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Photostability of commercial sunscreens upon sunlight exposure

Fotoestabilidade de protetores solares comerciais expostos a radiação solar

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ABSTRACT

Introduction: The use of sunscreens is recommended to reduce skin damage and prevent skin cancer. However, evidence has shown that sunscreen can undergo degradation processes induced by ultraviolet (UV) radiation which can lead to reduction or loss of photoprotective capacity, generation of free radicals and toxic intermediates which react with skin structures generating biological damage. **Objective:** To evaluate the photostability of four sunscreen formulations with Sun Protection Factor (SPF) 30 added by different chemical and physical UV filters. **Material and Methods:** Each product was exposed to solar radiation from 10 a.m. to 15 p.m. (UV index: 6.0). The areas under the curves (AUC) of the absorbance spectrum of the formulations before and after radiation exposure were used to calculate the ratio between the AUC before and after the solar radiation (AUCI). **Results:** Only two formulations, which presented the AUCI higher than 0.8, were considered photostable. Despite having the same SPF 30, formulations showed different absorption spectrum in regions of UVA1, UVA2 and UVB and the photostability of the products tested varied considerably. **Conclusion:** The development of photostable formulations is critical because degradation products of UV filters can act as photo-oxidants. Furthermore, increased exposure to UV radiation due to the reduction of the photoprotective capacity of unstable products increases the risk of burns and skin cancer.

Palavras-chave: Sunscreenig Agents; Ultraviolet Filters; Cosmetic Stability; Photodegradation.

RESUMO

Introdução: O uso de protetores solares é recomendado para reduzir os danos na pele e na prevenção do câncer de pele. No entanto, tem sido demonstrado que os filtros solares podem sofrer processos de fotodegradação induzidos pela radiação ultravioleta (UV), podendo levar a redução da capacidade fotoprotetora, geração de radicais livres e produtos intermediários tóxicos que podem reagir com as estruturas da pele causando danos biológicos. **Objetivo:** Avaliar a fotoestabilidade de quatro formulações fotoprotetoras com fator de proteção solar (FPS) 30 adicionados de diferentes filtros UV químicos e físicos. **Material e Métodos:** Cada produto foi exposto a radiação solar entre 10h e 15h (Índice UV: 6.0). As áreas sobre as curvas (ASC) dos espectros de absorção das formulações antes e após a exposição à radiação foram utilizados para calcular a relação entre a ASC antes e após a radiação solar. **Resultados:** Somente duas formulações, que apresentaram o índice de área sobre a curva (IASC) maior que 0.8, foram consideradas fotoestáveis. Os resultados mostraram que apesar das formulações possuírem o mesmo FPS 30, apresentaram diferentes espectros de absorção nas regiões do UVA1, UVA2 e UVB e que a fotoestabilidade das formulações testadas variou consideravelmente. **Conclusão:** O desenvolvimento de formulações fotoestáveis é uma etapa crítica uma vez que os produtos de degradação dos filtros UV podem agir como foto-oxidantes. Além disso, o aumento da exposição à radiação UV devido a redução da capacidade fotoprotetora de formulações instáveis aumenta o risco de queimaduras e câncer de pele.

Key-words: Protetores Solares; Filtros Ultravioleta; Estabilidade de Cosméticos; Fotodegradação.

INTRODUCTION

Although ultraviolet radiation (UVR) plays crucial role to human health, especially with regard to the biosynthesis of vitamin D,[1] protection against this radiation is extremely important to prevent skin damages such as sunburn, photoaging, and skin cancer.[2-5]

The disease attributable to sun exposure to UVR corresponds to 0.1% of global disease and is associated with a large part of the individual's morbidity and mortality exposed to UVR. Skin cancer is the main damage resulting from this exposure but this risk factor can be reduced with preventive actions (sun exposure in periods of lower incidence, use of appropriate clothing and accessories) and especially, the use of broad spectrum sunscreens with reapplication.[1,6-8] In this sense, the use of UV-filters incorporated in sunscreen formulations is the most indicated method for preventing skin injury induced by sun over-exposure.[1,9,10-12,13]

