

# Study of the influence of alcohol on the photostability of four UV filters

C. COUTEAU<sup>1</sup>, A. PHILIPPE<sup>2</sup>, A. ALI<sup>1</sup>, M. BERNET<sup>1</sup>, M. LECOQ<sup>1</sup>,  
E. PAPARIS<sup>1</sup>, L. COIFFARD<sup>1</sup>

<sup>1</sup>Université de Nantes – Laboratoire de Pharmacie industrielle et de Cosmétologie, Faculté de Pharmacie, Nantes - France

<sup>2</sup>Université de Nantes – Laboratoire de Mathématiques Jean Leray, Faculté des Sciences et des Techniques, Nantes, France

**Abstract. – OBJECTIVE:** Spray formulations are currently under development in the field of topical photoprotection. Such forms are characterized by their high fluidity, a property that is obtained by the presence of alcohol in the formula. The purpose of this work was to study the influence of ethanol in sunscreens on the photoprotective efficacy as well as the photostability of UV filters.

**MATERIALS AND METHODS:** The filters tested were octyl methoxycinnamate (OMC), PEG-25 PABA, octyl salicylate and butyl methoxydibenzoylmethane (BMDBM) at their maximum concentration authorized by European regulations and in the presence of increasing amounts of alcohol, up to 15% (w/w).

**RESULTS:** The effect of the presence of alcohol on the efficacy of the filters and their photostability varies depending on the molecule considered. Alcohol has no effect on octyl salicylate, either on its efficacy or its photostability. However, filter stabilization is seen for BMDBM and PEG-25 PABA.

**CONCLUSIONS:** Although these differences are significant, they are not great enough to justify large-scale use of ethanol in sunscreen products due to some of its properties, such as flammability.

*Key Words:*

Sunscreens, Photostability, SPF, UVA-PF, Alcohol.

## Introduction

Skin cancer is the most common form of cancer worldwide<sup>1,2</sup>. It is classified into basal cell carcinoma (BCC), squamous cell carcinoma (SCC) and melanoma<sup>2,3</sup>. Approximately 80% of skin cancer cases are BCC, about 16% are SCC and the remaining 4% are melanomas<sup>4,5</sup>. In 2010, Narayanan et al<sup>6</sup> reported between 2 and 3 million

patients with non-melanoma skin cancer (NMSC) and 132,000 cases of melanoma worldwide. The incidence of all types of skin cancer continues to rise due to various factors. The pathogenesis of skin cancer is, in fact, multifactorial, but it is now clear that the main causative agent is ultraviolet (UV) radiation<sup>7</sup>. Ultraviolet radiation is capable of causing DNA damage, genetic mutations, immunosuppression, oxidative stress and inflammatory reactions, all of which play a significant role in photoaging of the skin and the genesis of skin cancers<sup>8</sup>. In this context, it is essential to ensure effective photoprotection during sun exposure. This relies on protective clothing and the use of sun protection products, which are part of the overall strategy for preventing skin cancers as well as photodermatoses<sup>9,10</sup>.

Sunscreen products are formulated using organic and/or mineral UV filters. In Europe, Regulation (EC) No. 1223/2009 currently authorizes 27 organic filters and two mineral filters (titanium dioxide and zinc oxide)<sup>11</sup>. Many formulations are available, including emulsions, which are more or less fluid (lotions, creams), with the more fluid forms packaged as sprays and known as sprayable forms, oils and sticks. An important property of the preparation is its photostability, which provides the user with sufficient UV protection between successive applications. The photostability of different filters is highly variable<sup>12</sup>, and excipients can play a certain role in this area. Any ingredient added to increase photostability may be of interest. We investigated forms containing alcohol, including the sprayable forms currently particularly popular with consumers<sup>13</sup>. In this regard, we studied the influence of alcohol on the photostability of four organic filters that are currently used and are characterized by their poor photostability.

## Materials and methods

### Materials

The filters tested were octyl methoxycinnamate (OMC), PEG-25 PABA, octyl salicylate and butyl methoxydibenzoylmethane (BMDBM). These were incorporated at their maximum usable dose per Regulation (EC) No. 1223/2009, i.e., 10% (w/w) for octyl methoxycinnamate and PEG-25 PABA, and 5% (w/w) for octyl salicylate and butyl methoxydibenzoylmethane, in an emulsion model whose composition has been previously described (Couteau et al<sup>12</sup>). Cetiolâ HE, stearic acid, glycerin, parabens and triethanolamin (TEA) were purchased from Cooper (Melun, France). Xanthan gum (Keltrolâ BT) was obtained from Kelco (Lille Skensved, Denmark). Up to 10% (w/w) alcohol was added to evaluate its influence on the photostability of the filters. The polymethylmethacrylate plates were purchased from Europlast (Aubervilliers, France).

