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## Copper chloride antiperspirant action

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Sir,

Copper compounds have been used for more than 4000 years for human cosmetic and topical "medical-dermatological" purposes.[1] Despite copper's ancient and premodern history of topical skin usage, the modern scientific utilization of topically applied copper compounds is limited. Regarding modern scientific antiperspirant preparations, these were originally based on, and remain based on, aluminum compounds,[2] not copper compounds. Since the commercialization of modern antiperspirants, many studies have been published on the efficacy of aluminum-based antiperspirant formulations, but there are no published papers of copper chloride in terms of antiperspirant efficacy. Therefore, we addressed the question: does copper chloride possess antiperspirant action?

The evaluation of the effect of copper chloride on axillary sweating was conducted as a controlled, clinical trial. The study conformed to the Declaration of Helsinki guidelines, and had IRB approval.

Sweating was quantitatively evaluated by measuring the size of sweat "circles" (wet areas) produced on the axillary area of cotton exercise shirts immediately after physical activity. The sweat "circles" were approximately oval in shape, and the total moist area was estimated from measuring the vertical and horizontal diameters of these "circles." The volunteers were pretrained and confirmed to properly perform the sweat circle measurements in a standardized manner and to wear a standardized 100% cotton shirt. Each subject measured

his own shirt sweat "circles" at the place and time of his/her site of normal exercise activity. Measurements were taken within 5 min of stopping exercise activity. Each volunteer was carefully followed/monitored during the study by means of clinic visits and/or telephone calls to confirm adherence to the protocol. The study was conducted as prospective, double-blinded, placebo-controlled trial. Pairs of bottles were filled with the control solution for one side and the experimental solution for the other. Right or left axilla was assigned randomly, in a double-blind fashion, using an appropriate computer-generated protocol.

Each volunteer was given two bottles: one contained the experimental solution and the other the control solution. The experimental solution contained 4% copper chloride dihydrate, 4% salicylic acid and 4% ethyl alcohol, dissolved in propylene glycol. The control solution contained 4% salicylic acid and 4% ethyl alcohol, dissolved in propylene glycol. (The combination of copper chloride with salicylic acid was chosen because salicylic acid appears to enhance antiperspirant activity of at least one metal salt, i.e., aluminum chloride.[3] There are no reported chemical incompatibilities between copper chloride and salicylic acid.) Colored FDandC food dyes were added to the control solution for color-balancing purposes.

The volunteers were instructed to apply approximately 0.75–1.5 cc to each armpit, twice daily. Times of application were immediately before bedtime and immediately on rising in the morning, at least 15 min before showering. They were instructed to shower each morning and to include washing the axillary area as part of the bathing routine.

Sweating measurements were to start 4 days, or later, after starting the regimen.

Volunteers were instructed to take no more than one set of measurements per day. Sweating measurements were to cease within 4 days of exhausting the supply of liquid in the bottle, i.e. approximately 2.5 weeks after starting the applications.

Six subjects were enrolled, and five completed the study. (One patient self-withdrew from the study before making sweat measurements.) All individual subjects performed from two to five sets of measurements during the study, depending on their personal physical activity schedules. For each subject, the ratios of sweat ring areas, i.e. the sweat "circle" area from the experimental side divided by control side, were computed for each individual day of data collection. These sets of sweat area ratio measurements were averaged for each subject.

For the five subjects, the average ratio of the moist area of the experimental side divided by the control side area was  $0.16 \pm 0.09$  (std. dev.) (n=5). Otherwise stated, this corresponds to a sweat area reduction of 84%  $\pm$  9% (std. dev.). The data for the decrease in sweating was statistically significant (P<0.001).

We conclude that copper chloride dihydrate is an antiperspirant, under our experimental conditions. However, aluminum chloride, not copper chloride, is, and has been, the gold standard for the treatment for sweating for more than 120 years.[2] The obvious question raised by this study is: Does copper offer any advantages over aluminum for the treatment of axillary hyperhidrosis? Future studies to address this question may wish to investigate the relative advantages (or disadvantages) of copper versus aluminum in four areas: (1) Does copper offer an absolute endpoint maximal efficacy advantage? That is, can it inhibit sweating – at some future optimal, maximal concentration/delivery system – better than

aluminum under its optimal delivery system? (2) Does copper offer a relative clinical advantage over aluminum in terms of the balance between efficacy and irritancy? (3) Is copper chloride more effective than aluminum chloride on the feet and/or palms? (4) Although aluminum, unlike nickel,[4] is a rare contact allergen, for those relatively few patients allergic to aluminum, perhaps the availability of an alternative metal ion, such as copper, would be helpful.

In terms of possible negative effects of topical copper application, we note that copper chloride can cause bleaching of clothing fabric colors due to the acidity of the formulation, and that copper compounds can cause irritation.[1] (Both these examples are also true with aluminum chloride). However, importantly, there are no reported long-term, negative health effects due to the application of copper chloride formulations on the skin.[1]

The present study utilized a direct quantitative measure of the real-life/patient-concerning aspect of axillary hyperhidrosis. Exercise-induced sweating, of course, is only one type of sweating, and future studies may wish to address the effect of copper chloride on psychologically induced sweating. Further, it would be interesting to use other available research techniques, such as the gravimetric or the silicone imprint method,[5] to measure the antiperspirant efficacy of copper chloride. Also, larger population studies using patient-to-patient design protocols (instead of the side-to-side axillae comparisons used here) would be interesting. Hopefully, these, and other scientific questions related to this ancient medicinal metal will be addressed in future studies.

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