The Role of Coenzyme Q10 in Skin Aging and Opportunities for Topical Intervention: A Review

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BACKGROUND: Coenzyme Q10 (CoQ10) is a naturally produced, lipid-soluble molecule crucial for cellular energy production and antioxidant activity. It diminishes with age and under external stress factors in skin, leading to signs of aging. Beyond its role in cellular energy production within the mitochondria, CoQ10 is vital to skin's defense against oxidative stress, a key contributor to premature aging. Use of topical skincare products with CoQ10 can be effective to replenish levels of CoQ10 and reverse skin aging. **OBJECTIVE:** This publication discusses the role of CoQ10 in skin aging along with the benefits of topical skincare products that incorporate CoQ10 as an ingredient. **METHODS:** We searched the PubMed database using terms "Coenzyme Q10" and "skin" and "aging." Overall, the search yielded 80 results, but a limitation of 10 years was then applied to restrict publications to those with the most up-to-date science. **RESULTS:** A total of 36 publications were identified and included as background for this article. These 36 publications encompassed both original research articles and review articles. **DISCUSSION:** Applying topical skincare products with CoQ10 replenishes CoQ10 cellular levels, helping to normalize cellular energy homeostasis and providing antioxidative effects to support and repair cutaneous damage including signs of skin aging. In *ex vivo* and *in vivo* studies, application of CoQ10 increased CoQ10 levels both on the skin surface (i.e., stratum corneum) and even more in deeper levels of the skin. Clinically, topical application of CoQ10-formulated products reduces the depth of cutaneous wrinkles, a sign associated with aging. **CONCLUSION:** Aging and stressed skin are, in part, the result of alterations in cellular metabolic homeostasis, which can be reversed via the benefits of topical application of CoQ10-enriched formulations that stimulate cutaneous energy metabolism and reduce free radicals via antioxidant function. By restoring physiological homeostasis, topical skincare products with CoQ10 replenish the skin's antioxidant levels, increase cellular (energy) metabolism, and reduce the signs of skin aging. **KEYWORDS:** Coenzyme Q10, skincare, aging, over-the-counter, antioxidants, homeostasis

Over-the-counter (OTC) skincare products formulated to prevent and minimize signs of aging skin have proliferated in recent years as the understanding of aging mechanisms has advanced. Cutaneous aging is determined by intrinsic as well as extrinsic factors—with ultraviolet (UV) radiation the main cause of accelerated skin aging.[1] Mitochondrial dysfunction, leading to impaired cellular energy metabolism and cellular senescence, represent two essential hallmarks of skin aging.[2–5] The changes in metabolic homeostasis are accompanied by visible structural changes and signs of skin aging, including wrinkles, fine lines, and loss of elasticity, among other signs.[3,6] Generation of reactive oxygen species (ROS), reactive nitrogen species (RNS) and other free radicals causes further damage to skin cells and the extracellular matrix, and impairs cellular energy metabolism.[6] These highly active molecules, which are generated secondary to deregulation in cellular respiration, are also associated with exposure to external insults, such as UV radiation.[6–8] This starts a vicious cycle: the skin's energy metabolism is disturbed, accompanied by increased formation of free radicals; as a result, the skin cells need increasing amounts of energy for repair and protection.[1,6–8]

Ubiquitous throughout the body, coenzyme Q10 (CoQ10) is an endogenous lipophilic molecule with a central role in cellular energy metabolism—more specifically, the mitochondrial electron transport chain. Additionally, CoQ10 functions as an effective antioxidant molecule involved in neutralization of reactive species and other free radicals.[6,9–12] CoQ10 levels in the skin decrease with age and exposure to UV radiation.[6,12–14] Topical supplementation of CoQ10 has been shown to ameliorate signs of skin aging both by stabilizing mitochondrial activity and by exerting antioxidant properties, which typically translates to regeneration of skin processes involved in cutaneous skin aging.[6,15,16]