### Methods

Fifty mg of product, exactly weighed, were spread over the whole surface of polymethylmethacrylate (PMMA) plates (25 cm<sup>2</sup>) using a finger coat to provide a homogenous layer over the entire plate. Three plates were prepared for each product to be tested; after the application, the plates were placed for 15 minutes in the dark at ambient temperature. The plates were irradiated for various times with a solar simulator (Suntest CPS+; Atlas, Moussy-le-Neuf, France) apparatus equipped with a xenon arc lamp (1500 W) and special glass filters restricting transmission of light below 290 nm. The temperature of the samples was kept low and constant using a tap water cooling circuit along the walls of the reactor. In order to eliminate turbulence inside the Suntest chamber, we have developed a system in our laboratory where the plates are blocked between two rails and covered with a quartz plate. The light source emission was maintained at 650 W/m<sup>2</sup> in accordance with global solar spectral irradiance at sea level, measured as specified by the International Commission on Illumination (CIE). Before and after irradiation, the SPF and UVA-PF of the creams was measured *in vitro* according to the protocol previously described. Nine measurements were performed on each plate. Transmission measurements between 290 (or 320) and 400 nm were carried out against a matching blank glycerin loaded PMMA plate using two different spectrophotometers equipped with an integrating

sphere, UV Transmittance Analyzer UV1000S and UV Transmittance Analyzer UV2000 (Lab-sphere, North Sutton, NH, USA). The minimum required dynamic range for this method is 2.2 absorbance units. The calculations for either term use the same relationship:

$$\text{SPF} = \frac{\sum_{290}^{400} E_{\lambda} S_{\lambda} \Delta\lambda}{\sum_{290}^{400} E_{\lambda} S_{\lambda} T_{\lambda} \Delta\lambda}$$

$$\text{PF} - \text{UVA} = \frac{\sum_{320}^{400} E_{\lambda} S_{\lambda} \Delta\lambda}{\sum_{320}^{400} E_{\lambda} S_{\lambda} T_{\lambda} \Delta\lambda}$$

where E is the CIE erythral spectral effectiveness, S is solar spectral irradiance, T is spectral transmittance of the sample at wavelength lambda and d is the wavelength increment (1 nm)<sup>14-16</sup>.

### Statistical Analysis

The first step of the statistical analysis consists in visualizing the data in order to highlight the effects of alcohol on the SPF and PF-UVA values. For each filter, the measurements are plotted as a function of the amounts of alcohol. We also summarize the data by the mean value with error bars representing the standard error of the mean. Then, we visualize the evolution of the mean as a function of amounts of alcohol.

Conclusions on the existence of an effect from the graphical analysis are then confirmed by statistical hypothesis tests.

For each of the filters, we want to check if the alcohol has an effect on the value of the SPF and PF-UVA. We define four groups corresponding to the amounts of alcohol: 0%, 5%, 10% and 15%. We test the hypothesis which states that the mean value is the same in all groups. This hypothesis means that the alcohol has no effect. A one-way analysis of variance is applied for testing the equality of means. This is the standard statistical method to test if the variability between the group is greater than the variability within the groups. Table I provides the result of one-way analysis of variance. If the *p*-value is less than .05, then all groups do not have the same mean at significance level 5%. In the other words the alcohol has an effect on SPF or PF-UVA. We also apply the one-way analysis of variance on three groups corresponding to the amounts of alcohol: 0%, 5% and 10% (Table II).

**Table I.** Numerical results of one-way analysis of variance for SPF or PF-UVA before irradiation [*left*] and for the difference Z (after-before) irradiation [*right*]. Comparison of the mean of 4 groups defined by their alcohol amounts: 0%, 5%,10% and 15%. The *p*-values in red indicate that there is an effect of alcohol at significance level 5%.

	Before irradiation					Difference after-before irradiation (Z)				
	df	Sumsq	meansq	Statistic	<i>p</i> -value	df	Sumsq	Meansq	Statistic	<i>p</i> -value
Octylsalicylate	3	0.116	0.039	16.288	0	3	2.061	0.687	178.085	0
Octylmethoxycinnamate	3	2.332	0.777	1.897	0.13	3	36.046	12.015	15.518	0
PEG-25 PABA	3	10.246	3.415	1090.512	0	3	5.512	1.837	445.008	0
Butylmethoxy dibenzoylmethane	3	1.664	0.554	133.375	0	3	2.419	0.806	183.371	0

We can also express the SPF and PF-UVA values as function of the amount of alcohol. We fix as reference group the one without alcohol and we write the model of the form:  $SPF = \mu + \alpha_1 \cdot 1(5\% \text{ (alcohol)}) + \alpha_2 \cdot 1(10\% \text{ (alcohol)}) + \alpha_3 \cdot 1(15\% \text{ (alcohol)}) + \text{error}$  or  $PF-UVA = \mu + \alpha_1 \cdot 1(5\% \text{ (alcohol)}) + \alpha_2 \cdot 1(10\% \text{ (alcohol)}) + \alpha_3 \cdot 1(15\% \text{ (alcohol)}) + \text{error}$ .

The parameter corresponds to the value of SPF or PF-UVA for the reference group and the  $\alpha_i$ 's represent the variation of this value with respect to the reference group. Let's take the first coefficient ( $i=1$ ) for example. It represents the variation of SPF when the amounts of alcohol vary from 0% to 5%. We test the hypothesis  $\alpha_i = 0$  against the alternative  $\alpha_i \neq 0$ . If the *p*-value is less than .05 (Table III) it means that, at significance level 0.05, the mean value of the SPF for the group with amounts of alcohol 5% is different from that of the reference group without alcohol.

