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SILVER DIHYDROGEN CITRATE: PRELIMINARY ASSESSMENT OF A POTENTIAL NEW ANTI-INFECTIVE FOR DERMATOLOGY

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Silver dihydrogen citrate (SDC), a new chemical entity, is a complex of ionic silver and citrate. SDC has broad-spectrum antimicrobial activity and may have utility as an anti-inflammatory agent and facilitate wound healing. *In vitro* microbicidal studies were performed on a panel of bacteria, fungi, and viruses. SDC was also evaluated in animal studies for acute dermal toxicity, oral toxicity, dermal irritation and sensitization, and eye irritation.

SDC, at 0.3 mmol/L, was bactericidal for cultures of *Propionibacterium acnes*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Salmonella choleraesuis*, *Listeria monocytogenes*, *Escherichia coli*, and *Enterococcus faecium*. Kill times (>99.9%) ranged from 15 seconds to 2 minutes. At 0.3 mmol/L, SDC inactivated viral strains of HIV type 1, herpes simplex type 1, rhinovirus, influenza A, and poliovirus type 2 with higher than 99.9% kill times, ranging from 30 seconds to 10 minutes. For the dermatophyte, *Trichophyton mentagrophytes*, 0.3 mmol/L SDC yielded a 99.9% kill in 10 minutes.

SDC was nonirritating on rat skin at a concentration of 0.3 mmol/L and slightly irritating on rabbit skin at 24.0 mmol/L, according to the Draize dermal irritation scale. Rabbits exposed to 0.3 and 24.0 mmol/L SDC in eye irritation studies experienced nonirritating and mildly irritating Draize scale responses to the respective doses. SDC was shown not to be a contact-sensitizing agent in guinea pigs. The highest nonirritating concentration on guinea pig skin was 12.0 mmol/L. The acute oral and dermal LD₅₀ values in rats were higher than 36 mg SDC per kilogram of body weight. There were no deaths or abnormal necropsy findings, associated with either route of administration. In summary, initial animal studies indicate that SDC is relatively nontoxic, nonsensitizing, and nonirritating to the skin and eyes.

The observed antimicrobial efficacy and excellent safety profile of SDC, in conjunction with the known beneficial properties of ionic silver, suggest a myriad of potential uses in dermatology as well as other health care applications. Details of these preliminary studies will be discussed and potential applications reviewed.

Therapeutics Incorporated owns the license for the technology.

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THE "DRY SKIN CYCLE": INTRODUCING A NEW MODEL FOR THE INDUCTION AND PROPAGATION OF XEROSIS IN NORMAL SKIN

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Classically, dry skin has been described in two ways: (a) as a condition that is simply either present or absent or (b) as a linear progression of sequelae, resulting in the concomitant development of clinical tools (e.g., linear visual grading scales).

Although not refuting the validity of the aforementioned dry skin models, it is proposed that the induction and propagation of dry skin conditions may be best and most intuitively expressed as a cyclical model, dependent on stratum corneum (SC) integrity and particularly on barrier function and homeostasis, which are essential for controlling SC water flux and content and enzyme reactions within the SC.

A cyclical model implies a spiraling deterioration in outcome that, without intervention, would lead to a progressive worsening in model endpoints. Additionally, it is implicit that intervention at one point, or preferably multiple points, within this cycle is necessary to arrest the progression of this continuing downward spiral. This is indeed the case with most dry skin conditions and, moreover, reflects extremely well the consumer's perception of dry skin—the seeming repetitive cycle of product usage, reusage, disappointment with treatment outcome, and, often, a corresponding loss of compliance.

This poster, therefore, describes a new cyclical model for induction and propagation of dry skin, with identified phases including (1) initial induction via a range of initiators, including abrupt change in external environment; (2) surface dehydration, loss of "natural moisturizing factors," and barrier disruption; (3) cytokine release and hyperproliferation; (4) dysfunctional keratinocyte differentiation; (5) functionally impaired SC desquamation and maturation; and (6) SC scaling.

