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Literature review : Nanoparticle Coatings for UV Protective Sunscreens

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Abstract: Ultraviolet radiation is a well-known cause of skin diseases. Sunscreen has become a contraceptive for skin diseases as effectively as possible to protect the skin from UV rays and radiation is also used in cosmetic preparations, but the use of chemicals in sunscreen causes irritation in some people, so it is necessary to administer active ingredients that can have serious side effects. small, namely with a new formulation of sunscreen in the form of nanoparticles. Nanoparticles are particles with dimensions of 1-100 nanometers. The purpose of nanoparticles is to overcome the solubility of poorly soluble drugs, improve poor bioavailability, modify drug delivery systems, improve drug stability and enhance absorption. The ethanol extract of suji leaves (Pleomele angustifolia) contains antioxidants that have potential as sunscreens as well as egg shell extract (CT) which is known to function as an active ingredient in sunscreens. Suji leaf extract is made into a cream preparation by mixing the aqueous phase (water, Tween 80, nipagin, glycerin, and propylene glycol) into the oil phase (mineral oil, nipasol, Span 80, and cetyl alcohol) at 60-70^{o}C, then Add the active ingredients according to the formula, stir until a homogeneous cream is formed. Egg shell extract (CT) through reduction of particle size and development of sunscreen formulations to increase the value of sun protection factors. CT was reduced in particle size through wet grinding using a ballmill tumbler followed by sonication to obtain a suspension of CT nanoparticles.

Keywords: Cream, Eggshell, Leaves suji *(Pleomele angustifolia)*, Nanoparticle, Sunscreen.

Introduction

Nanoparticles are a technology that is currently developing. The advantage of nanoparticles is their very small particle size, which is <100 nm. Metal nanoparticles attract a lot of attention because of their wide application and can be applied to detectors, electronics, catalysts, cosmetics and medicines (Wahyudi & Rismayani, 2008). Silver nanoparticles have been shown to have good abilities as a antimicrobial namely against bacteria, viruses and eukaryotic microorganisms (Gong*et al.*,2007). Silver nanoparticles are synthesized by several methods and conditions such as chemical reduction methods, photochemistry, sonochemistry, solvothermal synthesis and others.(Wahyudi & Rismayani, 2008). Ray spectrum the sun emits a certain amount of energy in the long range UVA with a wavelength range of 320-400 nm and the UVB region in the range 290-320 nm (Lowe et al., 1990). The mechanism for preparing sunscreen is divided into two groups, namely the chemical sunscreen group that works to absorb UV rays, and the physical blocking group (sunscreen that works physically). Physical blocking sunscreens work by reflecting or deflecting UV radiation. Physical sunscreens are generally inorganic compounds that are proven to provide benefits in preventing skin damage due to sun radiation (Mursiti et al, 2017). However, the formulation of these inorganic compounds is generally opaque in nature (Amir et al, 2022), because the size of the powder particles will affect the appearance of

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the skin when applied. Transparent, so that it can be better accepted as a cosmetic (Maulana et al, 2022). The particle size of the very fine physical blocking agent allows this preparation to also act as a sunscreen by absorbing UV light (Newmann et al., 2009). Research conducted by Prangdimurti et al., (2006) stated that suji leaves contain antioxidants. Antioxidants have various activities in the body, one of which is as a photoprotector which can be used as a sunscreen (Black, 1990). Chitosan as a polymer, can coat the extract and is able to protect it from instability due to exposure to high temperatures and light (Mohanraj and Chen, 2006). Cream preparations are of interest to consumers, including because they are easy to apply, provide a feeling of comfort when used, not sticky and easily rinsed with water when compared to ointments and pastes (Sari, 2017). The emulsifier determines whether or not a cream preparation is formed. One of the emulsifiers that can be used is non-ionic surfactants, because they are safer, do not irritate (Rowe et al. 2009). The combination of a nonionic surfactant such as Tween 80 with a viscosity increasing agent such as cetyl alcohol can improve the stability of the preparation (Rowe et al., 2009).

Materials and Methods

The cream preparation was made by mixing the aqueous phase (water, Tween 80, nipagin, glycerin, and propylene glycol) little by little into the oil phase (mineral oil, nipasol, Span 80, and cetyl alcohol) at 60-70C while continuously stirring. .

The water phase and the oil phase were heated to 70°C, then stirred using ultraturax at a speed of 9600 ppm for 25 minutes. Emulgel preparations were made by the trituration method, namely mixing a cream base with 40% PVP solution at 40oC to get an emulgel containing 2% PVP.

