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Using Copper to Improve the Well-Being of the Skin

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Abstract: Copper has two key properties that are being exploited in consumer and medical device products in the last decade. On the one hand, copper has potent biocidal properties. On the other hand, copper is involved in numerous physiological and metabolic processes critical for the appropriate functioning of almost all tissues in the human body. In the skin, copper is involved in the synthesis and stabilization of extracellular matrix skin proteins and angiogenesis. This manuscript reviews clinical studies that show that the use of textile consumer and medical device products, embedded with microscopic copper oxide particles, improve the well-being of the skin. These include studies showing a) cure of athlete's foot infections and improvement in skin elasticity, especially important for individuals suffering from diabetes; b) reduction of facial fine line and wrinkles; and c) enhancement of wound healing; by copper oxide embedded socks, pillowcases and wound dressings, respectively. The manuscript also reviews and discusses the mechanisms by which the presence of copper in these products improves skin well-being.

Keywords: Biocide, copper, extracellular matrix, skin, textiles, wound healing.

Copper has two key properties that endow it as an excellent active ingredient to be used in products, which come in contact with the skin, aiming to improve the skin's well-being. Copper plays a key role in the synthesis and stabilization of skin proteins, and it also has potent biocidal properties. This manuscript discusses how these two important distinct properties are utilized in consumer and medically related products.

SKIN AGING

The skin is the largest organ of the body that protects our internal tissues from chemical, physical, and microbial damage. It also helps to prevent loss of water and other endogenous substances, participates in thermoregulation of the body and serves as an excretory organ [1, 2]. The skin is differentiated into the epidermis, dermis and subcutaneous layers. The external non-vascularized layer, the epidermis, consists of differentiating keratinocytes that overlay a basement membrane, melanocytes and langerhans cells, and serves as the main semipermeable protective barrier. The dermis, below the basement membrane, consists of fibroblasts, nerves, hair follicles, sebaceous glands, sweat glands, lymphatic and blood vessels. The dermal layer gives shape, firmness, sensation and nourishment to the skin. Finally, the subcutaneous layer consists mostly of adipose tissue, acting primarily as a heat insulator and a mechanical cushion [1, 2].

With age, the skin undergoes vast changes, becoming wrinkled and rigid, losing its firmness, elasticity, tone, texture, thickness, flexibility and moisture content [3]. Skin aging is attributed to several changes. These include alterations in the dermal extracellular matrix (ECM) made up mainly by collagen (which provides strength and structure) and elastin (which provides elasticity and resilience) fibres. Collagen and elastin are secreted mostly by fibroblasts [4, 5]. Transforming growth factor- β (TGF-β) is the primary stimulator of the collagen and elastin fiber formation and deposition [4, 6], and plays a significant role in scar formation [7]. Lysyl oxidase (LOX) is a key protein involved in the lysine-derived crosslinks of the ECM dermal proteins [8-10]. Heat shock protein-47 (HSP-47) is a collagen-specific chaperone needed for the formation of the collagen triple helical structure [11]. During aging, there is a reduction of elastin and collagen production by dermal fibroblasts, alterations in LOX, and break-

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down of the collagen/elastin fibers forming the ECM by matrix metalloproteinases (MMP) [5, 6, 8-10, 12-16]. These events, accelerate by inflammation and oxidative stress in photoaged skin [3, 17, 18], are controlled chiefly via the mitogen activated protein kinase (MAPK) and NF-κB/p65 signal transduction pathways [17, 19, 20].

COPPER AND ITS PHYSIOLOGICAL ROLE IN THE SKIN

Copper is one of those nine minerals that are recognized as essential nutrients for humans, as it plays a crucial role in different physiological normal processes in basically all human tissues [21], as well as in the skin [22]. The body of a 70-kg healthy individual has about 110 mg of copper, 50% of which is found in the bones and muscles, 15% in the skin, 15% in the bone marrow, 10% in the liver and 8% in the brain [23]. The uptake, distribution to different tissues, secretion of excess, and metabolism of copper, are very precise and efficient coordinated events [23, 24]. Copper is naturally found in many food sources such as meats, vegetables and grains, and the recommended daily intake of copper for adults is ~1 mg [22, 25].

In the skin, copper a) stimulates dermal fibroblasts proliferation [26] (Fig. **1**); b) upregulates collagen (types I, II, and V) and elastin fiber components (elastin, fibrillins) production by fibroblasts [27] (Fig. **2**), seemingly through the induction of TGF-β [27]; c) stimulates HSP-47, essential to collagen fibril formation [27]; d) serves as a cofactor of LOX needed for efficient ECM protein cross-linking [10]; e) stabilizes the skin ECM once formed, as increased crosslinking of collagen and elastin matrices occurs in a copper dose dependant manner [28, 29]; f) serves as a cofactor of superoxide dismutase, an antioxidant enzyme present in the skin, important for protection against free radicals [30, 31]; g) inhibits cellular oxidative effects such as membrane damage and lipid peroxidation [27]; and h) serves as a cofactor of tyrosinase, a melanin biosynthesis essential enzyme responsible for skin and hair pigmentation [32, 33].

In accordance with the above, Cu-GHK, a peptide found in human serum and cerebrospinal fluid that strongly binds copper, increases protein synthesis of collagen and elastin [34]. Cu-GHK also promotes proliferation and survival of epidermal basal stem cells, which are associated with increased expression of integrin [35]. Accordingly, this peptide has been found to improve wound healing. [34]. In addition, patients with an incapacity to metabolize copper (Menkes patients) have reduced LOX activity and collagen formation [36]. Copper is essential to wound healing, as it promotes angiogenesis and skin ECM formation and stabilization [37-41]. For a comprehensive review of the physiological processes in which copper is involved in the skin please see reference [17].

