

Effects of Structure on the Solubility of UV Filters

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Abstract: In recent years, one of the most concerning topics in healthcare is the constant exposure to ultraviolet (UV) light being the cause of numerous skin diseases. This issue created a keen interest in sun-care cosmetics, and particularly in sunscreens, since it has been proven to significantly reduce human skin disorders. Usually, sunscreens are formulated as emulsions with organic UV-absorbers dissolved in the oil phase; thus, the solubility of these UV-filters in the emollients is crucial. In this work we expose the properties of different emollients, correlating the chemical structure with the ability to dissolve organic UV-filters.

Keywords: UV-filters; solubility; emollients; liquid chromatography; sunscreen; cosmetics

1. Introduction

Over the last decades, there has been a depletion in the earth's stratospheric ozone, causing a dramatic rise of UV radiation reaching the earth's surface [1]. This leads to an increase in human exposure to harmful UV radiation, provoking a huge variety of skin-related disorders: from the loss of skin elasticity or wrinkling to immunosuppression or even cancer [1–5].

The most popular approach to deal with this issue is the use of sunscreens since it has been proven to significantly reduce the adverse effects of UV radiation [6–8]. Generally, sunscreens are prepared as emulsions due to the huge versatility they provide; these formulations are made by mixing an oil phase and a water phase, the latter being the main component [9].

The active ingredients are classified into two groups: inorganic and organic sunscreen agents. The inorganic or physical agents reflect or scatter a broad range of the light spectra (from infrared to UV radiation); the more used agents are titanium dioxide and zinc oxide, characterized by being photostable and requiring thick applications for proper reflection. These sunscreen agents present a very undesirable effect of whitening in the formula [10]. On the other hand, there are the organic or chemical agents that absorb a narrow part of the light spectrum; these UV filters present some advantages with respect to the inorganic counterpart in some cosmetic and safety properties, like not having a whitening effect, being non-irritant and having higher stability, amongst others [3,9]. Usually, the commercially available sunscreens are created with a blend of chemical and physical UV filters granting the beneficial effects and the coverage of the deficiencies of both types [3,9–11].

The organic UV filters are critical for the absorption activity of these emulsions [9], and, taking into consideration that, as mentioned before, the main component of sunscreens is water, the proper solubilization of those UV filters is crucial to ensure a good efficacy [12]. The fundamental components that are used to dissolve UV filters are emollients, thereupon we expose a correlation study between the structure of some emollients with the capacity to dissolve UV filters.



Citation: Del Olmo, M.; Navarro, À.; Garcia, C.; Ehara, T.; Beltran, L. Effects of Structure on the Solubility of UV Filters. *Cosmetics* **2022**, *9*, 60. <https://doi.org/10.3390/cosmetics9030060>

Academic Editors: Carmen Garcia-Jares and Laura Rubio

Received: 25 May 2022

Accepted: 2 June 2022

Published: 7 June 2022

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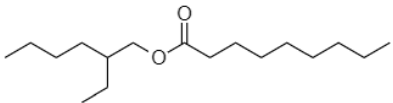
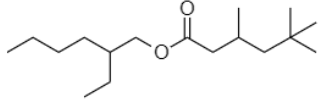
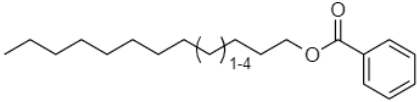
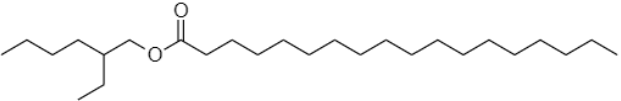
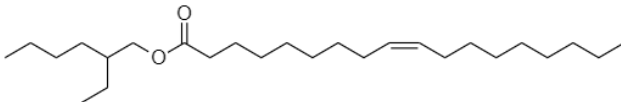
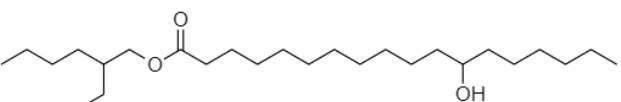
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2. Materials and Methods

2.1. Materials

Soldoc[®] VF 9 N (INCI: Ethylhexyl Pelargonate; from Industrial Quimica Lasem); Soldoc[®] VF 9 (INCI: Ethylhexyl Isononanoate; from Industrial Quimica Lasem; Waglinol[®] AB 1215 (INCI: C12-C15 Alkyl Benzoate; from Industrial Quimica Lasem); Lasemul[®] 130 (INCI: Ethylhexyl Stearate; from Industrial Quimica Lasem); Weichol[®] 130 (INCI: Ethylhexyl Oleate; from Industrial Quimica Lasem); Salacos[®] EH (INCI: Ethylhexyl Hydroxystearate; from Nisshin Oillio Group). These emollients were prepared, with the corresponding organic acid and alcohol, according to the standard, broadly described, esterification methods [13,14]. All mentioned products are summarized with its corresponding structure in Table 1.

