Cocos nucifera and glycerine afterwork moisturizers for secondary prevention of hand dermatitis among fabric worker: a randomized, double- blind, cross over trial

Windy K Budianti
wkeumala@gmail.com
University of Indonesia
Retno W Soebaryo
University of Indonesia
Muchtaruddin Mansyur
University of Indonesia
Franciscus D Suyatna
University of Indonesia
Minarma Siagian
University of Indonesia
Joshita Djajadisastra
University of Indonesia
Cita RS Prakoeswa
Airlangga University

Article

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Abstract

Introduction: The use of skin barrier-enhancing topical medication is a favorable approach for the treatment of occupational hand dermatitis (OHD). Cocos nucifera or coconut oil is one of the best sources of lipid enriched with laurate acid, and glycerin is a well-known humectant that improves skin hydration. This study is aimed is to evaluate the effectiveness of Cocos nucifera and glycerin for secondary prevention of OHD among batik (Indonesian traditional fabric) workers. Methods: In a randomized, double-blind, crossover trial, the effect of glycerin-Cocos nucifera cream vs. glycerin-only was considered with multiple afterwork applications of moisturizer over a 2-week period on batik workers with OHD. Assessment of trans-epidermal water loss (TEWL), skin capacitance, and a clinical assessment using the Hand Eczema Severity Index (HECSI) were carried out at day 0 and 14. Results: Thirty-two batik dyeing and/or rinsing workers were enrolled in the study with mild to moderate OHD. Clinical improvement was demonstrated by 20% decrease in HECSI and TEWL, and 20% increase in skin capacitance. Both moisturizers were equally effective for the secondary prevention of OHD. Conclusion: Glycerin-Cocos nucifera and glycerin-only cream are equally effective for secondary prevention for OHD among batik worker to reduce the prevalence of hand dermatitis.

Introduction

Batik is well-known as an intangible cultural heritage in Indonesia, claimed by United Nations Educational, Scientific and Cultural Organization (UNESCO) in 2009.[1] Batik is handwriting, a way of decorating by covering a part of the clothing with a coat of wax, followed by a dyeing process. Batik has become more popular over the years due to the dynamic development in the technological, esthetical, functional, and economic aspects.[1] The process of batik manufacturing is similar in different areas, but each region has its own characteristic of pattern and colour. Batik processing requires some materials that act as irritants or allergens, which can cause occupational hand dermatitis (OHD).[2] The hazards exposure includes excessive water, synthetic dyes (naphtol), caustic agents, and detergents.[2]

Physical personal protective equipment (PPE) was not standardised and often locally modified by the workers.[2] There are not many studies reported regarding the use of moisturizers specific to a particular job.[2] The goal of treatment for hand dermatitis is to improve the skin barrier function with appropriate moisturizers.[3,4] Various studies have demonstrated that regular use of hand lotions or creams can increase skin hydration and treat allergic or irritant contact dermatitis.[5,6] Moisturizers have many effects on the skin.[7,8] They may form a form of coating, which acts as a barrier for chemicals from the exterior and restricts the loss of water and other important substances from the interior. Moisturizers are used as an adjuvant besides physical PPE and its limitations.[4] Nevertheless, evidence supporting the superiority of moisturizers containing lipids over the more traditional moisturizers is still lacking.[2]

Because OHD may be concerned, not many studies with repeated usage and application of moisturizer have been done. [6,9] Nowadays, studies regarding herbal products and its efficacy in dermatologic

diseases is evolving.[10] This study aimed to examine whether the regular use of a moisturizer containing laurate acid from *Cocos nucifera* and glycerin cream in batik workers with OHD would prevent hand dermatitis from worsening. Improvement of the proportion of patients with OHD is deemed to be the goal of this study. This study was set in a real work situation as the batik workers still work under the evaluation of the moisturizer's effectiveness, and clinical effects were determined by using Hand Eczema Severity Index (HECSI), transepidermal water loss (TEWL), and skin capacitance.[11,12]

