



LETTER TO THE EDITOR

Indications that topical L-carnitin-L-tartrate promotes human hair growth *in vivo*
KEYWORDS

L-Carnitine-L-tartrate; Anagen; Hair follicle; Trichoscan

L-Carnitine is essential for the intramitochondrial transport of long-chain fatty acids for β -oxidation [1–3]. Recently, we have shown that L-carnitine-L-tartrate (CT) is able to increase hair shaft elongation and prolong anagen by upregulation of proliferation and downregulation of apoptosis in organ-cultured human scalp hair follicles [4]. In order to test whether CT is also able to stimulate hair growth in human scalp hair follicles (HF) *in vivo*, we have performed a small, double-blind, randomised, placebo-controlled observational study of topical CT administration over 6 months twice a day. Penetration of CT into the skin, employing a liposomal hair tonic (Henkel, Düsseldorf, Germany) versus a conventional hair tonic was investigated, using the BUS (bovine udder model).

For the penetration study, we performed a one-time, open application of the formulas in udder skin ($1 \text{ g}/100 \text{ cm}^2$) [5]. Using 2% CT, the applied quantity corresponds to $200 \text{ }\mu\text{g}/\text{cm}^2$ of skin. The 2% CT was solved in a proprietary liposomal (water, allantoin, cetareth-25, perfume, ethanol 96%, Soy lecithin) or conventional hair tonic. The liposomal or conventional hair tonic alone served as vehicle control. The minimum separation between the application areas was 2 cm. Skin samples were taken after 1.0 and 5.0 h. The skin of the lateral udder wall with HFs was prepared in four layers parallel to the skin surface. Level I: epidermo–dermal:0–150 μm (incl. stratum corneum), level II: sebaceous glands:

400–600 μm , level III: hair bulbs: 800–1000 μm , level IV: subcutis: >1100 μm . The quantitative analysis of the CT was performed using high-pressure-liquid-chromatography/mass-spectroscopy (HPLC/MS).

For the prospective, double-blind, randomised, placebo-controlled observational study of topical CT administration, 60 healthy volunteers (age 21–60 years, 19 males, 32 females) with clinically diagnosed mild to moderate androgenetic alopecia (inclusion criteria were: androgenetic hair loss (i.e. anagen status <80%, telogen status >20%), and/or thin and diffuse hair (total amount of hairs/test area <270 h) received either CT 2% solution ($n = 25$) or a placebo (the vehicle only: water, allantoin, Cetareth-25, perfume, ethanol 96%) ($n = 26$) locally twice a day for 6 months. Before treatment as well as after 4, 12 and 24 weeks of treatment, the anagen/telogen ratio and the number of terminal hair shafts were assessed by phototrichogram, using the trichoscan technique and by surface evaluation of living skin (SELS) technique [6,7]. For the phototrichogram, a defined reference area of the scalp was shaved and photographed [8]. After 3 days, the same area was measured again and the percentage of hairs was calculated. For a specific area of 1 cm^2 scalp hairs are shortened. After 3 days these hairs get coloured and photodocumented. The trichoscan video software assumes that anagen HFs grow 0.3 mm/day, while telogen hairs do not grow at all. Using this trichoscan software, the total number of terminal hair shafts/ 0.65 cm^2 and the anagen/telogen ratio is calculated. The sequential photodocumentation before and after therapy allows comparison of hair growth and density with statistical calculation after external treatment [6,7]. Statistical significance was calculated using the Wilcoxon test. Clinical checks were performed at all examination time points.

Five hours after the application of the liposomal hair tonic in the BUS model, the quantity of CT at the level of the hair papillae was approximately eight times as high as that in the untreated skin, as measured HPLC/MS of appropriate dermatome

Abbreviations: HFs, hair follicles; CT, carnitine tartrate; BUS, bovine udder skin.

