DERMACLAIM
Test & Trust

Project Reference

DC.289.36.102

Sponsor and Test Product

DEAD SEA & ARAVA SCIENCE CENTER

BRACELET TANKA T-MIGRAINE

Title of Study

HUMAN USE TEST IN 22 VOLUNTEERS AFTER TOPICAL TREATMENT FOR 8 WEEKS

Dermaclaim Lab S.L. ® || VAT: B16909699 || www.dermaclaim.com

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TABLE OF CONTENTS

1. EXECUTIVE SUMMARY

OBJECTIVE: To evaluate the volunteers' perception about "Bracelet T-Migraine" in 22 volunteers with frequent headache and migraine episodes, after topical treatment for 8 weeks.

PROCEDURE: 22 volunteers, aged from 27 to 66 years (mean 44.5 ± 11.3) were initially recruited for a human use test with Bracelet T-Migraine after topical treatment for 8 weeks (wearing 1 bracelet per month in one of the wrists). The volunteers were required to be between 30 and 65 years, with frequent headache and migraine episodes (≥ 56 in scale HIT-6 for headache and ≥ 2 in positive responses for ID Migraine Test), without using any medical treatment 15 days before and/or during the study, and a willingness to comply with instructions. All the subjects participating in the study gave their informed consent signed before the start of the treatment. The study was in compliance with the tenets of the Declaration of Helsinki. The selected volunteers were ordered according to the date of recruitment and worn the bracelet in one of the wrists for 8 weeks, according to client's needs. All the 22 volunteers completed the treatment. Before the start of the treatment, subjects attended clinical facilities to receive the samples and sign the corresponding informed consents. After 28 and 56 days of treatment, subjects attended clinical facilities and participant's subjective perception of the product efficacy was assessed with an individual questionnaire. The ordinal scale used was (1 = Poor | 2 = Fair | 3 = Good | 4 = Very good | 5 = Excellent). Satisfaction was considered for scores 3 - 5, and a remarkable percentage of acceptance was considered when average result is ≥ 80 %.

RESULTS: Data indicated an overall acceptance of 77.9 and 83.0, after 28 and 56 days of treatment, respectively. Specifically, significant positive evaluations (overall acceptance ≥ 80 %) were obtained for 6 out of 15 items after 4 weeks of treatment and 12 out of 15 items after 8 weeks.

CONCLUSION: The **topical application with "Bracelet T-Migraine" for 8 weeks in 22 volunteers shows good cutaneous compatibility and may claim "Dermatologically Tested", "Clinically Tested", and "Tolerance Tested"**. With regard to the volunteers' perception, data indicated an **overall acceptance of 77.9 and 83.0, after 28 and 56 days of treatment**, respectively.

Regarding cutaneous compatibility and acceptability, none of the 22 volunteers initially recruited showed any acceptability problem neither manifested any adverse symptom

or Serious Undesirable Effects (SUE) throughout the period of treatment or the following 7 days.

QUESTIONNAIRE AFTER 28 DAYS						
SENSORY EXPERIENCE	**1**	**2**	**3**	**4**	**5**	**% Satisfaction**
1. How much the application of the Bracelet is simple	0	0	2	3	17	**100**
2. How much the appearance of the Bracelet is pleasant	0	0	8	6	8	**100**
3. How much the feeling (texture) of the Bracelet is pleasant	0	1	5	9	7	**95**
4. How much the odor of the Bracelet is pleasant	0	2	3	11	6	**91**
5. How much the design of the Bracelet is attractive	1	2	10	6	3	**86**
TREATMENT EFFECTIVENESS	**1**	**2**	**3**	**4**	**5**	**% Satisfaction**
6. How the Bracelet reduce your migraine frequency	3	2	5	10	2	77
7. How much the Bracelet helps you to decrease migraine severity	4	3	3	10	2	68
8. How much the Bracelet improves your daily tasks	3	3	4	8	4	73
9. How much the Bracelet reduce the use pain killer (medicine)	3	3	4	6	6	73
10. How much the Bracelet improve your sleep quality	6	5	3	3	5	50
12. How much the Bracelet help you overcome pain	3	4	4	7	4	68
13 How much the Bracelet reduces your discomfort?	3	4	5	6	4	68
14. How much time is needed for you to feel relief/improvement? Please rate in days	**8,5**					
CONSUMER BEHAVIOUR	**1**	**2**	**3**	**4**	**5**	**% Satisfaction**
15 .I am satisfied with the treatment	3	4	0	6	9	68
16. I would use the Bracelet again	2	2	3	4	11	**82**
16. I would recommend the treatment	2	5	0	4	11	68
17. Have you ever used a similar product such as a food supplements (Y/N)	**NO (22) 100 %**				YES (0) 0 %	
18. I think the price of the Bracelet for 1 month should be (€)	16 €					
OVERALL ACCEPTANCE	**77,9**					

Table 1. Self-assessment questionnaire results after 28 days. *Volunteer's perception obtained for the different parameters regarding sensory experience, treatment effectiveness, and consumer behaviour, after 28 days of topical treatment with Bracelet T-Migraine in 22 volunteers. The ordinal scale used was (1 = Poor | 2 = Fair | 3 = Good | 4 = Very good | 5 = Excellent). Satisfaction was considered for scores 3, 4, and 5, and a remarkable percentage of acceptance was considered when average result is ≥ 80 % (in bold).*

QUESTIONNAIRE AFTER 56 DAYS						
SENSORY EXPERIENCE	**1**	**2**	**3**	**4**	**5**	**% Satisfaction**
1. How much the application of the Bracelet is simple	0	0	0	4	18	**100**
2. How much the appearance of the Bracelet is pleasant	0	4	4	8	6	**82**
3. How much the feeling (texture) of the Bracelet is pleasant	0	3	3	8	8	**86**
4. How much the odor of the Bracelet is pleasant	2	1	3	7	9	**86**
5. How much the design of the Bracelet is attractive	0	4	5	6	7	**82**
TREATMENT EFFECTIVENESS	**1**	**2**	**3**	**4**	**5**	**% Satisfaction**
6. How the Bracelet reduce your migraine frequency	2	2	8	8	2	**82**
7. How much the Bracelet helps you to decrease migraine severity	2	2	6	7	5	**82**
8. How much the Bracelet improves your daily tasks	1	2	8	5	6	**86**
9. How much the Bracelet reduce the use pain killer (medicine)	3	2	4	7	6	77
10. How much the Bracelet improve your sleep quality	3	1	8	6	4	**82**
12. How much the Bracelet help you overcome pain	3	1	6	9	3	**82**
13 How much the Bracelet reduces your discomfort?	3	1	8	6	4	**82**
14. How much time is needed for you to feel relief/improvement? Please rate in days	**16,0**					
CONSUMER BEHAVIOUR	**1**	**2**	**3**	**4**	**5**	**% Satisfaction**
15 .I am satisfied with the treatment	3	1	4	5	9	**82**
16. I would use the Bracelet again	3	2	1	6	10	77
16. I would recommend the treatment	3	2	1	8	8	77
17. Have you ever used a similar product such as a food supplements (Y/N)	**NO (22) 100 %**				YES (0) 0 %	
18. I think the price of the Bracelet for 1 month should be (€)	15 €					
OVERALL ACCEPTANCE	**83,0**					

Table 2. Self-assessment questionnaire results after 56 days. *Volunteer's perception obtained for the different parameters regarding sensory experience, treatment effectiveness, and consumer behaviour, after 56 days of topical treatment with Bracelet T-Migraine in 22 volunteers. The ordinal scale used was (1 = Poor | 2 = Fair | 3 = Good | 4 = Very good | 5 = Excellent). Satisfaction was considered for scores 3, 4, and 5, and a remarkable percentage of acceptance was considered when average result is ≥ 80 % (in bold).*

2. IDENTIFICATION OF STUDY

PROJECT REFERENCE: DC.289.36.102

SPONSOR: Dead Sea & Arava Science Center

TEST PRODUCTS: Bracelet T-Migraine

TITLE: Human use test in 22 volunteers after topical application for 8 weeks.

CLINICAL PROJECT MANAGER: Lucía Fernández Gómez, MSc

STUDY DIRECTOR: Alejandro Pérez Fernández, PhD

DERMATOLOGICAL SURVEILLANCE: Eduardo Bernía Petit, MD **License No**.: 464624840

3. PROVIDER AND EXPERIMENTAL CENTRE

COMPANY: Dermaclaim Lab S.L.