Materials and Methods

Study design and subjects

This was a randomized, double-blind, crossover, clinical trial done in few centres of batik enterprises in Indonesia. The ethical protocol was approved by The Research Ethics Committee of our institution (Protocol number 16178) and registered to *clinicaltrials.gov* with ID No. NCT03617068. Subjects enrolled in this study were batik workers involved in the dyeing and rinsing process, male, and aged 25–60 years, with mild–moderate OHD suitable to Mathias' criteria and investor global assessment for assessing the severity (Fig. 1.). They were required to stop applying topical products on their hands and arms other than those given during this study.[13,14] Exclusion criteria included individuals with a history of allergy or irritation to moisturizers or coconut oil, severe dermatitis or sign of infection, and subjects undergoing treatment with topical or systemic immunosuppressant agent.

Materials

Cocos nucifera-glycerin and glycerin cream were obtained from Faculty of Pharmacy, Universitas Indonesia, packaged into uniform opaque plastic pots, and physico-chemically tested to show no differences between both creams in colour, viscosity, and scent.

Local produced coconut oil was chosen after a gas chromatography testing for five sources of coconut oil from different islands in Indonesia, and all were found to have identical compositions and characteristics. Sterile laboratory conditions and good manufacturing practices were ensured so that the cream was manufactured safely.[15]

Randomization, treatment allocation, and blinding

A list of random numbers was generated by the study statistician. The investigator and subjects were blinded to the codes, treatments were allocated randomly, and the packaged pots were dispensed appropriately. The codes were not disclosed to the investigators until the end of the study.

Study intervention

Before initiation of the study, all participants were asked to stop using of topical treatments and moisturizing cream for a 1-week wash-out period. Thirty-two participants were randomized into 2 groups: 16 subjects were asked to use *Cocos nucifera-glycerin* (product A) cream and 16 subjects were asked to

use glycerin-only (product B) twice daily for two weeks each group, and between crossover a wash-out period for eight weeks was implemented. Aside from topical treatments used in the study, no other topical treatment was allowed. All subjects were requested to complete daily journals to record the frequency of the products were used each day and to refrain from using other products on their hands. Each subject was given one pot (10 grams) of Cocos nucifera-glycerin cream or glycerin –only cream for 2 days and was instructed to apply the cream to both hands and arms after bath.

Clinical assessment

Clinical evaluation of the effect of moisturizer containing coconut oil and glycerin application over a 2-week period was compared with a glycerin-only moisturizer over the same period. Secondary endpoints included the percentage changes from baseline in HECSI values, TEWL, skin capacitance, and the adverse events during the study. The study endpoints and digital photographs were obtained at every visit.

The clinical severity of OHD was determined using a validated scoring system, Hand Eczema Severity Index (HECSI).[9] This severity grading accounts for the extent and intensity of the lesion. TEWL and skin capacitance were measured on the anterior and posterior aspects of the dominant hand using a tewameter model TM300 and corneometer model CM825 (Courage & Khazaka Electronic GmbH) from Germany, respectively.[16]

The study was terminated for those who had severe adverse events, and dropouts were defined as subjects who did not attend for follow-up within two weeks and whose outcomes were unknown by the end of the study period.

Sample size

The sample size was calculated based on a crossover study and would give a power of 80% to detect at least 20% difference in the mean TEWL assuming an SD of 3.0, using a paired t-test with a 5% two-sided significance level. A sample of 32 subjects would be needed, assuming 10% dropout rate.

Results

Thirty-two batik workers with hand dermatitis were enrolled in the study after informed consent was obtained (Table 1). The flow of subject enrollment is shown in Fig. 1. The patients were recruited from several traditional batik enterprises in Yogyakarta, Central Java, Indonesia.

In the initial period, one subject did not come at the second visit, while at the second period, one subject did not come at both visits. Both subjects denied protocol or side effects of the study as the reason for absence. Before data analysis, data clearance was conducted, and 1,875% missing value was found. However, the data was still fit to be processed using SPSS 22, and the distribution test was done with the Shapiro-Wilk normality test.

