

Inorganic and organic UV filters: Their role and efficacy in sunscreens and suncare products

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Dedicated to Professor Vincenzo Balzani

Abstract

Minerals such as titanium dioxide, TiO₂, and zinc oxide, ZnO, are well known active semiconductor photocatalysts used extensively in heterogeneous photocatalysis to destroy environmental pollutants that are organic in nature. They are also extensively used in sunscreen lotions as active broadband sunscreens that screen both UVB (290–320 nm) and UVA (320–400 nm) sunlight radiation and as high SPF makers. When so photoactivated by UV light, however, these two particular metal oxides are known to generate highly oxidizing radicals ([•]OH and O₂^{-•}) and other reactive oxygen species (ROS) such as H₂O₂ and singlet oxygen, ¹O₂, which are known to be cytotoxic and/or genotoxic. Hydroxyl ([•]OH) radicals photogenerated from photoactive TiO₂ specimens extracted from commercial sunscreen lotions [R. Dunford, A. Salinaro, L. Cai, N. Serpone, S. Horikoshi, H. Hidaka, J. Knowland, FEBS Lett. 418 (1997) 87] induce damage to DNA plasmids in vitro and to whole human skin cells in cultures. Accordingly, the titanium dioxide particle surface was modified to produce TiO₂ specimens of considerably reduced photoactivity. Deactivation of TiO₂ diminishes considerably, in some cases completely suppresses damage caused to DNA plasmids, to human cells, and to yeast cells compared to non-modified specimens exposed to UVB/UVA simulated solar radiation. The photostabilities of sunscreen organic active agents in neat polar and apolar solvents and in actual commercial formulations have been examined [N. Serpone, A. Salinaro, A.V. Emeline, S. Horikoshi, H. Hidaka, J. Zhao, Photochem. Photobiol. Sci. 1 (2002) 970]. With rare exceptions, the active ingredients undergo photochemical changes (in some cases form free radicals) and the sunscreen lotions lose considerable Sun protection efficacy only after a relatively short time when exposed to simulated sunlight UVB/UVA radiation, confirming the recent findings by Sayre et al. [R.M. Sayre, J.C. Dowdy, A.J. Gerwig, W.J. Shields, R.V. Lloyd, Photochem. Photobiol. 81 (2005) 452].
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1. Introduction

A variety of marketing strategies have led consumers to believe and rely on the notion that sunscreen lotions are meant to prevent skin damage (e.g., sunburns, skin cancers) while permitting gradual tanning, both of which are achieved when sunscreens absorb UVB {290–320 nm}

and UVA {320–400 nm} sunlight radiation. To preclude sunburns and protect people from serious skin damage, sunscreens must possess several attributes. They must be photostable (ideally 100%) and must dissipate the absorbed energy efficiently through photophysical and photochemical pathways that rule out the formation of singlet oxygen, other reactive oxygen species, and other harmful reactive intermediates. They should not penetrate the skin, and should not be transported into the human cells where they can cause deleterious damage to DNA. Sunscreens should also minimize the extent of UVB and UVA radiation that might reach DNA in cell nuclei.

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With few exceptions, sunscreens contain *chemical* filters (organic; absorb mostly UVB radiation) and *physical* filters (e.g., TiO₂ and ZnO). The latter have been said to block UVB/UVA sunlight through reflection and scattering [1]. If this were so, since reflection and scattering are physical phenomena, the term *physical UV filters* was coined. However, these inorganic UV filters absorb considerable UV radiation [2].

Mineral compounds such as TiO₂ and ZnO are used extensively in such cosmetics as foundations, powders, eye shadows and pencils. Indeed, titanium dioxide (TiO₂) was reported as a sunscreen agent as long ago as 1952 [3]. The required feature of inorganic sunscreen filters is to screen/block UV light over the whole UVA/UVB range (290–400 nm) through absorption, scattering and reflection properties that in turn are determined by the intrinsic refractive index, the size of the particles, dispersion in the emulsion base, and by the film thickness. The ability of some minerals to act as the so-called physical filters in sunscreen lotions is determined by two major characteristics: the absorption/scattering property of the inorganic filter and its cosmetic acceptability.

