SYNERGIE SKIN
CLEAN SCIENCE

CLINICAL DATA – COENZYME Q10

Coenzyme Q10 is an important mitochondrial component and naturally occurring lipid-soluble antioxidant present in all human cell membranes. It plays a crucial role in the generation of cellular energy, enhances the immune system, and acts as a free radical scavenger.

Ageing, poor eating habits, stress, and infection – they all affect the organism's ability to provide adequate amounts of CoQ10. After the age of about 35, the organism begins to lose the ability to synthesise CoQ10 from food and deficiency develops. Many researchers suggest that using CoQ10 supplements both in supplements and skin care can aid in the health and vitality of cells.

Antioxidant activity

The protective antioxidant effect is extended to lipids, proteins and DNA in all cells. CoQ10 in its reduced form as Ubiquinol is a potent lipophilic antioxidant that has a great importance as a free radical scavenger. CoQ10 protects the stability of the cell membranes, protects DNA from free radical induced oxidative damage, and is capable of recycling and regenerating other antioxidants, such as tocopherol and ascorbate (Crane 2001). Other important functions of CoQ10 for cell signalling and epigenetic gene expression have also been described (Bhagavan & Chopra 2006).

Another direct demonstration of the elimination of free radicals is shown by topical coenzyme Q 10 treatment of skin in elderly subjects. Damaged cell luminescence is eliminated via free radical scavenging when a skin cream containing coenzyme Q is applied (Hoppe *et al.* 1999).

Topical supplement

CoQ10 plays a key role in the skin protective network. In the skin. Ageing, poor eating habits, stress, and infection all affect the ability to provide adequate amounts of CoQ10 in the skin. After the age of 35, humans lose the ability to synthesise CoQ10 from food and its deficiency develops. CoQ10 increases in the skin from childhood to maturity and then decreases with age, environmental stress and under irradiation with UVA rays. It has been concluded that oral supplementation with CoQ10 may be very helpful to skin health.

CoQ10 has become a key active ingredient in many topical products. There are numerous topical formulations containing CoQ10, claiming to possess of antioxidant effects, skin repair and regeneration abilities as well as anti-wrinkling and anti-ageing capability (Hojerova *et al.* 2006). Vinson and Anamandla (2006) demonstrated *in vivo* antioxidative effects in the skin of young and middle-aged subjects of two forms of CoQ10 after a single dose and after a long-term supplementation.

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Clinical study: Topical treatment with CoQ10-containing formulas improves skin's Q10 level and provides antioxidative effects

Results demonstrate that stressed skin benefits from the topical Q10 treatment by reduction of free radicals and an increase in antioxidant capacity.

Introduction

Skin as the outermost human organ is in direct contact with the environment and is, therefore, exposed to external stress factors. To combat resulting damages, cutaneous cells are constantly involved in tissue regeneration and repair, processes that require a high amount of energy and a well-regulated cellular metabolism. With increasing age, however, energy production as well as mitochondrial activity decline. As a consequence, cell and tissue functions are impaired and visible structural alterations occur including the appearance of lines and loss of elasticity.

Reactive oxygen species (ROS) and free radicals represent predominant causes of damages to cellular components. In aging cells, ROS are frequently generated due to changes in cell respiration. Especially in skin cells, formation of ROS is also promoted by exposition to external insults such as ultraviolet (UV) light, IR light, HEV blue light and pollution.

ROS damage not only affects cell membranes and DNA but also structural and catalytic proteins which play a crucial role in cellular energetic pathways. As a result, the energy metabolism is further impaired by actions of free radicals, which are not only the cause of the aging process, but also its result.

During the process of energy production and in extracellular enzymatic processes, ubiquinone is converted into its reduced form (ubiquinol) which serves specific functions as a lipid-soluble antioxidant. Ubiquinol acts as a radical scavenger and protects mitochondria, lipid membranes, lipoproteins, and also DNA from oxidative damage.

Coenzyme Q10 (Q10), also known as ubiquinone, is an important coenzyme that is present in all human cells. It was originally shown to be a necessary component of the mitochondrial respiratory chain, working as an electron carrier and is crucial for energy production in the human body. It has also been well established that Q10 has many other important functions,

A recent publication showed that loss of Q10 levels in a mouse model leads to gradual loss of mitochondrial function, the development of aging-like disease traits and reduced lifespan. This condition is reversible when ubiquinone levels are restored. This illustrates the importance of Q10 and its epigenetic impact for optimal function of the entire organism.