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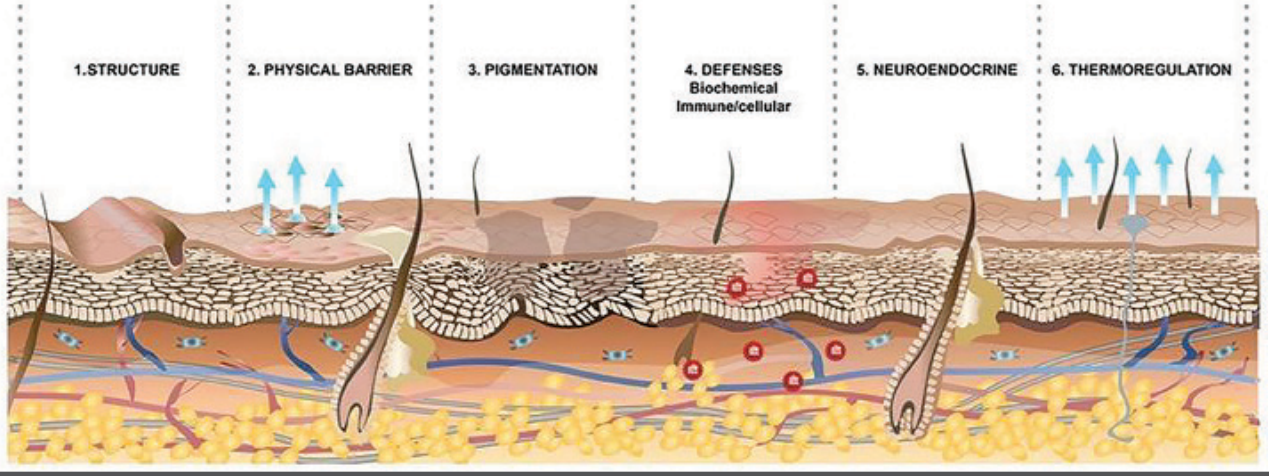

FIGURE 1. Effect of stressors on skin functions. Impacted functions include structure (matrix and adnexa), skin barrier function, melanocytes including hyperpigmentation, biochemical immune and cellular defenses, neuroendocrine delivery, and thermoregulation. Adapted and used with permission from Bravo et al.[19]

Given the variety of skincare products available, it is important for dermatology healthcare professionals to have a thorough knowledge of active ingredients such as CoQ10 to educate and advise patients. Because many patients feel that maintaining a youthful and pleasant facial appearance is important, facial aging can impact quality of life.

In the present review, we discuss the currently available literature supporting use of CoQ10 in anti-aging topical skincare products.

DISCUSSION

Cellular metabolism and cutaneous aging. Skin aging involves a variety of factors, encompassing chronological processes as well as exposure to factors in the environment, lifestyle, and chronic disease that impair overall function (Figure 1).[3,15,19] The interaction of these intrinsic and extrinsic factors leads to metabolic and molecular changes, including deteriorating cellular and extracellular structures and reduction of the skin's ability to regenerate and maintain appropriate homeostasis.[1,9,20]

Clinically, cutaneous aging is characterized by thinning skin, loss of elasticity, and increased wrinkling.[2,20,21] Pigmentation changes can occur (e.g., lentigines and other pigmentation), veins and bones can become more visible, and injuries take longer to heal.[2,20] Cellular activity decreases at a molecular level, collagen production decreases while degradation increases, and there is an increase in nonfunctional elastic fibers.[2,12,22] Deterioration of mitochondrial function leads to ROS

