

# Assessment of the influence of licochalcone on selected functional skin parameters in patients with impaired vasomotor disorders and rosacea

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## Abstract

**Introduction:** Rosacea is a dermatosis of 0.2-2% of the population which occurs in both sexes, although more often in women. The onset of illness usually occurs after 30 years of age, rarely before. It occurs in four forms. One of them is erythemato-telangiectatic rosacea, which is characterized by paroxysmal transient change in the type of skin redness (pre-rosacea) associated with vascular hyperreactivity. Persistent changes may be a diffuse erythema and telangiectasia, accompanied by a burning sensation and burning skin. Among others, flavonoids are used in the treatment of rosacea.

**Aim:** To evaluate the impact of the flavonoid licochalcone, a component of creams – soothing moisturizer designed for day and night for a soothing effect in patients with vasomotor disorders and patients with rosacea.

**Material and methods:** The study group included 35 patients (31 women and 4 men) aged from 30 years to 60 years (average age 48.3 years). Twenty patients had pre-rosacea and 15 rosacea skin lesions. Before the enrolment of patients in the study, in 20 patients after 6 and 8 weeks and 15 patients after 8 weeks of application of the preparations, the severity of erythema, visible on the skin, skin hydration and transepidermal water loss (TEWL) were assessed using the Courage-Khazaka equipment.

**Results:** A significant reduction in the severity of erythema after 6 and 8 weeks of treatment with the creams was demonstrated. A significant increase in the degree of hydration of the epidermis and the reduced average value of TEWL were observed.

**Conclusions:** The use of creams containing licochalcone in patients with pre-rosacea and rosacea helps to reduce the severity of erythema. These creams also affect the reduction in TEWL values and increased hydration of the epidermis.

**Key words:** pre-rosacea, rosacea, mexametry, transepidermal water loss, hydration.

## Introduction

Sensitive skin with vasomotor disorders is a common therapeutic and cosmetic problem. It is especially present in the parts of the body that are more exposed to environmental influences [1].

The problem of skin sensitivity may relate to all skin types, but especially dry ones. Its pathogenesis is associated with damage to the protective barrier of the epidermis, which favours deeper penetration of irritants and allergens, dysfunction of the water-lipid coat, stimulation of hypersensitive sensory receptors (even under the influ-

ence of mild external stimuli) and a tendency towards excessive formation of new blood vessels [2].

Evidence of sensitive skin is present in rosacea: chronic dermatosis associated with seborrhoeic base and vasomotor disorders, manifested by the presence of redness, vasodilation, and telangiectasia as well as inflamed erythematous papules and pustules. The clinical picture of rosacea varies, with four varieties of the disease being identified: erythemato-telangiectatic, papulo-pustular, phymatous and ocular. The first of these, the early variety, is classified by many authors as a neurosis of vascular skin and is accompanied by migraine, irritable bowel

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syndrome, excessive sweating and others. Determining the lesions in this variant uses the concept of so-called vasomotor skin or pre-rosacea, which refers to increased vascular reactivity, and manifests itself as periodically occurring erythema which is associated with vascular damage [3-5].

Redness can be transient or persistent. The transient changes are characterized by paroxysmal erythema, for example when under the influence of emotions, while persistent forms manifest themselves by the presence of fixed diffuse erythema, dilated blood vessels and telangiectasia.

Clinical symptoms associated with sensitive skin are accompanied by burning, itching, dryness, exfoliation and a subjective sense of the skin being "pulled" [6, 7].

The causes of skin redness may be related to either endogenous factors such as hypertension, neurological and endocrine diseases, skin dermatoses and menopausal factors, or exogenous factors, often with an environmental basis, such as increased exposure to UV radiation, ambient temperature changes (wind, high or low temperature), air pollution, the use of sunbeds as well as certain foods such as alcohol, caffeine and theine, as well as spices such as pepper, hot pepper, cinnamon or ginger, and drugs that cause vasodilation [8].