Sunscreens are photochemical systems containing UV active substances capable of absorbing, reflecting and/or dispersing the radiation that penetrates the skin. These substances can be divided into organic and inorganic filters.[14,15] Typically, the organic filters are called chemical filters, as their mode of action is related to chemical changes in their molecules that prevent UV radiation reaching the skin. On the other hand, the inorganic UV filters are called physical, since their mode of protection against solar radiation is associated with physical phenomena, such as scattering and reflection of UVR.[16,17]

Solar radiation is composed of 56% of the infrared light (> 780 nm), 39% visible light (400-780 nm) and 5% by ultraviolet (UV) light (100-400 nm). UVR is subdivided into ultraviolet C (UVC, 100-280 nm), ultraviolet B (UVB, 290-320 nm) and ultraviolet A (UVA, 320-400 nm).[16,18,19] The ozone and other gases of the atmosphere absorbs 100% of UVC radiation (not reaching the earth's surface), approximately 90% of UVB radiation and practically does not absorbs the UVA radiation.[18-21] The UVB component is the most energetic and harmful portion of UVR, act mainly on the most superficial layer of the skin (epidermis), and the UVA deeply penetrate the epidermal and dermal layers of the skin causing cellular damage mediated by reactive oxygen species (ROS).[9,22-24]

It is important to emphasize to consumers the necessity of sunscreens that offer broad-spectrum protection, with coverage of both UVA and UVB radiation. The main UV filters used in cosmetic formulations belonging to the class of para-amino benzoates (PABA), salicylates, cinnamates, benzophenones, dibenzoyl methanes, camphor derivatives, and inorganic particulates.[14]

The National Health Surveillance Agency (ANVISA) is the Brazilian regulatory agency that is responsible for the regulation of sunscreen in cosmetics, through a Resolution RDC nº 30, of June 1, 2012.[25] The regulation applies rules for the classification of the degree of SPF; establish *in vivo* methods for determination of SPF and protection against UVA radiation, water resistance tests and labeling requirements for sun protection products. However, the regulation does not describes tests for assessing the stability of photoprotective formulations when exposed to solar radiation.

Studies have shown that when exposed to RUV, some UV filters may undergo spectral changes or act as photooxidants producing reactive compounds (free radicals and ROS). These reactive substances can interact with other components of the formulation when they come into direct contact with the skin and result in by-products without sunscreen effectiveness.[26,27]

There is a substantial literature on measurement of photostability behaviour of isolated UV-filter and sunscreen formulations upon UV radiation employing several solar simulator apparatus.[4,15,28-33] However, studies with artificial UV light source do not produce the level of sunscreen instability as does the natural sunlight.[26] Despite this, few papers appear to focus on the sunscreens' photoinstability upon outdoor sunlight exposure.[26,34-36]

Therefore, the aim of this study was to assess the photostability of four commercial products containing UV-filters after exposure to natural sunlight irradiation. Additionally, the present research presents a simple and low cost methodology that can be used at the development of the formulations step in order to help in the direction of more stable and safe formulations.

MATERIAL AND METHODS

Sunscreen formulations

Four products (SPF = 30) containing different UV filter associations most commonly used commercially were selected (convenience sampling) (table 1). Three formulations (F1, F2, F3) were purchased from local handling pharmacies in Juiz de Fora (Minas Gerais, Brazil) and one industrialized formulation (F4) was purchased from local drugstore in the same city. All analyzes were performed within the expiration dates of the formulations declared on their labels. The formulations obtained from handling pharmacies presented 3 months of expiration date and the industrialized one had an expiration date of 2 years.

Sample preparation and UV irradiation

Identical quantities of each product (32 mg) was applied and carefully spread onto a 16cm^2 area of a glass plate, corresponding to a 2.0 mg/cm^2 area density according to the European Cosmetic, Toiletry and Perfumery Association (COLIPA) guidelines

Table 1: Photoactive compounds in investigated sunscreen products having the same label SPF 30.