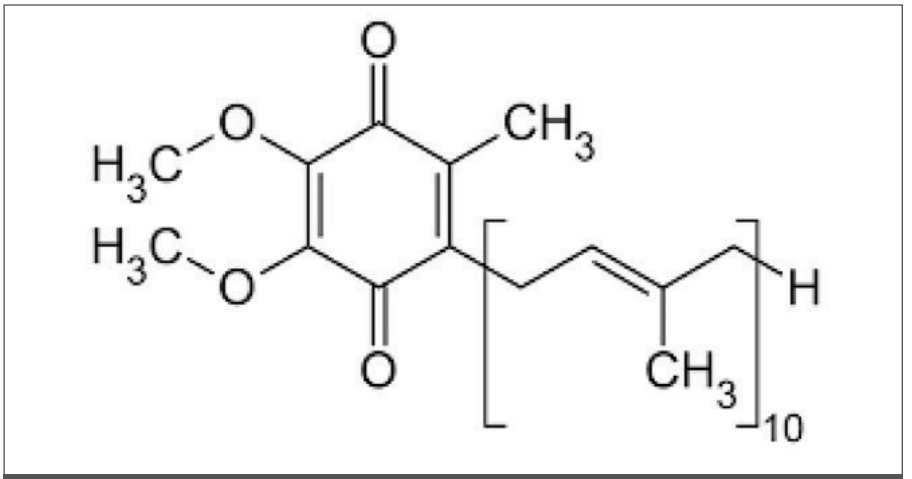

FIGURE 2. Structure of CoQ10

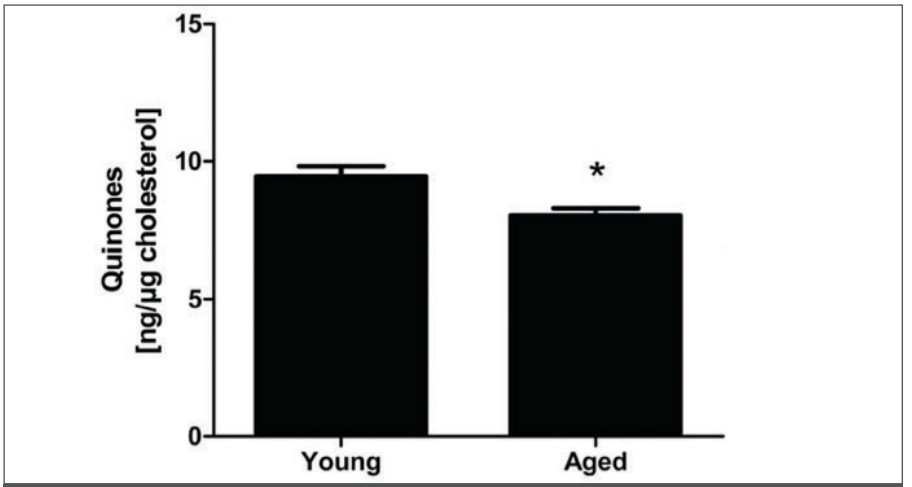

FIGURE 3. Age-dependent decline in CoQ10 levels in skin. Used with permission from Knott et al.[6]

