



Published by  
Department of Dermatology and  
Venereology, Universitas Udayana

# The effectiveness of ceramide moisturizing cream in pruritic papular eruption treatment of HIV/AIDS patients



Ayu Wikan Sayekti<sup>1\*</sup>, Ann Kautsaria Putri<sup>1</sup>, Satiti Retno Pudjiati<sup>1</sup>,  
Dwi Retno Adi Winarni<sup>1</sup>

## ABSTRACT

**Background:** Pruritic papular eruption (PPE) is one of the most common skin manifestations in HIV/AIDS patients. Pruritic papular eruptions are due to immune dysregulation, causing dominance of interleukin-4, which causes a decrease in ceramide synthesis (CER) and impaired skin barrier function. This study aimed to investigate the effectiveness of CER over non-CER moisturizing cream in HIV/AIDS patients with PPE.

**Methods:** Double-blind experimental design. The research subjects are PPE patients at Dr. Sardjito General Hospital. CER and non-CER moisturizing cream are applied for three weeks, respectively. Analysis of the trans-epidermal water loss (TEWL), skin hydration, and itching were analyzed using an unpaired T-test or the Mann-Whitney test with a significance of  $p < 0.05$ .

**Results:** Ceramide synthesis moisturizing cream decreased the TEWL value by  $3.56 \pm 2.38$  g/m<sup>2</sup>/hour; increased the value of skin hydration by  $16.39 \pm 7.19$  a.u.; decreased skin lesions by  $0.79 \pm 4.95$ ; reduced itching by  $1.54 \pm 0.78$  and without causing side effects. Non-CER moisturizing cream decreased the TEWL value by  $1.57 \pm 2.00$  g/m<sup>2</sup>/hour; increased the value of skin hydration by  $12.03 \pm 6.88$  a.u.; decreased skin lesions by  $1.42 \pm 3.00$ ; reduced itching by  $1.17 \pm 0.70$  and also without causing side effects.

**Conclusion:** Ceramide cream is more effective than non-CER moisturizing cream in reducing TEWL and increasing skin hydration. Ceramide and non-CER moisturizing creams have the same effectiveness in reducing the number of lesions and reducing itching. Ceramide and non-CER moisturizing creams do not cause side effects.

**Keywords:** ceramide moisturizer, pruritic papular eruption, skin hydration, TEWL.

**Cite This Article:** Sayekti AW, Putri AK, Pudjiati SR, Winarni DR, The effectiveness of ceramide moisturizing cream in pruritic papular eruption treatment of HIV/AIDS patients. *Bali Dermatology Venereology and Aesthetic Journal*. 2024;7(1):4-9. DOI: 10.51559/balidervenaesthj.v7i1.96

<sup>1</sup>Department of Dermatology and Venereology, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia.

\*Corresponding author:  
Ayu Wikan Sayekti;  
Department of Dermatology and Venereology, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia;  
ayuwikansayekti@gmail.com

Submitted: 2024-01-24

Accepted : 2024-03-27

Published: 2024-03-30

## INTRODUCTION

Pruritic papular eruption (PPE) is one of the manifestations of skin disorders commonly found in patients with human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS), which is chronic and difficult to treat. This disorder is reported quite often, in tropical and subtropical countries with a mean prevalence of 11-46%.<sup>1</sup> The etiology and pathogenesis of PPE are not fully understood. Several factors considered to play a role in the etiology and pathogenesis of PPE are hypersensitivity to insect bites in HIV/AIDS patients, host cellular immune response to abnormal infection processes, drugs, skin autoimmune reactions, and direct effects of viruses through immune dysregulation and skin tissue.<sup>2,3</sup>

Pruritic papular eruptions are associated with an increased role of Th2 lymphocyte cytokines in the advanced stages of HIV/AIDS infection and result in impaired skin barrier function. Research in the United States (2010) which measured skin barrier function in HIV patients with xerotic dermatitis, without xerotic dermatitis, and healthy non-HIV controls showed a significant decrease in skin barrier function in HIV patients without xerotic dermatitis compared to healthy controls and impaired barrier function increasingly significant in patients with xerotic dermatitis through an “inside-to-outside” mechanism mediated by the dominant Th-2 lymphocyte cytokine in HIV/AIDS infection.<sup>4</sup> The potential role of Th2 lymphocyte cytokines, especially the increase in IL-4, will suppress ceramide synthesis through interference with

catalytic enzymes, thereby disrupting the skin barrier function. Increased IL-4 also induces vascular cell adhesion molecule (VCAM), which increases eosinophil and macrophage migration. Increased IL-4 is associated with reduced E-cadherin, inhibition of involucrin synthesis, desmosome maturation, and inhibition of profilaggrin synthesis into filaggrin, which is a natural moisturizing factor (NMF) precursor. These factors impair skin barrier function, increasing skin sensitivity and itching sensation.<sup>5</sup>