COPPER AS A BIOCIDE

Copper has also potent biocidal properties (reviewed in [42, 43]) and has been used as a biocide for centuries by many different civilizations [44, 45]. Both gram positive and gram negative bacteria, including antibiotic resistant bacteria as well as hard to kill bacterial spores, fungi and viruses, when exposed to high copper concentrations, are killed [42, 43]. In some cases, they are killed within minutes of exposure to copper or copper compounds (e.g. [46-48]). Accordingly, copper biocides have become indispensable, and many thousands of tons are used annually, all over the world, in agriculture [49], wood preservation [50], and in antifouling paints [51]. More recently, copper compounds are introduced into textiles and solid surfaces for odor and microbial control [52-55], including for reduction of microbial bioburden in medical institutions [43, 56-61].

Copper exerts its toxicity to microorganisms through several parallel mechanisms. These include direct contact killing and damage caused by exposure to released copper ions [42, 43, 62-64]. The damage is nonspecific and includes harm to the microorganisms' envelope phospholipids, microbial envelope or intracellular proteins, and nucleic acids [48, 63-69]. Many bacteria and fungi, excluding viruses, deal with excess copper via intra- and extracellular sequestration through the cell envelopes and membrane efflux pumps. Furthermore, tolerance and adaptation occur by upregulating necessary genes in the presence of copper and by the precipitation of copper by secreted metabolites (reviewed in [42]). However, microorganisms cannot deal with copper overload. Therefore, when exposed to high concentrations of copper they are irreversibly damaged and killed.

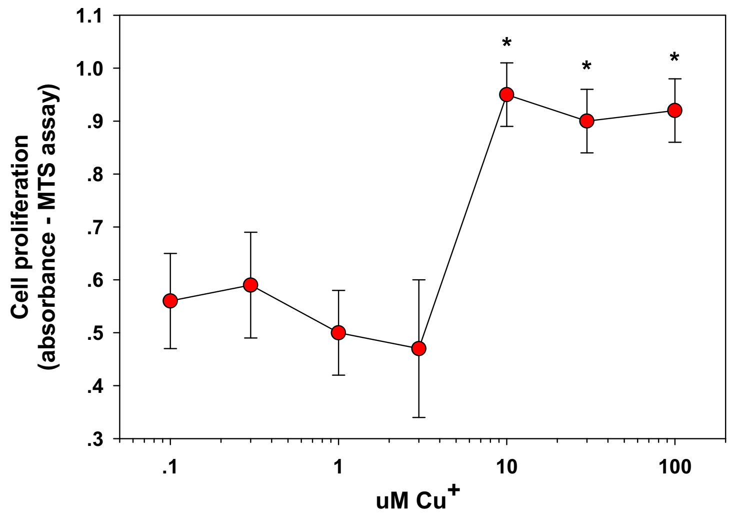


Fig. (1). Stimulation of Fibroblast Proliferation by Copper. Fibroblasts were exposed to 0–100 μM copper for 24 hr. The cells were examined for proliferation by MTS assay. Effects are represented as absorbance units; ∗ = $p < 0.05$, relative to control (0 Cu^{2+}). Error bars represent standard deviation, n = 4. Data taken from [26].

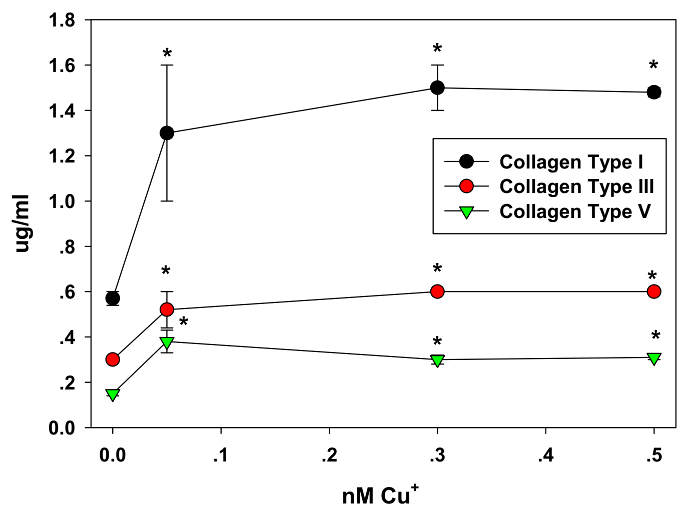


Fig. (2). Upregulation of Fibrillar Collagens Secretion from Fibroblast by copper. Fibroblasts were dosed with 0, 0.05, 0.3, or 0.5 nM copper for 24 hr and examined for type I, type III and type V collagen protein levels. ∗$p < 0.05$ relative to control; Error bars represent standard deviation, n = 4. Data taken from [27].

Copper can exist in several oxidation states, i.e. metallic copper (Cu^0), monovalent copper (Cuprous, Cu+) or divalent copper (cupric, Cu++) ions. Cu+ ions may exhibit more cytotoxic effects with respect to bacteria in comparison to Cu++ ions [70, 71] (Fig. **3A**). As shown in Figure 3B, cuprous ions exhibit greater cytotoxicity with respect to fungi. Importantly, redox cycling between Cu++ to Cu+ can catalyze the production of short lived hydroxyl radicals, which in turn may contribute to superior biocidal activity and thus the combined activity of both cuprous and cupric ions provide greater cytocidal activity than either oxidation state alone.

