

Skin Tolerance of a New Bath Oil Containing St. John's Wort Extract

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Key Words

Bath oil • Contact dermatitis • Detergents • *Hypericum perforatum* • Skin barrier • Transepidermal water loss • Sodium lauryl sulfate

Abstract

Background: Dry and atopic skin requires skin care with lipid-rich emollients and moisturizing bath or shower oils. However, it has been shown recently that some bath oils may even impair the skin barrier. **Objective:** To investigate the skin-irritating potential of a new bath oil containing a lipophilic St. John's wort (*Hypericum perforatum*) extract. **Methods:** In this single-center, randomized, double-blind, prospective study, 3 bath oils together with positive and negative controls were applied under occlusion on test areas on the volar forearms of 18 volunteers (visit 1). After 24 h, the tapes were removed, and the test areas were evaluated by a visual score and the instrumental measurement of skin erythema and transepidermal water loss (TEWL) using a Mexameter and a Tewameter (visit 2). The test substances were applied a second time, and the measurements were performed after another 24 h (visit 3). **Results:** The positive control, 1% vol/vol sodium lauryl sulfate (SLS), caused a significant increase in skin erythema and TEWL. In contrast, distilled water as a negative control did not influence these parameters. The new bath oil containing St. John's wort extract and 1 of the

other 2 commercial products were not different from the water control. The third bath oil displayed a skin-irritating effect similar to SLS. **Conclusion:** The results of this study confirm the different skin-irritating potential of bath oils and demonstrate good skin tolerance of the new bath oil containing St. John's wort extract.

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Introduction

The human skin represents a physical barrier which is constituted by a lipid- and keratin-containing water-repellent layer, the stratum corneum. Extraction of lipids by repeated contact with soaps and detergent agents leads to sustained deterioration of the skin barrier function. An impaired barrier function results in an increased susceptibility of the skin to further irritation, accompanied by epidermal hyperplasia and inflammation [1]. First signs of irritated skin are itchiness, dryness, redness and tightness [2], possibly turning into contact dermatitis [1, 3]. Since regular skin cleansing is important for healthy as well as for diseased skin, the choice of the cleansing agent is of critical importance. Some surfactants are

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poorly tolerated by the skin [4]. The majority of irritant or allergic reactions to cosmetics is considered to be caused by cleansing agents such as soaps, shower gels or bath foams [2]. Recently, an irritating potential of various shower and bath oils has been demonstrated in an occlusive patch test model compared to distilled water and sodium lauryl sulfate (SLS) as negative and positive controls, respectively [5]. Moreover, it has been demonstrated that irritating amounts of surfactants from soaps remained on the skin after rinsing, which was considered the cause for skin irritations [6].

The identification and avoidance of irritant and allergenic substances is a prerequisite for the prevention of contact dermatitis. Additionally, treatment with moisturizing agents contributes to skin protection, reducing dryness and the risk of eczema. It has been shown that the use of moisturizers improves the skin barrier function and renders the skin less susceptible to irritant agents [7, 8]. Continued use of moisturizers reduces skin dryness within symptom-free intervals of a skin disease [9, 10]. The consistent use of shower and bath oils leaves a protective lipid layer on the skin [11–13]. The use of bath oils displays positive effects such as cleansing, disinfection, reduction of pruritus and improvement of psychological well-being [14–16].

Recent investigations suggest anti-inflammatory and antibacterial effects of hyperforin, which is a major lipophilic constituent of *Hypericum perforatum* L. (St. John's wort). It has been shown that a cream containing St. John's wort alleviates the symptoms of atopic eczema significantly better than placebo [17]. The aim of the present study was to determine the skin tolerance of a new bath oil containing St. John's wort extract for daily skin care of dry and inflammatory skin conditions.

Methods

In the prospective randomized trial, 18 subjects aged between 21 and 55 years were investigated. The study was approved by the ethics committee of the University of Freiburg, Germany, and was performed according to established good clinical practice guidelines. All subjects enrolled in the study gave their written informed consent. Healthy persons of both sexes, aged at least 18 years with full contractual capability, were included. Exclusion criteria were inflammatory skin diseases, metabolic diseases, use of any drugs except for contraceptives, alcohol consumption, infections, impaired contractual capability as well as participation in other clinical studies during the previous 30 days. Furthermore, no skin care products were allowed on the test areas 3 days before the onset of the study. Also, the volunteers had to avoid contact of the test sites with water, soap and shower gel.