The PPE therapy in people living with HIV/AIDS is still a challenge because various treatment modalities have not been able to solve the problems that patients complain about.<sup>6</sup> Impaired skin barrier function, which results in dryness of the skin and the appearance of itching in dermatoses generally improves with the

application of moisturizers. Moisturizers are topical products designed to improve and maintain skin barrier function. The latest generation of moisturizers contains better ingredients than classic moisturizers. The latest generation of commonly used moisturizers are ceramides (CER), free fatty acids, and cholesterol, which help replace fat deficiency in several skin diseases with impaired skin barrier function.<sup>7</sup> The skin barrier function can be assessed through non-invasive biotechnological methods based on the amount of water lost through the stratum corneum or transepidermal water loss (TEWL) and skin hydration level.<sup>8</sup>

A CER is a heterogeneous and complex sphingolipid group with the main structure containing sphingosine, phytosphingosine, or 6-hydroxy sphingosine, a C18-sphingoid base bound to an amide group by various non-hydroxy,  $\alpha$ -hydroxy, or hydroxy acids. A CER is the stratum corneum's predominant lipid component, comprising 30-40% of stratum corneum lipids. It also plays an important role in the structure and maintenance of the skin's water-permeability barrier function.<sup>9</sup> The skin barrier was interestingly investigated to determine whether a moisturizer containing CER is effective for the treatment of PPE in HIV/AIDS patients. To the best of the author's knowledge, no studies have measured the effectiveness of giving a moisturizing cream containing CER to patients with PPE. This study aimed to evaluate the moisturizing cream containing CER for treating PPE in HIV/AIDS patients in the context of TEWL, skin hydration, and itching.

## MATERIALS AND METHODS

This study is an analytical study with a double-blind experimental design. The research was conducted at Dr. Sardjito General Hospital, Yogyakarta, Indonesia, and the Research Laboratory of the Department of Dermatology and Venereology, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada. Each subject received a ceramide moisturizing cream (CER) and non-CER, which was applied to the volar part of the forearm on different sides. The measurements taken were the

rate of evaporation of water through the epidermis (TEWL) using a tewameter TM 300<sup>®</sup>, skin hydration using a corneometer CM 825<sup>®</sup>, the number of lesions, and itching with a VAS (visual analog scale) assessment as well as subjective side effects. Measurements were made in weeks 0 and 3.

The research population is HIV/AIDS sufferers with PPE who seek treatment at Dr. Sardjito General Hospital and meet the inclusion and exclusion criteria. Analysis of the results was done using an unpaired T-test or Mann-Whitney test. Multivariate analysis using MANOVA aims to determine what variables have changed after using ceramide moisturizing cream with a 95% confidence degree and declared significant if the p-value <0.05.

## RESULTS

### Characteristics of Research Subjects

At the end of the study, the envelope was opened containing information on the contents of cream A and cream B. Cream A was a CER moisturizing cream (right arm), and cream B was a non-CER moisturizing cream (left arm). The characteristics of the research subjects are shown in [Table 1](#).

Lesions on the upper extremities were found in all subjects (100%), followed by lesions on the lower extremities (67%), back (63%), chest (46%), and abdomen (33%). Efflorescence lesions in the form of hyperpigmented papules, excoriations, macules, and hyperpigmented patches were found in all subjects (100%) and followed by erythematous papules (96%). The normality test using the Saphiro-Wilk test showed that the data was normally

distributed in addition to the variable number of lesions.

### Results of Bivariate Analysis

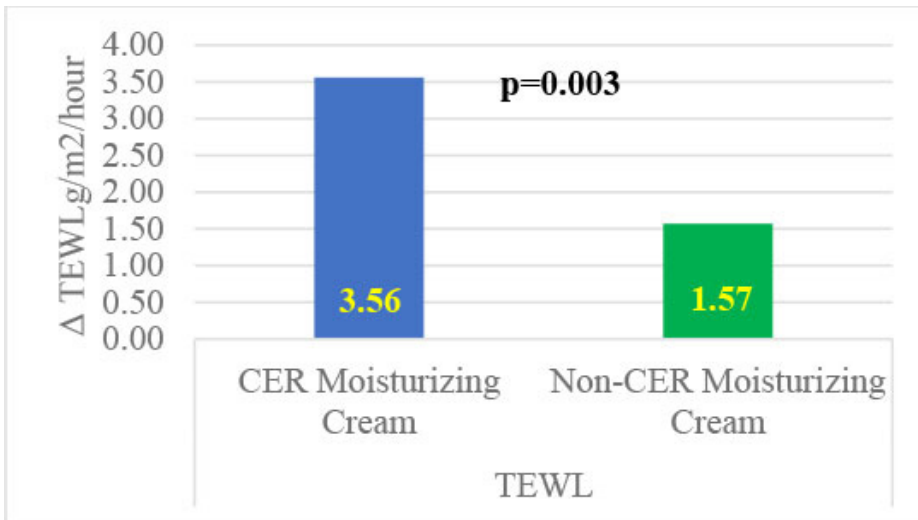
The mean difference analysis in TEWL of CER and non-CER moisturizing cream using independent t-test. The average TEWL of week 0 of CER moisturizing cream was  $13.19 \pm 3.78$ , and the average TEWL of week 0 of non-CER moisturizing cream was  $11.79 \pm 3.69$  ( $p=0.201$ ). The average TEWL of the 3rd week of CER moisturizing cream was  $9.63 \pm 3.18$ , and the average TEWL of the third week of non-CER moisturizing cream was  $10.23 \pm 3.51$  ( $p=0.543$ ). The results of the mean difference delta in TEWL are shown in [Figure 1](#).

