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Original Research Article

Formulation and effectiveness test of clove flower oil (*Syzygium aromaticum* L.) nanoemulsigel preparations against *Propionibacterium acnes* bacteria

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ABSTRACT

Background: Acne is a chronic inflammatory process in the pilosebaceous glands. The appearance of acne is a process of follicular hyper-keratinization, which causes blockage of the pores so that the hair follicles are blocked by bacteria known as *Propionibacterium acnes*. Clove flower oil contains eugenol compounds which have the strongest activity against gram-positive and gram-negative bacteria.
Methods: In this research, antibacterial activity tests were carried out on clove flower oil with various concentrations and nano-emulsion gel preparations were made with a clove flower oil concentration of 1.5%; 3%; 5.5%, which was then tested for antibacterial activity on the nano-emulsion gel preparations of clove flower oil measured using a caliper and the diameter of the inhibition zone produced was recorded.
Results: the results of the organoleptic research showed that the color was yellow, transparent and had a distinctive odor, homogeneity showed that there were no coarse particles, viscosity was still within the required range, pH showed that the pH was still within the required range of 4.5-6.5, particle size test was below 200 nm, cycling test showed that it was stable during storage at hot and cold temperatures for 6 cycles of *P. acnes* inhibitory clove flower oil nano-emulsion preparation with a concentration of 1.5%; 3%; 5.% respectively have resistance of 11.60 mm, 13.53 mm, 15.76 mm
Conclusions: From the results of the research that has been carried out, it is concluded that clove flower oil can be formulated into a nano-emulsion gel preparation, is stable during cycling tests, and has a particle size below 200 nm. Nano-emulsion gel formulations have the greatest antibacterial activity compared to emulsion gel formulations.

Keywords: Clove flower oil, Nano-emulsion gel, Antibacterial

INTRODUCTION

Skin is the outermost layer of the human body which is in direct contact with the external environment. One way to make skin healthy and well-maintained is to use skin care products.[1] Facial skin is different from the skin of other parts of the human body because facial skin contains more sebaceous glands, which produce fatty acids called "sebum".[2] The accumulation of sebum and dead skin cells in the sebaceous follicles increases the microbial load, which disrupts the follicle walls, causing inflammation of the skin called acne.[3] Acne is a skin disease where the

pores become blocked, causing inflamed pockets of pus and a skin condition characterized by the appearance of spots on various parts of the body, including the face, neck, back, and chest.[4] Acne occurs due to active oil glands under the skin. This activity is stimulated by the androgen hormone, which increases when a person enters puberty, and their oil glands also increase in height.[5] *Propionibacterium acnes* is a gram-positive anaerobic bacterium that is the most dominant bacteria in acne lesions.[6] At puberty, there is an increase in hormones, which will have an effect on increasing sebum production, causing an increase in the growth of *P. acnes*.[7] *P. acnes* plays a role in the pathogenesis of acne by breaking down sebum components, namely triglycerides, into free fatty acids, which are mediators of inflammation

Clove (*Syzygium aromaticum L.*) is a type of spice plant that is often found in Indonesia. From several parts of the clove plant, such as stalks, flowers, and clove leaves, essential oil can be obtained with the main component of the phenol group, namely eugenol. According to research by.[8] The eugenol content of clove flowers is between 78-95% with the essential oil reaching 6%, and from the leaves, the eugenol content is between 80-85% with the essential oil content of clove leaves reaching 2-3%. Carvacrol and eugenol are isomer of eugenol and are included in the phenol group of compounds that have the strongest activity against gram-positively and gram-negative bacteria. To make it easier to use, clove oil can be formulated in the form of a nano-emulsion gel, which is a gel-based nano-emulsion preparation. This preparation has a small particle size; therefore, 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 (Jivani et al).[8]

Thus, increasing penetration into sebaceous tissue, which is influenced by nano-sized particlels.[9] The smaller the particle size, it is expected to increase the contact area of the particle with the membrane and make it easier for the particle to enter through the melmbrane.[10] The aim of this research is to make a nano-emulsion gel formulation from clove flower oil and test the antibacterial activity of the nano-emulsion gel preparation against the bacteria *Propionibacterium acnes.*

