

The Effect of a Moisturizing Cream Containing Saccharide Isomerate and Ceramide on Reducing Transepidermal Water Loss in Eczema

Helen Hartini¹, Vlorensia¹, Hairus Abdullah², Ahmad Raif Martinus¹, Refi Ikhtiari^{1,2*}

¹Laboratory of Biomolecular Chemistry, Graduate School of Biomedical Science
Universitas Prima Indonesia

²Laboratory of Materials Chemistry, Faculty of Industrial Engineering,
Universitas Prima Indonesia

Emails: (helen, vlorensia, hairusabdullah, ahmadraif, refiikhtiari)@unprimdn.ac.id

Keywords: Moisturizer, saccharide isomerates, ceramide, TEWL, eczema

Abstract: Dermatitis is a disorder of dry skin or a state of skin sensitization due to exposure to external substances. Moisturizing treatments can reduce TEWL (transepidermal water loss). This study is aimed to determine the effectiveness of using moisturizing creams that contain saccharide isomerates and ceramide to reduce TEWL in eczema sufferers. The moisturizing creams have been applied in the lower limbs of eczema sufferers as subjects. The research subjects were 12 people for each group, namely the Saccharide Isomerates (SI), non-SI, Ceramide (S) and non-S. Tewameter/Corneometer 350 treatment used to measure TEWL values before treatment (Week 0) and after treatment (Week II). Data analysis using the unpaired t-test. The results showed that the use of moisturizing creams containing saccharide isomerates and moisturizing creams containing ceramide effectively reduced the TEWL value in eczema sufferers ($p = 0.032$).

1 INTRODUCTION

The skin is a living organ that lines the entire surface of the human body, functions to protect and receive stimuli from the environment (Tyas, 2014). Aesthetic functions are also an important function of the skin because the skin can describe one's health, beauty, social status, and economic status (Mescher, 2013).

Various factors both from outside and inside the body can affect the structure and function of the skin, for example, dry air, low humidity, sunlight, age, various skin diseases and diseases in the body. Because these factors can occur excessive evaporation in the skin epidermis so that the water content in the stratum corneum <10% and causes dry skin (Wasiatmadja, 2011).

Dry skin is a disorder on the surface of the skin due to reduced fluid or oil content in the skin so that the moisture on the surface of the skin layer decreases (Nuzantry, 2015). Dry skin is a condition characterized by damage to the stratum corneum due to lipid modification and disturbed hydration. Dry skin is indicated by the condition of skin becomes rough, scaly, wrinkled and less elastic than normal and dry skin on touch (Kusumaningrum, 2017). Dry

skin occurs if the balance of oil content is disturbed. The content of fat on dry skin is very small, so it is easy to occur premature aging marked by wrinkles and the skin looks tired and looks rough (Kusantati, 2008).

Dermatitis or eczema is a disorder of dry skin or a state of skin sensitization due to exposure to external substances. Based on its etiology, dermatitis can be divided into exogenous dermatitis if it is caused by factors outside the patient's body, and endogenous dermatitis (constitutional) if caused by factors from within the body itself (Harrianto, 2013). Dermatitis is an inflammatory condition of the skin that varies in terms of its severity, is non-infectious, and cannot be transmitted from one person to another (Krishnan et al., 2013).

In response to the influence of exogenous factors or the influence of endogenous factors, Eczema or dermatitis causing clinical abnormalities in the form of polymorphic efflorescence (erythema, edema, papules, vesicles, squama) and itching complaints (Djuanda, 2011). Dermatitis is an inflammation of the epidermis and dermis that is characterized by objective symptoms in the form of lesions that are polymorphic and subjective symptoms of itching, can

be caused by endogenous or exogenous factors (Maryunani, 2010).

According to Febriana (2012), eczema is characterized by reddish, scaly, cracked skin, feeling itchy especially at night, small bubbles appear filled with water or pus, swollen, blistered, red, very itchy and feel hot. The cause is an allergy to specific chemical stimuli, or sensitivity to specific foods like shrimp, sea fish, alcohol, MSG. Eczema prevention can be done by avoiding things or ingredients that can cause allergies. Dermatitis is characterized by polymorphic skin inflammation that has broad characteristics, including itching, erythema (redness), edema (swelling), papules (solid protrusions with diameters less than 55 mm), vesicles (protrusions containing a liquid diameter of more than 55mm), crust and squama.

