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The effect of electrical stimulation on skin vulnerability to irritants

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Abstract

Purpose: Electrical stimulation (ES) is a widely used technique in the medical field for various purposes. The effect of ES on several skin properties has been investigated; however, its effect on skin vulnerability to irritants remains unknown. This study aimed to investigate the effects of ES application on skin vulnerability to external irritants.

Materials and methods: An experimental study on 12 healthy male subjects (Mean ± SD, 22.9 ± 3.6 years) who completed the study. The subjects were free of skin abnormalities in the volar aspect of both forearms. Three areas were allocated to each forearm and marked as areas 1, 2, and A in the treated forearm, and areas 3, 4, and B in the control forearm. ES was applied to the volar aspect of the treated forearm for 30 min three times a week, for 2 weeks. The effect of ES on skin vulnerability was investigated using 5% and 0.5% sodium lauryl sulfate (SLS) patches applied to both treated and control forearms. The skin response to irritants was evaluated using transepidermal water loss (TEWL) and a visual erythema score 24 h after patch removal.

Results: Compared to the control forearm, ES increased skin permeability and erythema in response to external irritants (SLS), as measured by the visual analog score ($Z = 2.75$, $p = 0.006$) and TEWL ($p < 0.05$), respectively.

Conclusions: ES escalates skin reactions to low concentrations of irritant substances, such as SLS, in the area between the two electrodes. This emphasizes the use of this substance, and similar irritants should be avoided in areas treated with ES.

KEYWORDS
electrical stimulation, physical therapy, skin irritation, skin vulnerability, transepidermal water loss

1 | INTRODUCTION

Numerous studies have investigated the clinical effects of electrical stimulation (ES) in humans. Studies have demonstrated that ES is an effective therapeutic modality for strengthening muscles,[1] reducing spasticity,[2] relieving pain,[3] promoting wound healing,[4] increasing skin blood flow,[5] and alleviating itching in certain dermatological conditions.[6]

When ES is applied, the current is typically delivered via noninvasive surface electrodes and electrically conducting media between the electrodes and skin. Depending on the condition being treated and the type of current employed, the electrodes must remain in contact

with the skin for 30 min to 24 h.[7] This procedure may compromise the integrity and properties of the skin beneath the electrodes. According to previous studies, the skin beneath electrodes is susceptible to skin contact irritation and allergic reactions. Approximately 40% of individuals who use transcutaneous nerve electrical stimulation (TENS) develop skin contact dermatitis.[8,9] Contact dermatitis has been reported following continuous TENS electrode use. It can be brought on by direct contact with allergens such as acrylic acid in self-adhesive electrodes,[10,11] propylene glycol in conductive gel,[12] or rubber and nickel in a TENS electrode.[13–15] Although the studies cited may have demonstrated limited skin irritation or dermatitis within the electrode boundaries, it is important to keep in mind that the electrical current has the potential to affect areas of the skin and other tissues that it passes through, which may lead to further adverse reactions.

It has been shown that ES can alter the properties of the epidermis between the electrodes. Nevertheless, this modification may not necessarily have a lasting effect on the epidermis. It has been observed that ES induced a transitional increase in transepidermal water loss (TEWL) that persisted approximately 30 min after ES ceased.[16] In a similar manner, an increase in skin blood flow has been observed between electrodes in both normal and injured epidermis.[5–7,16,17] Moreover, research suggests that ES can improve the absorption and efficacy of skincare products by augmenting the skin's absorption of topically applied substances.[18] Since ES can alter the skin's properties and increase its permeability, it is crucial to consider whether this immediate effect will make the skin area between the electrodes more sensitive to external irritants or chemicals.[19]

The chemical compound sodium lauryl sulfate (SLS) is recognized as the standard stimulant. This substance was used to evaluate the skin irritation to exogenous stimulants.[20] SLS is commonly found in cleaning and personal care products.[21] It has been demonstrated that skin irritation affects the constant state of water vapor loss through the skin layers, also known as TEWL.[22] The TEWL is a crucial indicator of the stratum corneum's performance as the primary barrier to water loss. It is frequently used to assess healthy, damaged, and diseased epidermis.[23,24] In our study, we used both visual erythema scoring and TEWL to determine the level of SLS-induced skin irritation after ES.

