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Study number 2110292240

Muenster, March, 4th, 2022

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

on 20 subjects with application of test product daily on the eyelids
over a period of four weeks
Examination for dermal tolerability including a final questionnaire
and macro photographs using the VISIA® system

Eyelid Cooling Patch

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1 General information

Title

Clinical application study under dermatological control

Testing body

Dermatest GmbH
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Specialists in dermatology

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Specialist in Dermatology
Venereology, Allergology,
Phlebology and Environmental Medicine

Dr. med. Gerrit Schlippe
Specialist in Dermatology and Venereology

Study coordinator

PhD Jens Klokkers
Biotechnologist

1.1 Synopsis

Table 1: Synopsis of the study

Study title	Clinical application study under dermatological control
Test product	**Eyelid Cooling Patch, consumer good**
Product type	Consumer good with cosmetic ingredients
Carrier material	Sodium polyacrylate
Study design	Single-centre
Testing body	Dermatest GmbH Engelstr. 37 D-48143 Münster
Expert report version and date	Version 1, Muenster, March, 4th, 2022
Test period	December 2021 – February 2022
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 - Digital recording / analysis with the VISIA® system - Photographs before and one hour after application , Visia TM, five subjects
Quantity of subjects	20, five subjects digital photographs with the VISIA® system
Application period	four weeks
Times of measurement	Questionnaire: $T_{28\,d}$ Skin moisture: $T_{0\,d}$ and $T_{28\,d}$
Test area	Both eyelids
Frequency of application	Once a day
Inclusion criteria	- 18 years and older - Female and male healthy volunteers - Skin type: any - Written informed consent of the subjects or legal guardian is available - subjects with swelling and tear sacs of the eyelids

Exclusion criteria	- Severe or chronic skin inflammations - Severe internal or chronic diseases - Taking of drugs that may interfere with skin reactions (glucocorticoids, antiallergics, topical immune modulators, etc.) - Application of active substance-containing products and care products 7-10 days before the start of the test - Severe allergies or any serious side effects of cosmetic preparations ever occurred - Sun baths or solarium visits during the study - Known neoplastic disease - Pregnancy and breast-feeding

1.2 Schedule

Table 2: Schedule of the study

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		✔
Digital recording / analysis VISIA®	✔	✔

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 **Eyelid Cooling Patch** 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 possibly sensitisation potential

- Application study

3.2 Secondary outcomes

Assessment of efficacy

- Query of the subjective impression by questionnaire
- Digital recording / analysis with the VISIA® system
- Photographs before and one hour after application , Visia TM, five subjects

3.3 Study parameters

Monocentric clinical trial over a period of four weeks

4 Selection of subjects

The study was carried out with 20 female and 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
- Skin type: any
- Written informed consent is present
- subjects with swelling and tear sacs of the eyelids

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 chronic skin inflammations
- Severe internal or chronic diseases
- Taking of drugs that may interfere with skin reactions (glucocorticoids, antiallergics, topical immune modulators, etc.)
- Application of active substance-containing products and care products 7-10 days before the start of the test
- Severe allergies or any serious side effects of cosmetic preparations ever occurred
- Sun baths or solarium visits during the study
- Known 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

Table 3: List of subjects of the study

Subject №	Initials	Sex [f/m]	Age	Visia TM photos
1	BaGe	f	39	-
2	BeJu	f	41	-
3	BeRe	f	69	yes
4	DuAl	f	22	yes
5	FrKa	f	34	yes
6	GrJe	f	26	-
7	HeVa	f	23	-
8	KaVe	f	35	yes
9	KeOk	f	46	yes
10	KlIs	f	28	yes
11	KoAr	m	29	-
12	LeVi	f	34	-
13	PiBi	f	41	yes
14	RaCh	f	30	-
15	SaJa	f	18	-
16	ScOl	f	53	-
17	ScDa	m	26	-
18	ScNi	f	37	-
19	StTi	m	39	yes
20	TaRo	f	27	-

5 Test product

5.1 Application of the investigational product

The product was applied on the eyelids 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

7.1 Query of the subjective impression

By means of a final questionnaire, very disparate and non-measurable parameters (subjectively experienced effect, smell, taste, consistency, influence on the appearance of the skin, etc.) can be determined. To this end, each subject independently fills in the respective questionnaire at the query times. In case of uncertainty, the attending study nurse or the attending dermatologist can be consulted and questioned at any time.

7.2 Digital imaging with the VISIA® System

The VISIA® system (Canfield Scientific, Inc.) allows taking of high-resolution digital images of the face under standardised conditions (distance from the camera, exposure, perspective, positioning of the face).

The following parameters can be visualised, analysed and compared using the VISIA® system:

In this study, no evaluations were made, but only the macro photographs were given to the client.