The main symptom felt by people with eczema is excessive itching of the skin. Then accompanied by reddened skin, scaly and cracked, small bubbles arise containing water or pus. Parts of the body that are often affected by eczema are usually the hands, feet, groin, and ears. Eczema is divided into two, namely dry and wet eczema. In wet eczema, excessive heat and cold will also feel on the skin. Eczema is caused due to allergies to certain chemical stimuli such as those found in detergents, soaps, drugs and cosmetics, sensitivity to certain types of food such as shrimp, sea fish, eggs, chicken meat, alcohol, MSG, etc. (Djuanda, 2011).

Eczema can also be caused by allergies to plant pollens, dust, climate disorders, even emotional disturbances. Eczema is more common in people who are prone to allergies. This disease often occurs repeatedly or relapse. Therefore, it must be considered to avoid things or substances that can cause allergies (allergens.) However, with proper treatment, this disease can be controlled properly so that it reduces the recurrence rate. In some cases, eczema will disappear with age as patients (Djuanda, 2011).

Moisturizers are commonly used to relieve dry skin include those that cause eczema or dermatitis by increasing barrier repair, creating temporary artificial barriers, and restoring skin softness. Moisturizers are complex formulations designed to improve the hydration mechanism of the skin and maintain the structure and function of the skin from various influences such as dry air, sunlight, old age, temperature, various skin diseases and diseases that can accelerate evaporation of water (Nuzantry, 2015).

Moisturizing treatments can reduce TEWL (transepidermal water loss) with a barrier repair mechanism, prevent water evaporation from the epidermis, play a role in replacing lipid compounds and restore skin softness (Kurnia, 2017).

Cream formulations are the most widely used dosage forms in drug and cosmetic delivery systems through the skin. Preparations used in the skin include physical effects, namely skin protectors, lubricants, softeners, drying agents, etc., or for special effects of existing medicinal ingredients. In general, the administration of drugs or cosmetics through the skin is intended to provide local effects. Absorption of medicinal substances from outside the skin to the bottom of the skin (percutaneous absorption) depends on the physical-chemical properties of the drug ingredients, drug carrier properties, and skin conditions (Ansel, 2008; Yanhendri and Satya, 2012).

Drug-penetration after topical application to the intact skin is mostly through the epidermis layer, and the other small part through the walls of the hair follicles, sweat glands or fat glands or between the horn membrane cells. Percutaneous absorption of a drug is generally caused by direct drug penetration through the stratum corneum which has a thickness of 10–15 μm . The stratum corneum consists of approximately 40% protein (generally keratin) and 40% water and fat especially triglycerides, free fatty acids, cholesterol, and phosphate fat. The fat component of the stratum corneum causes low drug penetration through the stratum corneum. A drug that can penetrate the stratum corneum can then continue through deeper epidermal tissue and enter the dermis when the drug reaches the blood vessels so the drug can be absorbed into the systemic circulation. The stratum corneum as a keratin tissue acts as a semi-permeable membrane, and drug molecules penetrate by passive diffusion. The amount of drug that can pass through various layers of the skin depends on the concentration of the drug, its solubility in water, and the coefficient of the partition of the drug in oil or water. Diffusion of drug molecules in the layers of the skin can occur through transcellular penetration (crossing cells), intercellular penetration (intercellular), and penetration through hair follicles, sweat glands, fat glands, and pilo sebaceous. Factors that influence percutaneous absorption include (Ansel, 2008).

There are various moisturizing products on the market with various active ingredients, namely those made from active Saccharide isomerates (SI). The Pentapharm pharmaceutical industry in Switzerland

in 2008 produced the active ingredient Saccharide isomerates (SI) which is a mucopolysaccharide carbohydrate complex (glycan) similar to that found in the human skin's stratum corneum. The active ingredient SI in the epidermis will form hyaluronic or hyaluronic acid. In accordance with this hyaluronic function, SI can function to maintain moisture by increasing the water content in the stratum corneum even in low air humidity (Pentapharm, 2009).

SI is a carbohydrate complex similar to that of the stratum corneum of human skin. Functioning to maintain humidity even in low humidity. SI can bind to the skin even in very low pH condition, so it is ideal when used together with moisturizers that contain Alpha hydroxy acid (AHA). SI composition by HA acts as an effective moisturizer to control skin moisture by binding to the lysine amino acid group present in the keratin stratum corneum. Because the bond is very strong, it will remain effective even in dry air and low humidity. SI has a strong bond with the stratum corneum which can only be released by the desquamation process, therefore it is very effective at moisturizing the skin, while also making the skin smoother and not itchy (Pentapharm, 2009).