Often, these symptoms also occur with improper skin care, i.e. the use of aggressive cleaning agents (detergents), chlorinated water, lotions with alcohol, cosmetics containing preservatives and dyes, and certain fragrances, as well as the preparation of fruit acids and mechanical peeling [9].

In turn, the occurrence of broken skin blood vessels and telangiectasia may cause genetic conditions, cardiovascular disorders, hormonal problems and vascular damage by external factors such as topical corticosteroids [3].

As not all medicines and cosmetics are universally well tolerated, the treatment and care of sensitive skin is difficult; each individual course of therapy for each particular patient demands a unique formulation based on pathogenesis and choice of individual procedure. Therefore, the introduction of new agents that are well tolerated and that repair the damaged protective barrier of the epidermis is vital [10, 11].

## Aim

The aim of this study was to assess the impact of creams containing licochalcone in controlling facial erythema skin hydration and TEWL in patients with rosacea.

**Table 1.** Severity of symptoms according to the NRS scale in subjects ( $n = 33$ )

Severity of symptoms on NRS scale	0	1	2	3
Number of patients	0	3	17	13

## Material and methods

The study involved 35 people (31 women and 4 men) aged from 30 years to 60 years (average age 48.3 years) with changes of rosacea. Two men did not complete the study. In the majority of patients, the facial skin lesions resembled the erythemato-telangiectatic subtype. Only one person demonstrated visible papulo-pustular changes in addition to erythema and telangiectasia. Clinical assessment was based on the four-step (0-3) NRS scale – National Rosacea Society (no symptoms, mild, moderate, severe) [3]. The severity of the symptoms in subjects is presented in Table 1.

Patients in the study used two face creams with licochalcone for 8 weeks. In addition to licochalcone, Eucerin® soothing moisturizer cream containing UVA/UVB SPF 15 sunscreen was used during the day, and soothing Eucerin® night cream containing panthenol was used during the night. Both the day and night creams had the same base. All patients completed treatment with other agents that could affect the results at least 2 weeks before the study. Photographic documentation was taken of each patient both before and after the study.

The severity of erythema, skin hydration and TEWL was evaluated in all patients. Measurements were performed before inclusion of patients in the study and after 8 weeks of using preparations for skin application. In addition, 16 people were measured after 6 weeks' application. The Courage-Khazaka Electronic GmbH (Germany) Multi Probe Adapter MPA-5 with appropriate probes was used. The severity of erythema was evaluated using a Mexameter MX 18. The degree of skin hydration was studied using a Corneometer CM 825. A Tewameter TM 300 was used to measure TEWL. Tests were performed on the facial skin, around both cheeks in a room with constant temperature and humidity, and an average value was calculated [12-14].

In addition, the patients made a subjective assessment of the creams, regarding the absorption and possible symptoms of poor tolerance.

Before starting the study, all patients expressed their written consent for measurements to be taken. The results were analysed with the following tests:

- skewness and kurtosis test for normality,
- ANOVA with repeated measures,
- Friedman's nonparametric two-way ANOVA,
- marginal homogeneity test,
- linear regression with robust standard errors,
- generalized linear models for discrete data.

The statistically significant level of significance in all analyses was  $p < 0.05$ .

## Results

Before using Eucerin® creams, the severity of erythema within the facial skin was found to be from 453 to 494 U

(mean 473.88 U). However, the average severity of erythema decreased significantly after 8 weeks' application of creams for day and night (mean 377.83 U,  $p = 0.002$ ). It was also observed to be lower in 16 patients after 6 weeks of treatment. The mean values for the severity of erythema and their median standard deviations before applying the creams and after 6 and 8 weeks of treatment are presented in Table 2.

Comparison of the severity of erythema before using licochalcone creams and after 6 and 8 weeks of application is shown in Figure 1.

The skin hydration states before applying creams and after 8 weeks of the application are respectively 62.22 U and 77.34 U. Similarly, after 6 weeks of treatment, the corneometric measurements increased compared to baseline by an average of 7.4 U. The observed increase in skin moisture level in the patients studied was statistically significant ( $p = 0.008$ ). The mean values of skin moisturizing creams before and after 6 and 8 weeks of their application is given in Figure 2.