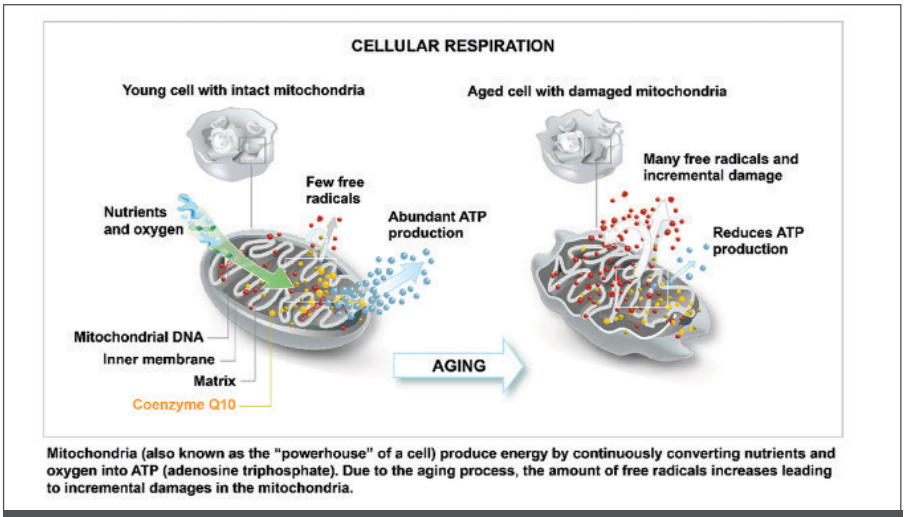

FIGURE 4. Impact of aging on CoQ10 cellular function in metabolic homeostasis

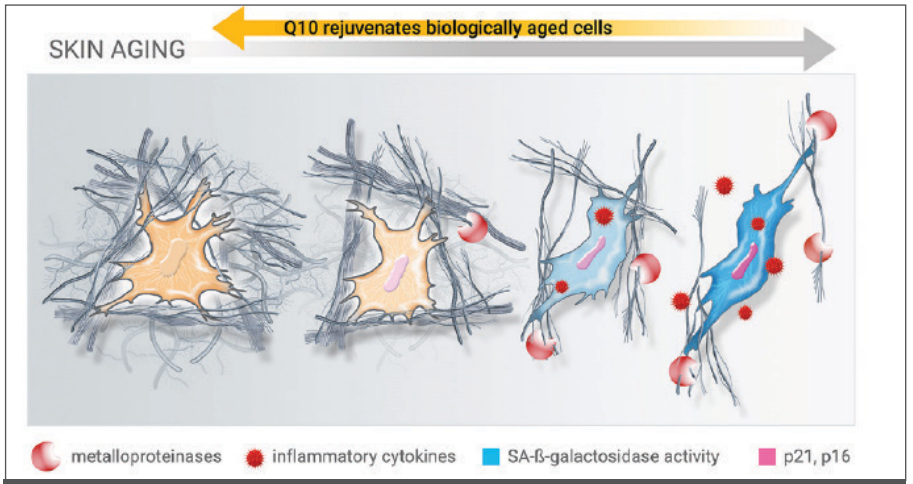

FIGURE 5. Role of diminished CoQ10 level on biological aging of skin cells

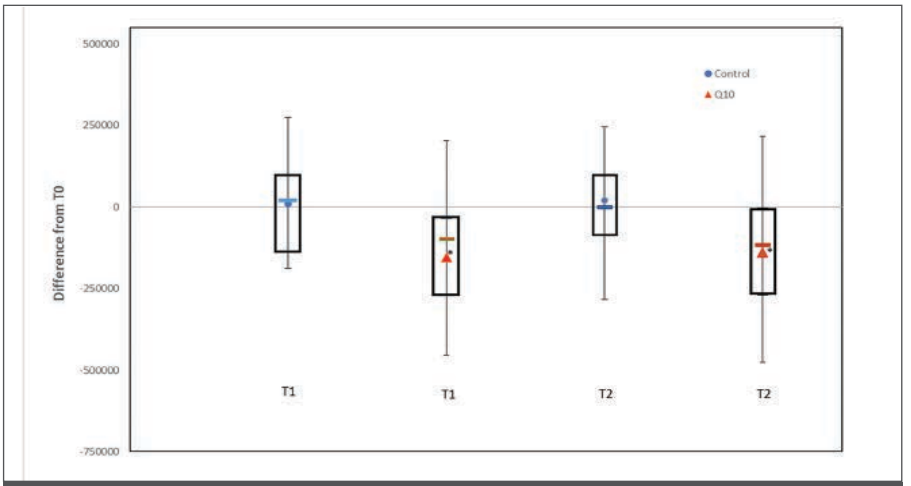

FIGURE 6. UVA-induced chemiluminescence. Box plots of differences to baseline T0, photon counts. The dot (•) corresponds to the mean values for control sites, the (x) indicate sites treated with CoQ10 lotion. The line inside the box (-) corresponds to the median. * $p<0.0001$ when compared with T0. Data on File Beiersdorf Study Report STDR-071541C.

generation, often overwhelming cellular redox homeostasis, thereby causing further damage to cellular structures and to the extracellular matrix, including collagen.[2,13] Aging epidermal keratinocytes may also shift energy generation from aerobic respiration to anaerobic glycolysis, a change that has been attributed to an attempt to compensate for reduced CoQ10 levels.[35] Cells may also enter a state of cellular senescence, or irreversible growth arrest.[2,21,23–25]