Sunscreen	Photoactive ingredient (INCI name abbreviation)	UV absorption	Chemical or Physical UV filter
F1	MBBT	UVA/UVB	Chemical
	BEMT	UVA/UVB	Chemical
F2	EHMC	UVB	Chemical
	BP-3	UVA/UVB	Chemical
	TiO_2	UVA/UVB	Physical
F3	EHMC	UVB	Chemical
	BMBM	UVA	Chemical
	EHS	UVB	Chemical
F4	OCR	UVB	Chemical
	BMBM	UVA	Chemical
	EHT	UVB	Chemical
	BEMT	UVA/UVB	Chemical
	TiO_2	UVA/UVB	Physical

MBBT: methylene bis-benzotriazolyl tetramethylbutylphenol (CAS 103597-45-1); BEMT: bis-ethylhexyloxyphenol methoxyphenyl triazine (CAS 187393-00-6);EHMC: ethylhexyl methoxycinnamate (CAS 5466-77-3);BP-3: benzophenone-3 (CAS 131-57-7);TiO_2: titanium dioxide (CAS 13463-67-7);BMBM: butyl methoxydibenzoylmethane (Avobenzone) (CAS 70356-09-1);EHS: ethylhexyl salicylate (CAS 118-60-5); OCR: octocrylene (CAS 6197-30-4); EHT: ethylhexyl triazone (CAS 88122-99-0).INCI: international nomenclature of cosmetic ingredients; CAS: chemical abstracts service number.

recommended concentration.[37] Then, the plates were dried form 15 min protected from light sources. Every sunscreen product under study was exposed for the same time to a natural sunlight from 10 a.m. to 15 p.m. The outdoors exposure was performed during a clear sunny day in late May, in Juiz de Fora city, latitude 21º46´39.0´´S, longitude 43º22´00.7´´W and altitude 796.89 m above sea level. Maximum of the daily temperature was 22ºC, and the UV Index forecast for the experimental day by National Institute of Space Research was 6.0, considered as high.[38] Control plates of each product were maintained protected from natural and artificial light sources. All exposures were performed in duplicate.

After that, exposed and non-exposed formulations were diluted in ethanol to reach a final concentration of 0.2 mg/mL. To obtain the absorption spectra, the solutions were analyzed in a spectrophotometer (Micronal B582, São Paulo, Brazil) in the wavelength range of 290-400 nm.[39]

Area under de curve index (AUCI)

The areas under the curves (AUC) of absorbance vs. wavelength before and after sunlight exposure were calculated for total UV spectrum (290-400 nm), UVA1 (340-400 nm), UVA2 (320-340 nm), and UVB (290-320 nm). If the area under the curve index (AUCI = AUC_{after}/ AUC_{before}) was higher than 0.8 the sunscreen product was considered photostable.[36] Determinations of AUC were performed using the GraphPad Prism® version 8.0.1 (GraphPad®, San Diego, CA, USA).

RESULTS

Considering the areas under the curves in the absorption spectra (290-400 nm), we observed that the F4 formulation provided the greatest absorption of irradiation (AUC=95.43), followed by formulations F1 (AUC=73.42), F3 (AUC=65.99), and F2 (AUC=63.66) (table 2).

Only formulations F1 and F4 were considered photostable, since they presented AUCI higher than 0.8, of (0.91 and 0.96, respectively). F4 formulation, the industrialized one, presented the highest absorption of UV radiation in the range of 290-400 nm. Also, it was considered the most photostable of all the formulations analyzed, being stable in the UVB (AUCI= 1.00), UVA2 (AUCI = 0.96) and UVA1 ranges (AUCI = 0.92).

DISCUSSION

Despite all commercial formulations had the same SPF of 30 stated on their labels and the same form (lotion), they had different UV absorption spectra and the photostability of the sunscreens tested varies considerably. It can be seen that they do not promote the same photoprotective efficiency. Two of the four formulations investigated in the present study showed to be photounstable, presenting significant changes in their UV absorption spectra after sunlight exposure.

Our results corroborate with previous studies that also evaluated the photostability of sunscreens with the same SPF using different UVR sources. Romanhole et al[18] studied four sunscreens formulations after exposure

Table 2: Summary of the AUC and AUCI values for the investigated sunscreens.

