

LETTER TO THE EDITOR

Topical corticosteroid or emollient product: Which to apply first?

Both topical corticosteroid (TCS) and emollients have important roles in the management of inflammatory dermatosis. Their combined use can be cumbersome for patients. Healthcare professionals are also challenged because recommendations of recognized professional societies regarding sequence and time between application of the two products are contradictory and poorly referenced (Table 1). Against this background, it is crucial to envision what exactly happens locally when products or rather their ingredients come together and are rubbed onto the skin. The vehicle designations (cream, ointment) as defined in pharmacopoeias refer to the *primary vehicle format* in the container (tube, bottle). The umbrella term *emollient* describes more of a function (making soft) than a vehicle format and is colloquially used for skin care products that may be very diverse in composition. During and after product application volatile vehicle ingredients evaporate, form temporarily a secondary and after complete evaporation a tertiary or final vehicle format on the skin. This phenomenon coined as 'metamorphosis of the vehicle' is often visibly noticeable by the changing surface aspect of the skin at the application site, is haptically palpable and is described as the product 'is well absorbed' or 'dries up well'.¹ It is obvious that due to the changing sum of vehicle ingredients, vehicle format and physicochemical environment at the application site change. This becomes even more complex when mixing two products. It can be deduced that, contrary to popular beliefs, it is not the primary vehicle format in the container that is responsible for effects of any kind, but exclusively the physicochemical properties of the sum of vehicle ingredients during and after application on the application site. When the vehicle ingredients from the TCS and emollient product come together

during application, a 'new' in situ formulation emerges in a locally limited area. Depending on the physicochemical properties of the vehicle ingredients of both products on the skin, they will mix more or less well. It follows that sequence and time between the applications play an important role. If volatile vehicle ingredients are still present from the first product when the second product is applied, the mixing behaves differently than if no volatile vehicle ingredients are present. With a simple experiment, we have visualized the effect when TCS and emollient come together on the skin (Figure 1). When TCS was applied first, a *hydrophilic* emollient was unable to dissolve the ingredients of the *lipophilic* TCS vehicle, while a *lipophilic* emollient was able to dissolve the *lipophilic* TCS vehicle very well. In the latter case, the TCS was distributed over the entire application area of the emollient, which is undesirable as it unnecessarily increases the application area and thus the percutaneous absorption of the TCS. This observation applied to TCS cream and ointment. As TCS cream and ointment are both very lipophilic, the observation is thus independent of product format. When hydrophilic or lipophilic emollients were applied first and then TCS, the latter remained locally. The experiments reveal two aspects: (1) When two topicals are mixed on the skin—even if one formulation has already been 'absorbed' or 'dried up'—the subsequently applied formulation may redissolve the vehicle ingredients of the initially applied formulation. This phenomenon is highly dependent on the physicochemical characteristics (e.g. hydro-/lipophilicity) of both formulations. (2) Vehicle designations are unsuitable for making recommendations, as they give no reliable indications for the physicochemical properties of the products and metamorphosis of the vehicle after application is

TABLE 1 Current contradictory recommendations of leading medical societies for combined application of topical corticosteroids (TCS) and emollients to the same skin area

Medical societies	Publication date/last update	Recommended application sequence	Recommended time interval between products
Primary Care Dermatology Society (PCDS), UK ³	2022	Emollient before TCS	15–20 min
National Institute of Health and Care Excellence (NICE), UK ⁴	2021	According to patient's preference	Several minutes
European Task Force on Atopic Dermatitis (ETFAD), European Academy of Dermatology and Venereology (EADV) ⁵	2020	Cream formulation before ointment formulation	15 min
German Society of Dermatology ⁶	2018	TCS before emollient	30 min

Abbreviation: UK, United Kingdom.

