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ANALYSIS OF MORINGA LEAF NANOEMULGEL (MORINGA OLEIFERA L.) AND ALOE VERA AS A MOISTURIZER FOR MALE RABBITS IN NEW ZEALAND

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ABSTRACT

Moisturizing lotion is an emollient group that contains more water which is useful for increasing skin hydration. One of the active ingredients in the moisturizing lotion is the antioxidant compounds found in Moringa oleifera L. and aloe vera leaves. Moringa leaves contain flavonoids such as quercetin, which have strong antioxidant activity that can neutralize free radicals. Aloe vera contains vitamins A, B, C, E, calcium, amino acids, enzymes and polysaccharides which are useful as moisturizing agents. The formulation of Moringa leaf extract and aloe vera was made in the form of nanoemulgel lotion as a skin moisturizer, before being formulated into a lotion preparation, a phytochemical screening was carried out to determine the content of the extract compounds. This study aims to determine the effect of using nanoemulgel lotion of moringa leaf extract and aloe vera on skin moisture. The formulation of nanoemulgel lotion of moringa leaf extract and aloe vera uses different concentrations of active substances of 3% (F1), 6% (F2) and 9% (F3). The physical evaluation carried out included organoleptic tests, homogeneity, pH, spreadability, viscosity and skin moisture. The results showed that all formulations with concentrations of 3%, 6% and 9% met the requirements for the evaluation test for nanoemulgel lotion for skin moisturizing. The higher the concentration of the active substance, the greater the spreadability and viscosity value obtained, no effect on pH. Nanoemulgel lotion preparations of moreinga leaf extract and aloe vera with a concentration of 9% (F3) have high ability as skin moisturizers.

Keywords: aloe vera; antioxidant; moringa leaf extract; nanoemulgel moisturizing lotion

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INTRODUCTION

Moringa leaf extract (Moringa leaf extract) is widely used and used traditionally because it has a lot of nutritional value and can be used as herbal medicine, because it has high activity as an antioxidant, immunomodulator, anticancer, antibacterial, antidiabetic and photoprotective effect on some parts of the moringa plant. The Moringa plant is called the tree of life(Satrimafitrah et al., 2022). Moringa plants in the leaves are rich in phenolic acids, flavonoids, glucosinolates and isothiocyanates(Ulandari & Sugihartini, 2018). Phenolic compounds and flavonoids are secondary metabolites produced in response to environmental conditions as UV filters, antioxidants and antihyperproliferative, so that Moringa leaves can be used to prevent skin aging, brighten the skin, protect the skin from exposure to radiation / free radicals, protect against skin damage, moisturizes the skin and can be used to rejuvenate the skin(Yuniarsih et al., 2023). Aloe vera contains various vitamins (except vitamin D), enzymes, minerals, saponins, and many types of amino acids in it, as well as biologically

active compounds such as anthraquinone mannans acetate, polymannans, antioxidants and various lectins. Aloe vera has major benefits for the skin as a stimulant for the formation of skin epidermal tissue and helps the skin cell regeneration process(Murnalis, 2019). Gel on aloe vera can moisturize the skin because there is a lot of water content, has a water content of around 95%, mucopolysaccharide compounds can bind skin moisture. Aloe vera stimulates fibroblasts to produce collagen and elastic fibers which can make skin elastic and reduce wrinkles, amino acids in aloe vera are useful as astringents to shrink pores(Khoirini, 2018). The content of antioxidant compounds found in Moringa leaves and aloe vera makes it suitable for use as additional ingredients for moisturizing lotion preparations.

