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Rapid communication

Effect of the combination of organic and inorganic filters on the Sun Protection Factor (SPF) determined by *in vitro* method

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Abstract

This paper describes the effect on Sun Protection Factor (SPF) of the combination of inorganic and organic filters in sunscreen products as determined by an *in vitro* method. O/W emulsions containing inorganic filters, such as titanium dioxide and zinc oxide, combined with 18 EU-authorized UV-B organic filters were tested. SPF measurements were carried out using a spectrophotometer equipped with an integrating sphere.

This study observed a synergic effect when titanium dioxide was combined with either anisotriazine or octyldimethylPABA. The combination of zinc oxide with 11 UV-B organic filters also exhibited a similar synergy; however, the measured SPF was systematically lower than the protection factor achieved with titanium dioxide.

Keywords: Inorganic; Organic; Filter; Combination; Synergy; SPF *in vitro*

1. Introduction

UV constitutes about 10% of the total solar radiation. There are two categories of UV radiation: UV-A and UV-B. UV-A (320–400 nm) has lower energy than UV-B, however, it penetrates more deeply and does not burn skin as easily. The 95% of UV radiation is UV-A. UV-B (290–320 nm) radiation has higher energy and penetrates only the outer skin layers, but induces skin burns more easily (Hoffman et al., 2000). UV radiation has both positive and negative effects. Positive effects of UV radiation include warmth, light, photosynthesis in plants and vitamin D synthesis in the skin (UV light converts a cholesterol derivative into previtamin D3) (Holick et al., 1980). Overexposure to UV radiation is the primary environmental risk factor in the development of UV-related adverse health conditions, which include diseases of the eye (Sliney, 2001), immune suppression (Norval, 2006) and skin cancers. Exposure to UV radiation appears to be the most important environmental factor in the development of skin cancer (Hussein, 2005). The increase in skin cancer has resulted from an increased outdoor leisure time and a decrease in the amount of protective clothing worn outdoors (Vanquerp et al., 1999; Marks, 1999; Couteau et al., 2001; Morison, 2003).

Sun Protection Factor (SPF) is the universal indicator for describing the efficiency of sunscreen products. It is the ratio of the least amount of ultraviolet energy required to produce a minimal erythema on sunscreen protected skin to the amount of energy required to produce the same erythema on unprotected skin (FDA, 1978). In this way, SPF indicates the ability of a sunscreen product to reduce UV-induced erythema. It is measured by both *in vivo* (Colipa method) and *in vitro* methods (Groves et al., 1979). It is recommended to use sunscreen products with an SPF of 15 or higher. This paper describes the study of the effect of the combination of organic and inorganic UV filter substances on the SPF of topically applied sunscreen formulations, using an *in vitro* method.

2. Materials and methods

2.1. Materials

Tables 1 and 2 present the filters (organic and inorganic) and their characteristics. Dimethicone (Abil®WE 09) was obtained from Goldschmidt (Montigny-le-Bretonneux, France). Cetiol® HE, stearic acid, glycerin, parabens and triethanolamin (TEA)

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Table 1
Characteristics of the organic sunscreens investigated

INCI name	Suppliers	λ_{max} (nm)	Solubility	Maximum concentration authorized (%)
PABA	Merck, Fontenay sous Bois, France	290.0	Hydrosoluble	5
Homosalate	Merck, Fontenay sous Bois, France	306.0	Liposoluble	10
Oxybenzone	BASF, Levallois-Perret, France	287.5	Liposoluble	10
Phenylbenzimidazole sulfonic acid	Merck, Fontenay sous Bois, France	305.5	Hydrosoluble after neutralisation with NaOH	8
Octocrylene	BASF, Levallois-Perret, France	304.0	Liposoluble	10
Octylmethoxycinnamate	BASF, Levallois-Perret, France	310.0	Liposoluble	10
PEG-25 PABA	BASF, Levallois-Perret, France	307.0	Hydrosoluble	10
Isoamyl *p*-methoxycinnamate	Symrise, Neuilly sur Seine, Paris	310.0	Liposoluble	10
Octyltriazone	BASF, Levallois-Perret, France	314.5	Liposoluble	5
Diethylhexylbutamidotriazone	Créations couleur, Dreux, France	310.5	Liposoluble	10
4-Methylbenzylidene camphor	Merck, Fontenay sous Bois, France	301.0	Liposoluble	4
3-Benzylidene camphor	Unipex, Rueil Malmaison, France	291.05	Liposoluble	2
Octylsalicylate	Alzo, Helsinki, Finland	306.0	Liposoluble	5
OctyldimethylPABA	Merck, Fontenay sous Bois, France	312.0	Liposoluble	8
Benzophenone-5	BASF, Levallois-Perret, France	287.5	Hydrosoluble	5
Methylene bis-benzotriazolyl tetramethylbutylphenol	Ciba, Grenzach-Wyhlen, Germany	305.5	Hydrosoluble	10
Anisotriazine	Ciba, Grenzach-Wyhlen, Germany	310.0	Liposoluble	10
Polysilicone 15	Roche, Fontenay sous Bois, France	312.5	Liposoluble	10

