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Increase in skin surface elasticity in normal volunteer subjects following the use of copper oxide impregnated socks

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Background: Copper is an essential mineral involved in the formation and stabilisation of extracellular skin proteins. As copper can be absorbed through intact skin, we reasoned that using socks containing copper-impregnated fibres may have an effect on skin elasticity.
Methods: A double blind, placebo controlled study was conducted in which one group of healthy volunteers (n = 32) wore socks with fibres containing microscopic copper oxide particles and the other group wore identical socks without copper oxide (n = 28). The socks were worn for at least 10 h a day for 4 weeks. Skin elasticity measurements were taken from three separate test sites on the side of the ankle using a Cutometer at baseline and after 2 and 4 weeks of product use.
Results: There was an increase in the mean net skin elasticity (R5) of 6.4% (P = 0.6) and 31.4% (P = 0.004) after 2 and 4 weeks respectively, in the group of individuals that used the copper oxide containing socks, but no increase in the group of individuals that used the control socks. Similarly, there was an increase in the mean biological elasticity (R7 values) of 3% (P = 0.55) and 20.7% (0.014) after 2 and 4 weeks, respectively, only in the group of individuals that used the copper oxide containing socks. The differences between treatments (i.e. socks used) were statistically significant at 4 weeks (P = 0.0058 and P = 0.0327 for R5 and R7, respectively).
Conclusion: Using copper oxide containing socks results in an increase in skin elasticity of the feet.

Key words: copper oxide – elasticity – skin – socks – placebo controlled clinical study

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THE DERMAL matrix contains extracellular matrix (ECM) proteins such as collagen, elastin, and proteoglycans that confer strength and elasticity to the skin. The dermal fibroblasts are primarily responsible for the synthesis of the ECM proteins (1, 2). A primary regulator of the ECM proteins formation is TGF-β (3). With ageing, there is a reduced expression of TFG-β (3) and loss/atrophy of structural ECM proteins (4–6) that results in reduced skin elasticity.

Copper is an essential trace element involved in numerous human physiological and metabolic processes (7), including synthesis and stabilisation of ECM skin proteins critical for skin formation (8, 9) and wound repair (10, 11). The recommended daily allowance of copper is approximately 1 mg and copper salts, such as copper oxide, can be found in dietary supplements. Copper is a cofactor of lysyl oxidase, the enzyme that oxidises lysine and hydroxylysine residues in elastin and collagen allowing for the formation of cross-links in the ECM (9, 12). Alterations in lysyl oxidase alters TGF-β activity, causes abnormalities in ECM formation and in skin ageing (9, 12, 13). Serum isolated copper peptides (Cu-GHK) stimulate expression of collagen and elastin and reduce the clinical manifestation of skin ageing (8). The presence of copper oxide has been shown to promote formation of elastin (14–16) and collagen (16) and to upregulate TGF-β (11, 16).

Copper oxide particles can be permanently introduced into textile products endowing them two main features, broad-spectrum biocidal properties (17–19) and skin altering properties, such as upregulation of key extracellular skin proteins and reduction in wrinkles (16, 20, 21). Copper oxide containing products are extremely safe, as demonstrated in more than 10 clinical trials, without a single adverse reaction recorded (22, 23).

This study was aimed to examine the hypothesis that under conditions of normal wear, a textile containing copper oxide particles would have an effect on skin elasticity.

Methods

The study was a 4 week double blind, parallel group comparison of the effect of socks impregnated with copper oxide (TS) compared with socks without copper oxide (CS) in a panel of 60 normal individuals. The study was conducted at Cutest Systems Ltd, Cardiff, UK (http://www.cutest.co.uk) and approved by the Cardiff Independent Research Ethics Review Committee (CIRERC). All individuals had the nature of the study explained to them and were given written information concerning the study. They were informed that they were able to withdraw from the study at any stage without obligation and without being required to state a reason. All study participants gave their written, witnessed, informed consent before starting the study. All subjects were normal subjects whose medical history was updated and recorded prior to participation in the study. The study participants were randomly assigned to either treatment according to a pre prepared randomisation code, such that there were 32 subjects in test group A and 28 subjects in test group B. The studied products were supplied coded by the sponsor so that the double blind nature of the study could be adhered to and the code was not revealed until after study closure. The study participants were allocated several pairs of socks that could be washed and worn in rotation. Study participants were instructed to (i) wear the socks they received daily for at least a 10 h wear period; (ii) use a pair of clean socks each day; (iii) not to use any other socks; (iv) wash the socks after use using normal household washing procedures, but without using fabric conditioners; (v) to use only closed shoes during the period of sock wear; (vi) not to excessively bathe, swim, or use saunas and foot spas that would lead to excessive hydration of the skin; (vii) not to use other foot products or creams during the study; (viii) not to have pedicures or use of abrasive products on the feet during the study; (ix) continue washing their feet using their normal washing procedures; and (x) shower/bath and wash their feet a minimum of 2 h before their appointment time the morning of their clinic visits. Subjects wore their allocated test socks (TS) for a period of 4 weeks. Subject's compliance was assessed by the study nurse who questioned the subjects at their week 2 and week 4 visits.