Although considerable research has been dedicated to the relationship between ES and skin irritation, no study has examined the impact of ES on skin susceptibility or hyperreactivity to irritants in the region between the electrodes. This study aimed to investigate whether ES enhances the vulnerability of the skin and its tendency to irritate the region between the ES electrodes using SLS. We hypothesized that ES would enhance skin vulnerability and make the skin more prone to irritation from SLS, as indicated by the elevated visual erythema score and TEWL.

2 | MATERIAL AND METHODS

Participants were recruited through advertisements at Hashemite University College of Applied Health Sciences in Zarqa, Jordan. The participants were healthy males with Fitzpatrick skin types II to V and were free of skin diseases and abnormalities (i.e., rashes, wounds, scars, atopic dermatitis, psoriasis, eczema, and erythema) in the volar aspect of both forearms. Female participants were not included in this study to avoid any cyclic hormonal effects on skin TEWL, and other skin properties shown by women during normal menstrual cycles.[25]

2.1 | Subjects

In accordance with the inclusion and exclusion criteria, this study included 22 (N = 22) healthy male participants with the following characteristics: age (MSD, 22.93.6 years), weight (77.613.3 kg), height (175.16.4 cm), and BMI (26.4 5.8%). All participants were prohibited from applying cosmetics, personal care products, or medicinal formulations to their forearms for 48 h prior to and throughout the study. They were instructed against applying shampoos or body soaps on the volar aspect of their forearms or using loofahs. However, routine bathing was permitted throughout the study period. Participants were provided with a no-exercise directive for the day preceding the study. Water and shaving should be avoided at the measurement locations 48 h prior to measurement. The participants were strongly encouraged to abstain from consuming caffeinated beverages for a minimum of 3 h before performing the measurements.

Only 12 participants completed the study, according to the study protocol. Ten subjects dropped out of the study; six subjects missed the measurement session, and four subjects did not adhere to the study protocols.

The study was conducted in accordance with the revised Declaration of Helsinki of 2000 and the National Institutes of Health procedures for healthy volunteers. All procedures and experimental methods were explained to each participant, who then signed an informed consent form. The study procedures and consent forms were approved by the institutional review board of the Hashemite University.

2.2 | Electrical stimulation

TNES was provided using a current-controlled electrical stimulator (Sonoplus 992, Enrouf, Holland). The stimulator provided a balanced current of biphasic square waves. The pulse width was 200 μs at a frequency of 30 pulse/s, with a maximum current intensity of 30 mA. The current was delivered through two carbon-based rubber electrodes (4 cm × 6 cm, Enrouf, Holland) by using an electrode gel (Spectra 360 electrode gel, Parker Laboratories, Inc. New Jersey, USA) to maximize the electrical conductivity with minimal skin impedance.[26]

2.3 | Skin TEWL measurement apparatus

TEWL was measured using a noninvasive Tewameter TM 300 as part of a Multiprobe Adapter System MPA (Courage + Khazaka Electronic

