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Study number 2305307026

Muenster, 21 November 2023

Expert report by dermatological specialists about a clinical-dermatological application study

(Test period June - November 2023)

on 20 subjects with application (home in-use) of test product once daily on the affected skin areas over a period of four weeks

Examination for dermal tolerability including a final questionnaire and
Determination of a modified SCORAD (SCORing Atopic Dermatitis)

anti-eczema cream

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1 General information

Title

Clinical application study under dermatological control

Testing body

Dermatest GmbH
Nevinghoff 30
D-48147 Münster

Specialist in dermatology

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Specialist in Dermatology
Venereology, Allergology,
Phlebology and Environmental Medicine

Study coordinator

PhD Janina Tiemann
Biotechnologist

1.1 Synopsis

Study title	Clinical application study under dermatological control
Test product	**anti-eczema cream**
Product type	cream
Study design	Single-centre
Testing body	Dermatest GmbH Nevinghoff 30 D-48147 Münster
Expert report version and date	Version 1, 21.11.2023
Test period	June - November 2023
Primary study objectives	Assessment of skin tolerability From the time of start of the study to the end of the study and 30 days beyond, all skin reactions and any other adverse reactions are recorded in the reaction file.
Secondary study objectives	Assessment of efficacy - Query of the subjective impression by questionnaire - Determination of a modified SCORAD (SCORing Atopic Dermatitis)
Quantity of subjects	20
Application period	four weeks (home in-use)
Times of measurement	Questionnaire: T_{28} Determination of a modified SCORAD: T_0 and T_{28}
Test area	affected skin areas
Frequency of application	one time a day
Inclusion criteria	- 18 years and older - Female and male healthy volunteers - All skin type - Subjects with eczema in the inflammation stage - Written informed consent of the subjects or legal guardian is available

Exclusion criteria	- Severe or acute skin inflammations - Severe internal or acute diseases - Short-term and acute intake of medications that may interfere with skin reactions (glucocorticoids, anti-allergics, immunomodulators, etc.) - Application of prescription preparations and skin care products 7-10 days before the start of the test - Severe allergies or any serious side effects of cosmetic preparations ever occurred - Intensive sun baths or solarium visits during the study - Acute neoplastic disease - Pregnancy and breast-feeding

1.2 Schedule

Study day	Day 0	Day 28
Information of the subjects	✔	
Informed Consent Form Sheet	✔	
Medical history	✔	
Dermatological examination	✔	✔
Compliance with the inclusion and exclusion criteria	✔	✔
Query of the subjective impression		✔
Determination of a modified SCORAD	✔	✔

2 Introduction

The human skin is the largest and functionally most versatile human organ. It delimits the organism against the outside world, protecting against dehydration and environmental influences. The skin consists of three layers: Epidermis (upper skin layer), dermis (true skin) and subcutis (hypoderm). The epidermis, in turn, is composed of five layers and consists of 90 % keratinocytes (horny cells). From outside to inside, the superimposed layers are: *Stratum corneum*, *Stratum lucidum*, *Stratum granulosum*, *Stratum spinosum* and *Stratum basale*.

These days a lot of products, in particular cosmetics, consumer goods and medical devices, are in contact with the skin daily and often over long periods. Good tolerability is a prerequisite for application of these products. Since alternative test methods such as animal testing are prohibited and results of cell culture experiments can be applied to humans only in limited extent, tests under medical supervision are currently required from an ethical and scientific point of view. For analysis of the skin tolerability of products, application studies, so-called home-in-use tests, can be carried out. The product to be tested is applied over a prolonged period on the intended application area. Inclusion and exclusion criteria of the subjects are adapted to the target group as far as possible. Before each testing the risk of all ingredients of the test product are assessed. All available information are systematically analysed in order to identify potential hazards and to avert risks.

3 Study objective

The objective of this study was to precisely investigate the skin tolerability and efficacy of the product **anti-eczema cream** according to clinical-dermatological test criteria.

Before inclusion the dermatological integument of all subjects was investigated regarding health and integrity. In case of necessary medical treatment the subjects were excluded. Furthermore, the conditions of the study were explained to all subjects as well as the rights and duties of the subjects in the context of the study by the attending study nurse or the attending dermatologist. All subjects were included into the study only, if they did not exhibit any pathological changes of the skin in the application area, signed the consent statement of their own free will or with agreement of their legal guardians and complied with all other inclusion and exclusion criteria. During the study all subjects could consult the attending study nurse or the attending dermatologist in case of any objective and subjective skin changes. According to the schedule, all dermatological examinations were done.