Test items

Two socks were included in the study: TS containing polyester yarn impregnated with copper oxide particles (Fig. 1) or identical control socks (CS) that contained polyester yarn but without copper oxide particles in them. The socks were composed of 88% polyester, 11% nylon and 1% lycra, with the Cupron polyester® being present only in the foot area of the sock at a composition of 75% polyester and 25% nylon. The test materials were coded as Product A and Product B and neither the study participants nor the staff members involved in the study knew or could identify the TS.

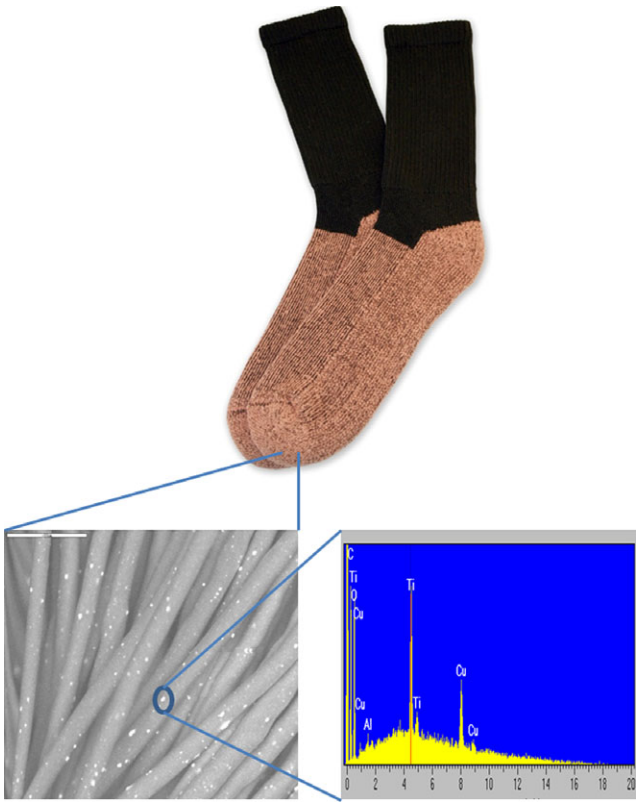

Fig. 1. A scanning electronic microscope image (lower left panel; taken with a Jeol JMS 840 scanning electron microscope) of the polyester yarn containing copper oxide particles found in the sole of the test sock (upper panel) is shown. The white dots are the copper oxide particles embedded in the polyester fibres. The chart (right lower panel) is an X-ray photoelectron spectra analysis (done with a Shimadzu XRD 6000, TN-5500 X-ray analysis system) of the encircled white dot, showing a peak at 8 KeV corresponding to copper.

Elasticity skin measurements

Measurements were carried out at baseline before product use and after 2 and 4 weeks of use in a room with controlled temperature (20–22°C) and relative humidity (40–50%). Study participants sat quietly in a controlled environment for 25 min (±5 min) before any measurements were taken. Subjects removed all footwear and socks at the beginning of the acclimatisation period.

The test site was defined as follows: The subject stood bare foot on a flat surface and a line drawn on the skin surface parallel to the flat surface at a distance of 2 cm from the flat surface. This line was the bottom edge of a rectangle 1.5 cm × 5 cm as shown in Fig. 2. The centre of the rectangle was immediately below the centre of the medial malleolus (ankle bone).

Skin elasticity measurements were taken from the test site using a Cutometer (www.courage-khazaka.de). The Cutometer is a suction chamber method for measuring the elasticity of the skin. The test site was at the side of the ankle in one foot only, the left or right foot being chosen at random. The 2 mm Cutometer probe was used by resting it on the skin and applying a negative pressure of 100 mbar for 5 s on/off cycles with three repetitions per cycle. Measurements were carried out at three separate test sites within the test area and were performed at week 0 (baseline) and repeated after 2 and 4 weeks of product use. The elevation of the skin into the chamber following the negative pressure applied is measured by a noncontact optical system built into the head of the device. A typical graph of a time strain curve where the vacuum is applied for 5 s is shown in Fig. 3. The Cutometer parameters R5 (Net elasticity) and R7 (Ratio of immediate retraction to total deformation, Biological elasticity) were recorded and analysed (see legend of Fig. 3 for more details).