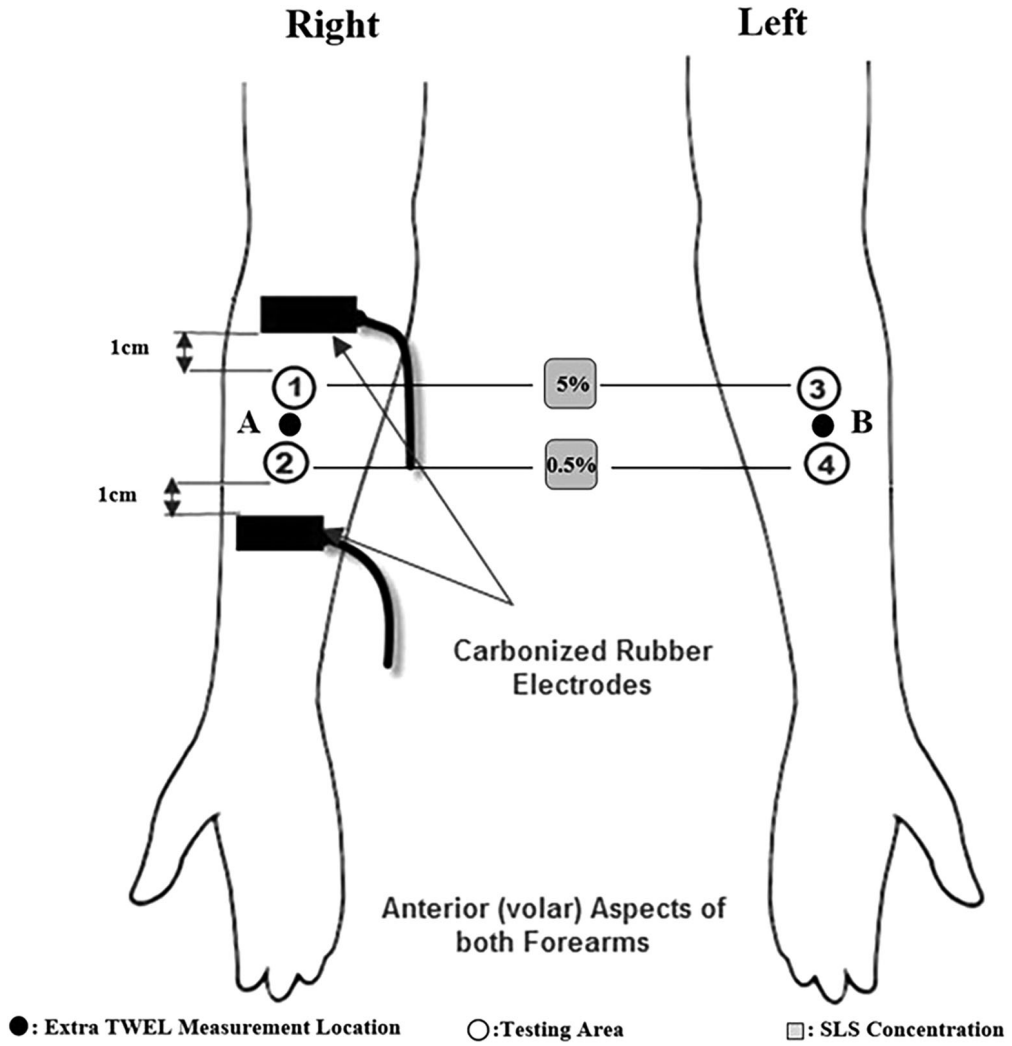

FIGURE 1 The figure depicts the electrode positions and the four measurement areas (1, 2, 3, and 4). Right areas 1 and 2 were electrically stimulated and patched with sodium lauryl sulfate (SLS) (5% and 0.5%). Control areas 3 and 4 on the left were patched at 5% and 0.5%, respectively. Electrodes were placed 8 cm apart. Each area was 2 cm wide and 2 cm apart. A and B are additional TWEL measurement locations used for pre- and 24-h post-patch comparisons.

GmbH, Germany). The system was connected to a PC via a USB cable, and all the TEWL readings were stored for subsequent analysis. TEWL was measured according to the approved guidelines of the European Society of Contact Dermatitis standardization group.[27] Measurement is based on the measurement of TEWL on the surface of the skin using two pairs of sensors placed in a cylindrical probe (relative humidity and temperature). The TEWL was measured by gently placing the probe head on the skin and pressing the probe button. The TEWL measurements were made 40 s after the probe was applied and when the TEWL level had stabilized. The values are recorded in $g/m^2/h$.

Skin susceptibility to irritants was assessed using two patches with different SLS concentrations (5% and 0.5%). A paper disc impregnated with 60 μL of 5% or 0.5% SLS (Sigma Ultra, Japan) was placed in an 11 mm Finn Chamber (Epitest Ltd., Finland) at four different locations on both forearms for 24 h (Figure 1). The test was performed in accordance with the European Association of Contact Dermatitis Standards Group Guidelines.[20] Then, 24 h after the removal of the SLS patch, both visual erythema scores and TEWL were recorded for each area.

2.4 | Core temperature

The core body temperature was measured using a tympanic infrared thermometer (Beurer, FT55, Germany). The thermometer measured the infrared heat generated by the eardrums and the surrounding tissues. Temperatures are expressed in centimeters.

2.5 | Procedures

In a room with a controlled ambient temperature of (21 ± 0.5°C) and a relative humidity of 25%–30%, ES and all measurements were taken.