Tools and materials

The tools used in this study were cutting mill instruments (Retsch type SM-1), mortar grinders (Retsch, type RM100), ball mill tumblers (Retsch), automatic sifters (Retsch), ovens (Binder), probe sonicator (Vibra cell), particle size analyser (delsaTM Nano C, Beckmen Coulter), UV B lamp (SMART), bath sonicator (Branson type 5510), ultraturax T25 (Janke & Kunkle, IKA labortechnik), analytical balance (Toledo), brookfield viscometer type DV-I, pH meter (Beckmann), water bath , shaver (WAHL), Rotary evaporator (Heidolph), magnetic stirrer (Scilogex MS-H280-Pro), a set of adhesive and spreadability test equipment, UV-Vis Spectrophotometer (Shimadzu UV 1800) and the ingredients are egg shells broiler chicken (obtained from Amanda steamed brownie factory), technical hydrochloric acid, technical Tween 80, sodium lauryl sulfate, setostearyl alcohol, stearic acid, TEA, lanolin, Span 80, VCO (Virgin Coconut Oil) obtained from SITH ITB, propylene glycol, PVP K-21, methyl paraben, propyl paraben, vitamin E acetate, aquadest, and titanium dioxide. Suji leave (*Pleomele angustifolia*). 70% ethanol, cetyl alcohol, Span 80, glycerin, propyl paraben, methyl paraben, mineral oil, sodium tripolyphosphate and glacial acetic acid, chitosan.

Preparation of Chitosan Nanoparticle Cream and Eggshells

The cream preparation was made by mixing the aqueous phase (water, Tween 80, nipagin, glycerin, and propylene glycol) little by little into the oil phase (mineral oil, nipasol, Span 80, and cetyl alcohol) at 60-70°C while continuously stirring. Before being mixed, the two phases were heated separately before reaching that temperature. The mixture is stirred continuously to form a creamy preparation, then the active ingredients are added according to the formula while continuously stirring to form a homogeneous cream (Rizkita et al, 2022).

The preparation of eggshell nanoparticles was carried out in several stages, namely cutting using a cutting mill and grinding using mortar

grinders. The crushed powder is then sieved. Particles with a size of less than 100 μm were suspended in a 1% Tween 80 solution with a 50% concentration of eggshell particles, then crushed using a ballmill tumbler. then dried in the oven. The dry powder was then suspended in a 1% Tween 80 solution with a concentration of 10% to make nanosuspensions using the sonication method (Rizkita et al, 2020). The obtained nanosuspension was evaluated including particle size, polydispersity index, and particle morphology using SEM.

Characterization of Chitosan Nanoparticle Cream and Eggshells

The KEEDS nanoparticle organoleptic showed that the system had a clear appearance with a particle size of 233.4 ± 1.37 and a polydispersity index of 0.651 ± 0.03 (Prihantini et al., 2019). KEEDS nanoparticles that have been formulated into cream preparations produce preparations that have a soft texture, brownish white in color, with an aroma typical of suji leaves**.**Meanwhile, eggshell organoleptic has a brownish white color, almost odorless, has a water content (%w/b) 1.75 ± 0.08 and particle size (nm) ranges from 453.97 ± 25.63 (Rizkita et al, 2021)

Test of Chitosan Nanoparticle Cream and Eggshell Homogeneity

The results of the KEEDS cream homogeneity test for all formulas showed homogeneous results, namely in all preparations there were no coarse particles on the slide. While Egg Shell preparations F1A and F1B are preparations in emulgel form, which are semi-solid preparations and can be in the form of oil-in-water emulsions or water-in-oil emulsions where the viscosity is increased by adding*gelling agent*, this preparation can increase comfort when used because this preparation provides the advantages of an emulsion and gel at the same time (Mohammed, 2004). Preparations F2A and F2B are water-in-water cream preparations, with an emulsifier *in situ* stearic acid and TEA which will form TEA-Stearate in the preparation. The addition of lanolin in the preparation can relieve the irritating effect of TEA-Stearate, while cetostearyl alcohol is useful to increase the viscosity of the preparation so that it is more stable (Wibowo et al, 2018).