A study of the effects of SI use on moisturizing formulations was conducted by Dewi (2010) who found that adding 5% saccharide isomerates in moisturizing formulations can improve skin hydration higher and maintain higher skin hydration after the administration was stopped compared to ordinary moisturizers.

SI can be an occlusive and humectant component. The moisturizer components can also contain other active ingredients that can improve skin softness by lubricating and filling the gaps between cells between dry cells, namely ingredients that are emollient (Simion & Story, 2005).

The synthetic moisturizers can also help deal with dry skin such as ceramide. Ceramid mimics natural substances in the outermost layers of the skin to help maintain moisture (Octavia, 2017). The original ceramide is naturally in the skin which is a component of epidermal lipids in the skin around the stratum corneum which has the effect of keeping the skin moist. Ceramide functions, among others, regulating water loss through epidermis (KAME) or transepidermal water loss (TEWL) (Trisnowati, 2015).

Ceramide is a water-retaining molecule in the extracellular space in the stratum corneum and a ceramide bond with a structural matrix protein that forms the skin's defense function. The lack of

ceramide in the skin causes the skin barrier function to be disturbed which results in increased fluid loss (TEWL) through the skin, so the skin becomes drier and sensitive to various physical and chemical influences (Jafar, 2015).

The chemical bond between ceramide and water will form a smooth emulsion so that it appears smooth and soft. The administration of ceramide-containing emollients has been carried out in cases of atopic dermatitis, which is caused by impaired skin barrier function. Research results show that the use of ceramide not only improves TEWL and erythema severity but also increases endogenous ceramide levels in the stratum corneum (Partogi, 2008). Ishikawa et.al's research (2013) shows that indicators of dry skin (dry, rough and scaly) are closely related to ceramide levels.

Ceramide formulation in moisturizing creams is generally a solid lipid nanoparticle (SLN) formulation. Nanoparticles in the form of very small particles with a diameter between 1-100 nm. Nanoparticles are a three dimensional particle, which has a nanometer scale. The nature of the nanometer-sized material has a difference with the properties of the larger size (bulk). Where nano-sized material has chemical, physical and biological properties that are superior to larger sized materials (Backdropissa, 2017).

SLN was developed by Muller in the 1990s. In his research, it was found that SLN can be applied for the administration of drugs and cosmetics in the form of liposomes, microemulsions and polymer nanoparticles. The advantage of SLN is that its lipid matrix is made of physiological lipids, thereby reducing the danger of acute and chronic toxicity. Because of these advantages, SLN has been introduced as a new carrier system for active compounds in the pharmaceutical and cosmetic fields (Background, 2017).

According to Amalia (2015), solid lipid nanoparticles offer unique properties such as relatively small particle size, large surface area, high drug absorption rate and potential as a carrier/preparation that can improve the performance of drugs and other nutraceutical ingredients.

Expansion of the use of nanomaterials in technology and consumer applications has increased the potential for accidental exposure to human skin. This has generated considerable interest in determining the conditions under which nanoparticles can penetrate the skin. Its main benefit is for therapeutic success but one that can also minimize the

potential for negative side effects. The wide use of nanoparticles as a sunscreen and topical cosmetics has resulted in the study of many nanoparticles formulations (Delouise, 2012). This research limits the effect of moisturizing creams containing isomerate and ceramide in the formulation of solid lipid nanoparticles on eczema.

2 RESEARCH METHODS

The research subjects consisted of 12 people for each group, the subjects who received saccharides isomerate (SI) moisturizing cream, non SI groups, the subject group treated with Ceramide (S) moisturizing cream and non Ceramide (non S). The research material was a moisturizing cream containing saccharides isomerate and ceramide in a solid lipid nanoparticle formulation. The research instrument used to measure the value of TEWL was Tewameter/ Corneometer 350. Measurement of TEWL values was carried out before treatment (Week 0) and after treatment (Week II).

The measurement data were analyzed for the mean TEWL values before and after treatment and a comparison between the SI treatment group and non SI with the S treatment group and non S. The test used when the normal data distribution was an unpaired t test while the Mann-Whitney test was used when the distribution was not normal. Data is processed statistically using the SPSS program.

The interpretation of TEWL values are 0- <25 gr / m² / hour for normal conditions and > 25 gr / m² / hour for disturbed conditions (high) (Black et al., 2005).