Table 4: Evaluable parameters of photos of the Visia™ system

Spots	Spots are brown or red lesions and include freckles, acne scars, hyperpigmentation and vascular lesions. Spots are to be distinguished from the conventional skin colour by colour and contrast. They vary in size and are predominantly circular.
Wrinkles	Wrinkles are creases, furrows or kinks in the skin that occur as a result of increased sun exposure and are associated with decreasing elasticity of the skin. This skin characteristic has the greatest variability from image to image, due to its dependence on the facial expression of the subject. Wrinkles are determined by the characteristics of the long and narrow shape.
Planeness	Texture is primarily an analysis of the uniformity of the skin. The "planeness" parameter measures the hue and uniformity of the skin by identifying the colour gradations, as well as the peaks and valleys on the skin surface that show variations in the surface texture.
Pores	Pores are circular openings of the sweat glands on the surface of the skin. Due to shading, pores appear darker than the surrounding skin tone, and they are identified by the darker colour and round shape. The VISIA® system distinguishes pores from spots by their size, since they are much smaller.
UV spots	UV spots occur in places when increased amounts of melanin are formed. UV spots are usually invisible under normal lighting conditions. The selective absorption of UV light by the epidermal melanin increases their appearance and detection by the VISIA® system.
Brown spots	Brown spots indicate melanin concentration on or under the skin. This appears in various forms of hyperpigmentation, such as sun damage or melasmata.
Red areas	Red areas represent blood or haemoglobin, respectively. Evaluation shows where under the skin surface there are signs of vascular diseases such as rosacea, telangiectasia (spider veins) or acne.
Porphyrins	*Propionibacterium acnes*, the bacterium that causes acne, synthesises and stores large amounts of porphyrins that are deposited in sebaceous glands. Porphyrins fluoresce under UV light and have a circular, white shimmering characteristic under this illumination.

For visualisation and analysis of the parameters, the face is exposed from the right and the left as well as frontally, using three procedures: IntelliFlash® (standardised light), cross-polarised light, and UV light (365 nm). Here, UV images allow the best possible evaluation and analysis of sun damage to the skin, and they visualise porphyrins. Images under polarised light increase contrast and saturation and reduce reflections and glare of shiny surfaces. Furthermore, Canfield's RBX® technology can be used to differentiate reddish and brownish skin so that telangiectasia (spider veins), hyperpigmentation, rosacea and acne can be optimally visualised. The fully automatic evaluation can be carried out in various ways:

Feature counts: Counting of frequencies with respect to a certain characteristic. This analysis allows the exact counting of the characteristics to be considered (e.g., wrinkles, pores, etc.). Only the number of these features is shown, regardless of the size or intensity of the respective feature.

Absolute scores: Comprehensive evaluation of a particular characteristic. Within this analysis, not only the frequency of a feature, but also its size, intensity and the effect on the condition of the skin are taken into account by means of an algorithm.

Per subject, three measurements are taken per time of measurement (from the left, from the right and from the front).

REFERENCES:

- http://www.canfieldsci.com
- VISIA User Guide CANFIELD Imaging Systems

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.

Table 5: Dermatological examination results

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 occur, the type of the reaction is assessed clinically-dermatologically, and the findings are documented using the following scale:

Table 6: Scale for assessment of possible skin reactions

–	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 do you like best about the eyelid cooling patches?**
   [2 x] Cooling effect
   [1 x] Cooling effect at the beginning
   [1 x] Pleasant cooling feeling during application
   [1 x] It cools, relaxes and there is an immediate effect.
   [1 x] The pads have a super decongestant effect. The care is visible and the easy handling is very practical.
   [1 x] Pleasant feeling
   [1 x] Soothing and cooling effect
   [1 x] Easy and quite comfortable to wear
   [1 x] Very good unexpected hold, comfortable to wear
   [1 x] Comfortable and cooling throughout application
   [1 x] Pleasantly cooling on the eyes
   [1 x] The pleasant scent
   [1 x] The cooling sensation on the skin
   [1 x] Easy to apply, pleasant cooling sensation
   [1 x] Very thin and pleasant on the skin
   [1 x] Pleasant to apply these cooling patches
   [1 x] The cool refreshment when applied
   [1 x] Pleasantly light on the eyes and super easy to apply
   [1 x] Easy to apply and the relaxing effect of the cooling patches

2. **What did you not like about the eyelid cooling patches?**
   [11 x] Nothing
   [1 x] You can't see anything for 15 minutes, it would be better to put it under the eyes.
   [1 x] The packaging (way too much plastic, doesn't fit in the yellow bag). (Please note: The yellow bag is a system for recycling plastic materials in Germany.)
   [1 x] The fact that you have to put it all over your eye and it is not practical because not being able to see for 15 minutes in the morning does not fit well into my daily routine.
   [1 x] Because it goes over the whole eye, it can burn a bit if you don't have your eyes completely closed all the time.
   [1 x] That it was on the eye.
   [1 x] After application, the skin on the eyes was a little tight.
   [1 x] That you have to keep your eyes closed for the time of the treatment.
   [1 x] I don't know anything.
   [1 x] The complete application on the eye and not just under the eyelid

