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Review Article

Characterization and application of moisturizer in skin treatment: A review

Ahmad Ainurofiq, Arfa Fairuziyah Firdausy Divinda Haya, Asifa Nurma Safitri, Ika Zuliana Solihatin, Safna Bina Nusriya, Tasya Saevita Nugroho

Pharmaceutical Technology and Drug Delivery, Department of Pharmacy, Sebelas Maret University, Ir. Sutami 36A, Surakarta, Indonesia.

Abstract

Repeated exogenous exposure can disrupt the skin barrier hence affecting its ability to maintain water levels and disrupt lipids in the stratum corneum to trigger transepidermal water loss (TEWL), causing skin to become scaly, dull, itchy, and more sensitive. The skin also contains a natural moisturizer called natural moisturizing factor (NMF). However, if NMF is insufficient to maintain skin moisture, additional protection is needed using a cosmetic moisturizer. A moisturizer is a product aimed to increase skin hydration and maintain normal skin pH. Moisturizer is classified as occlusive, humectant, and emollient moisturizers with different work mechanisms. Although reports on the side effects of moisturizer are rare, moisturizer can cause xerosis and positively modifies the skin barrier. Other harmful reactions for the skin include abnormal sensations, such as pain, burning and stinging over facial skin. Therefore, the ingredients in moisturizers need to be considered to prevent toxicity or adverse effects. This review aims to evaluate published studies on cosmetics, advantages, disadvantages and characterization of moisturizers. The characteristics discussed in this review include organoleptic/light test, pH determination, stability, spreadability, saponification value, density, viscosity, homogeneity, irritability, in vitro and in vivo skin hydration.

Key words
Cosmetics; Moisturizer; Application; Advantages and disadvantages; Characteristics.

Introduction

Skin is a vital organ that forms a barrier between body and external environment, forming layers with stratum corneum (SC) as its outermost layer. A more detailed illustration is depicted in **Figure 1**. The stratum corneum is a thin tissue with around 20 µm thickness that acts in protecting the skin barrier function.[1] Skin exhibits natural protection from external factors such as chemical exposure, ultraviolet radiation, and microorganisms.[2] This function is very important to maintain balance in the body, preventing outside substances from entering and regulating water evaporation from the body. However, dry air, ultraviolet radiations (external factors), aging and stress (internal factors) interrupt the physiological function of SC?, lipid disruption, and transepidermal water loss (TEWL), leading to hypersensitivity to various stimuli. The skin contains a natural moisturizer known as natural moisturizing factor (NMF). NMF aids in maintaining skin moisture, keeping it healthy, and preventing skin problems by absorbing water. However, if NMF is inadequate to maintain skin moisture, additional protection is needed using cosmetic skin moisturizers.[2] Furthermore, moisturizer is applied to prevent a dry environment and add moisture or oil. The importance of skincare with moisturizer for conditions related to dry skin has been recognized within the last few years.[1]

Address for correspondence
Dr. Ahmad Ainurofiq, Associate Professor, Associate Professor Pharmaceutical Technology and Drug Delivery, Department of Pharmacy, Universitas Sebelas Maret, Ir. Sutami 36A, Surakarta, Indonesia, 57126
E-mail: rofiq@mipa.uns.ac.id

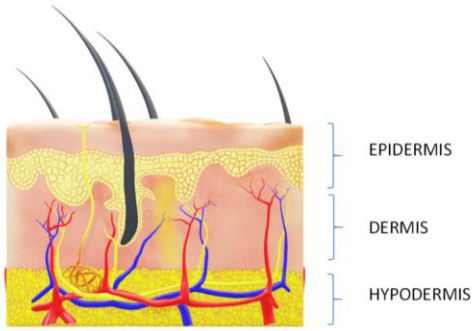

Figure 1 Structure of skin layers.