In the presence of air, under ambient conditions, the external metallic copper layer oxidizes to Cu_2O. Only at very high temperatures (>200°C), the Cu_2O layer further oxidizes to CuO [72]. Significantly higher amounts of copper ions are released by metallic copper followed by Cu_2O and CuO layers under different environmental conditions [73]. The Cu_2O layer is as effective in contact killing as is metallic copper [73].

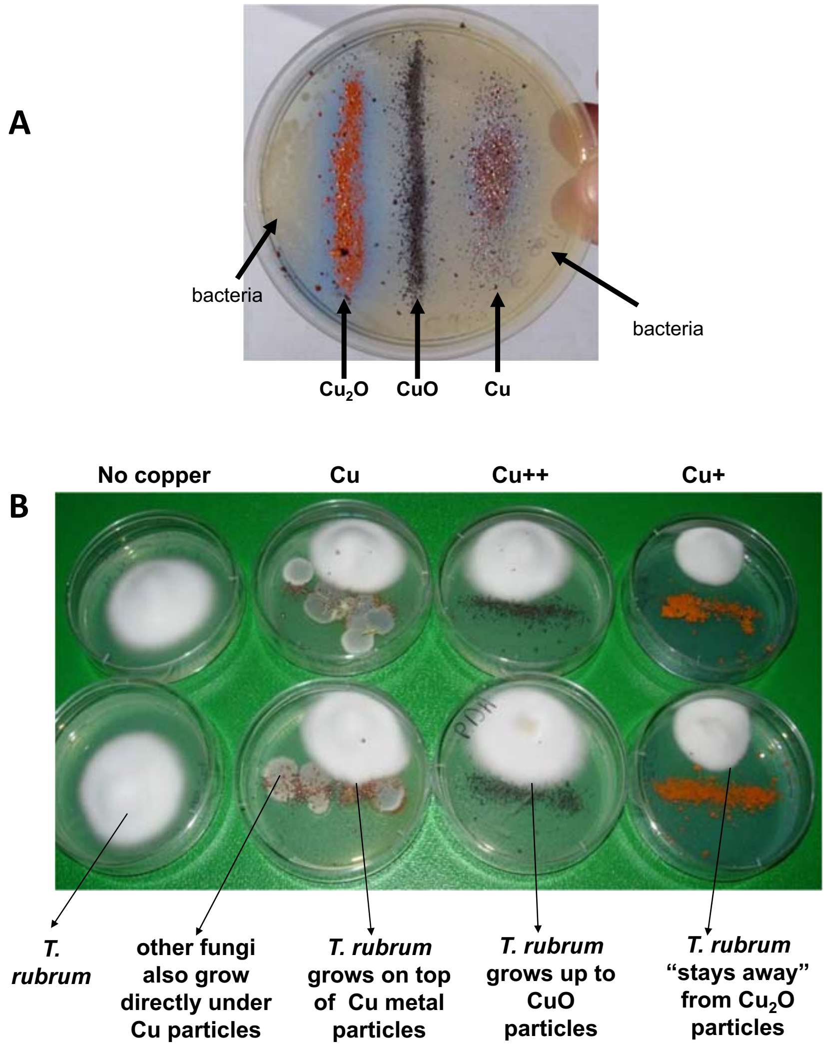


Fig. (3). Antibacterial and antifungal efficacy of Cu, Cu++ and Cu+ ions. A) *Staphylococcus aureus* bacteria were homogenously plated in agar plates, followed by the addition of Cu, CuO and Cu_2O particles (in strips). After 24 hours of culture at 37°C the bacteria formed colonies (beige areas). Notice no growth of bacteria especially around the strip of Cu_2O particles; **B**) Cu, CuO and Cu_2O particles (in strips) were added to agar plates. A *Trichophyton rubrum* colony was plated at the side of the plate. The pictures show the growth of the fungi after 4 days of culture at 37°C. Plates without copper served as a negative control. Notice the inhibition of growth of the fungi especially when exposed to the cuprous particles. Experiment was conducted in duplicates.

HISTORICAL USES OF COPPER FOR SKIN TREATMENT AND DISINFECTION

Interestingly, many different civilizations throughout human history, some in completely separate geographical locations, and mostly independent from one another, have discovered the capacity of copper to help improve/resolve skin and other tissue maladies (for a review see references [44] and [45]).

These include: the Sumerians (~4000–2300 B.C.), who used pulverized malachite (basic cupric carbonate) for generic medical purposes; the ancient Egyptian cultures (~3900–1550 B.C.), who also used pulverized malachite for the prevention and cure of eye infections, and later on (~1550 B.C. to 30 A.D.) additionally for healing postoperative wounds; the Babylonian-Assyrian culture (~1750–539 B.C.), who used different compounds containing copper, as well as copper bracelets, as generic therapeutic remedies; the ancient Indian culture (~2800–1000 B.C.), who used copper sulfide or copper sulfate for nonspecific medical purposes; the ancient Chinese culture (~3000 B.C. TO 1100 A.D.), who used copper (sulfate or sulfide) for topical treatment of skin and eye diseases and also for treatment of systemic infections by oral administration of copper; the Mayan, Aztec, and