The mean difference analysis in skin hydration of CER and non-CER moisturizing creams using independent t-test. The average skin hydration week 0 CER moisturizing cream was  $34.94 \pm 6.15$ , and the average skin hydration week 0 non-CER moisturizing cream was  $34.63 \pm 6.82$  ( $p=0.807$ ). The average skin hydration in the 3<sup>rd</sup> week of the CER moisturizing cream was  $51.33 \pm 8.35$ , and the average of the 3<sup>rd</sup> week of the non-CER moisturizing cream was  $46.66 \pm 9.31$  ( $p=0.074$ ). The results of the mean difference delta in the average skin hydration are shown in [Figure 2](#).

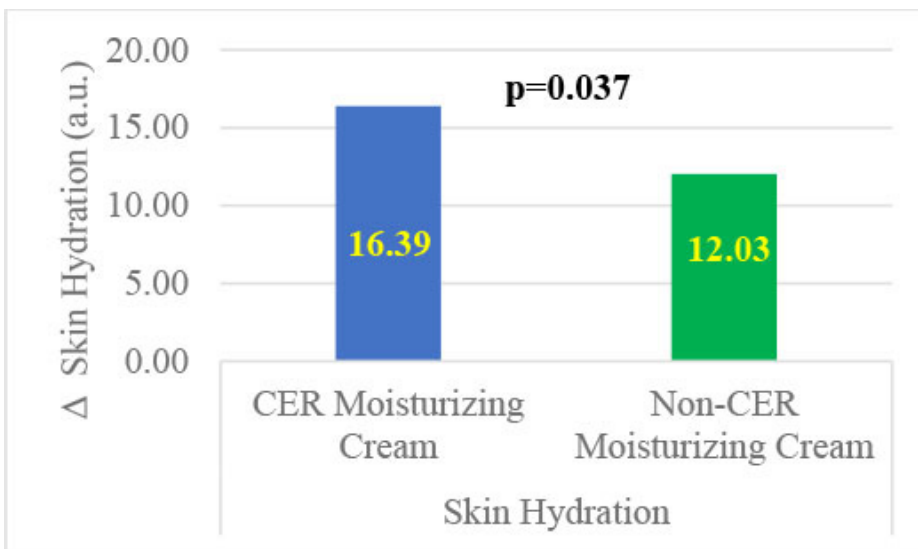
The mean difference analysis in the mean number of CER and non-CER moisturizing cream lesions using the Mann-Whitney test. The average number of lesions in week 0 of CER moisturizing cream was  $23.58 \pm 1.39$ , and in week 0 of non-CER moisturizing cream was  $17.38 \pm 1.14$  ( $p=0.043$ ). The mean number of

**Table 1. Characteristics of research subjects**

No.	Characteristics	n	%	Mean
1.	<b>Age (years)</b>			
	Youngest	24	-	$32.67 \pm 6.68$
	Oldest	50	-	
2.	<b>Sex</b>			
	Male	23	95.83	-
	Female	1	4.17	
3.	<b>Length of PPE (months)</b>			
	Lowest	1	12.6	$10.46 \pm 1.17$
	Longest	36	4.17	
4.	<b>Number of CD4 T lymphocyte cells (cell/mm<sup>3</sup>)</b>			
	Lowest	7	4.17	$76.04 \pm 7.92$
	Highest	321	4.17	



**Figure 1.** The mean difference delta of TEWL reduction in CER and non-CER moisturizing creams.



**Figure 2.** The mean difference delta of skin hydration improvement in CER and non-CER moisturizing creams.

lesions in the 3<sup>rd</sup> week of CER moisturizing cream was  $22.79 \pm 1.31$ . This value was higher than the average of the 3<sup>rd</sup> week of non-CER moisturizing cream of  $15.96 \pm 0.97$  ( $p=0.046$ ). The results of the mean difference delta in the average number of lesions are shown in [Figure 3](#).