Skin cells are continuously involved in repairing and regenerating tissue; these processes generally require a high amount of energy, along with well-regulated cellular metabolism to withstand exposure to external and internal stressors.[21] The intrinsic aging process is driven by oxygen free radicals (ROS); these molecules damage cellular and extracellular structures, including DNA and lipid membranes, and upregulate matrix metalloproteinases (MMPs). The net result is increased cutaneous breakdown and reduced levels of collagen and elastin.[3,21,26] The subsequent imbalance is known as oxidative stress, which occurs due to an imbalance between ROS and endogenous antioxidants.[3] The most common oxygen species are hydrogen peroxide, singlet oxygen, and hydroxyl radicals.[12] Accumulation of ROS results in inflammation, cellular senescence, and skin aging.[3] To defend against this, the skin has enzymatic and non-enzymatic antioxidant mechanisms. Enzymes that help prevent radical damage can include superoxide dismutase (SOD), catalase, and glutathione peroxidase, while non-enzymatic antioxidants present in skin include vitamin E, ascorbate (vitamin C), and CoQ10, which has a dual action as an antioxidant and energy metabolizer.[12]

Mechanism of action of CoQ10. The structure of CoQ10 is similar to vitamin K, but it can be synthesized in the body (Figure 2).[27] In the skin, CoQ10 functions as both an integral part of cellular energy metabolism and as a barrier against ROS. Skin's CoQ10 level decreases with age, declining through the ages of 20 to 66 years (Figure 3); this decline contributes to an age-dependent metabolic alteration.[6] Low CoQ10 can be associated with oxidative stress, mitochondrial dysfunction, and cellular senescence in dermal fibroblasts, resulting in a disruption of cellular homeostasis.[12,23,25]

Cellular respiration. CoQ10 has an essential

physiological role as a cofactor for mitochondrial enzyme pathways within cells.[28] Even small increases in CoQ10 concentrations in the inner mitochondrial membrane are thought to lead to increased respiration.[28] Alterations in mitochondrial function impair cellular adenosine triphosphate (ATP) production and thereby inhibit the fuel for cellular repair mechanisms and function (Figure 4).[28] As a consequence, ROS accumulate, which in turn can damage mitochondria, cellular membranes, and mitochondrial DNA, accelerating skin aging in a negative feedback loop.[28] In response to reduced mitochondrial energy generation, other sources of intracellular energy—such as switchover to anaerobic pathways—attempt to compensate.[28, 35] Anaerobic pathways, such as glycolysis, favor formation of advanced glycation end products, which also may harm cellular processes, including generation of nonfunctional cytoskeletal proteins, inflammation, and potentially, cellular apoptosis. This sequence highlights why it is important to preserve mitochondrial energy generation.[28] The ability of CoQ10 to positively impact mitochondrial function underlies its ability to maintain appropriate energy levels.[6,12,23,25] In turn, this helps prevent aging skin from converting to anaerobic energy production.[28, 29]

Antioxidant function. Outside of the mitochondria, CoQ10 in its reduced form acts as an antioxidant to stabilize cellular membranes by protecting against peroxidation of phospholipids.[12,13,28, 30] In addition, it may slow the chain propagation of ROS and regenerates oxidized vitamin C and vitamin E.[31,32] CoQ10 sustains skin function against free radicals and their ability to activate the mitogen-activated protein kinase (MAPK) pathway. Activation of MAPK stimulates production of MMPs, including collagenases, which damage collagen fibers.[36–38] Finally, CoQ10 reduces damage caused by lipid peroxidase to lipids, proteins, and DNA.[14,26] Overall, the unique dual functionality of CoQ10 in skin may stimulate collagen production, primarily via its energetic function in delivering ATP for synthesis, and also mitigate skin aging by protecting mitochondrial function and decreasing the activity of reactive oxygen species.[3]

Anti-aging evidence of Coq10. Anti-aging benefits associated with CoQ10 have been shown in early aging and in mature skin.[27] In 1999, Hoppe et al[12] showed that CoQ10 not only penetrated into the living layers of human skin to reduce oxidation, but also reduced the depth of wrinkles following topical application around the skin of the eyes for six months (n=20). In addition, these researchers found that CoQ10 reduced collagenase expression in human dermal fibroblasts exposed to UV radiation.[12] Hoppe et al also showed that CoQ10 had no cytotoxicity in cultured keratinocytes, even at concentrations much higher than used in skincare products.[12] Further, its irritancy potential was similar to vehicle (e.g., absent) even in individuals with sensitive skin.[12,33] A reduction in wrinkle depth was also shown by Ashida et al,[17] while Innui et al[36] demonstrated that CoQ10 decreases production of cytokines by keratinocytes, which in turn reduces MMPs and associated wrinkles.