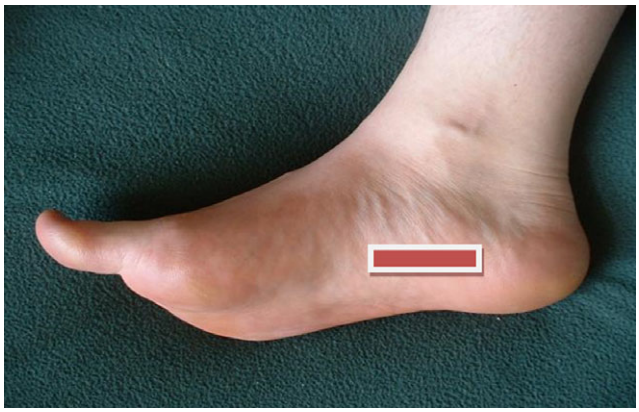

Fig. 2. Test site. Cutometer skin elasticity measurements were taken from either the left or right foot at within the delineated area.

Statistical analysis

Two-way Analysis of variance (ANOVA) was carried out on all data to determine any time and treatment effects. A secondary analysis was carried out using the Mann–Whiney *U*-test on baseline subtracted data; i.e. the increase or decrease in a given parameter was calculated according to the following equation:

$$\left(\frac{\text{Initial score at baseline} - \text{Score after use (2 or 4 weeks)}}{\text{Initial score at baseline}}\right) \times 100$$

A difference was considered statistically significant if $P \leq 0.05$.

Results

Participants characteristics

All 47 female and 13 male subjects recruited finished the trial. The age of the 60 subjects that finished the trial varied between 21 and

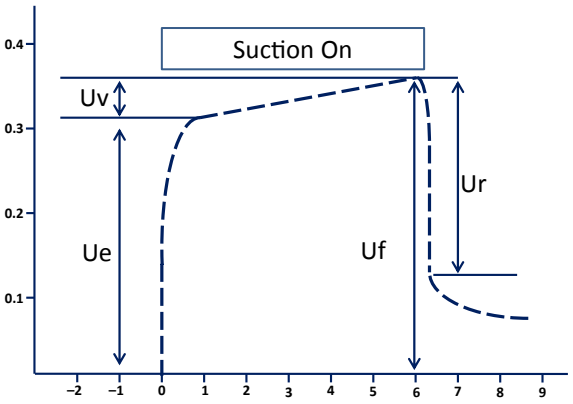

Fig. 3. Cutometer record of the skin surface elasticity. The resistance of the skin to being sucked upwards by the negative pressure (firmness or distensibility) and its ability to return to its original position (elasticity) are displayed as a series of these curves. Initially there is a rapid displacement of the skin upwards (immediate deformation, Ue) followed by a slower deformation (delayed deformation, Uv), which is related to the viscoelastic properties of skin. The parameter Uf is the total distension (Ue plus Uv). When the suction is released the skin undergoes an immediate retraction (Ur) followed by a gradual reduction to Ua (the final position after removal of the vacuum). Skin elasticity can be described by two main ratios: the net elasticity (R5 = Ur/Ue) and the biological elasticity (R7 = Ur/Uf).

65 years (mean 48 years). Following the random allocation to both groups, there were no statistical significant differences between both groups in terms of age and gender (Table 1).

Elasticity measurements

As can be seen in Fig. 4, at baseline (week 0) there were no significant differences between both group participants in terms of the R5 and R7 measurements. However, the control group using socks without copper demonstrated no significant changes in both elasticity measurements over time, while in the test group using the socks containing copper oxide particles, there was an increase in mean net skin elasticity (R5) of 6.4% ($P = 0.6$) and 31.4% ($P = 0.004$) at week 2 and 4 respectively, and in the mean biological elasticity (R7) of 3% ($P = 0.55$) and 20.7% (0.014) after 2 and 4 weeks respectively. The difference between the groups using the TS and the CS at 4 weeks was statistically significant for both elasticity parameters ($P = 0.0058$ and $P = 0.0327$ for R5 and R7, respectively).