Preparation of pH

The pH of sunscreen cream preparations ranges from 4.5 to 7.5. If the sunscreen cream preparation is too alkaline, it can make the skin dry quickly, slippery and scaly. The results of pH measurements of KEDDS nanoparticle sunscreen cream were 4.7-4.8. The pH of the eggshell preparations tended to be above the basic pH, namely 6.19 for F1and 6.53 for F2. This is due to CaCO3 which is contained in the egg shell dissolved in water as the outer phase of the preparation becomes Ca(OH)2 which is alkaline so that the pH of the preparation is higher than the pH of the base. In the figure it can be seen that during storage at 40^{o}C for 20 days there was no significant change in pH in F1A and F1B. This is due to the amount of CaCO3 dissolved in the water phase is saturated, so even if stored above room temperature the amount of CaCO3 dissolved does not increase. The pH values of F2A and F2B increased when stored at 40^{o}C but there was no significant difference between F2A and F2B even though the number of egg shells added to F2B was one and a half times greater than F2A. This indicates the saturated solubility of CaCO3 has been reached at a concentration of 5% eggshell, so that the addition of the number of eggshells does not increase the pH significantly.

Viscosity

The results of the viscosity test showed that the thickness of the KEDDS nanoparticle sunscreen cream increased with the influence of the concentration of Tween 80 and cetyl alcohol to increase the consistency of the cream preparation to become thicker. The viscosity of topical preparations is generally 50-1000 dPas (Lachman et al, 1994). The results of the homogeneity and normality tests on the viscosity value data showed that the data were homogeneously distributed (sig. > 0.05), but not

normally distributed (sig. <0.05), so the data analysis was continued with the test *Kruskall–Wallis*. The results of the eggshell viscosity test for the three formulas showed that there were differences between the formulas, and the test was followed by the Mann-Whitney test to analyze which formulas gave significant differences. The results of the analysis showed that formula I and II were not significantly different (sig. > 0.05), while the difference in viscosity values between formulas I and II and formula III had a significant difference because the significance value was <0.05. While the viscosity of the eggshell preparation during the accelerated stability test did not change significantly in F1A and F1B, this indicated that the preparation was in a stable condition during storage. The viscosity of F2A and F2B decreased when stored at 40°C, but no phase separation occurred during 28 days of storage at that temperature (Wibowo et al, 2017).

Results and Discussion

Cream Preparation

The KEEDS nanoparticle sunscreen cream formula is presented in Table I. The formula refers to Ardianti's research (2019) where the active ingredient was modified using the chitosannanoparticle system of ethanol extract of suji leaves. The manufacture of KEEDS nanoparticles refers to Prihantini (2019).
KEEDS nanoparticle cream formulas are shown in Table I.

Table 1. Suji leaf ethanol extract formula encapsulated in the system nanoparticle as sunscream cream

Material	Composition (gram)		
	Formula I	Formula II	Formula III
Nanopartikel KEEDS (mL)	0,1	0,1	0,1
Minyak mineral	29	29	29
Setil alkohol	3	10	10
Tween 80	3	3	10
Span 80	1,15	1,15	1,15
Gliserin	10	10	10
Nipagin	0,2	0,2	0,2
Nipasol	0,1	0,1	0,1
Aqua demineralisata, genapkan	100	100	100

The water phase and the oil phase were heated to 70°C, then stirred using ultraturax at a speed of 9600 ppm for 25 minutes. Emulgel preparations were made by the trituration method, namely mixing a cream base with 40% PVP solution at 40°C to get an emulgel containing 2% PVP.

The preparations that have been made are then tested for their stability against extreme storage temperatures using the test method *freeze-thaw*. An emulsion system can experience physical instability that is characteristic *reversible* (*creaming* and flocculation) as well *irreversible* (*coalescent* and phase inversion). Characteristic instability *reversible* can return to initial state with little agitation. Meanwhile, the instability in the form of coalescence and phase inversion can end in phase separation (Eccleston, 2007). The results obtained from the test *freeze-thaw* showed that the basic formulas F1 and F2 had good physical stability, while the basic formula F3 showed that there was a phase separation in the cycle *freeze-thaw* second. Based on test results *freeze-thaw* Therefore, the F1 and F2 formulas were chosen to be developed into sunscreen preparations with the addition of eggshell nanoparticle powder.