3 RESULTS AND DISCUSSION

The characteristics of the subjects in the SI treatment group and non-SI according to the age of the majority aged 30-35 years 11 people (45.8%). Characteristics of the respondents according to ethnic groups are mostly Batak 11 people (45.8%). The characteristics of respondents according to marital status mostly married 20 people (83.3%). The characteristics of respondents according to occupation of most housewife's were 11 people (45.8%). Characteristics of subjects in the S treatment group and non S (control group) according to age were mostly aged 30-35 years 14 people (58.3%). Characteristics of the

respondents according to ethnic groups are mostly Javanese 11 people (45.8%). The characteristics of respondents according to marital status mostly married 22 people (91.7%). Characteristics of respondents according to occupation of housewife are 12 people (50%). In more details, subject characteristics is presented in the Table 1 with statistical analysis of each group of treatment.

Table 1. Subjects characteristics based on ages, ethnics, marital status and occupations.

No	Subject Characteristics	SI Treatment Group and non SI (n = 24)		S Treatment Group and non S (n = 24)	
		f	%	f	%
1.	Age				
	a. 30-35 years	11	45,8	14	58,3
	b. 36-40 years	13	54,2	10	41,7
2.	Ethnic				
	Batak	11	45,8	10	41,7
	Java	8	33,3	11	45,8
	Chinese	5	20,8	3	12,5
3.	Marital Status				
	a. Single	4	16,7	2	8,3
	b. Married	20	83,3	22	91,7
4.	Occupation				
	Civil servants	1	4,2	-	-
	Private Employees	9	37,5	10	41,7
	Housewife	11	45,8	12	50,0
	Unemployment	3	12,5	2	8,3

Based on the homogeneity test using Levene's test, both the SI and non SI groups and the S and non S groups at the time before and after the treatment, obtained a significance value > 0.05, this means the data is assumed to be homogeneous.

The results of the normality test using the Shapiro-Wilk test, the TEWL value of the subjects in the SI and non SI groups before being treated with moisturizing cream each obtained a significance value of > 0.05, this means that the data is assumed to be normally distributed. The TEWL value of subjects in the SI treatment group and non SI after receiving treatment with each moisturizing cream obtained a significance value of > 0.05, containing the meaning that the data was assumed to be normally distributed.

The TEWL value of subjects in the S treatment group and non S before receiving treatment with each moisturizing cream, obtained a significance value of > 0.05, this means that the data is assumed to be normally distributed. The TEWL value of subjects in the S treatment group and non-S after receiving

treatment with each moisturizing cream, obtained a significance value of > 0.05, containing the meaning that the data was assumed to be normally distributed.

3.1 Effectiveness of the Use of Moisturizing Cream Containing Saccharide Isomerate Reducing TEWL Value in Eczema

The data of TEWL values showed that the use of saccharide isomerate moisturizing cream for 2 weeks can significantly reduce TEWL in patients with eczema. Compared to the control group (non SI) the decrease in TEWL values in the SI group was higher. The data of TEWL values has been evaluated statistically as shown in Table 2.

Table 2. TEWL Value of Skin in Lower Limbs of SI and Non SI Subjects Before and After Treatment.

Treat ment	Groups	TEWL Value (gr/m ² /hour)	p value
		Mean	
Before	SI	23,67 (21,65-26,25)	0,270
	Non SI	24,31 (21,53-26,25)	
After	SI	13,98 (11,55-15,25)	0,036
	Non SI	15,22 (12,55-17,50)	

Statistical data analysis of TEWL values showed a significant decrease after treatment in the SI group with saccharide isomerate moisturizing cream. Decrease in TEWL value from 23.67 gr/m²/hour range (21.65-26.25) before treatment to be 13.98 gr/m²/hour (11.55-15.25) with a significance value p = 0.036.

We have not found a previous study of the use of saccharide isomerate moisturizing cream in eczema sufferers to be compared with this study. However, there are studies in subjects that are normal (not eczema sufferers), namely Dewi (2010) who found that saccharide isomerates can improve skin hydration higher and maintain higher skin hydration after administration is stopped compared to ordinary moisturizers.

