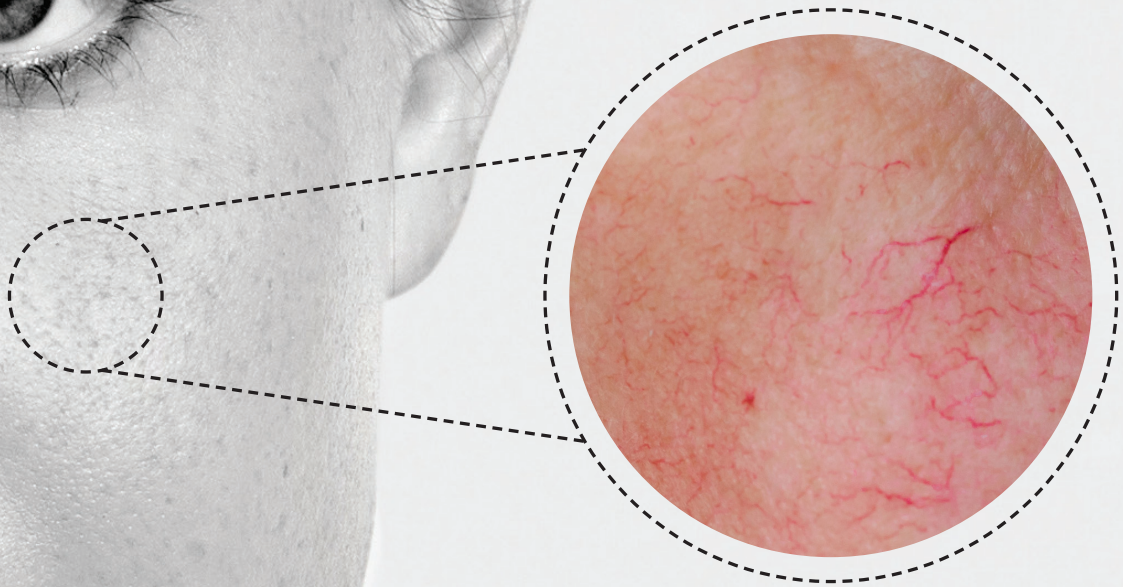


CLINICAL
STUDY
BOOKLET

CLINICAL EVALUATION OF
THE EFFICACY IN REDNESS
REDUCTION AND SKIN
BARRIER RESTORATION
OF C.R. 1 COMPLEX
TREATMENT



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Inflammation is part of the body's defence mechanism. It is the process by which the immune system recognises and removes harmful and foreign stimuli and begins the healing process. Inflammation can be acute or chronic.

Chronic inflammation, also referred to as slow, long-term inflammation lasting for prolonged periods of several months to years. Generally, the extent and effects of chronic inflammation vary with the cause of the injury and the ability of the body to repair and overcome the damage.

Most of the features of acute inflammation continue as the inflammation becomes chronic, including the expansion of blood vessels (vasodilation), increase in blood flow, capillary permeability, and migration of neutrophils into the affected tissue through the capillary wall. However, the composition of the white blood cells changes soon, and the macrophages and lymphocytes begin to replace short-lived neutrophils.

The hallmarks of chronic inflammation topical treatment are to reduce the pro-inflammatory state, regulating inflammatory cytokines that contribute to the progression of the tissue damage and strengthen the impaired skin barrier.^[1]

Rosacea is a common chronic inflammatory skin condition, which predominately affects women after the age of 30. The pathogenesis of rosacea is poorly understood, but deviant neurovascular signalling, dysregulation of the innate and possibly the acquired immune system, colonisation with microorganisms such as *Demodex folliculorum* and *Demodex brevis* on the skin, and *Helicobacter pylori* in the gastric mucosa have all been proposed as pathogenic factors. Traditional environmental triggers include exposure to ultraviolet irradiation, cold, heat, alcohol, spicy food, stress, and physical activity. A family history of rosacea is common, although few established genetic risk variants have been identified.^[2]

Rosacea typically affects the skin of the central face. Symptoms consist of transient or persistent erythema of the face with the appearance of telangiectatic vessels, papules, and pustules, up to hypertrophy of the sebaceous glands of the nose (rhinophyma). Patients also suffer from cutaneous symptoms, such as facial flushing, stinging, pain or burning sensations.^[3] Rosacea has been classified into four subtypes: erythematotelangiectatic, papulopustular, phymatous, and ocular.^[4]

Research reported the prevalence of erythematotelangiectatic rosacea among rosacea patients to be between 72-80% and papulopustular rosacea between 18-28%^[2]

Since rosacea affects the highly visible area of the facial skin, it has a high impact on the quality of life of those suffering, including discomfort, stigmatisation, loss of self-esteem, depression, and limitations on social activities. Many patients do not receive treatment (topical, systemic, lifestyle changes) until later.^[4]

TREATMENT / MANAGEMENT

The first step in the treatment of rosacea is to advise the patient to identify and then avoid triggers. Universal skin care recommendations for all patients with rosacea include pH-balanced skin cleansers, broad-spectrum sunscreen with SPF 30 or higher and regular use of moisturisers. The choice of therapy is guided by the signs and symptoms present for the individual patient. The majority of the therapies aim to reduce inflammation. The persistent erythema and telangiectasias are not completely secondary to inflammation and often require treatment targeting the skin vasculature. The phymatous changes of rosacea result in irreversible changes to the skin that require surgical intervention when indicated.^[5]

Numerous treatment modalities are emerging in the treatment of rosacea, although the avoidance of known triggering factors remains the first step toward relieving symptoms. Among the various therapeutic options, the determination of optimal treatment modalities depends on the clinical severity of the patient and the underlying mechanism of action of each treatment. Topical azelaic acid and retinoids have been proposed to manage inflammation.^[3]

Topical azelaic acid has shown to exert its anti-inflammatory properties by inhibiting the production of ROS and the UVB-induced upregulation of pro-inflammatory cytokines such as IL-1, IL-6, and TNF- α .^[3]

Retinoids have shown to downregulate TLR-2 expression and further regulate TLR-2-mediated abnormal innate immune responses in rosacea. It can also have a profound effect in papulopustular rosacea.^[3]

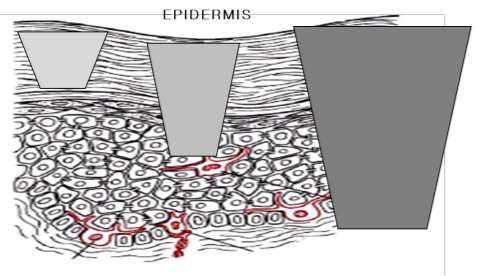
Hallmarks in rosacea's topical treatment are to improve the levels of pro-inflammatory cytokines, angiogenesis-related inflammatory factors, and attenuate the VEGF-induced pathophysiology of rosacea, reducing tube formation, cell migration, and endothelial cell proliferation.^[6]

(Layer and time dependent and not neutralised).
Typically administered by trained pHformula skin specialists.

Controlled dermatological chemical skin resurfacing represents an advanced approach in professional skincare. Unlike traditional chemical peels primarily focused on epidermal exfoliation, controlled chemical skin resurfacing actively triggers an accelerated process of epidermal cell turnover and regeneration. pHformula formulates skin resurfacing products with a sophisticated delivery system called the PH-DVC™ (Bio-Availability Delivery Vehicle Complex) to facilitate precise and controlled delivery of protons.

This controlled delivery mechanism provides targeted and efficient penetration of active ingredients while minimising the potential for adverse effects commonly associated with traditional peeling procedures. In essence, controlled dermatological chemical skin resurfacing is a scientifically advanced strategy for optimising skin health and quality with a reduced risk of undesirable side effects.

TRADITIONAL MEDICAL-STRENGTH PEELING

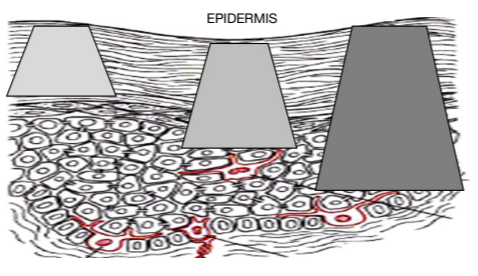


EPIDERMIS

DISADVANTAGES

- High superficial trauma and irritation.
- Excessive skin inflammation.
- No control in uniformity of the peel.
- Possible painful and unwanted complications.
- Possible side effects.