VAT NUMBER: B16909699

ADDRESS: Parc Cientific Universitat de Valencia (PCUV). Calle Agustín Escardino Benlloch, 9. 46980, Paterna (Valencia), España

EMAIL: dermaclaim@dermaclaim.com **PHONE**: +34 644 41 61 12

TESTING FACILITIES: Calle Doctor Vicente Zaragozà, 38 Bajo. 46020, Valencia (Valencia), España

EMAIL: clinica@dermaclaim.com **PHONE**: +34 644 03 50 20

4. SPONSOR

COMPANY: Dead Sea & Arava Science Center

ID TAX: 580458776

ADDRESS: Masada National Park. M.P. Dead Sea, 8691000. Israel

PROJECT RESPONSIBLE: Nimrod Vardi, CEO

EMAIL: amnonvardi@gmail.com

5. TEST PRODUCT

PRODUCT NAME: BRACELET TANKA T-MIGRAINE

REFERENCE & BATCH: Not provided

INCI: Not provided

DERMACLAIM REFERENCE: DC.0400

GALENIC: Not applicable

NUMBER AND TYPE OF SAMPLES: 50 bracelets

CONTENT: 1 Bracelet (one month)

STORAGE CONDITIONS: Room temperature (23 ± 1 ºC)

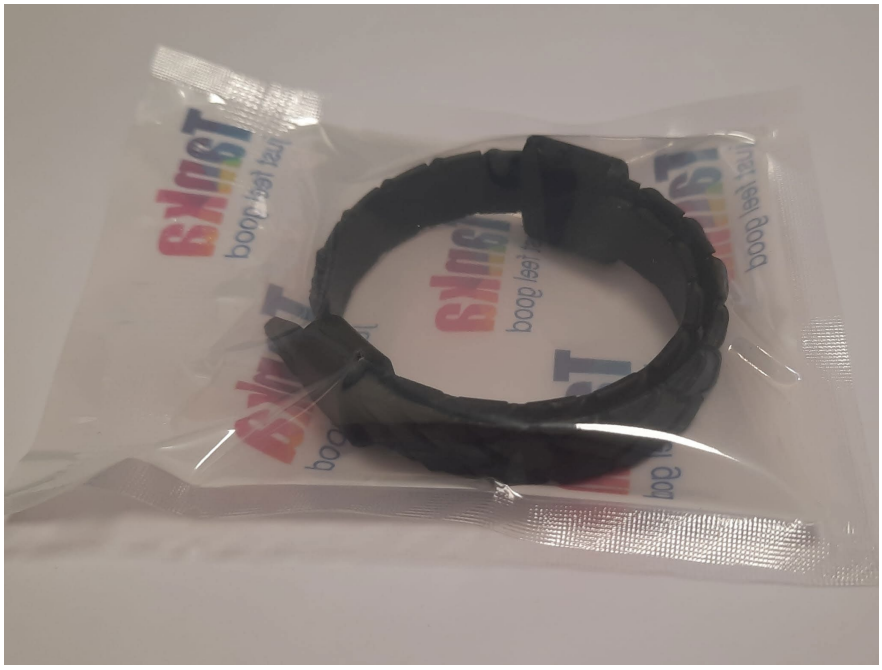

Figure 1. *Image showing Bracelet T-Migraine in its original container, used for the clinical study.*

Upon arrival at Dermaclaim Lab S.L. facilities, the test material was assigned a unique laboratory code number and registered into a daily log identifying sponsor, product name, batch number, number of units and quantity received, date of reception, status of the reception, storage conditions and reference of the project in which the sample is being analyzed.

Samples are kept for a period of 12 months, beyond submission of final report, unless otherwise specified by the sponsor.

6. DATES OF STUDY

STUDY START DATE: 10/07/2023

DATE OF SAMPLES' RECEPTION: 19/07/2023

PROCEDURE'S START DATE: 11/09/2023

PROCEDURE'S END DATE: 08/11/2023

FINAL REPORT DATE: 15/11/2023

REPORT REVIEWED DATE: 15/11/2023

REPORT DELIVERY DATE: 16/11/2023

7. ETHICAL RELEVANCE

This study was performed under clinical surveillance at the testing facilities. Experimental controls are the same participants whose parameters are evaluated upon product application, prior to initiate the treatment. This study has been conducted according to the general conditions of Dermaclaim Lab S.L., established for research studies involving human volunteers.

Before the beginning of the study, Dermaclaim internally assessed and approved its suitability for the product type and the methodology to be used. The study aimed at a better knowledge of the efficacy of the test product and the foreseeable risk incurred by the volunteers who took part in the study were minor, thus, there was a suitability between the aim of the study and its possible risks.

The experimental conditions adopted (type of treatment, quantity of product, frequency, duration, etc.) reproduced the normal conditions of use of the test product, and the test performed on a "small scale" reflected the application by the future consumers.

The study protocol is in accordance with the Scientific Committee on Consumer Safety (SCCS) guidance. It meets all international standards for research studies involving human subjects, Structure and Content of Clinical Study Reports from ICH Harmonised Tripartite Guideline; International Recommendations ICH Topic E6, European Parliament and Council Guideline 2001/20/CE, the Good Clinical Practices (ICH-GCP), and the World Medical Association. It has been conducted pursuant to the Declaration of Helsinki (1964), with the amendments of Tokyo (1975), Venice (1983), Hong Kong (1989), South Africa (1996), Edinburgh (2000), Seoul (2008), and Fortaleza (2013).

8. INTRODUCTION

Migraine, a complex neurological condition, affects millions worldwide, causing recurrent and often debilitating headaches accompanied by a spectrum of symptoms. According to the definition of International Headache Society, migraine is a recurrent headache disorder manifesting in attacks lasting 4 to 72 hours (when untreated or unsuccessfully treat). Migraine affects approximately 1 out of every 6 American adult population and 1 in 5 women over the past 3-month period [*Burch et al., 2018*]. Unlike other chronic diseases, people who are usually healthy, young and meddle-aged are more likely to get sick and women are more prone than men, especially for those aged 18 to 44 years [*Peters, 2019*].

The impact of migraine extends beyond the physical realm, significantly influencing an individual's quality of life, daily functioning, and productivity. Repeated migraine attacks can lead to anxiety, depression, cognitive decline, injury of vascular endothelium, and even increase the risk of stroke, which may be related to the pathogenesis of migraine Despite being a prevalent ailment, the mechanisms triggering migraines remain intricate and multifaceted, making its treatment a challenging endeavor [*Faurot et al., 2023*].

Many strategies for treating migraine improve the frequency and/or duration of attacks but may be associated with side effects that have a negative overall impact on quality of life. Overuse of medication for the treatment of frequent episodic migraine is a risk factor for developing chronic daily headache. Hence, it is critical to consider all symptoms related to quality of life when judging the therapeutic effectiveness of strategies for reducing migraine [*Buse et al., 2009*].

The research and evaluation of non-pharmacological or alternative interventions of migraine is therefore warranted. In this project, we aim to evaluate the volunteers' perception about "Bracelet T-Migraine" in 22 volunteers with frequent headache and migraine episodes, after topical treatment for 8 weeks.

9. PANEL OF VOLUNTEERS

9.1 Number

The number of volunteers initially recruited for the study was 22. All the 22 recruited volunteers attended to all the measurements and complete the treatment, and corresponding data was included in the analysis.

According to the date of recruitment, the subjects were ordinally assigned a permanent identification number within the study, from 1 to 22.

9.2 Inclusion criteria

The specific inclusion criteria, defined in the protocol, were as follows:

- ✓ Gender: Female/Male.
- ✓ Age: Between 30 and 65 years.
- ✓ Presenting frequent headache and migraine episodes, through ≥ 56 in scale HIT-6 for headache and ≥ 2 in positive responses for ID Migraine Test (Attachment 7) [*Shin et al., 2008; National Headache Foundation*]
- ✓ Last participation in a clinical study, ending at least one month before the start of this experiment.
- ✓ Wash-out period of 15 days before the start of the treatment with no medical treatment.
- ✓ Individuals with overall good health status and free of relevant health problems, including neurological, dermatological, or systemic disorders that could interfere with the results, under the Clinical Project Manager and the Study Director criteria. To be assessed by the principal researcher.
- ✓ Individuals who understand the instructions of use and are willing to cooperate with the study, as stated.
- ✓ Reading, understanding, and signature of the Protection of Personal Data and Communication consent.
- ✓ Reading, understanding, and signature of the Informed Consent for the study DC.289.36.102.

9.3 Exclusion criteria

- Subjects with a history of any form of skin cancer, melanoma, lupus, psoriasis, connective tissue disease, diabetes, or any disease that would increase risk associated with study participation.
- Allergy or reactivity to any of the components of the test product, or a product within the same or similar category than the tested one.
- Individuals currently undergoing medical treatment that may mask or interfere with the test results, under the Clinical Project Manager and the Study Director criteria.
- Relevant treatments (surgery procedures, etc.), on the experimental area finishing less than 6 months before the start of the study.
- Females who are pregnant or lactating or have been pregnant or given birth within the six-month period immediately preceding the start of the study.
- Forecast of change of routine or relevant way of life, during the period of study.

9.4 Recruitment tools and panel management

Panel recruitment is accomplished through advertisements in social media (Facebook, Instagram, or LinkedIn), direct communication (WhatsApp or SMS), any other electronic media, or any combination thereof.

Panel management is conducted by using Clinic Cloud v20220215.1 premium application (DOCTORALIA INTERNET SL, B62834981).

9.5 Constraints of the study

The constraints imposed on the volunteers were as follows:

- Full respect of the test products conditions of use.
- No application or intake of other products intended to treat headache or migraine during the period of study.