METHODS

Materials

The materials used in this research were an incubator (Memmert), laminar air flow cabinet (Astec HLF 1200 L), magnetic stirrer (Thermo), particle size analyser (Horiba Scientific, viscometer (NDJ-8S), micro-pipette (Eppendorf), pH meter (Hanna), sonicator (Elma), clove flower oil (*Syzigium aromaticum L.*), distilled water, 96% ethanol (PT. Nitra Kimia), carbopol 940 (PT. Nitra Kimia), rabbit skin membrane, Triethanolamine (PT. Nitra Kimia), Tween 80 (PT. Nitra Kimia), and propylene glycol (D PT. Nitra Kimia). This research was conducted from February 2023 to March 2023 in the physical pharmacy and microbiology laboratory, faculty of pharmacy, university of North Sumatra.

Nanoemulsigel formulation

The process of making nanoemulgel uses a spontaneous emulsification method consisting of a water phase and an organic phase. The aqueous phase consisted of tween 80 (surfactant) and distilled water stirred continuously at a speed of 5000 rpm. The organic phase consisted of clove flower oil and propylene glycol 400 (cosurfactant) stirred at a constant speed of 5000 rpm. The organic phase was injected into the water phase with constant stirring at a speed of 5000 rpm and sonicated for 30 minutes until a clear preparation was formed. In a separate container, carbopol 940 was dispersed in distilled water, then triethanolamine was added and homogenised at 500 rpm until a transparent gel was formed. In the final step, nanoemulsion is slowly added to the gel base and homogenised at 2000 rpm for 10 hours.[11-12] The nanoemulgel formula is shown in Table 1.

Table 1: The clove flower oil nanoemulsion formulation.

Ingredients	Concentration (%) b/b		
	NEG1	NEG2	NEG3
Clove flower oil	1.5	3	5.5
Tween 80	35	35	35
Propylene glycol	5	5	5
Methyl paraben	0.1	0.1	0.1
Propyl paraben	0.02	0.02	0.02
Alcohol 96%	15	15	15
Aquadest	6	6	6
Carbopol	1	1	1
Triethanolamine	0.8	0.8	0.8
Aquadest	100	100	100

Evaluation of nanoemulsigel

Organoleptic test

Organoleptic tests were carried out on nanoemulgel, which were visually observed for changes in color, odor, and shape.[14]

Homogeneity test

Homogeneity tests were carried out on nano emulsified gels by applying a certain amount.

Viscosity measurement

Viscosity measurement aim to determine the viscosity of nanoemulgel preparation. Viscosity measurement using an NDJ-8S viscometer. Viscosity measurements were carried out by placing the preparation in a 50 ml beaker and using a spindle accordingly.[11]

Sample onto a glass object. The sample should show a homogeneous composition as well as no visible coarse grains.[11]

pH measurement

The determination of the pH of nanoemulgel was carried out using a calibrated pH meter, first with buffer solutions (pH 7.01) and (pH 4.01) until the instrument showed the pH value. Then the electrode was washed with distilled water and dried with tissue. Then the electrode is dipped into the sample until the instrument shows a constant pH value. According to skin pH, the required pH range is 4.5-6.5.[15]

Particle size measurement

Particle size measurements were carried out by diluting 0.5 g of sample with 1 mL of distilled water. Then 1 mL was taken to test the particle size. Particle size measurements were carried out at the Bandung institute of technology using the Horiba scientific nanoparticle analyzer SZ-100. Particle size testing is carried out to determine the size of the globules formed in nanoemulgel and elmulgel.[16]

Study of physical stability of nanoemulgel

The purpose of carrying out a cycling test is to determine stability. Accelerated cycling test by storing the preparation at a temperature of 4±20ºC for 24 hours, then moving it to a temperature of 40±20ºC for 24 hours. This treatment is 1 cycle. The treatment was repeated for 6 cycles and the phase separation was observed. Physical conditions after the experiment were compared with those before the experiment.[17]

Antibacterial activity

Antibacterial activity tests were carried out on nanoemulgel preparations. Using the agar diffusion method (Kirby-Bauer), this test was carried out. The sterile petri dish was first filled with 0.1 mL of inoculum, then 15 mL of nutrient agar (NA) medium was added while maintaining a temperature of 45-50°C and homogenised until solid. Each petri dish is placed on a paper disk that has a drop of test solution on it. After 24 hours of incubation at 36-37°C, the diameter of the clear zone was measured. Use a calliper expressed in millimetres. Testing was carried out in triplicatel.[18-19]

RESULTS

Gell nano emulsion and gel emulsion formulation

The nanoemulgel and emulgel formulations consist of clove flower oil, tween 80, PEG 400, distilled water, propyl paraben, methyl paraben, carbopol 940, and triethanolamine. Clove flower oil is used as a carrier oil and an ingredient that has antibacterial, antiseptic, and anti-inflammatory activity. Tween 80 (surfactant), PEG 400 (cosurfactant), carbopol 940 (gelling agent), and triethanolamine (pH balance) The results of the nanoemulgel and emulgel formulations are shown in Figure 1.