Clinical evaluation

Prior to the study, clinical characteristics of 32 subjects based on location, type of dermatitis, and nail discolouration were observed. The lesions occurred on the dorsum aspect of the hand of 2 subjects (6.3%), palmar of 17 subjects (53.1%), the finger of 10 subjects (31.3%), and ginger tips of 3 subjects (9.4%). For the types of hand dermatitis, there was no chronic hand eczema (0%), 2 subjects had recurrent vesicular hand eczema (6.3%), 18 subjects had hyperkeratotic palmar eczema (56.3%) as pictured in Fig. 2. Three subjects had pulpitis (9.4%), and 5 subjects had interdigital eczema (15.6%), while 4 had nummular hand eczema (12,5%). In this study, the predominant location of hand dermatitis was the palmar aspect, with hyperkeratotic palmar eczema as the most prevalent type. Most subjects had nail discolouration (96.97%), while only one subject had no nail discolouration.

Hand Eczema Severity Index

HECSI score was determined (ranging 0-360) based on observation of morphological lesions. Common morphologies were erythema, infiltration, vesicles, fissures, squamous, and edema. During the first period, the lowest baseline HECSI score was 10, and the highest was 54. During the second period, the lowest baseline was 7 and the highest was 54. Compared to the baseline, both groups showed a decrease in the HECSI score. The change in median HECSI score after treatment between periods 1 and 2, in the A-B treatment sequence, was not statistically significant ($p = 0.477$). Likewise, the median change in the HECSI score after treatment in periods 1 and 2, in the B-A treatment sequence, was not statistically significant ($p = 0.166$) (Table 3.). A positive change from baseline indicates a decrease in HECSI and, therefore, an improvement in the skin conditions. Both moisturizers showed a clinically significant treatment effect on HECSI from baseline to day 14.

Effect of treatment on trans-epidermal water loss

The mean value of TEWL for dorsum A-B, and B-A after receiving coconut oil and glycerine-only cream is presented in Fig. 2. In the AB period 1 sequence group, the first group to get coconut oil moisturizing cream, the final TEWL value was 29.6 (9.03) g / m^2 / hour after application of product A, and 18.1 (4.71) g / m^2 / hour after application of product B. The inter-individual difference is 11.5 (9.45) g / m^2 / hour. In the BA group, the mean final TEWL value of the hand dorsum was 18.8 (7.79) g / m^2 / hour after application of product A and 25.9 (6.11) g / m^2 / hour with inter-individual differences of − 7.1 (8.51) g / m^2 / hour.

The final skin capacitance value of the subject's hand in the AB treatment sequence group after the use of product A was 70.77 (28.01) AU, whereas for product B it was 60.52 (10.33) AU, with inter-individual differences of 10, 3 (27.39) AU. Whereas in the B-A treatment sequence group, the final TEWL value on the dorsum of the subject's hand was 67.52 (16.47) AU after using product A, and 78.47 (26.39) AU after application of product B.

Based on the difference in mean HECSI score, the TEWL value and skin capacitance of dorsum hand and palmar skin capacitance between before and after the treatment shown in Table 4,established a difference in batik workers who received coconut oil-glycerin moisturizing cream (product A) and glycerin only (product B). It was determined that the difference is considered meaningful if there is a decrease in the HECSI score of 20%, a decrease in TEWL of 20%, and an increase in skin capacitance of 20%. A 10% decrease in HECSI value was found in 93.8% of subjects, as was the case with the product B group. A decrease in TEWL greater than 20% in the dorsum of the hand was more notable in product B group (81.3%) compared to the product A group (65.6%), and an increase from the baseline was found in 5 subjects for each treatment group.

Of the 32 subjects, no adverse effects were found due to the use of product A and glycerine-only cream. Among 32 subjects, there were 27 (84%) subjects who stated that they liked the distinctive smell of coconut oil in the test cream. Both were given coconut oil aroma for blinding purposes. All subjects felt comfortable using the cream after bathing and do not feel the work is interrupted by the use of both test creams and stated the skin is softer after the use of both test creams.