9.6 Panel features

Number of subjects initially recruited | completing the study Drop-outs (N, % of total)	22 | 22 0 (0 %)
Age range (Mean)	27 - 66 (44.5 ± 11.3)
Gender	Female: 16 | Male: 6
Ethnicity (race)	Caucasian: 21 | Latin: 1
Skin type (according to sebum levels)	Dry: 8 | Normal: 11 | Oily: 3
Skin phototype (according to Fitzpatrick)	II (white): 8 III (light brown): 14

Skin phototype is classified according to *Fitzpatrick, 1988*; whereas skin type is classified according to *Kim et al., 2006*:

Type	U-zone (cheek, chin)	T-Zone (forehead, nose)
Dry	< 70 µg/cm^2	< 100 µg/cm^2
Normal	70 – 170 µg/cm^2	100 – 210 µg/cm^2
Oily	> 170 µg/cm^2	> 210 µg/cm^2

Table 3. *Classification of the objective facial skin type by reference values of sebum casual levels measured with Sebumeter SM 815 (µg/cm^2).*

9.7 Informed consents

Informed consent forms describing reasons for the study, possible adverse effects, associated risks and potential benefits, and their limits of liability were obtained from volunteers prior to initiating the study. The participants read, signed, and dated the informed consent document to indicate their authorization to proceed and acknowledge their understanding of the contents (Attachment 5).

Additionally, all the volunteers included in this study had previously read, understood, and signed the Protection of Personal Data and Communication consent.

10. METHODOLOGY

10.1 Experimental conditions of use of the test product

The experimental conditions, defined in the protocol, were the following:

- Experimental areas: Wrist / Arm.
- Guidelines of use for the test product: To wear 1 bracelet in the same wrist / arm for 8 weeks (bracelet at D28 is substituted for 1 new bracelet).
- Application at research center: Plastic bag containing the bracelet was open in the clinical facilities and placed into volunteers' wrist, in order to start the treatment.
- Application at home: 1 bracelet per month, in the same wrist / arm.

10.2 Verification of the panel

On the first day of attendance to the experimental center, the Clinical Project Manager verified the inclusion and exclusion criteria previously defined for this study. In case of non-compliance with any of the criteria, the volunteer was excluded prior to the start of the study.

10.3 Environmental conditions

Not applicable.

10.4 Measurement site and frequency of measurements

Not applicable.

10.5 Instrumental assessment of the efficacy

Not applicable.

10.6 Calibration of the instrumental equipment

Not applicable.

10.7 Subjective evaluation of the efficacy

The efficacy of the treatment was subjectively assessed by participants via an individual questionnaire, filled in after 28 and 56 days of treatment, which covered items concerning sensory experience, treatment effectiveness, and consumer behavior, previously defined with the Sponsor. Volunteers' opinion was considered since it could reflect that of the potential consumer.

All the volunteers included in the study were considered to assess the cosmetic efficacy via questionnaire. For each item, the volunteers had to express their satisfaction according to an ordinal scale. The ordinal scale used was (1 = Poor | 2 = Fair | 3 = Good | 4 = Very good | 5 = Excellent). Satisfaction was considered for scores 3-5 and a remarkable percentage of acceptance was considered when average result is ≥ 80 % (in bold).

10.8 Checking of the acceptability

A visual examination of the experimental area was performed by the responsible technician before and after the application of the test product. The protocol and complete data were supervised, approved, and signed by the dermatologist.

The volunteers were requested to highlight any reaction observed and sensation of discomfort felt after the use of the test product, to the responsible technician conducting the study.

In case of reactivity or discomfort, the main sensations were described as heating, stinging, pruritus (itching), pulling, burning, or watering. The intensity of the sensations of discomfort was assessed according to an ordinal scale (slight, moderate, severe). The main visible signs that might be noted could be erythema, oedema, vesicle, bulla, papule, sab, dryness, coloration, or macula.

According to the specific information reported by the volunteer and the definitions provided by The European Cosmetic and Perfumery Association (Colipa), the reaction is classified as undesirable event, undesirable effect (UE), or serious undesirable effect (SUE) (Table 4, Attachment 15.3).

Undesirable event	Undesirable effect (UE)	Serious undesirable effect (SUE)
0	0	0

***Table 4. Undesirable events table**. Table showing undesirable events, undesirable effects (UE), and serious undesirable effects (SUE), taken place during the period of treatment.*

Participants showed no Serious Undesirable Effects (SUE) and declared neither discomfort nor Undesirable Effects (UE) throughout the period of treatment or the following 7 days.

10.9 Statistical analysis

For each item, the volunteers had to express their satisfaction according to an ordinal scale. Satisfaction was considered for scores 3 - 5 and the threshold to consider a remarkable satisfaction percentage was set at 80 % by Dermaclaim scientific staff.

10.10 Consumption control

Product samples assigned to volunteers were weighed before the start of the treatment and at each of the timepoints (D28 and D56) and the applied amount was calculated by subtraction (D28/D56 – D0) (Table 5, Attachment 3).

N Vol	QUANTITY OF SAMPLES USED (g)		
	D28	D56	Per day
MEAN	0,046	0,118	0,002
SD	0,139	0,198	0,004

***Table 5. Consumption control results**. Mean average and standard deviation with regard to the quantity of sample used during the study after 4 and 8 weeks of treatment (in grams).*

10.11 Volunteers' diary

Beyond the consumption control, compliance and participant adherence during the clinical trial is assessed by using a diary. At the initial visit, volunteers were ordered to fill the diary daily for each application of the test treatment during the whole study. In case of specific comments or adverse reactions, they can also use the daily register to note them.

Physical documents are kept during 12 months, after finishing the study, in paper format. An example of volunteers' diary is shown in Attachment 6.

10.12 Follow-up of volunteers during the period of treatment

In order to keep all the volunteers involved in the study, reduce the possibilities of abandonment, and assure the correct application of the corresponding treatment, Dermaclaim is in direct contact with the volunteers through the following:

- Reminder email for each appointment.
- Reminder WhatsApp before each specific appointment.
- Individual contact with each volunteer every 2 weeks.

10.13 Protocol deviations

The consumption control yielded negative values for some of the samples, when subtracting the weight of the plastic bag to the initial weight at D0. Similar effect was obtained for some samples after the second month of treatment. This effect might be due to the slight variability of the weighing scale between measurements at different timepoints, due to an absence of extract release within some specific bracelets, or due to possible interferences with external fluids or particles the bracelets could have acquired (e.g. sweating, water, urban dust…).

11. RESULTS

The number of volunteers that assigned each possible score to the indicated item and the percentage of satisfied volunteers (also indicated as percentage of acceptance), is described in Table 6-7.

QUESTIONNAIRE AFTER 28 DAYS						
SENSORY EXPERIENCE	**1**	**2**	**3**	**4**	**5**	**% Satisfaction**
1. How much the application of the Bracelet is simple	0	0	2	3	17	**100**
2. How much the appearance of the Bracelet is pleasant	0	0	8	6	8	**100**
3. How much the feeling (texture) of the Bracelet is pleasant	0	1	5	9	7	**95**
4. How much the odor of the Bracelet is pleasant	0	2	3	11	6	**91**
5. How much the design of the Bracelet is attractive	1	2	10	6	3	**86**
TREATMENT EFFECTIVENESS	**1**	**2**	**3**	**4**	**5**	**% Satisfaction**
6. How the Bracelet reduce your migraine frequency	3	2	5	10	2	77
7. How much the Bracelet helps you to decrease migraine severity	4	3	3	10	2	68
8. How much the Bracelet improves your daily tasks	3	3	4	8	4	73
9. How much the Bracelet reduce the use pain killer (medicine)	3	3	4	6	6	73
10. How much the Bracelet improve your sleep quality	6	5	3	3	5	50
12. How much the Bracelet help you overcome pain	3	4	4	7	4	68
13 How much the Bracelet reduces your discomfort?	3	4	5	6	4	68
14. How much time is needed for you to feel relief/improvement? Please rate in days	**8,5**					
CONSUMER BEHAVIOUR	**1**	**2**	**3**	**4**	**5**	**% Satisfaction**
15. I am satisfied with the treatment	3	4	0	6	9	68
16. I would use the Bracelet again	2	2	3	4	11	**82**
16. I would recommend the treatment	2	5	0	4	11	68
17. Have you ever used a similar product such as a food supplements (Y/N)	**NO (22) 100 %**				YES (0) 0 %	
18. I think the price of the Bracelet for 1 month should be (€)	16 €					
OVERALL ACCEPTANCE	**77,9**					

Table 6. Self-assessment questionnaire results after 28 days. *Volunteer's perception obtained for the different parameters regarding sensory experience, treatment effectiveness, and consumer behaviour, after 28 days of topical treatment with Bracelet T-Migraine in 22 volunteers. The ordinal scale used was (1 = Poor | 2 = Fair | 3 = Good | 4 = Very good | 5 = Excellent). Satisfaction was considered for scores 3, 4, and 5, and a remarkable percentage of acceptance was considered when average result is ≥ 80 % (in bold).*