Because SC barrier function is pivotal to this model, there are important implications for treatment of xerotic skin conditions. In other words, to truly attenuate this self-perpetuating degenerative process, an intervention is required that targets the barrier itself, not just the symptoms of dry skin.

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THE EFFECT OF HERBAL EXTRACT ON HAIR GROWTH IN FEMALE ANDROGENETIC ALOPECIA

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In androgenetic alopecia, whether in men or in women, the action of 5 α -reductase is recognized as one of the most etiologically important. Recent studies have now demonstrated that even low levels of cytochrome P-450 aromatase, which convert C19 androgens into estrogens, in the scalp of women affected by androgenetic alopecia is a further requisite in the expression of this disease.

Therapy using antiandrogen substances aimed at 5 α -reductase, such as finasteride, is able to reduce the progression of androgenetic alopecia, diminishing the shrinking of hair follicles, the apoptosis of the dermal papilla.

Use of finasteride in young women is not recommended because of the risk of side effects involving the fetus. For this reason, the efficacy of an herb, *Niponivea bobeminesis*, has been assessed in female androgenetic alopecia, in the I and II stages of Ludwig's classification.

The effectiveness has been tested *in vitro* (with radioenzymatic assay) and compared with other antiandrogen 5 α -reductase substances already noted. Then a test was carried out in double-blind fashion versus placebo on 150 women affected with female androgenetic alopecia. In addition to specific photographic techniques (macrophotography, epiluminescence), histological assessment was carried out.

The aerial extract of *N bobeminesis* has demonstrated to be active *in vitro* (20% activity inferior to finasteride, 60% superior to saw palmetto) and *in vivo* has demonstrated good effectiveness in 78% of the treated cases. No side effects were noted.

The efficacy of *Niponivea*, the absence of side effects, and the lack of teratogenicity make this substance a useful therapeutic alternative in the treatment of female androgenetic alopecia.

Nothing to disclose.

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THERAPEUTIC EVALUATION OF A TOPICAL COMPOSITION WITH CAFFEINE IN THE TREATMENT OF GYNOID LIPODYSTROPHY WITH THE ORTHOGONAL POLARIZATION SPECTRAL METHOD

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Introduction: Gynoid lipodystrophy is a very common disease that affects women worldwide. It is supposed that topical caffeine is able to increase the blood flow rate to the dermis, thereby reducing some manifestations of gynoid lipodystrophy, such as edema and would be a suitable drug to improve the clinical manifestations of the disease.

Patients and methods: We evaluated 99 women, 18 to 40 years old, with grade II-III gynoid lipodystrophy. The body mass index was between 20 and 26 and any weight variation more than 1.5 kg was an exclusion criterion. Patients were treated in one thigh with a topical gel containing caffeine, for continuous use, for 30 days. Patients were evaluated with an orthogonal polarization spectral (OPS) imaging method, a new noninvasive technology for *in vivo* observation of dermal capillaries. We studied the following microcirculatory parameters: capillary density (per microliter), blood flow rate, and dermal papillary diameter. Other clinical parameters included thigh and hip circumferences at the beginning and end of the study.

Results: The main reduction of thigh circumferences was 0.5 cm ($P < .003$) when compared with the control thigh. Microcirculation evaluation detected increase in capillary density (no statistical significance), better response to the drug in patients with regular exercise habits ($P < .04$), and a worse response among those who were smokers ($P < .06$).

Discussion and conclusions: Topical caffeine applied for 30 days was very well tolerated and was also effective in the clinical management of gynoid lipodystrophy. The OPS imaging method was a secure and effective noninvasive method to evaluate microcirculation in fair-skinned patients. Microcirculatory parameters were well correlated with clinical parameters in the evaluation of the therapeutic response to topical caffeine among women with grade II-III gynoid lipodystrophy.

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