Inca cultures (~600 B.C. TO 1500 A.D.), who used gauzes soaked in a copper sulfate solution to ''disinfect'' surgical wounds afflicted during widely practiced drilling of a hole in the skull as a physical, mental, or spiritual treatment, with estimated survival rates above 50%; the ancient Greek culture (1300–323 B.C.), who used copper preparations for purifying drinking water and for the treatment of various cutaneous and eye diseases, pulmonary, vaginal and gastrointestinal disorders, and copper bracelets for arthritis; the early Phoenicians (1550 BC to 300 B.C.) nailed copper strips to the bottom of their ships to inhibit fouling to increase speed and maneuverability; the ancient Roman culture (~600 B.C. TO 476 A.D.), who used various copper compounds for the treatment of eye and skin diseases, inflammation of the tonsils, hemorrhoids and generally wound treatment; and the Hindu store for centuries "holy water of the Ganges" in copper utensils to keep the water clean. Finally, copper sulphate is widely used by many inhabitants of the African continent for healing sores and skin diseases.

Today, copper and copper compounds are widely used in many medical related applications. Metallic copper is used already for many years in dental fillings [74] and in copper intrauterine devices for reversible contraception by millions worldwide [75, 76]. Copper compounds are widely used in anthroposophical medicine [77], via oral, subcutaneous injections, or topical applications, in order to stimulate the body to heal itself. Ointments containing copper, which liberate copper ions that are absorbed through the skin [77, 78], are used, for example, in the treatment of cramps, disturbances of renal function, peripheral, venous hypostatic circulatory disturbances, rheumatic disease and swelling associated with trauma [79]. There are also cosmetic facial creams that contain copper as their active ingredient (e.g. Neutrogena Visibly Firm® Face Lotion SPF 20).

SAFETY OF COPPER

As reviewed above, copper has been used throughout history by different civilizations, not only in utensils and adornments, but for many medicinal purposes. The topical or systemic forms of copper and copper compounds used included metallic copper, copper carbonate, copper silicate, copper oxide, copper sulfate, and copper chloride [44, 45], and in general were perceived as safe. As indicated above, copper is widely used today in dental amalgams and in IUDs, and their use is considered very safe [74-76, 80]. The use of copper, as the coating on the surface of hospital furniture, for the reduction of bioburden is gaining momentum following successful trials [59, 61]. Copper is a very weak sensitizer as compared with other metal compounds, and the risk of adverse reactions, due to dermal contact with copper, is exceptionally low [81, 82]. Application of ointment preparations, containing up to 20% metallic copper, were found not to cause any adverse reactions or toxicity [77].

INTRODUCTION OF COPPER OXIDE INTO POLYMERIC PRODUCTS

A novel durable platform technology has been industrialized, via which copper oxide particles are embedded (Fig. **4**) in polymeric carriers (e.g. polyester, polypropylene and nylon). From these copper oxide embedded polymers, an endless variety of textile, extruded and cast products can be made, endowing these products with potent biocidal properties [52, 61, 83, 84]. The current consumer and health-related products made using this technology include: a) hospital linens, nurse clothing, patient robes and pajamas, with the aim of reducing bioburden and nosocomial infections [52, 55, 83, 85]; b) antiviral and antibacterial copper-impregnated personal protective equipment (PPE), such as protective respiratory masks [55]; c) socks for the prevention and treatment of fungal foot infections (athlete's foot) [86] and for reducing the risk of skin pathologies, especially in diabetic patients [54]; d) pillowcases that reduce wrinkles [87, 88]; and e) wound dressings that reduce dressing and wound contamination, and enhance wound repair [38, 89].

The safety of using copper oxide containing products has been examined in several non-clinical studies and in more than 10 clinical trials. In all the studies, not even one adverse reaction was recorded. The products were found to be non-irritating, non-sensitizing, and safe to use, both when in contact with intact and broken skin [89-91].

Copper oxide particles are practicably non-soluble at aqueous solutions with a pH 5.5 and above. Textile products impregnated with copper oxide particles continue to be efficacious even after 50 repeated home or industrial washings [56, 86]. The copper oxide particles serve as a reservoir of copper ions. These ions are slowly liberated in the presence of humidity; for example as that present in the interior of the shoe or in the skin surface.