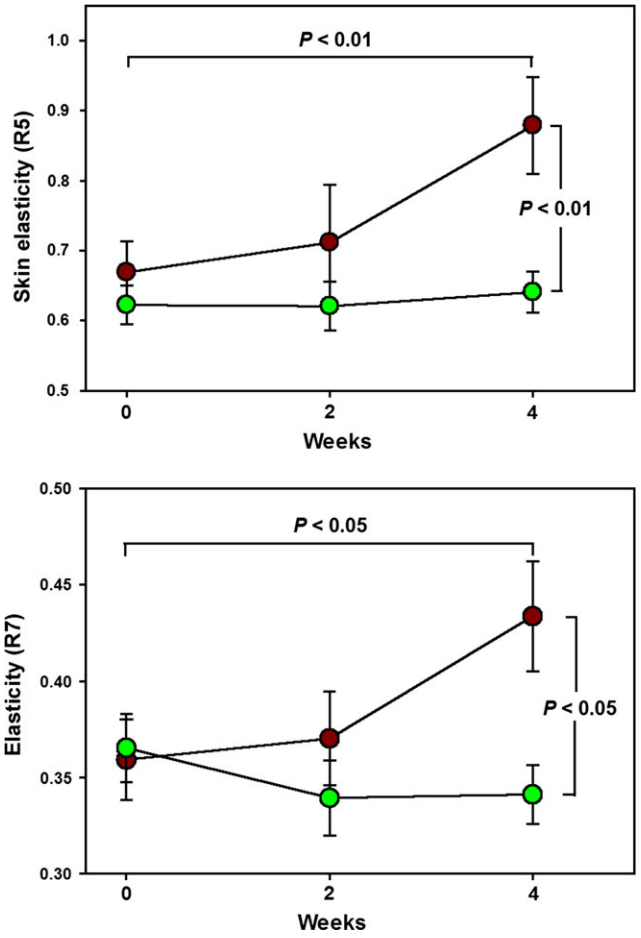

Fig. 4. Increase in skin elasticity in subjects using the copper oxide containing socks. The statistical significant differences in the R5 and R7 measurements between both groups at Week 4 are shown. Also, the statistical significant increase in the R5 and R7 parameters in the test group between week 0 (baseline) and at week 4 are shown.

Discussion

Copper is absorbed through skin (24, 25) and is widely considered as safe for human use (22). For example, copper intrauterine devices as a contraceptive are in widespread use worldwide. Copper-containing ointments 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 (26). Copper oxide containing wound dressings have also been shown to enhance wound closure in diabetic mice (11). Currently, different textile products, such as linens, towels, and socks impregnated with copper oxide particles, are widely sold in the consumer and industrial markets, due to the beneficial biocidal properties of copper. For instance, clinical manifestations of acute or chronic fungal infections are significantly improved or resolved when wearing copper oxide impregnated socks (27–31).

We hypothesised that the continuous contact of copper oxide impregnated textiles with human skin may lead to altered skin elasticity based on the following observations: (i) absorption of copper or copper oxide applied on skin has been demonstrated (24, 25); (ii) copper stimulates dermal fibroblasts proliferation (2); (iii) dermal fibroblasts are primary cells responsible for ECM maintenance; (iv) elastin, which provides firmness and resiliency/elasticity characteristics

TABLE 1. Participant demographics

		Age (years)				Gender			
Test group	Number	Range	Mean	Median	Mann–Whitney rank sum test	F (*n*)	M (*n*)	F/M ratio	Mann–Whitney rank sum test
Test group	32	23–61	46.8	48.5	$P = 0.46$	23	9	2.55	$P = 0.2$
Control group	28	21–65	48.7	50.0		24	4	6	

to the skin, is one of proteins that constitute the skin ECM; (v) copper oxide stimulates *in vitro* the formation of elastin by dermal fibroblasts (16); (vi) several proteins, such as lysyl oxidase, needed for efficient ECM protein cross-linking, including of elastin, require copper as a cofactor (12); (vii) human peptide Gly-(L-His)-(L-Lys) or GHK, when it interacts with copper ions, increases protein synthesis of elastin (8); and (viii) Menkes patients (patients with incapacity to metabolise copper) have reduced lysyl oxidase activity (32). In addition, several double blind clinical trials and other observations have demonstrated that continuous contact with the skin of copper oxide impregnated textiles has a positive effect on the skin (20, 21, 28, 30, 31). For instance, sleeping daily on copper oxide containing pillowcases for a period of 1 month resulted in a statistically significant reduction in the mean depth of wrinkles by approximately 9% (21).

Indeed, as demonstrated in this double blinded, placebo controlled study, 1 month of continuous use of copper oxide containing socks resulted in increased foot skin elasticity. Thus, the use of copper oxide containing socks not only is beneficial in regards to protecting the feet from infections (27–31), it has also a clear effect on the mechanical properties of the skin surface. It is generally accepted that skin elasticity decreases with age, i.e. the skin is less firm (4–6). The changes observed in this study are intriguing and suggest a firming of the skin.

No adverse reactions related to the test product and to the presence of copper oxide were recorded in the study. This is in accordance with the results obtained in all previous 10 clinical studies carried out with copper oxide containing textiles in which not even one adverse reaction was recorded (22, 23) and in accordance with the extremely low risk of adverse reactions due to dermal copper contact (33).

In conclusion, this study confirms our hypothesis that using copper oxide containing socks that liberate copper ions alters skin elasticity of the foot.

Funding source

The study was funded by Cupron Inc, Richmond, Virginia.

Conflict of interests

The study was funded by Cupron Inc, Richmond, Virginia, the manufacturers of the studied socks.

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