3.1 Primary outcomes

Assessment of skin tolerability and possible sensitisation potential

- Application study

3.2 Secondary outcomes

Assessment of efficacy

- Query of the subjective impression by questionnaire
- Determination of a modified SCORAD

3.3 Study parameters

Monocentric clinical trial over a period of four weeks in total.

4 Selection of subjects

The study was carried out with 14 female and 6 male subjects in the age of 18 years and older according to the inclusion and exclusion criteria. All subjects were selected from the subject database or recruited by flyers, social networks and newspapers.

4.1 Information of the subjects

Before the study all subjects were informed about the course of the study by the attending study nurse or the attending dermatologist. Participation in the study was voluntary. All subjects could discontinue the study at any time and without giving any reason as well as without any negative consequences for the subjects.

4.2 Inclusion criteria

- 18 years and older
- Female and male healthy volunteers
- All skin type
- Subjects with eczema in the inflammation stage
- Written informed consent is present

The subjects had to be able to communicate with the attending study nurse or the attending dermatologist and to understand and follow the requirements of this clinic-dermatological application study.

4.3 Exclusion criteria

- Severe or acute skin inflammations
- Severe internal or acute diseases
- Short-term and acute intake of medications that may interfere with skin reactions (glucocorticoids, anti-allergics, immunomodulators, etc.)
- Application of prescription preparations and skin care products 7-10 days before the start of the test
- Severe allergies or any serious side effects of cosmetic preparations ever occurred
- Intensive sun baths or solarium visits during the study
- Acute neoplastic disease
- Pregnancy and breast-feeding

4.4 Exclusion of subjects from the clinical-dermatological application study

The investigator could exclude a subject from the clinical-dermatological application study if any of the following conditions occurred:

- Revocation of the consent
- Occurrence of an undesirable event
- Deterioration of the clinical condition

If premature withdrawal of a subject happened, it was documented completely. Supervision of these and all subjects continues for reasonable time in order to control clinical condition and occurrence of adverse events.

4.5 List of subjects

Subject №	Sex [f/m]	Age
1	m	43
2	w	28
3	w	27
4	m	67
5	w	48
6	m	47
7	m	39
8	w	24
9	w	35
10	w	46
11	w	35
12	w	45
13	w	60
14	w	39
15	m	54
16	w	45
17	w	55
18	w	51
19	w	27
20	m	38

5 Test product

5.1 Application of the investigational product

The product was applied on the affected skin areas once daily over the entire application period. The subjects were instructed not to use any equivalent product in the test area during the test period.

5.2 Interruptions / Discontinuation of the application

Application of the test product could be discontinued at any time by the subject or according to the decision of the investigator, if the clinical condition required so. Each discontinuation was documented completely. It was the responsibility of the investigator to assess, whether conditions for discontinuation were given.

6 Benefit-risk consideration and precautions

There was no known risk for use of the product. If a residual risk was recognised or if a change in acceptance of the product was evident, the sponsor was notified immediately.

If during the study 10 % or more of the test subjects experienced a product-related reaction, that was not acceptable for the corresponding product category, the study was terminated immediately and the sponsor was informed accordingly.

7 Methods

In order to minimise fluctuations caused by external influences such as room temperature and relative humidity, all measurements were always carried out at the same physical ambient conditions in rested status (≈20 °C, humidity 40–60 %).

7.1 Query of the subjective impression

Very disparate and non-measurable parameters (subjectively experienced effect, smell, taste, consistency, influence on the appearance of the skin, etc.) can be determined by means of a final questionnaire. Correspondingly each subject answered independently the respective questionnaire at scheduled times. In case of uncertainty, the attending study nurse or the attending dermatologist could be consulted and questioned at any time.

7.2 Determination of a modified SCORAD (SCORing Atopic Dermatitis)

Atopic dermatitis is a chronic or chronic recurrent, non-infectious skin disease with age-related, typical morphology and localisation of the skin symptoms. The pathophysiology of the disease is multifactorial and not yet fully understood. In addition to environmental factors, various genloci appear to be involved in the development of an atopic disease (Flohr et al., 2013). Atopic dermatitis is one of the most common clinical diseases in dermatology. Its incidence has risen sharply in industrialised countries and is also increasing in other parts of the world (Deckers et al., 2012). 10 - 15 % of all European children suffer from atopic dermatitis at times from birth up to seven years (Flohr et al., 2013).