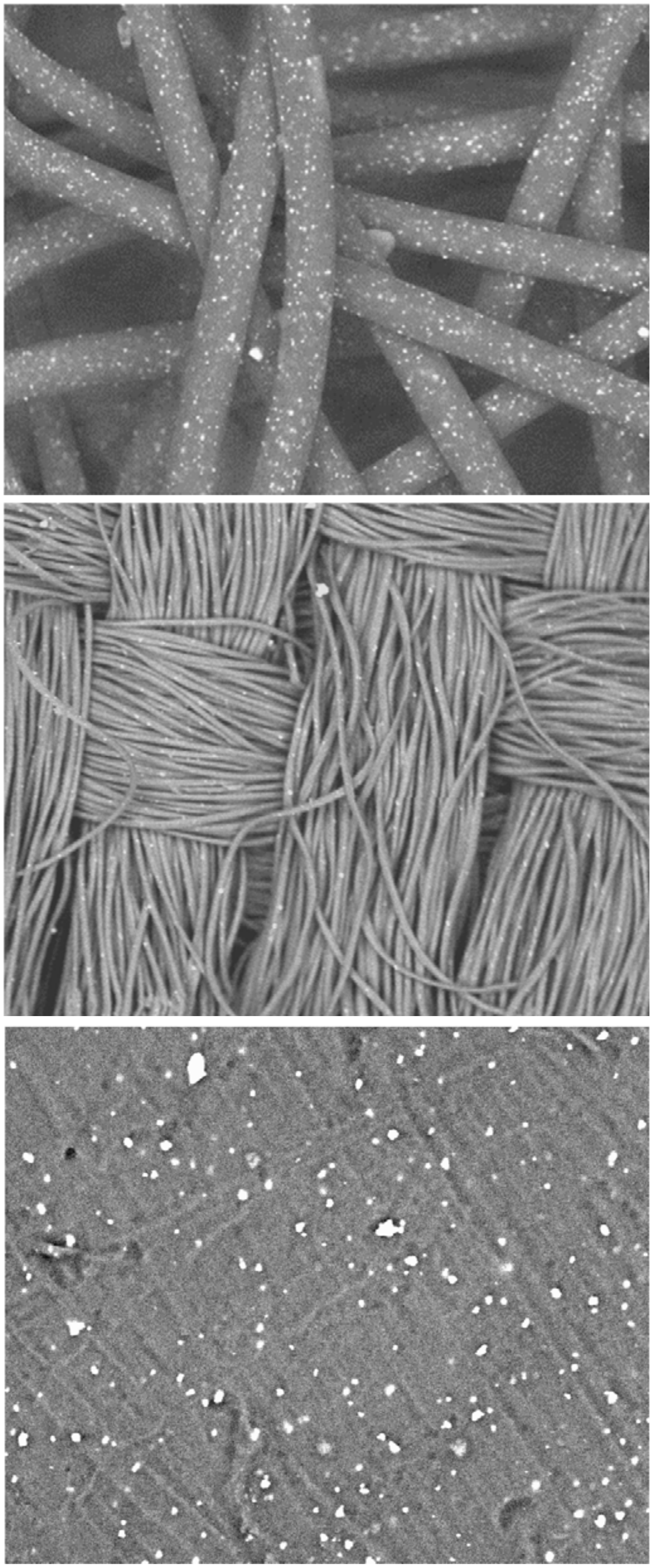


Fig. (4). Scanning electronic microscope pictures of non-woven, woven and plastic plate containing the copper oxide particles. The white dots are the copper oxide particles embedded in the polymeric matrices. For more detailed information please see references [52, 83].

The following section summarizes the studies conducted with various textile products containing copper oxide that have been found to exert positive effects on the skin.

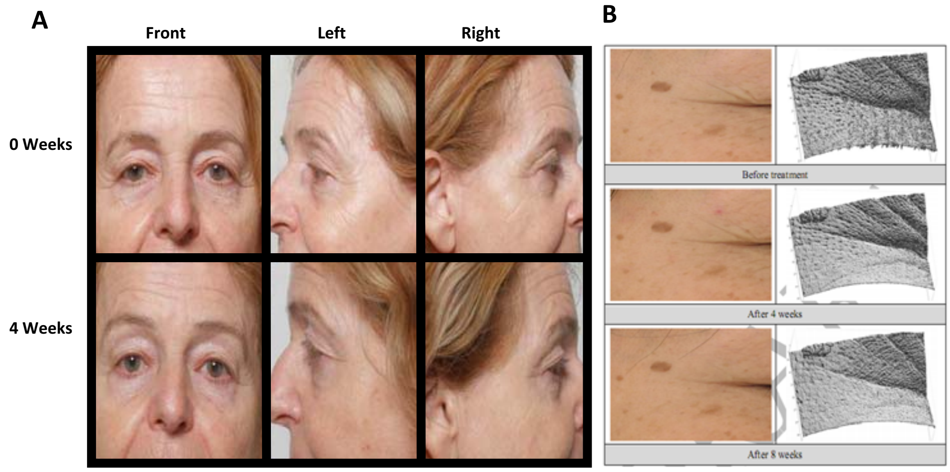
PILLOWCASES

The capacity, of pillowcases containing copper oxide, in reducing wrinkles and improving the well-being of the skin was determined in several double blind placebo controlled clinical trials. These trials were conducted by independent researchers and specialized labs. In all the trials, half of the trial participants used pillowcases containing copper oxide while the other half used similar control pillowcases not containing copper oxide. The participants used the pillowcases during sleep for 4 or 8 weeks. In two studies, both the test and control groups used also a cleanser and moisturizing cream. The skin surface topography and condition was analyzed at the commencement of the trials and after 2, 4 and 8 weeks (where relevant) by skin imaging equipment (e.g. 3D Image Analysis GFM Phaseshift Rapid in vivo Measurement of Skin (PRIMOS) system), photography, and by expert graders. In all studies, a statistically significant higher reduction of wrinkles and crow's feet/fine lines occurred in the group of individuals using the copper oxide containing pillowcases as compared to the control group [87, 88]. Some representative data and pictures are shown in (Fig. **5**).

SOCKS

The first trial included 56 subjects suffering from chronic or acute severe tinea pedis (athlete's foot infections). During the study, the participants used the socks for at least 8 hours a day. Within 8-12 days of use, there was a significant improvement or complete resolution of the podiatric conditions from which the patients suffered (erythema, fissuring, vesicular eruptions, scaling, burning, and/or itching) [86, 92] (Fig. **6**). The results included improvement in the skin condition of 21 diabetic patients. Diabetes hinders the capacity to deal with skin damage and infections. Also, in areas of the foot where no fungal infection was present, the skin looked healthier (unpublished observations).