Figure 1: Nanoemulsigel formulations.

Evaluation of nanoemulgel

Organoleptic test

Organoleptic tests are visually observed on all formulas including color, odor and shape. The organoleptic results are in Table 2.

Table 2: Results of nanoemulsigel formulations.

Formula	Color	Shape	Odor
NEG1	Yellow	Transparent	Distinctive aroma
NEG2	Yellow	Transparent	Distinctive aroma
NEG3	Yellow	Transparent	Distinctive aroma

The organoleptic results of nanoemulgel concentrations of 1.5%, 3% and 5.5% are yellow, have a distinctive aroma of clove leaf oil and are transparent.

Homogeneity test

The aim of the homogeneity test is to determine the homogeneity aspect of nanoemulgel. The homogeneity test results are in Table 3.

Table 3: Results of organoleptic examination of nanoemulgel and emulgel.

Formula	Homogeneity
NEG1	Homogeneous
NEG2	Homogeneous
NEG3	Homogeneous

Viscosity measurement

Viscosity measurement aim to determine the viscosity of a preparation to flow. Viscosity measurement using a Brookfield NDJ-8S. The viscosity measurement results are shown in Table 4.

Table 4: Viscosity measurement results of nanoemulgel.

Formula	Viscosity (C. Pas)
NEG1	3997.90±0.70
NEG2	4365.20±0.10
NEG3	4432.46±0.15

The viscosity value states the amount of resistance a liquid has to flow. The higher the viscosity value, the higher the viscosity value, the greater the resistance to flow. Carbopol is a type of gelling agent that provides excellent stability.[13]

pH measurement

The pH test aims to determine the safety of the preparation when used so that it does not irritate the skin and also to determine the stability of the preparation. The results of pH measurements are shown in Table 5.

Table 5: Results of pH measurements for nanoemulgel.

Formula	pH
NEG1	5.2±0.4
NEG2	5.4±0.1
NEG3	5.3±0.2

The results of pH measurements show that the higher the concentration of oil used, the pH of the oil preparation also increases. The pH measurement results were obtained at NEG1 5.2, NEG2 5.4, NEG3 5.3, For example 6.41. The pH results obtained are in accordance with the skin's pH, namely between 4.5-6.5, so it is safe to use and does not cause irritation to the skin.

Particle size measurement

Measurement of nano-emulsion gel and emulsion gel particles were carried out using a particle size analyser (Horiba Sz-100) at room temperature when preparation was complete. The results of particle size measurements are shown in Table 6.

Table 6: Results of pH values for nanoemulgel gel and emulgel particle size.

Formula	Particle size (nm)
NEG1	45.49±0.02
NEG2	50.24±0.06
NEG3	66.68±0.08

Particle size is an important parameter in nanoemulgel preparation. The smaller the particle size will increase the surface contact area; the higher the surface contact, the faster the incoming and outgoing material is absorbed into the skin so that it can produce the desired effect optimally.[20] The size at the nanoscale is determined by the homogenization time, stirring speed, and concentration of surfactant and cosurfactant used in the formulation. The particle size results for NEG1, NEG2, and NEG3 are not more than 200 nm. The small particle size of the nanoemulgel will bel absorbed morel quickly by the skin, which can increase the stability of the active substance, thereby increasing drug absorption. Study of the physical stability of nanoemulgel and emulgel. Physical observations of the nanoemulgel and emulgel preparation were carried out for three cycles, and there was no change in color, change in odor, or phase separation (Figure 2). It was concluded that the nanoemulgel and emulgel preparations were stable during storage.

Study of physical stability of nanoemulgel

Physical observations of the nanoemulgel preparations were carried out for three cycles and there was no change in color, change in odor or phase separation (Figure 2). It was concluded that the nanoemulgel preparations were stable during storage.