Table 1. Summary of used emollients. Structure, INCI and trade name.

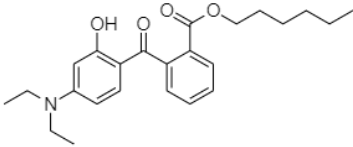
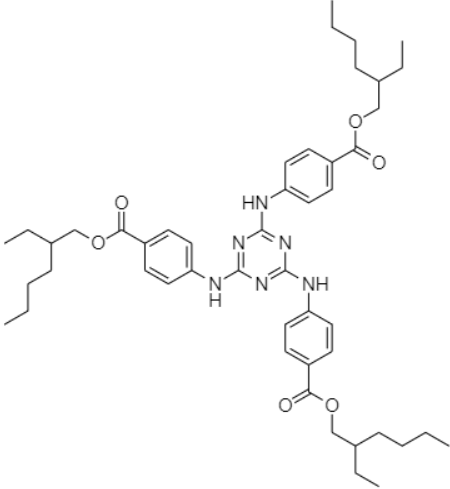
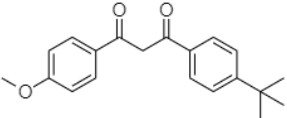
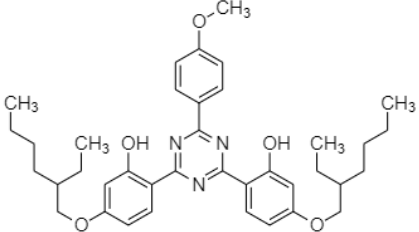
Structure	INCI	Trade Name and Supplier
	Ethylhexyl Pelargonate	Soldoc [®] VF 9 N (Industrial Quimica Lasem)
	Ethylhexyl Isononanoate	Soldoc [®] VF 9 (Industrial Quimica Lasem)
	C12-C15 Alkyl Myristate	Waglinol [®] AB 1215 (Industrial Quimica Lasem)
	Ethylhexyl Stearate	Lasemul [®] 130 (Industrial Quimica Lasem)
	Ethylhexyl Oleate	Weichol [®] 130 (Industrial Quimica Lasem)
	Ethylhexyl Hydroxystearate	Salacos [®] EH (Nisshin Oillio Group)

There was an initial intent of using all emollients with the Ethylhexyl scaffold to limit the structural differences between the molecules, but Ethylhexyl Benzoate has been labelled as a teratogen [15]; consequently, a non-toxic substitute was desired. C12–C15 Alkyl Benzoate was taken as the alternative, since it was available to us, and it doesn't have any apparent toxicity [16].

Diethylamino Hydroxybenzoyl Hexyl Benzoate (DHHB), Ethylhexyl Triazone (EHT), Butyl Methoxydibenzoylmethane (BMDBM) and Bis-Ethylhexyloxyphenol Methoxyphenyl Triazine (BEMT) were the UV filters used for this work; the structure, the trade name and the supplier are summarized in Table 2.

Other UV-filters were proposed to evaluate in this study such as Ethylhexyl Salicylate (or Octylsalate) [17] but could not be accurately examined with the current method.

Table 2. INCI name, structure, trade name and supplier of UV filters used.

INCI	Structure	Trade Name and Supplier	Maximum Allowed Concentration (Regulation EC No 1223/2009) [18]
Diethylamino Hydroxybenzoyl Hexyl Benzoate (DHHB)		Uvinul® A Plus (BASF)	10%
Ethylhexyl Triazone (EHT)		Uvinul® T150 (BASF)	5%
Butyl Methoxydibenzoylmethane (BMDDBM)		Parsol 1789 (DSM)	-
Bis-Ethylhexylphenol Methoxyphenyl Triazine (BEMT)		Tinosorb® S (BASF)	10%

2.2. UV Filter Solubility and HPLC Analysis

A 40 mL brown vial with screw cap (Supelco 27182) was filled with a magnetic stir bar, 20 mL of respective emollient, and 0.2 g (1% (*w/v*)) of respective solid UV filter, and then capped. If the solution was clear, 0.2 g of the UV filter was added; this process is repeated until the saturation of the solution is observed by the precipitation of the UV filter. Next, the prepared capped vial was stirred during 7 days at a rate of around 200 to 300 rpm using a magnetic stirrer (MultiMix Heat D MMH90E) in a room at 25 °C. The solutions were monitored ensuring that the solution remain saturated during the whole 7-day stirring process.