The mean difference analysis in the average itching feeling of CER and non-CER moisturizing cream using independent t-test. The average itching week 0 of the CER moisturizing cream was  $7.08 \pm 1.06$ , and the average itching week 0 of the non-CER moisturizing cream was  $6.96 \pm 1.08$  ( $p=0.675$ ). The average itching at the 3<sup>rd</sup> week of CER moisturizing cream was  $5.54 \pm 0.83$ . This value was

lower than the average itching in week 3 of non-CER moisturizing cream, which was  $5.79 \pm 0.93$  ( $p=0.241$ ). The results of the mean difference delta of itching are shown in [Figure 4](#).

The CER and non-CER moisturizing creams showed no side effects in all subjects. Mild erythema that disappeared in the first three days of use was found in one subject (4.17%) on the arm using CER and non-CER moisturizing cream.

#### Multivariate analysis

The multivariate test in this study used the MANOVA (multivariate analysis of variance) test. The variables included in the multivariate analysis were p-value <

0.25 in the bivariate analysis, including changes in TEWL, skin hydration, and itching. The results of the multivariate test are shown in [Table 2](#).

## DISCUSSION

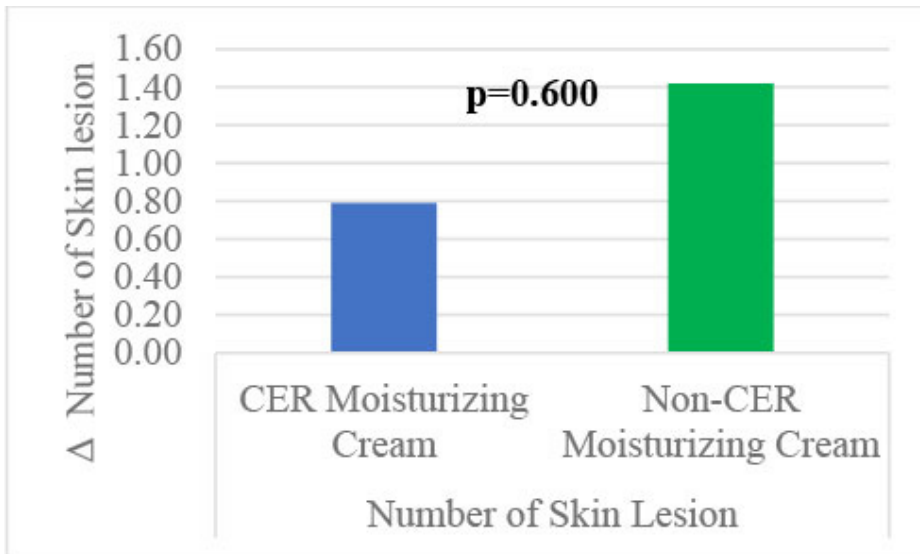
The youngest age of the subjects with PPE in this study was 24 years, and the oldest was 50 years, with a mean age of  $32.67 \pm 6.68$  years. Most of the subjects were male (95.83%). A large proportion of people living with HIV/AIDS in this age group is associated with higher-risk sexual behavior and increased commercial sex services by men.<sup>10</sup> Research by Afonso *et al.* (2012) in Brazil also reported that the mean age of PPE sufferers was 38.3 years, the age range was 28-61 years, and the predominance of male subjects (72.2%).<sup>11</sup>

This study showed that the mean number of CD4 T lymphocytes was  $76.04 \pm 7.92$  cells/mm<sup>3</sup>, and most of the subjects had a CD4 T-lymphocyte count < 200 cells/mm<sup>3</sup> (87.5%). Research by Wiraguna and Adam (2018) also reported that most of the CD4 T lymphocyte cells in PPE patients was < 200 cells/mm<sup>3</sup> with a CD4/CD8 T lymphocyte ratio lower than normal.<sup>3</sup>