The SCORAD is a validated measuring instrument of international acceptance developed by the European Task Force on Atopic Dermatitis to assess the severity of atopic dermatitis (Kunz et al., 1997). It is a cumulative indicator (index) that is composed of the objective eczema size (skin area) and intensity of skin lesions (redness, oedema [swelling], crust formation, skin abrasion, lichenification and dryness) and subjective parameters (itching during the day and sleep disturbance). Mild dermatitis has an overall SCORAD score of up to 25 points, moderate dermatitis is 25 to 50 points and severe dermatitis is over 50 points (Oranje, 2011; Charman et al., 2003).

Part A of the SCORAD was used to determine the percentage of skin area affected in this study. Part B of the SCORAD was used to determine the intensity of the morphological skin changes.
A representative atopic eczema was used for assessment. The expression of the parameters erythema, oedema/papule formation, oozing / crust formation, excoriations and lichenification were evaluated using the prescribed point system of 0 - 3 (0 = no intensity, 1 = mild intensity, 2 = moderate intensity, 3 = strong intensity).
The subjective level of suffering was assessed using the parameter C of the SCORAD. The intensity of itching and insomnia was determined on a visual analogue scale (0 = no itching or no insomnia, 10 = very severe itching or insomnia).

The SCORAD was determined before the first application and after the application period. The SCORAD was calculated in this way: SCORAD = A/5 + 7*B/2 +C.

The following exclusion criteria apply (no recruitment at the beginning of the study).

- Exclusion from the study with an index value > 50
- Exclusion in case of sleep loss > 3 (VAS scale 0 - 10)

- Exclusion in case of sole infestation of the palms of the hands, soles of the feet or pubic area
- Exclusion in case of oedema and secreting or bleeding atopic eczema

Literature

- Charman C, Chambers C, Williams H. Measuring atopic dermatitis severity .in randomized controlled clinical trials: What exactly are we measuring? J Invest Dermatol.120 (2003), Jun, 6: 932–941.
- Flohr, C., Mann, J. New insights into the epidemiology of childhood atopic dermatitis. Allergy. 69 (2013), 3–16.
- Kunz B, Oranje, A P, Labreze, L, Stalder J F, Ring J, Taieb A. Clinical validation and guidelines for the SCORAD index: consensus report of the European Task Force on Atopic Dermatitis. Dermatology 195 (1997), 1: 10–19.
- Oranje A P. Practical issues on interpretation of scoring atopic dermatitis: the SCORAD index, objective SCORAD and the three-item severity score. Curr Probl Dermatol 2011, 41:149-155.
  Deckers I A G, McLean S, Linssen S, Mommers M, van Schayck C P, Sheikh A. Investigating international time trends in the incidence and prevalence of atopic eczema 1990-2010: a systematic review of epidemiological studies. PLoS One. 2012, 7 (7)

7.3 Descriptive Statistics

The values of the individual measurements are averaged, and the differences of the before and after values and the relative change of the mean values are calculated.

8 Results

8.1 Dermatological examination results

The examinations were carried out according to clinical-dermatological evaluation criteria. All test persons showed healthy skin in the test area before, during and after the application study. No pathological skin lesions were found in any form. No test interruption, even less treatment by a specialist in dermatology was performed in any case. The product named was very well tolerated, and it did not lead to dermatologically relevant skin changes in any subject.

Subject №	Findings before	Findings after	Type of reaction
1	–	–	
2	–	–	
3	–	–	
4	–	–	
5	–	–	
6	–	–	
7	–	–	
8	–	–	
9	–	–	
10	–	–	
11	–	–	
12	–	–	
13	–	–	
14	–	–	
15	–	–	
16	–	–	
17	–	–	
18	–	–	
19	–	–	
20	–	–	

If skin reactions occurred, the type of the reaction was assessed clinically dermatologically and documented according to following scale:

–	no pathological findings
1	mild reaction
2	moderate reaction
3	severe reaction

8.2 Query of the subjective impression

The question of the subjective impression was made with the help of a final questionnaire.