QUESTIONNAIRE AFTER 56 DAYS						
SENSORY EXPERIENCE	**1**	**2**	**3**	**4**	**5**	**% Satisfaction**
1. How much the application of the Bracelet is simple	0	0	0	4	18	**100**
2. How much the appearance of the Bracelet is pleasant	0	4	4	8	6	**82**
3. How much the feeling (texture) of the Bracelet is pleasant	0	3	3	8	8	**86**
4. How much the odor of the Bracelet is pleasant	2	1	3	7	9	**86**
5. How much the design of the Bracelet is attractive	0	4	5	6	7	**82**
TREATMENT EFFECTIVENESS	**1**	**2**	**3**	**4**	**5**	**% Satisfaction**
6. How the Bracelet reduce your migraine frequency	2	2	8	8	2	**82**
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8. How much the Bracelet improves your daily tasks	1	2	8	5	6	**86**
9. How much the Bracelet reduce the use pain killer (medicine)	3	2	4	7	6	77
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12. How much the Bracelet help you overcome pain	3	1	6	9	3	**82**
13 How much the Bracelet reduces your discomfort?	3	1	8	6	4	**82**
14. How much time is needed for you to feel relief/improvement? Please rate in days	**16,0**					
CONSUMER BEHAVIOUR	**1**	**2**	**3**	**4**	**5**	**% Satisfaction**
15. I am satisfied with the treatment	3	1	4	5	9	**82**
16. I would use the Bracelet again	3	2	1	6	10	77
16. I would recommend the treatment	3	2	1	8	8	77
17. Have you ever used a similar product such as a food supplements (Y/N)	**NO (22) 100 %**				YES (0) 0 %	
18. I think the price of the Bracelet for 1 month should be (€)	15 €					
OVERALL ACCEPTANCE	**83,0**					

Table 7. Self-assessment questionnaire results after 56 days. *Volunteer's perception obtained for the different parameters regarding sensory experience, treatment effectiveness, and consumer behaviour, after 56 days of topical treatment with Bracelet T-Migraine in 22 volunteers. The ordinal scale used was (1 = Poor | 2 = Fair | 3 = Good | 4 = Very good | 5 = Excellent). Satisfaction was considered for scores 3, 4, and 5, and a remarkable percentage of acceptance was considered when average result is ≥ 80 % (in bold).*

Data indicated an overall acceptance of 77.9 and 83.0, after 28 and 56 days of treatment, respectively.

Specifically, significant positive evaluations (overall acceptance ≥ 80 %) were obtained for 6 out of 15 items after 4 weeks of treatment and 12 out of 15 items after 8 weeks.

- 1. How much the application of the Bracelet is simple (D28 – D56).
- 2. How much the appearance of the Bracelet is pleasant (D28 – D56).
- 3. How much the feeling (texture) of the Bracelet is pleasant (D28 – D56).
- 4. How much the odor of the Bracelet is pleasant (D28 – D56).
- 5. How much the design of the Bracelet is attractive (D28 – D56).
- 6. How the Bracelet reduce your migraine frequency (D56).
- 7. How much the Bracelet helps you to decrease migraine severity (D56).
- 8. How much the Bracelet improves your daily tasks (D56).
- 10. How much the Bracelet improve your sleep quality (D56).
- 12. How much the Bracelet help you overcome pain (D56).
- 13. How much the Bracelet reduces your discomfort? (D56).
- 15. I am satisfied with the treatment (D56).
- 16. I would use the Bracelet again (D28).

12. CONCLUSION AND SIGNATURES

The goal of this study was to evaluate the volunteers' perception about "Bracelet T-Migraine" in 22 volunteers with frequent headache and migraine episodes, after topical treatment for 8 weeks.

To achieve this goal, 22 volunteers, aged from 27 to 66 years (mean 44.5 ± 11.3) were initially recruited for a human use test with Bracelet T-Migraine after topical treatment for 8 weeks (wearing 1 bracelet per month in one of the wrists). The volunteers were required to be between 30 and 65 years, with frequent headache and migraine episodes (positive response in questionnaire HIT-6 and ID Test for migraine), without using any medical treatment 15 days before and/or during the study, and a willingness to comply with instructions. All the subjects participating in the study gave their informed consent signed before the start of the treatment. The study was in compliance with the tenets of the Declaration of Helsinki. The selected volunteers were ordered according to the date of recruitment and worn the bracelet in one of the wrists for 8 weeks, according to client's needs. All the 22 volunteers completed the treatment. Before the start of the treatment, subjects attended clinical facilities to receive the samples and sign the corresponding informed consents. After 28 and 56 days of treatment, subjects attended clinical facilities and participant's subjective perception of the product efficacy was assessed with an individual questionnaire. The ordinal scale used was (1 = Poor | 2 = Fair | 3 = Good | 4 = Very good | 5 = Excellent). Satisfaction was considered for scores 3 - 5, and a remarkable percentage of acceptance was considered when average result is ≥ 80 %.

Results indicated an overall acceptance of 77.9 and 83.0, after 28 and 56 days of treatment, respectively. Specifically, significant positive evaluations (overall acceptance ≥ 80 %) were obtained for 6 out of 15 items after 4 weeks of treatment and 12 out of 15 items after 8 weeks.

In conclusion, the **topical application with "Bracelet T-Migraine" for 8 weeks in 22 volunteers shows good cutaneous compatibility and may claim "Dermatologically Tested", "Clinically Tested", and "Tolerance Tested"**. With regard to the volunteers' perception, data indicated an **overall acceptance of 77.9 and 83.0, after 28 and 56 days of treatment**, respectively.

Regarding cutaneous compatibility and acceptability, none of the 22 volunteers initially recruited showed any acceptability problem neither manifested any adverse symptom or Serious Undesirable Effects (SUE) throughout the period of treatment or the following 7 days.

Clinical Project Manager

Lucía Fernández Gómez, MSc **Date:** 08/11/2023

… declares the study was conducted in accordance with the spirit of the Good Clinical Practices (International Recommendations ICH topic E6), and the results reported in this final report accurately and completely reflect the raw data of the study.

Study Director

Alejandro Pérez Fernández, PhD **Date:** 15/11/2023

… declares the study was carried out under my responsibility, the content of the study report is reliable and takes into account the "Guidelines for the evaluation of the efficacy of cosmetics products" (May, 2008) from Colipa. The test product may claim Clinically Tested.

Dermatologist

Eduardo Bernía Petit, MD. College Number 464624840 **Date:** 13/11/2023

… declares the clinical protocol was designed and conducted under my surveillance, in accordance with the Scientific Committee on Consumer Safety (SCSS) guidance. The test product may claim Dermatologically Tested and Tolerance Tested.

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13. ARCHIVING AND DISCLOSURE

All original raw data, including data sheets, clinical protocols, technical procedures, laboratory notebooks, correspondence files, copies of final reports, and remaining samples, are maintained on the premises of Dermaclaim Lab S.L., in limited access marked storage files. Altogether, including the information provided by the sponsor, volunteers' data, information about materials, reagents or methodology, and all the information generated by Dermaclaim Lab S.L. (statistical analysis, graphical representations, etc.) is considered Confidential, and will not be shared with third parties.

To prevent loss of and protect intellectual property, the final report has been electronically signed using the official signature of Dermaclaim Lab S.L. (VAT: B16909699). Any attempt to remove the signature will irreversibly damage the label and leave an immediate trace, thus invalidating the document.

Only reports containing the Dermaclaim Lab S.L. electronic signature intact, will be recognized by Dermaclaim Lab S.L. as a certified original.

Dermaclaim Lab S.L. represents filly independent testing facilities committed to the highest standards of unbiased testing and reporting. Dermaclaim Lab S.L. is not in partnership, affiliation and/or association, in any way, with any other corporation, company, sole proprietorship, partnership, client, laboratory, and/or any other business entity. Dermaclaim Lab S.L. is not legally responsible or bound to any claim(s) provided by a third party claiming any kind of association with Dermaclaim Lab S.L.

The industrial and intellectual property rights that may arise from the contracted services, as well as the ownership of the results, belongs entirely to the Sponsor, unless expressly stated otherwise in the corresponding budget.

14. CERTIFICATIONS AND REGULATIONS

The study protocol is in accordance with the Scientific Committee on Consumer Safety (SCCS) guidance. It meets all international standards for research studies involving human subjects, Structure and Content of Clinical Study Reports from ICH Harmonised Tripartite Guideline; International Recommendations ICH Topic E6, European Parliament and Council Guideline 2001/20/CE, the Good Clinical Practices (ICH-GCP), and the World Medical Association. It has been conducted pursuant to the Declaration of Helsinki (1964), with the amendments of Tokyo (1975), Venice (1983), Hong Kong (1989), South Africa (1996), Edinburgh (2000), Seoul (2008), and Fortaleza (2013).