For all filters, the SPF and PF-UVA values are measured before and after irradiation. Thus, we have matched samples from which we can test the stabilizing effect of alcohol. In order to analyze the evolution of the index before and after irradiation, we apply the same analysis as previously on the difference:  $Z = SPF \text{ (after irradiation)} - SPF \text{ (before irradiation)}$  or  $Z = PF-UVA \text{ (after irradiation)} - PF-UVA \text{ (before irradiation)}$ .

The one-way analysis of variance is applied to test the effect of the alcohol as well as the following model:  $Z = \mu + \alpha_1 \cdot 1(5\% \text{ (alcohol)}) + \alpha_2 \cdot 1(10\% \text{ (alcohol)}) + \alpha_3 \cdot 1(15\% \text{ (alcohol)}) + \text{error}$ .

The analysis of the data presented is performed with the R software.

## Results

We studied the influence of adding alcohol in an emulsion model, up to 15% (w/w), on the stability of the filters by looking for possible changes in the SPF and UVA-PF values for octyl methoxycinnamate, octyl salicylate, PEG-25 PABA and butyl methoxydibenzoylmethane, before and after irradiation.

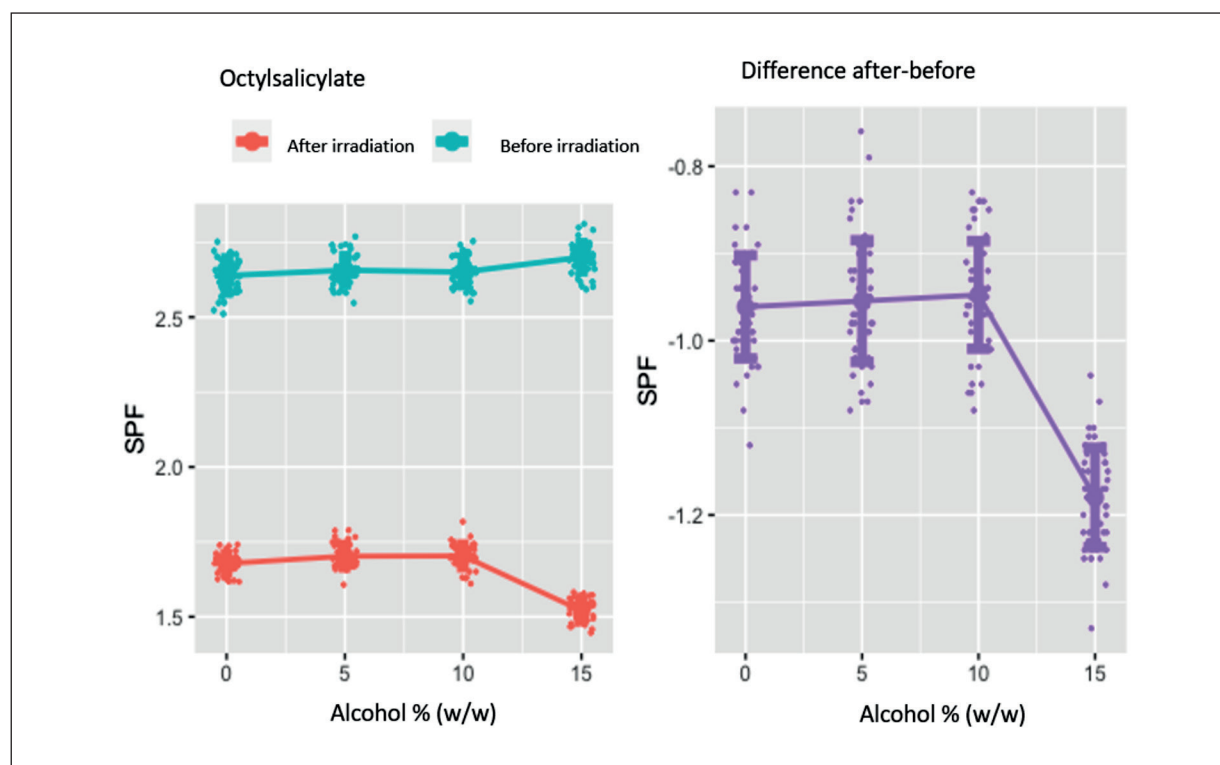
The results for octyl methoxycinnamate and octyl salicylate are shown in Figures 1 and 2 [left]. Before irradiation, it seemed that these two UVB filters behaved similarly in the presence of alcohol at the levels tested, namely 5 and 10%. If the amount of alcohol is less than 15%, then, the alcohol has no effect on SPF for octylmethoxycinnamate but it does have an effect for octylsalicylate. The presence of alcohol has no effect on the SPF value, which was not changed by the incorporation of this solvent. To evaluate

**Table II.** Numerical results of one-way analysis of variance for SPF or PF-UVA before irradiation [*left*] and for the difference Z (after-before) irradiation [*right*]. Comparison of the mean of 4 groups defined by their alcohol amounts: 0%, 5% and 10% The *p*-values in red indicate that there is an effect of alcohol at significance level 5%.