The average TEWL value before treatment was found to be 11.5 g/m<sup>2</sup>/h, while it was seen to decrease to 9.55 g/m<sup>2</sup>/h after 8 weeks of treatment. It also decreased significantly by 0.94 g/m<sup>2</sup>/h after 6 weeks of application. Significant reductions in TEWL values were seen in subjects during application of the creams ( $p = 0.014$ ). These results are compared in Table 3 and Figure 3.

Beneficial effects associated with Eucerin® cream were observed in almost all subjects: both reducing the severity of erythema and resolving telangiectasia (Figs. 4, 5). Only two individuals did not achieve significant improvement. Clinical evaluation of the severity of symptoms based on the 4-point NRS scale before treatment and after 8 weeks application of creams in 33 subjects are presented in Table 4 and Figure 6.

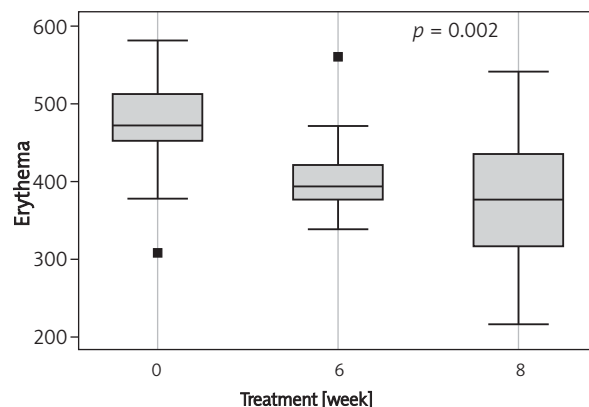
Clinical results were also satisfactory according to the subjective assessment of patients. Most people (73%) participating in the study noted total or significant reduction in severity of erythema and in the amount of telangiectasia around the face skin. The results are shown in Figure 7.

Clinical evaluation of regression of lesions after 8 weeks of using creams based on a 4-point NRS scale correlates strongly with subjective assessment of the final result, presented by the patients ( $p = 0.61$ ,  $p < 0.001$ ) (Fig. 8).

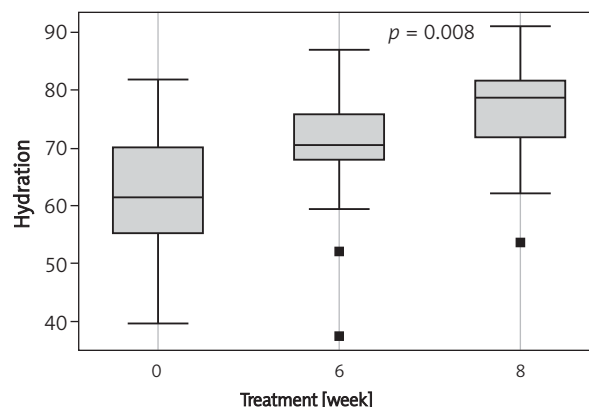
**Table 2.** Mean values of severity of erythema, standard deviation and the median before applying creams and after 6 and 8 weeks of treatment

	Erythema [U], $\bar{x} \pm SD$	Median, Me
Before using licochalcone creams	473.88 ± 57.80	472.84
After 6 weeks of use	408.98 ± 51.64	394.00
After 8 weeks of use	377.83 ± 78.58	377.00

Applied creams were also well tolerated by patients. Day cream was very well evaluated by 23 patients, i.e. 70% of respondents, and night cream by 82% of patients. All tested persons confirmed their good absorption, especially the night cream. There were no signs of irritation and hypersensitivity. Only part of the respondents report-