The whole process involving this assay was performed following UNE-EN-ISO 9001/2015 Quality Management System guidelines, certified on August 5th, 2022 (reference code, EC-10984/22) and positively reviewed on July 10th, 2023.

The studies follow the "Guidelines for the Evaluation of the Efficacy of cosmetic Products", COLIPA, May 2008.

14.1 GENERAL PRINCIPLES FOR ALL TESTS (Rev. Efficacy Evaluation Guidelines – May 2008, COLIPA)

Studies must be relevant and comprised of methods which are reliable and reproducible. The studies should follow a well-designed and scientifically valid methodology according to good practices. The criteria used for evaluation of product performances should be defined with accuracy and chosen in compliance with the aim of the test.

Studies conducted on volunteers should naturally respect ethical rules and products tested should have previously undergone a safety investigation. Human studies should be conducted on the target population, when necessary, defined by strict inclusion / exclusion criteria.

Depending on the aim of the study, tests can be open, single- or double-blind.

A study protocol must be drawn up and validated by the parties involved. This is essential to enable the study manager / promoter to monitor the study and the experimenter to carry out the test in order to ensure its quality.

The test laboratories must have standardized operating procedures. The equipment must be the subject of documented maintenance adapted to its use. Whatever the type of study, it is important that the person conducting the study:

- has the appropriate qualifications.

- has the training and experience in the field of the proposed study; and

- is respected for ethical quality and professional integrity.

A study monitoring system must be set up in order to ensure that the protocol and the operating procedures are correctly followed.

Data processing and the interpretation of results must be fair and should not overstep the limits of the test's significance. Data recording, transformations, and representation in tabular or graphical form should be transparent or clearly explained if complex. It should not be designed to overstate the effect(s) measured. Appropriate statistical analysis of the data should be performed.

A critical point for the validity of consumer tests is the wording of the questionnaire. The questions and proposed answers should be clear enough to be unequivocally understood by participants. The answers scale should be well balanced (e.g., same number of positive and negative answers) and not capable of influencing the answer. Special attention should be paid to the wording of questions for which responses will be used to substantiate the claim: the claim should be directly substantiated by the results related to the relevant question without any questionable interpretation.

14.2 SUBSTANTIATION OF CLAIMS (EU Regulation 655/2013)

Cosmetic claims must comply with EU Regulation 655/2013 that provides the Common Criteria to ensure that the information conveyed to the end-users through claims is useful, understandable, and reliable so that consumers can make informed decisions.

Claims for cosmetic products, whether explicit or implicit, shall be supported by adequate and verifiable evidence regardless of the types of evidential support used to substantiate them, including where appropriate expert assessments. Evidence for claim substantiation shall consider the state-of-the-art practices.

Products may bear claims that relate to the nature of experimental studies. Consumer expectations regarding these claims may vary depending upon the presentation of the claim and its specific context. However, in all circumstances, consumers will expect that such claims are made only when the effects tested are favorable.

Use test claims such as tolerance tested, under medical surveillance, clinically tested, dermatologically tested, etc… should be substantiated, according to the following explanation:

TOLERANCE TESTED	CLINICALLY TESTED	DERMATOLOGICALLY TESTED
The product underwent tests under the supervision of a scientifically qualified professional intended to study its tolerance on a target group and that the results of those tests show that the product was well tolerated by this group.	The product was tested on humans under the supervision of a medically qualified professional or another scientifically qualified professional according to a clinical protocol or in a clinical setting.	The product was tested on humans under the supervision of a dermatologist. Depending on the presentation of the claim, it may refer to a specific efficacy or tolerance of the product. Consumer self-perceptions studies are not appropriate to support such claims.

14.3 CLASSIFICATION OF ADVERSE REACTIONS (Colipa, March 2016)

An **undesirable or adverse event** is defined as any human adverse health event which is voluntarily reported by consumers, healthcare professionals, Competent Authorities, and any other individuals to have occurred during or after normal or reasonably foreseeable use (exclude misuse and abuse) of a cosmetic product. It is not necessarily related to the product.

Undesirable effect (UE) means an adverse reaction for human health attributable to the normal or reasonably foreseeable use of a cosmetic product. Undesirable Effects include but are not limited to irritant or allergic reactions that can affect the skin, eyes or mouth. Undesirable effects caused by product misuse and abuse are not included in this definition.

A **serious undesirable effect (SUE)** means an undesirable effect which results in temporary or permanent functional incapacity, disability, hospitalization, congenital anomalies or an immediate vital risk or death.

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16. ATTACHMENTS

16.1 Attachment 1. Volunteers' data

VOLUNTEERS'S DATA							
Nº Volunteer	ID Volunteer	Gender	Age	Ethnicity	Skin Type	Skin Phototype	Left / Right
1	2635	Female	40	Caucasian	Dry	III (light brown)	R
2	1449	Male	66	Caucasian	Combination	III (light brown)	L
3	76	Female	46	Caucasian	Dry	II (white)	L
4	1036	Female	45	Caucasian	Combination	II (white)	L
5	2167	Female	42	Latin	Combination	III (light brown)	R
6	1140	Female	37	Caucasian	Dry	III (light brown)	R
7	109	Female	31	Caucasian	Combination	III (light brown)	R
8	2627	Female	49	Caucasian	Combination	III (light brown)	R
9	1943	Female	35	Caucasian	Dry	II (white)	L
10	2195	Female	41	Caucasian	Combination	II (white)	L
11	839	Female	30	Caucasian	Combination	III (light brown)	L
12	52	Female	39	Caucasian	Oily	II (white)	L
13	370	Female	56	Caucasian	Combination	III (light brown)	R
14	1726	Female	48	Caucasian	Dry	III (light brown)	R
15	785	Female	27	Caucasian	Combination	II (white)	R
16	2668	Male	64	Caucasian	Oily	III (light brown)	R
17	1032	Male	32	Caucasian	Oily	III (light brown)	L
18	1948	Male	62	Caucasian	Dry	III (light brown)	R
19	2044	Male	58	Caucasian	Dry	II (white)	R
20	2667	Male	49	Caucasian	Combination	III (light brown)	L
21_extra	2670	Female	36	Caucasian	Dry	II (white)	R
22_extra	685	Female	45	Caucasian	Combination	III (light brown)	L

***Table 8**. Panel data. Data (Number of volunteers within the study, Dermaclaim's ID for each volunteer, age, gender, skin ethnicity, skin type, sensitive skin, skin phototype, wrist wearing the bracelet during the study, and results for the initial tests) of the volunteers included in the study.*

16.2 Attachment 2. Daily visit registration

DAILY REGISTRATION			
Nº Volunteer	**Day 0**	**Day 28**	**Day 56**
1	11/09/2023 16:15	10/10/2023 16:30	08/11/2023 16:30
2	13/09/2023 10:15	06/10/2023 10:30	08/11/2023 12:00
3	11/09/2023 9:30	10/10/2023 9:30	08/11/2023 13:00
4	12/09/2023 9:45	11/10/2023 9:45	08/11/2023 8:45
5	11/09/2023 10:00	10/10/2023 10:00	08/11/2023 10:00
6	11/09/2023 17:00	10/10/2023 15:30	08/11/2023 15:30
7	11/09/2023 13:00	11/10/2023 9:45	08/11/2023 13:00
8	12/09/2023 10:00	11/10/2023 10:30	08/11/2023 10:30
9	11/09/2023 12:15	10/10/2023 12:15	08/11/2023 12:15
10	11/09/2023 12:30	10/10/2023 12:00	08/11/2023 12:00
11	12/09/2023 11:00	11/10/2023 13:15	08/11/2023 13:30
12	12/09/2023 14:30	11/10/2023 10:00	08/11/2023 10:00
13	12/09/2023 16:30	10/10/2023 16:45	08/11/2023 16:15
14	11/09/2023 15:30	10/10/2023 7:30	08/11/2023 15:00
15	11/09/2023 8:30	10/10/2023 8:30	08/11/2023 8:30
16	11/09/2023 11:00	10/10/2023 10:30	08/11/2023 10:15
17	12/09/2023 16:30	10/10/2023 16:45	08/11/2023 16:30
18	11/09/2023 11:00	10/10/2023 14:45	08/11/2023 12:00
19	12/09/2023 9:15	11/10/2023 9:00	08/11/2023 9:15
20	11/09/2023 15:00	10/10/2023 14:45	08/11/2023 15:00
21_extra	11/09/2023 14:00	10/10/2023 12:30	08/11/2023 11:00
22_extra	12/09/2023 15:30	10/10/2023 0:00	08/11/2023 15:30

Table 9. Daily visit registration*. Date and time for each of the visits conducted for each of the volunteers.*