The second study included 53 soldiers undergoing basic training. This population is prone to fungal infections and related skin problems. The soldiers used the socks daily for 3 weeks during



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Parameter	Group	Week	N	Mean[1]	SD	Decrement (%)	p-value
Rz (Average maximum height of the profile)	Copper	0	30	130.33	37.57	-	
		4	30	117.98	29.96	9.84▼	0.002*
	Placebo	0	31	123.06	27.5	-	
		4	31	122.34	26.9	0.59▼	0.798
Rp (Maximum profile peak height)	Copper	0	30	77.15	19.15	-	
		4	30	70.82	17.65	8.29▼	0.001*
	Placebo	0	31	74.25	13.18	-	
		4	31	77.23	14.83	4.01∆	0.082
Ra (average value of profile peaks)	Copper	0	30	23.49	5.85	-	
		4	30	21.33	4.47	9.19▼	<0.001*
	Placebo	0	31	22.71	4.7	-	
		4	31	22.38	4.74	1.46▼	0.493
Rmax (Maximum of all peak-to-valley values)	Copper	0	30	192.24	66.49	-	
		4	30	179.68	56.31	8.27▼	0.028*
	Placebo	0	31	176.51	46.26		
		4	31	181.64	53.58	5.42∆	0.132

Fig. (5). Representative pictures (**A**) and 3D images (**B**) data analysis showing reduction of fine lines in the group of individuals using the copper oxide containing pillowcases. Pictures and data taken from references [87, 88]. [1]Decrement of the mean value represents improvement of skin wrinkles (▼). *Statistically significant difference compare to before treatment ($p<0.05$).

Fig. (6). Representative pictures showing improvement in the foot skin well-being after using the copper oxide impregnated socks for 12 days. Pictures taken from reference [54].

which a clear improvement in their skin condition was recorded [93]. Similarly, in an additional trial with ~ 200 soldiers that used the socks continuously for one week under harsh field conditions, the number of soldiers reporting to the infirmary due to foot problems was significantly lower as compared to soldiers using regular socks without copper (unpublished data).

Based on antifungal in vitro testing, conducted by independent laboratories, using the highest laboratory standard (GLP), Cupron Inc. obtained a unique registration with the USA Environmental Protection Agency (EPA) to make public health claims, that their fibers/fabric kill 99.9% of the fungus that causes athlete's foot, including following repeated washings (EPA registration numbers 84542-10 and 84542-11).

The positive effect of the socks on the skin, is not only due to the biocidal properties of the socks, but as determined in a double blind, placebo controlled study that was conducted with healthy volunteers by CuTest, a UK company that conducts dermatological clinical trials, the copper oxide containing socks improved significantly the elasticity of the skin [94] (Fig. **7**).

The capacity to heal minor wounds and cuts is significantly reduced in diabetic individuals, often resulting in hard to treat chronic ulcers. We hypothesized that part of their reduced capacity to heal wounds is related to the low *in situ* copper levels present, due to the reduced blood circulation that mainly occurs in the extremities [37]. We further hypothesized that using copper oxide containing socks, by diabetic individuals, may significantly reduce their risk of developing skin disorders in their feet [54]. We hypothesized that the copper impregnated socks continuously release copper ions that are absorbed through the skin. This results in the upregulation of the production of extracellular skin proteins and the stabilization of the ECM, which improve the skin's well-being. Furthermore, the released copper ions reduce the risk of fungal and bacterial infection of minor wounds and cuts. In addition, especially in larger wounds, the copper ions stimulate angiogenesis and enhance wound healing. We thus suggested the use of copper impregnated socks as a preventive modality [54]. Indeed, such socks, designed specifically for diabetic patients, are sold in pharmacies (e.g. in Israel, by Perrigo).

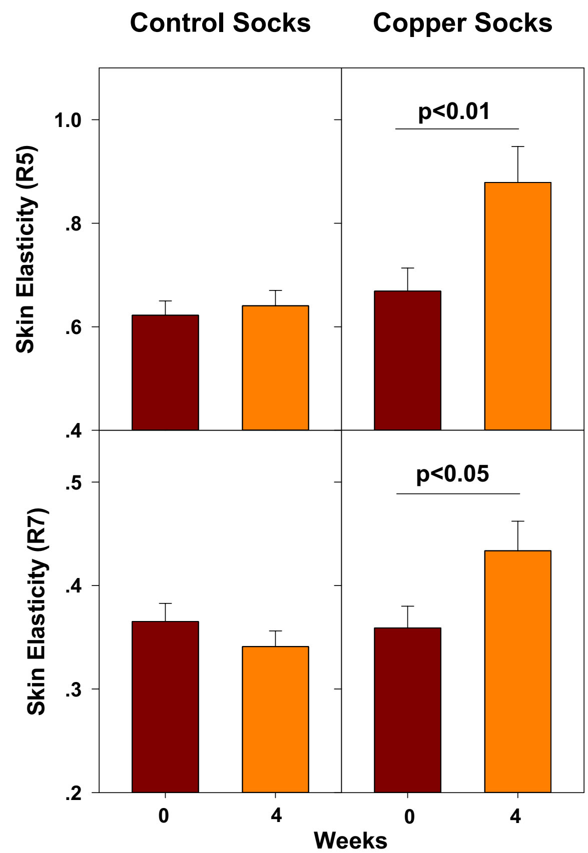

Fig. (7). Increased skin surface elasticity following the use of copper oxide containing socks. Using copper oxide containing socks for at least 10 h a day for 4 weeks resulted in 31.4% increased net skin elasticity (R5)($p = 0.004$) and 20.7% increased mean biological elasticity (R7) ($p=0.014$). Data is taken from [94].