Table 2
Characteristics of the inorganic sunscreens investigated

INCI Name (Trade name)	Suppliers	Solubility	Maximum concentration authorized (%)
Titanium dioxide, hydrated silica, aluminium hydroxide, dimethicone/methicone copolymer (T-Lite SFS)	BASF, Levallois-Perret, France	Liposoluble	25
Zinc oxide, diphenyl capryl methicone (Z-Cote Max)	BASF, Levallois-Perret, France	Liposoluble	–

were purchased from Cooper (Melun, France). Xanthan gum (Keltrol® BT) was obtained from Kelco (Lille Skensved, Denmark). Polymethylmethacrylate (PMMA) plates were purchased from Helioscience (Creil, France). Powder-free latex finger cots were obtained from Cooper (Melun, France).

2.2. Preparation of sunscreen creams

Each O/W emulsion was prepared in the laboratory by combining organic and inorganic filters, in the highest EU-authorized concentration, to a basic formula (Table 3) were manufactured by the authors. Hydrophilic-phase and oil-phase were heated separately to between 78 and 82 °C, until the ingredients of each part were solubilized. Next, the oily preparation was added slowly to the hydrophilic preparation with constant stirring (Yellow line OST basic mixer, IKA, Staufen, Germany). It was necessary to continue stirring until the resulting emulsion was cooled to room temperature (20 °C). In addition, sunscreen agents were incorporated at various concentrations into this emulsion. A filterless cream was used as a blank (Couteau et al., in press-a,b).

2.3. Study of effectiveness

Thirty milligrams of precisely weighed product were spread across the entire surface (25 cm^2) of a polymethylmethacrylate (PMMA) plates using a cot-coated finger. Plates have both a smooth and a rough surface. The roughness was measured between 5 and 10μ. After spreading, 15 mg of the product remained on the finger cot. The SPF of the creams was then measured *in vitro*. Three plates were prepared for each product to be tested and nine measurements were performed on each plate. Transmission measurements between 290 and 400 nm

Table 3
Composition of the emulsion

Ingredients	Percent by weight
Abil® WE 09 (polyglyceryl-4 isostearate; cetyl PEG/PPG-10/1 dimethicone; hexyl laurate)	5
Paraffin oil	12
Cetiol® HE (PEG-7 glyceryl cocoate)	5
Butylhydroxytoluene	0.01
Stearic acid	5
Eumulgin® B1 (Ceteareth-12)	1.5
Eumulgin® B2 (Ceteareth-20)	1.5
Glycerine	4
Sodium propylparaben	0.05
Sodium methylparaben	0.1
Keltrol® BT (xanthan gum)	0.9
TEA	0.3
Distilled water	qsp 100.0