	UV 290-400 nm			**UVA1** 340-400 nm			**UVA2** 320-400 nm			**UVB** 290-320 nm		
	AUC before	**AUC** after	**AUCI**	**AUC** before	**AUC** after	**AUCI**	**AUC** before	**AUC** after	**AUCI**	**AUC** before	**AUC** after	**AUCI**
F1			0.91	30.87	27.23	0.88	18.65	16.84	0.90	23.90	22.47	0.94
F2			**0.57**	2.63	2.09	**0.79**	16.20	8.81	**0.54**	44.83	25.28	**0.56**
F3			**0.29**	10.29	0.48	**0.05**	15.28	3.66	**0.24**	40.42	13.68	**0.34**
F4		91.8	0.96	36.57	36.65	1.00	20.35	19.62	0.96	38.52	35.52	0.92

The AUCI is defined as AUCa$_{fter}$/AUC$_{before}$. The bold numbers show when AUC is < 0.80 (photounstable).

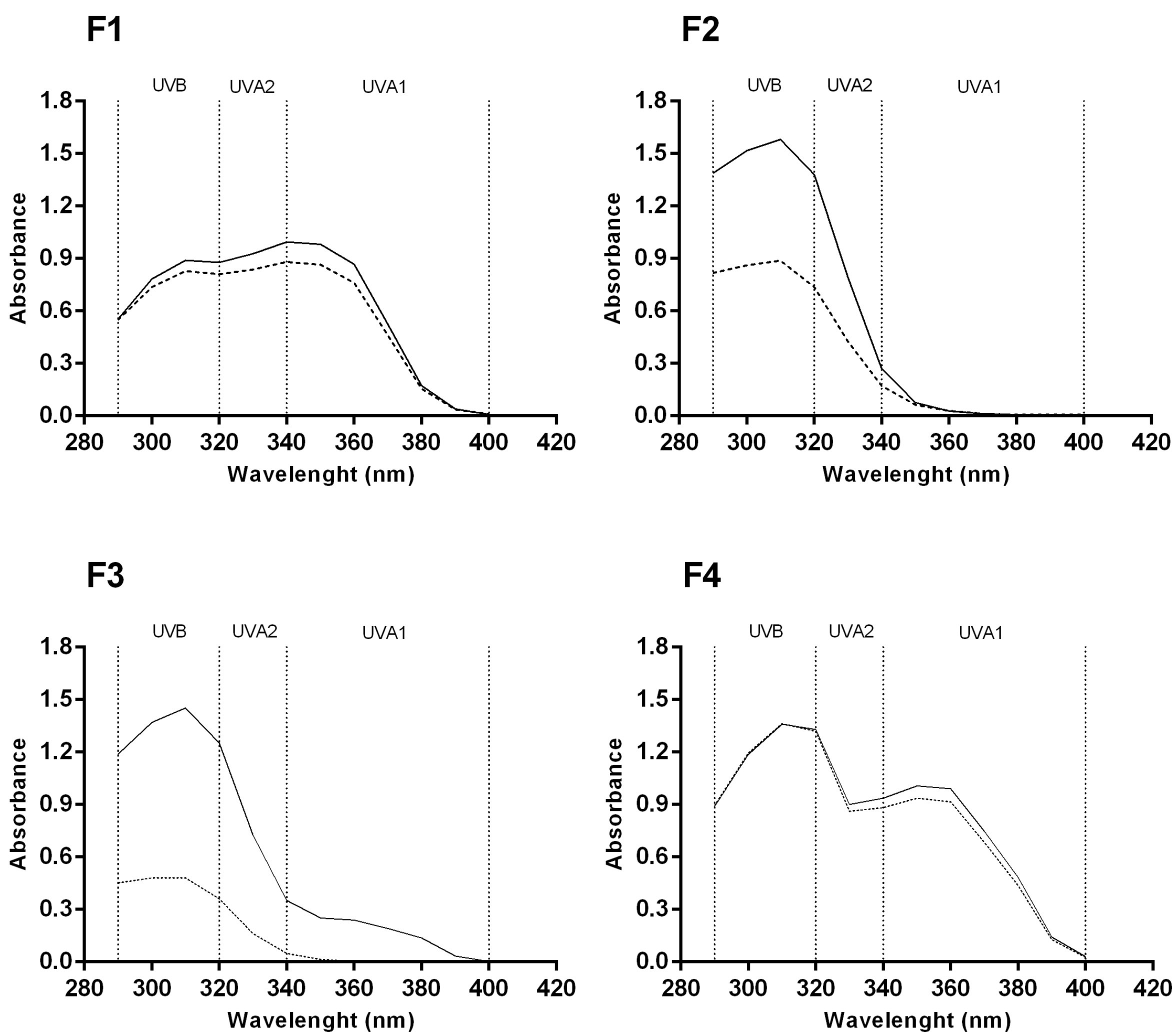

Figure 1: UV absorbance profiles (290-400 nm) of 0.2 mg/mL ethanolic solutions of F1, F2, F3 and F4 sunscreen formulations before (full line) and after (dashed line) sunlight exposure.

to fluorescent indoors light radiation such as from light emitted by commercial lamps present in homes and offices. They found that three formulations did not show photostability, suffering significant changes in their UV absorption spectra, and only one of the selected formulations were considered photostable.

Gonzalez et al[36] investigated the photostability of seven commercial sunscreens products after natural and artificial UV exposure. Several products were photountable. Most sunscreens offered good protection against UVB while the UVA photostability of some products decreased substantially during UV exposure.

Studies also carried out using natural sunlight showed that seven products out of a total of fifteen evaluated exhibited photoinstability in the total UV range.[26] Another study that investigated sunscreens photostability after irradiation with light simulating the sun radiation showed that only seven products meet SPF requirements after irradiation from set of 20 tested sunscreens.[30]