CONTROLLED CHEMICAL SKIN RESURFACING



EPIDERMIS

ADVANTAGES

- Maximum and even, controlled penetration.
- Targeted cell regeneration.
- Controlled irritation and inflammation.
- No superficial trauma or complications and side effect.
- Excellent skin tolerance.

CONTEXT

Specifically formulated as active resurfacing treatment for skin showing typical signs of redness. What makes this treatment unique and the core of pHformula's choices in the professional treatment room, is that C.R.1 complex is not only showing results in vascular-inflammatory issues such as Rosacea-prone skin, it can also be chosen as the first step in helping to reduce the inflammatory signs that are typically showing in acne, ageing and hyperpigmented skin.

The multifunctional ingredients of the C.R. 1 complex offer skin restoration. The synergistic action of Mandelic-, Salicylic-, and Lactic acids enhance cell renewal by allowing easier exfoliation of dead skin cells. Lactic acid contributes to improve skin hydration and Mandelic acid gently helps to reduce rosacea-aggravating microorganisms. Retinol improves epidermal thickness. The C.R. 1 complex is formulated to assist in reinforcing the skin barrier.





To evaluate the efficacy of a skin resurfacing protocol under dermatological control to reduce redness and restore the skin barrier in rosacea skin.

- Effect on the redness of the face (by scoring).
- Assessment of the redness (photo analysis – C CUBE®) on D0, D14, D28, D56 and D84.
- Capacity to maintain the integrity of skin by (clinical examination under dermatological control).
- Assessment of the effect on trans epidermal water loss (Tewameter) on D0, D14, D28, D56, and D84 before and after use of the treatment.
- Assessment of the moisturising effect (Corneometer) on D0 and D84 before and after use of the treatment.
- Cosmetic acceptability (subjective questionnaire).

INCLUSION CRITERIA

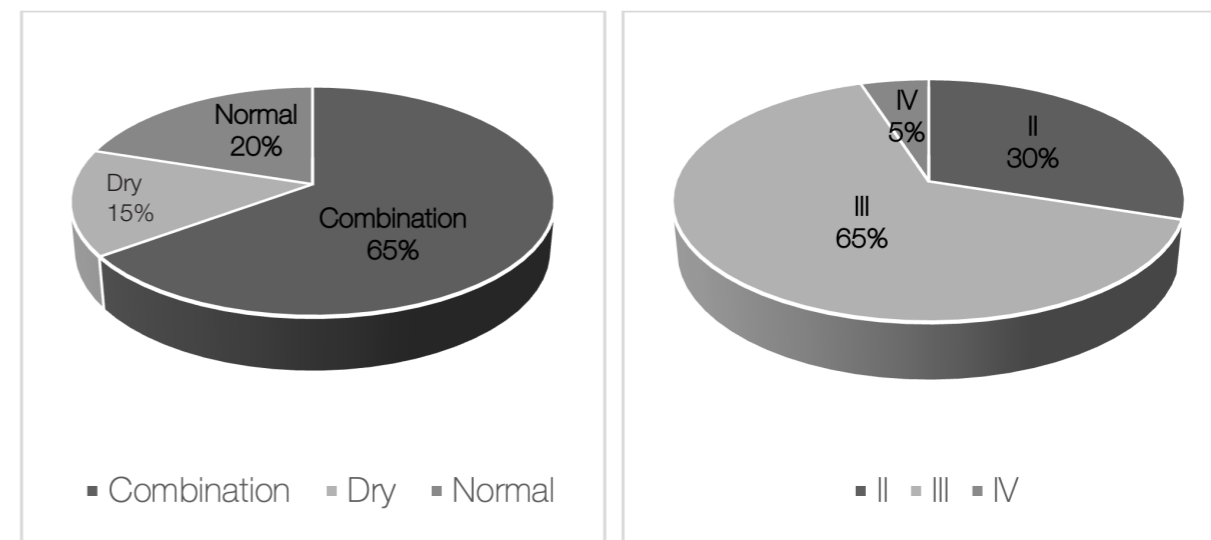
- 20 female and male subjects.
- 40-70-years-old (average age 55).
- Sensitive skin*.
- 100% of subjects with Rosacea mild stage I, II, and III.
- 100% of subjects with Redness skin / Couperose (due to sensitive skin factors).
- 100% of subjects with Cutaneous inflammation (swollen skin).

*Blushing or flushing episodes, facial redness (permanent or temporary), burning / stinging skin, sensitivity to any product(s) or ingredient(s), skin on the face feels hot, dry, flaky skin appearance (rough skin texture).

NON-INCLUSION CRITERIA

- For women: pregnant or nursing woman or woman planning to get pregnant during the study;
- Cutaneous pathology on the study zone (eczema, irritations etc);
- Use of topical or systemic treatment during the previous weeks liable to interfere with the assessment of the cutaneous acceptability/efficacy of the study product;
- Subjects with Lupus Erythematosus (SLE), Dermatomyositis, Sarcoidosis, Seborrheic dermatitis, Acne vulgaris, Steroid dermatitis, Keratosis pilaris rubra, Periorificial dermatitis, Contact dermatitis, Chronic gastritis, Irritable bowel syndrome (IBS), Leaky gut syndrome, Proton pump inhibitors;
- Subjects having undergone a surgery under general anesthesia within the previous month;
- Subjects having received acid treatments or microneedling 1 month before the start of the study;
- Subjects who have undergone to facial depilation that have caused a visible irritation or men with facial hair / beards;
- Excessive exposure to sunlight or UV-rays within the previous month;
- Subjects enrolled in another clinical trial during the study period.

SKIN- AND PHOTO-TYPE OF THE FACE






PROFESSIONAL PROTOCOL

PROTOCOL					
E.X.F.O. cleanse		S.K.I.N. primer		C.R. 1 complex	
		P.U.R.E. rosehip oil		P.O.S.T. recovery cream	
				U.V. protect SPF 50+	

1. Cleanse: E.X.F.O. cleanse
2. Degrease: S.K.I.N. primer
3. Resurface: C.R. 1 complex – 1 layer
 - Session 1 (D0): 3 minutes
 - Session 2 (D14): 6 minutes
 - Session 3 (D28): 9 minutes
 - Session 4 (D42): 12 minutes
 - Session 5 (D56) and 6 (D70): 15 minutes
4. P.U.R.E. rosehip oil
5. Hydration: P.O.S.T. recovery cream
6. Protection: U.V. protect SPF 50+

HOME CARE PROTOCOL

AM HOME CARE ROUTINE			
E.X.F.O. cleanse		C.R. recovery	
		P.O.S.T. recovery cream	
		U.V. protect SPF 50+	

PM HOME CARE ROUTINE			
E.X.F.O. cleanse		A.C.T.I.V.E. formula	
		P.O.S.T. recovery cream	

Prior to the professional treatment room protocol the subjects arrived in the investigation center and spend a period of 15 minutes of acclimatisation. The room temperature and relative humidity were controlled during the measurements and evaluations in the study being $22 \pm 2^\circ\text{C}$ and between 40-60% respectively.



**E.X.F.O. cleanse
professional and homecare**

Specifically formulated for use during and after the professional pHformula skin resurfacing procedure to gently cleanse, help exfoliate, soothe, calm, and rehydrate the skin. A soft, hydrating cleanser that thoroughly removes make-up and impurities maintaining the essential moisture of the skin.

Lactobionic acid – is a polyhydroxy acid (PHA) that provides multiple skin benefits such as assisting to increase cell turnover time and providing antioxidant properties. It helps to improve wound healing processes. Lactobionic acid has strong moisturising and water-binding properties and is a film-forming and non-irritating agent.

Rooibos extract – contains two particularly potent flavonoids (quercetin and luteolin) and polyphenol antioxidants which are potent free radical scavengers that help to protect the skin cells against ageing-causing free radicals.

Pro-vitamin B⁵ – attracts moisture from the environment (humectant). It absorbs easily into the skin and has calming, soothing, and excellent hydrating properties.

Resumoist complex – consists of water, calcium pantothenate, xanthan gum, caprylic glycol, proline, alanine, serine, magnesium lactate, potassium lactate, magnesium chloride, sodium citrate, glycerin, urea, papain, and ethylhexylglycerin. Is a molecular film designed to obtain an optimised delivery of papain, a proteolytic enzyme that selectively degrades the corneo-desmosomal linkages between damaged or dead skin cells. It also provides an improved moisturisation to the skin and preserves the natural barrier function of the epidermis, due to the ingredients comprising of natural moisturising factor.