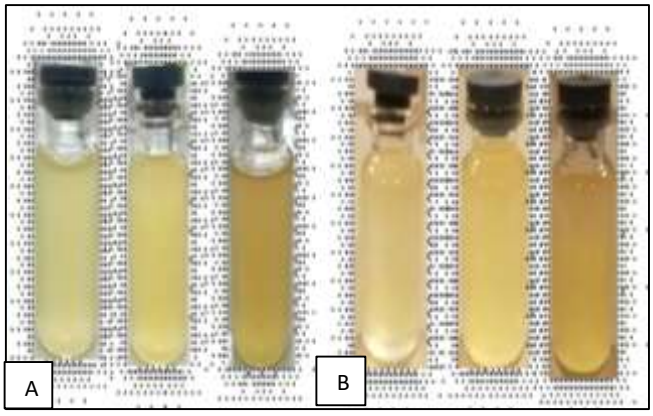

Figure 2 (A and B): Before cycling the nano-emulgel and after cycling the nano-emulgel test.

Anti-bacterial activity

Antibacterial activity tests were carried out on nanoemulgel preparation. Using the agar diffusion method (Kirby-Bauer). The result of measuring the diameter of bacterial growth inhibition are shown in Table 7. Growth inhibition of nanoemulgel and clove flower oil

Table 7: Results of measuring bacterial diameter.

Formula	Obstacle zone
NEG1	11.60±0.02
NEG2	13.53±0.05
NEG3	15.76±0.05

Based on the table above, it can be seen that the higher the concentration of clove flower oil used, the higher the concentration of clove leaf oil used, the greater the inhibitory power produced. This proves that the eugenol contained in clove leaf oil can bel used as an anti-bacterial, especially against bacteria that cause acne. Table 6 also shows that the concentration is 5.5%, nano-emulsion gel has greater inhibitory power.

DISCUSSION

The formulation of this nano-emulsion gel preparation consists of clove flower oil, ethanol 96%, Tween 80, propylene glycol, carbopol 940, methyl paraben, TEA, and distilled water. Clove flower oil in this formulation is used as an anti-acne ingredient. Tween 80 as a dispersing agent, propylene glycol functions as a humectant, the gel base used is carbopol 940, methyl paraben and propyl paraben as a preservative, TEA is used to neutralize kerboxylic groups and polymers and ionize, electrostatic repulsion occurs between negatively charged particles thereby increasing the properties development and thickening of (rigid) polymers (Magbool et al). In the initial stage of making nano-emulsion gel preparations, nano-dispersion is first made which mixes the organic phase with the water phase. Before proceeding with the manufacture of nano-emulsion gel, nano-dispersion F1 50.91 nm, F2 53, 30 nm, and F3 58.12 nm. Based on previous research, the size of nano-dispersions ranges from 100 to 200 nm.[20] The resulting nano-emulsion formulation is yellow, thick, and has a distinctive aroma.

The homogeneity test was carried out to determine whether the mixing was even or not when making the dosage formula, and also to determine the evenness of the nanogel texture when applied to the skin. The homogeneity observation results showed that the three formulas had good and even homogeneity, showing no particles when applied to glass objects. The preparation is said to be homogeneous when there is an even color and no different particles are found. Spread-ability is an important characteristic in a formulation that ensures ease when the preparation is easily applied to the skin, influencing consumer acceptability.[21] Spread-ability testing was carried out at room temperature for weeks 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 and 12 using the same method. Results of the spread-ability test of the clove flower oil gel nano-emulsion preparation during storage.

pH measurements were carried out when it was finished and during 12 weeks of storage at room temperature every 1 week, carried out 3 times and then the pH value was averaged. pH measurements were carried out to determine the pH of the nano-emulsion gel preparation according to the skin, because the preparation is in direct contact with the skin and will affect the condition of the skin. showed that during storage all preparations, both nanoemulsion gel which were stored at room temperature for 12 weeks showed a pH but it was not very significant but the resulting pH value still met the skin pH requirements, namely 4.5-6.5.[22] If the pH of the preparation is too acidic it can cause skin irritation, while a pH that is too alkaline can cause dry and scaly skin. Decrease in pH that is too significant can cause preparation to become watery, which can cause the preparation to become unstable.

