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Niosome gels encapsulate green mangosteen peel extract (*Garcinia mangostana* L.) as an anti-acne-inducing bacterial and anti-inflammatory activity

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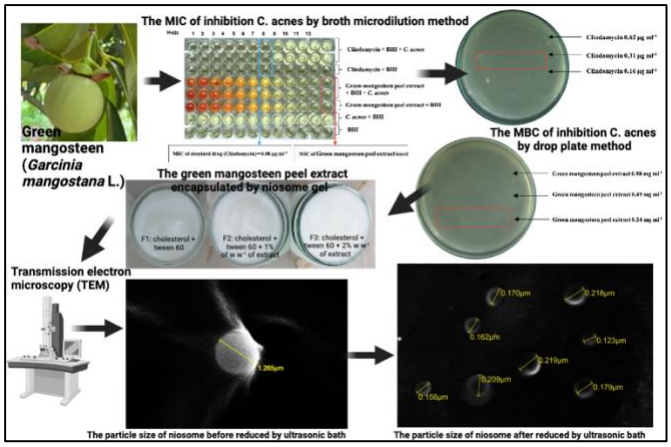
Abstract

This research aims to develop a niosome gel from green mangosteen peel extract (*Garcinia mangostana* L.) by maceration with an ethanol solvent. The result of the yield percentage was 14.35 ± 0.90. The result of analyzing the phytochemicals by high-performance liquid chromatography (HPLC) was that tannin and xanthone were equal to 0.7483 ± 0.0825 mg per 100 mg of extract and 0.02964 ± 0.0088 mg per 100 mg of extract, respectively. The results of the determination of the effect include anti-inflammatory and anti-bacterial (*Cutibacterium acnes)* as anti-inflammatory with nitric oxide from LPS-induced macrophage cells up to a maximum equal to 29.10 ± 4.78% as a concentration at 1 mg mL^{-1} as acetonide can inhibit nitric oxide equal to 33.12 ± 3.62% as a concentration at 1 mg mL^{-1}. and anti-bacterial (*Cutibacterium acnes)* by broth microdilution and drop plate methods, it was found that clindamycin has a minimum inhibitory concentration (MIC) and a minimum bactericidal concentration (MBC) of 0.08 μg mL^{-1} and 0.31 μg mL^{-1}, respectively. The development of niosomes consisting of cholesterol, tween 60, and mangosteen peel extract at 1% w w^{-1} and 2% w w^{-1} in every formula showed good stability. The reduction of particle size in the formula by an ultrasonic bath at 30 minutes and measurement of particle size with a transmission electron microscope (TEM) were found to be equal to 1,265 and 123 – 219 nm, respectively. The polydispersity index (PDI) was in the range of 0.1 – 0.2, and the zeta potential value was in the range of –26.15 to –28.61 mV. The result of hydration and trans epidermal water loss (TEWL) was found to be that after 4 weeks of use, the formula containing the niosomes of mangosteen peel extract concentrated at 2% w w^{-1} maximizes skin moisture. It has a value of 346 ± 39.27 and has the least surface water loss.



Keyword: Green mangosteen; Tannins; Xanthone; Anti-inflammatory; Anti-bacterial (*C. acnes*); Niosome

1. Introduction

The application of nanotechnology in cosmetic products enhances the efficiency of natural active ingredients and the delivery of active ingredients into the skin by developing vectors or delivery systems that can transport and protect active ingredients to reach specific targets. In addition, it is able to increase the stabilizers of natural active ingredient in cosmetic products. Particulate active carriers are made up of small particles that encapsulate the important active inside small vesicles. These vesicles are characterized by the structure of the cell wall as a bilayer membrane, which is formed by the self-assembly of molecules with polar and nonpolar properties in the same molecule, also known as amphiphilic molecules, arranged by bringing the hydrophobic parts together to form a wall of the same thickness as that of the molecule. The walls envelop the solution internally and release it through membranes outwards. Niosomes are vesicles made from nonionic surfactants. It also has a number of properties suitable for use as carriers, including blocompatible, biodegradable, non-toxic, and able to store large amounts of ingredient compared to the volume of very small vesicles [1]. Most niosomes have particle sizes in the range of 30 – 120 nm. It can be produced in various forms of cosmetics and cosmeceuticals [2, 3].

