patient confidence in a dermatologic surgery practice. *J Am Acad Dermatol*. 2016;74:1185-1193.
2. McGinness JL, Goldstein G. The value of preoperative biopsy site photography for identifying cutaneous lesions. *Dermatol Surg*. 2010;36:194-197.
3. Nijhawan RI, Lee EH, Nehal KS. Biopsy site selfies—a quality improvement pilot study to assist with correct surgical site identification. *Dermatol Surg*. 2015;41(4):499-504.
4. Python. Python Software Foundation. Available at: https://www.python.org/. Accessed July 1, 2018.
5. Kazemi V, Sullivan J. One millisecond face alignment with an ensemble of regression trees. In: *2014 IEEE Conference on Computer Vision and Pattern Recognition*. Columbus, OH; June 23-28, 2014:1867-1874.

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Cutaneous absorption of tretinoin in 0.05% cream and 5% chemical peel formulas

To the Editor: Tretinoin chemical peels have been used for over 2 decades as an adjuvant therapy for melasma, photoaging, and acne.[1] The available literature does not elucidate to what degree a chemical peel at 5% may concentrate tretinoin in the epidermis and dermis to target nuclear retinoic acid receptors compared with the conventional 0.05% cream. This study aimed to quantify the cutaneous absorption of tretinoin in 0.05% (cream) and 5% (chemical peel) formulas.

A side-randomized, evaluator-blinded trial was conducted on 24 postmenopausal female volunteers older than 60 years, with Fitzpatrick skin types II to III, who were treated for photoaging. Tretinoin 0.05% and 5% emulsions were compounded 1 day before with the same vehicle, containing water, glycerin, polyacrylamide, $C_{13\text{-}14}$ isoparaffin and laureth-7, caprylic/capric triglyceride, phenoxyethanol, caprylyl glycol, ethylenediaminetetraacetic acid tetrasodium salt, butylhydroxy toluene, butylhydroxy anisole, and pentaerythrityl tetra-di-t-butyl hydroxyhydrocinnamate (School of Pharmacy, Federal University of Sao Paulo). Sealed 0.5-g sachets were kept refrigerated and photoprotected until topical application over a 250-cm^2 rectangle in each dorsal aspect of the forearm after gentle degreasing with acetone/ethanol 1:1, and left unoccluded for 6 hours before washing.[2] A delimited area had the corneal layer stripped by tape technique,[3] followed by a 3-mm punch biopsy for the quantification by liquid chromatography with tandem mass spectrometry of tretinoin extracted from the corneal layer and the epidermis or dermis.