Table 4
Combination of UV-B filters and titanium dioxide

Filter (INCI name)	SPF (filter) (mean ± S.D.)	SPF (filter + titanium dioxide combination) (mean ± S.D.)	Increase or decrease of SPF compared to predicted SPF (SPF units)
PABA	5.48 ± 0.62	41.04 ± 6.05	–
Homosalate	4.25 ± 0.96	38.09 ± 3.27	−4
Oxybenzone	5.10 ± 0.57	39.07 ± 4.11	−4
Phenylbenzimidazole sulfonic acid	13.39 ± 1.60	49.37 ± 11.07	–
Octocrylene	9.40 ± 1.42	43.42 ± 3.79	–
Octylmethoxycinnamate	12.09 ± 1.20	53.12 ± 4.69	–
PEG-25 PABA	4.09 ± 0.56	35.87 ± 3.08	−6
Isoamyl *p*-methoxycinnamate	13.49 ± 1.90	52.84 ± 5.85	–
Octyltriazone	12.54 ± 2.15	36.57 ± 3.67	−14
Diethylhexylbutamidotriazone	10.73 ± 1.44	47.27 ± 3.89	–
4-Methylbenzylidene camphor	6.44 ± 0.88	43.38 ± 2.99	–
3-Benzylidene camphor	2.84 ± 0.47	33.47 ± 4.03	−7
Octylsalicylate	2.89 ± 0.37	38.81 ± 4.13	–
OctyldimethylPABA	8.98 ± 0.81	53.55 ± 4.07	+7
Benzophenone-5	5.59 ± 0.88	35.77 ± 3.61	−7
Methylene bisbenzotriazolyltetramethyl butylphenol	6.68 ± 1.80	19.50 ± 4.03	−25
Anisotriazine	29.63 ± 4.19	73.06 ± 4.96	+6
Polysilicone 15	4.25 ± 0.95	38.77 ± 4.32	–

were carried out using a spectrophotometer equipped with an integrating sphere (UV Transmittance Analyzer UV1000S, Labsphere, North Sutton, US). The SPF were carried out according to the following equation:

$$\mathrm{SPF} = \frac{\sum_{290}^{400} E_\lambda S_\lambda \Delta_\lambda}{\sum_{290}^{400} E_\lambda S_\lambda T_\lambda \Delta_\lambda} \qquad (1)$$

where E_λ is CIE erythemal spectral effectiveness, S_λ is solar spectral irradiance and T_λ is spectral transmittance of the sample (Ferrero et al., 2003; Villalobos-Hernandez and Müller-Goymann, 2007).

3. Results and discussion

The SPF of the cream containing 25% titanium dioxide or 25% zinc oxide was, respectively, 37.65 ± 3.90 and 7.14 ± 1.22.

Table 5
Combination of UV-B filters and zinc oxide

Filter (INCI name)	SPF (filter) (mean ± S.D.)	SPF (filter + zinc oxide combination) (mean ± S.D.)	Increase or decrease of SPF compared to predicted SPF (SPF units)
PABA	5.48 ± 0.62	10.94 ± 1.22	–
Homosalate	4.25 ± 0.96	11.94 ± 2.25	–
Oxybenzone	5.10 ± 0.57	13.42 ± 1.61	–
Phenylbenzimidazole sulfonic acid	13.39 ± 1.60	24.76 ± 3.82	+4
Octocrylene	9.40 ± 1.42	25.74 ± 2.57	+9
Octylmethoxycinnamate	12.09 ± 1.20	26.63 ± 2.98	+7
PEG-25 PABA	4.09 ± 0.56	15.06 ± 3.18	+4
Isoamyl *p*-methoxycinnamate	13.49 ± 1.90	29.07 ± 3.56	+8
Octyltriazone	12.54 ± 2.15	25.88 ± 2.94	+6
Diethylhexylbutamidotriazone	10.73 ± 1.44	49.28 ± 4.37	+31
4-Methylbenzylidene camphor	6.44 ± 0.88	15.16 ± 2.06	–
3-Benzylidene camphor	2.84 ± 0.47	12.72 ± 1.77	+3
Octylsalicylate	2.89 ± 0.37	9.08 ± 1.40	–
OctyldimethylPABA	8.98 ± 0.81	28.51 ± 2.94	+12
Benzophenone-5	5.59 ± 0.88	15.28 ± 1.42	+3
Methylene bis-benzotriazolyltetra methyl butylphenol	6.68 ± 1.80	12.92 ± 1.90	–
Anisotriazine	29.63 ± 4.19	36.89 ± 3.29	–
Polysilicone 15	4.25 ± 0.95	15.55 ± 1.37	+4