Mangosteen (mangosteen), scientific name *Garcinia mangostana* L., family Guttiferae, is a tropical plant species in deciduous forests. Its young fruits in the outer peel are yellow-green with yellow ribbed inside, as the matures fruit, the outer peel is dark pink-red (exocarp), thickness of 6 – 10 cm. There are many research reports to phytochemicals in mangosteen peel, consisting of tannin [4] 8.8 – 10.5%, xanthone [5 – 6] and α-mangostin. Several previously reported main active of mangosteen peel extract such as antibacterial[7], antihistamines, anti-inflammatory [8] and antioxidant [9].

Therefore, the researcher is interested phytochemicals consisting of xanthone and tannin in mangosteen peel extract. In addition, interested about cosmetic effects such as anti-inflammatory activity by compared activity with triamsinolone acetonide as an anti-inflammatory drug after that studied the anti-bacteria of *Cutibacterium acnes* as bacteria causing acne. Development of gel products containing niosomes from mangosteen peel extract and test the efficiency of the product. It is the development of cosmetic products using natural raw materials to increase the value of extracts by developing extracts in the form of niosome small particles as an interesting source of raw materials. It can be applied in the cosmetic industry.

2. Materials and Methods

Materials

The samples of green mangosteen peel *(Garcinia mangostana* L.) from Bannasan district, Surat Thani province, Thailand, are presented in Fig. 1. The chemicals consisted of ethanol (Merck, Germany), tannin standard (Sigma-Aldrich,Germany), xanthone standard (Sigma-Aldrich, Germany), triamcinolone standard (Fluka), macrophage cells (Raw 264.7), *Cutibacterium acnes* (Faculty of medicine, Chiang Mai University, Thailand), clindamycin standard (RPC International Co., Ltd., Thailand), cholesterol (Chemipan, Thailand), and tween 60 (Chemipan, Thailand). Additionally, the other chemicals used in this research experiment were of analytical grade. The equipment consisted of high-performance liquid chromatography (HPLC) (Bindea, Germany), a microplate reader (Versa Max, USA), particle size, and a zeta potential analyzer (Malvern (Zetasizer ZS), United Kingdom), an ultrasonic bath (GT Sonic D-series), and scanning electron microscopy (SEM) (JEOL, JSM-6610LV). The nanoparticle size distribution was

determined on a particle analyzer (Beckman counter, Delsa Nano C). The skin hydration test and transepidemal water loss (TEWL) (Cortex, Dermalab's Series, SkinLab 2.1.1.1). The stability of the niosome was tested on centrifuge equipment (Hettich Mikro 22r).

Fig. 1 The morphology of green mangosteen

Preparation of extracts

Preparation of green mangosteen peel extract (*Garcinia mangostana* L.) by the maceration method First, cut and wash in part of the peel, then dry with a hot air oven (Memmert, Germany) at 60 ± 2 °C until dry, then grind with a grinder to become powder, which is stored in a zip bag at room temperature. (25 ± 2 °C) [10] Second, in the extraction [11, 12], by mixing 50 g of dry powder with an ethanol solution (SNP General Trading Co., Ltd., Thailand) in a volume of 500 ml for 7 days, filter and evaporate the solvent with a rotary vacuum evaporator (Buchi Model R-205/V, Switzerland) at 50 ± 2 °C Finally, store the extracts at 15 °C until analysis.

Characterization of mangoteen peel extract

The green mangosteen peel extract analysis consists of 2 botanical substances, xanthone and tannin, diluted to a concentration of 100 µg ml^{-1} in ethanol solution. After that, it was analyzed with a high-performance liquid chromatography (HPLC) using C18 column reverse phase (4.6 x 250 mm, 5 µm), flow rate equal to 1 ml min^{-1}, injection volume equal to 20 µl. Wavelength 320 nm. The mobile phase are acetonitride (A) and phosphoric acid (B), with the ratio of the two moving phase adjusted at different times.

Anti-inflammatory activity test

The dissolved extract and triamsinolone acetonide, an anti-inflammatory drug, were dissolved in 10% DMSO (v v^{-1}) in colorless cell culture media and sterilized by filtering through a porous membrane measuring 0.2 microns. Dilute the test sample solution to concentrations of 0.0001, 0.001, 0.01, 0.1, 1, and 10 mg m L^{-1} and test for inhibition of nitric oxide generation from LPS-induced macrophage cells [13]. Nitric oxide was quantified with a Griess reagent solution, and the percentage of nitric oxide generation inhibition was calculated compared to the control group.