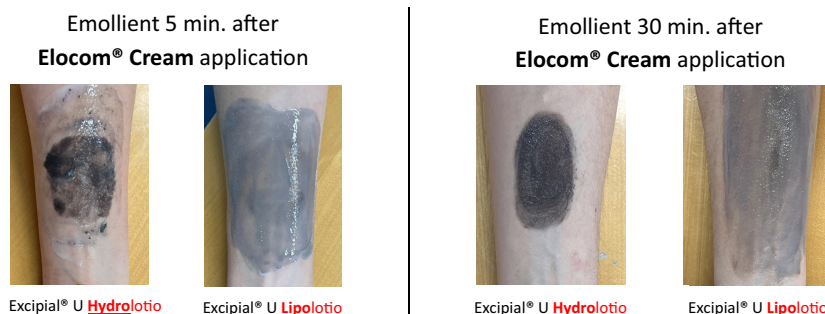


FIGURE 1 Elocom® cream and ointment (Mometasone Furoate, 0.1%, Organon GmbH) were spiked with black iron oxide pigments (iron oxide black C33-7734, BASF, 10 mg/g Elocom®) to visualize their distribution on the skin after subsequent application of a hydrophilic and a lipophilic emollient. With the hydrophilic emollient (Excipial® U Hydrolotio, oil-in-water emulsion, lipid content 11%, Galderma SA), the area of the Elocom® cream remained largely in place, whereas with the lipophilic emollient (Excipial® U Lipolotio, water-in-oil emulsion, lipid content 36%, Galderma SA), the Elocom® cream was distributed from its initial application area to the entire application area of the emollient. The patchy pigment distribution of Elocom® cream after 5 min is due to remaining traces of hydrophilic ingredients mixing with the hydrophilic ingredients of the emollient. This phenomenon was not observed after 30 min because all volatile topical corticosteroid vehicle ingredients have evaporated. Very similar pattern was seen with the application of Elocom® ointment and the aforementioned hydrophilic and lipophilic emollients (images not shown).

not accounted for. As the sum of vehicle ingredients and the physicochemical properties of TCS and emollient products can vary considerably and are usually unknown to prescribers, we recommend applying the emollient first and then—after a ‘drying time’ of several minutes to allow evaporation of volatile ingredients—the TCS to prevent unnecessary distribution of TCS over skin areas larger than intended. From a therapeutic perspective, as observed in a small study, the order of application of TCS and emollient did not appear to influence the treatment efficacy.² For practical reasons, it may be more convenient for patients to split product application according to the time of day (morning/evening). Other application modalities may also be practical to increase patients' adherence.

ACKNOWLEDGMENT

None.

CONFLICT OF INTEREST


The authors have no conflict of interest.

DATA AVAILABILITY STATEMENT

Data are available on request from the corresponding author.

ETHICS STATEMENT

The volunteers in this manuscript have given written informed consent to the publication of their case details.

Christian Surber^{1,2} 
 Jasmin Robertis³
 Daphne Reinau³

¹Department of Dermatology, University Hospital Zurich, Zurich, Switzerland

²Department of Dermatology, University Hospital Basel, Basel, Switzerland

³Hospital Pharmacy, University Hospital Basel, Basel, Switzerland

Correspondence

Christian Surber, Department of Dermatology, University Hospital Zurich, Rämistrasse 100, 8091 Zurich, Switzerland.

Email: christian.surber@unibas.ch

ORCID

Christian Surber  <https://orcid.org/0000-0001-5027-4112>

REFERENCES

1. Surber C, Knie U. Metamorphosis of vehicles: mechanisms and opportunities. *Curr Probl Dermatol*. 2018;54:152–65. <https://doi.org/10.1159/000489529>
2. Ng SY, Begum S, Chong SY. Does order of application of emollient and topical corticosteroids make a difference in the severity of atopic eczema in children? *Pediatr Dermatol*. 2016;33(2):160–4. <https://doi.org/10.1111/pde.12758>
3. Primary Care Dermatology Society (PCDS). Eczema: atopic eczema [cited 2022 August 17]. Available from: <https://www.pcds.org.uk/clinical-guidance/atopic-eczema>
4. National Institute for Health and Care Excellence. Atopic Eczema in under 12s: Diagnosis and Management. Clinical Guideline [CG57], last updated 02 March 2021. [cited 2022 August 17]. Available from: <https://www.nice.org.uk/guidance/CG57/chapter/1-Guidance#treatment-2>
5. Wollenberg A, Christen-Zäch S, Taieb A, Paul C, Thyssen JP, Bruin-Weller M, et al. ETFAD/EADV Eczema Task Force 2020 position paper on diagnosis and treatment of atopic dermatitis in adults and children. *J Eur Acad Dermatol Venereol*. 2020;34(12):2717–44. <https://doi.org/10.1111/jdv.16892>
6. Wohlrab J, Staubach P, Augustin M, Eisert L, Hünnerbein A, Nast A, et al. S2k guidelines for the use of topical preparations on the skin. *J Dtsch Dermatol Ges*. 2018;16(3):376–92. <https://doi.org/10.1111/ddg.13473>