

## Identification of titanium dioxide on the hair shaft of patients with and without frontal fibrosing alopecia: a pilot study of 20 patients

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DEAR EDITOR, Frontal fibrosing alopecia (FFA) has increased markedly in incidence since it was first reported in 1994.<sup>1</sup> A possible role of cosmetic ingredients has been suspected, especially ultraviolet (UV) blockers, as these were added to products in the late 1980s. Daily year-round use of facial moisturizers, most of which contain a sunscreen, has been associated with FFA in both women and men.<sup>2,3</sup> An additional large study has reported that the use of facial sunscreens is the only common risk factor for FFA in both men and women.<sup>4</sup> Patch testing in patients with FFA shows a high prevalence of sensitization to cosmetic ingredients but not to a specific culprit, possibly indicating that these patients utilize more cosmetic products than the general population.

A case report has shown hair regrowth in a woman with FFA who discontinued use of sunscreen along the hairline,<sup>5</sup> and another single case report has shown the presence of titanium species on the hair shaft of a patient with the disease.<sup>6</sup> Contact allergy to titanium dioxide and a photocontact allergy to other UV blockers were excluded in a recent study.<sup>7</sup>

Nanoparticle titanium dioxide is a common ingredient in cosmetic products, used not only as a sunscreen but also as a pigment and a thickener. Titanium dioxide has significant photocatalytic activity with UV irradiation. This UV-induced oxidative reaction suggests that there may be tissue damage and associated inflammation in the skin when the titanium dioxide is exposed to UV. Zinc dioxide has a lower level of photocatalytic activity. The photocatalytic activity in titanium and zinc dioxide is significant enough that most sunscreen and cosmetic products use titanium and zinc dioxide that has been coated with a nonreactive chemical. Finally, nanoparticles of titanium and zinc dioxide, which have a particle size of only 40 nm, are common ingredients in cosmetic products and it is possible that these nanoparticles can enter skin cells. The impact on cellular function from intracellular passage of titanium dioxide is not known.

We tested hair shafts from 16 women with biopsy-proven FFA using scanning electron microscopy with energy-dispersive X-ray spectroscopy (SEM/EDX). For each patient, a single hair shaft was plucked from the frontal hairline in a clinically affected region. Patients were asked not to wear make-up or cosmetics on the day of sampling and the area was cleaned with alcohol before plucking. Multiple SEM/EDX instruments were used for the detection, one of which was a Hitachi

FlexSEM (Hitachi America, Ltd. Tarrytown, NY, U.S.A.) equipped with an Oxford 30 mm<sup>2</sup> SDD EDX detector (Oxford Instruments America, Inc., Concord MA, U.S.A.).

Titanium species was identified in all 16 hair shafts, with some shafts having more titanium present than others. Titanium species was also identified on the hair shaft of three female control patients who had no evidence of FFA. A single male control with no evidence of FFA who reported no use of facial moisturizer, sunscreen or hair dye was negative. Testing along the hair shaft, from the follicular ostia to > 5 mm out showed the presence of titanium along the entire length. As shown in Fig. 1, a backscattered electron image taken from one of the typical hair shafts with SEM indicates the presence of particles with brighter contrast on the hair shaft. EDX spectra collected from individual brighter particles are shown in Figure 1a. Particles 1 and 3 indicate the presence of titanium species, but titanium species was not found on particle 2. Some particles also contained simple salts, with calcium, aluminium, chloride, iron and sodium being identified and a few contained silica, a common element in sand/dirt. The EDX detector also identified elements that comprise the normal hair, such as carbon, nitrogen, oxygen and sulfur.

Facial moisturizers, foundations, sunscreens and hair dye contain numerous ingredients that could be involved in the development of FFA. Although some studies linked FFA to chemical sunscreens,<sup>4</sup> our experience and the results of a very recent case-control study confirming a possible association between FFA and cosmetic application<sup>8</sup> show that patients often use multiple products and recall brands more often than product names. In addition, many sunscreens found in foundations can contain both chemical and physical filters, which are used daily by women and have titanium dioxide as an ingredient.

One hypothesis of how titanium dioxide could be involved in developing FFA is that the titanium dioxide penetrates down to the isthmus, wherein a lichenoid reaction develops near the bulge. This hypothesis could also explain why vellus follicles are primarily involved in FFA. Another hypothesis, proposed by Cranwell and Sinclair, is that the use of sunscreen suppresses the anti-inflammatory and immunomodulatory effects of sunlight.<sup>8</sup> In both hypotheses, chronic inflammation may eventually lead to a breakdown of the special immune privilege of the follicle, allowing an autoimmune disease to develop.