Table 1. International Cosmetic Ingredient (INCI) labeling of the tested bath oils

Oil	INCI declaration
A	Caprylic/capric triglyceride, oleum ricini, polyglyceryl-2-laurate, polyglyceryl-3-palmitate, <i>Brassica oleifera</i> oil, soybean oil, <i>Argania spinosa</i> oil, <i>Prunus armeniaca</i> oil, <i>Hypericum perforatum</i> extract, tocopherol, oleum menthae piperitae, L-ascorbic acid-6-palmitate
B	Soybean oil, butylhydroxytoluol, L(+)-6- <i>o</i> -palmitoyl ascorbic acid, laurmacrogol-400, propylene glycol, N,N-bis(2-hydroxyethyl)oleamide, citric acid monohydrate, fragrance
C	<i>Persea gratissima</i> , lecithin, MIPA-laureth sulfate, laureth-4-paraffinum liquidum, ploxamer 101, cocoamide DEA, sodium lactate, fragrance

The study visits were on 3 consecutive days. On the first day (visit 1), 3 test areas were marked on each volar side of both forearms. Subsequently the transepidermal water loss (TEWL) was measured on each test area using the Tewameter (Mobile Skin Center® MSC 100, Tewameter® 300, Courage & Khazaka Electronic GmbH, Cologne, Germany). The measurement was performed according to the guidelines of the European Society of Contact Dermatitis [18]. Additionally, photometric measurements of skin erythema were performed on the test areas with a Mexameter MX 16 (Courage & Khazaka Electronics) as described [19]. The test substances, each 50 µl/test area, were applied under occlusion in a randomized manner on the volar sides of the forearms using extra large Finn test chambers of 12 mm inner diameter (Epitest Ltd. Oy, Tuusula, Finland) on Scanpor® fleece tape (Alpharma AS, Norway). The chambers were fixed with Fixomull® stretch stripes (Beiersdorf AG, Hamburg, Germany).

On the second day (visit 2), the tape was removed 24 h after substance application, 1 h prior to evaluation of the test areas to prevent false measurements due to reactions to the tape. Subsequently the instrumental measurements mentioned above were performed. The extent of barrier damage and inflammation was additionally assessed by a visual score according to the European Society of Contact Dermatitis guidelines on clinical scoring of acute SLS irritant reactions [20].

The visual score was graded as follows: 0 = negative, no skin irritation; 0.5 = arguable, weak erythema or slight scaling; 1 = weak, moderate erythema or edema or slight scaling or slight roughness; 2 = moderate, moderate erythema and edema, scaling, roughness or slight chemical burn or vesicles, crusts, rhagades; 3 = strong, distinct erythema and edema and scaling or chemical burn, vesicles, bullae, crusts, rhagades; 4 = very strong, like score 3 with necrotic areas.

The test areas were taped occlusively a second time with the substances for 24 h. On the third day (visit 3), the tapes were removed again 1 h prior to the measurements, and visual scoring and instrumental measurements were performed as described above. The test products were 3 different bath oils: A = Bedan bath and shower oil (containing St. John's wort extract), Cassella-med,

Table 2. Visual scoring of the test areas at visit 2 (V2) and visit 3 (V3)

Severity level	A		B		C		D		E		Untreated	
	V2	V3	V2	V3	V2	V3	V2	V3	V2	V3	V2	V3
0	12	13	10	11	3	1	2	1	10	13	14	17
0.5	5	5	5	6	7	4	7	3	6	5	4	1
1	1	0	3	1	7	5	6	7	2	0	0	0
2	0	0	0	0	0	4	3	5	0	0	0	0
3	0	0	0	0	1	4	0	2	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
TPS, %	4.9	3.5	7.6	5.6	18.8	37.5	21.5	34.0	6.9	3.5	2.8	0.7

The number of volunteers in each severity level is indicated. A–C = Bath oils; D = SLS; E = distilled water.

Berlin, Germany; B = Balneum Hermal bath oil, Hermal, Hamburg, Germany; C = Sebamed lipid shower oil, Sebapharma, Boppard, Germany; D = the positive control, SLS (1% vol/vol); E = the negative control, distilled water. One empty test chamber served as background reading (F). The International Cosmetic Ingredient declaration of the tested bath oils is shown in table 1. Bath oils B and C were chosen as additional controls with good and poor skin tolerance, respectively, as shown by Lodén et al. [5].