WOUND DRESSINGS

We tested how the continuous application of copper oxide impregnated wound dressing could help heal full thickness skin wounds inflicted in genetically engineered diabetic mice. We found that the wounds healed statistically significantly faster ($p<0.01$) than wounds treated with control wound dressing without copper or with wound dressing containing silver [38]. Histological analysis revealed normal epidermal and dermal regeneration, granulation tissue formation, formation of numerous new blood vessels, generation of new hair follicles and sebaceous glands, chronic inflammatory infiltrate, and fibroplasia, with no precancerous changes or atypia of any kind (Fig. **8A**). mRNA expression analysis of biopsies taken from the wound beds at several days following wounding, revealed significant upregulation of key proteins involved in wound healing in the mice

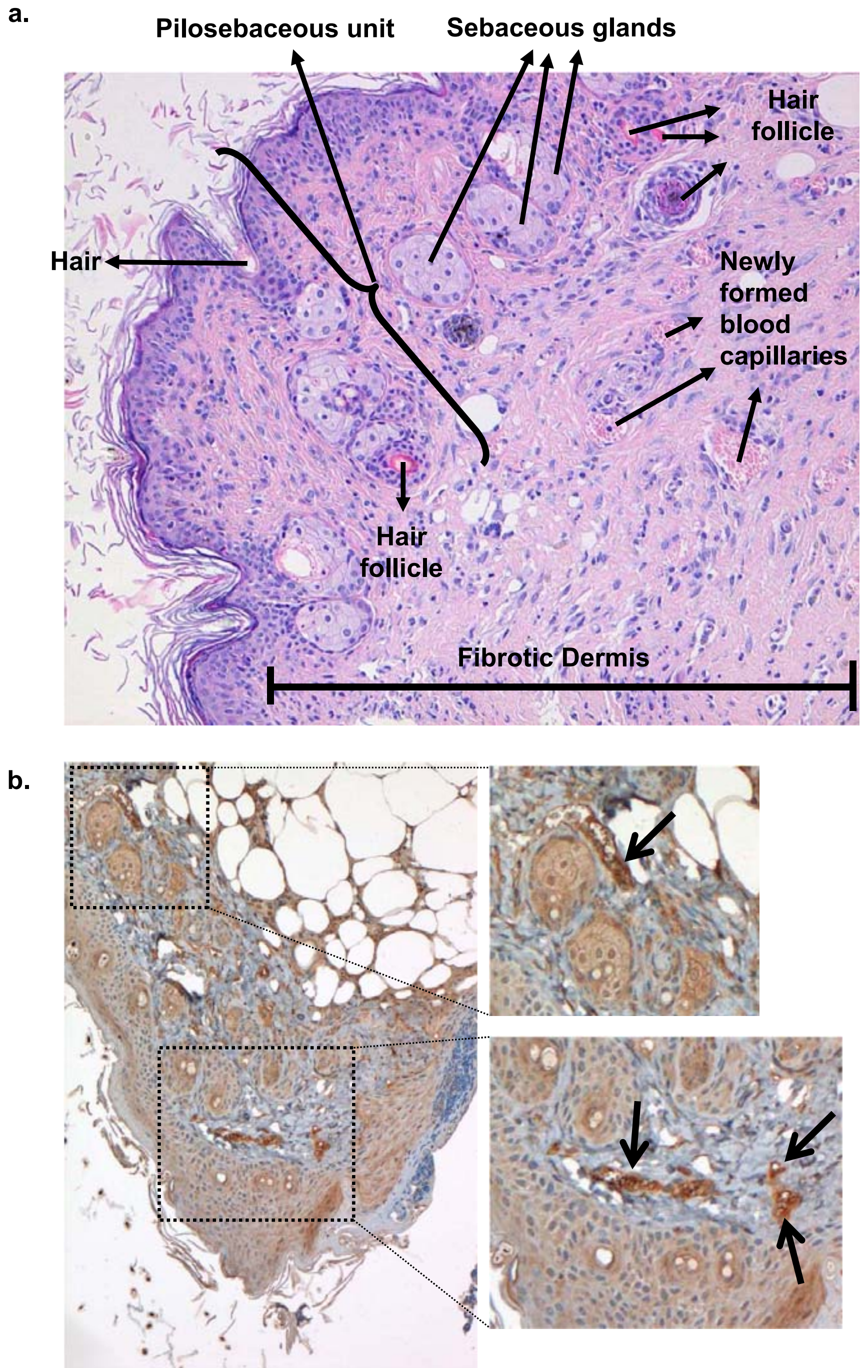

Fig. (8). Improved wound healing. Following wounding and treatment with copper oxide containing wound dressings there is **a**) normal skin regeneration (histological analysis after 17 days of wounding) and **b**) upregulation of angiogenic related factors, such as Vascular Endothelial Growth Factor (VEGF) – Immuno-histological analysis. Arrows show VEGF specific staining. For comparative data to control treated mice and other details, please see reference [38].

treated with the copper oxide wound dressings as compared to the control mice (Fig. **9**). For example, one day after wounding there was ~6 fold increase in integrins (proteins that bind extracellular matrix proteins and transduce signals crucial for cell processes in wound healing [95]) and 22 fold increase in placental growth factor (PLGF; an angiogenic factor known to be markedly reduced in diabetic wounds). Five days after wounding there was a 33, 141 and 112 fold increase in TGF-β1, TGF-β2 and TGF-β3, proteins that stimulate collagen and elastin fiber formation and deposition

