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Holistic Exploration of Lipidic Interfaces for Enhanced Skin-Formulation Interaction

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1. Introduction

Cosmetic innovation draws inspiration from nature, much like Leonardo da Vinci's creations [1]. At the heart of this progress lies biomimicry, a guiding principle that bridges science and nature to craft effective, sustainable solutions [2]. Advances in green chemistry now enable natural ingredients that meet the demand for clean and responsible beauty. These ingredients are biodegradable, eco-friendly and multifunctional, addressing high performance with minimal social and ecological impact [3]. By prioritizing skin safety, environmental respect and resource efficiency, this holistic approach aligns cosmetics with the needs of both human beings and the planet preservation. In the pursuit of more effective and sensorially appealing cosmetic products, growing attention is being paid to how ingredients interact with the skin's structure and functions, particularly the lipid film, a key component in maintaining skin integrity and resilience [4,5].

The skin's lipid matrix is a highly complex and dynamic structure. It starts with the synthesis of lipids precursors into the keratinocyte form *stratum spinosum* which are first packed into lamellar granules, also called Odland bodies [6–8]. They are then dumped into *stratum corneum* intercellular space as a result of fusion of the lamellar body with the cell membrane of the keratinocyte at the boundary between the *stratum granulosum* and the *stratum corneum* [9,10]. Due to a wide range of enzymatic processes, lipid precursors will turn into well-known *stratum corneum* lipids: ceramides, free fatty acids and cholesterol mainly in an approximately equimolar ratio arranged in lamellaes [5,11,12]. These components form the intercellular lipid,

also called “mortar”, and corneocytes “bricks” [13]. Due to their self-compact crystalline organization [14], they make a major contribution to the skin's permeability by forming an occlusive film [4]. Otherwise, it is well known that a lack of one or more of these components leads to cutaneous disorder of varying degrees of severity like atopic dermatite [14,15].
Esters are widely used in cosmetics formulations, primarily as emollients to provide softness, enhance texture, and help maintain skin hydration [16]. While their diverse chemical structures contribute significantly to the sensory properties of cosmetic products [17], their specific interactions with other cosmetic ingredients and skin lipids remain poorly understood to date. Although there is clear evidence of their benefits on the skin, such as the formation of protective or moisturizing occlusive films thanks to their physicochemical properties [17], the mechanisms of these molecular interactions are not really known to date. In other words, their impact of esters on the microstructure of the skin lipid lamellae, as well as the mechanisms by which esters interact with the native lipids to the *stratum corneum* remain largely unexplored, despite their apparent importance in the formulation of cosmetic and pharmaceutical skincare products addressing various consumer needs. Beyond these fundamental questions, advancing this knowledge could open the door to even more impactful innovations, such as the development of optimized formulations, capable of forming a perfectly homogeneous film. This could allow for the uniform integration of UV filters, thereby enhancing their efficacy while minimizing their release into aquatic environments, one of the major challenges currently facing both the cosmetics industry and public health.

By combining *in vivo* biometrological analysis of TEWL with appropriate statistical treatment, this study offers new insights into ester–skin interactions. Such a bio-inspired approach leverages the strategy of formulators for implementing the strategy for the use of esters as emollients in cosmetics. It also brings original knowledge and skills for the benefit of the scientific community in fields as varied as skin biology, physiochemistry, formulation or sensory and biometrological approaches.

2. Materials and Methods

Cosmetic formulation:

Eleven esters, mostly biosourced, were chosen for this project (Table 1).

Table 1: Tested esters (INCI name)

Physical state	INCI Name	NOI (%)
Liquid at AT	Coco-Caprylate/Caprate	100
	Ethyl Oleate	100
	C18-36 Acid Triglyceride	100
	Propylene Glycol Dicaprylate/Dicaprate	100
	Polyglyceryl-3 Diisostearate	100
	Caprylic/Capric Triglyceride	100
	Hexyl Laurate	100
Solid at AT	C10-18 Triglycerides	100
	Myristyl Myristate	100
	Hydrogenated coco-glycerides	100
	Methyl Palmitate	88

To better discriminate the emollient esters impact on the skin, they were formulated in emulsion by following the same formula (Table 2).