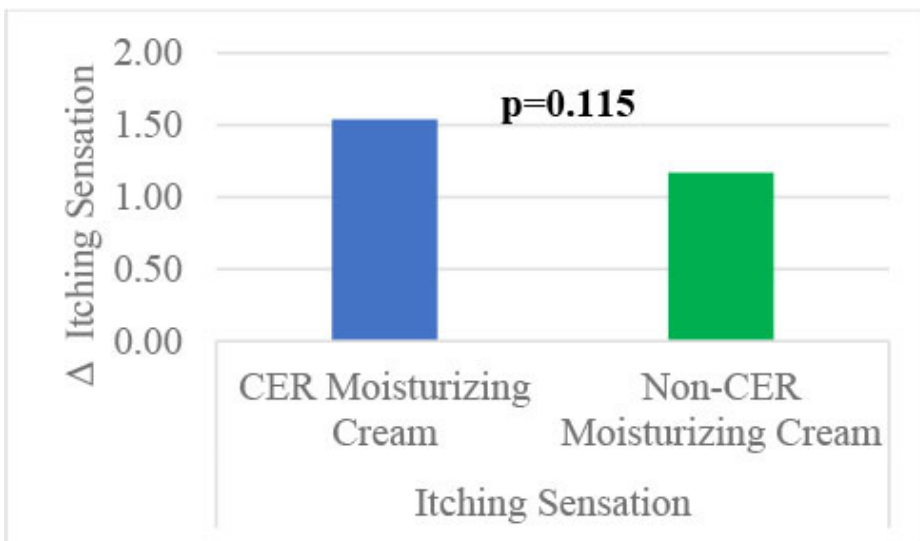
The pruritic papular eruption is a chronic itchy dermatosis in HIV/AIDS patients. Previous studies have shown that more than half of people with HIV/AIDS reported PPE as an early manifestation that appeared several months before the diagnosis was made.<sup>2,12</sup> The results of this study indicate that the length of PPE suffers from 1 to 36 months, and the mean suffers from PPE is  $10.46 \pm 1.17$  months.

Research by Chua *et al.* (2014) stated that lesions on the extremities (arms and legs) were found in most patients with PPE. These findings are consistent with the results of this study, namely lesions on the upper extremities were found in all subjects (100%), followed by lesions on the lower extremities (67%), back (63%), chest (46%) and abdomen (33%). This confirms the alleged role of insect bites in the etiopathogenesis of PPE due to the predilection for dominant lesions in exposed skin areas.<sup>13</sup>

Research by Arista and Murtiastutik (2015) showed that the main skin lesions of PPE were hyperpigmented papules (58.6%), followed by hyperpigmented



**Figure 3.** The mean difference delta of skin lesion number in CER and non-CER moisturizing creams.



**Figure 4.** The mean difference delta of itching sensation in CER and non-CER moisturizing creams.

**Table 2.** MANOVA multivariate test results

Variable	p-value	F	Adjusted R squared
Changes in TEWL	0.003	9.83	15.80%
Changes in skin hydration	0.037	4.59	7.10%
Changes in itching sensation	0.086	3.07	4.20%

macules (14.6%) and erythematous papules (13.8%).<sup>14</sup> this study found hyperpigmented papules, macules, and hyperpigmented patches in all subjects (100%), followed by erythematous papules (96%).

Bivariate analysis (test of difference in mean change) of TEWL showed that the difference (decrease) in the mean TEWL of CER moisturizing cream was higher than the difference (decrease) in the mean

of non-CER moisturizing cream, so it can be concluded that there was a difference in TEWL between the arms using CER and non-CER moisturizing creams. CER, a CER moisturizing cream, is more effective in reducing TEWL than non-CER moisturizing creams. The subjects' mean at the beginning of the study was in good TEWL condition (11 – 14 g/m<sup>2</sup>/hour). The approach to interpreting the results of this study after applying moisturizing

cream showed that in TEWL, there was an improvement in TEWL from good category (11 – 14 g/m<sup>2</sup>/hour) to very good (<11 g/m<sup>2</sup>/hour).

Several studies have shown that CER is an important component of intercellular lipids needed to connect corneocytes to the skin barrier to protect the underlying skin tissue. The CER morphology holds corneocytes from adhering to the intercellular matrix, thereby maintaining skin integrity. The tightly packed lipid array forms a system to prevent the increase in TEWL and makes the stratum corneum impermeable/waterproof. A decrease in CER, especially CER 1 and 3, is associated with a significant increase in TEWL, the main factor affecting skin dryness.<sup>15,16</sup> CER moisturizing cream (ceramide-3) can improve skin barrier function disorders (reduce TEWL) through a semi-occlusive moisturizing effect that limits water evaporation from the skin.<sup>17</sup>

Bivariate analysis (difference test of mean change) of skin hydration parameters showed the difference (increase) in the mean skin hydration of CER moisturizing cream was higher than the average increase in skin hydration of non-CER moisturizing cream so it could be concluded that there was a difference in skin hydration between the arms using CER moisturizing cream and non-CER moisturizing cream, namely CER moisturizing cream is more effective in increasing skin hydration than non-CER moisturizing cream. The subjects' mean at the start of the study was dry skin hydration (34 – 35 a.u.). The approach to interpreting the results of this study after giving moisturizing cream showed an improvement in the dry hydration category (34 – 35 a.u.) to good hydration (46 – 52 a.u.).