In skin, endogenous Q10 levels decline with increasing age 14. Additionally, UV-irradiation, which leads to oxidative damage, significantly reduces skin's Q10 levels 20. In this context, the objective of this study was to investigate whether human skin may benefit from a topical Q10 treatment with regards to the two aforementioned

important points of action: increase in cellular energy metabolism as well as antioxidant effects.

In Vivo trials with Q10-Containing Formulas

A controlled, randomized study was carried out enrolling 73 healthy, non-smoking, female volunteers (20–66 years).

For the study, two formulas, a cream and a serum, containing Q10 in different concentrations were used (cream 348 µM ubiquinone [formula 1]; serum 870 µM ubiquinone [formula 2]).

During a 5-day preconditioning period and throughout the study, volunteers were required to desist from using skin care products and to avoid excessive contact with surfactants and sun exposure on both forearms. Visits to saunas, solariums, swimming-pools as well as very demanding exercise were prohibited for 1 day prior to measurements. Measurements were performed by trained and experienced personnel after acclimatization for at least 30 minutes.

One inner forearm of each volunteer was used for product treatment (two test areas) and the other forearm was left untreated and utilized as control (one test area). The positioning of treatment locations was left–right randomized and a stencil was used to mark the test areas. Volunteers applied the test formulas twice daily (morning and evening; 2 mg/cm2) for 2 weeks according to written instructions.

Collection of Skin Samples

After 2 weeks of application, the following skin samples were obtained on the morning after the last treatment: (I) uppermost layers of stratum corneum (skin surface), (II) suction blister fluid, and (III) suction blister epidermis (Fig.1).

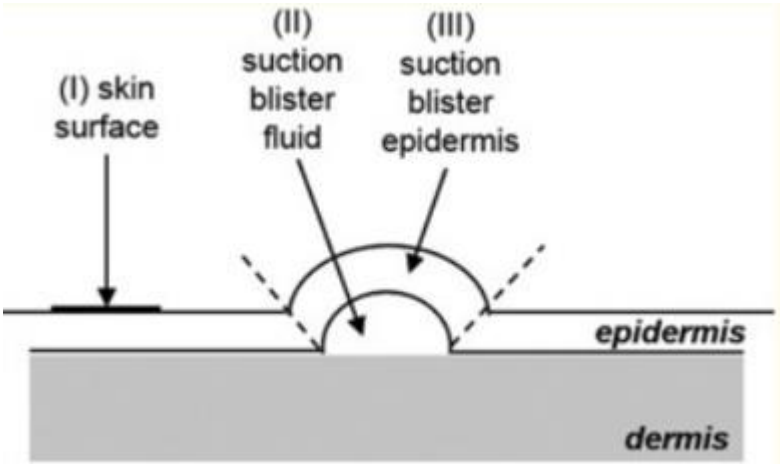

Figure 1 – Schematic illustration of collection of skin samples (not shown to scale). Samples from the skin surface (I) were obtained using adhesive sampling discs (D-Squames). After raising suction blisters, the blister fluid (II) was collected using a sterile syringe. In the last step, suction blister epidermis (III) was harvested using sterile forceps and scissors (III).

Preparation of Extracts from Suction Blister Epidermis and sampling discs.
Suction blister epidermis and sampling discs were analysed.

Analysis of Suction Blister Fluids

Freshly isolated suction blister fluid samples were analysed using the FORM Analyzer (Micro-Medical Instrumente GmbH). The concentration of hydroperoxides was determined in untreated skin utilizing the Free Oxygen Radicals Test (FORT, Calligari).

Baseline levels in suction blister fluids were ≤160 FORT units. According to reference values of blood samples given by the manufacturer and obtained from a recent publication 24, increased oxidative stress levels are considered as such starting at a value of 55% over baseline. Thus, the limit value for oxidative stress in our samples starts at 250 FORT units and was displayed by 16 out of 73 volunteers which are depicted in Fig. 2