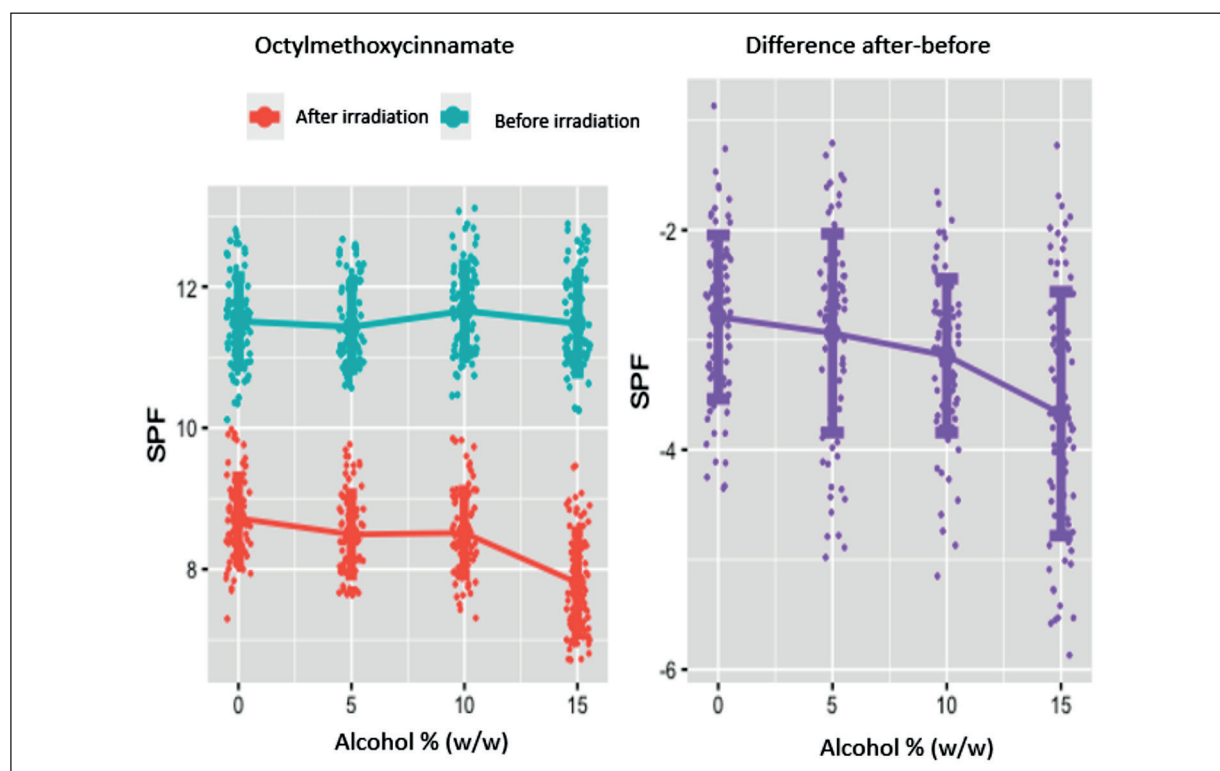
	Before irradiation					Difference after-before irradiation (Z)				
	df	Sumsq	meansq	Statistic	<i>p</i> -value	df	Sumsq	Meansq	Statistic	<i>p</i> -value
Octylsalicylate	2	0.009	0.005	1.848	0.161	2	0.005	0.003	0.625	0.537
Octylmethoxycinnamate	2	2.153	1.076	2.791	0.063	2	5.063	2.531	4.074	0.018
PEG-25 PABA	2	7.114	3.557	1085.986	0	2	4.529	2.264	582.79	0
Butylmethoxy dibenzoylmethane	2	0.866	0.433	129.78	0	2	0.706	0.353	106.14	0

**Table III.** Estimations of the parameters with the standard deviation and the  $p$ -value of  $t$ -test for SPF or PF-UVA before irradiation [left] and for the difference  $Z$  (after-before) irradiation [right].

	Before irradiation			Difference after-before irradiation		
	Estimate	Std.error	$p$ -value	Estimate	Std.error	$p$ -value
<b>Octylsalicylate</b>						
(Intercept) $\mu$	2.639	0.007	0	-0.961	0.008	0
(Alcohol 5%) $\alpha_1$	0.018	0.009	0.057	0.007	0.012	0.578
(Alcohol 10%) $\alpha_2$	0.012	0.009	0.207	0.014	0.012	0.253
(Alcohol 15%) $\alpha_3$	0.061	0.009	0	-0.219	0.012	0
<b>Octylmethoxycinnamate</b>						
(Intercept) $\mu$	11.512	0.071	0	-2.791	0.098	0
(Alcohol 5%) $\alpha_1$	-0.082	0.101	0.418	-0.147	0.138	0.288
(Alcohol 10%) $\alpha_2$	0.146	0.101	0.148	-0.352	0.138	0.011
(Alcohol 15%) $\alpha_3$	-0.033	0.101	0.744	-0.880	0.138	0
<b>PEG-25 PABA</b>						
(Intercept) $\mu$	3.045	0.008	0	-0.925	0.009	0
(Alcohol 5%) $\alpha_1$	0.024	0.011	0.029	0.333	0.012	0
(Alcohol 10%) $\alpha_2$	0.456	0.011	0	0.373	0.012	0
(Alcohol 15%) $\alpha_3$	0.438	0.011	0	0.391	0.012	0
<b>Butylmethoxy dibenzoylmethane</b>						
(Intercept) $\mu$	2.856	0.012	0	-1.636	0.013	0
(Alcohol 5%) $\alpha_1$	-0.182	0.018	0	0.182	0.018	0
(Alcohol 10%) $\alpha_2$	-0.244	0.018	0	0.211	0.018	0
(Alcohol 15%) $\alpha_3$	-0.340	0.018	0	0.422	0.018	0