For statistical analysis the percentages of the total possible score (TPS) of the visual readings were analyzed as given in table 2. TPS is closely related to mean values. It is defined as

$$\text{TPS} = \frac{\text{mean}}{\text{highest possible score}} \cdot 100\%.$$

In contrast to the arithmetic mean, the TPS is independent of linear scale transformations.

Instrumental readings were adjusted by subtracting background readings before treatment. The difference from baseline was evaluated for visits 2 and 3. The differences between the test substances were analyzed using the nonparametric Friedman rank sum test for paired data. The Friedman rank sum test is used to compare data for multiple observations on the same individuals that are not normally distributed. In case of a significant finding, post hoc tests for pairwise comparisons (Wilcoxon and Wilcoxon) were performed [21]. *p* values <0.05 were regarded as statistically significant. All statistical evaluations were carried out using SPSS 12.01.

Results

Visual Score

The medical bath and shower oils A–C were applied on 3 out of 6 test areas in each volunteer. During the course of the trial, 17 out of 18 subjects developed an irritant contact dermatitis within some test areas. Nine subjects showed just slight irritations, corresponding to a visual score of 0–1 with moderate erythema and/or slight

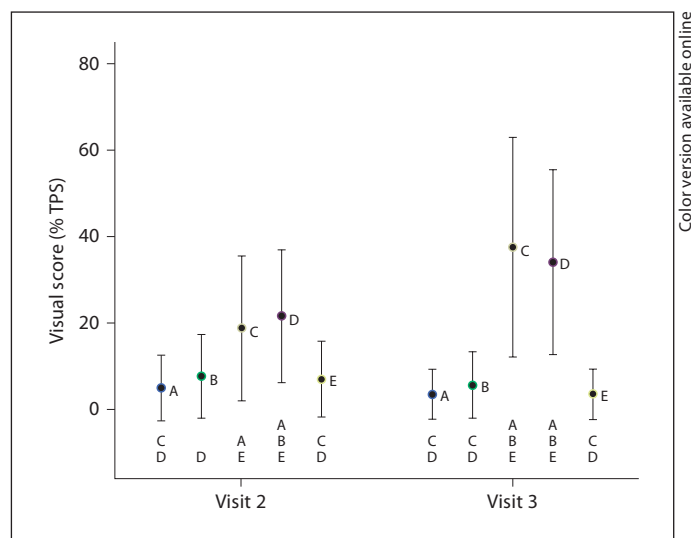


Fig. 1. Visual score at visits 2 and 3. A–C = Bath oils; D = SLS; E = distilled water. Means and standard deviations are depicted. Capital letters under the bars indicate significant differences to the corresponding substances.

edema and/or slight scaling. Eight subjects displayed a distinct irritation with a visual score of 2–4. The moderate to severe skin irritation was exclusively caused by test substance C. At visits 2 and 3, highly significant differences between the test substances were detected by visual assessment (*p* < 0.0005). The distribution and grading of the visual score are shown in table 2. The percentage of the total possible score is calculated for each test substance at visits 2 and 3 (table 2, fig. 1). Paired comparison according to Wilcoxon and Wilcoxon revealed a significantly lower irritation of substances A and B com-