16.3 Attachment 3. Consumption control

N Vol	WEIGHT OF SAMPLES (g)				QUANTITY OF SAMPLES USED (g)		
	Wristband I		Wristband II				
	D0	D28	D28	D56	D28	D56	Per day
1	7,99	8,01	8,60	8,54	-0,02	0,04	0,001
2	8,28	8,31	7,99	7,94	-0,03	0,02	0,000
3	8,05	8,07	8,05	7,98	-0,02	0,05	0,001
4	8,01	8,06	8,23	8,30	-0,05	-0,12	-0,002
5	8,00	7,98	8,06	7,96	0,02	0,12	0,002
6	8,07	8,00	8,03	7,95	0,07	0,15	0,003
7	8,00	7,97	8,06	8,01	0,03	0,08	0,001
8	8,07	8,18	8,22	8,20	-0,11	-0,09	-0,002
9	8,29	8,22	8,35	8,26	0,07	0,16	0,003
10	8,00	7,95	8,20	8,12	0,05	0,13	0,002
11	8,03	8,02	8,03	7,98	0,01	0,06	0,001
12	8,30	8,31	8,00	8,00	-0,01	-0,01	0,000
13	8,18	8,16	8,05	7,93	0,02	0,14	0,003
14	7,98	7,94	8,12	7,98	0,04	0,18	0,003
15	8,36	7,91	8,28	7,94	0,45	0,79	0,014
16	8,05	8,09	8,32	8,31	-0,04	-0,03	-0,001
17	8,20	8,16	8,01	8,00	0,04	0,05	0,001
18	8,05	8,02	8,01	7,94	0,03	0,10	0,002
19	8,20	8,27	8,04	8,01	-0,07	-0,04	-0,001
20	8,01	7,98	8,32	8,21	0,03	0,14	0,002
21	7,99	7,93	8,22	8,14	0,06	0,14	0,003
22	8,26	7,81	8,21	8,13	0,45	0,53	0,009
MEAN	**8,108**	**8,061**	**8,155**	**8,083**	**0,046**	**0,118**	**0,002**
SD	**0,125**	**0,136**	**0,155**	**0,162**	**0,139**	**0,198**	**0,004**

Table 10. Raw data for consumption control*. Raw data (g) regarding the weight of the samples belonging to each volunteer, and calculation of the quantity used at each of the time points, and the mean quantity used per day.*

16.4 Attachment 4. Panelist self-assessment

QUESTIONNAIRE AFTER 28 DAYS	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
SENSORY EXPERIENCE																						
1. How much the application of the Bracelet is simple	5	5	5	5	4	5	5	5	5	3	5	5	5	5	5	4	5	5	5	5	4	3
2. How much the appearance of the Bracelet is pleasant	5	4	5	3	4	5	3	5	3	3	3	4	5	3	3	5	4	5	4	5	3	4
3. How much the feeling (texture) of the Bracelet is pleasant	4	5	5	5	3	5	4	5	3	3	3	4	5	3	2	4	4	5	4	4	4	4
4. How much the odor of the Bracelet is pleasant	5	3	4	5	4	4	4	5	4	3	4	4	5	2	4	5	5	4	4	3	2	4
5. How much the design of the Bracelet is attractive	4	3	4	3	4	5	2	3	3	3	3	4	3	3	1	5	5	3	4	4	3	2
TREATMENT EFFECTIVENESS																						
6. How the Bracelet reduce your migraine frequency	4	3	4	4	4	5	2	1	3	4	2	3	3	5	4	3	4	4	4	1	1	4
7. How much the Bracelet helps you to decrease migraine severity	4	2	4	3	4	5	2	1	1	4	2	3	4	4	5	4	4	4	3	1	1	4
8. How much the Bracelet improves your daily tasks	4	3	4	4	4	5	2	2	1	4	2	3	4	5	5	4	4	5	3	1	1	3
9. How much the Bracelet reduce the use pain killer (medicine)	4	3	5	4	4	5	2	2	1	4	2	3	5	5	5	3	5	4	3	1	1	4
10. How much the Bracelet improve your sleep quality	5	2	4	4	1	5	2	1	1	2	1	2	3	5	3	3	5	5	4	1	1	2
12. How much the Bracelet help you overcome pain	4	2	4	3	4	5	2	2	1	4	2	3	5	5	4	3	4	5	3	1	1	4
13 How much the Bracelet reduces your discomfort?	4	2	4	3	4	5	2	2	1	4	2	3	5	5	4	3	4	5	3	1	1	3
14. How much time is needed for you to feel relief/improvement? Please rate in days	15		20	12	1	7			7	7	15	7	28	3	3	4	0	10	2			3
CONSUMER BEHAVIOUR																						
15 .I am satisfied with the treatment	5	4	5	4	5	5	2	2	1	4	2	2	5	5	5	4	5	5	4	1	1	4
16. I would use the Bracelet again	5	4	5	5	4	5	2	3	3	5	1	2	5	5	5	5	5	5	4	1	3	4

16. I would recommend the treatment	5	4	5	5	5	5	2	2	1	5	2	2	5	5	5	4	5	5	4	1	2	4
17. Have you ever used a similar product such as a food supplements (Y/N)	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
18. I think the price of the Bracelet for 1 month should be (€)	20 €	30	20	15	15	16	10	20 €	10 €	18	15	10		25 €	10	15 €	15	20		10		15 €

Vol	11. How much the Bracelet reduce your migraine frequency compared to before treatment (number)
1	Before 5 a month now 2 a month
2	-
3	Before month 6 now I have had 2
4	This month I have only had 1
5	Before 5 now 2
6	I have noticed a difference before 4 now 1
7	I've noticed that I don't get a migraine as often, but I've still had it on several days for more than half the day.
8	Before 3 or 4 now 3
9	-
10	Before 5, now 2
11	Before 4 a week now 3 a week
12	Same number, less intensity
13	Before every other day, and now once a week or so, it has improved a lot.
14	-
15	Before 17 a month, now 2-3 a month
16	Before 15 a month now 6 a month
17	Before 4 a month now 1 a month
18	Before 2 a month, this month none
19	To the half
20	-

21	Same
22	Before 2 or 3 a month, for now I have only had 1 migraine

Vol	19. Comment
1	Great smell and phenomenal results
2	I have not had strong migraine episodes. Temporary headaches
3	It has been fantastic, I would buy it without thinking about it
4	My experience has been gratifying, I only had a crisis one day, but in general I am happy, I also highlight that its smell is very relaxing.
5	As the days go by, the appearance deteriorates, it looks very worn out.
6	I liked it
7	I haven't noticed much improvement, maybe I haven't had a migraine so recently but I don't know, if this would have been the same without the bracelet. I have had to take medication due
8	The bracelet is quite loose, it is somewhat rigid. I would use it again, because I believe that migraine treatments are slow in effectiveness and need time to start to take effect.
9	The smell is pleasant and relaxing
10	It would be ideal if it were smaller and more flexible, the color is fine. The smell it has is only the first few days, it is not unpleasant and in my opinion it reduces the migraine a lot although
11	At night it usually opens, it is too wide and is a bit uncomfortable to wear with a watch or other bracelets.
12	I feel slight relief, but the frequency has not decreased
13	That it does not deteriorate, and that the perfume will last longer
14	I don't know if it's suggestion, but it's effective from the first days. The most annoying thing is the smell, it is too strong
15	I really love it, it's incredible, I want to know how it really does it, what formulas it has inside, I'm speechless. After 10 years with almost daily migraines...I can't believe that a month went b
16	After two or three days you have to adjust the bracelet.
17	It has improved my daily life
18	Good feeling, without discomfort and with good results
19	Sebdesgasta un poco por la parte interior
20	It wears a little on the inside
21	I have noticed that the mild headaches have reduced, but the migraines have continued. The smell of the bracelet is quite strong at first and if you work with your hands it deteriorates quic
22	Measurements should be improved.

QUESTIONNAIRE AFTER 56 DAYS	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
SENSORY EXPERIENCE																						
1. How much the application of the Bracelet is simple	5	5	5	5	5	5	5	5	5	4	5	5	5	5	5	4	5	5	4	5	4	5
2. How much the appearance of the Bracelet is pleasant	5	4	5	4	4	3	2	3	4	4	3	4	5	2	2	4	5	5	4	5	3	2
3. How much the feeling (texture) of the Bracelet is pleasant	4	5	5	5	5	5	3	2	4	4	2	4	5	2	3	4	5	5	4	4	4	3
4. How much the odor of the Bracelet is pleasant	5	4	5	5	1	4	5	5	5	3	4	5	5	1	4	4	5	3	4	3	2	4
5. How much the design of the Bracelet is attractive	3	5	5	4	5	3	2	3	4	4	3	4	4	2	2	4	5	5	5	5	3	2
TREATMENT EFFECTIVENESS																						
6. How the Bracelet reduce your migraine frequency	5	3	3	4	5	4	2	1	3	3	2	4	3	3	4	3	4	4	3	1	4	4
7. How much the Bracelet helps you to decrease migraine severity	5	4	3	4	5	5	2	1	3	3	2	4	3	3	5	3	4	4	4	1	4	5
8. How much the Bracelet improves your daily tasks	5	3	3	4	5	5	2	3	3	3	2	4	4	3	5	3	5	5	3	1	4	4
9. How much the Bracelet reduce the use pain killer (medicine)	5	4	3	4	5	5	1	1	3	3	2	4	5	3	4	2	5	4	4	1	4	5
10. How much the Bracelet improve your sleep quality	3	3	3	4	5	4	1	1	4	3	2	4	3	3	5	3	5	5	4	1	4	3
12. How much the Bracelet help you overcome pain	5	4	3	4	5	3	2	1	3	3	1	4	4	3	5	3	4	4	4	1	4	4
13 How much the Bracelet reduces your discomfort?	5	3	3	4	5	3	2	1	3	3	1	4	4	3	5	3	4	4	3	1	4	5
14. How much time is needed for you to feel relief/improvement? Please rate in days	15	3	45	3	0	15			30	20	0	36	18	12	2	7	7	10	6		40	35
CONSUMER BEHAVIOUR																						
15 .I am satisfied with the treatment	5	4	5	5	5	5	2	1	3	3	1	4	4	3	5	3	5	5	4	1	4	5
16. I would use the Bracelet again	5	4	5	5	5	5	2	1	2	4	1	4	5	5	5	3	5	4	5	1	4	4
16. I would recommend the treatment	5	4	5	5	5	5	2	2	1	4	1	4	5	4	5	3	5	4	4	1	4	4