**Figure 1.** Evolution of the SPF as a function of the alcohol level before and after irradiation [left] and the difference ( $Z$  value) [right] for octylsalicylate.



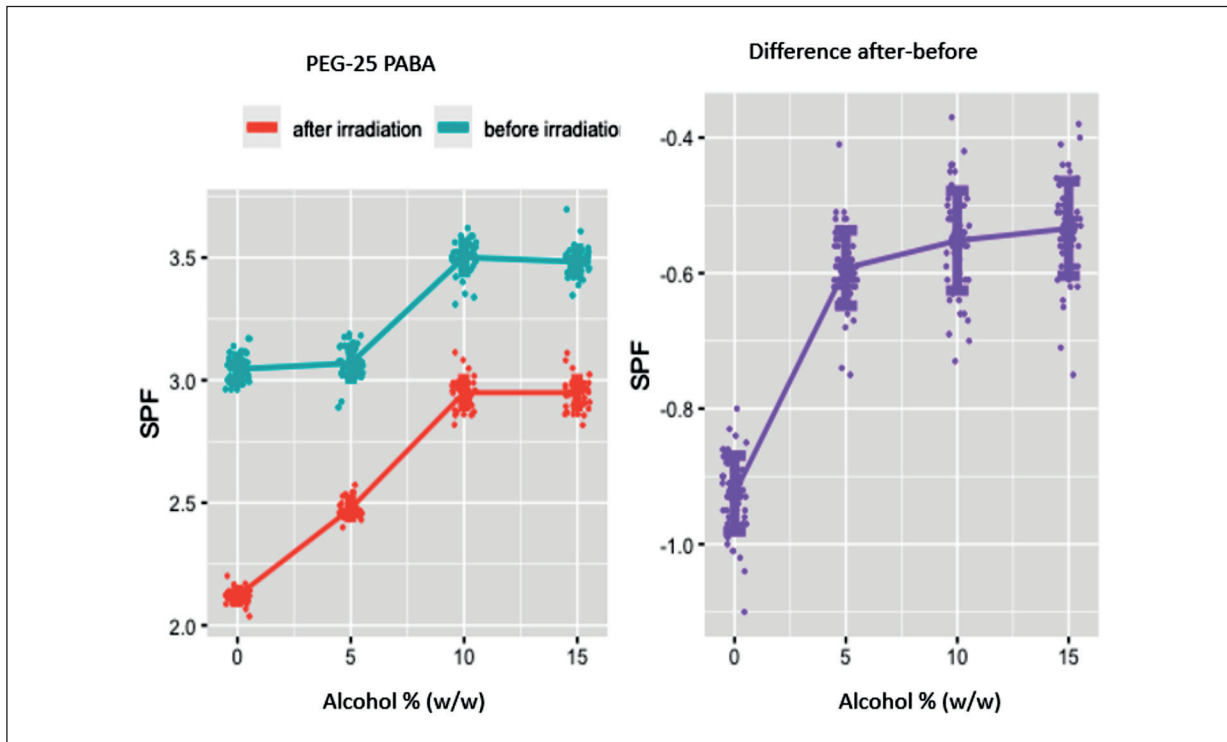
**Figure 2.** Evolution of the SPF as a function of the alcohol level before and after irradiation [left] and the difference (Z value) [right] for octyl methoxycinnamate.

the influence of alcohol on the photostability of the filters, we considered the Z variable = SPF (after irradiation) – SPF (before irradiation) (Figures 1 and 2 [right]). The difference before and after irradiation (Z) is significant. The SPF value decreased after exposure, since both these filters are known to be photolabile<sup>12,17</sup>. The presence of alcohol had no effect on the photostability of octyl salicylate (except for the amounts of 15%), and the decrease in SPF after irradiation is consistent, regardless of the ethanol content. In contrast, in the case of octyl methoxycinnamate, alcohol potentiates the UV effect on the filter. Alcohol also had a significant effect on the value of the Z difference. There is a greater decrease in the SPF as the percentage of alcohol increases. This could be explained by a ratio of *trans* and *cis* isomers at the photostationary state, which depends on the solvent due to variations in the quantum isomerization yield<sup>18</sup>.