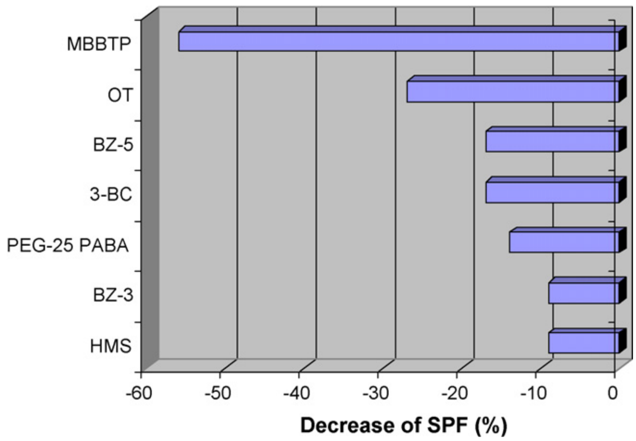

Fig. 1. Decrease of effectiveness (%) for the combination between titanium dioxide and methylene bis-benzotriazolyl tetramethylbutylphenol (MBBTP), octyltriazone (OT), benzophenone-5 (BZ-5), 3-benzylidene camphor (3-BC), PEG-25 PABA, benzophenone-3 (BZ-3) and homosalate (HMS).

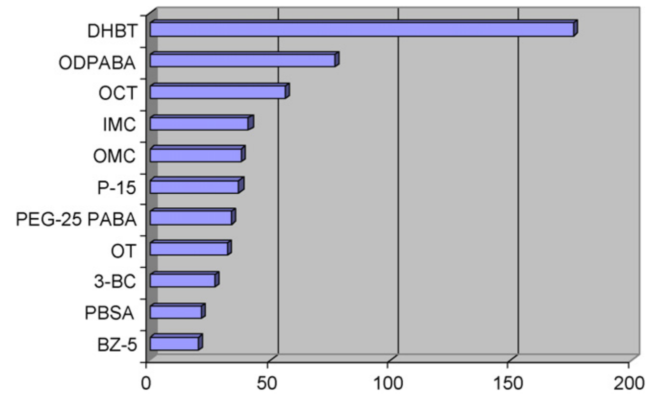

Fig. 2. Increase of effectiveness (%) for the combination between zinc oxide and diethylhexylbutamidotriazone (DHBT), octyldimethylPABA (OD-PABA), octocrylene (OCT), isoamyl *p*-methoxycinnamate (IMC), octylmethoxycinnamate (OMC), polysilicone-15 (P-15), PEG-25 PABA, octyltriazone (OT), 3-benzylidene camphor (3-BC), phenylbenzimidazole sulfonic acid (PBSA) and benzophenone-5 (BZ-5).

We noted a clear superiority of TiO_2 over ZnO in terms of effectiveness. A previous study established that SPF is a function of filter concentration (Couteau et al., in press-a,b). Therefore, by knowing the equation SPF = *f*(*c*) for each filter and each separately added screen, it will be possible to predict the SPF of sun creams combining both filter and screens. We expect manufacturers to question the relevance of all of these combinations, a query that will be answered by this paper.

The effect of the combinations was evaluated statistically by a Student's *t*-test ($N = 27$; $p < 0.05$) (Tables 4 and 5). A combination was considered relevant if the SPF of the cream combining filter and screen was higher or equal to the SPF obtained separately, filter only or screen only. On the other hand, we considered a combination to be irrelevant if the SPF of the combination remains inferior to the expected result. In 9 out of 18 trials, the creams formulated with TiO_2 revealed a purely additive effect. Seven creams turned out to be less promising than predicted (with a loss of SPF compared to predicted results between 4 and 25) (Fig. 1). We found two synergistic combinations worth noting: the cream formulated with TiO_2 and anisotriazine resulted in a SPF value of about 70 (an increase of 6 SPF units). The second interesting combination was obtained with octyldimethylPABA (an SPF about 55). The increase was about 7 SPF units. So it is possible to predict the SPF of all the combinations between the various molecules.

In a large majority of the cases (11 out of 18), a combination with zinc oxide was more promising because it generated more synergy (Fig. 2). In terms of an increase in SPF protection, two combinations are particularly worth mentioning: the combination with diethylhexylbutamidotriazone (an increase of 31 SPF units) and the combination with octyldimethylPABA (an increase of 12 SPF units).

The formulated creams made with zinc oxide turned out to be more reliable than those made with titanium dioxide in the sense that there was no unexpected loss of SPF compared with the predicted results. It will be necessary, however, to further investigate the use of titanium dioxide because high SPF (70 for example) products can be created with it; these high values cannot be attained with zinc oxide (maximum SPF of 49). By referencing Tables 4 and 5 of this paper as well as the linear curves (SPF = *f*(*c*)) established in an earlier study (Couteau et al., in press-a,b), it is possible to select filter–screen combinations in function of a desired protection level.

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