1. What did you particularly like about the product?
answer
• compatibility, smoothness, fast absorption, spreadability • that it helps to use well • the consistency and that it is absorbed quickly • fragrance-free and pleasant consistency • the product was very easy to apply and was pleasant on the skin • / • the light texture, which spread well and was absorbed quickly and the fairly neutral fragrance • easy to spread • it spreads well • Ointment is absorbed very quickly, pleasant feeling on the skin • the cream has good suppleness and is absorbed quickly, improves the chapped skin very well • Consistency, spreads well • is easy to apply and relieves itching • easy to spread, quickly absorbed, long-lasting care effect, rapid improvement • itching relief and the feeling of application on the skin (smooth) • absorbs quickly, spreads well • good effectiveness • no unpleasant odor, odorless, easy to apply • absorbs quickly • the cream had a very pleasant consistency and was absorbed quickly

2. What did you not like about the product?
answer
• the smell could be more subtle • the smell • it helped very well but not 100% • nothing! • / • it is difficult to handle from the can • nothing • does not eliminate the eczema of the hands in the long term • lack of effect • there was nothing negative in my opinion • / • there is nothing to complain about • the first applications to the affected area caused a prolonged burning sensation on the skin. This lasted about 10 minutes. Only after 4-5 days did the burning no longer occur. • nothing • the quantity could have been slightly larger

3. How would you rate the product overall?		
answer	**number**	**percent**
very good	10	50,00%
good	7	35,00%
neither good nor bad	3	15,00%
bad	0	0,00%
very bad, because	0	0,00%

4. How would you rate the skin tolerance of the product?		
answer	**number**	**percent**
very good	13	65,00%
good	6	30,00%
neither good nor bad	1	5,00%
bad	0	0,00%
very bad, because	0	0,00%

5. How would you rate the statement: „The product calms down sensitive skin.“		
answer	**number**	**percent**
totally agree	13	65,00%
rather agree	6	30,00%
neither	1	5,00%
rather disagree	0	0,00%
do not agree at all	0	0,00%

6. How would you rate the statement: „The product reduces skin irritation.“		
answer	**number**	**percent**
totally agree	13	65,00%
rather agree	6	30,00%
neither	1	5,00%
rather disagree	0	0,00%
do not agree at all	0	0,00%

7. How would you rate the statement: „The product is gentle to the skin.“		
answer	**number**	**percent**
totally agree	15	75,00%
rather agree	4	20,00%
neither	1	5,00%
rather disagree	0	0,00%
do not agree at all	0	0,00%

8. How would you rate the statement: „The product does not irritate my skin.“		
answer	**number**	**percent**
totally agree	15	75,00%
rather agree	4	20,00%
neither	1	5,00%
rather disagree	0	0,00%
do not agree at all	0	0,00%

9. How would you rate the statement: „The product moisturises intensively.“		
answer	**number**	**percent**
totally agree	8	40,00%
rather agree	12	60,00%
neither	0	0,00%
rather disagree	0	0,00%
do not agree at all	0	0,00%

10. How would you rate the statement: „The product is also suitable for sensitive skin.“		
answer	**number**	**percent**
totally agree	15	75,00%
rather agree	4	20,00%
neither	1	5,00%
rather disagree	0	0,00%
do not agree at all	0	0,00%

11. How would you rate the statement: „The product is also suitable for skin prone to atopic dermatitis.“		
answer	**number**	**percent**
totally agree	11	55,00%
rather agree	6	30,00%
neither	2	10,00%
rather disagree	1	5,00%
do not agree at all	0	0,00%

12. How would you rate the statement: „The product makes the skin feel cared for immediately.“		
answer	**number**	**percent**
totally agree	11	55,00%
rather agree	9	45,00%
neither	0	0,00%
rather disagree	0	0,00%
do not agree at all	0	0,00%

13. How would you rate the statement: „The product reduces itching.“		
answer	**number**	**percent**
totally agree	9	45,00%
rather agree	8	40,00%
neither	1	5,00%
rather disagree	1	5,00%
do not agree at all	0	0,00%
I do not have feelings of itching	1	5,00%

14. How would you rate the statement: „The product reduces redness.“		
answer	**number**	**percent**
totally agree	6	30,00%
rather agree	11	55,00%
neither	2	10,00%
rather disagree	1	5,00%
do not agree at all	0	0,00%
I do not have rednesses	0	0,00%

15. How long after starting to use the product you see a visible improvement in your skin condition?		
answer	**number**	**percent**
after one day	2	10,00%
after two days	6	30,00%
after one week	9	45,00%
after two weeks	2	10,00%
after four weeks	0	0,00%
I do not see any improvement	1	5,00%

16. How would you rate the statement: „The product helping to restore skin natural barrier, making it more resilient.“		
answer	**number**	**percent**
totally agree	3	15,00%
rather agree	12	60,00%
neither	5	25,00%
rather disagree	0	0,00%
do not agree at all	0	0,00%

17. How would you rate the product texture and absorbance?

answer	number	percent
very good	10	50,00%
good	9	45,00%
neither good nor bad	1	5,00%
bad	0	0,00%
very bad, because	0	0,00%

