ekstrak daun kelor (moringa oleifera lamk)," *Ind. J. Teknol. dan Manaj. Agroindustri*, vol. 8, no. 3, pp. 165–170, 2019, doi: 10.21776/ub.industria.2019.008.03.1.