Before the investigation began, the participants sat comfortably in this room for at least 15 min to acclimate. To prevent weather-related skin or body temperature effects. An acclimatization period was required because the study was conducted in the morning hours of autumn when the temperature was still warm. Following the acclimatization period, the experimental and control arms were randomly assigned. The measurement points on both forearms were marked with a template made up of two circles, each 2 cm in diameter and spaced 2 cm apart. Areas 1 and 2 were assigned to the experimental forearm, whereas areas 3 and 4 were assigned to the control forearm. Two carbonized rubber electrodes (4 cm× 6 cm, Enraf-Nonius, Germany) placed 8 cm apart were used to deliver ES to the experimental forearm. The electrodes were secured to the participant's skin on the volar aspect of the forearm by using medical adhesive tape. Without producing any pain or discomfort, the electrical current intensity was clamped slightly below each subject's threshold at the beginning of the muscle contraction. ES was applied to the experimental forearm three times a week for 30 min over a 2-week period. Each session lasted 45 min on average for the participants.

At the end of the 2 weeks of ES application, baseline readings of core temperature, TWEL, and visual erythema scores were recorded for all areas (1 to 4). Subsequently, we studied the susceptibility of the skin to irritants. Fresh 5% and 0.5% aqueous SLS solutions were patched on the subjects at the four locations listed above (Figure 1) and left for 24 h. In a 12 mm Finn Chamber, a paper disc impregnated with 60 μL of 5% or 0.5% SLS was placed and then the chambers were fixed in their designated locations. Area 1 in the experimental forearm received SLS 5%, Area 2 received SLS 0.5% and Areas 3 and 4 in the control forearm received 5% and 0.5% SLS, respectively. Before the patch was removed 24 h later, the TWEL and erythema scores were measured at two additional locations: location A between areas 1 and 2 and location B between areas 3 and 4. In addition, core temperatures were measured (Figure 1). The patches were then removed and the targeted regions were cleaned with distilled water for at least 60 s. The participants were then told to return after 24 h. The core temperature, TEWL, and visual erythema scores were recorded 24 h after patch removal in Areas 1, 2, 3, 4, A, and B. The new measurements in areas A and B were compared with the initial readings to rule out any skin changes that occurred within the previous 24 h, which could have influenced the results. TWEL's mean value was calculated by averaging three individual measurements. The Tewameter TM 300 probe was placed directly and horizontally on the designated skin areas of both forearms for 40 s, while providing modest and continuous pressure.

Visual erythema scores were obtained in accordance with the European Association of Contact Dermatitis guidelines for the clinical assessment of acute SLS irritant reactions.[20] The level of irritation was visually measured using the following scale: 0, no visible reaction; 1, tobacco paper appearance without erythema; 2, slight patches of erythema; 3, homogeneous erythema; 4, erythema with edema; 5, erythema, edema, and veins/bulla12. An IScope 10× camera (Iscope, Japan) was used to capture digital images of the treatment and control sites. The procedure is summarized in a flow chart (Figure 2).

2.6 | Statistical analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) for Windows (version 23.0, SPSS Inc., NY, USA). All statistical analyses were conducted at a significance level of $p < 0.05$. The mean values of the TWEL measurements were expressed as mean ± standard deviation (M ± S). A paired *t*-test was used to determine how the mean values of the two TWEL measurements changed within the group. The ordinal variable scores for visual erythema were analyzed based on the ranking of the differences between the scores. The nonparametric Wilcoxon signed-rank test was used to compare the differences in visual erythema scores before and 24 h after SLS patch removal from both the forearms.

3 | RESULTS

During the research, the average ambient temperature of the experimental room was (21 ± 0.5°C), and the average electrical current intensity was (12.5 ± 4.7 mA). The average tympanic temperature for all subjects was (36.6 ± 0.3°C), and there was no significant increase in core temperature between 24 h prior to the application of the patch and 24 h after its removal. In addition, no participant experienced any type of skin irritation during or after the ES application.

At the time and after 24 h after patch removal, two additional TWEL readings were taken between allocated areas 1 and 2 (area A) on the experimental forearm and areas 3 and 4 (area B) on the control forearm (Figure 1). These readings were compared with the baseline readings on the same forearm to ensure that no other changes could occur in the skin during the patching time and 24 h after patch removal in the TWEL measurements. No significant differences were found between the two readings in areas A and B or between them and the baseline readings in each forearm.

