Reviewer's report

Title: Topically applied vitamin C increases the density of dermal papillae in aged human skin

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Reviewer: salvador gonzalez

Reviewer's report:

General
In this manuscript the authors use confocal laser scanning microscopy to show that the papillary index decreases with age and that topical vitamin C can correct this regression.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

There are several points which concern me, some due to presentation and others with data acquisition and interpretation.

In the otherwise lengthy Introduction, the authors fail to use standard guidelines to address the aim of their study. They state at the end of the Introduction that Vit C partially restores a “functioning dermo-epidermal interface” but this claim is not present in the Abstract, substantiated in the Results nor addressed in the Discussion. Do the authors equate increased papillary index with undulating dermo-epidermal interface?

The authors use unconventional parameters to evaluate the number of dermal papillae per surface unit, which is not even used in conventional histology studies. The authors describe this parameter to be tightly linked to the number of capillary loops and do not contemplate other possibilities, such as epidermal hyperplasia with increased basal layer for example.

The authors also assess granular cells diameter of the most apical plane. However the granular layer is not so uniform. In the same image you can have a digital section of different cell planes. This parameter is very unreliable.

In the Materials and Methods section, the authors do not specify the number of female volunteers for their first study. Why was the dose of 3% Vit C used? Is there a dose-response?

In the Results section, in the second study, it would be useful to show the results as mean +/- standard deviation and the p value. There is also what appears to be a significant difference between baseline median values for the treated and untreated areas (25.3 vs 22.7), which should be considered.

The authors discuss angiogenesis as the mechanism responsible for the therapeutic effect of Vit C but they have no data to back this and it remains speculative. Angiogenesis is also broached in the Abstract, and with no data to support it, should be omitted. Have the authors explored the literature on the particular effects of vitamin C on the papillary dermis? For example, ascorbic acid has been shown to decrease papillary dermal thickness in stretch marks, which is contrary to the effect described by the authors in normal aged skin.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Discretionary Revisions (which the author can choose to ignore)

**What next?:** Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** No

**Declaration of competing interests:**

None