Directions for use

Apply a small amount of E.X.F.O. cleanse on clean, dry, gloved hands. Spread onto a dry face, neck, and décolleté. Massage with circular movements until the entire area is covered. Wet fingertips with water when the skin becomes too dry (struggling to make circles). Massage with circular movements until the entire area is covered again. Remove with damp gauze, cotton pads, or a disposable compress. Dab the skin dry with a clean towel or tissue. Repeat if necessary.



**S.K.I.N. primer
professional**

pHformula's S.K.I.N. primer assists in cleansing and degreasing the skin, which provides optimum penetration of the ingredients.

Isopropyl alcohol – degreasing vehicle for every professional resurfacing treatment.

Directions for use

Spray 2-3 sprays of S.K.I.N. primer onto dry gauze or cotton pads. Wipe over the entire treatment area. Repeat in areas with excess oil secretion. Continue with resurfacing protocol.



C.R. 1 complex professional

The pHformula C.R. complexes are specifically formulated as active resurfacing treatments for skin showing typical signs of redness. The multifunctional ingredients of the C.R. complexes offer skin restoration. The C.R. complexes are formulated to assist in reinforcing the skin barrier.

Mandelic acid – has powerful antimicrobial properties which help to reduce bacteria associated with rosacea-prone skin. It is a very gentle acid and particularly effective for skin types which cannot tolerate aggressive topical treatments.

Salicylic acid – is a powerful keratolytic, allowing additional active ingredients to penetrate more effectively.

Retinol – The use of retinol helps to increase epidermal thickness and to improve the dermal extracellular matrix.

Lactic acid – helps to break down the desmosomes (bonds between cells) to allow easier exfoliation of dead surface cells while hydrating the skin.

PH-DVC™ (delivery vehicle complex) – An advanced delivery complex used in the pHformula formulations to enhance the penetration of active ingredients. It is composed of a delivery system, a soothing ingredient, and a cell activator complex named Respiderm. Respiderm assists to increase cellular oxygenation as well as wound healing, promoting collagen and elastin synthesis. Cellular activation is enhanced while having a soothing effect. Respiderm can potentiate the activity of other active ingredients.

Directions for use

Decant 1 pipette of the C.R. 1 complex, into a dry, clean, small glass bowl. Apply a thin layer with a fan brush. Application should start from the forehead, working from the centre outward and continuing along one side of the face working downwards from the cheek, then continuing on the other side. Check skin sensitivity levels. Leave on the skin for 3-15 minutes and remove thoroughly with E.X.F.O. cleanse and dampened cotton pads. If not well-tolerated, severe erythema will be observed and / or light frosting may occur in some areas. Remove immediately and thoroughly with E.X.F.O. cleanse and dampened cotton pads.



P.U.R.E. rosehip oil professional

This highly nutritive, pure Rosehip oil contributes to revitalise and rejuvenate the skin thanks to its unique composition. Rich in essential fatty acids, it helps to increase the moisture levels of the skin and improve its barrier function, contributing to prevent the loss of water. Due to the presence of antioxidants and vitamins (β-carotene, vitamins C and E) in its composition, P.U.R.E. rosehip oil promotes cell regeneration and strengthens the health of the skin.

Rosa Canina Fruit Oil – is rich in essential fatty acids (omega 6 and omega 3 EFAs) with an important action on the regulation of skin elasticity and the restoring of skin moisture by contributing to strengthen skin barrier function. These fatty acids, in conjunction with its content of tannins, flavonoids, vitamin C, and Beta-carotene, make this oil an ideal product for a healthier complexion.

Vitamin E – is an important lipid-soluble antioxidant vitamin that helps to protect cell membranes from oxidation. An excellent moisturiser with powerful soothing and wound healing properties.

Directions for use

Dispense 5 drops in the palm of your hands. Rub your hands together to warm up and spread the product evenly. Apply onto the face, neck, and décolleté. Massage into the skin. DO NOT REMOVE. Continue with treatment.



**P.O.S.T. recovery cream
professional and homecare**

The P.O.S.T. recovery cream is a rich emollient cream containing a blend of humectants that contributes to attract water to the skin to enhance hydration. The P.O.S.T. recovery cream contributes to protect and hydrate the skin whilst delivering continuous moisture throughout the day to support and enhance skin comfort. The P.O.S.T. recovery cream has very good skin compatibility.

Panthenol – helps to improve and increase skin moisture, making the skin feel softer and more elastic. It contributes to soothe irritated skin, promotes epithelialisation, and helps to heal the skin.

Niacinamide – has potent antioxidant properties, helps to improve the epidermal barrier function, reduces skin yellowing as well as erythema and blotchiness. Niacinamide helps to reduce the appearance of fine lines, wrinkles, and hyperpigmentation.

Prunus amygdalus dulcis oil – Sweet Almond oil is extracted from the seeds of almonds. Rich in triglycerides and fatty acids (oleic, linoleic, myristic), vitamin E and some B-vitamins. It helps to retain skin moisture, improve skin hydration, and restore skin barrier function. Sweet Almond oil is a soothing emollient with antioxidant properties.

Lactobionic acid – PHA with multiple skin benefits: cell turnover, antioxidant, wound healing accelerator, moisturising and water-binding properties, film-forming agent.

Glycyrrhetic acid – has antioxidant and skin soothing properties when applied to the skin. It is also a tyrosinase inhibitor that contributes to the reduction of hyperpigmentation.

Bisabolol – helps to protect and heal the skin from the effects of daily stress. It is a naturally occurring active ingredient that helps to accelerate the healing processes of the skin.

Directions for use

Use 5ml / 2 pumps. Apply the P.O.S.T. recovery cream to the face, neck, and décolleté and massage until completely absorbed. Follow with U.V. protect SPF 50+.



**U.V. protect SPF 50+
professional and homecare**

An essential skin defence product with a unique combination of innovative ingredients. The U.V. protect SPF 50+ provides, very high, broad-spectrum protection against harmful UVA/UVB rays. U.V. protect SPF 50+ helps to prevent visible signs of photo-ageing such as lines, wrinkles, pigmentation spots, dehydration, and dryness. It provides very high sun protection yet is comfortable and gentle on the skin. This unique formula, especially for the face, can also be applied after skin resurfacing procedures as well as outdoor activities and sports.

UVA filters – consisting of Titanium Dioxide (nano), Methylene Bis-Benzotriazolyl Tetramethylbutylphenol (nano), Bis-Ethylhexyloxyphenol Methoxyphenyl Triazine, Butyl Methoxydibenzoylmethane, and 4-Methylpropanediol Camphor for daily broad-spectrum protection.

UVB filters – consist of Titanium Dioxide (nano), Octocrylene, Phenylbenzimidazole Sulfonic acid, Methylene Bis-Benzotriazolyl Tetramethylbutylphenol (nano), Bis-Ethylhexyloxyphenol Methoxyphenyl Triazine, and 4-Methylpropanediol Camphor for daily broad-spectrum protection.

Enzymatic Photo-Protector – biotechnological ferment containing multifunctional and stable enzymes. It fights IR-induced damage: lessens the inflammatory conditions, improves hydration, and maintains dermal architecture in order to limit wrinkle formation. It prevents IR-induced stress in response to an increase in heat, offers proportional detoxifying activities and counteracts ROS production generated by IR. Contributes to hydration improvement.

Co-enzyme Q10 – helps to reduce free radical damage with its antioxidant properties. It also assists cells in building collagen and therefore helps to reduce the appearance of fine lines and wrinkles.

Vitamin C – is one of the best sources to help neutralise free radicals and combat photo-ageing. It promotes skin repair processes and contributes to cellular restoration.

Vitamin E – helps to protect the skin against environmental pollution and has a protecting action against UV radiation. It is an excellent moisturiser and powerful antioxidant with soothing, and wound healing properties.

Directions for use

Apply 5ml U.V. protect SPF 50+ on all exposed areas (including ears), to the face, neck, and décolleté. Massage until completely blended into the skin and allow to absorb for 20 minutes prior to daytime exposure. Avoid prolonged sun exposure during the professional pHformula skin resurfacing program, even when using sun protection.



**A.C.T.I.V.E. formula
homecare - evening**

A.C.T.I.V.E. formula is specifically formulated to be used as a homecare skin resurfacing product, assisting in normalising our 4 identified skin disorders and maintaining overall results.

Glycolic acid – is an alpha hydroxy acid (AHA) that has clinically been proven to loosen the glue-like bonds that hold skin cells together, thus shedding the top layer of dull, damaged, and ageing skin.