In the experimental forearm, the mean TEWL (Table 1) values increased significantly in area 1 (18.9 ± 7.8 g/m^2/h, $p = 0.002$) and area 2 (13.6 ± 3.7 g/m^2/h, $p = 0.003$), in comparison to their baseline values of (10.8 ± 3.7 g/m^2/h) and (10.6 ± 4.1 g/m^2/h) for areas 1 and 2, respectively (Figure 3). In the control forearm, there was a significant increase in TWEL in area 3 (16.8 ± 6.1 g/m^2/h, $p = 0.001$) and no significant increase in area 4 (12.4 ± 3.4, $p = 0.09$) g/m^2/h in comparison to their baseline values (10.4 ± 3.3 g/m^2/h) and (11.0 ± 3.6 g/m^2/h) for area 3 and 4, respectively (Figure 3). When comparing the mean TEWL values of the two forearms 24 h after patch removal, areas 1 and 2 were significantly higher than areas 3 ($p = 0.04$) and 4 ($p = 0.005$).

The visual score of erythema showed that the 5% SLS solution was strong enough to cause obvious irritation in both areas: area 1 ($Z = -2.7$, $p < 0.01$) in the experimental forearm and area 3 ($Z = -2.1$, $p = 0.03$) in the control forearm. Furthermore, the visual erythema scores for area 1 were significantly higher than those for area 3 ($Z = -2.2$, $p = 0.03$). However, the low concentration of SLS (0.5%) was not sufficient to induce a significant change in visual erythema scores