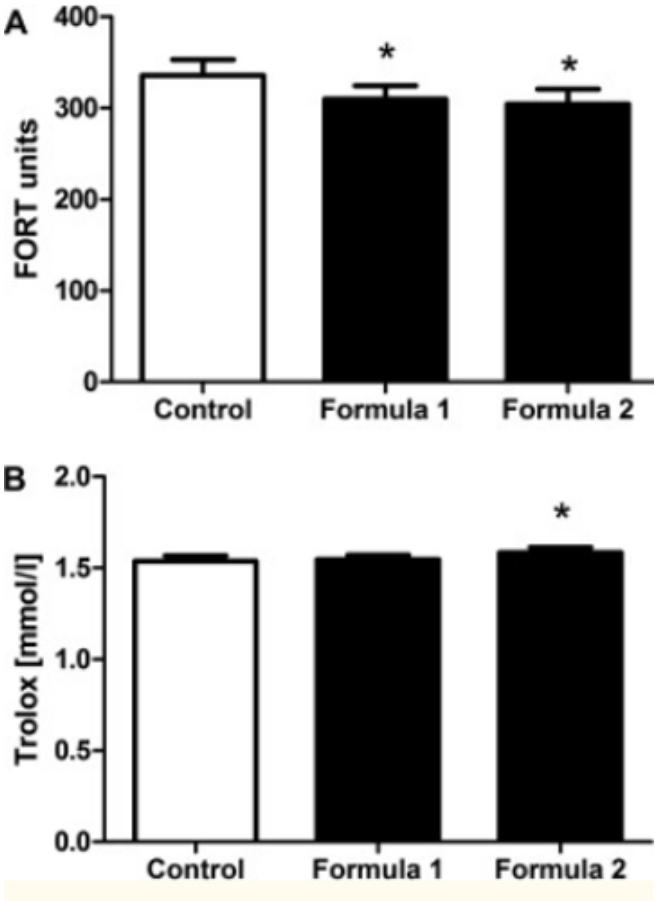

Figure 2 – Antioxidant properties of stressed skin are improved after treatment with Q10-containing formulas. Volunteers displaying elevated oxidative stress (≥250 FORT units) in untreated skin, were analysed following a 14-day treatment with formula 1 and formula 2. The level of free oxygen radicals **(A)** and the free oxygen radical defence **(B)** were determined in suction blister fluid obtained from treated compared with untreated control samples. Results are depicted as mean ± SEM (*n = 16)*. Significant difference are marked with an asterisk [*P<0.05 with respect to the untreated control (repeated measures analysis of variance, Dunnett's *post hoc* test)].

1. Quinone Levels are Reduced with Age in Human Epidermis

To investigate total quinone (ubiquinone plus ubiquinol) levels and connected biological effects in human skin in more detail, suction blister epidermis material was used for the determination of quinone concentrations. A comparison of samples obtained from young and aged volunteers showed that the quinone content in aged epidermis (8.04 ± 0.26 ng/µg cholesterol) was significantly lower than in young epidermis (9.45 ± 0.37 ng/µg cholesterol) indicating a loss of quinones with age (Fig 3). With this information it was investigated whether the epidermal quinone content can be improved by topical application.

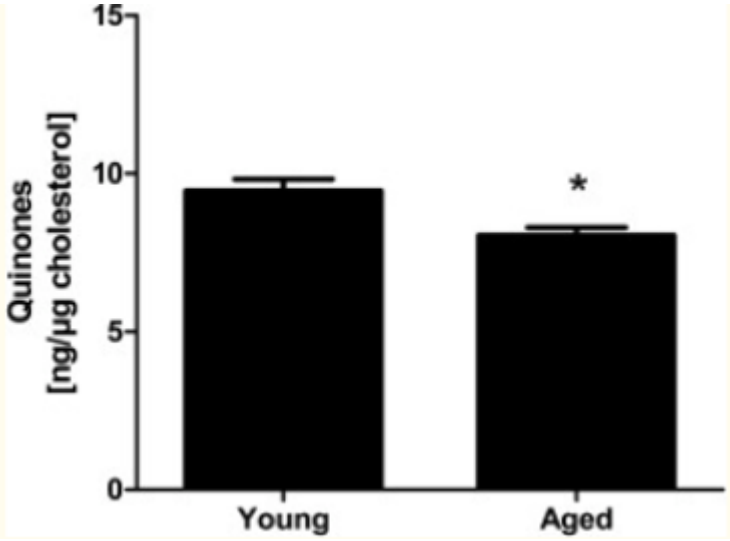

Figure 3 – Age-dependent decline of quinone levels within human epidermis. Quinone concentrations of young (20-25 years; *n=28)* and aged (60-66 years; *n= 28)* volunteers measured in suction blister epidermis obtained from untreated forearm skin. Data are depicted as mean ± SEM. Significant differences are marked with an asterisk [**P<0.05* for comparison between young and aged subjects (Student's *t*-test)].