Considering the formulations evaluated in the present study, F4 contains multiple UV filters in combination (OCR, BMBM, EHT, BEMT, and TiO_2), which may have contributed for stabilization of the formulation. Formulation 4 contains the physical filter (TiO_2) considered photostable and more effective in photoprotection than zinc oxide when associated with organic UV filters.[15] In general, sunscreen with TiO_2 particles seem to be more photostable.[36] It`s photoprotection occur by reflecting the UV radiation. The filter BEMT is considered a stable and a broad band absorber and together with OCR helps to stabilize BMBM (avobenzone), a photolabile UV filter.[12,40] Studies showed that the presence of the OCR and BEMT filters in sunscreen formulations were able to reduce the photodegradation of BMBM by 40% and 27%, respectively.[12]

Formulation F1 were stable in UVA1 (AUCI = 0.88), UVA2 (AUCI= 0.90), and UVB (AUCI= 0.94) ranges. The mixture of MBBT and BEMT filters present in this formulation was expected to be photostable. The MBBT and BEMT exhibit excellent photostability since it has the ability to undergo reversible isomerization (tautomerism) via the orthohydroxy group resulting in hydrogen bonds that guarantee stability.[40] These UV filters present broad UVB and UVA absorbance. The BEMT filter is considered the most efficient broad-spectrum absorber and the addition of low concentration of MBBT is capable of reaching the critical wavelength of 370 nm.[40]

The formulations F2 and F3, which presented AUCI of 0.57 and 0.29 respectively, were unstable after 5 h of natural sunlight exposition. The formulation F3 was the most photounstable, showing total UV protection reduction of 72.98%, suggesting high degradation of UV filters in the range of UVA1 (AUCI= 0.05), UVA2 (AUCI= 0.24) and UVB (AUCI= 0.34). It is important to emphasize that this formulation offers a low protection against UVA1 radiation, due the small area under the curve observed in the spectrum of the unexposed formulation. Since this formulation is not added to physical filters that could protect the skin by reflection of the radiation, it can be concluded that this formulation does not offer a broad spectrum protection.