Anti-Bacteria activity test

The antibacterial activity test was performed using extract dissolved with ethanol to an initial concentration of 1,000 mg mL^{-1} and standard clindamycin at an initial concentration of 10 µg mL^{-1}, sterilized by filtering through a membrane with a pore size of 0.2 µm, then pipette the liquid culture medium into 96 well microplates of 100 µL per well. 100 µL (2-fold serial dilution), then add *C. acnes* bacterial suspension, which has adjusted turbidity to close to 0.5 McFarland standard, to all wells. 100 µL per well, which will obtain the concentration of extract and standard clindamycin used in the test incubated in an incubator at 37 ± 1 °C for 48 hours in anaerobic conditions. Next, read the minimum inhibition concentration (MIC) by observing the last clear well with no sediment at the bottom of the pit and find the (MBC) value by sucking the food in a clear well with a volume of 5 µL and dripping it onto the brain heart infusion (BHI) agar culture medium, leaving it to dry and incubating in the incubator at 37 ± 1 °C for 48 hours in anaerobic conditions. Finally,

read the minimum bactericidal concentration (MBC).

Preparation of niosome base

The niosome base is prepared by dissolving surfactants (Tween 60) and cholesterol in 10 ml of chloroform in a round bottom flask with a ratio of surfactant to cholesterol (1:1). After that, evaporate the solvent using a rotary evaporator at 60°C, add 10 ml of water, shake, and heat to 60°C for 60 minutes. Store the niosome base at room temperature for 12 hours. [14, 15]

Preparing of niosome containg mangoteen peel extract

The preparation involves filling the extract to an initial concentration of 0.25, 0.5, or 1.0 mg mL^{-1}, measuring the solution in 10 mL of chloroform, adding surfactants and cholesterol, stirring well, baking under the pressure of a vacuum at 40°C for 4 hours, adding 10 mL of water, shaking, and heating to 60°C for 60 minutes. Store the noisome mangoteen peel extract at room temperature for 12 hours.

Evaluation of niosomes containing mangosteen peel extract

The observation of appearance, observe the external characteristics of the niosomes, such as the color of both the base niosome and the niosome containing mangosteen peel extract, pH. The particle shapes as niosomes drop on a carbon-coated copper grid; set aside; niosomes adhere to the skin for 1 – 2 minutes; blot the excess with filter paper; and let the sample dry in the desiccant before viewing it with a transmission electron microscope. For the measurement of particle size and zeta potential, prepare a sample of 0.1 ml and dilute it with some water (1.9). After that, fill in disposable folded capillary cells of the zeta sizer (Malvern Zetasizer ZS). Every measurement is done at 25 ± 0.5 °C.

Niosome efficacy Test

The skin hydration test measured the moisture of the skin by testing at the arm using a multi-probe skin analyzer. Hydration probes were used to test the efficacy of gel-based and gel-based products containing extracts with concentrations of 0.5, 1, 1.5, 2 and 2.5 %w w^{-1}, respectively. A comparison was made before and 4 weeks after using.

The transepidemal water loss (TEWL), in the test for loss of water on the skin by testing at the arm by using a multi-probe skin analyzer as efficacy compared measurements before and 4 weeks after using the product.

Statistical data analysis

The results of the experiment were repeated three times and the data was analyzed using the SPSS program.

3. Results and Discussion

The result of extraction

The extraction of mangosteen peel (*Garcinia mangostana* L.) with ethanol solvent was done by the maceration method. The results showed that the characteristics of the extract are tough and viscous, as the color of the crude extract is dark brown-green. The percentage yield of crude extract was 14.35 ± 0.90 % w w^{-1}. According to previous research, Mangosteen extract with an ethanol solvent can be extracted in high quantities.

The Results of phytochemical analysis

Analysis of phytochemicals consisting of tannin and xanthone by high-performance liquid chromatography (HPLC) showed that the standard chromatography tannin at a concentration of 2 mg mL^{-1} had a retention time of 8.155 minutes. The calibration curve of tannin standards at different concentrations ($y = 312789x + 10944$, $R^2 = 0.9995$). The analysis results showed that mangosteen peel extract in a concentration of 20 mg mL^{-1} had a peak of tannin in the chromatogram of the extract at 8.146 ± 0.004 min. and tannin was found at 0.7483 ± 0.0825

mg per 100 mg extract, respectively. (Table 1) Previous research has shown that mangosteen contains high amounts of tannin [16]. The chromatography of the xanthone standard at a concentration of 0.05 mg mL^{-1} has a retention time of 4.160 minutes, as does the calibration curve of the xanthone standards at various concentrations ($y = 308x + 84631$, $R^2 = 0.9956$). The results of the analysis showed that mangosteen peel extract at a concentration of 2 mg mL^{-1} showed the peak of xanthone in the chromatogram of the sample at 4.074 ± 0.012 minutes. Xanthone was found at 0.02964 ± 0.0088 mg per 100 mg extract, respectively. (table 1)