Research by Spada (2018) reports that a moisturizer with CER-3 content is the latest generation of moisturizer that increases skin hydration because it resembles the skin's natural moisturizing system. Increased skin hydration can reduce therapy duration and disease symptoms with impaired skin barrier function.<sup>7</sup> Increased skin hydration occurs through an increase in the expression of the FLG gene that encodes filaggrin, resulting in increased levels of natural moisturizing factor (NMF) to maintain

homeostasis of the stratum corneum. Low NMF levels are associated with mutations in the FLG gene, a major factor in skin barrier disruption.<sup>18</sup>

The subjects in this study used the right arm as the dominant arm when working and doing daily activities. Research by Novak Bilic et al. (2018) showed that the dominant arm was more affected by exposure, thus allowing more skin lesions.<sup>19</sup> This is similar to this study in that the dominant arm has more skin lesions.

This study showed that CER moisturizing cream was not more effective than non-CER moisturizing cream in reducing the number of lesions. Most of the subjects had a CD4 T lymphocyte count < 200 cells/mm<sup>3</sup> (87.5%), so the more severe the disruption of skin barrier function occurred. This increases skin sensitization to exposure to antigens and environmental stimuli, including arthropod bites that can activate the inflammatory process.<sup>2</sup> This causes new PPE lesions before the old ones disappear or exacerbate existing ones.

Research by Kubba *et al.* (2009) showed that post-inflammatory hyperpigmented lesions took 3 – 24 months to fade completely.<sup>20</sup> Research by Udompataikul (2015) showed that CER has an anti-inflammatory effect both in vitro and in vivo. Still, the anti-inflammatory response, especially the parameters of edema and erythema, is slower and weaker than the corticosteroid response.<sup>21</sup> Research by Kim *et al.* (2002) showed that CER can inhibit melanogenesis by activating extracellular-signal-regulated kinase (ERK), but CER cannot directly suppress tyrosinase.<sup>22</sup> The number of lesions is greater in the dominant arm, the anti-inflammatory and depigmentation effects were weak, and due to the short observation time, it was possible that the changes in lesion reduction were not significant.

Scratching due to severe itching that lasts chronically (itch-scratch cycle) results in mechanical disruption of the skin barrier in the form of a decrease in the skin's natural moisturizing content. Topical ceramide administration aims to improve skin barrier function and reduce itching to break the chronic itching-scratch cycle.<sup>23</sup> The results of the different tests of this study showed that CER moisturizing

cream reduced itching more than non-CER moisturizing cream, but this was not statistically significant. This is a weakness of this study because the two creams were applied to two different arms but on one subject, so it was difficult to assess the subjective taste caused by the use of the cream.

The CER and non-CER moisturizing creams in this study showed no side effects in all subjects. Mild erythema in one subject that disappeared in the first three days could be due to preservatives in the content of the two creams. Preservatives are important components that inhibit the development of microorganisms, extend the shelf life of cosmetic products, and prevent oxidation of active ingredients. Still, they have been reported to cause skin irritation and are a common source of cosmetic allergies.<sup>24</sup> Parabens (*methyl- and propyl-paraben*) in various cosmetic products were safe and effective in 0.1–0.2% concentrations.<sup>25</sup> Parabens of 0.1% concentration (safe range) were used in this study. Parabens are the cause of T-cell-mediated sensitization, thereby inducing inflammation that can lead to rapid-type hypersensitivity.<sup>26</sup>

CER moisturizing cream is an emollient with a mechanism of action on fluidity and permeability of cell membranes to improve the skin barrier function.<sup>27</sup> This is in accordance with the results of the multivariate analysis of this study, namely that CER moisturizing cream has an effect, especially on changes in TEWL, by 15.8%, followed by an effect on changes in TEWL. Skin hydration by 7.1% compared to non-CER moisturizing creams.

## CONCLUSION

The CER moisturizing cream is effective and more effective than the non-CER moisturizing cream in lowering TEWL. CER moisturizing cream is effective and more effective than non-CER moisturizing cream in increasing skin hydration. CER and non-CER moisturizing creams have the same effectiveness in reducing the number of lesions. CER and non-CER moisturizing creams have the same effectiveness in reducing itching. CER and non-CER moisturizing creams do not cause side effects.

## CONFLICT OF INTEREST

There is nothing to declare.

## ETHICS IN PUBLICATION

The research has obtained an ethical suitability letter on 2<sup>nd</sup> June 2020 from the Medical and Health Research Ethics Committee (MHREC) Faculty of Medicine Public Health and Nursing Universitas Gadjah Mada - Dr. Sardjito General Hospital with reference number KE/FK/0622/EC/2020.

## FUNDING DISCLOSURE

Faculty of Medicine, Public Health and Nursing Universitas Gadjah Mada Community Fund Program.

## AUTHORS CONTRIBUTION

Sayekti A.W. wrote the manuscript with support from Putri A.K. Both Pudjiastuti S.R. and Winarni D.R.A. supervised the project.