3. **How do you rate the eyelid cooling patches overall?**
   [4 x] very good
   [12 x] good
   [4 x] sufficient
   [0 x] bad
   [0 x] very bad

   Additional comments:
   [1 x] I did not notice any decongestant effect.
   [1 x] Pleasant to wear, but not very practical for me in everyday life

4. **How do you rate the skin compatibility of the eyelid cooling patches?**
   [13 x] very good
   [6 x] good
   [1 x] sufficient
   [0 x] bad
   [0 x] very bad

   Additional comments:
   [1 x] It does well, no irritation.
   [1 x] No irritation or the like

5. **How do you judge the following statement: "My skin was not irritated from using the eyelid cooling patches?"**
   [16 x] I strongly agree
   [3 x] I tend to agree
   [0 x] I neither agree nor disagree
   [1 x] I tend to disagree
   [0 x] I strongly disagree

6. **How do you judge the following statement: "After application, have you experienced any type of discomfort such as stinging or itching?**
   [2 x] Yes, I felt

   [1 x] As already mentioned, it burns quickly if you don't have your eyes closed all the time.
   [1 x] The eyelashes were stuck together. This took a few minutes and did not work completely in the first wash.

   [18 x] No

7. **Was the patch comfortable to wear for each treatment?**
   [8 x] I strongly agree
   [10 x] I tend to agree
   [1 x] I neither agree nor disagree
   [1 x] I tend to disagree
   [0 x] I strongly disagree

8. **Was the patch gentle enough for everyday use?**
   [20 x] Yes
   [0 x] No, because

9. **How do you rate effectiveness eyelid cooling patches in reducing swollen eyelids?**
   [2 x] clearly visible
   [8 x] visible
   [10 x] slightly visible
   [0 x] unchanged

10. **How do you rate effectiveness eyelid cooling patches in reducing tear bags?**
    [1 x] clearly visible
    [5 x] visible
    [10 x] slightly visible
    [4 x] unchanged

11. **How do you rate this statement: "The daily application of the eyelid cooling patches does not dry out the skin at the application site?"**
    [5 x] I strongly agree
    [13 x] I tend to agree
    [0 x] I neither agree nor disagree
    [1 x] I tend to disagree
    [1 x] I strongly disagree

12. **How do you rate this statement: "The daily application of the eyelid cooling patches soothes swollen eyelids and tired eyes in the application area?"**
    [5 x] I strongly agree
    [13 x] I tend to agree
    [2 x] I neither agree nor disagree
    [0 x] I tend to disagree
    [0 x] I strongly disagree

13. How do you rate this statement: "The daily application of the eyelid cooling patches soothes reddened eyelids and tired eyes in the application area?"

[2 x] I strongly agree
[13 x] I tend to agree
[4 x] I neither agree nor disagree
[1 x] I tend to disagree
[0 x] I strongly disagree

14. Would you recommend the eyelid cooling patches?

[14 x] Yes
[6 x] No, because

[1 x] The application directly on the eye, with closed eyes in everyday life is not so practical.
[1 x] It is not practical to put something on your eyes for 15 minutes in the morning so that you can no longer see.
[1 x] I wouldn't necessarily recommend the patches to others, as I don't find it very pleasant to have them over the whole eye. However, as far as effectiveness and tolerance are concerned, there were no problems at all!
[1 x] Didn't like it so much on the eye
[1 x] Not effective and unpleasant skin feeling after use
[1 x] Not practical for me in everyday life. You can't do anything else during application.

Additional comments:

[1 x] It is worth trying out.

15. Would you buy the eyelid cooling patches after this application test?

[14 x] Yes
[6 x] No, because

[1 x] With its application not to be accommodated in the daily rhythm
[1 x] If I get severe discomfort in the eye region, then I would buy them.
[1 x] For the reasons mentioned before
[1 x] I think if I were looking for patches for the eyelids, I would rather get ones that don't cover the whole eye.
[1 x] Result was not as desired.
[1 x] See previous answer, not practical for me

9 Assessment of the study results

9.1 Skin tolerability

The test product **Eyelid Cooling Patch** was applied once a day onto the eyelid 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.

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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

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Certificate

about the consumer good with cosmetic ingredients

Eyelid Cooling Patch

Clinical application study under dermatological control

The test product was applied over a period of four weeks by 20 subjects once daily on both eyelids. 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 viewpoint, there is no high potential for irritation and sensitisation for the tested product when this is used as intended.

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