Table 1 The retention time and volume of mangosteen peel extract

Phytochemicals	Retention time (min)	Volume (mg per 100 mg extract) (Mean ± SD)
Tannin	8.146 ± 0.004	0.7483 ± 0.0821
Xanthone	4.073 ± 0.012	0.0296 ± 0.0088

The result of anti-inflammatory activity

The anti-inflammatory activity test in macrophage cells (RAW 264.7) as a result of inhibition of nitric oxide from LPS-induced macrophage cells up to 29.10 ± 4.78% at a concentration of 1 mg mL^{-1} at the same time anti-inflammatory drug (triamsinolone acetonide) can inhibit nitric oxide up to a maximum of 33.12 ± 3.62% at a concentration of 1 mg mL. Therefore, the test of mangosteen peel extract at a concentration of 1 mg mL^{-1} showed anti-inflammatory activity in macrophage cells (RAW 264.7) as 0.88 times that of the anti-inflammatory drug (triamsinolone acetonide), as shown in Table 2. In compliance with previous research [17], mangosteen (*Garcinia mangostana* L.) has anti-inflammatory potency, especially the component of xanthone, in various inflammatory conditions and diseases such as skin disease, psychiatric disease, arthritis, and soft tissue inflammation.

Table 2 The percentage inhibition of nitric oxide

Sample / Concentration (mg ml^{-1})	Percentage inhibition of nitric oxide					
	0.0001	**0.001**	**0.01**	**0.1**	**1**	**10**
Mangosteen peel extract	NA	18.58 ± 3.10	26.32 ± 1.60	28.79 ± 2.58	29.10 ± 4.78	38.39 ± 3.26*
Drug (Triamsinolone Acetonide)	26.11 ± 3.36	28.45 ± 4.99	29.91 ± 3.30	30.78 ± 3.22	33.12 ± 3.62	NA

Note : The values shown are the result of repeated experiments 4 time (Mean ± S.D.),

* The color of the sample interferes with the measured absorption spectrophotometric value, NA = Not tested

The result of inhibition Cutibacterium acnes

The results of inhibition of *Cutibacterium acnes* consist of the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) by the broth microdilution method (Fig. 2). The effect of MIC and MBC can inhibit C. acnes bacteria less than 0.24 mg mL^{-1} as shown in 3.7 – 3.8 At the same time, the standard antibacterial drug (Clindamycin) has MIC and MBC equal to 0.08 μg mL^{-1} and 0.31 μg mL^{-1}, respectively, as shown in Fig. 3.

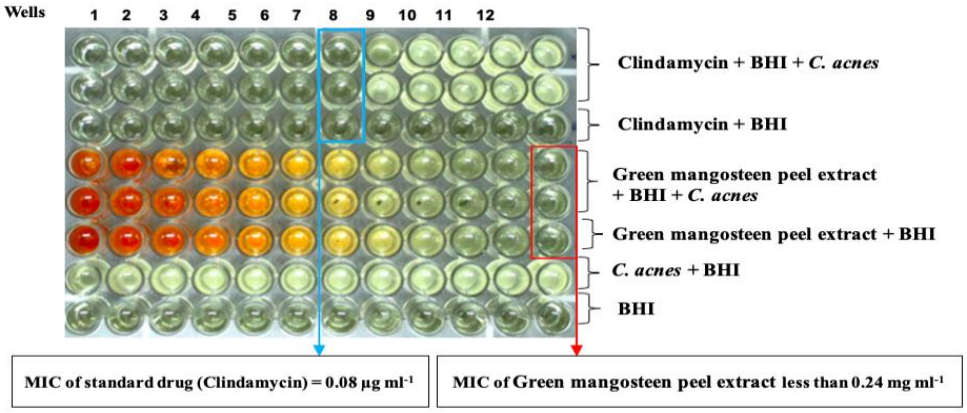


Fig. 2 The MIC of inhibition C. acnes by broth microdilution method between mangosteen peel extract and drug (clindamycin)