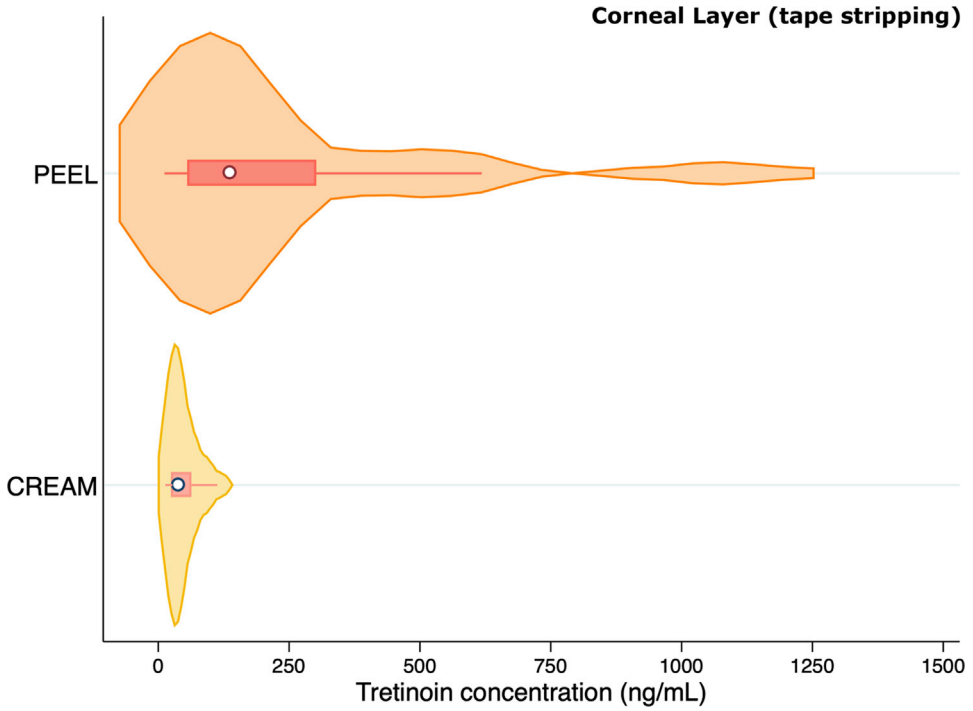

Fig 1. Corneal layer concentration. Violin plots of the distributions of tretinoin concentration extracted from the corneal layer of 24 side-randomized volunteers, after a treatment time of 6 hours, in cream formulas containing 0.05% tretinoin ("cream" on the *y* axis) and 5% tretinoin ("peel" on the *y* axis), followed by washing with soap and tape stripping (10 times) for the removal of the corneal layer. Tretinoin was extracted from the tapes and quantified by liquid chromatography with tandem mass spectrometry.

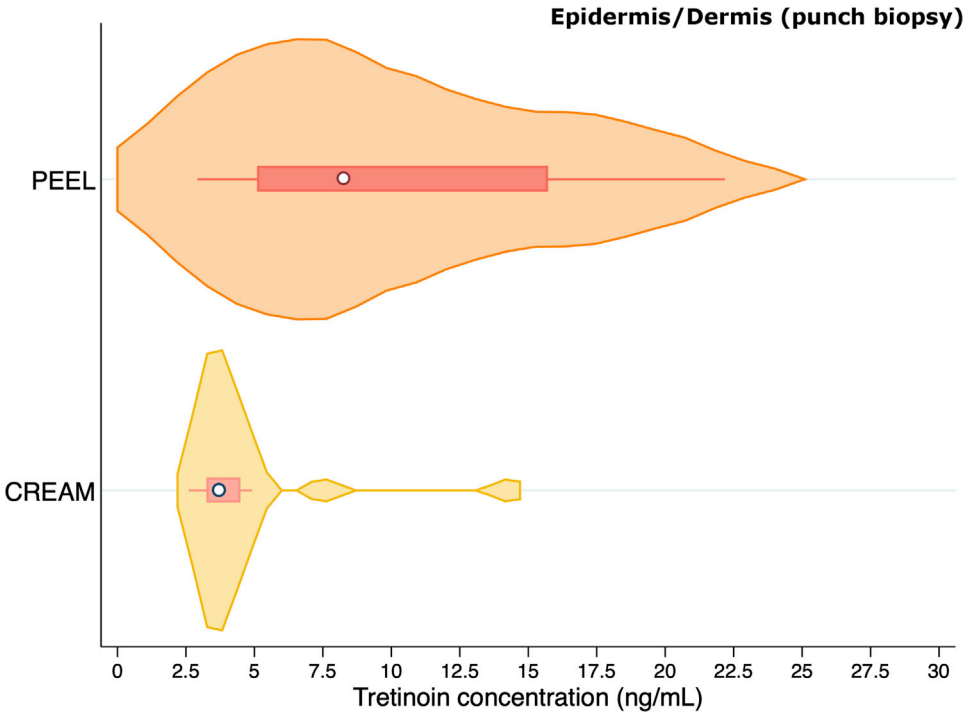

Fig 2. Epidermis/dermis concentration. Violin plots of the distributions of tretinoin concentration extracted from the dermis and epidermis (3-mm punch biopsies) of 24 side-randomized volunteers, after a treatment time of 6 hours of cream formulas containing 0.05% tretinoin ("cream" on the *y* axis) and 5% tretinoin ("peel" on the *y* axis). The biopsies were performed after washing with soap and stripping 10 consecutive times with tape for the removal of the corneal layer. After processing of the specimens, tretinoin was quantified by liquid chromatography with tandem mass spectrometry.

Tretinoin concentrations extracted from the corneal layer ranged from 13.4 to 129.2 ng/mL (median 39.7 ng/mL; interquartile range 37.9 ng/mL) for the 0.05% formula versus 12 to 1166.45 ng/mL (median 138.5 ng/mL; interquartile range 263.9 ng/mL) for the 5% formula (Fig 1). The amount of tretinoin extracted from the corneal layer was significantly higher in the peel group ($P < .001$).

Tretinoin concentrations extracted from the dermis or epidermis devoid of corneal layer ranged from 2.6 to 14.3 ng/mL (median 3.7 ng/mL; interquartile range 1.2 ng/mL) for the 0.05% formula versus 2.9 to 22.2 ng/mL (median 8.3 ng/mL; interquartile range 10.6 ng/mL) for the 5% formula (Fig 2). The absorbed amount was significantly higher in the peel group ($P < .001$).