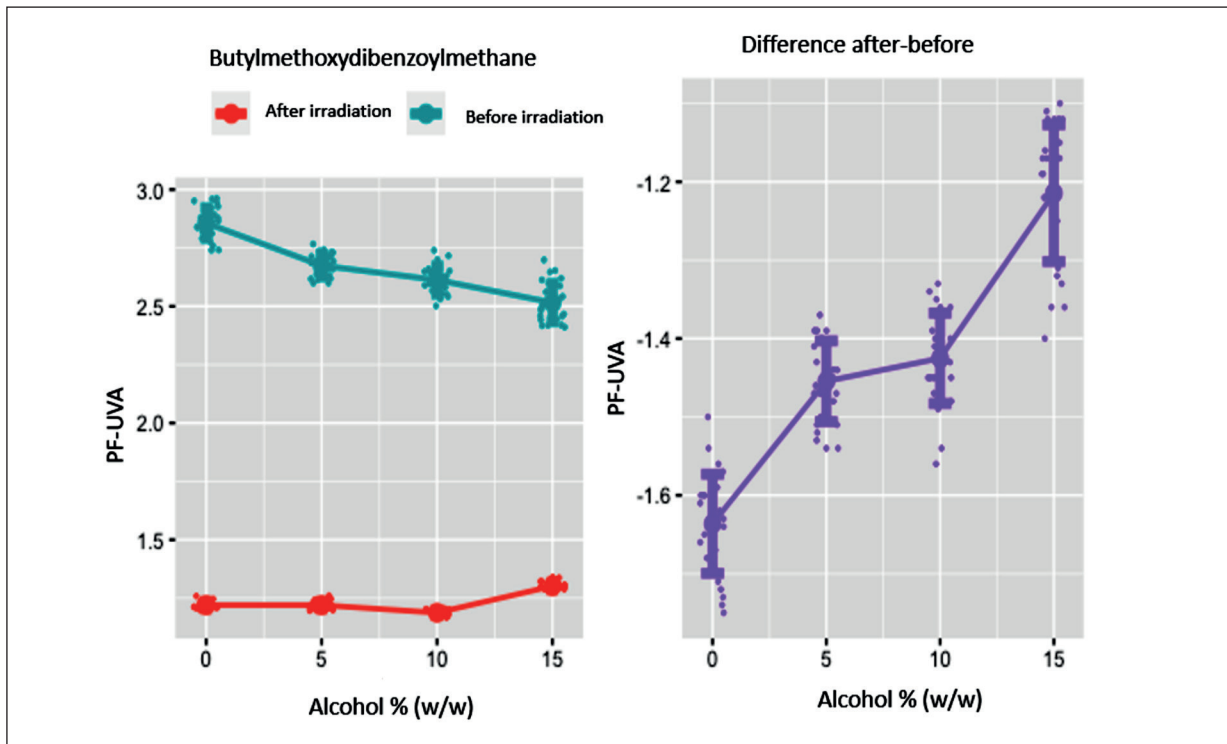
The results for PEG-25 PABA are shown in Figure 3. In this case, alcohol has an effect on the performance of the filter and this effect is nonlinear. The difference before and after irradiation (Z) was evaluated, and we observed that

the presence of alcohol had a significant effect on its value. The demonstrated SPF decrease is less marked as the percentage of alcohol increases in the emulsion. As the maximum authorized dose for this filter in Europe is 5%, there is a dose-response relationship regarding the influence of the solvent on the filter, with the effect of the alcohol being stronger since it is present in excess compared with that of the filter. As this compound is a polyoxyethylated ester of *p*-aminobenzoic acid, it is one of the rare water-soluble filters. Given that ethanol is a polar solvent, its addition will cause an increase in the polar phase of the emulsion and may result in hydrolysis, leading to transformation into para-aminobenzoic acid, which has greater photostability.

With regard to butyl methoxydibenzoylmethane, alcohol was found to have an effect on the PF-UVA value (Figure 4). The presence of ethanol negatively influences the performances of this filter with respect to UVA. As with the UVB filters studied, we then evaluated the effect of alcohol on the photostability of this UVA filter. To do this, we studied the influence of alcohol on the difference between the PF-UVA values



**Figure 3.** Evolution of the SPF as a function of the alcohol level before and after irradiation [left] and the difference (Z value) [right] for PEG-25 PABA.



**Figure 4.** Evolution of the PF-UVA as a function of the alcohol level before and after irradiation [left] and the difference (Z value) [right] for butylmethoxydibenzoylmethane.

before and after irradiation. The difference is significant, and alcohol plays a photostabilizing role for BMDBM. When the percentage of alcohol increases in the emulsion, there is a decrease in the loss of PF-UVA units. It has been demonstrated that the photostability of avobenzone is related to the environment in which it is found, being relatively stable in polar protic solvents and considerably photolabile in non-polar media<sup>19,20</sup>. The presence of alcohol in the medium is therefore favorable to its stability.