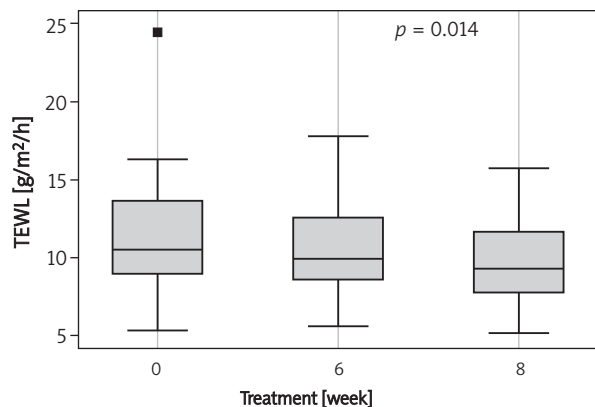
**Fig. 1.** Comparison of the severity of erythema before using licochalcone creams and after 6 and 8 weeks of their application



**Fig. 2.** Comparison of epidermal hydration before using licochalcone creams and after 6 and 8 weeks of application

**Table 3.** Mean values of TEWL, standard deviation and the median before applying creams and after 6 and 8 weeks of treatment

	TEWL, $\bar{x} \pm SD$ [g/m <sup>2</sup> /h]	Median
Before using licochalcone creams	11.50 ± 3.80	10.55
After 6 weeks of use	10.56 ± 3.11	9.95
After 8 weeks of use	9.55 ± 2.78	9.30



**Fig. 3.** Comparison of TEWL before using licochalcone creams and after 6 and 8 weeks of application

ed lacrimation during the first applications; this resolved after a few minutes and did not require discontinuation of the use of creams. Figure 9 shows in a graphic way tolerance of creams assessed by the subjects.

### Discussion

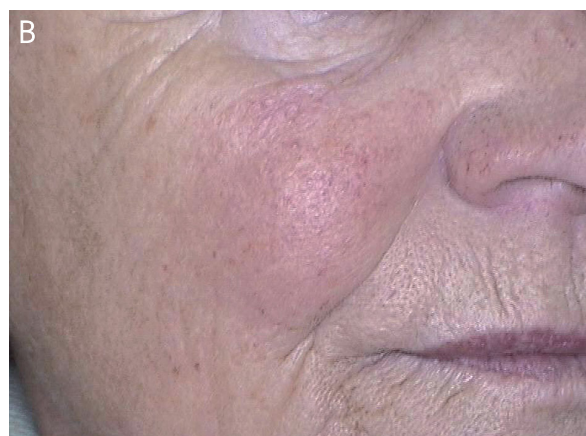
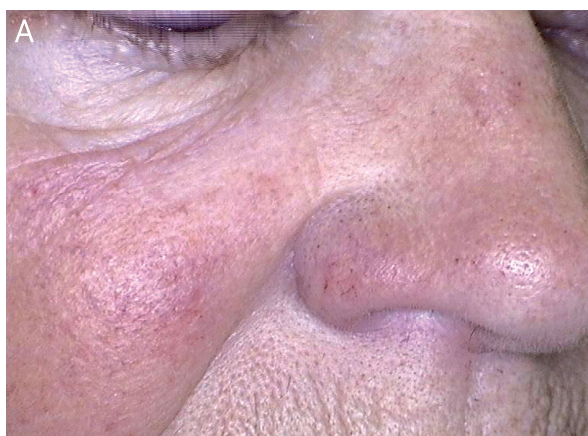
Sensitive skin problems are met as part of daily dermatological practice and occur frequently in patients with rosacea. Patients with sensitive skin tolerate creams and cosmetics most poorly; burning, itching, redness, dryness, exfoliation, and a subjective feeling of pulling, especially immediately after washing, occur after application of external cosmetics. Hence it is important to find a cosmetic preparation which will not irritate the skin and will be well tolerated by patients.

When selecting cosmetics, it is important to take into account the lack of fragrances, preservatives and dyes. Active ingredients used in cosmetics for sensitive skin should have a moisturizing effect: urea, hyaluronic acid and glycerine are good examples. In turn, essential unsaturated free fatty acids demonstrate a regenerating effect, while allantoin and d-panthenol have a soothing effect. Flavonoids possess anti-inflammatory effects, which also improve microcirculation [10, 11].