Discussion

The effectiveness of moisturizers is determined by various components, including active ingredients, vehicle, penetration ability, ease of application, cosmetics acceptance, comfort, and minimal intersection effects.[17] In making moisturizers specifically for occupational fields, it is also necessary to consider the reactions that can occur between the material found in moisturizers and exposure to the workplace environment.[18] The use of moisturizers is expected to not facilitate the penetration of irritant or allergen material, which exacerbates the occurrence of occupational dermatitis.[3] Moisturizing texture needs to be designed so that it does not interfere with work. Adherence to the use of moisturizers is very important to note, workers need to understand the importance of using moisturizers for prevention of dermatitis, as well as the correct use, both frequency and volume of moisturizers.[4,8]

The lipid concentration used, the amount and type of emulsion, humectant, and preservative materials need to be considered, including the pH of the moisturizer.[3,8,15] The active ingredients used in this study were 30% coconut oil and 20% glycerin, as well as the excipients that matched the base cream to obtain oil emulsions in water (o/w). With this composition moisturizer give an occlusive effect and humectant, so that it effectively protects the skin barrier.

This study used 20% glycerin as a humectant in both test creams. Glycerin is an effective humectant and is able to activate transglutaminase in the stratum corneum, accelerate the maturity of corneocytes and act as corneodesmolytics in the process of desquamation, as well as esterification of ceramide.[19] Glycerin also has unique characteristics because it is capable of maintaining moisture of the skin for quite some time even though the material is undetectable on the skin. The effectiveness of glycerin improves skin hydration is closely related to the presence of AQP-3 or aqua-glycoprotein, a membrane

protein expressed most in the basal stratum and serves to facilitate the transport of water in the epidermis.

The most type of hand dermatitis in this study was hyperkeratotic hand eczema. Pro-inflammatory cytokines namely interleukin (IL)-1a, IL-1b, and TNF-a (7), and the chemokine CCL21 that hones naıve T-lymphocytes to the skin, shown to be elevated in the skin during irritant contact dermatitis.[19] Other hand dermatitis found in batik artisans was the interdigital type of eczema in 15.0% of subjects, nummular hand eczema 12.5% of subjects, 9.4% of pulpitis subjects, and recurrent vesicular hand eczema types were found at least. In interdigital eczema type hand dermatitis papule lesions, vesicles, plaques, and squares are found with signs of inflammation.[21] The lateral side of the finger is the transition zone between palmar and dorsum of the hand. There is a progressive evolution between the two-thirds anterior part and the posterior third of the finger. The suspected hand dermatitis is greater if there is involvement of the anatomic location because it is a location that is prone to irritant or allergic contact dermatitis. Nail discoloration was found in 96.9% worker, Discoloration of nails occurs because the gloves used are degraded so that the color material can penetrate the glove and then penetrate into the nails.

The normal TEWL value for the palmar area was 41.69–46.37 g/m2/hour and hand dorsum were 10.00–13.16 g/m2/hour. After the use of moisturizer for 2 weeks, in both groups there was a decrease in TEWL on the dorsum hand and palmar ompared to the baseline. Decreasing the TEWL value of the dorsum of the hand and palmar after administration of product B in the A-B sequence turned out to be greater than the administration of coconut oil moisturizing cream. Possibly the conditions in the second period of the subject have not returned to the baseline due to the carry-over effect being removed with a long wash out period of 8 consecutive weeks. Unlike the case with the B-A group who received product B first, both the decrease in TEWL value of the dorsum of the hand and the palmar was greater in giving product A than product B, but the therapeutic effect on TEWL of the hand dorsum and palmar after the administration of coconut oil or product B moisturizing cream is similar. Clinically, the decrease in palmar TEWL values in the two treatment groups was not as large as the decrease in TEWL value on the dorsum of the hand. Only 46.9% experienced a decrease in TEWL of more than 20% in the product A group, and 43.8% in the product B group. The palmar location is the area most experienced by workers in the form of hyperkeratotic lesions. This can affect the penetration of coconut oil and product B moisturizing creams, making it less effective in reducing TEWL values.

This study was carried out on the actual conditions of Batik artisans, who continue to work with exposure to irritants and allergens as usual. Thus, the results obtained can reflect the real situation and are expected to contribute to improving the health of batik workers. The limitations of this study are the work environment and surrounding factors, temperature and humidity at work, and the workload per day cannot be controlled from time to time. This condition can affect the value of TEWL and skin capacitance during the use of the test cream.