2. Topical Treatment with Q10 Formulas Increases Epidermal Quinone Content on Multiple Levels

After 14 days of treatment with Q10-containing formulas, quinone levels were assessed in D-Squame® disc samples collected from the skin surface. To take the size of the treatment area into account, values were related to the area of the sample (mm2). The untreated control sample was compared with two individual samples which were obtained from test areas treated with ubiquinone-containing formula 1 or formula 2 (containing more than twice as much ubiquinone than formula 1). The untreated control sample displayed a level of 0.024 ± 0.003 ng quinones/mm2. Compared with the untreated control, treatment with formula 1 resulted in a significant increase to 0.133 ± 0.02 ng quinones/mm2, whereas application of formula 2 led to an even more pronounced and significant augmentation to 0.717 ± 0.083 ng quinones/mm2 (Fig. (Fig.4)

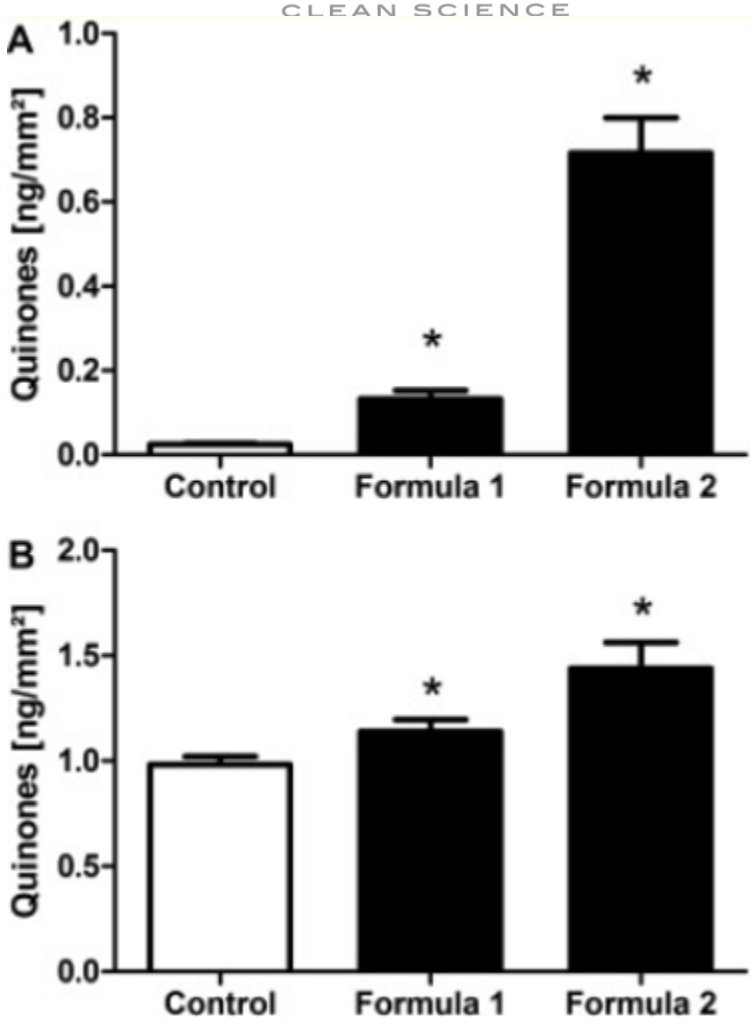

Figure 4 – Increase in quinone levels after treatment with Q10-containing formulas. Following a 14-day treatment with Q10-containing formulas 1 and 2, quinone levels were assessed on the skin surface using samples obtained from D-Sqaumes **(A)** and within the epidermis using suction blister material **(B).** Results are shown as mean ± SEM (20-66 years; *n=73).* Significant differences are marked with an asterisk [**P<0.05* with respect to the untreated control (repeated measures analysis of variance, Dunnett's *post hoc* test)].

It was further investigated whether topical treatment can increase quinone levels also in deeper layers of the epidermis. For this purpose, quinone content was analysed in suction blister epidermis obtained from the treated and untreated areas described above. Quinone values determined in the respective D-Squame® disc samples were subtracted to exclude quinone residues present on the skin surface. After treatment with formula 1, quinone levels were significantly increased (1.14 ± 0.06 ng quinones/mm2) compared with the untreated control (0.98 ± 0.04 ng quinones/mm2). Application of formula 2 elevated the quinone content even more (1.44 ± 0.12 ng quinones/mm2) and also showed a significant augmentation compared with the untreated control (Fig. (Fig.33B).