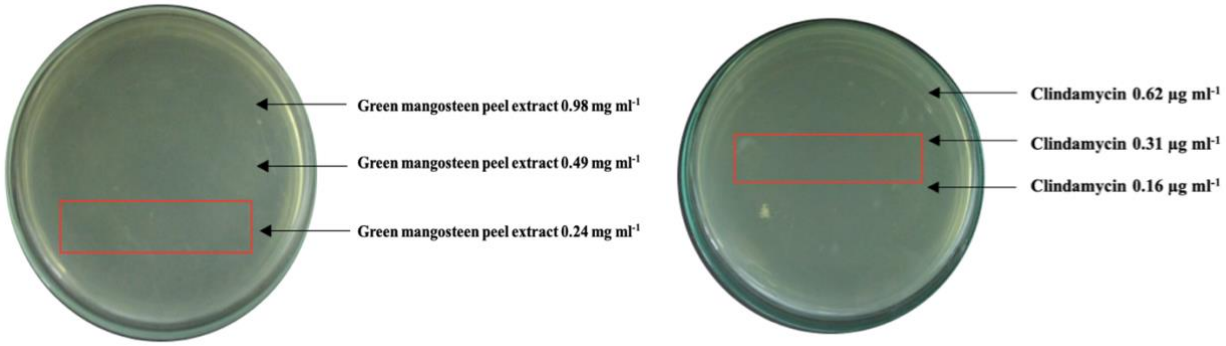


Fig 3 The MBC of inhibition C. acnes between green mangosteen peel extract and drug (Clindamycin) by drop plate method

Effects of niosomes and stability test

The result of niosomes consists of three formulas: white solution and opaque. The stability of niosomes, as all formulas don't allow separation of layers, is shown in Table 3.

Table 3 The stability of niosomes encapsulated mangosteen peel extract

Sample	Centrifugation	H–C*	Inference
cholesterol + tween 60	+	+	Passed
cholesterol + tween 60 + 1% w w^{-1} extract	+	+	Passed
cholesterol + tween 60 + 2% w w^{-1} extract	+	+	Passed

Note: H–C* = Heating–Cooling cycle, + = No separate layers, - = Separate layers

The results of the niosome encapsulate mangosteen peel extract

The results of gelling agents of various types, In the test, 3 types of gelling agents were used, including poly gel, aristroflex AVC, and any gel, as shown in Fig. 4(A), at the same concentration of 0.5%w w^{-1}. Polygel has been found to provide the best

properties. It has a clear gel texture, medium viscosity, good texture, fineness, is easy to spread, and is well absorbed into the skin. The aristroflex AVC has a clear gel texture that is more liquid than poly gel with slow drying, and any gel has an opaque gel texture and excessive liquid. Therefore, the research team selected poly gel as a gelling agent to develop gel products that contain niosomes and encapsulate mangosteen peel extract.

Evaluation of niosomes encapsulating mangosteen peel extract, The physical properties of niosome gel 3 products by F1 (cholesterol + tween 60), F2 (cholesterol + tween 60 + 1% w w^{-1} of extract), and F3 (cholesterol + tween 60 + 2% w w^{-1} of extract) (Fig.4(B)) When comparing the color of the product, it was found that at a concentration of 2 % w w^{-1} it had the most opaque white color, as shown in Table 4.6. After that, bring the three products reduce the molecular particle size with an ultrasonic bath for 30 minutes. The stability test of every product, stored at room temperature for 4 weeks and tested in accelerated conditions in all tests, doesn't change.

(A) (B)

Fig. 4 The niosome encapsulate mangosteen peel extract (A) = The type of gelling agent , (B) = The physical properties of niosome gel 3 products consist of F1: cholesterol + tween 60, F2: cholesterol + tween 60 + 1% of w w^{-1} of extract, F3: cholesterol + tween 60 + 2% w w^{-1} of extract

The result of measurement particle size by transmission electron microscopy

The determinations of particle size and particle size distribution of the formulations are important for transmission electron microscopy (TEM) in the examination of the morphology and structure of the niosome. The shape of the niosome is spherical in every formula at 30 min., and it was found that before reduction, the particle size was equal to 1,265 nm. (Fig. 5), and after reduction by ultrasonic bath at 30 min., it was in the range of 123 – 219 nm., which was a suitable size for penetration into the skin.