3.2 Effectiveness of the Use of Moisturizing Creams Containing Ceramide in Reducing TEWL Value in Eczema

The effectiveness of moisturizing cream has been evaluated statistically and showed that a significant decrease in TEWL value after treatment in group S with moisturizing cream containing ceramide solid lipid nanoparticle formulation. Decreasing of the TEWL value from 24.50 gr/m²/hour range (22.95-26.10) before treatment became 14.98 gr/m²/hour (13.55-16.95) with a significance value p = 0.035. These data show that the use of ceramide moisturizing cream in solid lipid nanoparticle formulation for 2 weeks can significantly reduce TEWL in patients with eczema. Compared with the control group (non-S) the decrease in TEWL value in the S group was higher. In details, effectiveness data shown in Table 3.

Table 3. TEWL Value of Skin in Lower Limbs of S and Non S Subjects Before and After Treatment.

Treat ment	Groups	TEWL Value (gr/m ² /hour)	p value
		Mean	
Before	S	24,50 (22,95-26,10)	0,207
	Non S	25,04 (23,68-26,52)	
After	S	14,98 (13,55-16,95)	0,035
	Non S	15,87 (14,50-17,37)	

The results of this study was in accordance with Ishikawa et al. (2013) which showed that indicators of dry skin (dry, rough and scaly) were closely related to ceramide levels. The Spada study (2018) which found moisturizing creams containing ceramide significantly reduced TEWL (p < 0.001) for 24 hours. The results of this study are also in accordance with the results of the Partogi (2008) study which found that the bond between ceramide and water will form a smooth emulsion, making it appear smooth and soft. Giving emollients containing ceramide has been carried out in cases of atopic dermatitis, which is caused by impaired skin barrier function. Research shows that administration of ceramide not only improves TEWL and erythema severity, but also

increases levels of endogenous ceramide in the stratum corneum.

We found a previous study supporting the results of this study but with different research subjects, Spada (2018) who found that 24 hours after application of Ceramide cream was significantly greater ($P < 0.05$) than measured for the three reference moisturizers tested. Ceramide cream significantly reduces TEWL ($P < 0.001$) for 24 hours, and is proven to not cause sensitization to the skin of adults and children and does not cause irritation to the skin, eyes and related eye area.

3.3 Effectiveness of the Use of Moisturizing Cream Containing a Combination of Saccharide Isomerate and Ceramide on Reducing TEWL Value in Eczema

To the best of our knowledge on literature, still no report on the differences in the use of moisturizing creams containing saccharides isomerate and ceramide in eczema sufferers to be compared with this study.

The effectiveness of combination of moisturizing cream showed that the results of the measurement of TEWL values in the SI and S groups before the treatment had no difference ($p = 0.092$). After treatment there were differences in TEWL values between the Saccharide Isomerate group and the Ceramide group ($p = 0.032$). In details, the statistical data analysis of TEWL values of combination cream is presented in the Table 4.

Table 4. TEWL Value of combination SI and S in eczema sufferers.

Treatment	Groups	TEWL Value (gr/m ² /hour)	p value
		Mean	
Before	SI	-0,84083	0,092
	S		
After	SI	-1,00167	0,032
	S		

Based on the statistical results of the independent t test, it was found the significant difference in the use

of moisturizing creams containing saccharide isomerate and ceramide in solid lipid nanoparticles formulations in reducing TEWL values in eczema sufferers.

The results of this study prove that the use of moisturizing creams containing saccharide isomerate can significantly reduce TEWL in eczema sufferers. Compared to the control group (non saccharide isomerate) the decrease in TEWL values in the SI group was higher. To the best of our knowledge, we have not found a previous study of the use of saccharide isomerite moisturizing cream in eczema sufferers to be compared with this study.

Voegeli et.al (2019) has reported that remarkable gradients of skin hydration, TEWL, skin surface pH and sebum exist within short distances across the face and the gradients are distinctive among different ethnic groups. In addition, these studies have demonstrated that darkly- pigmented individuals do not necessarily have a better skin barrier function than their less- pigmented counterparts and that Caucasians have a lower facial skin surface pH compared with more pigmented subjects. Overall, there are no correlations between capacitance, TEWL and skin surface pH including individual topology (Voegeli et. Al 2019).

The results of this study are in accordance with the results of Pentapharm (2009) study that the active ingredient of saccharide isomerate in the epidermis will form hyaluronic or hyaluronic acid. In accordance with this hyaluronic function, the isomerate saccharide can function to retain moisture by increasing the water content in the stratum corneum even in low air humidity (Pentapharm, 2009).