## REFERENCES

1. Serling SLC, Kieron, Toby M. Approach to Pruritus in the Adult HIV-Positive Patient. *Seminars in Cutaneous Medicine and Surgery*. 2011;30(2):101–6. DOI: [10.1016/j.sder.2011.04.004](https://doi.org/10.1016/j.sder.2011.04.004).
2. Eisman S. Pruritic Papular Eruption in HIV. *Dermatologic Clinics*. 2006;24(4):449–57. DOI: [10.1016/j.det.2006.06.005](https://doi.org/10.1016/j.det.2006.06.005).
3. Wiraguna AAGP, Adam AM. Pruritic Papular Eruption (PPE) Pada Penderita HIV/AIDS. In: Hidayati AN, et al, editors. *Manifestasi dan Tatalaksana Kelainan Kulit dan Kelamin Pada Penderita HIV/AIDS*. Jakarta: Badan Penerbit FKUI. 2018:207–226.
4. Gunathilake R, Schmutz M, et al. Epidermal Barrier Dysfunction in Non-Atopic HIV: Evidence for an inside to outside Pathogenesis. *J Invest Dermatol*. 2010;130(4):1185–1188. DOI: [10.1038/jid.2009.367](https://doi.org/10.1038/jid.2009.367)
5. Hatano Y, Hiroto T, Shoko A, Kazumoto K. Interleukin-4 Suppresses the Enhancement of Ceramide Synthesis and Cutaneous Permeability Barrier Functions Induced by Tumor Necrosis Factor- $\alpha$  and Interferon- $\gamma$  in Human Epidermis. *Journal of Investigative Dermatology*. 2005;124(4):786–92. DOI: [10.1111/j.0022-202X.2005.23651.x](https://doi.org/10.1111/j.0022-202X.2005.23651.x).
6. Navarini AA, Stoeckle M, Navarini S, Mossdorf E, Jullu BS, Mchomvu R, Mbata M, Kibatala P, Tanner M, Hatz C. Antihistamines Are Superior to Topical Steroids in Managing Human Immunodeficiency Virus (HIV)-Associated Papular Pruritic Eruption. *International Journal of Dermatology*. 2010;49(1):83–86. DOI: [10.1111/j.1365-4632.2009.04279.x](https://doi.org/10.1111/j.1365-4632.2009.04279.x).

