

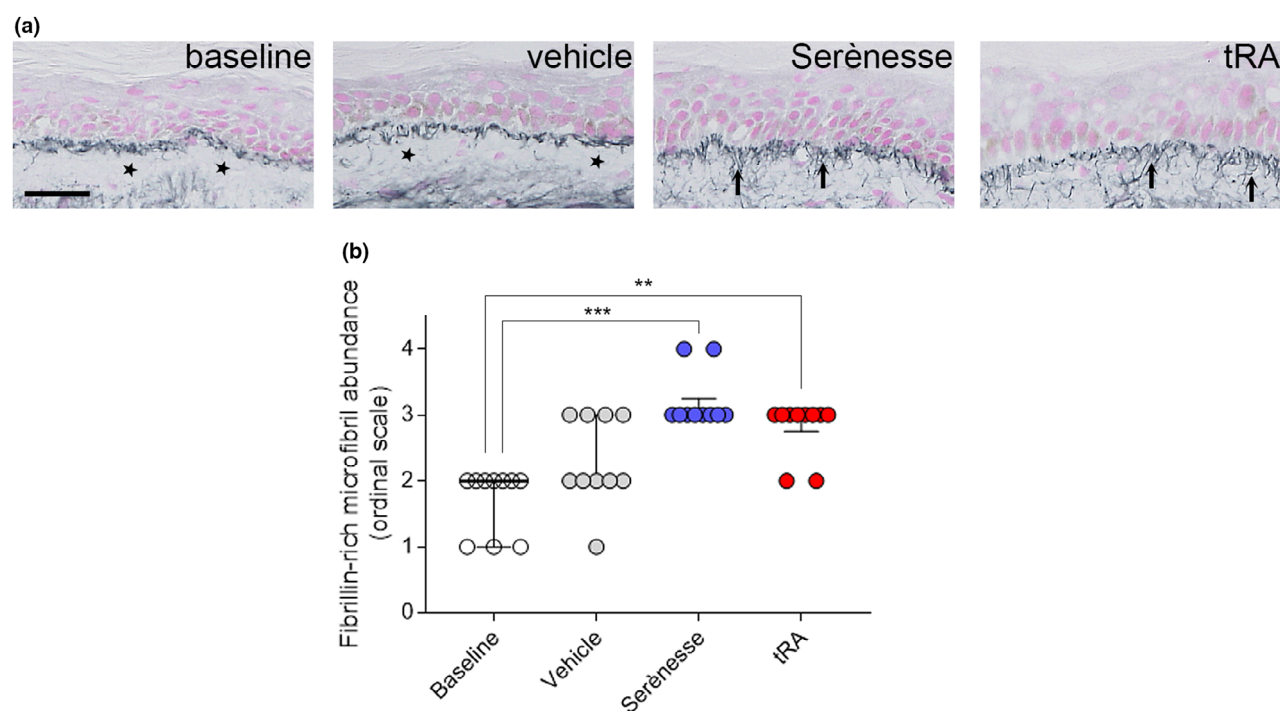
## LETTER TO THE EDITOR

## Restoration of collagen and elastic fibre networks following treatment of photoaged skin with Serènesse, a novel over-the-counter anti-ageing product

Chronic sun exposure induces profound changes to the dermal extracellular matrix (ECM) resulting in the loss of fibrillin-rich microfibrils (FRM)<sup>1</sup> and fibrillar collagen.<sup>2</sup> The gold standard topical treatment for photoaged skin is all-*trans* retinoic acid (tRA).<sup>3</sup> The 'Manchester Patch-Test' (MPT) assay was first developed in 2001 as a short-term, exaggerated-use patch-test protocol to test the potential efficacy of topical anti-ageing products.<sup>4</sup> Since its inception, the assay has provided evidence that some over-the-counter cosmetic 'anti-ageing' products, as well as topical retinoids, can induce FRM deposition at the dermal–

epidermal junction (DEJ) of photoaged skin.<sup>4–6</sup> We used the MPT assay to assess the effect of a novel, over-the-counter topical anti-ageing product (Serènesse, CG Skincare Ltd, Manchester, UK) on the dermal collagen and elastic fibre network in photoaged skin. The study was performed on 10 healthy, photoaged volunteers (mean age  $73.1 \pm 3.9$  years; 3 M; 7F) and approved by The University of Manchester Research Ethics Committee; all subjects gave written informed consent. Test substances (vehicle and Serènesse) were applied, under occlusion, to photoaged extensor forearm for 12 days; tRA (0.025%; Retin-A® cream; Janssen-Cilag Ltd, Beerse, Belgium; 20  $\mu$ L) was used as a positive control and applied for 4 days. At the end of the test period, 3-mm punch, skin biopsies were obtained under 1% lignocaine local anaesthesia from each test site and analysed histologically.