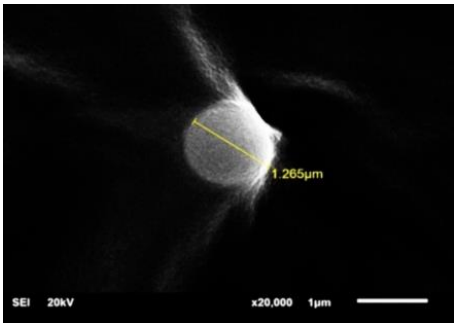


Fig. 5 The particle size of niosome encapsulate extract with TEM before reduced by ultrasonic bath

The measurement of particle size and zeta potential

The result of particle size and zeta potential after being reduced by an ultrasonic bath to a niosome gel base consisting of cholesterol and Tween 60 with a ratio of 1:1 has a particle size equal to 104.62 ± 0.03 nm

and a zeta potential equal to –26.15 ± 3.61. The niosome gel encapsulate mangosteen extract 2 formula as deference of concentrate by niosome gel encapsulate 1% w w^{-1} of extract has a particle size of 203.33 ± 0.56 nm and a zeta potential of –37.87 ± 2.56 and niosome gel encapsulate 1% w w^{-1} of extract has a particle size of 292.69 ± 5.32 nm and a zeta potential of –28.61 ± 2.38. The average particle size of niosomes is generally between 20 – 200 nm due to their small droplet size, which affects their stability and efficacy in delivery through the skin. The polydispersity index (PDI) of the niosomes at 25 °C is generally droplet size, with a narrow distribution equal to not more than 0.25. [18, 19], as the PDI values of this experiment ranged from 0.1 to 0.2, as shown in Table 4.

Table 4 The physical properties of niosome gels

Systems Gel	Particle size (nm)	Polydispersity index (PDI)	Viscosity (cP)	Zeta potential (mV)
Cholesterol + Tween 60	104.62 ± 0.03	0.261 ± 005	0.8893 ± 0.01	–26.15 ± 3.61
Cholesterol + Tween 60 + 1% w w^{-1} of extract	203.33 ± 0.56	0.116 ± 0.04	0.8701 ± 0.01	–27.87 ± 2.56
Cholesterol + Tween 60 + 2% w w^{-1} of extract	292.69 ± 5.32	0.156 ± 0.07	0.8626 ± 0.02	–28.61 ± 2.38

The result of efficacy using niosome gel

The skin hydration test, the efficacy of niosome gel base (Cholesterol + Tween 60), and niosome gels containing extract concentrations of 1% w w^{-1} of extract and 2% w w^{-1} of extract, respectively, were compared before and after using the product for 4 weeks. The result of skin hydration value before using product range 302 – 304 uS and after using product range 304 – 346 uS as niosome gels containing extract concentrations of 2% w w^{-1} of extract was the highest moisture value on the skin, as shown in Table 5.

Table 5 The results of the skin hydration test (mean ± SD) (n = 3).

Parameter of test	Hydration (uS)		
	Niosome gel base	Niosome gel + 1%w w^{-1} of extract	Niosome gel 2% w w^{-1} of extract
Before using product	302 ± 15.13	305 ± 14.79	304 ± 26.80
After using product	382 ± 25.90	351 ± 15.79	394 ± 32.17
After using product for 2 weeks	312 ± 14.89	336 ± 28.94	358 ± 13.58
After using product for 4 weeks	304 ± 13.68	324 ± 26.89	346 ± 39.27

The trans epidermal water loss (TEWL) test

The result of trans epidermal water loss (TEWL) on the skin before using products was a TEWL value equal to 2.32 – 2.58 g/m^2/h and after using products for 4 weeks, a TEWL value equal to 1.65 ± 1.35 g/m^2/h of niosome gel 2% w w^{-1}. It has the best value and the least water loss in the skin, as shown in Table 6.

Table 6 The trans epidermal water loss (TEWL) test (mean ± SD) (n = 3)

Parameter of test	The trans epidermal water loss (TEWL) (g/m^2/h)		
	Niosome gel Base	Niosome gel + 1%w w^{-1} of extract	Niosome gel 2% w w^{-1} extract
Before using product	2.36 ± 2.79	2.58 ± 3.35	2.32 ± 1.55
After using product	2.14 ± 0.46	2.13 ± 1.35	2.02 ± 1.38
After using product for 2 weeks	2.02 ± 1.27	1.91 ± 0.26	1.89 ± 1.24
After using product for 4 weeks	1.92 ± 1.25	1.82 ± 1.35	1.65 ± 1.35