According to the specific aim of this study, it can be concluded that both interventions group showed decrease in HECSI more than 20% for about 93.8% of the subjects. The treatment effects of product A and B was found to be exactly same. Most common hand dermatitis type was palmar hyperkeratosis (56.5%) found at 90.63% subjects, as well as nail discoloration at 31% of the subjects (96.97%). Decrease of TEWL score for more than 20% at dorsal and palmar parts of the hand after 14 days of product A application compared to product B. The treatment effects of product A and the product B was found to be exact. Increase in skin capacitance for more than 20% at dorsal and palmar parts of the hand after 14 days of product A application compared to product B. There were no side effects occurring due to product A nor the product B found among the 32 workers, after subjective and objective evaluations. There were no signs and symptoms of poor interactions between moisturizers and exposure to materials used at work. A total of 27 (84%) subjects stated that they liked the distinctive smell of product A. All subjects did not feel work was interrupted by the use of product A and B.

According to the result of this study, several factors need to be implemented such as: recommending the use of coconut oil containing moisturizers and glycerine among Batik worker in the rinsing and dyeing sections, that support the occupational safety health program.

Conclusion

Both glycerin-Cocos nucifera combination and glycerin-only formulation cream are equally effective for secondary prevention for OHD among fabric workers in Indonesia. Afterwork moisturizers as secondary prevention of hand dermatitis among fabric workers should be encouraged as means to reduce disease prevalence.

Declarations

Conflict of Interest

All authors have declared no conflict of interest.

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Tables

Table 1. Sociodemographic Characteristics of Subjects (N=32)

No	Variables	n	(%)
1.	Age (year)		
	25 – 40	16	(50.0)
	41 – 60	16	(50.0)
3.	Batik Processing Section		
	Dyeing	11	(34.4)
	Rinsing	3	(9.4)
	Dyeing and Rinsing	18	(56.3)
4.	Period of Work (years)		
	1 – 5	15	(46.9)
	6 – 10	7	(21.9)
	> 10	10	(31.3)
5.	Working Time (hours)		
	< 8	7	(21.9)
	³ 8	25	(78.1)
6.	Use of PPE		
	No	19	(59.4)
	Yes	13	(40.6)
10.	History of atopic dermatitis		
	No	29	(90.6)
	Yes	3	(9.4)
14.	Onset of dermatitis (years)		
	< 1	8	(25.0)
	1-5	17	(53.1)
	> 5	7	(21.9)

Table 2. HECSI, TEWL, and Skin capasitance *Baseline* against subject groups (Mean (Standard Deviation))

No	Variales	Product A (N=32)	Product B (N=31)	P
1.	Hand Eczema Score Index	21.00(12.75)	22.00(13.75)	0.59
2.	Trans epidermal water loss (g/m^2/hour)			
	Dorsal hand	39.69(14.27)	44.10(15,66)	0.17
	Palmar	54.93(10.89	56.44(9.82)	0.46
3.	Skin capacitance (AU)			
	Dorsum hand	53.96(24.30)	52.79(19,11)	0.83
	Palmar	54.46(22.91)	50.66(25.67)	0.51

Table 3. HECSI Score after treatment based on Sequence group (median (IQR))

Sequence group	Treatment period 1	Treatment period 2	p-value
A-B	8.5 (12)	10.0 (8)	0.477
B-A	9.5 (6)	11.5 (6)	0.166

Note :

Non parametric test: Wilcoxon.