The higher the concentration of clove flower oil and the longer the storage time, the larger the average particle size, however this size is still within the accepted range for nanoemulsion gel particle sizes, namely less than 1000 nm.[23] The increase in particle size due to nano preparations also has several shortcomings that often arise during preparation, such as rapid aggregation and uneven particle size uniformity, resulting in the stability of the disperse system being difficult to control.[24] The resulting particle size is influenced by the speed of the homogenizer, where to produce small particle sizes, high-speed homogenization or sonication is often used. However, during storage there is no stirring, which can trigger the particles to become large.[25]

The stability test using a cycling test was carried out by conditioning the gel nanoemulsion preparations in extreme hot (45ºC) and cold (4ºC) cycles alternately for 24 hours each. This treatment is called 1 cycle, and this test is carried out for 6 cycles (12 days). In this way, an overview of the stability of the preparation under long-term storage conditions during an accelerated test period is obtained. After 6 cycles, the nanoemulsion gel preparations were qualitatively observed showing no changes in shape, odor and color in the three preparation formulas. So, this is declared physically stable during the cycling test. The Cycling test aims to determine the stability of the preparation at extreme temperature differences. This test is carried out to speed up changes that usually occur under normal conditions.[26]

Testing the antibacterial activity of clove flower oil used the agar diffusion method, this method was used because it allows the nanoemulsigel preparation test material to come into direct contact with the walls of the agar medium, so that measuring the diameter of the inhibition zone will be easier and can be seen visually.[27] It shows that in F1 the preparation is able to inhibit the growth of *Propionibacterium acnes* bacteria by 11.6±0.1, in F2 it is able to inhibit the growth of *Propionibacterium acnes* bacteria by 13.53±0.05, in F3 it is able to inhibit the growth of *Propionibacterium acnes* bacteria by 15.76±0.05. Based on these results, the clove flower oil nanoemulsion preparation with a concentration of 5.5% was more effective in inhibiting the growth of *Propionibacterium* bacteria, increasing the diameter of the clove flower oil inhibition zone after it was made in the form of a clove flower oil nanoemulsigel preparation. This is because the nano-emulsion gel preparation has a smaller particle size so that it can increase the contact area of the particles with the membrane and make it easier for the particles to penetrate the membrane so that the release of the active ingredient is easier.[28] The inhibition zone diameter results

obtained in this study were only for the *Propionibacterium acnes* bacteria

CONCLUSION

From the results of the research that has been carried out, it is concluded that clove flower oil can be formulated into a nanoemulgel preparation, is stable during cycling tests, and has a particle size below 200 nm. F3 nanoemulsion preparation has the best antibacterial activity of 15.76±0.05.