The photounstable behavior of F3 formulation could be explained mainly by the combination of BMBM and EHMC that present a great challenge for stabilization.[41] Studies have shown that BMBM degradation increases in the presence of EHMC.[42] Under UV exposure, these filters engage in a reaction known as the De Mayo reaction, which consists in a reaction of an enol with an alkene to produce a [2+2] cycloaddition followed by a retro aldol cleavage. In this reaction it was observed the intermolecular triplet-triplet energy transfer from BMBM to EHMC, photodegrading both compounds and producing reactive species.[41-43]

Moreover, avobenzone (BMBM) is one of the most common UVA-filters in sunscreens and is known to be photounstable.[44-46] In its enol form it exhibits an excellent UVA absorption at 357 nm but in its diketo form its absorption is in the UVC region and thereby ineffective as a UVA or UVB filter. In addition, it has been reported to fragment when exposed to UV radiation into reactive species.[15,44,47]

In this sense, octocrylene (OCR), among other triplet quenchers like methylbenzylidene camphor, is the most effective at stabilizing avobenzone.[30] Despite this, no stabilizer was added to the formulation 3 in order to improve avobenzone photostability. Thus, the decrease in absorption after exposure of F3 may also be related to photodegradation of BMBM.

The F2 formulation, also considered photounstable (AUCI= 0.57), showed a total reduction in UV protection capacity of 43.16%, with the highest photoinstability in the UVA2 range (AUCI= 0.54), followed by UVB (AUCI= 0.56) and UVA1 (AUCI= 0.79). The formulation F2 also has poor absorption in the UVA1 range. However, unlike the F3 formulation, F2 is added to the physical filter titanium dioxide, which can provide protection in the skin by reflecting the incident UV radiation, compensating for the lack of chemical filters in the UVA1 region.

Formulation 2 were highly unstable mainly in UVB region. A hypothesis for this instability involve the degradation of EHMC that might undergoes isomerization of the cis-trans type upon exposure to irradiation, generating cis-octylmethoxycinnamate. The cis isomer has a lower capacity to absorb UV irradiation and a consequent reduction in its photo-protective activity.[39,48-50]

The reduction of the photoprotection presented by the photounstable formulations, in addition to compromising the effectiveness of the protectors, not conferring adequate protection to the skin can also trigger the formation of degradation products potentially harmful to the skin, which can interact with skin components, mediating phototoxic and/or photoallergic processes.[28,51,52] It is worth considering that even if the product were reapplied to the skin at time intervals to ensure photoprotection, the problem of skin contact with the toxic degradation products would not be eliminated, since the sunscreen would be applied on the skin layer already containing the filters products of degradation.

It should be emphasized that sunscreen should not be used in order to prolong the duration of sun exposure. However, studies have shown that using sunscreen makes people feel protected against erythema and is much more exposed to the sun than when they do not use sunscreen. Therefore, this attitude becomes much more dangerous when the sunscreens are photo-labile, giving a false sense of security.[53,54]

It is very important that the development of a photoprotective formulation be very well performed, so that the combination of the sunscreens provides an adequate stability of the product.[15] This step involves the proper choice not only of the filters, but also of the carrier, solvents and appropriate cosolvents, which also contribute to the stability of sunscreens.[55] Some UV filters acting as stabilizers of photounstable UV filters.[15]

Moreover, the use of stabilizers is also essential to ensure efficacy and safety of sunscreen formulations containing photounstable filters. These stabilizers include glass beads, polymer microspheres, antioxidants and triplet-triplet quenchers.[47]

The present study is relevant because it shows that SPF, which is the parameter considered by the consumer at the time of purchase, does not reflect the photostability of the formulation. Although the products have the same SPF 30, it was seen that some are more stable than others.

Brazilian legislation requires *in vivo* testing to determine SPF, the level of UVA protection and water resistance.[25] However, photostability tests are not required. It is also worth mentioning that handling pharmacies are not required to performed these *in vivo* tests.

In order to ensure the sunscreen efficacy, it´s important that these compounds remain stable for the entire time of sun expose for the purpose of obtain the expected photoprotection and safety.[44,56,57] Once a formulation is photounstable, the consumer may come into contact with degradation products resulting from UV filters that can be toxic and also be susceptible to sunburn. In this perspective, there is a need for standardized and robust measurements of photostability.[58]

CONCLUSIONS

The present study presents a simple technique for evaluating the photostability of sunscreens in order to develop more stable products. Although brazilian legislation does not yet have methods for evaluating sunscreens stability when exposed to natural sunlight exposure, photostability studies are very important to ensure the products safety and efficacy.

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