Moisturizer is a product that aims to improve skin hydration and maintain normal skin pH.[2] It is also the most used topical product to treat skin barrier dysfunction. Water retention in SC depends on two main components: natural hygroscopic agents in corneocytes and regularly structured lipids between SC cells to form a barrier from the TEWL process. Thus, skin barrier dysfunction is related to TEWL improvement and low water levels in SC.[3] Moisturizers can have the characteristics of humectant, occlusive, and intercellular lipids in SC. Occlusive and humectant moisturizers contain a mixture of lipids and are widely formulated because they can restore moisture to the skin. On the other hand, intracellular lipid moisturizers are usually formulated to treat skin infections.[4] Wide varieties of commercial moisturizers are available. However, the best moisturizer depends on individual's needs and preferences. The use of moisturizer can cause skin irritation and inflammatory symptoms. The reason is any substance can cause skin reactions in sensitive areas with a specific condition for each individual.[5] Therefore, this review aims to provide information related to cosmetics, moisturizers, moisturizer application, advantages, disadvantages, and characteristics of moisturizers.

Cosmetics

Cosmetics are ingredients or dosage forms that are poured, attached, rubbed, sprinkled, or sprayed on the outer part of the human body (epidermis, nail, hair, lip, and external genitalia), or teeth and mucous membranes, especially to clean, change appearance, scent, and/or improve body odor or protect and maintain body health. Skin cosmetics are categorized based on their function into cosmetics for skincare, body cosmetics, and makeup cosmetics.[6] Skincare cosmetics function to protect, clean, and improve skin conditions. Based on its function, skincare cosmetics include cleanser cream or foam, lotion and massage cream (conditioner), and moisturizer. Moisturizers used for the body can be in the form of facial moisturizers, body and hand moisturizers, and eye creams.[7] The objective of cosmetics is to maintain skin hygiene and health.[8]

Moisturizers

There is no agreed definition of moisturizer. The term moisturizer is coined by marketers to promote the ability of a product to moisturize skin. Even after occlusive and humectant are included, the term moisturizer and emollient are often used alternately.[9] Moisturizers becomes an important part of skincare because of their ability to improve skin hydration. The ability of moisturizers to increase skin hydration can be measured by subjective and objective parameters. The function of a moisturizer is to restore the ability of the intercellular lipid bilayer to absorb, retain, and redistribute water.

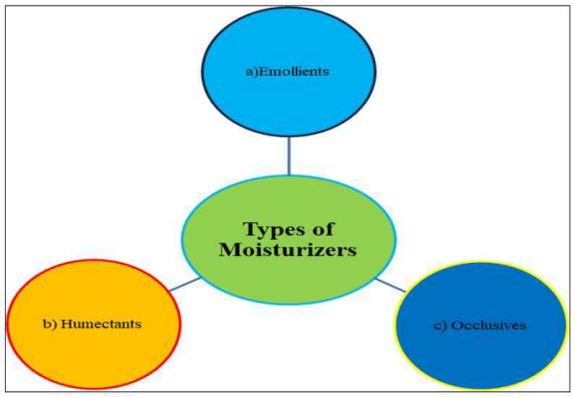

Figure 2 Types of moisturizers.

Based on the mechanism, moisturizers are divided into emollient, humectant, and occlusive, presented in **Figure 2**.[9]

The use of occlusive and humectant moisturizers is the primary mechanism to hydrate SC.

Emollient moisturizers work by filling desquamated intercorneocyte gaps to smoothen and improve skin texture. Emollient also acts to prevent water evaporation in the skin.[10] It is an important fatty acid found naturally in wool, palm oil, and coconut, which is generally used for the formation of cosmetics or topical therapies. Emollient has various effects on the skin barrier function that includes the formation of eicosanoid, membrane fluidity, cell cycle, and increased healing ability as well as skin permeability, which increases therapeutic benefits of topical medication. The categorization of emollients is shown in **Figure 3**. Some examples of emollients include stearate, linoleate, oleate, lauric acid, alcohol fat, squalene, cholesterol, and fatty acid.[9,11]

Humectant moisturizers act by attracting water from a deeper epidermis layer to SC. Theoretically, humectants can improve hydration in SC. It can also increase TEWL by increasing water absorption from the dermis to the epidermis to be evaporated easily.

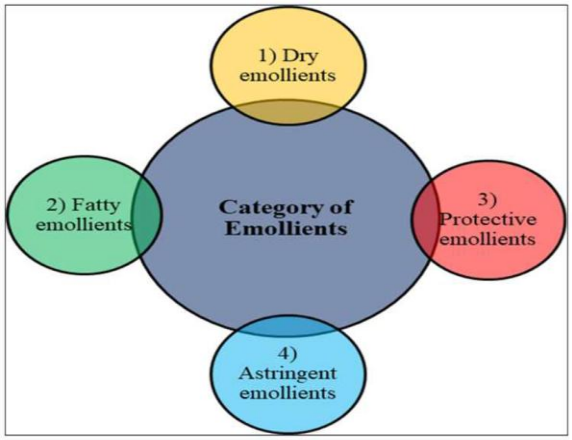

Figure 3 Emollient category.