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REFERENCES

1. Prianto JLA. Cantik Panduan lengkap merawat Kulit Wajah. Jakarta: PT Gramedia Pustaka Utama. 2014.
2. Dwikarya M. Merawat Kulit dan Wajah. Tanggerang. PT. Kawan Pustaka. 2007.
3. Hsieh M, Pan S, Setiono R. Validating service convenience scale and profiling customers: A study. J Management. 2011;3(2):1949-55.
4. Kusbianto D, Ardiansyah R, Hamadi DA. Implementasi Sistem Pakar Forward Chaining Untuk Identifikasi dan Tindakan Perawatan Jerawat Wajah. J Informatika Polinema. 2017;4(1):72-3.
5. Sylvia L. Hubungan Antara Jenis Mikroorganisme yang Ditemukan Pada Lesi Akne dengan Be, Tesis, Padang: Program Pendidikan Dokter Spesialis Fakultas Kedokteran Universitas Andalas. 2010.
6. Jappe U. Pathological Mechanism of Acne with Special Emphasis on *Propionibacterium acnes* and Related Therapy. Acta Derm Venereol. 2003;83:241-8.
7. Nurdjanah N. Diverifikasi tanaman cengkeh, J. Perspektif. 2004;3(2):61-7.
8. Malay NJ, Chandresh PP, Bhupendra GP. Nanoemulgel Innovative Approach for Topical Gel Based Formulation. Res Rev Health Care Open Acc J. 2018;1(2):RRHOAJ.MS.ID.000107.
9. Thassu D. Nanoparticulate drug delivery system. New York: Informa Healthcare USA Inc. 2007.
10. Syahfitri EL, Reveny J, Nainggolan M. Formulation and Antibacterial Activity Tests of Nanoemulsion Gel Black Cumin (*Nigella Sativa* L.) Ethanol Extract. Asian J Pharm Res Dev. 2020;8(4):07-11.
11. Wulansari A, Jufri M, Budianti A. Studies on the formulation, physical stability, and *in vitro*-antibacterial activity of tea tree oil (Melaleuca alternifolia) nanoemulsion gel. Int J Appl Pharm. 2017;9:135-9.
12. Hariyadi DM, Rosita N, Isnaeni, Sudarma S, Rezania D. Virgin Coconut Oil Emulgel: Effect of VCO and Carbopol 940 Concentration on Characterization and Antibacterial Activity. Res J Pharm Technol. 2022;15(5):2087-92.
13. Amalyuri AG, Reveny J, Dalimunthe A. Antibacterial Potential of Ethanol Extract of Tamarind Seed Bark (*Indica* L.) And Formulation of Anti-Acne Nanogel. Int J Sci Technol Manag. 2022;3(3):598-604.
14. Jufri M, Iswandana R, Wardani DA, Malik SF. Formulation of Red Fruit Oil Nanoemulsion Using Sucrose Palmitate. Int J Appl Pharm. 2022;14(5):175-80.
15. Yadav VD, Shinde AD, Jadhav PD. Formulation and Evaluation of Liposomes Containing Fluconazole. Int J Drug Deliv Technol. 2022;12(1):98-102.
16. Verma V, Easwari TS. A Novel Approach of Leflunomide Nanoemulgel for Topical Drug Delivery System. Int J Pharm Investig. 2022;12(2):199-204.
17. Fitri R, Reveny J, Harahap U, Dharmawan H, Nasri N. Anti-Acne Activity from Biocellulose Mask Formula Containing (*Aloe Vera* (L.) *Burm*. F) Essence Combined with Vitamin E. Indones J Pharm Clin Res. 2021;4(1):1-7.
18. Harahap U, Dalimunthe A, Hertiani T, Muhammad M. Antioxidant and antibacterial activities of ethanol extract of Vernonia amygdalina Delile. Leaves. AIP Conf Proc. 2021;1:2342
19. Algahtani MS, Ahmad MZ, Ahmad J. Nanoemulgel for improved topical delivery of retinyl palmitate: Formulation design and stability evaluation. Nanomaterials. 2020;10(5):848.
20. Sharma A, Garg T, Aman A, Panchal K, Sharma R, Kumar S, et al. Nanogel-an Advanced Drug Delivery Tool: Current and Future. Artificial Cells, Nanomedicine, And Biotechnology. Halaman. 2024;2(1):165-77.
21. Garg A, Aggarwal D, Garg S, Sigla AK. Spreading of Semisolid Formulation: An Update. Pharmaceut Tecnol. 2002;84-102.
22. Muadifah A, Astutik TK, Amini HW, Tarigan IL. Studi activities extract ethanol dan sediaan gel daun melinjo (*Gnetum gnemon* L.) sebagai antibakteri terhadap *Staphylococcus Aureus*, Chempublish J. 2019;4(2):89-100
23. Muniraj N, Siddharth S, Shriver M, Nagalingam A, Parida S, Woo J, et al. Induction of STK11-Dependent Cytoprotective autophagy in breast cancer cells upon honokion treatment. Cells Deaeh Discovery. 2020;6(1):81.
24. Nagavarma BVN, Hemant Y, Ayaz A, Vasudha LS. Different Techniques for Preparation of Polymeric Nanoparticles-A Review. Asian J Pharm and Cli Res. 2012;5(3):16-23.
25. Dwiastuti R, Noegrohati S, Istyastono EP, Marchaban M. Metode Pemanasan dan Sonikasi Menghasilkan Nanoliposom dari Fosfolipid Lesitin Kedelai (Soy Lecithin). J Pharmaceut Sci Comm. 2016;13(1):23-7.

26. Niazi SK. Handbook of Pharmaceutical Manufacturing Formulation: Compressed Solid Formulations. 2nd Ed. New York: Informa Healthcare. 2004.
27. Jawetz. Mikrobiologi Kedokteran. Salemba Medika. Jakarta. 2005.
28. Thassu D. Nanoparticulate drug delivery system. New York: Informa Healthcare USA Inc. 2007.

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