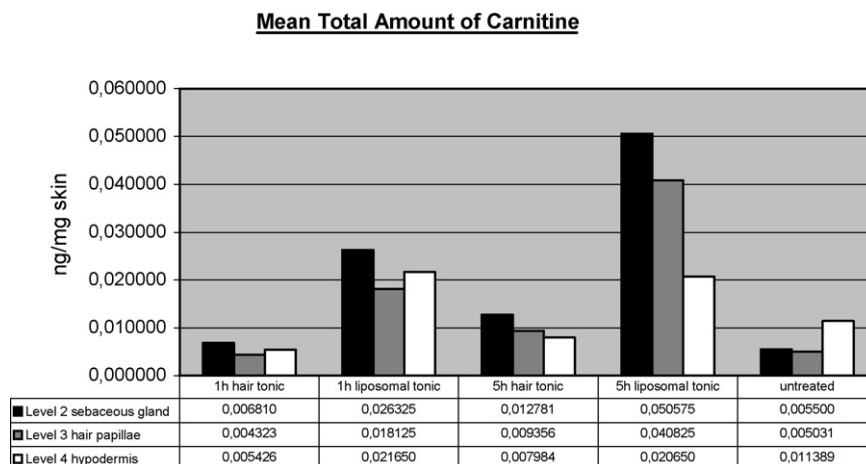


Fig. 1 Penetration of locally applied CT into the skin is increased when solved in a liposomal hair tonic compared to a conventional hair tonic. CT penetration into the skin was tested using the BUS (bovine udder skin model). CT was labeled, and the concentration of CT in the different levels of sectioned skin was measured by HPLC/MS.