LotionsThis includes softening preparations that contain a lot of water because lotion functions as a defense against skin moisture, cleans, prevents water loss and maintains the content of active substances in it.(Mulyani et al., 2018). The components that make up the lotion are moisturizers, emulsifiers, fillers, cleansers, active ingredients, solvents and preservatives(Ambari & Suena, 2019). Lotion has the advantage of being easy to spread evenly on the surface when smeared on the skin, easy to use and how it works directly on the local tissue so that the desired therapeutic effect is more easily achieved(Iskandar et al., 2019). The delivery of active drug substances in a preparation is influenced by the size of the particles, because there is a skin membrane barrier, the smaller the particle size, the easier it is to penetrate the skin membrane barrier and the better the effect obtained, one of the preparations is made of nanoemulgel(Imanto et al., 2019). Nanoemulgel is an emulsion preparation with a droplet size of around 1-100 nm which is suspended in a hydrogel.(Choudhury et al., 2017). Oil components in nanoemulgel preparations such as surfactants and constructants are useful for increasing the penetration of active substances so that they can increase the expected therapeutic effect.(Algahtani et al., 2020). In research conducted by(Azzahra et al, 2023)Moringa leaf extract and aloe vera are used as a lotion formulation that functions as a sunscreen. Due to the presence of phenolic and flavonoid compounds which are useful as antioxidants, this research formulated nanoemulgel lotion of moringa leaf extract and aloe vera as skin moisturizers. This study aims to formulate extracts of Moringa leaves and aloe vera in nanoemulgel preparations using different concentrations of active substances between formulas. Nanoemulgel lotion of moringa leaf extract and aloe vera is expected to increase the effectiveness of the resulting moisture therapy.

METHOD

The research method used was the experimental method with the type of post test only control group design research at the Pharmacy Laboratory of the Kendal High School of Health Sciences, with the following procedure: Moringa leaves were obtained from a farmer who cultivates Moringa leaves in Kendal City, Central Java. The obtained moringa leaves are washed thoroughly with running water, then dried directly in the sun until dry and finely blended. Moringa leaf powder was weighed as much as 30 g, wrapped in filter paper, tied with thread at both ends and put in a Soxhlet tube. The Soxhlet flask was filled with boiling stones and 96% ethanol, using a ratio of 1:20 (30 gr/600 ml) to solvent. The socket unit is installed with a return cooler and heated to the temperature of the boiling point of the solvent, allowed several circulations to occur until the Moringa leaf powder in the socket tube is clear. The soxhletation results obtained were then evaporated over a water bath until the desired thick extract was obtained.

Aloe vera was obtained from an aloe vera plantation in the Kendal area, Central Java. The aloe vera obtained is washed thoroughly with running water, cut off the ends and the base. Slice the outside and take the meat and aloe vera gel on the inside. Cut it into several pieces

and then put it in the container. Do the same steps until you get a wet yield of 58.02 grams. Enter the gel results in a blender then puree. The results obtained were filtered using filter paper to separate from the dregs. After that, get aloe vera gel and store it in a container(Zarwinda et al., 2022). Mortar and stamper, lotion pot, analytical balance, digital balance, stir bar, spatula, porcelain cup, universal pH meter, measuring cup, round bottom flask, beaker glass, parchment paper, knife, Rion viscometer, dropping pipette, measuring cup, aluminum foil, test tube, water bath, filter paper, watch glass, object glass, square glass, blender. Moringa leaf powder, 96% ethanol, VCO, tween 80, propylene glycol, carbopol, glycerin, propyl paraben, methyl paraben, aquadest and 0.1 N NaOH.

Formulation of Nanoemulgel Lotion

Nanoemulgel lotion was made in 3 formulations, which were distinguished by the concentration of the active substances of the extracts of Moringa leaves and aloe vera namely 3%, 6% and 9% and the negative control without the active substances of the extracts of Moringa leaves and aloe vera. Each preparation is 100 grams in the same basic composition. The formula for making nanoemulgel preparations in this study can be seen in table 1.

Table 1.
Formula Nanoemulgel Lotion

	Formula Nanoemulgel Lotion						
Material	Function	Formulas (%)					
		I	II	III	K(+)	K(-)	
Moringa leaf extract	Active	3	6	9		-	
-	substance						
Aloe Vera Gel	Active	3	6	9	•		
	substance				"Marina		
VCO	Oil phase	25	25	25	Hydro	25	
Tweens 80	Surfactant	3.50	3.50	3.50	Cool Gel	3.50	
Propylene glycol	Consurfactant	4	4	4	Lotion"	4	
Carbopol	Gelling agent	3	3	3	•	3	
Glycerin	humectants	15	15	15	•	15	
Propyl paraben	Preservative	0.02	0.02	0.02	•	0.02	
Methyl paraben	Preservative	0.15	0.15	0.15	•	0.15	
NaOH 0.1 N	Emulsifiers	10	10	10	•	10	
Aquadest	Water phase	100	100	100	•	100	