17. Have you ever used a similar product such as a food supplements (Y/N)	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
18. I think the price of the Bracelet for 1 month should be (€)	30 €	10	15	15	10	20	8	15 €	10 €	15	5	20	20	12 €	10	20 €	15	20		5	15	15 €

Vol	11. How much the Bracelet reduce your migraine frequency compared to before treatment (number)
1	Before, 4 or 5 per month, now 1 or none
2	1 per month
3	Half
4	1 per month
5	Before 4, now 2
6	Before 3, now 1
7	Before it was almost every day if not every day and not now…
8	Before 1-4 now 1-4
9	Before 3 now 1
10	2 times 3rd time out of 5
11	Before 4 per week, now the same
12	6 a month now 1
13	Before almost every day and now less than half.
14	I have not noticed a difference although it may be due to having had COVID
15	Before 4 per week, now 4 per month
16	Before every 2 days, now every 4 or 5 days
17	Before 3-4 per month now 1 a month
18	Before 2 a month now 0
19	Before 3-5 a month now 12
20	It doesn't reduce it
21	Before 5 now 1

22	Before 2 per month, this month none

Vol	19. Comment
1	I would use it again and I am interested in knowing where they sell it because it has helped me a lot with my severe headaches.
2	I entered the migraine phase and it was not as strong as before. However the duration was three/four days.
3	The smell will go away soon
4	The smell relaxes me a lot and the truth is that I will ask about purchasing it.
5	The first day it makes me dizzy and anxious
6	At first it smells quite a bit... then the strong smell disappears... it unscrews and you have to secure it so that it tightens
7	The feeling I have is that I don't know what it would have been like without the bracelet so it is difficult to buy
8	I still think it is very uncomfortable and rigid. The smell is exceptional but in my case I have not noticed any improvement.
9	pleasant perfume
10	It reduces migraines by more than half and I would only change the shape of the bracelet if it were closed because the tip gets caught on clothing for example
11	For comfort it could be a little narrower and by design it could be chosen in brown or black.
12	During the first month I didn't see much relief but from then on my migraines have improved
13	I would like it to give off that smell for longer.
14	At first it had a too strong smell it gave me more headaches. I don't think I have noticed results as a result of COVID. I would try it again in a while to be more objective.
15	I loved it I told my family that I can't believe it that I have been able to have my daily activity without migraines...it's incredible
16	It does not bother and appears to reduce the frequency and intensity of migraines.
17	Very good result
18	Improvement in the cadence and intensity of migraines
19	Very easy to wear and very discreet
20	It hasn't helped me at all
21	I have noticed the results when wearing the second bracelet. It has greatly reduced my headaches.
22	Suggestion: option for a more feminine design.

16.5 Attachment 5. Informed consent

1

CONSENTIMIENTO INFORMADO DE PARTICIPACIÓN EN EL ESTUDIO DE INVESTIGACIÓN COSMÉTICA DC.289.36.102

${nombreyapellidos}** con DNI **${dni_contacto} he sido invitado a participar en el estudio DC.289.36.102 de investigación cosmética, el cual será llevado a cabo por Dermaclaim Lab S.L., CIF: B16909699, con sede fiscal en Parc Cientific de la Universitat de Valencia, Calle Catedràtico Agustín Escardino Benlloch, 9, 46980 Paterna (Valencia).

El objetivo de este consentimiento informado es que usted reciba la información correcta y suficiente para que pueda evaluar y juzgar si quiere o no participar en el estudio. Para ello, lea esta hoja informativa de atención y nosotros le aclararemos las dudas que le puedan surgir al respecto.

Debe saber que su participación en este estudio es voluntaria y que puede decidir no participar y retirar el consentimiento en cualquier momento, sin que por ello se altere la relación con Dermaclaim Lab S.L.

OBJETIVO DEL ESTUDIO

El objetivo principal del estudio es evaluar los efectos beneficiosos de una pulsera para la reducción de ataques de migrañas. Para ello, se obtendrá información subjetiva de la percepción de los voluntarios sobre la eficacia del producto, mediante un cuestionario de evaluación.

FUNCIONAMIENTO

Esta nueva tecnología funciona mediante el contacto directo con la piel. Los principios activos se liberan de forma controlada, de forma que una pulsera pueda ofrecer tratamiento durante semanas. Su formulación es natural y libre de medicamentos. Ensayos clínicos humanos han demostrado con anterioridad la eficacia de los principios activos que contienen, reduciendo al menos en un 50% el número de migrañas que sufrían los pacientes.

MODO DE USO

Deberá llevar puesta una pulsera 24 horas durante la duración del estudio. Es resistente al agua, al sudor, al calor... por lo que no deberá preocuparse por quitársela. Una vez puesta correctamente, puede olvidarse de ella.

Es más, **solo funciona cuando está en contacto directo con la piel**, por lo que no debe quedar mucho espacio entre su muñeca y la pulsera.

IMPORTANTE: No debe usar otros dispositivos o suplementos alimenticios para la prevención de las migrañas durante el estudio. Sin embargo, si sufriera alguna, puede mantener sus hábitos y medicación habitual.

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FT-03-04 | Rev.00

CONTRAINDICACIONES

No utilizar en niños, embarazadas o mujeres lactantes.

Duración de Tratamiento y Medidas

Duración del tratamiento: 56 días

Medidas: 3 visitas

1) Inicial (Día 0): 11 SEPTIEMBRE
2) Intermedia: 10 OCTUBRE (¡Atención! Entre festivos. Asegurar su disponibilidad)
3) Final: 9 NOVIEMBRE

OBLIGACIONES

- **No utilizar** ningún dispositivo o suplemento alimenticio para prevenir las migrañas durante la duración del estudio.
- No modificar sus hábitos, rutina o dieta de forma sustancial durante el estudio.
- Ponerse en contacto con Dermaclaim en caso de duda, molestia o cambio que perjudique al correcto funcionamiento del estudio.
- Completar los cuestionarios de evaluación subjetiva en la fecha indicada.
- Completar el diario de registro, añadiendo cualquier información relativa al producto o dolores de cabeza sufridos durante el estudio.
- No retirar ni aflojar la pulsera durante el estudio bajo ninguna circunstancia.

Compensación económica

- En el caso de completar el estudio siguiendo las indicaciones correspondientes, recibirá una compensación económica de 35€.

  *La compensación económica se recibirá vía transferencia bancaria al finalizar el tratamiento si se han cumplido todas las condiciones de estudio, lo cual puede detectarse con el control de consumo y los resultados analizados en clínica.

Persona de contacto durante el estudio

Lucía Fernández Gómez, Clinical Project Manager

clinica@dermaclaim.com +34 644 03 50 20

CONSENTIMIENTO INFORMADO DE PARTICIPACIÓN

Yo, **${nombreyapellidos}** a fecha **${fecha_hoy}**:

3

- He recibido suficiente información sobre el estudio y he comprendido la información que se me ha facilitado.
- He podido hacer preguntas sobre el estudio a las personas responsables del mismo.
- Comprendo que mi participación es voluntaria.
- Confirmo que los datos personales aportados son ciertos, soy mayor de 18 años y capaz de firmar un contrato jurídicamente vinculante.
- Autorizo a Dermaclaim Lab S.L. a comunicarse conmigo por los medios que consideren oportunos.

16.6 Attachment 6. Volunteer's diary

1

DC.289.36.102	DIARIO DE REGISTRO

Este documento se utiliza para registrar la aplicación diaria del tratamiento en estudio. Anota el día/mes y el momento de aplicación, durante todo el tratamiento. Asimismo, anota los posibles efectos adversos (picor, rojez, escozor, sequedad, etc.) que puedan tener lugar durante la aplicación, así como cualquier comentario que desees resaltar, en relación con el tratamiento.