Using x-ray fluorescence and iodine labeling, Staufer et al[34] assessed cellular uptake and distribution of CoQ10 *in vitro* in human skin cells.[34] After exogenous application, there was a large accumulation of CoQ10 in skin cells.[34] Schniertshauer[16] further demonstrated increased mitochondrial respiration—along with ATP production—in human epidermis samples after exogenous CoQ10 administration. Similar findings were reported by Knott et al,[6] along with reduction of ROS and increase in antioxidative capacity. Marcheggiani et al[23] showed that CoQ10 supplementation improved cellular oxidative status, and conversely, inhibition of CoQ10 is associated with a shift toward a senescent phenotype in skin cells, indicating CoQ10 is not a sidebar to skin aging but rather a main cause.[25] Prahl et al[35] demonstrated that CoQ10 application protected and stabilized function of mitochondria against UV irradiation.

In 2020, Mine et al[39] showed that CoQ10 application increased proliferation of fibroblasts and mRNA expression of collagen (types I, II and VII), elastin, and heat shock protein 47. Additionally, Marcheggiani et al[23] revealed that in a CoQ10 deprivation model, the cells with reduced CoQ10 levels enter cellular senescence and secrete inflammatory cytokines as well as show reduced collagen and elastin expression. These effects can be reversed by CoQ10 replenishment (Figure 5).[25] Collagen and elastin

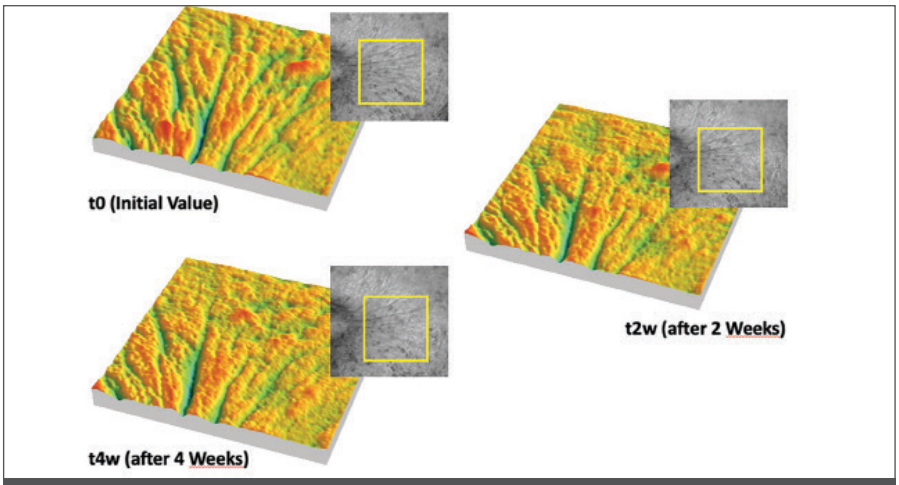

FIGURE 7. Decrease in wrinkles and roughness after exogenous CoQ10 topical application. Data on File Study Report STDR-072057C.

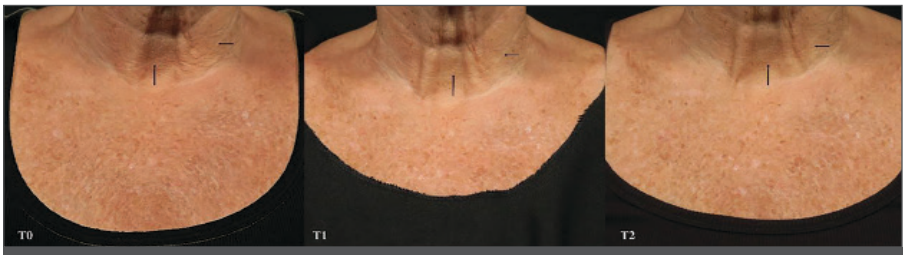

FIGURE 8. Illustrates the décolletage images at baseline (T0), 2 weeks (T1) and at 4 weeks (T2). Arrows show the areas of improvement. Data on File, Study Report STDR-077530C.[43]

are both important to maintain skin structure and function, and decreases are associated with wrinkle formation that is accelerated by both aging and UV exposure.[36] Further, CoQ10 inhibited MMP expression and subsequent collagen degradation.[36]