Unlike treatment with tRA, occluded application of vehicle and Serènesse for 12 days did not induce significant acanthosis of the epidermis. Immunohistochemical assessment of

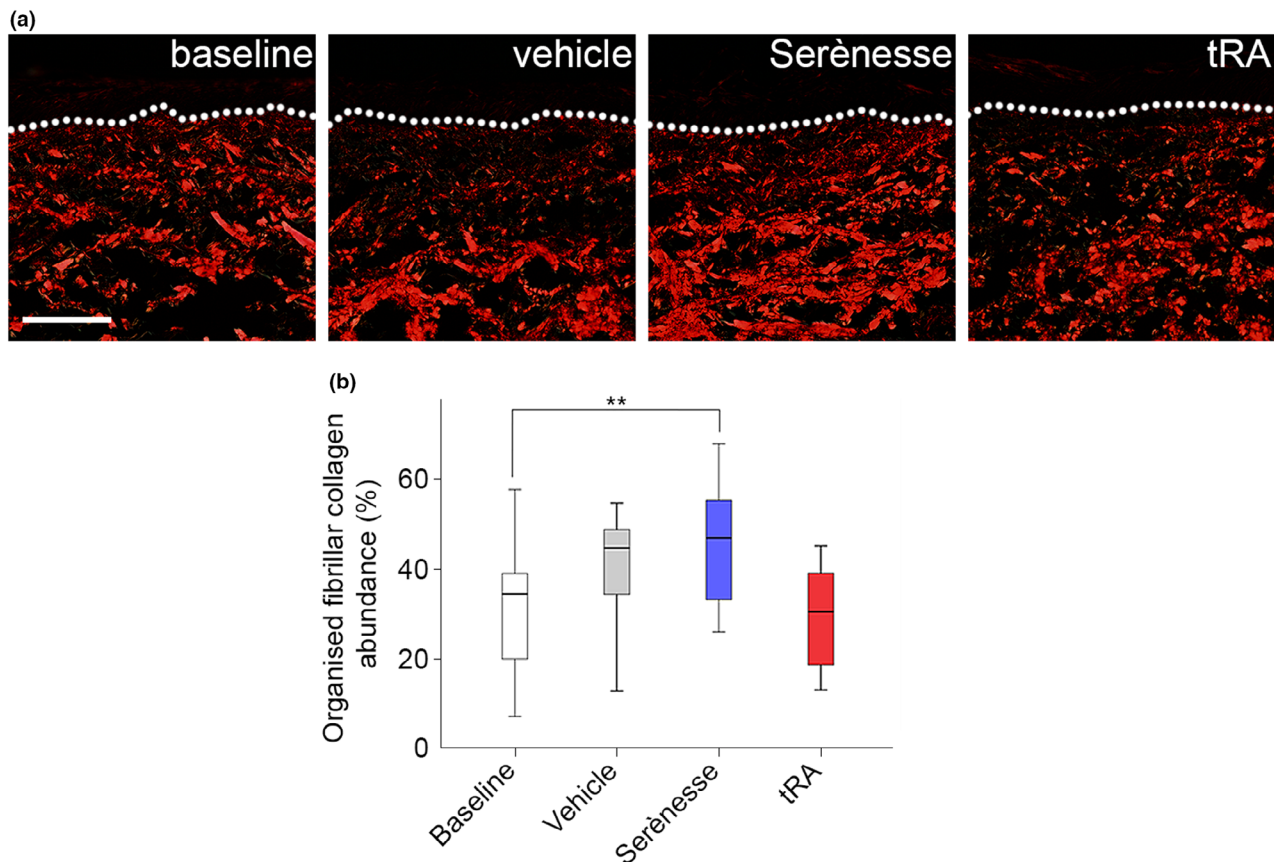


**Figure 1** Serènesse induced deposition of fibrillin-rich microfibrils following 12-day application using the Manchester Patch-Test assay. (a) The effects of vehicle, Serènesse and all-*trans* retinoic acid (tRA) application under patch-test conditions were assessed immunohistochemically. Untreated baseline and vehicle skin display a pronounced Grenz zone within the papillary dermis (stars). (b) Application of Serènesse and tRA resulted in a significant deposition of fibrillin-rich microfibrils (FRMs; arrows) at the DEJ and a diminished Grenz zone, as compared with untreated baseline. \*\* $P < 0.01$ ; \*\*\* $P < 0.001$ ; scale bar = 50  $\mu$ m.