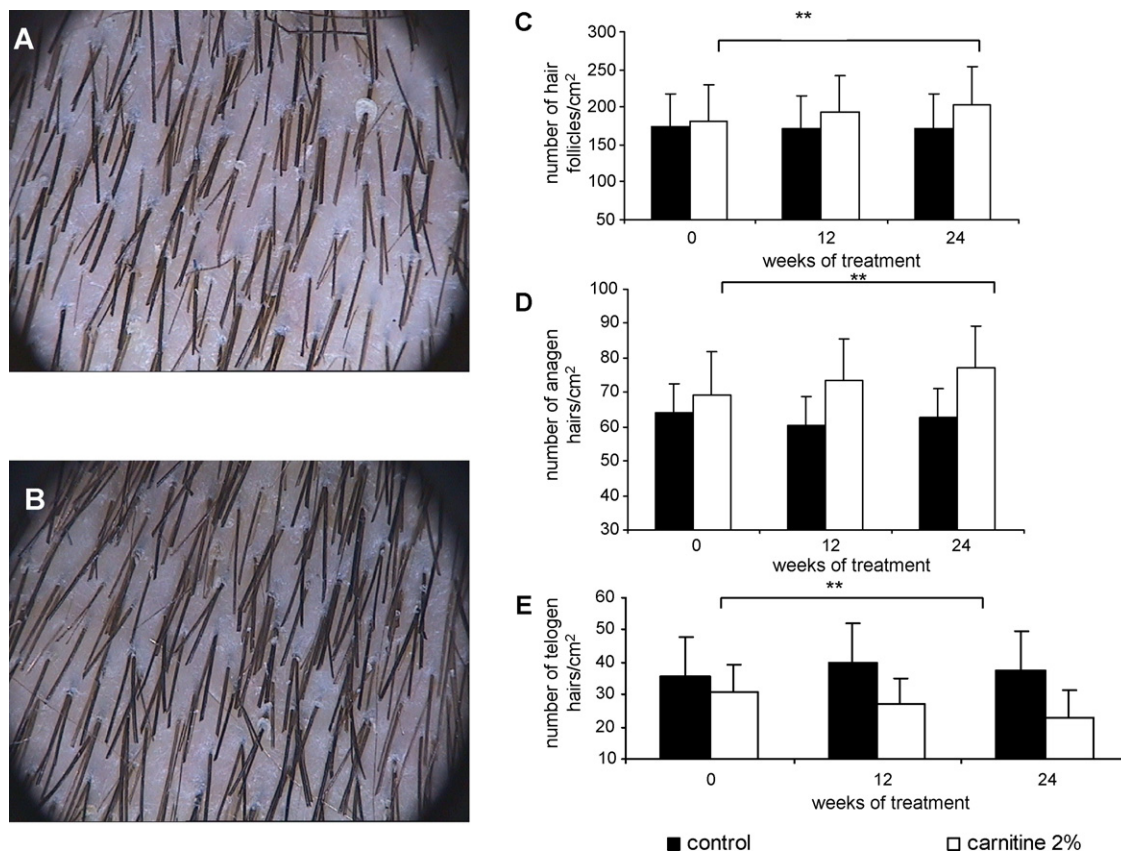


Fig. 2 Trichoscan assessment. (A) Before treatment, (B) after 6 months treatment of scalp HF_s *in vivo* with CT 2% solution. Note significantly more scalp HF_s in the test group after 6 months. (C) The total number of HF_s/2 cm², counted by using the trichoscan method increased significantly after treatment with carnitine 2% solution for 24 weeks compared to the placebo control group (vehicle only). (D) Number of anagen VI HF_s increased, while (E) number of telogen HF_s decreased in the CT treated group after 12 and 24 weeks. ***p* = 0.05.

transections (Fig. 1). With the conventional hair tonic, an increase in the CT concentration at the level of the hair bulb was also observed; however, it was substantially lower (0.013 ng/mg skin) than when CT had been encapsulated in the liposomal hair tonic (0.05 ng/mg skin). This demonstrates that the employed liposomal preparation is very effective to promote skin penetration of CT and its delivery to the hair bulb level.

After 6 months, the observational study had been successfully completed by 51/60 volunteers, 26 in the CT 2% treated group, and 25 in the vehicle control group. Nine volunteers dropped out after 3 months due to noncompliance or personal reasons (e.g. change of residence to a distant town). Only two volunteers in the test group reported mild, one volunteer reported strong itching (occurrence of reddish papules or a light burning sensation; two test subjects in the CT 2%-treated group reported increased dandruff).

Evaluation of hair growth, using the trichoscan technique, showed a significant increase (13.5%, $p < 0.05$) in the total number of terminal scalp hair shafts, comparing volunteers before (170 hairs/cm²) and after 24 weeks of treatment with CT 2% solution (197 hairs/cm²) (Fig. 2A–C). The number of anagen HFs increased (75%) and the number of telogen HFs was significantly downregulated (25%) in volunteers receiving topical CT 2% solution twice daily (Fig. 2A, B, D, E) compared to the placebo group (38% telogen HF, 62% anagen HF) after 24 weeks. Thus, local treatment with CT 2% solution showed a significant hair growth-stimulating effect, while vehicle-treated volunteers did not show any significant changes in the number of terminal hairs or in the anagen/telogen ratio during the study. The use of the skin surface evaluation of living skin (SELS) technique [8] confirmed that the percentage of a specific measured reference area of scalp skin covered with hair was significantly higher in the CT-treated group compared to the placebo group (mean: CT, 8.1; placebo, 4.7; S.E.M.: TCT, 3.6; placebo, 3.1; $p < 0.05$).

In this prospective, double-blind, randomised, placebo-controlled observational study, topical treatment of volunteers with moderate-level androgenetic alopecia with a 2% CT solution increased the total number of terminal scalp hairs/cm² and the anagen/telogen ratio after 6 months of treatment. This small pilot study, evidently, requires repetition with a much larger n of volunteers and a prolonged observational period. However, the currently available data confirm our *in vitro* data with organ-cultured human scalp hair follicles [4], and further support the concept that CT is able to promote

human hair growth at a favourable ratio of benefits to risks/undesired effects.

Conflict of interest statement

This study was commissioned by Henkel AG, Düsseldorf.

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