Table 2: Formula

Phase	Raw material (INCI name)	Role	% (w/w)
A1	Aqua	Solvent	78,70
	Carbomer	Thickener	0,40
A2	Methyl propanediol	Solubilizer	4,00
	Xanthan Gum	Thickener	0,40
B	PEG-8 Caprylic/Capric Glycerides	Emulsifier	1,00
	ESTER	Emollient	15,00
C	Phenoxyethanol & propylene glycol & decylene glycol	Preservative	0,50
		TOTAL	100,00

The stability of the formulated emulsions was ensured by organoleptic and rheological monitoring (data not shown).

Biometrological studies:

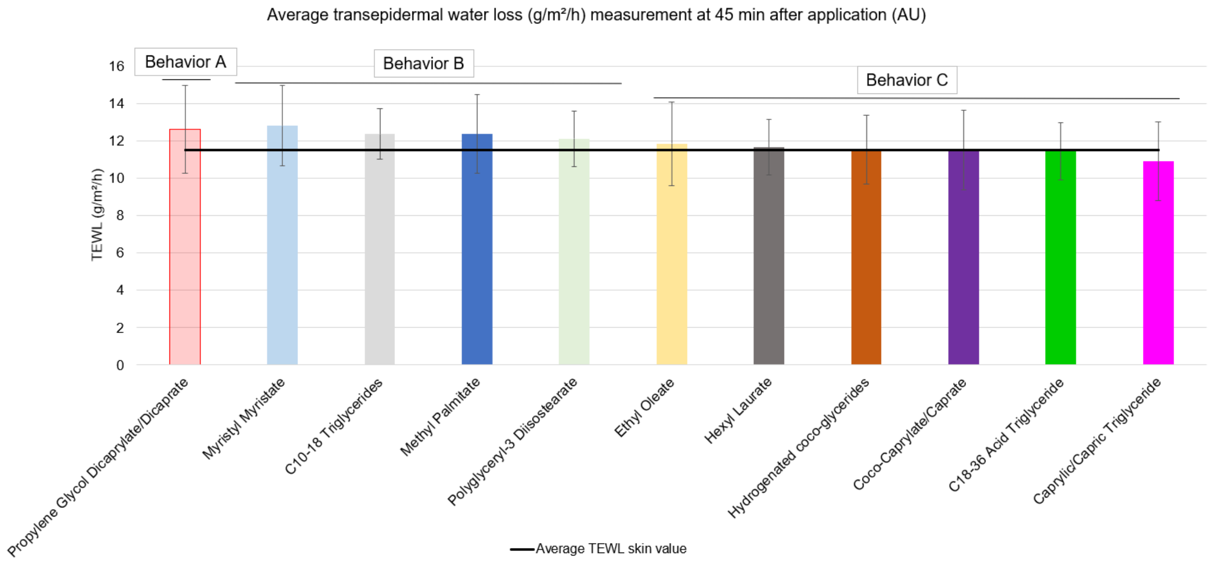
Biometrological studies were performed by using a Tewameter® TM300 and MPA CT Plus software (Courage+Khazaka electronic GmbH, Cologne, Germany). A panel of 26 female volunteers, aged between 19 and 36 years, all with healthy skin, was recruited. An informed written consent document was obtained from each participant before the study. The study was approved by the Ethical committee of Université Le Havre Normandie. Prior to the study, volunteers were asked not to apply any cosmetic products to their forearms for at least two hours before the start of the test. Measurement sessions were performed in a closed room with a humidity level of between 48 and 52% and a temperature of between 18°C and 22°C. A 10-minute acclimatization period was imposed before the start of the study. Two 20 cm² areas were drawn on each of the volunteers forearms using a template. Trans-Epidermal Water Loss (TEWL) was measured at T0 on bare skin, as control. 40 µL of product was then applied onto the test area. TEWL measurements were performed 45 minutes and 2 hours after application of the product, respectively. Each measurement was taken in at least in triplicate.