Manufacture of Preparations

Weigh all the ingredients needed according to the formulation. The oil phase was prepared beforehand by inserting (Tween 80, Propyleneglycol and VCO) into it beaker glassStir using a magnetic stirrer at 800 rpm for 30 minutes until the preparation is homogeneous. The water phase, namely aquadest and NaOH, was added to the oil phase mixture, stirred using a magnetic stirrer for 20 minutes until it became homogeneous and an emulsion was formed. Activate carbopol in a hot mortar with hot aquadest, stirring in a ratio of 1:20 until a homogeneous gel is formed, then add Moringa leaf extract. Dissolve methyl paraben and propyl paraben in glycerin, then set aside. The emulsion that has been formed is put in a mortar containing Moringa leaf extract gel, stir until homogeneous, then add methyl paraben and propyl paraben which have been dissolved with glycerin, stir until well blended, put in a lotion pot.

Preparation Evaluation

The prepared Moringa leaf extract nanoemylgel lotion was observed physically which included odor, color, homogeneity and concentration of the preparation. Test the pH using a universal pH stick. pH measurements were carried out 3 times. The pH test aims to determine whether the prepared nanoemulgel preparations are in accordance with the pH of nanoemulgel preparations or not, nanoemulgel preparations must have a skin pH value in accordance with the provisions of the Indonesian National Standard (1996), namely a pH value ranging from 4.5-8. So it does not cause irritation to the skin when used(Purwaningsih et al., 2020). The viscosity of the lotion gel was measured using a Viscometer Rion rotor no. 1 and rotor no. 2. The gel sample was put in a pot to be tested. The rotor is placed in the middle of the pot which already contains nanoemulgel lotion, then the tool is turned on. The numbers obtained will appear on the screen, after they are stable, the scale on the viscometer is read. The test was carried out 3 times.

Good gel spreadability, which is around 5-7 cm(Kharisma & Safitri, 2017). The lotion gel sample was weighed as much as 0.5 gram and placed in the center of the first petri dish that had been given a millimeter block. The second petri dish is placed on top of the first petri dish as an initial load for 1 minute. Measure the diameter of the spread of the nanoemulgel on 4 sides of the petri dish. The spreadability test was repeated with an additional load of 50 grams every 1 minute. Spreadability test was carried out 3 times. The adhesion of topical preparations greatly affects the therapeutic effect. This test aims to determine how much the ability of the nanoemulgel preparation to stick to the skin in a certain time so that it can function optimally for drug delivery(Kindagen et al., 2018). Nanoemulgel as much as 0.15 grams was placed on the object glass and affixed to another glass object, then pressed with a weight of 1 kg for 5 minutes. The object glass is mounted on the test kit and 80 grams of load is released It is carried out using a skin detector measuring instrument to determine the ability of the preparation to reduce water evaporation on the skin(Megantara, 2017). The percentage of skin moisture is measured for 2 minutes after application(Iskandar et al., 2019). The results of the percentage of water content obtained are processed with scale, namely, dry (34% -37%), normal or moist (38% -42%), very moist (43% -46%)(Anggiarti et al., 2022).

RESULTS

After determining the plants and calculating the yield with >10% susceptibility, an organoleptic evaluation test was carried out which stated that the preparation was homogeneous. Then a pH test is carried out which is still within normal levels, then a spreadability test with a diameter that meets the requirements. After that, the adhesion test and viscosity test with results that meet the requirements. After going through several tests of physical properties, then a moisture test was carried out on the rabbit's skin and resulted in the most optimum average moisture. The product in the form of nanoemulgel moisturizing lotion was made in 2 types, namely with and without Moringa leaf extract as a test and as a test control. In the formulation of moringa leaf extract gel lotion, various concentrations of active substances are used. Formulas I, II, and III with concentrations of 3%, 6% and 9%, respectively. The nanoemulgel lotion formula consists of Moringa leaf extract and aloe vera gel as active ingredients, VCO as the oil phase, Tween 80 as a surfactant, carbopol as a gelling agent, methyl paraben and propyl paraben as preservatives, glycerin as a humectant, propilenglycol, as a cosurfactant, NaOH as an emulsifier, and distilled water as a solvent.