Thus, humectants are usually used in relation to occlusives to aid in increasing the function of the epidermis barrier in addition to hydration. Common ingredients used as humectants include glycerin, sorbitol, urea, glucose, and alpha hydroxy acid (lactic acid, sodium pyrrolidine, and carboxylic acid).[9,12] Aside from their hygroscopic properties, alpha hydroxy acid and ammonium lactate can also reduce abnormal thickening of SC, increase the cohesion between corneocytes, reduce the appearance seen in ichthyosis, and other hyperkeratotic conditions.[13] Other examples of humectants are honey, panthenol, gelatin, hyaluronic acid, propylene glycol, and butylene glycol.[9]

The working mechanism of occlusive is preventing TEWL from SC. Occlusive can block TEWL in SC and helps maintain the water level.[12] When applied to wet skin, occlusive provides the highest impact, forming a hydrophobic barrier in the skin and contributing to the intercorneocyte matrix. The effectivity of occlusive is increased by diffusion to intercellular lipid areas.[9] Lanolin and petrolatum are examples of ingredients used as occlusive.[14] Liquid paraffin and petrolatum are the most important ingredients. Petrolatum is one of the most effective traditional occlusive moisturizers compared to olive oil. Petrolatum with a minimum concentration of 5% can limit moisture loss 170 times and limit TEWL to more than 98%.[9] These types of moisturizers have adverse effects. Emollients can irritate (rare), humectants can also irritate (urea, lactic acid), while occlusive can cause folliculitis (mineral oil) and contact dermatitis (lanolin). Moisturizers can be formulated in various pharmaceutical preparations such as ointment, cream, and lotion. The formulation of moisturizers available in the market uses a mixture of emollients, occlusive, and humectants formulated in a mixture of lipids and water.[5]

Application

Moisturizers are often used in preventive therapy or adjunctive therapy for various dermatological conditions. The application of moisturizer is generally used to make the skin look youthful because it can make the skin smooth and reduce facial wrinkles and keep the skin moist.[15] The majority of facial moisturizers usually use the oil-in-water (O/W) formulation. The O/W type can be identified by its cold feeling and matte appearance, while the W/O type can be recognized by its warm feeling and appearance which is the opposite of the O/W type, which is glossy. Moisturizing compositions usually consist of ingredients mixed in the oil phase such as vegetable oil, dimethicone, propylene glycol, as well as the aqueous phase including minerals, glycerin, distilled water in fulfilled amount to form a lotion or cream. Moisturizing products can be used for variety of skin types by developing and adjusting the occlusivity of the ingredients.[16] Moisturizing products for oily skin types consist of ingredients that contain little oil such as water and dimethicone, which are non-clogging and do not cause allergic reactions. Meanwhile, moisturizing products for dry skin types usually contain hydrating water, vegetable oils, mineral, petrolatum, and propylene glycol. Then, products designed for normal or combination skin types consist of equal parts oil and water.[17]

Occlusive moisturizers are usually used on moist skin, such as after a shower.[18] The right way to apply moisturizer is to rub it on your palms and then rub it on your facial skin in the direction of the hair follicles.[19] This thing is done to prevent oil folliculitis in the skin layer. Meanwhile, the application of ointment is more even compared to product formulations with low viscosity and easily evaporated ingredients. The penetration of ingredients to the skin surface is easier for cream and ointment compared to lotion and tincture.[20] After being applied to the skin, the material will slowly penetrate into the skin, then it will be metabolized or disappeared from the skin due to evaporation, peeling or due to contact with other ingredients.[4]

Moisturizers can hydrate skin and prevent excess water loss from the skin through the occlusive mechanism. In this case, they act to return the water level to the skin using humectants by attracting water from the epidermis layer to the SC. The use of humectant moisturizers is suitable for outdoor activities. Furthermore, occlusive ingredients in moisturizers can prevent excess TEWL. Moisturizers also contain epidermal lipid that maintains the skin permeability barrier and improve its plasticity. Wounded or damaged skin will heal itself through the lipid synthesis mechanism, thus moisturizer can help in healing the damaged epidermis barrier. Other than that, moisturizers can smoothen the skin through emollients. They also reduce friction by using ingredients that can increase lubrication, such as alcohol and ester.[17] Moisturizers ideally have properties that can carry out the 4 basic needs of consumers, as listed below:

Improve skin smoothness and softness The final result that is needed by consumers from using moisturizer on the face is to make the skin soft and smooth. Softness and smoothness of skin can be measured by the layer of dead keratinocytes (corneocytes) on the surface of the facial skin. When the layer of lipids are lost due to moisturizer use, folded corneocyte sides create friction when the hands are rubbed onto the skin surface, so it can make the skin feel smoother and softer when using an emollient from of moisturizer.[21]

Improve skin hydration Scientifically relevant moisturizers must keep the skin sufficiently hydrated via the transepidermal water loss

(TEWL) mechanism. This moisturizer will slow down and inhibit the evaporation of water from the surface of the skin. The TEWL mechanism is obtained by providing a material with a waterproof layer and applying it to the surface of the skin to attract water and prevent its rapid evaporation. Increased skin hydration can reduce dehydration wrinkles, especially around the eyes that have the thinnest layer of skin. The TEWL mechanism can temporarily hydrate the skin until the moisturizer is lost from facial cleansing. Several ingredients that can reduce TEWL are occlusive, including petroleum, paraffin, dimethicone, cyclomethicone, and mineral oil.[4]

Improve skin appearance Another function of a moisturizer is to improve skin appearance, also called luminosity. As people get older, the levels of skin constituents, such as melanin and hemoglobin, as well as the distribution of collagen become disrupted. Therefore, facial moisturizer is needed because it can provide a thin pigmented layer on the skin or increase reflection from the skin surface which can improve the appearance. Several ingredients that can improve skin appearance in moisturizers are pigments and optical reflective ingredients such as fish scales or mica, iron oxide that have anti-aging benefits.[16]

Has the potential to deliver materials to the skin surface Several types of emulsions such as double emulsions, micro or nanoemulsion, quick breaking emulsions, and gel emulsions have been used in skincare products as or moisturizer delivery agent. Different moisturizers with different physico-chemical properties can be modified by mixing them with cosmetic bases such as gels and creams. This will deliver moisture efficiently to skin tissues, thus increasing skin moisture.[22]

Advantages and disadvantages

The safety profile of moisturizers is considered quite high compared to traditional medicines, this is reinforced by the rare reports regarding the adverse effects of using moisturizers. Moisturizers function to increase moisture and improve skin xerosis.[16] Xerosis cutis or commonly known as dry skin is a condition in which moisture is lost or reduced in the stratum corneum. Xerosis cutis is a skin abnormality, with the characteristics of rough, scaly, wrinkled skin with a lack of elasticity compared to normal and dry skin during palpation.[23] The water content in the SC must be in the range of 10% to 30%, this is to avoid a hydration effect on the skin. With evaporation, the lost water must be replaced by water from the epidermis and dermis. Damage to the skin barrier causes xerosis, marked by thick, cracked, and irregular SC as seen in the electron micrograph.[16]

Another common adverse effect of moisturizers is a sensory reaction, or subjective sensation (no inflammatory signs), including pain, burning and stinging in sensitive facial skin. The level of ingredients in moisturizers must be considered to prevent toxicity or adverse effects.[24] Humectant, as pyrrolidone carboxylic acid (PCA) and lactic acid is known to cause a subjective sensation. Propylene glycol can also cause unfavorable skin reactions in dermatitis patients with a low 2% concentration.[25] Excessive and repeated use of moisturizers in sensitive areas can cause dermatitis. Herbal moisturizers often cause adverse reactions. However, some herbal drugs can cause an allergic reaction and several others can cause photosensitization, such as olive oil, aloe vera, tea tree oil, chamomile, black cumin oil, and inula helenium have been reported to cause allergiccontact dermatitis.[25]