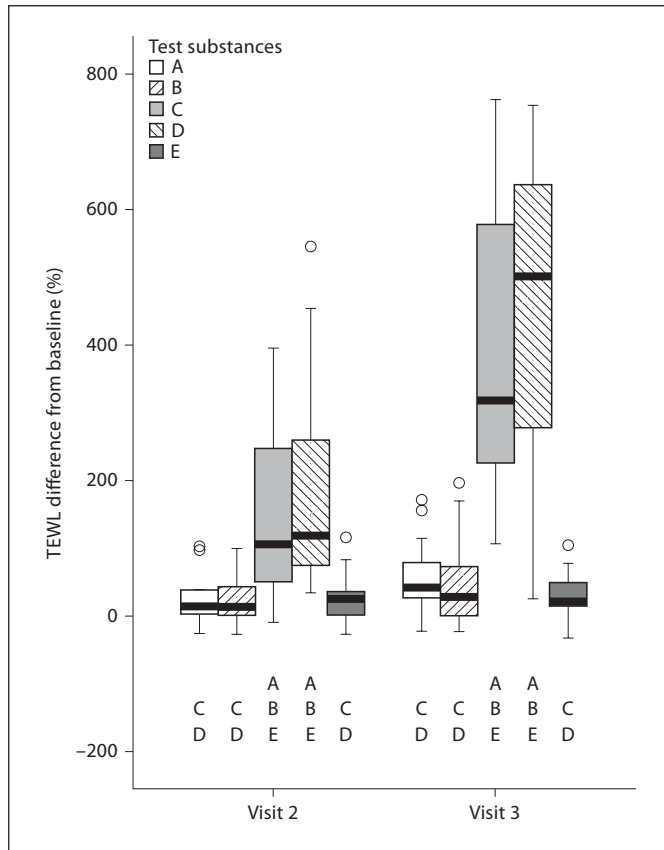


Fig. 2. Distribution of relative TEWL values at visits 2 and 3. A–C = Bath oils; D = SLS; E = distilled water. Capital letters under the boxes indicate significant differences to the corresponding substances.

pared to substance C and the positive control D (SLS) at visit 3. At visit 2 substance A showed a significantly lower irritation than C and D whereas C only differed from D significantly. No significant difference could be assessed between A, B and the negative control E (water). Substance C was not significantly different from the positive control D (SLS).

The frequency and severity of irritations increased after the second application of the bath oils. For example, 15 out of 18 subjects already showed an irritated test area at visit 2, 24 h after application of test substance C. Two additional subjects developed a skin irritation after the second application. Only 1 subject did not show any irritation caused by the bath oils (table 2). Except for 1 subject, the positive control SLS led to irritated test areas in all subjects. The negative control (distilled water) did not affect the skin in 13 subjects. However, 5 subjects displayed an arguable skin irritation, visually scored as 0.5.

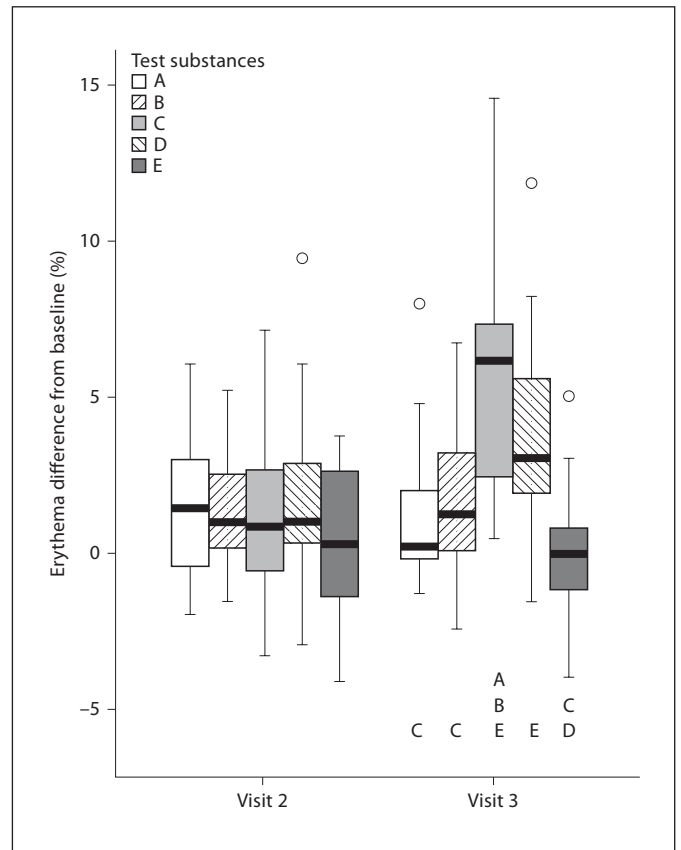


Fig. 3. Distribution of relative erythema values at visits 2 and 3. A–C = Bath oils; D = SLS; E = distilled water. Capital letters under the boxes indicate significant differences to the corresponding substances.

Transepidermal Water Loss

The TEWL was measured in each test area using a Tewameter. Box plots of relative TEWL values at visits 2 and 3 are shown in figure 2. There was a significant difference of the TEWL between the test substances A and B compared to test substance C and the positive control D (SLS). The TEWL was significantly higher after application of the test substances C and D in contrast to application of the test substances A and B. No significant difference could be detected between C and D, and between A, B and the negative control E on the other side. Thus, the Tewameter measurements confirm the results of the visual score.