Statistical analysis:

Statistical analysis was performed using XLSTAT Software Version 2016.02.27444 (Addinsoft, France). A one-way ANOVA was applied to the dataset to evaluate esters discrimination. When significant differences between products were detected ($p < 0.05$), product groupings were identified using Fisher pairwise comparison post hoc test ($\alpha < 0.05$).

3. Results

(A)



(B)

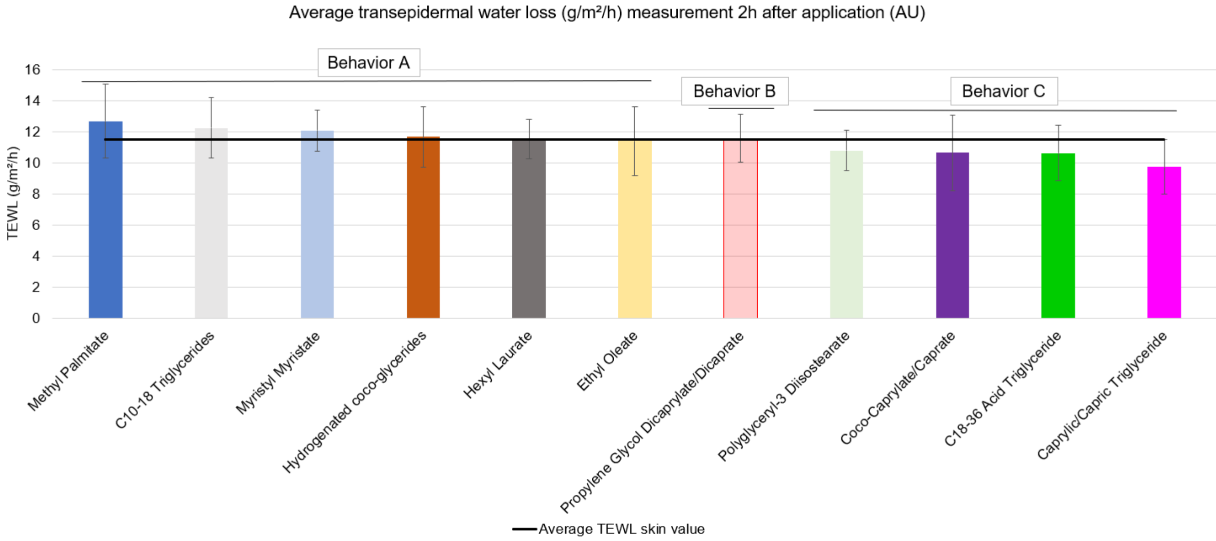


Figure 1: Mean value and standard deviation for Trans Epidermal Water Loss (TEWL) measurement 45 minutes (A) and 2 hours (B) after application.

A closer look at the results (Figure 1) reveals several interesting features. The different formulations, with the only difference being the ester integrated into the chassis, show several behaviors, whether 45 minutes after application or 2 hours. For each time interval, several groups emerge: some show an improvement in TEWL like capric/caprylic triglycerides at 45 minutes and 2h after application or C18/36 triglyceride and polyglyceryl-3 diisostearate 2h after application. Two distinct behaviors were observed among the emollient esters tested: some, such as hexyl laurate, appeared to have no noticeable impact on TEWL values, while others, like myristyl myristate and C10/18 triglyceride (45 minutes post-application) or methyl palmitate (after 2 hours), led to a significant TEWL increasing.