A-B : group receiving coconut cream treatment followed by product B

B-A: group receiving product B treatment followed by treatment

Table 4. Relative Differences of Baseline Score of HECSI, TEWL dan Scap between two groups

Parameter	Cream (n=32)				Statistical analysis
	Product A		Product B		
	n	%	n	%	
HECSI Score					p=0.59
Decrease > 20%	30	93.8	30	93.8	
Decrease 0.1–20%	1	3.1	0	0.0	
Score from baseline	1	3.1	0	0.0	
Increase from baseline	0	0.0	2	6.2	
TEWL dorsal hand					p=0.17
Decrease > 20%	21	65.6	26	81.3	
Decrease 0.1–20%	6	18.8	1	3.1	
Increase from baseline	5	15.6	5	15.6	
TEWL palmar					p=0.46
Decrease > 20%	15	46.9	14	43.8	
Decrease 0.1–20%	7	21.9	12	37.5	
Increase from baseline	10	31.3	6	18.8	
Skin Capacitance dorsal hand					p=0.83
Increase > 20%	20	62.5	21	65.6	
Increase 0.1–20%	7	21.9	4	12.5	
Decrease from baseline	5	15.6	7	21.9	
Skin Capacitance palmar					p=0.51
Increase > 20%	20	62.5	21	65.6	
Increase 0.1–20%	5	15.6	5	15.6	
Decrease from baseline	7	21.9	6	18.8	