Skin Erythema

The erythema of the test areas was photometrically assessed by a Mexameter, and relative values are shown in figure 3. The erythema measurements at visit 3 confirm

the findings of the visual score. The erythema was significantly lower after application of substances A and B compared to the application of substance C, and this difference was significant (fig. 3). However, in contrast to the visual score, no significant difference could be detected between A, B and C compared to the positive control D (SLS). The Mexameter measurements revealed a slight initial increase in erythema in all test areas at visit 2, implicating an increased blood flow of the skin after occlusive application of the test substances (fig. 3). At visit 3, the erythema caused by substances C and D increased, whereas the erythema due to substances A, B and E slightly decreased again (fig. 3).

Discussion

St. John's wort is a herbal remedy that is effective in the treatment of mild to moderate depression [22]. In traditional medicine, lipophilic extracts of St. John's wort have been used for the topical treatment of wounds, burns and myalgia. Most of the beneficial effects of these preparations are attributed to the lipophilic phloroglucin derivative hyperforin, a major constituent of St. John's wort that displays antibacterial and anti-inflammatory effects [23, 24]. These effects might also be useful in the topical treatment of infected wounds and inflammatory skin diseases [25]. It has been shown recently that a cream containing St. John's wort extract is effective in the treatment of atopic dermatitis, being significantly superior to placebo [17]. Because of its beneficial effects and good skin tolerance, the lipophilic St. John's wort extract has now also been incorporated in a skin-cleansing product in the form of a newly developed bath and shower oil.

Skin care products with high lipid content are recommended for the care of dry skin and inflammatory skin conditions. It has been shown that bath oils with no or only small amounts of surfactants are leaving a protective lipid layer on the skin [11–13]. Therefore, such bath and shower oils are useful for the treatment of dry and sensitive skin. Especially patients with eczematous skin disorders are in need of nonirritating moisturizing skin care products. In addition to lipids, various other substances such as surfactants and fragrances are added to the bath oils that display cleansing and antiseptic effects and reduce itching [14–16]. However, recently an irritant potential of different bath and shower oils has been described [5]. This prompted us to test the skin-irritating potential of the bath oil containing St. John's wort extract in comparison to 2 commercially available bath oils. The results

of our study have demonstrated a good skin tolerance of the new bath oil that was comparable to distilled water. The skin irritation model we used in this study has been adapted from Lodén et al. [5]. We confirmed the usefulness of this patch test method to assess the skin tolerability of cleansing products [5]. The application of 1% SLS caused an irritant-toxic contact dermatitis in over 90% of the subjects, whereas water did not alter the barrier function of the skin in this model [5, 26]. Surprisingly, in our hands the visual scoring method was superior to the photometric measurement of erythema at visit 2. At this time point, no significant differences were detected with the Mexameter. In contrast, the visual score detected significant differences that were similar to those detected at visit 3. This may be due to the fact that the Mexameter, in contrast to blood flow measurement, only evaluates skin reddening. The visual score is a combined score considering several variables such as erythema, swelling and exudation. This method seems to be superior to the measurement of skin reddening at an early stage of irritant dermatitis. However, both methods corresponded well after 2 days of irritation (visit 3). Also, the Tewameter measurement yielded similar results compared to the Mexameter and visual readings.

The most frequently used surfactants in bath oils are laureth sulfate and SLS [5]. The surfactants differ in their irritation potential that also depends on their interaction with other ingredients and physical parameters such as the critical micelle concentration [5, 27, 28]. Consequently, the skin-irritating potential of bath oils with a similar composition may differ considerably. Therefore, it seems useful to test a new product in an appropriate patch test model to avoid problems with skin tolerance after launching the product. Although the patch test model we used here is not directly transferable to the situation in daily skin care, it has several advantages. First, the test is easy to perform and requires little special equipment. Second, the test is standardized and only small numbers of volunteers are required to detect significant differences between the test preparations. Finally, suitable positive and negative controls also used in daily skin care compositions are available, and their use results in positive and negative reactions as required.

In conclusion, the results of this study confirm the different skin-irritating potentials of bath oils and demonstrate good skin tolerance of a new bath oil containing St. John's wort extract.

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