Table 2. Orientation of sunscreen base formulas

Substance name	**Amount substance in the formula (%b/b)**		
	F1	F2	F3
VCO	31	31	31
Natrium lauril sulfat	9	-	-
Setostearil alkohol	1	1	-
Lanolin	-	2	-
Asam stearat	-	8	-
TEA	-	1,6	-
Tween 80	-	-	9,36
Span 80	-	-	0,64
PVP	2	-	2
Aquadest ad	100	100	100

Description : F1 = emulgel; F2 = krim; F3 = emulgel

Cream Characterization

Figure 1. Sunscreen cream containing the active ingredient suji leaf ethanol extract encapsulated in the nanoparticle system A:FI (T80:SA (3:3)% w/v), B:FII (T80:SA (3:10)% b/v), C:FIII (T80:SA (10:10)% b/v).

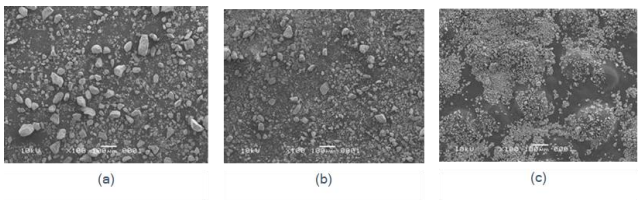


Figure 2. The results of examining eggshell powder in several stages of the process using SEM with a magnification of 100 times. The reduction process is < 100 µm (a), process*Ballmill*(b); sonication process (c).

Preparations of egg shell

Cream Test

Eggshell preparations F1A and F1B are preparations in emulgel form, which are semi-solid preparations and can be in the form of oil-in-water emulsions or water-in-oil emulsions where the viscosity is increased by adding *gelling agent*, this preparation can increase comfort when used because this preparation provides the advantages of an emulsion and gel at the same time (Mohammed, 2004). Preparations F2A and F2B are water-in-water cream preparations, with an emulsifier*in situ*stearic acid and TEA which will form TEA-Stearate in the preparation. The addition of lanolin in the preparation can relieve the irritating effect of TEA-Stearate, while cetostearyl alcohol is useful for increasing the viscosity of the preparation so that it is more stable in table 3.

Table 3. Shell sunscreen preparation formulation egg

Substance name	Amount substance in the formula (%b/b)			
	F1A	F1B	F2A	F2B
VCO	31	31	31	31
Natrium lauril sulfat	9	9	-	-
Setostearil alkohol	1	1	1	1
Lanolin	-	-	2	2
Asam stearat	-	-	8	8
TEA	-	-	1,6	1,6
PVP	2	2	-	-
Serbuk cangkang telur	5	8	5	8
Metil paraben	0,18	0,18	0,18	0,18
Propil paraben	0,02	0,02	0,02	0,02
Vitamin E asetat	0,01	0,01	0,01	0,01
Aquadest ad	100	100	100	100

Ranges pH the sunscreen cream

The pH of sunscreen cream preparations ranges from 4.5 to 7.5. If the sunscreen cream preparation is too alkaline, it can make the skin dry quickly, slippery and scaly. The results of pH measurements of KEDDS nanoparticle sunscreen cream were 4.7-4.8.

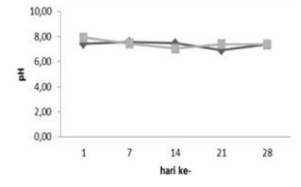
Table 4. KEEDS nanoparticle sunscreen cream pH

pH of KEEDS nanoparticle sunscreen cream	
Formula	pH
FI	4,74 ± 0,62
FII	4,84 ± 0,33
FIII	4,88 ± 0,04

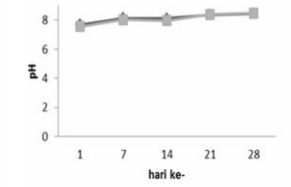
Preparation pH

Eggshell tend to be above the base pH, namely 6.19 for F1 and 6.53 for F2. This is due to CaCO3 which is contained in the egg shell dissolved in water as the outer phase of the preparation becomes Ca(OH)2 which is alkaline so that the pH of the preparation is higher than the pH of the base. In the figure it can be seen that during storage at 40^{o}C for 20 days there was

no significant change in pH in F1A and F1B. This is due to the amount of CaCO3 dissolved in the water phase is saturated, so even if stored above room temperature the amount of CaCO3 dissolved does not increase. The pH values of F2A and F2B increased when stored at 40°C but there was no significant difference between F2A and F2B even though the number of egg shells added to F2B was one and a half times greater than F2A. This indicates the saturated solubility of CaCO3 has been reached at egg shell concentration of 5%.