Nombre: [redacted] **Nº Vol:** 13

FECHA (día / mes)	¿DOLOR DE CABEZA? ¿MIGRAÑA? Añade detalles sobre la duración y la intensidad del ataque, o cualquier información relevante.
11 SEPT	
12 SEPT	Empiezo el tratamiento
13 SEPT	NADA
14 SEPT	NADA
15 SEPT	dolor de cabeza, intensidad Leve.
16 SEPT	NADA
17 SEPT	NADA
18 SEPT	Al levantarme dolor de cabeza, medio.
19 SEPT	NADA
20 SEPT	NADA
21 SEPT	NADA
22 SEPT	NADA
23 SEPT	NADA
24 SEPT	Al levantarme al rato se pasa y por la tarde volvió fuerte.
25 SEPT	NADA
26 SEPT	NADA
27 SEPT	NADA
28 SEPT	UN POCO POR LA TARDE
29 SEPT	NADA
30 SEPT	Me levanto con dolor muy fuerte tomo 2 pastillas y se pasa un poco y vuelve [illegible]
01 OCT	NADA
02 OCT	NADA
03 OCT	NADA
04 OCT	NADA
05 OCT	NADA
06 OCT	NADA
07 OCT	NADA
08 OCT	NADA

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16.7 Attachment 7. HIT-6 scale & ID Migraine questionnaires

INICIALES _ _ _

Escala HIT-6 **Fecha:** ☐☐/☐☐/☐☐

INSTRUCCIONES: En cada pregunta debe marcar con una cruz la casilla que corresponda a su respuesta.

1. Cuando usted tiene dolor de cabeza, ¿con qué frecuencia el dolor es intenso?

Nunca	Pocas veces	A veces	Muy a menudo	Siempre
☐	☐	☐	☐	☐

2. ¿Con qué frecuencia el dolor de cabeza limita su capacidad para realizar actividades diarias habituales como las tareas domésticas, el trabajo, los estudios o actividades sociales?

Nunca	Pocas veces	A veces	Muy a menudo	Siempre
☐	☐	☐	☐	☐

3. Cuando tiene dolor de cabeza, ¿con qué frecuencia desearía poder acostarse?

Nunca	Pocas veces	A veces	Muy a menudo	Siempre
☐	☐	☐	☐	☐

4. En las últimas 4 semanas, ¿con qué frecuencia se ha sentido demasiado cansada/o para trabajar o realizar las actividades diarias debido a su dolor de cabeza?

Nunca	Pocas veces	A veces	Muy a menudo	Siempre
☐	☐	☐	☐	☐

5. En las últimas 4 semanas, ¿con qué frecuencia se ha sentido harta/o o irritada/o debido a su dolor de cabeza?

Nunca	Pocas veces	A veces	Muy a menudo	Siempre
☐	☐	☐	☐	☐

6. En las últimas 4 semanas, ¿con qué frecuencia el dolor de cabeza ha limitado su capacidad para concentrarse en el trabajo o en las actividades diarias?

Nunca	Pocas veces	A veces	Muy a menudo	Siempre
☐	☐	☐	☐	☐

Valoración (a completar por el investigador):

Nunca	6 puntos x _____ (nº respuestas)	
Pocas veces	8 puntos x _____ (nº respuestas)	
A veces	10 puntos x _____ (nº respuestas)	Puntuación total: ☐
Muy a menudo	11 puntos x _____ (nº respuestas)	
Siempre	13 puntos x _____ (nº respuestas)	

INICIALES — — —

Descripción e Interpretación de HIT:

El Examen del Impacto del Dolor de Cabeza (HIT) es una herramienta utilizada para medir el impacto que los dolores de cabeza tienen en su capacidad para funcionar en el trabajo, la casa, la escuela y en situaciones sociales. Su puntuación le muestra el efecto que los dolores de cabeza tienen en la vida diaria normal y en su capacidad para funcionar. HIT fue desarrollado por un equipo internacional de expertos en dolores de cabeza de neurología y de medicina de cuidados primarios en colaboración con los psicólogos quienes desarrollaron la herramienta de valoración de la salud SF-36.

Si obtuvo una puntuación de 60 ó más: IMPACTO MUY SEVERO

Sus dolores de cabeza están teniendo un impacto muy severo en su vida. Usted puede estar experimentando dolor que lo inhabilita y otros síntomas que son aún más severos que los de aquellos otros afectados por dolores de cabeza. No permita que sus dolores de cabeza le impidan disfrutar de las cosas importantes en su vida como la familia, el trabajo, la escuela o las actividades sociales. Haga una cita **hoy** para que comente los resultados de su HIT-6 y sus dolores de cabeza con su doctor.

Si obtuvo una puntuación entre 56-59: IMPACTO IMPORTANTE

Sus dolores de cabeza están teniendo un impacto importante en su vida. Como resultado usted puede estar experimentando dolor severo y otros síntomas, ocasionándole que pierda la oportunidad de pasar el tiempo con la familia, el trabajo, la escuela o en actividades sociales. Haga una cita **hoy** para que comente los resultados de su HIT-6 y sus dolores de cabeza con su doctor.

Si obtuvo una puntuación entre 50-55: CIERTO IMPACTO

Sus dolores de cabeza están teniendo un cierto impacto en su vida. Sus dolores de cabeza no deberían hacerle perder la oportunidad de pasar el tiempo con la familia, el trabajo, la escuela o en actividades sociales. Asegúrese de comentar los resultados de su HIT-6 y sus dolores de cabeza en la próxima cita con su doctor.

Si obtuvo una puntuación de 49 ó menos: POCO O NINGÚN IMPACTO

Sus dolores de cabeza están teniendo poco ó ningún impacto en su vida en este momento. Lo alentamos que tome el HIT-6 cada mes para continuar el seguimiento de cómo sus dolores de cabeza afectan su vida.

Cuando su puntuación sea de 50 ó más:

Debería compartir los resultados con su doctor. Los dolores de cabeza que están alterando su vida podrían ser migraña. Lleve consigo el HIT-6 cuando visite a su doctor porque la investigación muestra que cuando los doctores comprenden exactamente qué tan mal afectan los dolores de cabeza la vida de sus pacientes, es más probable que proporcionen un programa de tratamiento exitoso, que pudiera incluir el medicamento. **HIT está disponible también en Internet en www.headachetest.com.** La versión de Internet le permite imprimir el informe personal de sus resultados así como una versión especial detallada de su doctor. No olvide tomar de nuevo el HIT-6 o intentar la versión de Internet para continuar vigilando su progreso.

Específicamente para los pacientes con migraña, en el Manual de Práctica Clínica en Cefaleas de la SEN[13] y en otras guías autonómicas[32,33] se recomienda indicar estudios de neuroimagen, tomografía computarizada con contraste o resonancia magnética, tras un primer episodio de migraña con aura de cualquier tipo, especialmente si el aura no es típica (nivel de evidencia IV, grado de recomendación C)[13,33], con cambios no explicados en la frecuencia o intensidad, migraña asociada a síncope y en caso de ansiedad o hipocondría del paciente[33]. Por su parte, no se recomienda el uso de la radiografía craneal o cervical, el estudio del líquido cefalorraquídeo (LCR) y las analíticas sanguíneas de manera rutinaria[32,33].

Otro aspecto que se debe tener en cuenta ante la sospecha de migraña es realizar el diagnóstico diferencial con los diferentes tipos de cefaleas. Se recomienda prestar especial atención a la cefalea tensional y a la cefalea en racimos y, en pacientes con sospecha de migraña con aura, se debe descartar que los síntomas correspondan a isquemia cerebral o crisis epilépticas focales[13,33].

En cuanto al proceso diagnóstico de la migraña en España, se ha estimado que el paciente puede tardar más de 6 años en ser diagnosticado[2] y que pueden pasar hasta 14 años desde la primera crisis de migraña hasta la primera consulta con atención especializada[34]. En este sentido, los expertos identifican que existe infradiagnóstico y retraso en el diagnóstico debido a falta de formación por parte de los profesionales, a dificultades para la derivación de pacientes a la consulta del especialista y a la falta de concienciación por parte de la sociedad, que no consideran su cefalea como motivo de consulta médica.

Los expertos mencionan que los criterios establecidos por la IHS no están adecuadamente extendidos entre los profesionales médicos y consideran que es difícil lograr integrarlos en la práctica clínica de todas las especialidades. En este sentido, los expertos consideran recomendable implementar herramientas que faciliten la detección de síntomas relacionados con la migraña, como, el test ***ID Migraine***, cuestionario conformado por 3 preguntas que, con dos respuestas positivas, permite identificar a las personas con migraña[91–93] (Fig. 10).

Figura 10. Test ID Migraine para el diagnóstico de la migraña

ID Migraine

Responder "sí" a dos de estas preguntas identifica eficazmente a los pacientes que sufren migraña.

1. ¿El dolor de cabeza ha limitado sus actividades durante un día o más en los últimos tres meses?
2. ¿Tiene náuseas o malestar estomacal cuando tiene dolor de cabeza?
3. ¿Le molesta la luz cuando tiene dolor de cabeza?

Fuente: Elaboración propia a partir de National Headache Foundation Resources[91] y Cousins G., et al. (2011)[92]

48