Flavonoids are a group of organic compounds found in plants which act as colorants and antioxidants. They



**Fig. 4.** **A** – patient (man) before applying licochalcone creams, **B** – patient (man) after 8 weeks of using licochalcone creams

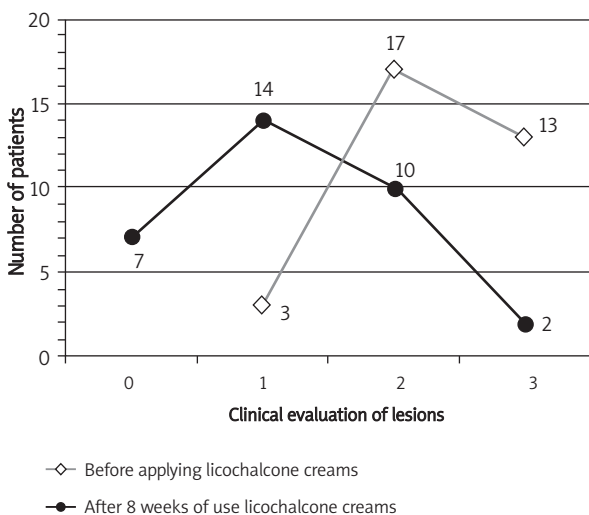


**Fig. 5.** **A** – patient (woman) before applying licochalcone creams, **B** – patient (woman) after 8 weeks of using licochalcone creams



**Table 4.** Clinical evaluation of lesions regression based on a 4-point NRS scale (n = 33)

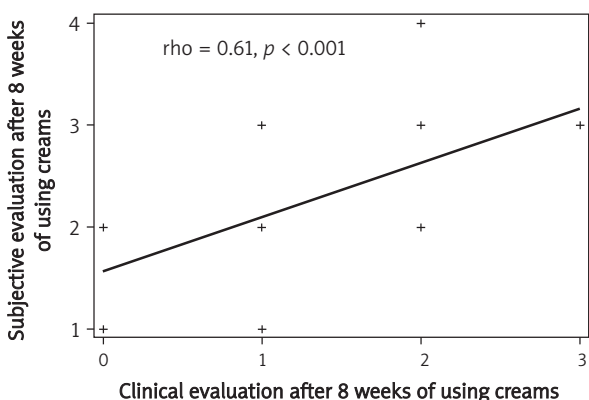
	Degree of severity of symptoms on NRS scale				Total
	0	1	2	3	
Before using licochalcone creams	0	3	17	13	33
After 8 weeks of use	7	14	10	2	33



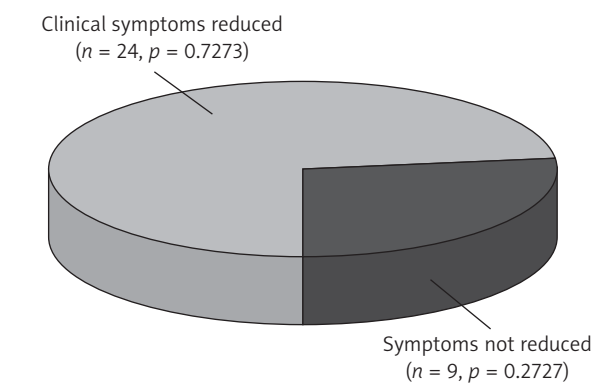
**Fig. 6.** Clinical evaluation of lesions regression based on a 4-point NRS scale

have the therapeutic effect of sealing blood vessels by inhibiting the activity of proteolytic enzymes (elastase, hyaluronidase), which improves the condition of the connective tissue in the vascular endothelium, increasing their flexibility and seals [15].

The paper presents the results of selected functional studies of skin after application of creams containing licochalcone, which is a natural flavonoid extracted from liquorice root (*Glycyrrhiza inflata*).