Figures

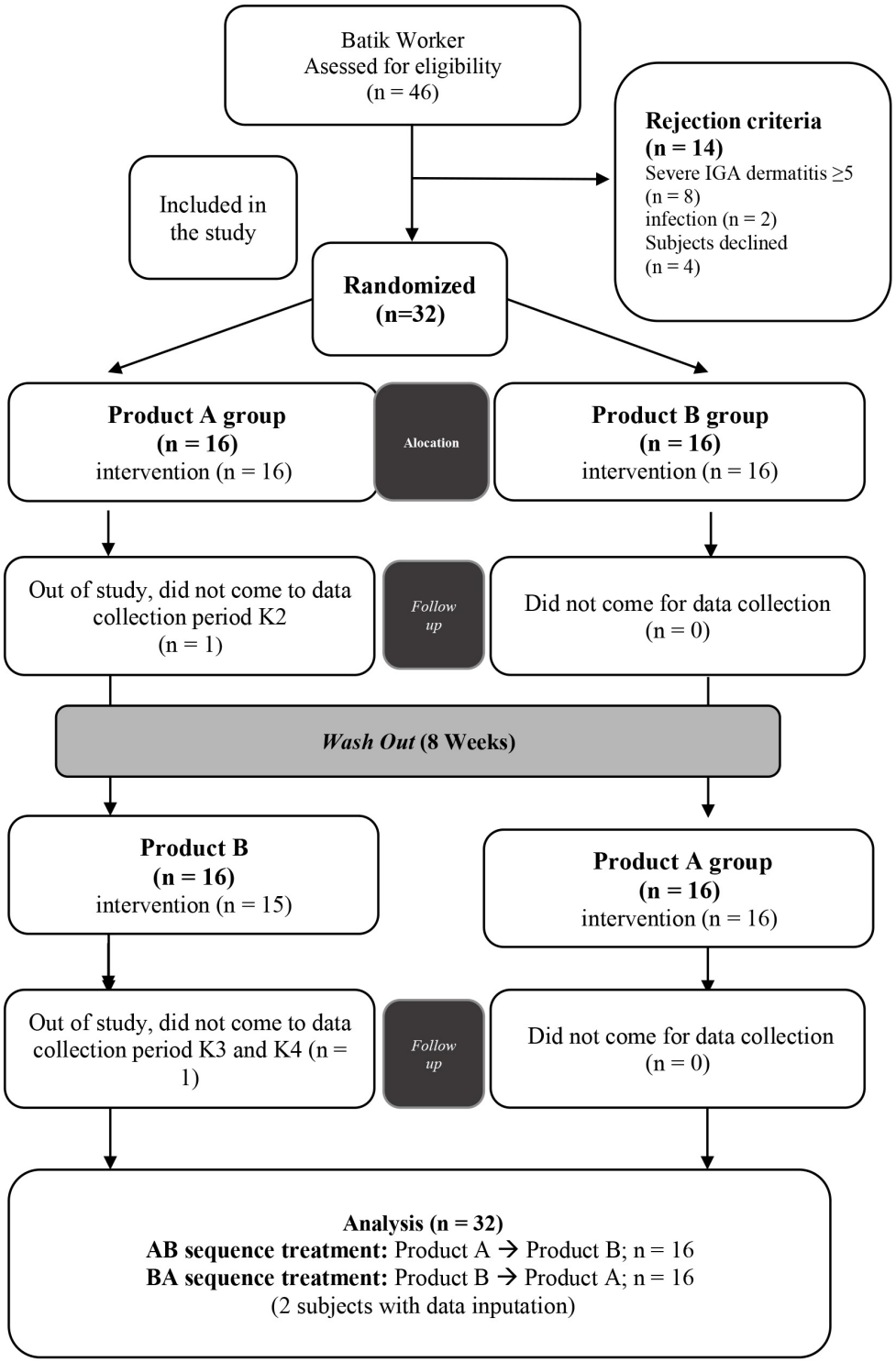

Figure 1

Flow of research study

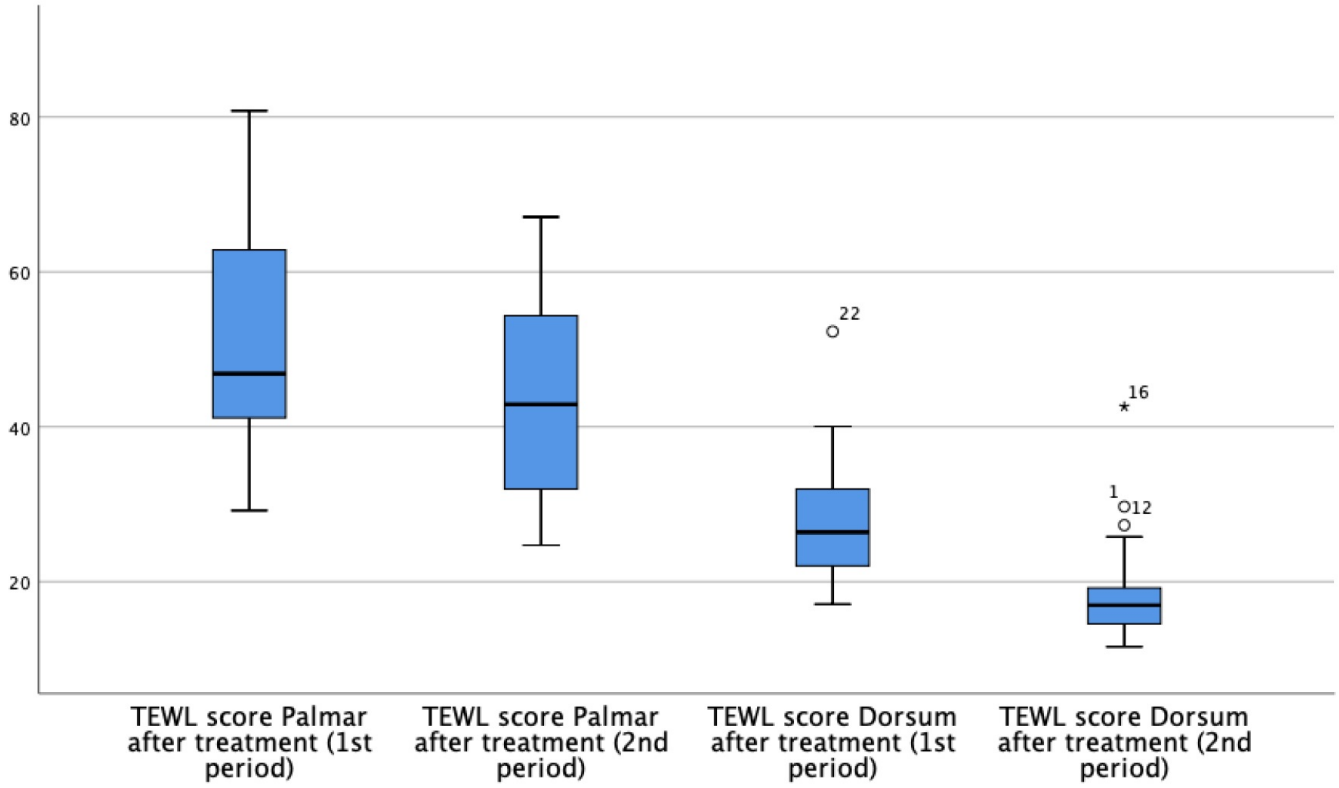

Figure 2

Mean of TEWL day 14 on Dorsal (left) and Palmar (right) Hand between 2 period for each Treatment Sequence