Before irradiation the results obtained by the one-way analysis of variance are confirmed by the results of modelling (Table III). For octylsalicylate, it means that alcohol has no effect. For octylmethoxycinnamate, we have and is different from zero. This confirms the existence of a significant effect of alcohol only on the 15% group. For butylmethoxy dibenzoylmethane and PEG-25 PABA all the parameters are different from zero, and so there is a significant effect of alcohol. For all filters, is different from 0 there is an effect on the irradiation and the sign of the parameter indicates a decrease of SPF or FP-UVA. For butylmethoxydibenzoylmethane and PEG-25 PABA all the parameters are different from zero, and so there is a significant effect of alcohol. The parameters are positive, it means that the decrease is less important compared to the reference group (0%). For octylsalicylate and is different from zero. There is a significant effect of alcohol for the 15% group. This decrease is more important in the presence of alcohol compared to the reference group (0%). For octylmethoxycinnamate we have and are different from zero. There is a significant effect of alcohol for the 15% and 10% groups. This decrease is more important in the presence of alcohol compared to the reference group (0%).

## Discussion

Three of the four filters studied are UVB filters. Only butylmethoxydibenzoylmethane is a UVA filter.

As the addition of alcohol reduces the viscosity of the preparations, it is especially used in spray formulations. In the case of the filters studied, the effects are variable and depend on the molecule tested, considering that we voluntarily selected these from four different chemical families. We observed that the presence of alcohol had no effect in the medium on the performances of OMC

or octylsalicylate, a positive effect for PEG-25 PABA and a negative effect for BMDBM. It is of note that even though the effect observed with PEG-25 PABA is significant, it remains weak (less than 1 SPF unit gained) and will therefore have no impact on the SPF. Similarly, the effect of the presence of alcohol on the photostability of the filters differs according to the molecule considered. In the case of octyl salicylate, alcohol does not modify the photostability of this UVB filter. In contrast, there is accentuated photodegradation of OMC and stabilization of PEG-25 PABA and BMDBM. However, once again, it should be noted that although these effects are significant, they remain minimal and there will be no impact on the final SPF of the formulation. Indeed, we recall here that the only SPFs that can be displayed on sunscreen products are 6, 10, 15, 20, 25, 30, 50 and 50+ (if the experimentally determined SPF is  $\geq 60$ )<sup>21</sup>. A gain in efficacy of a half to one whole SPF unit therefore has no impact on the protection of the product user. Our tests show that alcohol is not essential for photostabilization of UV filters in sunscreen products, especially since it is a penetration enhancer<sup>22,23</sup>. This is an unwanted phenomenon since UV filters, such as butylmethoxydibenzoylmethane, show increased transdermal penetration, known as passing the skin barrier<sup>24</sup>.

In addition, it seems difficult for the user to know whether they have applied a sufficient quantity of the product when it is a very fluid formula containing alcohol<sup>25</sup>. It appears that consumers tend to put less product on their skin<sup>26</sup>, which is detrimental to them in terms of protection since the level attained depends on the amount of product applied to the epidermis<sup>27</sup>.

Lastly, with regard to alcohol, it is important to remember its highly flammable nature. Cases of serious adverse reactions have already been reported following the use of sunscreens with alcohol packaged in the form of sprays. For example, in 2012, an American, Brett Sigworth, suffered serious burns while cooking a barbecue in his yard after having applied this type of product<sup>28</sup>.

## Conclusions

It therefore seems that the presence of alcohol in sunscreen products causes more problems than it solves in terms of improving the formulation. Combining molecules remains the best solution

at this time for stabilizing the filters<sup>29</sup>, which is required to obtain high indexes and broad photoprotection as required by the 2006 recommendations. The originality of our work demonstrates the uselessness of alcohol in sunscreens, especially since it has undesired properties.

### Conflict of Interest

The Authors declare that they have no conflict of interests.