DISCUSSION

Table 2.

Organoleptic Test Results of Nanoemulgel Lotion Extract of Moringa Leaves and Aloe Vera

Lotion	Organoleptic						
Formulas	Color Aroma Homogeneity Texture						
F0	Light green	Fresh specialty	Homogeneous	Semi solid easy to pour			
F1							
	Light green	Fresh specialty	Homogeneous	Semi solid easy to pour			
F2	Light green	Fresh specialty	Homogeneous	Semi solid easy to pour			
F3	Light green	Fresh specialty	Homogeneous	Semi solid easy to pour			

Information:

- F0: Preparation of nanoemulgel lotion without active substance
- F1: Preparation of 3% moringa leaf extract and aloe vera lotion nanoemulgel
- F2: Nanoemulgel lotion preparation of Moringa leaf extract and aloe vera 6%
- F3: Nanoemulgel lotion preparation of Moringa leaf extract and aloe vera 9%

Based on table 3.1. It can be seen that the organoleptic properties of all the formulas are light green, homogeneous, with a semi-solid texture with a distinctive aroma, because the formula contains Moringa leaf extract and aloe vera gel which have a distinctive odor. The acceptable pH of the lotion on the skin varies between 4.5 and 8. pH measurements were carried out 3 times from adjacent locations and the average pH results of the two lotions were determined with each of these formulas.

Table 3. pH Test Results of Nanoemulgel Lotion Extract of Moringa Leaves and Aloe Vera

Lotion Formulas	pH (3 repetitions)		pH Range	Information	
F0	5,1	5,1	5.0	5.0-5.1	Qualify
F1	5,3	5,2	5,2	5,2-5,3	Qualify
F2	5,5	5,5	5,5	5,5	Qualify
F3	5,9	5,9	6.0	5.9-6.0	Qualify

Information:

- F0: Preparation of nanoemulgel lotion without active substance
- F1: Preparation of 3% moringa leaf extract and aloe vera lotion nanoemulgel
- F2: Nanoemulgel lotion preparation of Moringa leaf extract and aloe vera 6%
- F3: Nanoemulgel lotion preparation of Moringa leaf extract and aloe vera 9%

Note: pH requirements = 4.5-6.5

The results of the pH test are based on table 3.2. All formulas meet the requirements of the pH test because they are included in the pH range of the skin.

Table 3.
Results of Spreadability Test of Nanoemulgel Lotion Extract of Moringa Leaves and Aloe
Vera

			. 0100		
Lotion Formulas	Deployment diameter (cm) (3 repetitions)			Average	Information
F0	5,7	6,9	7.0	5.7-7.0	Qualify
F1	5,8	5,8	5,8	5,8	Qualify
F2	6,3	6,3	6,3	6,3	Qualify
F3	5,4	5,5	5,5	5.4-5.5	Qualify

Information:

- F0: Preparation of nanoemulgel lotion without active substance
- F1: Preparation of 3% moringa leaf extract and aloe vera lotion nanoemulgel
- F2: Nanoemulgel lotion preparation of Moringa leaf extract and aloe vera 6%

F3: Nanoemulgel lotion preparation of Moringa leaf extract and aloe vera 9%

Note: Requirements 5-7 cm

The results of the spreading power test are based on table 3.3. all formulas meet the requirements.

Table 4 Viscosity Test Results for Nanoemulgel Lotion Extract of Moringa Leaves and Aloe Vera

Lotion Formulas	Viscosity(cps)	Information
F0	1978	Qualify
F1	2010	Qualify
F2	3721	Qualify
F3	2843	Qualify

Information:

F0: Preparation of nanoemulgel lotion without active substance

F1:Preparation of 3% moringa leaf extract and aloe vera lotion nanoemulgelF2 : Nanoemulgel lotion preparation of Moringa leaf extract and aloe vera 6%

F3: Nanoemulgel lotion preparation of Moringa leaf extract and aloe vera 9%

Note: Requirements 2000-50000 cps

The results of the viscosity test are based on table 3.5. all formulas meet the requirements.