An inorganic mineral sunscreen which functions well at reflecting light, however, tends to be opaque and white on the skin and consequently is unacceptable for cosmetic use. Cosmetic acceptability of metal-oxide sunscreens has required that the particle size of TiO₂ and ZnO, among others (e.g., alumina, ceria and zirconia) be around 20–50 nanometers (nm). Occasionally, iron oxide (Fe₂O₃) pigments are added to give the cosmetic a brown tinge to improve the appearance of the sunscreen product. The so-called *micronized* metal-oxide particles are used in cosmetic products [4], as they are easily incorporated into emulsions, are transparent to visible radiation, reflection from the particle surface is minimal, and in some cases (TiO₂ and ZnO) absorption is maximized. Partial light attenuation by these smaller particles is due mostly to Rayleigh scattering with the intensity of scattered light following the power law $I_s \propto \lambda^{-4}$ (where λ is the wavelength). Thus, such small particles scatter UVB and UVA wavelengths more than the longer visible light wavelengths.

In 1978, an OTC Panel [5] reported that "...as a physical sunscreen agent, titanium dioxide (TiO₂) is a safe, opaque and effective product that provides a barrier to sun-sensitive individuals against sunburns, because it reflects and scatters UVA and UVB radiation 290–400 nm) rather than absorbing the rays...". However, TiO₂ is a much stronger absorber of UV light than is a scatterer of UVB and UVA radiation [2,6]. Particle sizes of TiO₂ that are tenfold greater (range 200–500 nm) are best at reflecting visible light, which on application on the skin has the disadvantage of being opaque, albeit acting as a true sunblock.

Titanium dioxide is available in three different crystalline forms: viz., rutile, anatase and brookite, in addition to an amorphous phase. Only the rutile (bandgap energy, 3.0 eV; onset of absorption at 400 nm) and anatase

(bandgap energy, 3.2 eV; absorption onset at 387 nm) polymorphs have relevance in sunscreen lotions and in heterogeneous photocatalysis, a technology that aims to remediate polluted soil, as well as aqueous and atmospheric ecosystems. The principal difference between rutile and anatase is the divergence in photoactivity with anatase being the more photoactive form of titanium dioxide; however, rutile is the more common form of titania even though anatase is the more stable form by about 8–12 kJ mol⁻¹ [7].

Chemical organic filters are classified into either UVA (benzophenones, anthranilates and dibenzoylmethanes) or UVB filters (PABA derivatives, salicylates, cinnamates and camphor derivatives). Sunscreen lotions containing these active ingredients and/or inorganic UV filters are typically commercialized as cosmetic products in most countries [8], except in some as for example in the United States where they are treated as over-the-counter (OTC) drugs and thus regulated by the US Food and Drug Administration (FDA). Chemical UV filters are almost always used in combination because no single active agent, used at levels currently allowed by the FDA [1], provides high enough SPF (sun protection factor) protection or broad-spectrum absorption. Because of the photoinstability and possible unfavorable synergistic interactions between these agents, recent restrictions by the FDA's Federal Register Administration Regulatory Affairs [1] have limited the choice of suitable combinations of UVB/UVA *chemical organic* UV filters.

A trend in sun protection is the increased use of inorganic UV filters, especially in sunscreen products for children and people with sensitive skin. This increased use of inorganic UV sunscreens is due partly to their low potential for producing irritant reactions, and partly to their cosmetic efficacy. Cosmetic chemists have formulated products with high SPF using only titanium dioxide. In combination with organic sunscreen agents, TiO₂ gives impressive SPF numbers as well as displaying broad absorption in the UVB and UVA region [9]. Formulators have also incorporated *micro-fine* titanium dioxide into sunscreen preparations to avoid the decrease of SPF that can occur from the photoinstability of organic UV filters [10].

Our involvement in this field of sunscreen research was our, albeit late, recognition in the mid-1990s² that sunscreen lotions inherently contained TiO₂ in combination with various *chemical organic* filters. Table 1 summarizes three commercial sunscreen formulations available in Europe in the late 1990s. Note that today's compositions are not very different from those that were available nearly a decade ago. We were rather concerned since TiO₂ had been used for over a decade [11] as a very active photocatalyst to destroy, indeed mineralize pollutants organic in nature

² Thanks to an FDA staff chemist and Prof. John Knowland of Oxford University.

Table 1
Sunscreen active agents found in three different commercial sunscreen products

Sunscreen 1	Sunscreen 2	Sunscreen 3
4-Mebenzylideneamphor, 6%	4-Mebenzylideneamphor, 6%	Octylmethoxycinnamate (OMC) ^a , 7.5%
Parsol 1789, 2% ^b	Parsol 1789, 2%	Oxybenzone, 5%
Mexoryl SX, 1% ^c	Mexoryl SX, 2%	2-PBSA, 2.3% ^d
Titanium dioxide, 3.2%	Titanium dioxide, 5%	Titanium dioxide, 4.5%
Pure melanin		
Vegetable extracts		

^a Also known as octinoxate.

^b Butylmethoxy dibenzoylmethane, also known as Avobenzone.