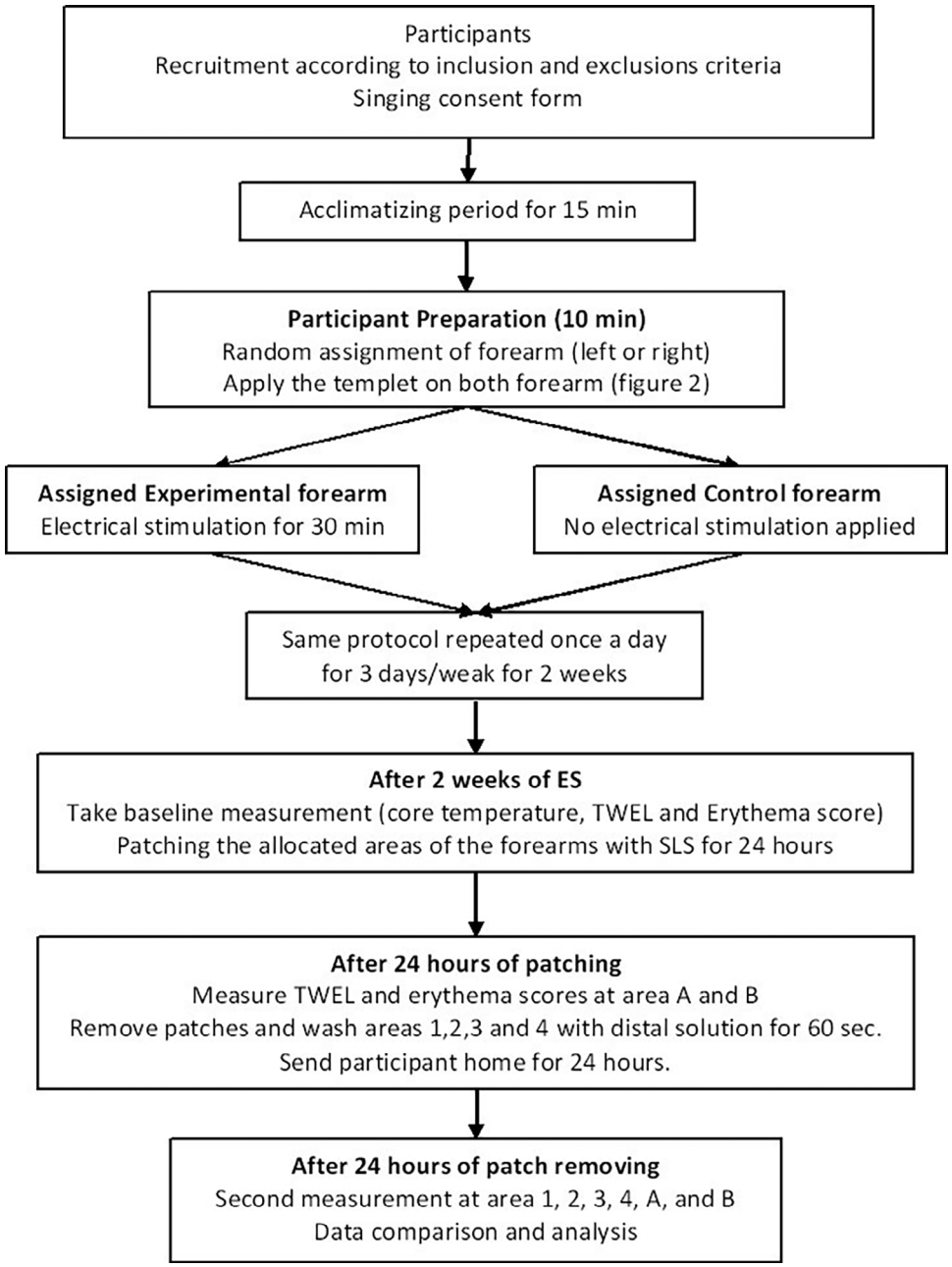

FIGURE 2 Flowchart of the study procedure.

for areas 2 ($Z = -1.36$, $p = 0.1$) and 4 ($Z = -1.36$, $p = 0.1$), and no significant differences ($Z = 0.0$, $p = 1.0$) were observed between them (Figure 4).

4 | DISCUSSION

We used TWEL and visual erythema scores to assess skin irritation, as they have been extensively utilized in several studies for this purpose.[19–24] This study demonstrated that ES makes the skin more sensitive to irritating stimuli such as SLS, even at concentrations as low as 0.5%. Even more so, with higher concentrations of SLS (5%) com-

TABLE 1 Transepidermal water loss (TWEL) mean values after 24 h of patch removal for areas 1, 2, 3, and 4 on the experimental and control forearms.

		Baseline		Post 24 h		*t*-test
		M	SD	*M*	SD	*p*
Experimental area	**1**	10.8	3.7	18.9	7.8*	0.002
	2	10.6	4.1	13.6	3.7*	0.003
Control area	**3**	10.4	3.3	16.8	6.1*	0.001
	4	11.0	3.6	12.4	3.4	0.086

Abbreviations: M, mean; SD, standard deviation.
*Significant compared to the baseline.

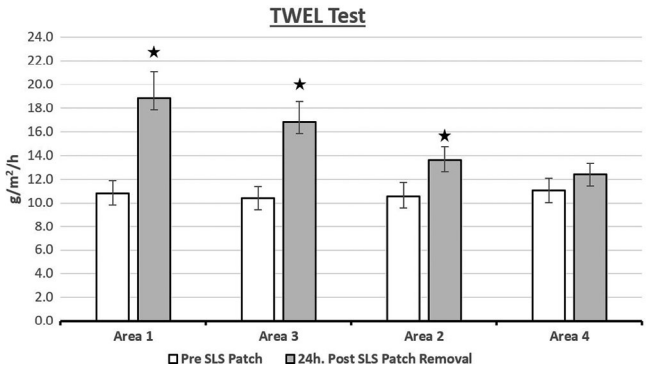

FIGURE 3 Transepidermal water loss (TEWL) 24 h after sodium lauryl sulfate (SLS) patch removal. Areas 1 and 2 on the experimental forearm and areas 3 and 4 on the control forearm were patched with 5% and 0.5% SLS, respectively. (*) TEWL results were significant compared to baseline.

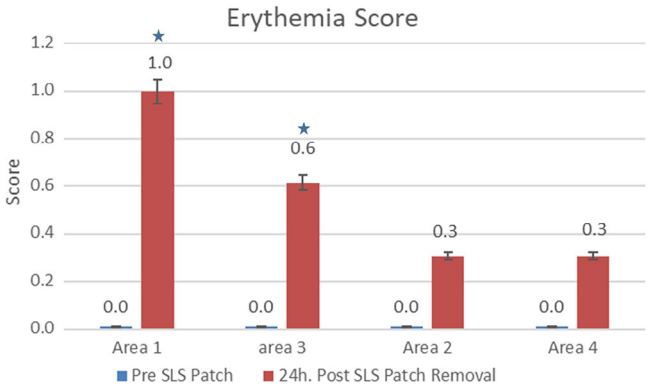

FIGURE 4 Visual skin erythema scores before and 24 h after patch removal. (*) Significant compared to baseline values.