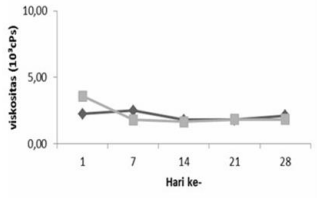
pH of F1A and F1B creams at accelerated stability test (♦ = F1A, ■ = F1B).



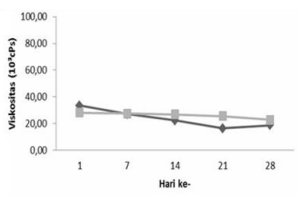
pH of F2A and F2B creams at accelerated stability test (▲ = F2A,♦ = F2B).

Viscosity

Table 5. KEEDS nanoparticle sunscreen cream viscosity



Viscosity of F1A and F1B creams at accelerated stability test (▲= F1A, ■= F1B).



Viscosity of F2A and F2B creams at accelerated stability test (■ = F2A, ▲= F2B).

Conclusions

The KEEDS nanoparticle cream visually looks homogeneous, with a brownish white color, soft texture, and the aroma of suji leaves. The pH value of the preparation was 4.74-4.88, type M/A cream. Variations in the T80:SA combination resulted in significant differences in the values of spreadability, adhesion, viscosity and activity of sunscreens between the three formulas (sig <0.05). SPF value on FI; FII; FIII respectively 33.41; 35.50; and 36.42 including the ultra protection category.

The cream formulation consisting of 1% lanolin, 2% cetosteryl alcohol, 8% stearic acid and 1.6% triethanolamine, with the active ingredients 5 and 8% eggshell nanoparticles added in a dispersed form in 1% Tween 80 solution, has physical stability. based on accelerated stability test for 28 days. The results of the skin irritation test showed that the preparation was mildly irritating with a primary irritation index value of 0.58 for a formula containing 8% eggshell nanoparticles and 10% titanium dioxide. The FPS value of preparations containing 5 and 8% eggshell nanoparticles were 3, respectively. 44 and 4.30.

References

Amir, R., Chaidir, C., Rizkita, A. D., & Herliyanti, A. (2022). Isolation And Characterization Of Jengkol (Pithecellobium jiringa) Skin Extract As Inhibitor Of Plasmodium falciparum Malaria Disease Enzym Malate Quinone Oxidoreductase. Journal of Pharmaceutical Sciences and Clinical Pharmacy, 19(1), 17-23

Ardianti. 2019. Formulasi dan Uji Aktivitas secara *In Vitro* Tabir Surya Sediaan Krim Ekstrak Etanol Daun Suji *(Pleomele angustifolia)* dengan Variasi Kombinasi Tween 80 dan Setil Alkohol, *Skripsi*, Universitas Wahid Hasyim, Semarang.

Ayuningrum, R. P., 2016, Uji Stabilitas Fisik dan Penentuan Nilai SPF Krim Tabir Surya Ekstrak Kulit Pepaya, *Skripsi*, Sekolah Tinggi Ilmu Kesehatan Ngudi Waluyo, Ungaran.

Cross, S. E., B. Innes, S. R. Roberts, T. Tsuzuki, T. A. Robertson, and P. McCormick, 2006, Human Skin Penetration of Sunscreen Nanoparticles: In vitro Assesment of Novel Micronized Zinc Oxide Formulation, Skin Pharmacol Physiol 2007:20, 148-154.

Damogalad, V., H.J. Edy, dan H.S. Supriati. 2013. Formulasi krim tabir surya ekstrak kulit nanas (Ananas comosus L. Merr) dan uji in vitronilai sun protecting factor (SPF). Pharmacon, J. Ilmiah Farmasi UNSRAT, 2(2):12- 16.

Davis, C. and R. Reg, 2002, *High Value Opportunitues From The Chicken Egg*, Rural Industries Research and Development Corporation, 30 – 31

Gadri, A., Darijono, S.A., Mauludin, R., dan Iwo. M.I. 2012. Formulasi Sediaan Tabir Surya dengan Bahan Aktif Nanopartikel Cangkang Telur Ayam Broiler. Jurnal Matematika & Sains, Vol. 17 Nomor 3. ITB

Kurniati, N., 2011, Uji Stabilitas Fisik dan Aktivitas Antioksidan Formula Krim Mengandung Ekstrak Kulit Buah Delima *(Punica granatum L.)*, *Skripsi*, Fakultas Matematika dan Ilmu Pengetahuan Alam, Universitas Indonesia, Depok, 29.