According to this data, topical application of the two test formulas increased quinone levels not only on the skin surface but also within the deeper levels of the epidermis.

Study conclusion:
Skin is constantly exposed not only to intrinsic but also to environmental stressors producing augmented internal ROS concentrations which cause damage throughout the tissue. Therefore, the "Free Radical Theory of Aging" 5 postulating that aging is the result of cellular damage inflicted over time by free radicals is not only one of the most prominent ideas concentrating on the complex phenomenon of aging, but also highly relevant for skin.

Coenzyme Q10 constitutes the only endogenously synthesized lipid-soluble antioxidant. At the same time, it plays a crucial role in cellular energy production. Intracellular synthesis is the major source of human CoQ10 but it can also be delivered through the diet or dietary supplements which can increase human total Q10 levels in plasma.

However, in skin, Q10 is not only found in living cells but also in the skin surface lipids (SSL), which are part of the stratum corneum, forming the outermost barrier of the skin. SSL are composed of a mixture of sebum secreted from sebaceous glands and lipids originating mainly from corneocytes. Due to their location on the skin surface SSL are constantly exposed to UV irradiation, air pollution, chemical oxidants, and microorganisms. SSL Q10 levels have been shown to decline with age and also decrease after UV exposure in vitro.

Quinone values on the skin surface were significantly increased after treatment with Q10-containing formulas demonstrating that the powerful antioxidant Q10 can be delivered directly to the uppermost layer of the skin. This data is significant since oral supplementation with Q10 did not result in the enhancement of Q10 content in skin surface lipids. With a topical Q10 treatment, however, short-term environmental stress-induced as well as age-related Q10 deficits, may be counteracted directly at the skin surface. Young individuals displaying normal Q10 values may benefit since spontaneously occurring external oxidative stress can be neutralized quickly. In the aged population already decreased Q10 levels may be replenished. Thus, using Q10-containing topical formulas on a regular basis to protect the outermost skin layer and is recommended for skin at any age.

There is a significant age-dependent decline in quinone levels in suction blister epidermis samples which is well in line with other findings documenting decreased Q10 levels not only in several human organs but also in the epidermis of volunteers aged 30–80 years. With advancing age, the decline of both quinones represents the major issue in skin. Besides the chronological aging process, occasional external stress events inside the epidermis may have an impact on the levels of both quinones as demonstrated by Podda *et al.* in human skin equivalents after UV-irradiation. In skin, both causes of Q10 decline (age-dependent and UV-induced) may be of significant physiological importance given that even small changes in Q10 concentration could result in substantial alterations in skin cell function.

According to the data, topical application of CoQ10 serves to replenish epidermal ubiquinone levels, which may be decreased with aging and environmental stress.

It was also found that, in cases of elevated levels of free radicals in the skin tissue, topical treatment with Q10-containing formulas may significantly reduce the oxidative stress level in cells.

In this context, it is interesting to note that dietary supplementation with ubiquinol is reported to exert beneficial effects in age-related diseases, such as cardiovascular disease, diabetes, age-related hearing loss, and Parkinson's disease. Moreover, decelerated age-related accumulation of oxidative damage was shown in ubiquinol-supplemented mice with accelerated senescence.

In summary, the data presented here show that topically applied Q10 can penetrate the skin exerts antioxidant effects, and can support the maintenance of cellular energy levels. These effects are not only beneficial for the aged population suffering from a Q10 deficit but also to replenish the Q10 level in skin which is lost over time through normal environmental stress.

Regular treatment with Q10-containing formulas enables the skin to cope more effectively with short-term insults inflicted by UV and IR irradiation and pollution stress. The broad benefits aid in cellular protection and long-term anti-aging effects for their skin.

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Anja Knott,[1] Volker Achterberg,[1] Christoph Smuda,[1] Heiko Mielke,[1] Gabi Sperling,[1] Katja Dunckelmann,[1] Alexandra Vogelsang,[1] Andrea Krüger,[1] Helge Schwengler,[1] Mojgan Behtash,[1] Sonja Kristof,[1] Heike Diekmann,[1] Tanya Eisenberg,[1] Andreas Berroth,[1] Janosch Hildebrand,[1] Ralf Siegner,[1] Marc Winnefeld,[1] Frank Teuber,[1] Sven Fey,[1] Janne Möbius,[1] Dana Retzer,[1] Thorsten Burkhardt,[1] Juliane Lüttke,[1] and Thomas Blatt[1]