7. Spada F, Barnes TM, Greive KA. Skin Hydration Is Significantly Increased by a Cream Formulated to Mimic the Skin's Own Natural Moisturizing Systems. *Clinical, Cosmetic and Investigational Dermatology*. 2018;11:491–97. DOI: [10.2147/CCID.S177697](https://doi.org/10.2147/CCID.S177697).
8. Antonov D, Schliemann S, Elsner P. Methods for the Assessment of Barrier Function. *Current Problems in Dermatology*. 2016;49:61–70. DOI: [10.1159/000441546](https://doi.org/10.1159/000441546).
9. Coderch L, López O, de la Maza A, Parra JL. Ceramides and Skin Function. *American Journal of Clinical Dermatology*. 2003;4(2):107–29. DOI: [10.2165/00128071-200304020-00004](https://doi.org/10.2165/00128071-200304020-00004).
10. Ditjen P2PL Kemenkes. Laporan Situasi Perkembangan HIV-AIDS dan PIMS Indonesia Januari-Desember 2017 [Internet]. 2018 (Cited on: 2018 Sept 2). Available from: [http://siha.depkes.go.id/portal/perkembangan-kasus-hiv-aids\\_pims](http://siha.depkes.go.id/portal/perkembangan-kasus-hiv-aids_pims)
11. Afonso JPJM, Jane T, Michalany NS, Nonogaki S, Porro AM. Pruritic Papular Eruption and Eosinophilic Folliculitis Associated with Human Immunodeficiency Virus (HIV) Infection: A Histopathological and Immunohistochemical Comparative Study. *Journal of the American Academy of Dermatology*. 2012;67(2):269–75. DOI: [10.1016/j.jaad.2011.11.923](https://doi.org/10.1016/j.jaad.2011.11.923).
12. Ekpe O. Pruritic Papular Eruption of HIV: A Review Article. *Our Dermatology Online* 2019;10(2):191–96. DOI: [10.7241/ourd.20192.22](https://doi.org/10.7241/ourd.20192.22).
13. Chua SL, Amerson EH, Leslie KL, McCalmont TH, Leboit PE, Martin JN, Bangsberg D, Maurer TA. Factors Associated with Pruritic Papular Eruption of Human Immunodeficiency Virus Infection in the Antiretroviral Therapy Era. *British Journal of Dermatology*. 2014;170(4):832–39. DOI: [10.1111/bjd.12721](https://doi.org/10.1111/bjd.12721).
14. Arista A, Murtiastutik D. Studi Retrospektif: Karakteristik Papular Pruritic Eruption (PPE) Pada Pasien HIV/AIDS (Retrospective Study: Characteristic of Papular Pruritic Eruption in HIV/AIDS Patients). *Berkala Ilmu Kesehatan Kulit Dan Kelamin*. 2015;27(3):204–10.
15. Draelos ZD. Clinical Situations Conducive to Proactive Skin Health and Anti-Aging Improvement. *Journal of Investigative Dermatology Symposium Proceedings*. 2008;13(1):25–27. DOI: [10.1038/jidsymp.2008.9](https://doi.org/10.1038/jidsymp.2008.9).
16. Kahraman E, Kaykın M, Bektay HS, Güngör S. Recent Advances on Topical Application of Ceramides to Restore Barrier Function of Skin. *Cosmetics*. 2019;6(3):1–11. DOI: [10.3390/cosmetics6030052](https://doi.org/10.3390/cosmetics6030052).
17. Kucharekova M, Schalkwijk J, Van De Kerkhof PCM, Van De Valk PGM. Effect of a Lipid-Rich Emollient Containing Ceramide 3 in Experimentally Induced Skin Barrier Dysfunction. *Contact Dermatitis*. 2002;46(6):331–38. DOI: [10.1034/j.1600-0536.2002.460603.x](https://doi.org/10.1034/j.1600-0536.2002.460603.x).
18. Danby SG, Brown K, Higgs-Bayliss T, Chittock J, Albenali L, Cork MJ. The Effect of an Emollient Containing Urea, Ceramide NP, and Lactate on Skin Barrier Structure and Function in Older People with Dry Skin. *Skin Pharmacology and Physiology*. 2016;29(3):135–47. DOI: [10.1159/000445955](https://doi.org/10.1159/000445955).
19. Novak-Bilić G, Vučić M, Japundžić I, Meštrović-Štefekov J, Stanić-Duktaj S, Lugović-Mihić L. Irritant and Allergic Contact Dermatitis – Skin Lesion Characteristics. *Acta Clinica Croatica*. 2018;57(4):713–20. DOI: [10.20471/acc.2018.57.04.13](https://doi.org/10.20471/acc.2018.57.04.13).
20. Kubba R, Bajaj AK, Sharma R, et al. Postinflammatory Hyperpigmentation in Acne Indian Journal of Dermatology Venereology and Leprology. 2009;75(Supplement 1):S54.
21. Udompataikul M. New Innovation of Moisturizers Containing Non-Steroidal Anti-Inflammatory Agents for Atopic Dermatitis. *World Journal of Dermatology*. 2015;4(2):108. DOI: [10.5314/wjdv4.i2.108](https://doi.org/10.5314/wjdv4.i2.108).
22. Kim DS, Kim SY, Chung JH, Kim KH, Eun HC, Park CY. Delayed ERK Activation by Ceramide Reduces Melanin Synthesis in Human Melanocytes. *Cellular Signalling*. 2002;9(9):779–85. DOI: [10.1016/S0898-6568\(02\)00024-4](https://doi.org/10.1016/S0898-6568(02)00024-4).
23. Harrison IP, Spada F. Breaking the Itch–Scratch Cycle: Topical Options for the Management of Chronic Cutaneous Itch in Atopic Dermatitis. *Medicines*. 2019;6(3):1–14. DOI: [10.3390/medicines6030076](https://doi.org/10.3390/medicines6030076).
24. Nowak K, Jabłońska E, Ratajczak-Wrona W. Controversy around Parabens: Alternative Strategies for Preservative Use in Cosmetics and Personal Care Products. *Environmental Research*. 2021;198:1–12 DOI: [10.1016/j.envres.2020.110488](https://doi.org/10.1016/j.envres.2020.110488).
25. Nanda S, Reddy BSN, Ramji S, Pandhi D. Analytical Study of Pustular Eruptions in Neonates. *Pediatric Dermatology*. 2002;19(3):210–15. DOI: [10.1046/j.1525-1470.2002.00061.x](https://doi.org/10.1046/j.1525-1470.2002.00061.x).
26. Macy E, Schatz M, Zeiger R. Immediate Hypersensitivity to Methylparaben Causing False-Positive Results of Local Anesthetic Skin Testing or Provocative Dose Testing. *The Permanente Journal*. 2002;6(4):17–21.
27. Purnamawati S, Indrastuti N, Danarti R, Saefudin T. The Role of Moisturizers in Addressing Various Kinds of Dermatitis: A Review. *Clinical Medicine and Research*. 2017;15(3–4):75–87. DOI: [10.3121/cm.2017.1363](https://doi.org/10.3121/cm.2017.1363).



This work is licensed under a Creative Commons Attribution