Lactobionic acid – PHA with multiple skin benefits: cell turnover, antioxidant, wound healing accelerator, moisturising and water-binding properties, film-forming agent.

Mandelic acid – helps to stimulate the production of collagen and shows advanced results in the treatment of photo-ageing by improving the appearance of fine lines and wrinkles without irritation. Mandelic acid is very effective as a tyrosinase inhibitor, actively treating several types of hyperpigmentation often associated with aged skin. Its powerful antimicrobial properties help to reduce microbes associated with acne eruptions.

Panthenol – promotes skin moisture, soothes irritated skin, helps epithelialisation, and skin healing.

Salicylic acid – is a powerful desmolytic and comedolytic allowing additional active ingredients to penetrate more effectively. The anti-inflammatory action of salicylic acid helps to soothe the skin. Salicylic acid also has antimicrobial properties.

Hydrolysed Soy protein – is rich in essential amino acids and helps to stimulate cellular renewal processes. It contributes to maintaining epidermal surface moisture by restoring the water balance.

Pyruvic acid – helps to stimulate collagen, elastin, and dermal glycoproteins.

Retinol – helps to regulate cell differentiation. Contributes to the stimulation of collagen and elastin synthesis and acts as a powerful antioxidant.

Melatonin – topical melatonin acts as a protector against oxidative damage, helps to prevent the proliferation of cancer cells, contributes to the reduction in inflammation, and promotes wound healing.

PH-DVC™ (delivery vehicle complex) – an advanced delivery complex used in the pHformula formulations to enhance penetration of the active ingredients. It is composed of a delivery system, a soothing ingredient, and a cell activator complex named Respiderm. Respiderm assists to increase cellular oxygenation as well as wound healing, promoting collagen and elastin synthesis. Cellular activation is enhanced while having a soothing effect. Respiderm can potentiate the activity of other active ingredients.

Directions for use
In the evening, dispense 1-2 pumps onto clean, dry skin. Optionally, proceed with the suggested pHformula corrective serum. Conclude your evening routine by using the recommended pHformula moisturiser.



**C.R. recovery
homecare - morning**

The C.R. recovery works in synergy with pHformula's professional skin resurfacing treatments, targeting skin displaying typical signs of redness, mild rosacea, impaired barrier function, and skin sensitivity. This formulation aids in stimulating skin repair processes, cell turnover, and sebum production regulation, providing moisturisation and water-binding properties.

Lactobionic acid – is a new generation of hydroxy acids that has the beneficial effects of AHAs and PHAs. It helps to provide moisture as lactobionic acid is a very hygroscopic product – it has multiple hydroxy groups that allows a greater absorption and retention of water, forming a gelatinous matrix on the skin. It contributes to wound healing as galactose is part of the dermal extracellular matrix where it contributes to the processes of cell migration and synthesis of glycosaminoglycans and collagen fibres. Lactobionic acid has antioxidant properties where it inhibits the production of free radicals by chelating iron, and it helps to prevent the oxidation of other substances. Lactobionic acid helps to improve skin barrier function as it stimulates cell regeneration and thanks to its moisturising properties, helps to increase the absorption of water as well as prevent trans epidermal water loss. Lactobionic acid has been described as a non-comedogenic, non-irritating, not photosensitising agent and helps to prevent and contributes to the treatment of photodamage.

Panthenol – helps to improve and increase skin moisture and helps to make dry skin softer and more elastic due to its hygroscopic properties. It helps to soothe irritated skin, promotes epithelialisation, and helps to heal the skin. *In vivo* and *in vitro* studies have demonstrated that panthenol is capable of activating fibroblast proliferation. *In vitro* studies on human fibroblast further noted the enhancement of proliferation, cell migration, attachment of fibroblasts and collagen synthesis during incubation of the cultures with pantothenic acid, or its derivatives.

Sodium ascorbyl phosphate – SAP is a water-soluble, highly stable form of vitamin C that has antimicrobial properties. It is a powerful antioxidant that helps to boost collagen.

Azeloglycine – is derived from azelaic acid and has increased moisturising and soothing properties. It is keratolytic and comedolytic, which helps to normalise cell turnover in the follicles.

Retinol – helps to regulate cell differentiation. Promotes the stimulation of collagen and elastin synthesis and acts as a powerful antioxidant.

PH-DVC™ (delivery vehicle complex) – an advanced delivery complex used in the pHformula formulations to enhance penetration of the active ingredients. It is composed of a delivery system, a soothing ingredient, and a cell activator complex named Respiderm.

Directions for use
Apply during both the treatment period and the recovery phase following treatments to enhance and uphold the overall skin resurfacing results. Dispense 1-2 pumps onto clean, dry skin in the morning and/or evening. Optionally, proceed with the suggested pHformula corrective serum. Conclude your morning/evening routine by using the recommended pHformula moisturiser.



C.R. TREATMENT

CLAIMS	EVALUATIONS	TIME POINTS
Dermatologically tested.	Dermatological control.	D0 and Dend (12weeks)
Redness visibly decreases.	Erythema index and Rosacea severity measurements with C-Cube (images and analysis).	D0, D2weeks, D4weeks, D8weeks, D12 weeks.
Reduces redness.		
Reinforces skin barrier.	TEWL	D0, D2weeks, D4weeks, D8weeks, D12 weeks.
Skin barrier restoration.		
Hydrates the skin.	Corneometer.	D0 and Dend (12weeks).
Suitable for sensitive skin.	Based on tolerance evaluation and recruitment of the subjects.	D0 and Dend (12weeks).
Suitable for mild rosacea skin.		
Well skin tolerated.		
Subjective claims.	Subjective questionnaire.	Dend (12weeks).

MEASURAMENTS

CRITERIA (VISUAL ASSESMENT)	SCALE
Redness.	0: none (same colour as skin). 1: very slight → fairly detectable, discreet pink. 2: slight → definite pinkness. 3: moderate → clearly distinguishable, dull red. 4: important → deep dark of fiery bright red.



AXIS / CLAIM

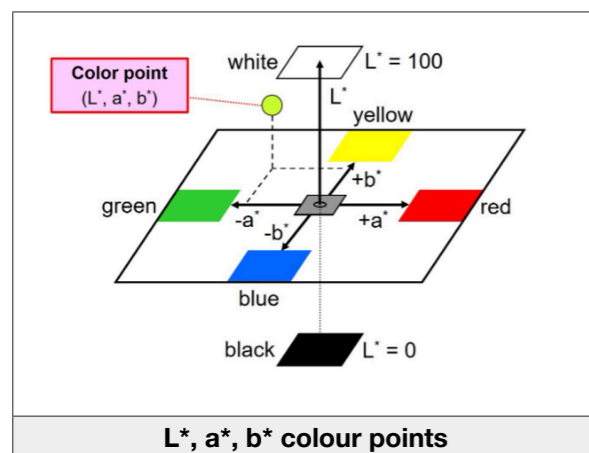
- Inflammation.
- Swelling.
- Soothing.
- Sensitive skin.

CONTEXT

The inflammatory response is a way for the body to defend itself. Local irritations are initiated by the contact of everyday substances. Anti-inflammatory agents are being incorporated into skin care products to improve skin tone and texture while reducing the appearance of redness. Most common cause for inflammatory processes is a disturbed and porous skin barrier.

TECHNIQUE

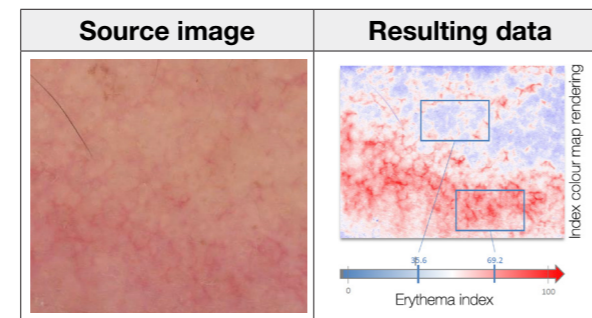
From the standard CIE L*a*b* (L* represents lightness, while a* and b* represent chromaticity; being a-axis the amount of green to red and b-axis the amount of blue to yellow) measurements given by the C-Cube for every pixel, a specific parameter (based on a*) is defined that can be used to grade erythema. This index can be displayed with a blue / red colour map to localise and illustrate the erythema.



Digital cameras present the advantage of enabling colour measurement for each pixel, thus greater colour discrimination within any defined region of interest (ROI).^[7] Drawing ROI on images, it is possible to monitor changes across time or to analyse differences of evolution between zones.