Humectants, occlusive, and emollients are three primary types of moisturizers. These ingredients have their characteristics. Humectants (PCA,

lactic acid, and urea) and preservatives (sorbic acid and benzoic acid) are known to cause sensory reactions. Moisturizers are generally not a strong irritant, but in sensitive areas they can cause mild irritation or even dermatitis if prolonged exposure occurs. Nevertheless, they are still recommended to be used as a no-rinse product, especially humectant with an impact of prolonged TEWL and application should be at least twice a day or based on the severity of skin dryness. The chemical properties of humectants as hygroscopic conditioning agents can function to attract and bind water from the layers of the epidermis and dermis. The existence of several hydroxyl ions (-OH) enables humectants to dissolve in water, aside from absorbing and keeping water molecules in SC. Humectants also supply moisture to skin tissues.[12,26] Examples of humectants include PCA, lactic acid, butylene glycol, propylene glycolglycerin, urea, sodium pyrrolidone, carboxylic acid, and panthenol.[27] The humectant most often used as a moisturizer is glycerin.[28-30] Increase in hydration varies between 1% to 25% or more, with the highest values between 20%-40% depending on the base.[31] Glycerin can function as a barrier regenerating agent and hydrates the skin surface.[32]

Occlusive agents can maintain a moist state in the stratum corneum by reducing excessive water loss. Although not all moisturizers are occlusive agents, they enable the water transfer required for normal skin function. Loss of dominant intercellular lipids which play an important role in regulating skin moisture by forming a double layer consisting of cholesterol, ceramides, and fatty acids, results in damage to the water barrier structure and dry skin. Most occlusive agents have no hydroxyl function group in their chemical structure; thus, they cannot bind to water.[15]

Other ingredient that needs to be considered in the formulation of moisturizers include 1% sodium lauryl sulfate solution which is used to induce irritation to the skin. Propylene glycol as a preservative can cause skin irritation at concentrations above 10% in occlusive conditions, above 2% concentration in dermatitis patients and higher concentration of topical treatment in burn patients. Therefore, the application of propylene glycol at concentrations greater than 20% is not recommended on areas of the body in children with abnormalities in skin barrier function.[15] Several adverse effects that may arise from the use of moisturizers are listed in **Table 1**.[24,33]

Characteristics

Organoleptic testing is performed by assessing the texture and color of moisturizers.[34] Clarity, odor, texture, and foreign particles in

Table 1 Adverse effect from moisturizer use**.**

Possible Effect	Possible Cause
Subjective irritation	Humectant: lactic acid, urea, preservatives such as benzoic acid or sorbic acid
Irritation	Protein in vegetable oil, urea, hydroxy acid, propylene glycol, solvent
Occlusive folliculitis	Petrolatum, mineral oil
Photosensitivity eruption or photomelanosis	Fragrance, hydroxy acid, preservative, sunscreen
Acne	Occlusive oil used in W/O preparations
Contact urticaria	Preservatives such as sorbic acid, fragrance, and balsam of Peru
Poisoning	Salicylic acid

moisturizers are also evaluated. Roughness and adhesiveness testing is determined by rubbing between two fingers.[35] This testing is suggested to be carried out randomly at different temperatures and at different storing durations to observe changes.[36]

Light test is carried out by placing moisturizers in a clear plastic container, followed by exposure to bright light for 15 days using a lamp with a photo periodicity system, which is 16 hours bright and 8 hours dark. Samples are analyzed for every physical characteristic difference (clarity, appearance, color, and liquefaction) at the end of the exposure. Each color change or phase separation is an indication of product instability.[37]

Determination of pH of moisturizers must not be too high or too low. High acidity in the skin might irritate the skin, while high alkalinity might cause dry skin.[38] A good pH should be similar to natural skin pH, between 4.5 to 6.5.[39] Determination of pH can be carried out with a standard digital pH meter.[34] Before using the pH meter, the equipment should be calibrated with a standard buffer solution (pH 4 and pH 7).[40]

Stability

Cycling test observation This cycling test was carried out as much as 6 cycles. Gel preparations are stored at cold temperature ± 4°C for the past 24 hours removed and placed at ± 40°C, this process is calculated as 1 cycle.[41]

Measurement of mean globule diameter The mean globule diameter is measured with an optical microscope. A moisturizer preparation is placed in an object glass and observed under certain magnification in the microscope. The observed image is captured and measured for its globule diameter.[42] Measurement of mean globule diameter is carried out at week 0 at room temperature and after the cycling test.[43]