^c Terephthalidenedicamphor sulfonic acid.

^d 2-Phenylbenzimidazole-5-sulfonic acid triethanolamine salt.

(e.g., chlorinated phenols, polychlorinated biphenyls, dioxins and the like) in aqueous ecosystems using the photogenerated highly oxidizing $\cdot\text{OH}$ radicals (see below), to remove and dispose off toxic metals (Hg , CH_3Hg^+ , and Pb) from the environment, and to recover precious metals with high selectivity from jewelry and photographic wastes (e.g., Au , Ag , Pt , and Pd).

Our studies on the photochemistry and photophysics of metal oxides have continued uninterruptedly during the past decade to further our collective level of understanding and knowledge of heterogeneous photocatalysis [11,12] as part of our objective to place this technology with metal-oxide photocatalysts on a more fundamental scientific base [13]. Knowledge thus acquired has proven crucial in our efforts to inactivate titanium dioxide for possible use in sunscreen lotions.

2. Photochemistry, photophysics and photobiology of metal-oxide semiconductors

Fig. 1 illustrates, in a simplistic fashion, some of the more relevant events of interest to the photobiology of metal oxides. On absorption of UV light, titanium dioxide particles produce conduction band electrons (e^-) and valence band holes (h^+). The electron is scavenged by the ubiquitous pre-adsorbed molecular oxygen to yield the superoxide radical anion ($\text{O}_2^{\cdot-}$), whereas the holes oxidize

the surface hydroxyl groups (and chemisorbed water) to generate hydroxyl radicals ($\cdot\text{OH}$) that initiate the oxidations [14]. The photoactivity of TiO_2 is set by a complex combination of factors, the most critical of which is the nature of the particle surface [15], a problem still under active debate and investigation [16]. In acidic media, the superoxide radical anion is protonated yielding the hydroperoxy radical, HO_2^{\cdot} , and ultimately hydrogen peroxide. The latter can also be produced by a radical chain termination step involving two $\cdot\text{OH}$ radicals. Fig. 1 also displays chemicals that interact with the photogenerated radicals or with H_2O_2 , and thus aid in identifying the more significant oxidizing agent(s) in surface photoredox reactions.

However, photophysical events that occur after UVA/UVB illumination of TiO_2 and subsequent formation of electron/hole pairs are, in fact, many and very complex. Following electron/hole separation, the two charge carriers migrate to the surface through diffusion and drift [17], in competition with a multitude of trapping and recombination events in the lattice bulk. At the surface, these carriers are poised to initiate redox chemistry with suitable pre-adsorbed acceptor and donor molecules in competition with recombination events to yield radiative and non-radiative emissions, and/or trapping of the charge carriers into shallow traps at lattice sites (e.g., anion vacancies, Ti^{4+} , and others). Some of these otherwise complex photophysical events occurring in several metal-oxide systems (e.g., TiO_2 , ZrO_2 , Sc_2O_3 and others) have been the object of systematic examination [13]. A complete picture is now evolving that will further enhance our understanding of the photoactivity of titanium dioxide and other metal oxides.

3. Titanium dioxide and DNA damage

To cause damage to DNA *in vivo*, titanium dioxide must penetrate the skin, and most importantly must penetrate the cell nucleus. Inferences that TiO_2 does penetrate the skin have been reported [18–21], although some of the data were somewhat inconclusive [22]. For instance, X-ray microanalyses and scanning electron microscopy failed to reveal the presence of TiO_2 in deep layers of the skin [23]. In a much earlier study, Dussert et al. [24] similarly found no intercellular or intracellular penetration of TiO_2 , although a time course of the penetration was not

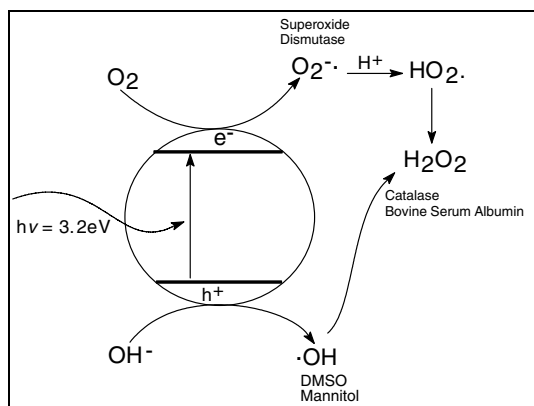


Fig. 1. Scheme illustrating, in simple terms, the photophysical and photochemical events that occur when metal-oxide semiconductors, such as TiO_2 and ZnO , are photoactivated by the absorption of UV radiation.