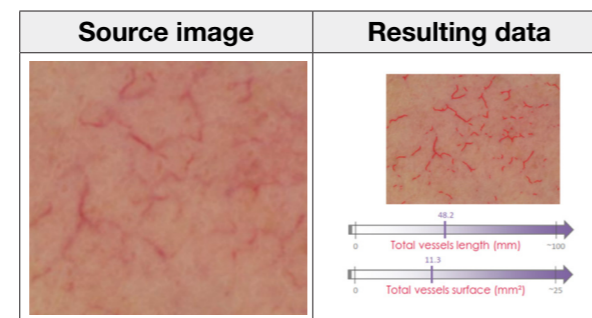
ERYTHEMA INDEX

The C-Cube is calibrated on 24 colour patches. This calibration makes it possible to obtain a colour measurement in L*a*b* space for each pixel of the image. The Erythema index is linked to the a* of this colour space. To produce the erythema rendering, each pixel of the image is replaced with the value of the Erythema index. When the index=0%, the pixel is blue; when the index is 100%, the pixel is red.



ROSACEA SEVERITY

Using state-of-the-art line detection algorithms, that is applied to the red channel, the most noticeable vessels at the surface of the skin can be detected. Then it can produce two different measurements: the total length of detected vessels (in mm) and the cumulated surface area of said vessels (in mm²) as a mean of expressing the average width. Illustrations are provided to show the location of detected vessels in the form of a red overlay on original images.



WHY WAS THE C-CUBE CHOSEN OVER OTHER FULL-FACE ANALYSERS?

The C-Cube has been designed to avoid having an impact of pressure in the skin that affects the final images. Through its closed chamber lighting technology, the C-Cube provides much more precise measurements compared to measurements carried out on full face devices. As these devices cannot produce 100% homogenous lighting due to the fact that the face is not flat.

The C-Cube measurement relies on a relatively large surface area (44.6mm²), resulting in greater detection sensitivity and therefore can detect a significant difference where other measures could not.^[8]

With C-Cube, measurements are obtained in a completely objective manner by fully automated image processing with a colour calibrated camera.^[9]

Trans epidermal water loss (TEWL) was measured regularly in order to provide further information on the epidermal permeability barrier – either normal, experimentally perturbed, or in diseased conditions. TEWL can be measured by evaporimeter, such as the Tewameter®, which was particularly designed according to Nilsson's Vapour Pressure Gradient Theory, with an open chamber method that provides minimal impact on the skin being examined with low statistical bias. ^[10]

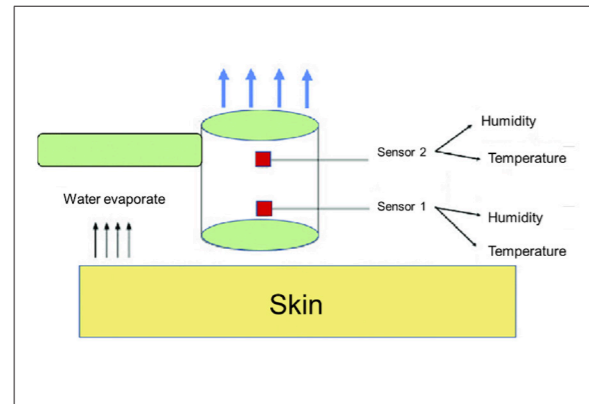


Illustration of the measurement principle, Tewameter®. ^[10]

The Tewameter® is a measuring device for the assessment of trans epidermal water loss (TEWL). This parameter provides information on the integrity of the skin protective barrier functions. The measurements are performed by the application of a probe to the skin surface for 30 seconds. Upon contact, the water evaporation rate (g/h/m²) is obtained. High values of TEWL reflect a damaged skin barrier function.

THE MEASURING PRINCIPLE

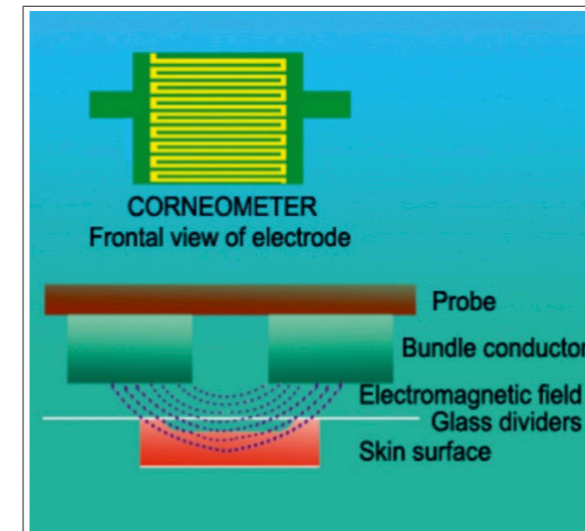
The TEWAmeter TM 300 probe measures the density gradient of the water evaporation from the skin indirectly by the two pairs of sensors (temperature and relative humidity) inside the hollow cylinder. This is an open chamber measurement. A microprocessor analyses the values.

ADVANTAGES

- The open chamber measurement is the only method to assess the TEWL continuously, which is necessary for most applications without influencing the skin surface.
- Numerous studies available.
- A stable measurement is achieved quickly, the next measurement can be done without waiting time.
- The small size of the probe head minimises the influence of air turbulence inside the probe.
- Its low weight has no influence on the skin structure and ensures easy handling.
- Check calibration can easily be done by a small chamber at any time.
- Available for C+K MPA-System, as stand-alone device, and wireless probe.



The Corneometer® CM 825 is the most used instrument worldwide to obtain exact reproducible values of the hydration level of the superficial layers of the skin (stratum corneum) via measurement of skin dielectric properties. The measurements are performed by the application of a probe to the skin surface. Upon contact, an electric field passes through the stratum corneum, and the dielectric constant is obtained. The value of the dielectric constant (in arbitrary units; 0-130AU) is directly proportional to the level of skin hydration.



Principle of the Corneometer. ^[11]

THE MEASURING PRINCIPLE

The measurement is based on capacitance measurement of a dielectric medium. The Corneometer® CM 825 measures the change in the dielectric constant due to skin surface hydration by capacitance differences of a precision capacitor.

Based on its working mechanism, when the water content of the epidermis is low, the Corneometer readings will settle at low values. The Corneometer is easy to use, efficient, and widely utilised in international studies for measurements in healthy or pathological conditions, for quantitative assessment of the effectiveness of various preparations intended for application to the skin surface, under well-controlled and standardised conditions. ^[11]

ADVANTAGES

- Substances on the skin (e.g., salts or residues of topical applied products) have only minimal influence due to capacitance measurement.
- The high-quality electronics of the probe allow a very quick measurement (1 s). This is important to avoid occlusion effects.
- The measurement depth is very small (10-20 µm of the Stratum corneum) to exclude the influence of water in deeper skin layers.
- The probe is small and lightweight for easy handling and measurement on all body sites.
- The spring in the probe head ensures constant pressure on the skin, enabling exact, reproducible measurements which do not influence the skin.
- Easy cleaning of the probe sensor.
- Worldwide established as "Corneometry" with a broad range of studies.
- Even used for space missions on the ISS*.
- Available for C+K MPA-systems, as stand-alone device (MDD) and wireless probe (operation with MPA Wireless software).

Each subject had to complete the questionnaire at the end of their treatment, D₈₄ (12 weeks).

1. The overall treatment is very good.
2. Treatment is suitable for my skin type: chronic redness.
3. Visibly decreases redness.
4. Improves the skin redness (redness is reduced).
5. Improves skin hydration / Moisturises the skin.
6. Restores the skin, improves the quality of the skin.
7. I feel that my skin recovery is faster.
8. Homecare products assist in normalising the skin discomfort / redness and maintaining overall results.
9. At the end of the treatment, the subject can visibly see a more radiant, younger-looking skin surface.
10. The hydration product helps to alleviate immediate skin dryness and provides soothing properties.
11. In general, the products have a pleasant texture.
12. In general, the products are easy to apply.
13. You are satisfied with the treatment plan.
14. The treatment provides a general comfort sensation.
15. The improvement of my skin is visible to other people.



Study preliminary results (3 sessions) – Subject 21.



Study preliminary and final results (3 & 6 sessions) – Subject 21.