18. Would you recommend the product after this application test?

answer	number	percent
yes	18	90,00%
no, because	2	10,00%

- it did not help me
- 1. burning sensation on the irritated skin at the beginning (approx. 3-5 days)
  2. relief of the itching and the reddened area only after more than a week

19. Would you also buy the product after this application test?

answer	number	percent
yes	18	90,00%
no, because	2	10,00%

- it did not help me
- 1. burning sensation on the irritated skin at the beginning (approx. 3-5 days)
- 2. relief of the itching and the reddened area only after more than a week

8.3 Dermatological assessment of a modified SCORAD

The SCORAD was assessed in the test area atopic eczema and the value of the index was calculated before and after an application period of four weeks.

Subject №	T_0	$T_{4\ weeks}$	Difference	Change [%]
1	38,50	14,00	24,50	-63,64
2	40,00	40,00	0,00	0,00
3	25,50	3,50	22,00	-86,27
4	17,50	6,50	11,00	-62,86
5	21,20	7,20	14,00	-66,04
6	31,50	9,00	22,50	-71,43
7	38,00	7,00	31,00	-81,58
8	16,50	4,50	12,00	-72,73
9	40,50	37,00	3,50	-8,64
10	27,70	0,20	27,50	-99,28
11	7,00	0,00	7,00	-100,00
12	34,50	9,00	25,50	-73,91
13	21,20	3,70	17,50	-82,55
14	32,70	4,70	28,00	-85,63
15	24,50	3,50	21,00	-85,71
16	46,50	30,50	16,00	-34,41
17	40,20	0,20	40,00	-99,50
18	33,50	16,00	17,50	-52,24
19	47,50	27,50	20,00	-42,11
20	34,70	0,20	34,50	-99,42
Mean	**30,96**	**11,21**	**19,75**	**-68,40**
Minimum	7,00	0,00	0,00	-100,00
Maximum	47,50	40,00	40,00	0,00
Std.Dev.	10,64	12,52	10,16	28,70

9 Assessment of the study results

9.1 Skin tolerability

The test product **anti-eczema cream** was applied once a day onto the affected skin areas over a period of four weeks by 20 subjects. From the clinical-dermatological perspective no relevant skin reactions arose, the product was tolerated very well. Neither intolerance reactions in terms of skin irritation nor allergic reactions (contact dermatitis) were detected.

Accordingly, from the dermatological point of view, the tested product **anti-eczema cream** exhibits no high potential for skin irritation and sensitisation, when used as intended.

9.2 Efficacy

The efficacy of the test product **anti-eczema cream** in terms of SCORAD was determined by dermatologist or trained personnel (study nurses). A change in SCORAD of -68,40 % was demonstrated.

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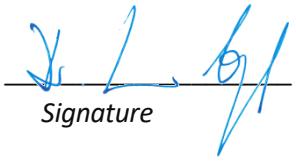
Signature

PhD Janina Tiemann
Biotechnologist


Signature

10 Addendum

10.1 Quality control, quality assurance and data protection

The quality of the study execution and of the data recording was ensured by ISO 9001 and checked in regular intervals internally as well as externally by monitoring through TÜV Rheinland.

The provisions of the applicable data privacy legislature were respected. All data of the subjects were handled confidentially and are disclosed to the sponsor only in a pseudonymised version. All data are stored for ten years.

10.2 Certificates

- Skin tolerability
- Efficacy

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Study number 2305307026

Muenster, 21 November 2023

Certificate

about the cosmetic product

anti-eczema cream

Clinical application study under control

(Test period June - November 2023)

The test product was applied over a period of four weeks by 20 subjects once daily on the affected skin area. From the clinical-dermatological point of view no relevant skin reactions occurred in the test area. The product was tolerated

excellently.

Neither intolerance reactions suggestive of irritation nor allergic reactions (contact dermatitis) were detected. Accordingly, from the dermatological point of view there is no high potential for irritation and sensitisation by the tested product when used as intended.

Based on the study design chosen and the confirmed skin tolerability, the 5-star seal can be used for the test product.

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Muenster, 21 November 2023

Certificate

about the cosmetic product

anti-eczema cream

Clinical application study under dermatological and control and determination of a modified SCORAD

(Test period June - November 2023)

The test product was applied during a period of four weeks by 20 subjects once day onto the affected skin areas. Determination of a modified SCORAD carried out under clinical-dermatological control showed

a change of a modified SCORAD by -68,40 %

in the test area.

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