The results of this study are also supported by Kurnia's statement (2017) that moisturizing treatments can reduce TEWL (transepidermal water loss) with a barrier repair mechanism, prevent water evaporation from the epidermis, play a role in replacing lipid compounds and restore skin softness.

4 CONCLUSION

The use of moisturizing creams containing Saccharide Isomerate and Ceramide in solid lipid nanoparticle formulations effectively reduced the TEWL value in eczema sufferers.

ACKNOWLEDGEMENTS

This research supported by Ministry of Research, Technology and Higher Education by Funding Contract No. 7/E/KPT/2019 and No. T/63/L1.3.1/PT.01.03/2019.

REFERENCES

- Amalia, Anisa. Preparation and Characterization of Gliclazide Solid Lipid Nanoparticle (SLN) Preparations. *Indonesian Pharmaceutical Sciences Journal*, April 2015, p. 108-114. ISSN 1693-1831.
- Dewi, Dian Andriani Ratna. Addition of 5% Saccharide Isomerates in Moisturizing Formulations Increases Skin Hydration Higher than Ordinary Moisturizers. Thesis. Denpasar: Udayana University, Postgraduate Program, 2010.
- Draelos Z. 2018. The science behind skin care: Moisturizers. *Journal of Cosmetic Dermatology* Volume 17, Issue 2.
- Engelbrechtsen KA, Kezic S, Jakasa I, Hedengran A, Linneberg A, Skov L, Johansen JD and Thyssen JP. 2018. Effect of atopic skin stressors on natural moisturizing factors and cytokines in healthy adult epidermis. *British Journal of Dermatology* 179: 560-561.
- Harrianto, R. Textbook on Occupational Health. Jakarta: EGC, 2013
- Ishikawa, K et.al. Cell growth control by stable Rbg2/Gir2 complex formation under amino acid starvation. *Genes Cells*, 2013;18(10):859-72. <https://www.yeastgenome.org/reference/S000154539>.
- Jafar. Formulasi Solid Lipid Nanoparticle Ceramide. *Jurnal Pharmascience*, Vol 2, No. 2, Oktober 2015, 80-87. ISSN-Online. 2460-9560. <http://jps.ppjpu.unlam.ac.id/>.
- Krishnan S, Darmada IGK, & Rusyati LMM. Occupational contact dermatitis. *J Udayana*. 2013; 1: 1-7.
- Kurnia, Tesha. Effectiveness of 2% Alga Chocolate (*Sargassum Sp.*) Extract in Moisturizers on Dry Skin. *Diponegoro Medical Journal*. Volume 6, Number 2, April 2017. ISSN Online: 2540-8844. <http://ejournal-s1.undip.ac.id>.
- Latarissa, Irma Rahayu. Article Review: Application of Nanoparticle Technology in Cosmetic Preparations. *Farmaka*. Supplement Volume 14 Number 1, 2017.
- Loden M. 2012. Effect of moisturizers on epidermal barrier function. *Clinics in Dermatology* 30, 286-296.
- Nuzantry, Juny Kurnia. Effectiveness of Mixture of Aloe Vera Extract and Olive Oil in Moisturizing Formulations against Skin Dryness. *Journal*. Semarang: Diponegoro University, Faculty of Medicine, 2015.
- Octavia, Sherly Ika. Care For Dry Skin, <http://corporate.kimiafarmaapotek.co.id>, 2017.
- Partogi, Donna. Dry skin. Medan: University of Sumatera Utara, Skin and Sex Health Sciences, 2008.
- Spada, Fabrizio. 2018. Skin hydration is significantly increased by a cream formulated to mimic the skin's own natural moisturizing systems. *Clinical, Cosmetic and Investigational Dermatology* 2018;11 491-497.
- Tippavajhala VK. 2018. In Vivo Determination of Moisturizers Efficacy on Human Skin Hydration by Confocal Raman Spectroscopy. *AAPS PharmSciTech* (19) 3177-3186.
- Trisnowati, Niken. Relationship between Stratum Corneum Hydration, Water Loss Through Epidermis and Skin Surface Fat Levels with Severity of Atopic Dermatitis. *Mdvi Journal*. Vol. 42 No. 4 of 2015; 164 - 166.
- Voegeli R, Gierschendorf J, Summers B, Rawlings AV. 2019. Facial skin mapping: from single point bio-instrumental evaluation to continuous visualization of skin hydration, barrier function, skin surface pH, and sebum in different ethnic skin types. *International Journal of Cosmetic Science* 41 (5).