The more the material dissolves in water, the lower the viscosity. Good viscosity value is about 50-80%.

Table 5.

Adhesion Test Results of Nanoemulgel Lotion Extract of Moringa Leaves and Aloe Vera

Measurement	<i>Lotions</i> Test	<i>Lotions</i> Control
I	0.076 sec	0.05 sec
II	0.088 seconds	0.043 sec
III	0.16 sec	0.031 sec
X (average)	0.2 sec	0.01 sec

Information:

F0: Preparation of nanoemulgel lotion without active substance

F1: Preparation of 3% moringa leaf extract and aloe vera lotion nanoemulgel

F2: Nanoemulgel lotion preparation of Moringa leaf extract and aloe vera 6%

F3: Nanoemulgel lotion preparation of Moringa leaf extract and aloe vera 9%

From table 5 it can be concluded that lotions made from moringa leaf extract and aloe vera have stronger adhesion compared to control lotions. This shows that the lotion with the extract has a maximum effect compared to the control lotion (without active substance).

Table 6.
Moisture Test Results of Nanoemulgel Lotion on Rabbit Skin

Formulas		Average Humidity (%)				
	1 hour	2 hours	3 hours	4 hours	5 Hours	
F0	25.35	23.00	22.00	19,10	15.50	
F1	36,89	33.55	32.00	30,20	28.54	
F2	42.00	36.00	32.00	31.67	29,67	
F3	51.00	49.80	47.55	45.00	41.89	

Information:

F0: Preparation of nanoemulgel lotion without active substance

F1: Preparation of 3% moringa leaf extract and aloe vera lotion nanoemulgel

F2: Nanoemulgel lotion preparation of Moringa leaf extract and aloe vera 6%

F3: Nanoemulgel lotion preparation of Moringa leaf extract and aloe vera 9%

Table 6 is the result of the average moisture content of the nanoemulgel lotion every hour in the skin treatment of each rabbit. The concentration of 9% (F3) has a high humidity value at the 1st hour, namely 51.00%, then decreases every hour with the lowest value, namely 41.89% at the 5th hour. Concentrations of 3% (F1) and 6% (F2) also decreased the humidity value every hour. The concentration of 3% (F1) has the highest humidity value, namely 36.89% at the 1st hour to the lowest at the 5th hour, namely 28.54%, while at a concentration of 6% (F2), the highest humidity value is at the 1st hour, namely 42% and the lowest at the 5th hour, namely 29.67%. The negative control or preparation base (F0) has a moisture value that decreases every hour with the highest value at the 1st hour at (F0) 23.35%, then the lowest value at the 5th hour at (F0) at 15.

CONCLUSION

From this study it can be concluded that the lotion produced does not cause significant side effects because the natural ingredients used are Moringa leaf extract which is rich in antioxidant compounds so that it can be formulated as a skin moisturizer. Formulation concentrations of 3%, 6%, and 9% all met the requirements for the semi-solid preparation evaluation test. The higher the concentration of the extract, the wider the distribution and viscosity values obtained, with no effect on viscosity and pH. Nanoemulgel lotion of Moringa leaf extract and aloe vera with a concentration of 9% (F3) has the ability to moisturize the skin with an average humidity of 51%.