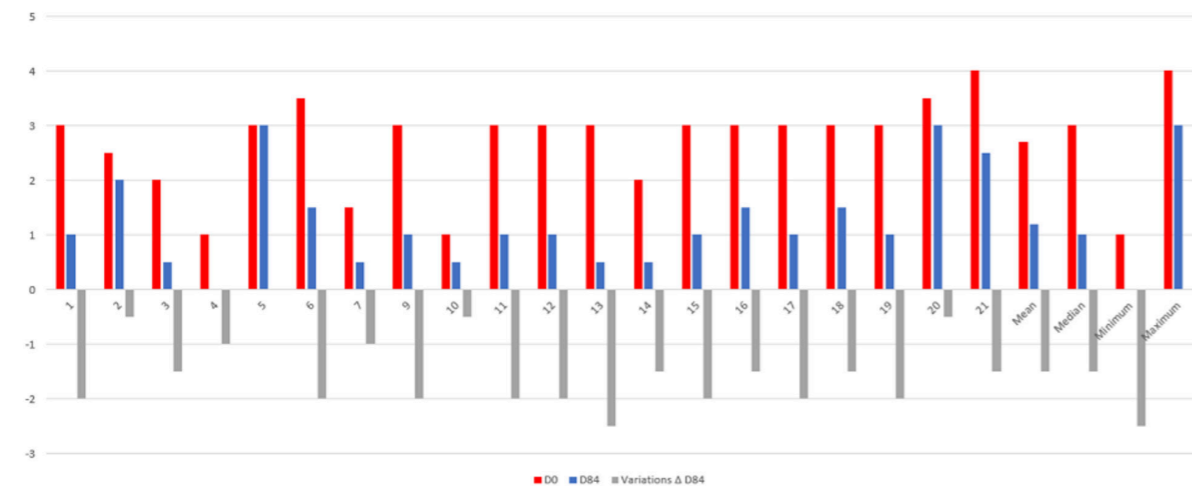


A decrease of the a* values have been observed on D14, D28, D56, and D84 when compared to D0. The analysis of the results shows a statistically significant decrease of the a* values after 14, 28, 56, and 84 days of product application. Therefore, the product reduces redness.

Redness: A statistically significant decrease in the values of redness on D84 of 55% has been observed, indicating that there is a visible decrease of the redness.

- 55% of redness decreases by clinical scoring in comparison with the initial state.
- 44% Rosacea length improvement (mm).
- 41% Rosace surface improvement (mm²).

REDNESS SCORE:

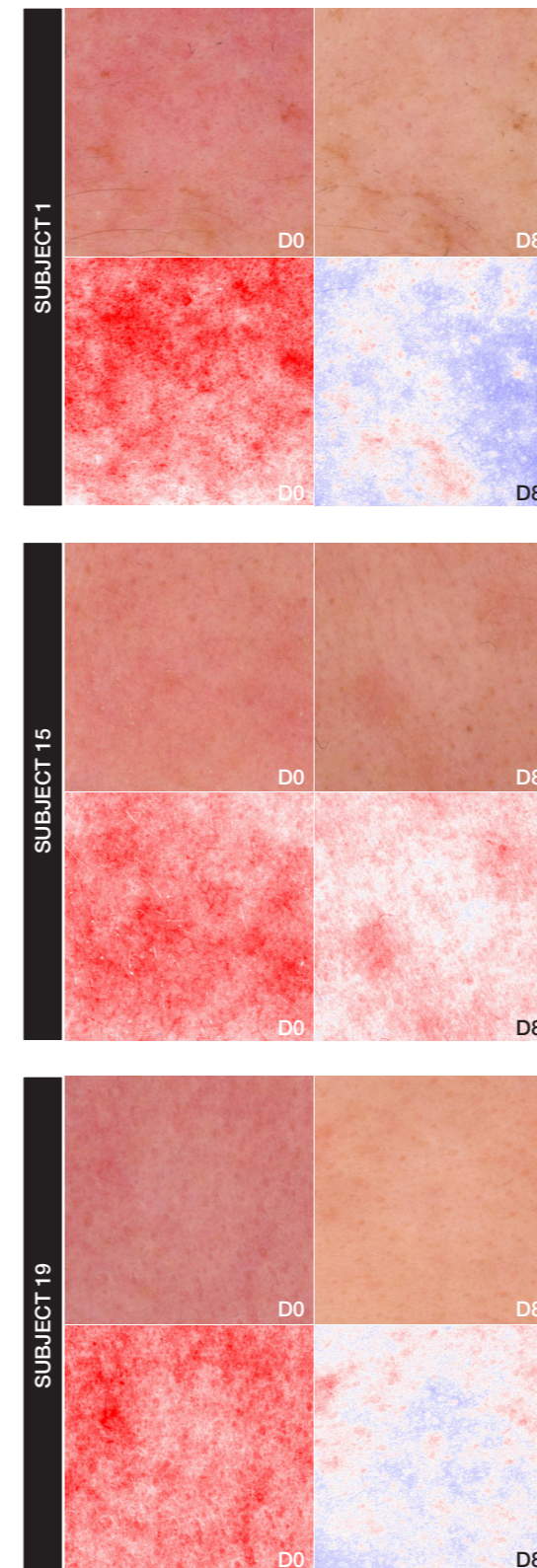


Every subject except n°5 (a subject that skipped using SPF protection for the last month of the study) showed a significant improvement in the redness score.

TEWL: A decrease in TEWL values has been observed on D14, D28, D56, and D84 of 18%, 23%, 13%, and 29% respectively, when compared to D0.

The analysis of the results shows a statistically significant decrease in the TEWL values after 14, 28, and 84 days of product application. Therefore, the product reinforces the cutaneous barrier integrity after 84 days of product application.

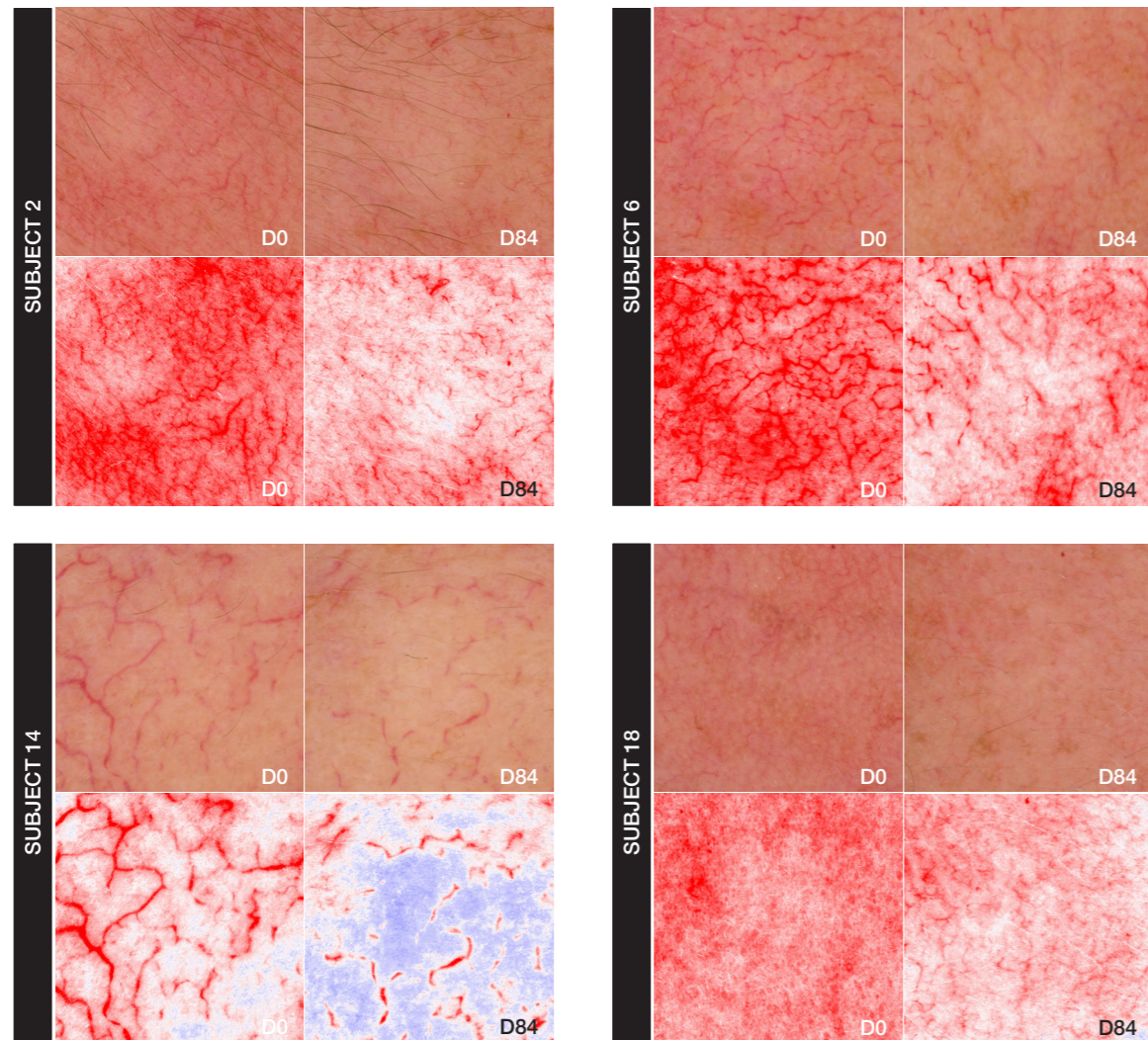
- 29% of TEWL decreased when compared to baseline.
- 19% hydration increase has been observed.