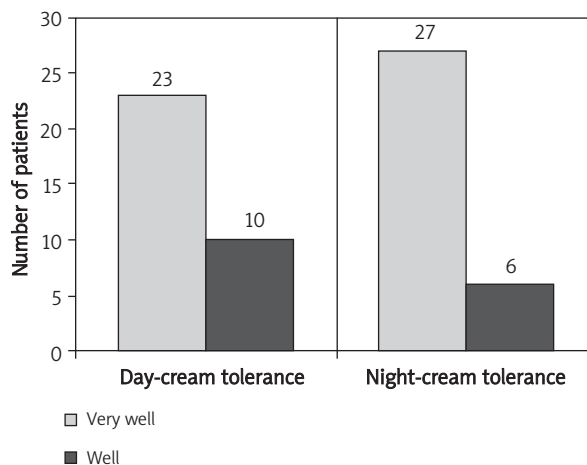


**Fig. 8.** Comparison of clinical and subjective evaluation after 8 weeks of using creams with licochalcone



**Fig. 7.** Reduction of degrees of erythema and telangiectasia in assessing subjective test

in the literature, a number of studies reporting on its antibacterial [16, 17], antiparasitic [18, 19], anticancer [20, 21] and immunomodulatory actions [22] can be found. Used in topical preparations, it has an anti-inflammatory effect and reduces irritation and severity of the erythema. Kolbe *et al.* [23] reported the anti-inflammatory action of licochalcone. They assessed the retention of erythema induced by shaving and UV irradiation in 57 subjects. They showed clear-



**Fig. 9.** Both creams tolerance assessment made by respondents

ly the soothing effect of the flavonoid on the irritation, which they believe is connected with the action of various mediators involved in inflammatory processes (PGE<sub>2</sub>, IL-6, TNF- $\alpha$ , LTB<sub>4</sub>). According to the authors, creams containing licochalcone are indicated for use in subjects with sensitive and irritated skin.

Increased skin sensitivity in patients with impaired vasomotor disorders is associated with epidermal barrier damage, which is manifested primarily by increased values of transepidermal water loss. In our own material study, measurements of selected functional skin parameters were made before applying Eucerin® creams, and after 8 weeks of use. They relate to the severity of erythema, skin hydration and TEWL. A search of the available literature reveals no reports on the effects of preparations containing licochalcone concerning the functional parameters of the skin. Our study showed that the severity of erythema decreased, skin hydration increased, and also TEWL values decreased in patients under the influence of Eucerin® creams. The results were statistically significant.

The anti-inflammatory action of licochalcone has also been reported by Weber *et al.* [24], who used flavonoid creams for 8 weeks on patients with a form of erythematotelangiectatic subtype of rosacea, with varying degrees of change. Using clinical evaluation, photographic documentation and data obtained from the survey, clear improvement of the skin was shown both after 4 and 8 weeks of their application. In addition, patients reported good toleration of preparations. The applied creams also affected the quality of life of patients [25].

Data from the literature and our own research results indicate a strong anti-inflammatory and anti-irritation action of licochalcone creams, and show their usefulness in application on patients with sensitive skin. They are used in rosacea, especially in its erythematotelangiectatic subtype, as well as in other skin conditions caused by exposure to UV radiation or other irritants.

## Conclusions

- The licochalcone creams tested have an anti-inflammatory action and soothe irritation; these activities are manifested by decreases in the severity of erythema and subjective symptoms such dryness, itching and burning skin.
- Ailments reported in patients with erythematotelangiectatic rosacea are associated with impaired function of the protective skin barrier.
- The regular application of creams with licochalcone reduced clinical symptoms associated with vasomotor disorders after only 6 weeks.
- The systematic use of licochalcone creams by patients 2 times a day for 8 weeks increased the degree of hydra-

tion of the epidermis, and the average TEWL value decreased, which suggests improvement in skin barrier function.

- Both test creams were well tolerated; there were no signs of irritation and hypersensitivity.

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