photoaged baseline skin identified the characteristic Grenz zone adjacent to the DEJ<sup>7</sup>; application of vehicle produced no significant effect on FRM deposition and the Grenz zone persisted. In contrast, application of both Serénisse and tRA resulted in significant deposition of FRMs at the DEJ and a marked diminishment of the Grenz zone ( $P < 0.001$  and  $P < 0.01$  respectively; Fig. 1). Reductions in fibrillar collagens are a further histological consequence of chronic photodamage<sup>8</sup>; however, neither tRA nor vehicle had affected the abundance of mature fibrillar collagen. In contrast, application of Serénisse significantly increased the amount of regularly ordered mature collagen bundles within the papillary dermis ( $P < 0.01$ ; Fig. 2); however, this was not associated with *de novo* deposition of pro-collagen (data not shown). Similarly, a failure to identify changes in matrix metalloproteinase activity by *in situ* zymography suggests that

remodelling of the pre-existing collagen does not occur in response to application of either Serénisse or tRA (data not shown).

Here, we demonstrate that application of a novel, over-the-counter ‘anti-ageing’ product – Serénisse – restores the structural architecture of photoaged dermal ECM. This finding is particularly important as remodelling and degradation of these key matrix components, particularly in ageing, cause profound structural and functional decline to overall skin health.<sup>9</sup> Consumers purchasing cosmetic skincare products – particularly those purporting ‘anti-ageing’ properties – are presented with a broad choice but only limited data regarding their efficacy. However, the results from this study are indicative of structural change in the skin following the use of a non-prescription, anti-ageing product. Furthermore, the difference in efficacy between



**Figure 2** Application of Serénisse significantly increased organized mature fibrillar collagen abundance in the Manchester Patch-Test assay. (a) Picrosirius red staining identifies the abundance and organization of mature fibrillar collagens when visualized under cross-polarized light. The slide background and epidermis appears black, and the collagen bundles are predominantly red with some yellow and green fibres interspersed. The mature collagen bundles display multiple orientations within the dermis for all samples. (b) Application of vehicle and all-*trans* retinoic acid (tRA) produced no significant effect on organized mature fibrillar collagen abundance. However, application of Serénisse resulted in significantly increased abundance of organized fibrillar collagen compared with untreated baseline control. \*\* $P < 0.01$ ; scale bar = 100  $\mu$ m.

the vehicle and Serénisse demonstrates that a correctly formulated skincare product can deliver clinically relevant repair of photoaged dermis, over and above that delivered by vehicle base alone. Importantly, Serénisse is better tolerated than tRA as it did not cause irritation, i.e. flaking, peeling or oedema following occlusion for 12 days – a common side effect observed for tRA-treated skin. Similarly, Serénisse did not induce histological epidermal thickening and it ‘out-performed’ tRA – with superior immunohistological data in the MPT assay. Taken together, these results indicate that Serénisse remodels photoaged dermis to an extent, whereby it recapitulates the structure found in more youthful, non-photodamaged skin. Previous experience with the MPT assay suggests potential for this non-pharmaceutical product as a plausible first-line therapeutic for signs of skin ageing particularly those ascribed to photoageing.

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### Conflict of interest

AKL has received research funding from Walgreens Boots Alliance and is a committee member of the BSID. JCMc has nothing to disclose. LFC and PH have received research funding from Walgreens Boots Alliance. TWG has received research funding from Walgreens Boots Alliance and is a Director and holder of stock options of CG Skincare Ltd. CEMG has received research funding and consulting fees from Walgreens Boots Alliance and is a Director and holder of stock options of CG Skincare Ltd. REBW has received research funding from CG Skincare Ltd, Walgreens Boots Alliance and a BBSRC-IPA with industrial part-

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