4. Discussion

Esters are commonly used in cosmetic formulations for their pleasant sensorial properties. This study aimed as to explore whether these ingredients can deliver functional benefits, particularly through interactions with the skin barrier. By adopting a holistic approach that considers both sensory perception and physiological effects, the concept of "**senso-functionality"** emerges, positioning esters as truly multifunctional ingredients. This exploratory study reveals a number of remarkable results. As shown, in Figure 1, two hours after application of ester-based creams, several trends emerge, reflecting different interaction profiles with the skin. A closer look on the data detailed in Figure 1 reveals several behaviors. First, some esters appear to have a neutral effect on the skin barrier. Among solid esters, this includes C10-18 Triglycerides, Methyl Palmitate, Methyl myristate and Hydrogenated coco-glycerides. Among liquid esters, hexyl laurate and ethyl oleate exhibit similar profiles. The latter do not significantly alter TEWL, suggesting either a transient or negligible effect on the skin barrier. Their non-occlusive and non-film-forming nature make them particularly suitable for lightweight formulations, especially for oily or combined skin types.

A second type of behavior was observed, as certain esters, namely C18-36 Acid Triglyceride, Caprylic/Capric Triglyceride, Coco-Caprylate/Caprate and Polyglyceryl-3 Diisostearate led to a statistically significant reduction of the TEWL two hours after application. Their film-forming properties therefore help to limit water evaporation. These results suggest that their film-forming properties help limit water loss through evaporation. Such behavior undoubtedly points out promising applications in intensive moisturizing treatments, particularly for dry or dehydrated skin.

An especially interesting case is that of Polyglyceryl 3 Diisostearate, which showed a dual and time-dependent effect: a significant increase in TEWL 45 minutes after application, followed by a notable reduction in the evaporation rate. This behavior may be linked to its multifunctional nature—beyond acting as a classic emollient, it also serves as a co-emulsifier in formulations. This dual role could influence the initial structure and dynamics of the formulation on the skin surface, potentially leading to a temporary disturbance of the skin barrier, followed by stabilization and the formation of a more coherent protective film. Such versatility highlights its interest as a multifunctional ingredient, both from a sensorial and functional standpoint.

Another interesting point is the behavior of Propylene Glycol Dicaprylate/Dicaprate. Paradoxically, this ester induced a significant increase in TEWL 45 minutes before application and allowing a return to the basal value of the skin two hours after application. This suggesting a temporary alteration in barrier function. This could be attributed to its amphiphilic structure conducive to fluidification of the *stratum corneum* or, a hygroscopic effect with no associated protective film. It could be used in drying products (intertrigo zones, antifungals), fast-absorbing serums combined with lipophilic active ingredients or in formulas that encourage the penetration of active ingredients (targeted skincare, gentle peels).

Several hypotheses can be considered to explain behaviors. An increase in TEWL is typically associated with a temporary disruption in the organization of the skin barrier [18]. The skin barrier is mainly governed by the compact crystalline organization of the lipid matrix in the *stratum corneum* [9]. Conversely, a decrease in TEWL is generally associated with the

formation of a protective occlusive film on the skin surface or to reparative processes induced by the incorporation of exogenous lipids within the *stratum corneum* lipid layers [19].
These finding prompt deeper consideration of the mechanisms triggered by ester-based formulations and how the chemical structure of esters may influence their interaction with the skin’s protective barrier.

5. Conclusion

This exploratory study shows the importance of esters in supporting the skin's barrier and hydration functions. However, depending on the ester incorporated into the formulation and its chemical structure, distinct behaviors can be observed, leading to specific effects on the skin. These observations underline the need for a more holistic approach to ingredient evaluation, one that integrates both sensorial and functional dimensions. In this context, esters can be considered as *senso-functional* ingredients, capable of delivering not only pleasant textures and sensations but also measurable biological benefits.
Several avenues of research are being considered to further explore these initial findings. Replicating the study on male or atopic skin would help determine how these esters perform across different skin types. To better understand how esters penetrate and interact with the intercellular lipid matrix of the *stratum corneum*, future work will combine biophysical and physicochemical approaches with skin permeation studies, biometrological tools, and cross-sensory analyses. For instance, correlating TEWL measurements with sensory perception could ultimately provide formulators with clearer guidance on the true benefits of each ester for skin barrier reinforcement.

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