### References

- 1) Fabris MR, Duraes ES, Martignago BC, Blanco LF, T.R. Fabris TR. Assessment of knowledge of skin cancer prevention and its relation with sun exposure and photo protection amongst gym academy members on the south of Santa Catarina, Brazil. *An Bras Dermatol* 2012; 87: 36-43.
- 2) Schierbeck J, Vestergaard T, Bygum A. Skin Cancer Associated Genodermatoses: A Literature Review. *Acta Derm Venereol* 2019; 99: 360-369.
- 3) Gordon R. 2013. Skin cancer: an overview of epidemiology and risk factors. *Semin Oncol Nurs* 2013; 29: 160-169.
- 4) Brandt MG, Moore CC. Nonmelanoma Skin Cancer. *Facial Plast Surg Clin North Am* 2019; 27: 1-13.
- 5) Einspahr JG, Stratton SP, Bowden GT, Alberts DS. Chemoprevention of human skin cancer. *Crit Rev Oncol Hematol* 2002; 41: 269-285.
- 6) Narayanan DL, Saladi RN, Fox JL. Ultraviolet radiation and skin cancer. *Int J Dermatol* 2010; 49: 978-986.
- 7) Kornek T, Augustin M. Skin cancer prevention. *J Dtsch Dermatol Ges* 2013; 11: 283-296.
- 8) Maden V, Leah JT, R.M. Szeimies RM. Non-melanoma skin cancer. *Lancet* 2010; 375: 673-685
- 9) Keeney S, McKenna H, Fleming P, McIlpatrick S. Attitudes, knowledge and behaviours with regard to skin cancer: A literature review. *Eur J Oncol Nurs* 2009; 13: 29-35.
- 10) Yeager DG, Lim HW. What's New in Photoprotection: A Review of New Concepts and Controversies. *Dermatol Clin* 2019; 37:149-157.
- 11) Regulation (EC) N° 1223/2009 of the European Parliament and the Council of 30 November 2009 on cosmetic products.
- 12) Couteau C, Faure A, Fortin J, Papis E, Coiffard LJM. Study of the Photostability of 18 Sunscreens in Creams by Measuring the SPF in Vitro. *J Pharm Biomed Anal* 2007; 44: 270-273.
- 13) Teplitz RW, Glazer AM, Svoboda RM, Rigel DS. 2018. Trends in US sunscreen formulations: impact of increasing spray usage. *J Am Acad Dermatol* 2018; 78: 187-189.
- 14) Sayre RM, Agin PP, LeVee GJ, Marlowe E. A comparison of in vivo and in vitro testing of sun-screening formulas. *Photochem Photobiol* 1979; 29: 559-566.
- 15) Couteau C, Pommier M, Papis E, Coiffard LJM. Study of the efficacy of 18 sun filters authorized in European Union tested in vitro. *Pharmazie* 2007; 62: 449-452.
- 16) Couteau C, El-Boury S, Papis E, Sébille-Rivain V, Coiffard LJ. In vitro UV-A protection factor (PF-UVA) of organic and inorganic sunscreens. *Pharm Dev Technol* 2009; 14: 369-372.
- 17) Freitas JV, Lopes NP, Gaspar LR. Photostability evaluation of five UV-filters, trans-resveratrol and beta-carotene in sunscreens. *Eur J Pharm Sci* 2015; 78:79-89.
- 18) Hanson KM, Narayanan S, Nichols VM, Bardeen CJ. Photochemical degradation of the UV filter octyl methoxycinnamate in solution and in aggregates. *Photochem Photobiol Sci* 2015; 14:1607-1616.
- 19) Matheny R, Lindemann S, Cho CG, Jiang P. Photodecomposition of several compounds commonly used as sunscreen agents. *J Photochem Photobiol A Chem* 1994; 80: 417-421.
- 20) Andrea I, Bringham A, Böhm F, Gonzenbach H, Hill T, Mulroy L, Truscott TG. A UVA filter (4-tert-butyl-4'-methoxydibenzoylmethane): photoprotection reflects photophysical properties. *J Photochem Photobiol B Biol* 1997; 37: 147-150.
- 21) Commission recommendation of 22 September 2006 on the efficacy of sunscreen products and the claims made relating thereto. Available from: <https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2006:265:0039:0043:en:PDF>.
- 22) Williams AC, Barry BW. Penetration enhancers. *Adv Drug Deliv Rev* 2004; 56: 603-618.
- 23) Cosmetic Ingredient Review Expert Panel. Final report of the safety assessment of Alcohol Denat., including SD Alcohol 3-A, SD Alcohol 30, SD Alcohol 39, SD Alcohol 39-B, SD Alcohol 39-C, SD Alcohol 40, SD Alcohol 40-B, and SD Alcohol 40-C, and the denaturants, Quassin, Brucine Sulfate/Brucine, and Denatonium Benzoate. *Int J Toxicol* 2008; 27 Suppl 1: 1-43.
- 24) Matta MK, Zusterzeel R, Pilli NR, Patel V, Volpe DA, Florian J, Oh L, Bashaw E, Zineh I, Sanabria C, Kemp S, Godfrey A, Adah S, Coelho S, Wang J, Furlong LA, Ganley C, Michele T, Strauss DG. Effect of Sunscreen Application Under Maximal Use Conditions on Plasma Concentration of Sunscreen Active Ingredients: A Randomized Clinical Trial. *JAMA* 2019; 321: 2082-2091.
- 25) Barr J. Spray-on sunscreens need a good rub. *J Am Acad Dermatol* 2005; 52: 180-181.
- 26) Sohn M, Herzog B, Osterwalder U, Imanidis G. Calculation of the sun protection factor of sunscreens with different vehicles using measured



- film thickness distribution — Comparison with the SPF in vitro. *J Photochem Photobiol B: Biol* 2016; 159: 74-81.
- 27) Couteau C, Paparis E, El-Bourry-Alami S, Coiffard LJ. Influence on SPF of the quantity of sunscreen product applied. *Int J Pharm* 2012; 43: 250-252.
- 28) Sunscreen Maker Promises Investigation After Stow Man Catches Fire. Available from: <https://boston.cbslocal.com/2012/06/02/sunscreen-maker-promises-investigation-after-stowe-man-catches-fire/>.
- 29) Chatelain E, Gabard B. Photostabilization of butyl methoxydibenzoylmethane (Avobenzone) and ethylhexyl methoxycinnamate by bis-ethylhexyloxyphenol methoxyphenyl triazine (Tinosorb S), a new UV broadband filter. *Photochem Photobiol* 2001; 74: 401-406.