The identification of titanium in all 16 FFA samples and three of the negative controls demonstrates the difficulty of assessing whether titanium dioxide is causative. Definitive proof of its role in FFA will likely require a carefully designed and large prospective study. Assessing the level of exposure, such as assessing the amount of titanium dioxide in each product, could

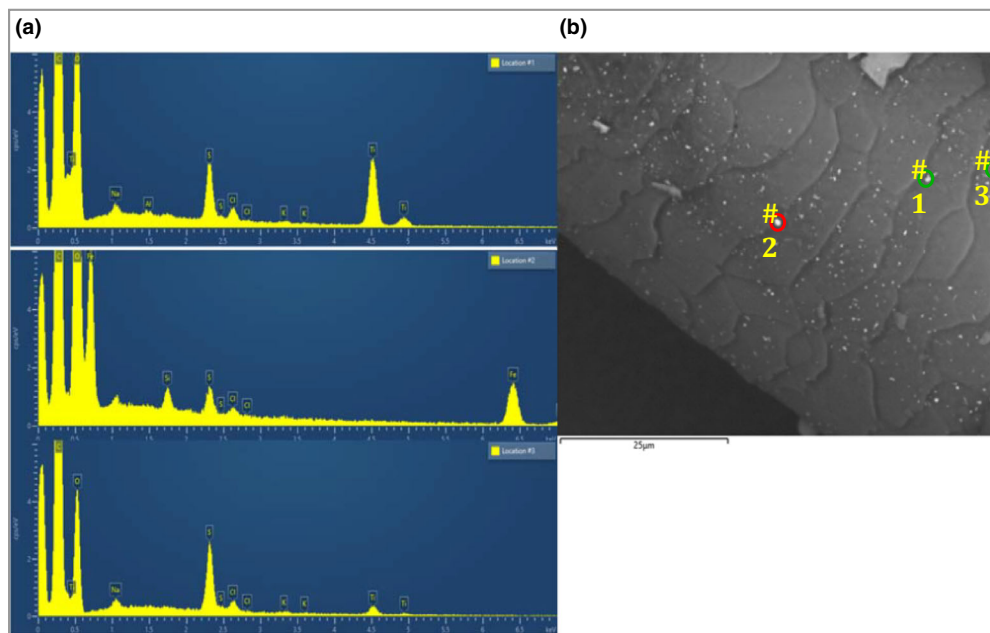


Fig 1. (a) Energy-dispersive X-ray spectroscopy spectra collected from particles 1–3 showing the presence of titanium species on particle 1 and 3. (b) A backscattered electron image taken from one of the typical hair shafts with scanning electron microscopy showing the presence of particles with brighter contrast on a hair shaft. Scale bar = 25 µm.

also be a helpful adjunct. Likewise, assessing the composition and source of the titanium dioxide being used, such as nanoparticle size and the presence or absence of an insert coating, may be helpful in further evaluation. In summary, the findings of this small study demonstrate the ubiquity of titanium dioxide, which was found on the hair of patients with and without FFA. Thus, it remains unknown whether titanium dioxide is causative of FFA. Perhaps final proof of causation could come only from observing a decrease in the incidence of the disease after the removal of suspect ingredients from foundations, facial moisturizers, sunscreens and hair dye.

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## References

- 1 Kossard S. Postmenopausal frontal fibrosing alopecia. scarring alopecia in a pattern distribution. *Arch Dermatol* 1994; **130**:1407.
- 2 Aldoori N, Dobson K, Holden CR et al. Frontal fibrosing alopecia: possible association with leave-on facial skin care products and sunscreens; a questionnaire study. *Br J Dermatol* 2016; **175**:762–7.
- 3 Debroy Kidambi A, Dobson K, Holmes S et al. Frontal fibrosing alopecia in men: an association with facial moisturizers and sunscreens. *Br J Dermatol* 2017; **177**:260–1.
- 4 Moreno-Arrones OM, Saceda-Corralo D, Rodrigues-Barata AR et al. Risk factors associated with frontal fibrosing alopecia: a multicentre case–control study. *Clin Exp Dermatol* 2019; <https://doi.org/10.1111/ced.13785>.
- 5 Cranwell WC, Sinclair R. Frontal fibrosing alopecia: regrowth following cessation of sunscreen on the forehead. *Australas J Dermatol* 2019; **60**:60–1.
- 6 Brunet-Possenti F, Deschamps L, Colboc H et al. Detection of titanium nanoparticles in the hair shafts of a patient with frontal fibrosing alopecia. *J Eur Acad Dermatol Venerol* 2018; **32**:e442–3.
- 7 Aerts O, Bracke A, Goossens A et al. Titanium dioxide nanoparticles and frontal fibrosing alopecia: cause or consequence? *J Eur Acad Dermatol Venerol* 2019; **33**:e45–6.
- 8 Cranwell WC, Sinclair R. Sunscreen and facial skin care products in frontal fibrosing alopecia: a case–control study. *Br J Dermatol* 2019; <https://doi.org/10.1111/bjd.17354>.

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