4. Conclusion

The green mangosteen peel extract (*Garcinia mangostana* L.) contains tannin equal to 0.7483 ± 0.0825 mg per 100 mg extract and xanthone equal to 0.02964 ± 0.0088 mg per 100 mg extract. Anti-inflammatory activity was tested in macrophage culture cells (RAW 264.7) by inhibiting nitric oxide production from LPS-induced macrophage cells up to 29.10 ± 4.78% at a concentration of 1 mg m L^{-1} while the anti-inflammatory drug triamsinolone acetonide can inhibit nitric oxide up to a maximum of 33.12 ± 3.62% at a concentration of 1 mg m L^{-1} Therefore, the test of mangosteen peel extract concentration of 1 mg mL^{-1} had anti-inflammatory activity in macrophage culture cells (RAW 264.7) that was 0.88 times that of anti-inflammatory drugs (Triamsinolone Acetonide). The mangosteen peel extract has the lowest inhibitory (MIC) and kill (MBC) concentrations of *C. acnes bacteria*, less than 0.24 mg mL^{-1}. Similar to standard antibacterial drugs, Clindamycin has minimum inhibitory (MIC) and kill-bacteria (MBC) concentrations of 0.08 μg mL^{-1} and 0.31 μg mL^{-1}, respectively. The particle size of niosomes encapsulates extracts before reducing particle size to 1,265 nm. and after reducing particle size to 123 – 219 nm. The skin hydration value before using the product was 302 – 304 uS, and after using the product for 4 weeks as niosome gel encapsulate extract, 2% w^{-1} of extract, the maximum moisture on the skin was 346 ± 39.27 uS. The result of the trans epidermal water loss (TEWL) value before using the product was in the range of 2.32 – 2.58 g/m^2/h and after using the product for 4 weeks, niosome gel encapsulated 2%w w^{-1} of extract, indicating that the skin has minimal water loss and is most moisturizing.

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6. References

[1] S.M. Mawazi, T.J. Ann, R.T. Widodo, application of niosomes in cosmetics: A systematic review, cosmetics. 9 (2022) 1 – 16. 10.3390/cosmetics9060127.

[2] P. Badri, P.Suchita, B. Sumati, M. Ayushi, P.Yuanwei, K.M. Prashant, K.S. Sunil, F. Ljiljana, Non-ionic small amphiphile based nanostructures for biomedical applications, R. Soc. Chem. 10 (2020) 42098 – 42115. 10.1039/d0ra08092f.

[3] S. Chen, S. Hanning, J. Falconer, M. Locke, J. Wen. Recent advances in non-ionic surfactant vesicles (niosomes): Fabrication, characterization, pharmaceutical and cosmetic applications, Eur J Pharm Biopharm. 144 (2019) 18 – 39. 10.1016/j.ejpb.2019.08.015.

[4] M. Malhotra, N.K. Jain, Niosomes as drug carriers, Indian drugs. 31 (1994) 81 – 86.