Most recently, a skincare product containing CoQ10 was evaluated, with ultra-weak photon emission and corneometer, after application on the forearm of 30 female subjects aged 35 to 60 years with dry skin (44%) or normal skin (66%).[40] This unpublished study was a controlled (non-treated site) and blinded evaluation in which the CoQ10 skincare product improved antioxidative status, as indicated by decreased UVA-induced ultra-weak photon emission after one (T1) and two (T2) weeks of regular application, and increased skin moisturization on Corneometer® assessments. The ultra-weak photon emission or chemiluminescence is described in Liebel et al.[41] Figure 6 shows the ultra-weak photon emission. In addition, the test product was well tolerated by the study population, with no discomfort observed or reported for any subject.

In an unpublished, split-face, randomized, blinded study of a CoQ10 skincare product applied twice daily for four weeks, effects on periorbital skin wrinkling versus untreated skin (n=41) were compared. Study participants were women aged 38 to 66 years with facial lines and wrinkles of any severity and Fitzpatrick Skin Phototypes I to IV. The evaluated CoQ10 product was associated with improvements in both wrinkle roughness and wrinkle depth as assessed by facial-wrinkle-analysis in high definition with $FOITS_{HD}$ technique, an optical method for non-contact measurement of skin microtopography (Figure 7).[42] In this study, after two weeks the untreated area had increased for the Rz (ten-point mean roughness) and Ra (arithmetical mean roughness) parameters by about 8 to 10 percent in comparison to baseline. After four weeks, increases for Rz and Ra parameters by about 4 to 5 percent were observed. For the test product formulated with CoQ10, after four weeks, decrease for Rz and Ra parameters were observed. Figure 7 shows the continuous improvement in skin roughness with the use of the CoQ10-based formula.

In another unpublished study, 36 women aged 40 or older, with Fitzpatrick Skin Phototypes I to IV, were enrolled.[43] Subjects included in the study had at least mild to moderate crepey skin on the neck, décolletage, dorsal forearms, and back of the hands. Overall, expert grader ratings showed that the product formulated with CoQ10 was associated with improvement in crepey skin and wrinkles after both two and four weeks of use compared to baseline (Figure 8). Pinch/recoil data from the back of the hand showed a large improvement in elasticity after both two and four weeks of use compared to baseline.

Limitations. The strength of the current review is limited by the fact that the data from the last three unpublished clinical studies discussed in this review[40,42,43] are not publicly available in the literature. More published clinical studies evaluating the efficacy of the CoQ10 skincare product that is discussed here should be conducted to confirm the results of these internally conducted clinical studies.

CONCLUSION

As described in this paper, CoQ10's dual functionality—as both a key component of cellular energy metabolism and as a powerful antioxidant—are favorable attributes when utilized in topical supplementation formulations. CoQ10 is present in the skin's own molecules, but its amount decreases with age. Topical CoQ10 replenishment is well tolerated by most skin types, including sensitive skin, allowing for a broader use of the ingredient for patients with most skin types.[6,12] The energy metabolism and antioxidative effects of CoQ10 support its daily use. In the clinical studies described here, we observed the anti-aging benefits of use of CoQ10. In a four-week study, an improvement in skin facial roughness and wrinkles was reported. In areas with crepey skin on the neck or the back of the hand, clinical improvement was documented.

CoQ10 has been shown to penetrate the skin following topical application and to be highly effective at protecting against skin damage at the cellular level while improving signs of cutaneous aging.[6] It has actions that target both intrinsic aging and extrinsic aging. Further, CoQ10 is safe and has very low irritation potential, including in individuals with sensitive skin.[12]

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