REFERENCES

- Algahtani, MS, Ahmad, MZ, & Ahmad, J. (2020). Nanoemulgel for improved topical delivery of retinyl palmitate: Formulation design and stability evaluation. Nanomaterials, 10(5).
- Ambari, Y., & Suena, NMDS (2019). Physical Stability Test of Citronella Oil Anti Mosquito Lotion Formulation. Medicamento Scientific Journal, 5(2), 111–115.
- Anggiarti, PI, Wisdom, I., & Purnama, SI (2022). Analysis of Air-conditioned Room Humidity on Microcontroller-Based Skin Humidity. Journal of Telecommunication, Electronics, and Control Engineering (JTECE), 4(2), 80–92.
- Azzahra et al. (2023). Moringa Leaves (Moringa oleifera): Activity of Sunscreen Extract and Formulation of Lotion Preparations. Pharmaceuticals, Research Magazine, Articles, 8(2), 133–147.
- Choudhury, H., Gorain, B., Pandey, M., Chatterjee, LA, Sengupta, P., Das, A., Moluglu, N., & Kesharwani, P. (2017). Recent Update on Nanoemulgel as Topical Drug Delivery System. Journal of Pharmaceutical Sciences, 106(7), 1736–1751.
- Imanto, T., Prasetiawan, R., & Retno Wikantyasning. (2019). Formulation and Characterization of Nanoemulgel Containing Aloe Vera L. Powder. In Indonesian Pharmaceutical Journal (Vol. 16, Issue 1).
- Iskandar, B., Frimayanti, N., Firmansya, F., Agustini, TT, & Putri, DD (2019). Evaluation of Physical Properties and Moisture Test of Lotion Preparations Sold Online-Shop. World Pharmacy Journal, 4(1), 8–16.
- Kharisma, IN Della, & Safitri, CINH (2017). Formulation and Physical Quality Test of Rice Bran Extract Gel (Oryza sativa L.). Articles of Parallel Speakers, 228–235.

- Khoirini, F. (2018). The Role of Aloe Vera Gel in Reducing Xerosis. Journal of Health Media, 9(1), 72–77.
- Megantara, INAP (2017). Variation of Triethanolamine Concentration as Emulgator and Hedonic Test on Abstract Lotion Raspberry (Rubus rosifolius) has high antioxidant activity which can be used in skin care. One of the cosmetics for skin care is. Udayana Pharmacy Journal, 6(2301–7716), 1–5.
- Mulyani, T., Ariyani, H., Rahimah, & Rahmi, S. (2018). Formulation and antioxidant activity of suruhan leaf extract lotion (Peperomia pellucida L.). Journal of Current Pharmaceutical Sciences, 2(1), 112–114.
- Murnalis, M. (2019). Benefits of Aloe Vera as a Mask for Dry Hand Skin Care. Journal of Education and Family, 11(1), 53.
- Purwaningsih, NS, Romlah, SN, & Choirunnisa, A. (2020). Literature Review Evaluation Test of Cream Preparations. Edu Masda Journal, 4(2), 108.
- Satrimafitrah, P., Afdal, M., Jusman, Razak, AR, Ridhay, A., & Inda, NI (2022). Viscosity and Antibacterial Activity of VCO-Based Liquid Soap with the Addition of Moringa Leaf (Moringa oleifera) Ethanol Extract Against Pathogenic Bacteria. COVALEN: Journal of Chemical Research, 8(1), 74–82.
- Sayuti, NA (2015). Research Article Formulation and Physical Stability Test of Chinese Ketepeng Leaf Extract Gel (Cassia alata L.) Formulation and Physical Stability of Cassia alata L. Leaf Extract. Indonesian Pharmaceutical Journal, 5(2), 74–82.
- Ulandari, Sri Atri, & Sugihartini, N. (2018). Evaluation of the Physical Properties of Lotion Preparations with Variations in the Concentration of Moringa (Moringa oleifera L.) Leaves. Journal of Health Scientific Research and Studies Volume, 6(1), 85–90.
- Yuniarsih, N., Dinanti, D., Susanti, EI, Latif, MZ, Irma, R., Rades, RA, Buana, U., Karawang, P., & Barat, J. (2023). Review Article: Body Lotion from Various Plant Extracts Review Article: Body lotion from Various Plant Extracts. Journal of Pharmaceutical and Sciences, 6(2), 810–815.
- Zarwinda, I., Elfariyanti, E., Adriani, A., & Agustina, M. (2022). Formulation of Hand Sanitizer Gel from Ethanol Extract of Belimbing Wuluh Leaves (Averhoa Blimbi L.) Combination of Aloe Vera Gel. Journal of Medicine and Health: Scientific Publications, Faculty of Medicine, Sriwijaya University, 9(3), 321–330.