pared to skin that had not been exposed to ES (Table 1). Previously, ES was observed to cause a transitory improvement in skin permeability, which dissipated shortly after ES was discontinued and did not result in a permanent increase in TEWL.[16]

Extensive research has shown that the use of ES in iontophoresis improves the delivery of topical medications through the skin by repelling or attracting ions.[7,18] Studies have revealed that the stratum corneum gait mechanism, known as electroporation, increases permeability.[18,28] Here, drug delivery occurs directly beneath the electrodes of the electrical stimulator. In none of these investigations were the regions between the electrodes considered. Almalty et al. found that the transient change in permeability is not restricted to the regions beneath the electrodes but also includes the space between them.[16] And as a consequence of this increased permeability, both drugs and irritant chemicals can more easily permeate the epidermis.

When ES is used in therapeutic applications, there is always a region between the electrodes that completes the circuit and makes the ES efficient. This area should be taken into account, especially for those who have to use ES for an extended period of time or multiple times a day.[7] Topical medications were suggested to be administered to this area immediately after ES, due to transient improved permeability for rapid penetration and absorption of the skin.[16] However, based on the findings of the current study, we do not recommend exposing this area to any products that contain irritating compounds such as SLS or other comparable irritants. These chemicals can be found in cleaning products, cosmetics, and personal care items such as soap, shampoo, creams, lotions, and skin cleansers. SLS has been found in a variety of cosmetic products at concentrations ranging from 1% to 50%,[21] as well as in a variety of cleaning products at concentrations ranging from 1% to 30%.[29]

The present study showed that a relatively low concentration of SLS (0.5%) was not capable of irritating normal healthy skin without ES, which is consistent with the findings of De Jongh et al.[30] who found that a concentration of 1% to 2% of SLS is needed to irritate normal healthy skin. Furthermore, irritation was worse with ES when a higher concentration of SLS (5%) was used, which was capable of irritating normal skin, even without ES. Therefore, when treating a patient with ES, be informed of the complications associated with exposing the patient to any of the aforementioned products. In these products, SLS concentrations can be 6 to 10 times higher than the concentration used in this study,[29] which may increase the risk of irritating the skin. Furthermore, repeated ES treatment and the use of one or more products containing irritants may expose patients to continuous skin irritation. This can lead to a reduction in the defense components of the skin barrier, such as natural moisturizing factors and the development of atopic dermatitis.[31] Furthermore, the area between the electrodes can range from a small area, such as that used in this study, to large or multiple areas, depending on the body part treated and the number and size of the electrodes used.

Previously, ES was administered under the supervision of professionals in clinical settings; however, it is now commercially available online or over the counter at a low price, and can be administered at home. In addition to medical applications, ES is also utilized in cosmetics and sports.[32,33] The market size for ES devices is projected to reach 5.48$ billion by 2030, up from an estimated 3.47$ billion by 2021.[34] Because of the expansion of the ES device industry and the unsupervised use of ES. Users of all types of electrical stimulators must be informed and warned about their adverse effects. Studies have shown that all types and configurations of electrical waves can increase the skin's permeability to topical medications and other chemical products that can be applied to the skin during or after ES sessions.[16,18] Therefore, the manufacturers of these devices must include a warning in the user manual regarding the potential for skin irritation when using chemical products during or immediately after using ES.

Despite the small sample size and the use of SLS as an irritant alone, this study opens the door for further research on SLS-like compounds. Our findings are based on patching subjects with SLS for 24 h, which is not the same as using irritant-containing products in everyday life. However, the regular use of products containing SLS or comparable irritants along with ES may result in the same results as those revealed in this study. As a result, this study can help to understand the effects of topical irritants, even at low concentrations, on the skin of patients who have received ES. Additional research is required to corroborate the

effect of irritant-containing products on the skin responses associated with ES.

5 | CONCLUSIONS

ES increases the vulnerability of the skin to irritants, such as SLS. The concentrations of these chemical compounds and associated irritants can be higher in many household cleaning and personal care products than the concentrations used in this investigation. This study introduces an additional warning regarding the utilization of ES by healthcare professionals who regularly incorporate it into their treatment methods as well as individuals who self-administer it. Healthcare practitioners and individuals who use ES should be cautious when using ES and products that include SLS or similar substances during or immediately after using ES, to avoid skin irritation.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Any data related to the study can be provided upon reasonable request.

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