After 7 days, the test solutions were centrifuged for 30 min at 13,000 rpm at 25 °C (DIGICEN 21, RT 152 rotor). The supernatant was filtered through a 0.45 µm non-sterile Membrex 25 PET filter (Membrapure GmbH, Bodenheim, Germany). The methodology to evaluate the UV filter solubility has been previously reported by B. Herzog, et al. [6].

The solubility analysis was performed using HPLC-UV (1260 Infinity II, Agilent Technologies) with a Poroshell 120 EC-C18, 2.7 µm column (column size 4.6 × 100 mm) at

35 °C. The mobile phase used a 1.0mL/min flow and the following gradient: five minutes with a constant mixture of 40%(v/v) water, 54%(v/v) acetonitrile and 6%(v/v) tetrahydrofuran, during the following 15 min the water proportion was linearly decreased to zero, then, the eluent composition was kept constant for additional 15 min. A diode array detector (DAD) was used to evaluate the various samples, considering the maximum intensity value, and correlating to the respective calibration curve (at the same wavelength) to measure the solubility quantitatively. The used wavelengths are the following: 358nm for DHHB and BMDBM, 340 nm for BEMT and 308 nm for EHT.

Each analysis was duplicated to check the consistency of the results.

3. Results

The solubility properties of the variety of emollients have been evaluated in different ranges to precisely compare the structural effects: branching, chain length and functional groups.

First, Ethylhexyl Pelargonate and Ethylhexyl Isononanoate were studied to gauge the effects on branching.

The differences between these results can only be attributable to the branching effect of the nine-carbon aliphatic chain since both emollients have the same Ethylhexyl scaffold. Even though we can appreciate a lower solubility of EHT and BEMT when compared to the other two UV filters, the general tendency is an overall higher solubility of Ethylhexyl Pelargonate (Figure 1). Having seen these results, we could deduce that ramification has a negative impact on the solubility.

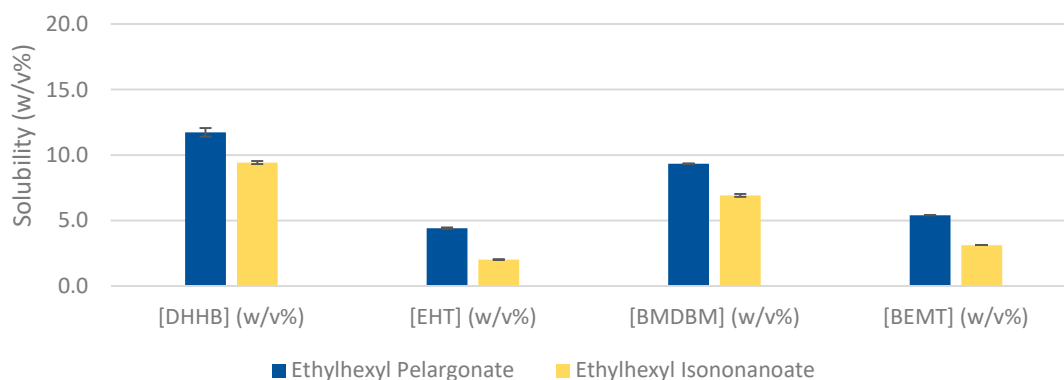


Figure 1. UV filter solubility of Ethylhexyl Pelargonate versus Ethylhexyl Isononanoate.

When comparing the repercussions of the chain length in the solubility, Ethylhexyl Pelargonate and Ethylhexyl Stearate present equivalent results as the previous analysis; where the less voluminous has better solubility, in this case the shorter the molecule the higher capacity of solubilizing UV filters (Figure 2).

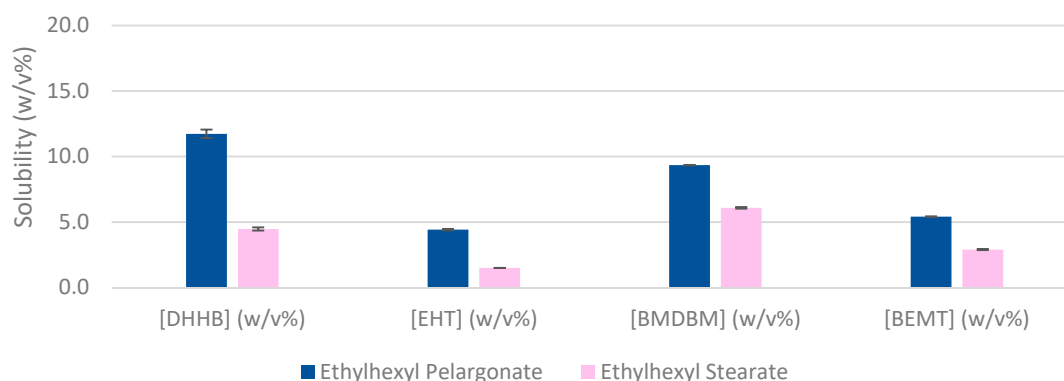


Figure 2. UV filter solubility of Ethylhexyl Pelargonate versus Ethylhexyl Stearate.