In baseline images the affected area exhibited noticeable redness associated with skin inflammation.

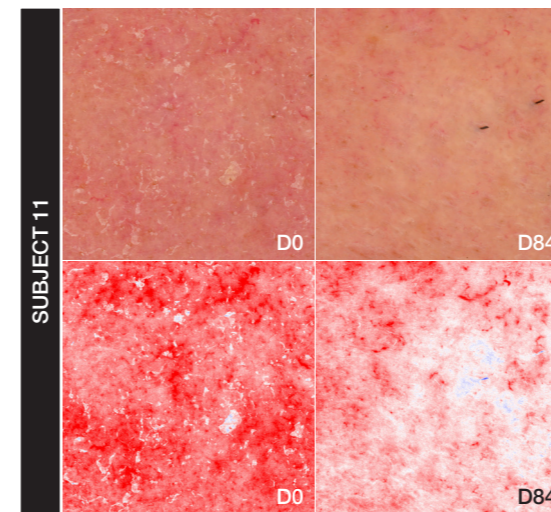
At the end of the study subject number 1 was showing a significant reduction in redness. The treated area appeared closer to the individual's natural skin tone.

The Erythema index is represented by colorimetric scale where red shows presence of erythema and blue absence of it. There is a significant reduction on erythema index from baseline to the end of the treatment.



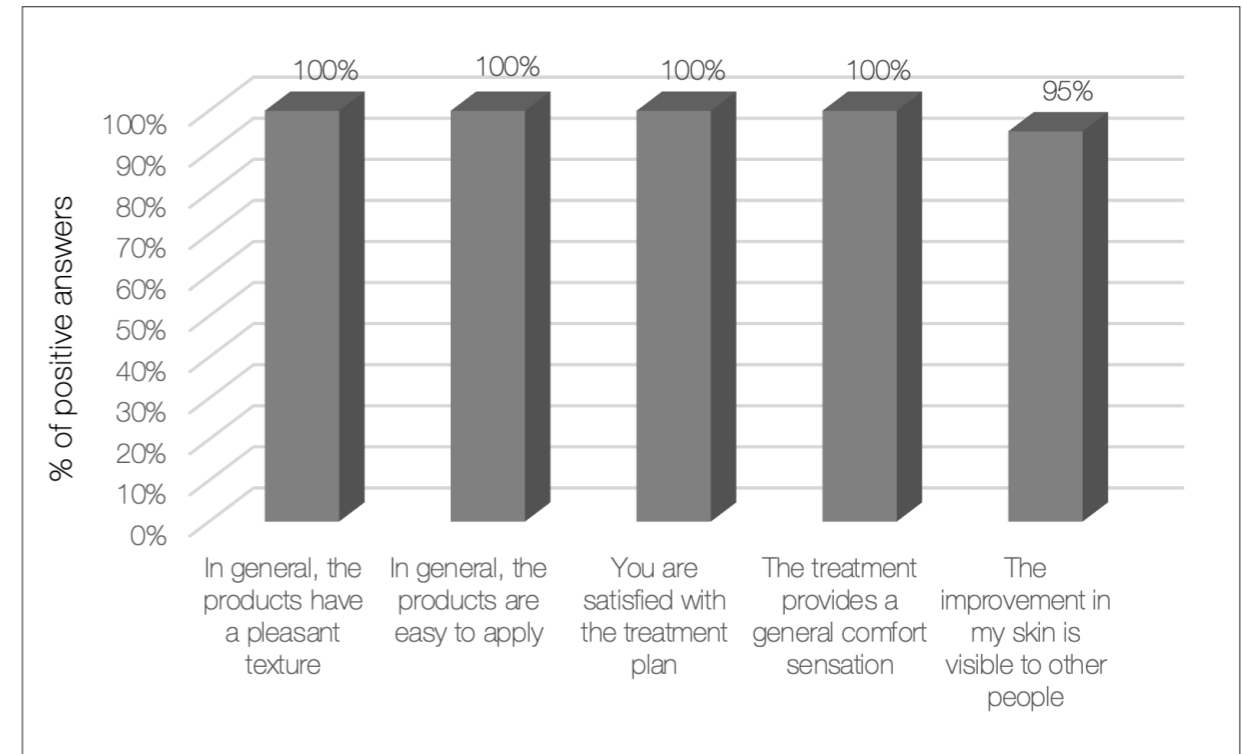
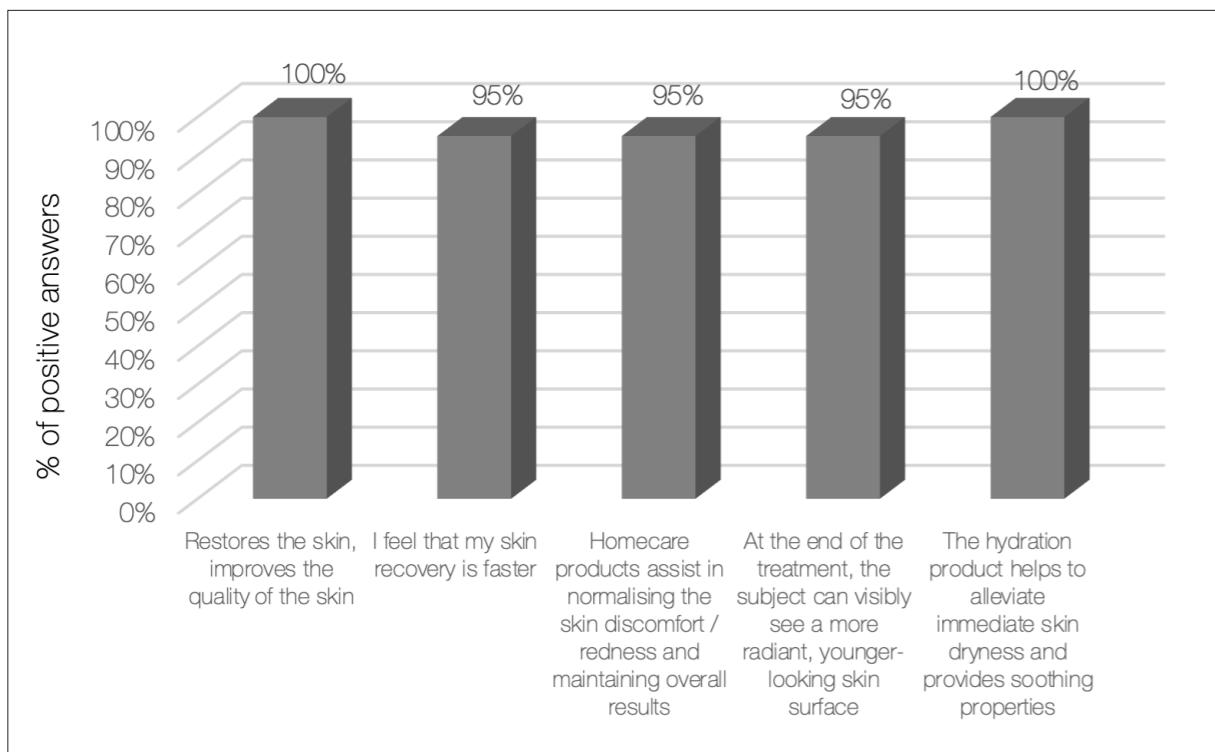
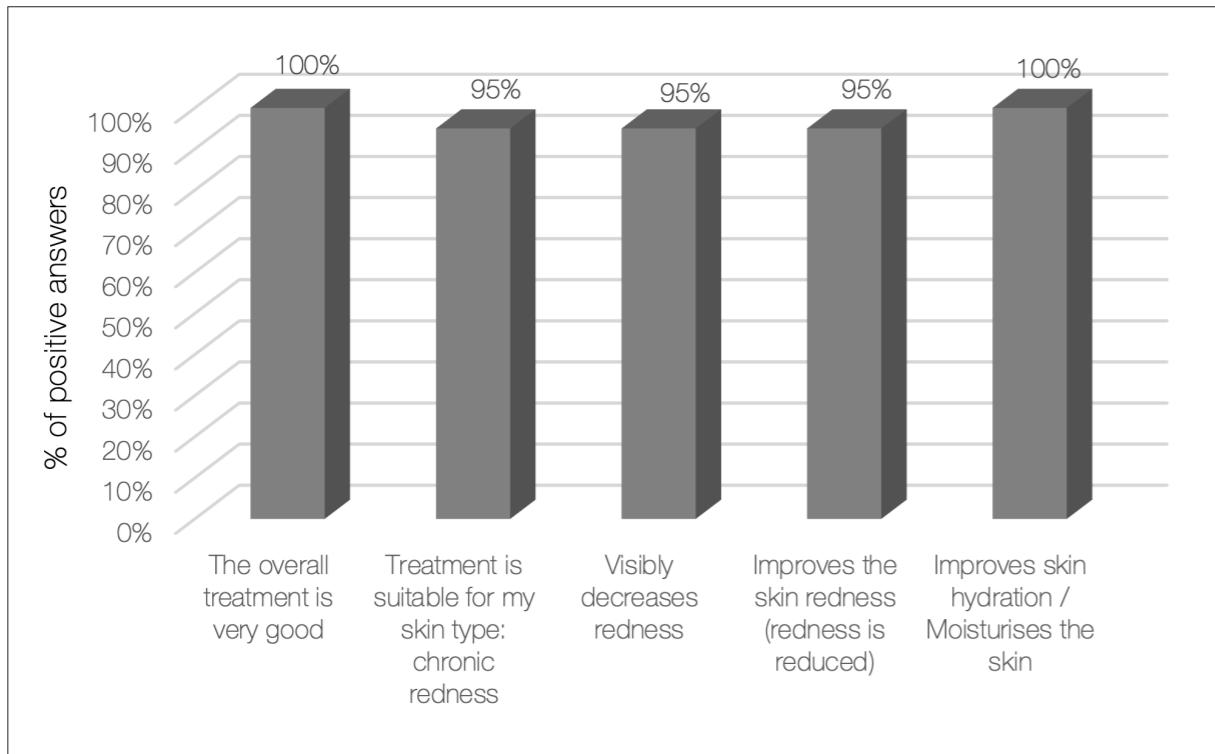
Prior to treatment the affected area exhibited visible telangiectasia, dilated blood vessels appearing as fine red lines on the skin surface. The vascular prominence was visible with notably extended vessels and redness.