Antibacterial activity Microbiological test to determine the antibacterial activity of moisturizers is carried out with the agar diffusion method by measuring the diameter of bacterial growth inhibition. The testing is carried out as follows: The testing solution is dropped into wells made in the testing media for 50 µl using a micropipette, then the media is incubated at 37 for 24-48 hours in the incubator. After that, diameter of inhibition area (clear zone) around the wells is measured using a caliper.[44]

Spreadability

A spreadability test is carried out to determine the ability of preparation to spread when rubbed on the skin. A good moisturizer can easily spread even in action areas to obtain optimum effectivity. The expected spreadability diameter is between 5-7 cm. A spreadability test can be carried out by taking 0.5 grams of gel and placing it on a transparent glass on graph paper. The preparation is allowed to spread over a certain diameter. Afterward, it is covered with transparent glass and given 50 grams of weight, and kept for 1 minute, then the diameter of spreadability is measured.[2]

Saponification value

Saponification value is amount of base needed to carry out saponification of fat samples. Another definition of saponification value is a measurement of the amount of free fatty acid esters in a sample which affects the stability of pH, formulation, and cleaning properties of ?. A high saponification value indicates that the short chain fatty acids are in glycerol bonds. In the formulation, the saponification value must be adjusted, if the fat content is high it will easily hydrolyze and can cause rancid odor and microbial growth. The saponification value is

evaluated by refluxing 2 preparation ingredients (30 minutes) with KOH (0.5 N) and alcohol (25 mL each), then adding 1 mL of Ph (phenolphthalein) and immediately titrating with HCl (0,5 N) and labeling the result with 'a'. Repeated procedure by removing the testing ingredient and labeling the result with 'b', and calculated using the following formula:[15]

$$\text{Saponification value} = \frac{(b-a) \times 28{,}05}{\textit{weight of substance (gram)}} \quad (1)$$

Density

Product density is measured with a pycnometer. An empty pycnometer weight with a cap is weighed, then filled with samples to full and reweighed. The density is calculated using the following formula:

$$\text{Sample density} = \frac{\textit{sample weight (gram)}}{\textit{water weight (gram)}} \times \textit{water density (g/ml)} \quad (2)$$

Viscosity

Viscosity is tested using the Brookfield Viscometer with a helipath stand and a certain speed (rpm) as needed. The tested samples were weighed at a certain number, then inserted into a beaker, and kept for 5 minutes before being measured with spindle T-D. Each speed reading is recorded and measured. After obtaining measurement results, the reading of each speed is multiplied by factors given in the Brookfield viscometer catalog. The mean measurement from replications is measured.[45]

Homogeneity

A certain amount of the preparation is spread on a watch glass. A homogeneity test is carried out by visual observation. The result is considered homogenous if there is no rough particles in the preparation. This test is important to determine of miscibility water and oil phase.[2]

Irritability

Based on the Effective Time-50 (ET-50) test used EpiDerm™ Skin Model (EPI 200) test protocol,[46] maintaining living tissue conditions was rated by Microtetrazolium test (MTT). MTT is prepared in Dulbecco's phosphate-buffered saline (DPBS) 1 mg/ml. In brief, samples (tissue) were taken from wells at the end of different treatment periods. Every sample insertion is rinsed entirely with DPBS free of Ca^{2+-} and Mg^{2+-} to eliminate residuals and placed in 24 new well plates that were previously filled with 300 µL/well MTT solution.

All incubated well plates for 3 hours (37±1°C, 5±1% CO_2, and 95% RH). After incubation, each insertion is released carefully. Smeared bottom part of the insertion was covered with sterile tissue paper and placed in 24 new well plates. In extraction phase, 2 ml of isopropanol is added to each well and the insertion is dipped into solution. Well was sealed with parafilm to prevent evaporation and placed into a plate shaker for 2 hours at room temperature.

After extraction, 200 µL each of two aliquots/tissue sample was dropped into 96 well plates for reading. Optical density (OD) of samples specified at a certain wavelength. The percentage (%) of tissue viability for each tissue specified using the following formula:

$$\%\ \text{tissue viability} = 100 \times \frac{\textit{Corrected OD (sample)}}{\textit{Corrected OD (negative control)}} \quad (3)$$

The value of ET-50 is specified from the dose-response curve. The value and benchmark classification of ET-50 can be seen in **Table 2** to categorize in vivo irritation response.[47]

Table 2 Interpretation of ET-50 Benchmark results.