[5] S.G. Bhokare, C.C. Dongaonkar, S.V. Lahane, P.B. Salunke, V.S. Sawale, M.S. Thombare, Herbal novel drug deliver, World J. Pharm. Sci. 5 (2016) 593 – 611.
[6] T. Oranuch, Niosome delivery systems in pharmaceutical applications, Isan J. Pharm. Sci. 8 (2012) 12 – 26. 10.1155/2018/6847971.
[7] M. Khanittha, W. Tanyaporn, S. La-ong, K. Wilasinee, Tannin extraction from mangosteen peel for protein precipitation in wine, KKU Res. J. 15 (2010) 377 – 385.
[8] R. Li, B.S. Inbaraj, B.H. Chen, Quantification of xanthone and anthocyanin in mangosteen peel by UPLC-MS/MS and preparation of nanoemulsions for studying their inhibition effects on liver cancer cells, Int. J. Mol. Sci. 24 (2023)1 – 29. 10.3390/ijms24043934.
[9] Y. Sukit, S. Anusak, W. Chatchai, Validation of LC for the determination of α-mangostin in mangosteen peel extract: a tool for quality assessment of *Garcinia mangostana* L., J. Chromatogr. Sci. 47 (2009) 185 – 189. 10.1093/chromsci/47.3.185.
[10] Z. Xin, D. Qingyin, H. Xi, Q. Zhiyong, Preparation and characterizations of antibacterial–antioxidant film from soy protein isolate incorporated with mangosteen peel extract, E-Polym. 21 (2021) 575 – 589. 10.1093/chromsci/47.3.185.
[11] W. Wahyu, D. Lusiana, S. Jo, F. Nurul, M. Maesaroh, P.E. Pande, Anti-inflammatory effect of mangosteen (*Garcinia mangostana* L.) peel extract and its compounds in LPS-induced RAW 264.7 Cells, Nat. Prod. Res. 22 (2016) 147 – 153. 10.20307/nps.2016.22.3.147. 10.20307/nps.2016.22.3.147.
[12] S. Weerayuth, M. Supranee, In vitro antioxidant properties of mangosteen peel extract, J Food Sci Technol. 51 (2014) 3546 – 3558. 10.1007/s13197-012-0887-5.
[13] I. Cavallo, F. Sivori, M. Truglio, Skin dysbiosis and *Cutibacterium acnes* biofilm in inflammatory acne lesions of adolescents. Sci. Rep. 12 (2022) 1 – 16. 10.1038/s41598-022-25436-3.
[14] Z. Zarina, S. Y. Tan, Determination of flavonoids in *Citrus grandis* (pomelo) peels and their inhibition activity on lipid peroxidation in fish tissue, Int Food Res J. 20 (2013) 313 – 317.
[15] L. Suklampoo, C. Thawai, R. Weethong, W. Champathong, W. Wongwongsee, Antimicrobial activities of crude extracts from pomelo peel of Khao-nahm-peung and Khao-paen varieties, KMITL Sci. Technol. J. 12 (2012) 55 – 57.
[16] J.J. Toh, H.E. Khoo, A. Azrina, Comparison of antioxidant properties of pomelo [*Citrus Grandis* (L.) Osbeck] varieties. Int Food Res J. 20 (2013) 1661 – 1668.
[17] T.R.Maria, G.C. Erika, B. Mark, M. Elvira, Anti-inflammatory and anti-oxidant effect of Calea urticifolia lyophilized aqueous extract on lipopolysaccharide-stimulated RAW 264.7 macrophages, J. Ethnopharmacol. 188 (2016) 266 – 274. 10.1016/j.jep.2016.04.057.
[18] S. Shafiq-un-Nabi, F. Shakeel, S. Talegaonkar, J. Ali, S. Baboota, A. Ahuja, R.K. Khar, A. Ali, Formulation development and optimization using nanoemulsion technique: a technical note, AAPS PharmSciTech. 8 (2007) 1 – 6. 10.1208/pt0802028.
[19] P. Palozza, R. Muzzalupo, S. Trombino, A. Valdannini, N. Picci, Solubilization and stabilization of β-carotene in niosomes: delivery to cultured cells, Chem. Phys. Lipids. 139 (2006) 32 – 42. 10.1016/j.chemphyslip.2005.09.004.
[20] T.H. Nguyen, D.H. Hoang, Q.H. Nguyen, T.T. Pham, T.M.T. Nguyen,

Study on extraction of tannins from the *Garcinia mangostana* Linn peel in viet nam. Vietnam J. Sci. Technol. 56 (2018) 113 – 120.

[21] Y. Vasin, S. Pao, K.K. Wiyada, V. Karthikeyan, W. Jittimon, P. Thanya, C. Narin, A review of the influence of various extraction techniques and the biological effects of the xanthones from mangosteen (*Garcinia mangostana* L.) pericarps, Molecules 27 (2022) 1 – 19. 10.3390/molecules27248775.

[22] A.S. Andreas, B. Jethro, P. Awal, Anti-inflammatory potency of mangosteen (*Garcinia mangostana* L.): a systematic review, J. Med. Sci. 11 (2023) 58 – 66. 10.3889/oamjms.2023.8746.

[23] C.R. Garcia, M.H. Malik, S. Biswas, V.H. Tam, K.P. Rumbaugh, W. Li, X. Liu, Nanoemulsion delivery systems for enhanced efficacy of antimicrobials and essential oils, Biomater. Sci. 10 (2022) 633 – 653.

[24] W. Rangsimawong, T. Ngawhirunpat, Nanoemulsions in transdermal drug delivery system, Thai. Bull. Pharm. Sci. 9 (2014) 46 – 1961.

[25] A.J. Nor, A.B. Syahrul, A.K. Khalilah, M.S. Wan, KW. Ng, I.A. Mohd, Development and optimization of nanoemulsion from ethanolic extract of centella asiatica (NanoSECA) using d-optimal mixture design to improve blood-brain barrier permeability, Evid. based Complement Alternat. Med. 2022 (2022) 1 – 18. 10.1155/2022/3483511.