Maulana, I., Hasanah, A. U., Tyas, R., & Rizkita, A. D. (2022). Effectiveness Test of Mouthwash Preparations from Ethanol Extract of Prasman Leaf (Eupatorium Triplinerve Vahl) Against Streptococcus Mutans. Mahardika Health Journal, 9(1), 28-34

Murrukmihadi, M., Ananda, R., Handayani, T.U, 2012, Pengaruh Penambahan Carbomer 934 dan Setil Alkohol sebagai emulgator salam Sediaan Krim Ekstrak Etanolik Bunga Kembang Sepatu *(Hibiscus rosa-sinesis L.,)* terhadap Sifat Fisik dan Aktivitas Antibakteri pada *Staphylococcus aureus.* Majalah Farmaseutik, 8(2):152-157.

Mursiti, S., Rizkita, A.D., & Dewi, S.A. (2017). Activity Test of Wani, Iler, and Mango Leaves as Antidiabetic using Streptozotocin, Alloxan, and TTGO Induction Methods. Proceeding of National Seminar on Chemistry and Chemical Education. 3: 105-109

Rizikiyan, Y., Sulastri, L., dan Indriaty, S., 2018, Formula Dan Uji Daya Hambat Krim Ekstrak Etanol Teh Hijau Terhadap *Propionibacterium Acnes, Jurnal Medical Sains*, 2(2): 65-74.

Rizkita, A. D., Dewi, S. A., Wibowo, E. A. P., & Maulana, I. (2021). Isolation and Identification of Saponins from Leunca Extract (Solanium ningrum L) by Infrared Spectrophotometry. Scientific Journal Of Science, 21(2), 166-169.

Rizkita, A. D., Handayani, S., & Dani, I. C. (2020, July). In vivo study of 8-OHdG as a biomarker DNA damage by combining the exposure of nonyl phenol and copper using ELISA technique. In IOP Conference Series: Materials Science and Engineering (Vol. 902, No. 1, p. 012054). IOP Publishing

Rizkita, A. D., Pamungkas, W. O., Dewi, S. A., Angganawati, R. T., Rochjana, A. U. H., Firmansyah, A., & Saputra, R. P. (2022, February). Proof of The Formation of OH Radicals from Methyl Paraben and Its Effect on Cancer Formation. In Proceeding International Conference on Religion, Science and Education (Vol. 1, pp. 489-492)

Santosa, M.R.P., dan Prihantini, M. 2021. Ekstrak Etanol Daun Suji *(Pleomele angustifolia)* Terenkapsulasi Nanopartikel Kitosan Dalam Sediaan Krim Tabir Surya dengan Variasi Tween 80-setil Alkohol. Jurnal Ilmu Farmasi dan Farmasi Klinik (JIFFK). Universitas Wahid Hasyim. Semarang.

Supriyadi, D., 2011, Pembuatan Nanopartikel Cangkang Telur Menggunakan Metode Sonikasi, *Tesis*, Program Pasca Sarjana Sekolah Farmasi ITB, 24-26.

Wenur, Susanti., Paulina V. Y Yamlean, dan Sri Sudewi, 2016, Formula dan Penentuan Nilai SPF dari Sediaan Losio Ekstrak Etanol Kulit Buah Pisang Goroho, *Jurnal Ilmiah Farmasi*, 5(4), 2302-2493

Wibowo, E. A. P., Arzanto, A. W., Maulana, K. D., & Rizkita, A. D. (2018). Preparation and Characterization of Nanosilica from Rice Straw. Scientific Journal of Science, 18(1), 35-40.

Wibowo, E. A. P., Hardyanti, I. S., Nurani, I., HP, D. S. H., & Rizkita, A. D. (2017). Study of Iron (Fe) and Copper (Cu) Metal Reduction in Embung Water Using Nanosilica Adsorbent. Scientific Journal of Science, 17(2), 131-134

Wood, C., and Murphy, E., 2000, *Sunscreen Efficacy. Glob. Cosmet. Ind.,* Duluth, 167: 38-44.

Yasin, R. A., 2017, Uji Potensi Tabir Surya Ekstrak Kulit Buah Jeruk Nipis *(Citrullus aureantifolia)* Secara In Vitro, *Skripsi*, Fakultas Farmasi, Universitas Islam Negeri Alaludin, Makasar.