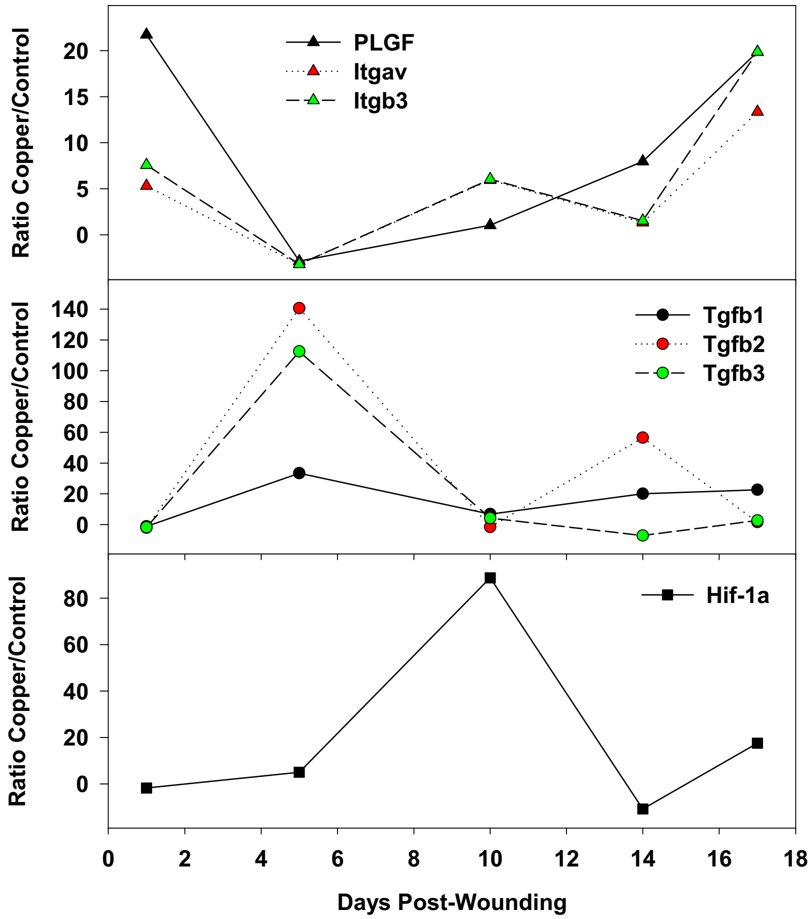

Fig. (9). Increased expression of angiogenic factors and other proteins involved in wound healing. Significant and differential upregulation of mRNA expression of key proteins involved in the wound healing process in the group of mice treated with the copper oxide wound dressings as compared to mice treated with control wound dressing without copper. Itgav - Integrin alpha V; and Itgb3 - Integrin beta 3. Data taken from reference [38].

[4, 6] and are involved in scar formation [7]. Hypoxia-inducible factor-1alpha (Hif-1α) was significantly upregulated by 5 and 88-fold at 5 and 10 days following wounding, respectively. Hif-1α, a regulatory protein involved in oxidative stress [96], activates many genes involved in wound angiogenesis and wound healing [97]. Redox between Cu_2O and CuO bring about the production of H_2O_2 and hydroxyl radicals [42], leading to the upregulation of Hif-1α. Accordingly, in the copper oxide treated mice, we found in-situ increased expression of pro-angiogenic factors, such as PLGF, Hif-1α and vascular endothelial cell growth factor (VEGF, Fig. **8b**) and consequently increased blood vessel formation ($p<0.05$), as compared to the control treated mice. For more detailed proposed molecular mechanisms of enhanced wound healing by the copper oxide containing wound dressings, please see reference [38].

Importantly, the wound dressings did not induce any adverse reactions in intact skin as determined in rabbits exposed to the dressing for 72 hours, following the ISO-10993 international standard. This included no erythema, eschar or edema formation [89]. Similarly, normal clinical pathology, normal histological patterns and no adverse effects were noted in open wounds in a pig. There were no significant differences in erythema, edema, and crust formation between the wounds treated with control or copper oxide containing wound dressings at 3 and 7 days post-wounding [89].

CONCLUSION

Copper is an essential mineral that plays a key role in many physiological and metabolic processes, including angiogenesis, skin generation and expression and stabilization of extracellular skin proteins. Copper has also potent wide spectrum biocidal properties. The combination of these two distinct properties of copper makes copper a very attractive active material for the improvement of skin well-being. It is thus, not surprising that copper and copper compounds have been used by many different civilizations for more than 2 millennia to treat skin diseases, as well as other maladies. In the last decade, a platform technology has been developed that introduces non-soluble copper oxide into polymeric yarns from which many textile and other consumer products are widely produced. Among these products, pillowcases, socks and wound dressing have been found to exert positive effects both on intact and broken skin. Pillowcases, containing copper oxide, have been demonstrated to reduce fine lines and wrinkles. Socks, containing copper oxide, have been found to increase skin elasticity and eliminate athlete's foot infections when used regularly. Wound dressings, containing copper oxide, enhance wound healing. Thus, the introduction of copper oxide into ordinary products transforms them into extraordinary products.

CONFLICT OF INTEREST

The author is the Chief Medical Scientist of Cupron Inc., who uses copper oxide as its active ingredient.

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