After treatment there was a significant reduction in telangiectasia visibility with a reduction on blood vessel length and diminished vascular prominence resulting in a substantial reduction in rosacea severity signs.



Prior to treatment the skin exhibited signs of an impaired skin barrier including redness and compromised ability to retain moisture. The skin was noticeably dry with visible flakes affecting the skin's appearance and leading to a rough texture.

After treatment there was a significant improvement in the skin barrier function proving a skin barrier restoration. The skin appeared less red, and the dryness-induced flakiness was markedly reduced. Not only did the skin appear smoother and healthier with a visible reduction in flakiness, but hydration was also enhanced, improving the skin's comfort.



FEEDBACK FROM SUBJECTS

*"The treatment was very good for me. It **improves the redness** on my skin and leaves my face **very soft**".*

*"My skin **looks perfect**".*

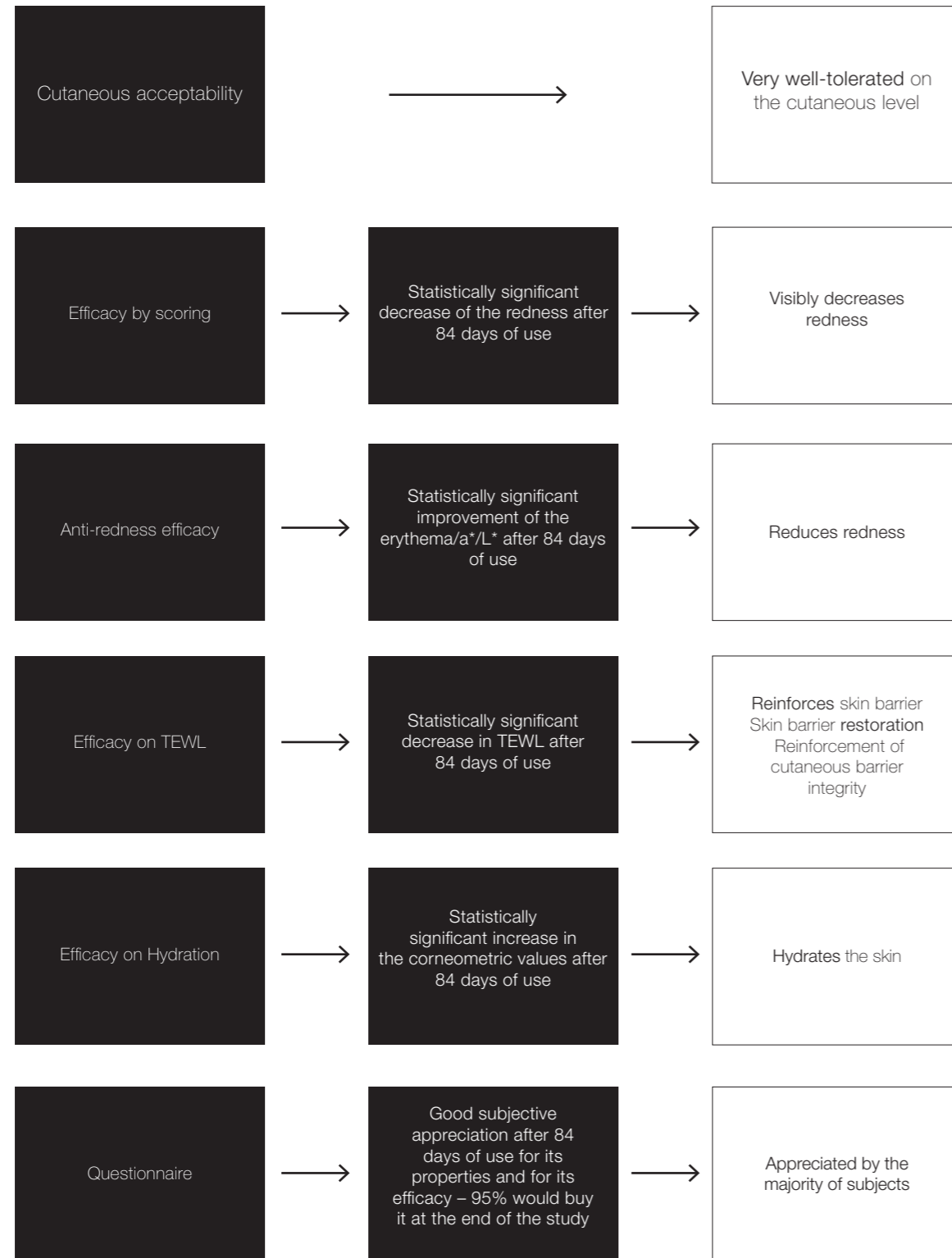
*"One of the **best** treatments that I tested".*

*"I like how the treatment leaves my skin like a **porcelain doll**".*

*"The skin is **visibly** seen more radiant in the application of the treatments in cabin. In homecare products the skin feels more **hydrated**".*

*"The **experience** was very good. I have chronic redness and sensitive skin but with the application of the treatment, I have improved a lot. It improves the **quality** of the skin, and the tone is more **even**".*

*"Good **quality** of the products".*



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↓ 55%

REDNESS

↓ 44%

ROSACEA LENGTH

↓ 41%

ROSACEA SURFACE

↑ 19%

HYDRATION

↓ 29%

TEWL

"Tolerance tested under dermatological control"

"Visibility decreases redness / reduces redness"

"Reinforces skin barrier / skin barrier restoration"

"Hydrates the skin"

"Suitable for sensitive skin"

"Suitable for mild rosacea"

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