Tretinoin peel formulas may contain undissolved crystals that cannot be absorbed in the epidermis.[4] Although studies have shown the efficacy of tretinoin peeling,[5] the advantages of high concentrations used in peels compared with the lower concentrations used daily are still controversial.[4] Absorption could be modified by aggressive degreasing, occlusion, different vehicles, volume, peel concentration, or time the formula is left on the skin. This study did not evaluate these absorption modifiers.

Five percent peels achieve approximately a trifold pulse of higher concentrations of tretinoin in the epidermis and dermis compared with the usual 0.05% cream formula with identical 6-hour time on the forearms.

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REFERENCES

1. Lee KC, Wambier CG, Soon SL, et al. Basic chemical peeling: superficial and medium-depth peels. *J Am Acad Dermatol*. 2019;81(2):313-324.
2. Sumita JM, Miot HA, Soares JLM, et al. Tretinoin (0.05% cream vs. 5% peel) for photoaging and field cancerization of the forearms: randomized, evaluator-blinded, clinical trial. *J Eur Acad Dermatol Venereol*. 2018;32(10):1819-1826.
3. Ascenso A, Salgado A, Euletério C, et al. In vitro and in vivo topical delivery studies of tretinoin-loaded ultradeformable vesicles. *Eur J Pharm Biopharm*. 2014;88(1):48-55.
4. Kligman DE. Regarding tretinoin peeling. *Dermatol Surg*. 2001;27(6):608.
5. Cucé LC, Bertino MCM, Scattone L, Birkenhauer MC. Tretinoin peeling. *Dermatol Surg*. 2001;27(1):12-14.

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Onychoscopy of allergic contact dermatitis caused by artificial nails: A double-center retrospective study on 34 patients

To the Editor: Artificial nails have gained popularity among women in recent years. They are associated with a high risk of developing allergic contact dermatitis because of the acrylates contained in the formers.[1-3] Artificial-nail-induced allergic contact dermatitis usually presents with acute dystrophic nail changes, often misdiagnosed as psoriasis, that occur at removal of the artificial nails. To date, no information about dermoscopy of this condition has been published, to our knowledge. A double-center retrospective study included 34 patients affected by allergic contact dermatitis caused by artificial nails, confirmed by patch-testing positivity. Demographic data, history, and clinical and dermoscopic features were collected (Table I). Age at presentation was variable, ranging from 26 to 80 years, with a peak incidence at aged 50 to 59 years. Median duration of the disease was 20 days.

Clinical examination showed nail color changes and onycholysis associated to some extent with subungual hyperkeratosis and paronychia as a sign of nail bed and periungual reaction. Onychoscopy was exhibited in all the affected patients as white discoloration, appearing as a distal color change of the nail plate in most cases (Fig 1). The presence of onycholysis was confirmed by dermoscopy, with a slightly dented onycholytic border that was more common than the linear one. An interesting finding was the low rate of an erythematous border of onycholysis, different from that commonly observed in nail psoriasis.[4]

Main clinical signs of nail bed psoriasis are onycholysis with erythematous border and salmon oil spot, whereas nonspecific signs are splinter hemorrhages and subungual hyperkeratosis. Onychoscopy is helpful in patients with fingernail onycholysis secondary to psoriasis, allowing visualization of the erythematous border surrounding the distal edge of the detachment. This is the most typical symptom of psoriasis and it appears as a bright orange-yellow border surrounding the distal edge of the detachment, which is observed as a slightly dented margin.[5] In our patients, subungual hyperkeratosis was commonly observed, but in most cases the extent was mild. Less than half the patients presented with a variable periungual tissue damage, ranging from mild paronychia to excoriations, thus probably indicating that in the remnant the allergic reaction was limited to nail tissue. The detection of splinter hemorrhages in a minority of patients made the differential diagnosis with nail psoriasis more challenging because these are nonspecific signs of nail psoriasis. Patch-testing results were similar to previously reported ones,[1] indicating that methacrylate was the most common allergen responsible for allergic contact dermatitis caused by artificial nails. The low rate of erythematous border and additional signs such as splinter hemorrhages, the mild hyperkeratosis, the history of a use of artificial nails, positivity of patch testing, and the absence of history for psoriasis could make the diagnosis of allergic contact dermatitis caused by artificial nails more likely.

Nail dermoscopy (onychoscopy) is used by experts in nail diseases to magnify the specific alterations on all visible parts of the nail unit, but also to provide important diagnostic information.

To our knowledge, our study was the first to describe specific onychoscopic features of allergic contact dermatitis caused by artificial nails. We believe our findings will help physicians in determining differential diagnoses of other common nail diseases such as psoriasis, which is often confused with allergic contact dermatitis. Dermoscopic findings were derived from a pilot double-center retrospective study, whose results should be confirmed by further studies.