ET-50(hr)	*Potential In Vivo skin irritation*
< 0.5	Strong/severe irritants, possibly corrosive
0.5-4	Moderate irritants
4-12	Moderate to mild irritants
12-24	Very mild irritation
24	No irritation

In vitro

In vitro testing can be carried out with cytotoxicity and phototoxicity tests using BALB/3T3 clone A31 culture of permanent murine fibroblast cell line. The cells are cultured in Dulbecco's Modified Eagle's Medium (DMEM) with fetal bovine serum (10% v/v) as a supplement, antibiotics, and glutamine (4 mM), controlled with standard conditions (5% CO_2, 37^{o}C, 97% RH for 24 hours). Cell release is carried out by using 0.05% (b/v) trypsin/0.02% EDTA (b/v) in phosphate buffer 7.2. Count released cells and placed on 96 well plates (20,000 cells/well).[45]

Cytotoxicity test

Cytotoxicity is evaluated with 3T3 neutral red uptake. Incubate samples for 2 hours then measure the absorbance. Evaluation is carried out with different concentrations. The value of IC10 and IC50 are counted. Cell viability (CV) is counted with the following formula:

$$\text{Cell Viability (CV)} = \left(1-\frac{OD_{sample}}{OD_{control}}\right) \times 100 \quad (4)$$

The approach mostly uses IC50 from in vitro basal cytotoxicity test to confirm cell viability concentration of 50%. There is maximum toxicity when viability is zero percent and non-cytotoxic when viability is 100%.[48]

Phototoxicity test

Phototoxicity is evaluated with 3T3 neutral red uptake with the same concentration as the cytotoxicity test. Samples are exposed to radiation (UVA+) for certain times to obtain a dose of 5 J/cm^2 and are then rated in the same concentration without light (UVA-). The results are measured in certain wavelengths. Data are analyzed using Phototox®.[48] Calculated Photo Irradiation Factor (PIF) and Mean Phototoxic Effect (MPE). Predictive parameters of PIF and MPE based on a validation study are listed in **Table 3**.[49]

Table 3 Interpretation of PIF and MPE results.

PIF and MPE	Phototoxicity Potential
PIF < 2 or MPE < 0.1	No phototoxicity
PIF > 2 or MPE > 0.1 and < 0.15	Possible phototoxicity
PIF > 5 or MPE > 0.15	Phototoxicity

In vivo

The compatibility of formulation in the skin is measured based on the guidance of International Contact Dermatitis Research Group. Evaluation is carried out on 18 volunteers aged 22-46 years after receiving informed consent. The involved volunteers had type II to IV Fitzpatrick skin type and were selected according to the exclusion and inclusion criteria. Safety evaluation of the formulation is carried out by applying the formulation to normal skin of upper back for 48 hours. Skin irritation response is evaluated after 30 minutes, 24 hours, and 48 hours after the product is removed from the skin. The formulation is considered safe if there is no edema, erythema or papules on the skin of volunteers.[48]

In vivo skin hydration

In vivo skin hydration is tested on volunteers aged 22-35 years, both men and women without any history of skin diseases. The volunteers are prohibited using any cosmetics products during two weeks before and on the day of test, except cleansing products like soap. This study was conducted monoblind, random, and placebo-controlled.[50] Before the test, volunteers stay in a room for at least 30 minutes to adapt the skin to the room temperature (21±2^{o}C) and RH (55±5%).[51] The water content in SC is determined by non-invasive biometric measurement with skin capacitance measurement (Corneometer® CM 825). Four

locations in the lower arm of the volunteers are chosen randomly. All formulations are smeared onto the skin with light massage for 10 seconds. TEWL is measured from the skin with evaporimeter (Tewameter® TM 300). TEWL and skin capacitance are determined before treatment, and after 1, 2, 3, 4, and 5 hours after application.[48]

Conclusion

Moisturizers can be a solution to dry skin because they can increase skin hydration with mechanisms and properties of humectant that attract water when smeared to the skin, occlusive that can block TEWL from SC and helps maintain water level, and emollients that can prevent water evaporation from the skin. Humectants, such as glycerin and propylene glycol are the most common ingredients for the formulation of skin moisturizers. The ingredients of moisturizers need to be considered to prevent problems. Moisturizer characteristics are evaluated to obtain safe and properly used moisturizers.

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