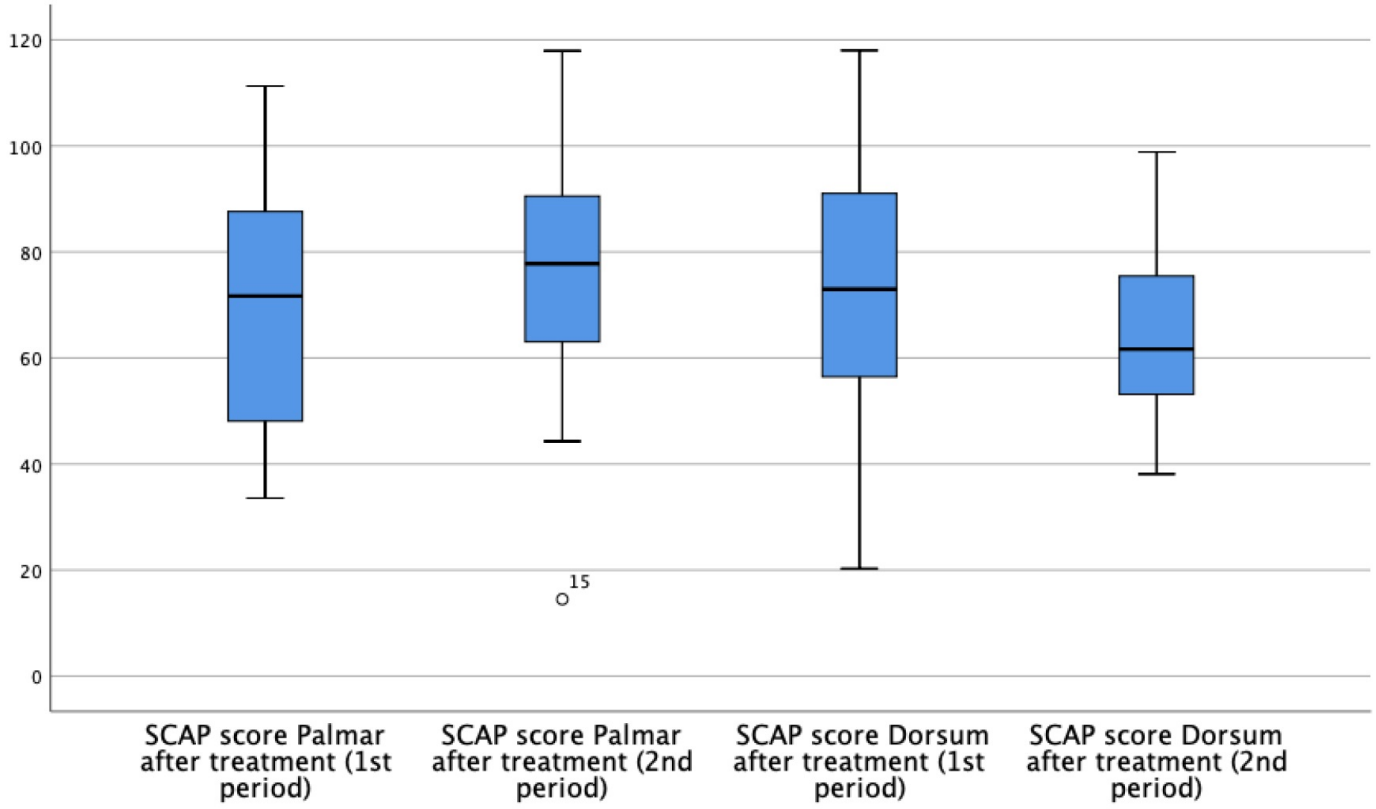

Figure 3

Mean of skin capacitance day 14 on Dorsum Hand (left) and Palmar Hand (right) between 2 period for each Treatment Sequence