Thus far we have been able to compare the impact of the hydrocarbon structure of the molecule; hereafter, we are going to evaluate the influence of different functional groups.

Considering the results presented in the Figure 3, we have observed an overall impressive solubility ability of C12-C15 Alkyl Benzoate. Even though this emollient does not have the same Ethylhexyl scaffold as the other ones, the clear cause of this higher solubility is the presence of the aromatic group.

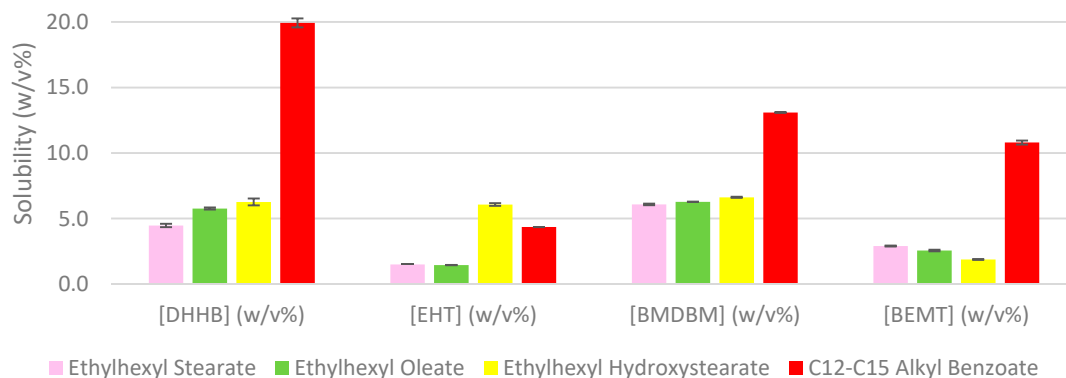


Figure 3. UV filter solubility of different emollients with similar scaffold.

On the other hand, the other three emollients that share the Ethylhexyl group present various behaviors depending on the evaluated UV filter. First, in the case of DHBB and BMDBM there's a general tendency in the solubility, the emollient without any functional group has the least ability to properly solubilize the UV filter while Ethylhexyl Hydroxystearate, which has an alcohol group, has the best solubility of the three. This slight increase in solubility could be caused by the presence of certain polarity in the emollient. Second, the solubility tendency of BEMT is the opposite of the previous mentioned UV filters. There could be a reasoning behind this evidence, but it could also be that since there is a small difference between the solubility values of the three emollients, that the functional group does not have a huge impact in the solubility of this UV filter. This argument could also be applied to BMDBM although the results follow the same order as in DHBB. Third, there is a peculiar case regarding EHT, where Ethylhexyl Hydroxystearate shows an astonishing solubility in comparison to the other emollients, even C12-C15 Alkyl Benzoate. This is probably due to some special affinity of Ethylhexyl Hydroxystearate with EHT.

4. Conclusions

Suncare cosmetics have been of great relevance, specially lately, and in consequence, emollients with the ability to properly dissolve UV filters. The exposed study of the correlation of the solubility and structure of the various emollients manifests some distinctive traits that favor the solubility of the UV filters: when evaluating fully saturated alkyl-chained emollients, shorter linear chains benefit the solubilization; when studying the effect of unsaturation, no great enhancement in the solubility has been observed; in contrast, alcohol and aromatic groups could significantly improve the solubility.

Author Contributions: Conceptualization, M.D.O., À.N., C.G., T.E. and L.B.; methodology, M.D.O., À.N., C.G., T.E. and L.B.; validation, M.D.O., À.N., C.G., T.E. and L.B.; formal analysis, M.D.O.; investigation, M.D.O.; resources, M.D.O., À.N., C.G., T.E. and L.B.; data curation, M.D.O.; writing—original draft preparation, M.D.O.; writing—review and editing, M.D.O., À.N., C.G., T.E. and L.B.; visualization, M.D.O., À.N., C.G., T.E. and L.B.; supervision, À.N., C.G., T.E. and L.B.; project administration, L.B. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Data Availability Statement: No new data were created or analyzed in this study. Data sharing is not applicable to this article.

Conflicts of Interest: The authors declare no conflict of interest.

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