performed [22]. More recently, however, several researchers report that TiO₂ particles can indeed enter the skin [25–28]. Thus to the extent that TiO₂ can also enter human cells [29], it was imperative that we examine details of the possible consequences of the role of titanium dioxide in sunscreen lotions, including the effect(s) it may have had on the integrity of DNA [30]. Although an evaluation reported in 1989 in a monograph on the safety of TiO₂ [31] concluded that TiO₂ is not mutagenic, and hence cannot damage DNA, it did not report on the effects of sunlight or on the particular preparations of TiO₂ specimens used in sunscreen formulations. This aspect is important because sunscreen TiO₂ particles are often coated with compounds (e.g. Al₂O₃, SiO₂, and ZrO₂) that form hydrated oxides which can capture hydroxyl radicals and thus reduce photosensitivity [32]. However, some TiO₂/Al₂O₃ and TiO₂/SiO₂ preparations have also been shown to exhibit enhanced photoactivity [33]. We have used chemical methods to examine photoinduced oxidation reactions catalyzed by TiO₂ specimens obtained from various sunscreens available in Europe and North America. We have also tested the ability of both illuminated TiO₂ and ZnO – also a sunscreen semiconductor with a band gap of 3.3 eV [34] – to attack DNA.

Fig. 2 depicts the experimental results of plasmid nicking assays of pure (100%) anatase and rutile TiO₂, together with a commercial sunscreen TiO₂ and ZnO. The plasmids were from an Sk+ pbluescript DNA, a circular and extrachromosomal DNA in *E. coli* bacteria. Three forms of DNA were detected by electrophoretic techniques: supercoiled (S), relaxed (R), and linear (L) forms.

Lanes 1–4 in the top panel of Fig. 2 illustrate results after illumination of the DNA plasmids with simulated sunlight UV radiation (Solarbox) alone for 0, 20, 40 and 60 min; lanes 5–8 display results in the presence of 1% anatase TiO₂; lanes 9–12 show results in the presence of 1% rutile TiO₂, whereas lanes 13–18 display the effect(s) of sunscreen TiO₂ for 0, 5, 10, 20, 40 and 60 min of UV illumination. In the bottom panel, lanes 1–5 show the results with 0.2% ZnO after illumination for 0, 10, 20, 40 and 60 min; lanes 6–10 show the effects after adding DMSO to the ZnO/DNA system; lanes 11–16 summarize the effects of

sunscreen TiO₂ on DNA plasmids for 0, 5, 10, 20, 40 and 60 min of UV illumination in the presence of 200 mM DMSO, whereas lanes 17–22 show the results for TiO₂/DNA in the presence of 340 mM mannitol. Note that both DMSO (dimethyl sulfoxide) and mannitol are ·OH-radical scavengers (see Fig. 1). Clearly, comparison of lanes 13–18 (top panel) with lanes 11–16 and lanes 17–22 (bottom panel) demonstrates that damage to the DNA plasmids is caused by the photogenerated ·OH radicals. Experiments with catalase, boiled catalase, and serum bovine albumin precluded the involvement of H₂O₂ (and thus the O₂^{·-} radical) [30]. UV light irradiated sunscreen TiO₂ specimens extracted from sunscreen lotions produced single-strand and double-strand breaks on the DNA plasmids, and on nuclei of whole human skin cells as determined by a comet assay method [30].

The above results indicate that the potential for DNA damage associated with using titanium dioxide (and zinc oxide also) as an inorganic UV filter in sun care products cannot be underestimated. Germane to the above findings, Huang and coworkers [35] also found that UVB/UVA-irradiated uncoated 10-nm TiO₂ particles induced oxidative damage to DNA leading to cell death, which could have been prevented in the presence of scavengers of reactive oxygen species. In a related study, Afaq et al. [36] reported that intratracheal exposure of rats to about 2 mg of uncoated small TiO₂ particles (size smaller than 30 nm) leads to lipid peroxidation and H₂O₂ production associated with enhancement of antioxidant enzyme activity and cytotoxicity to pulmonary alveolar macrophages. Nakagawa and coworkers [37] showed that under dark conditions, TiO₂ particles have no or else display only weak genotoxicity toward DNA. However, when irradiated with UV radiation from a solar simulator, TiO₂ caused significant damage to DNA (comet assay) and in the chromosomal aberration test. In spite of these findings, however, the US Federal Register of May 21, 2000 [1] continues to state that although “The (FDA) agency is aware that sunscreen manufacturers are using *micronized TiO₂* to create high SPF products that are transparent and aesthetically pleasing on the skin... Based on data and information presented at the September 19–20, 1996, public meeting on the pho-

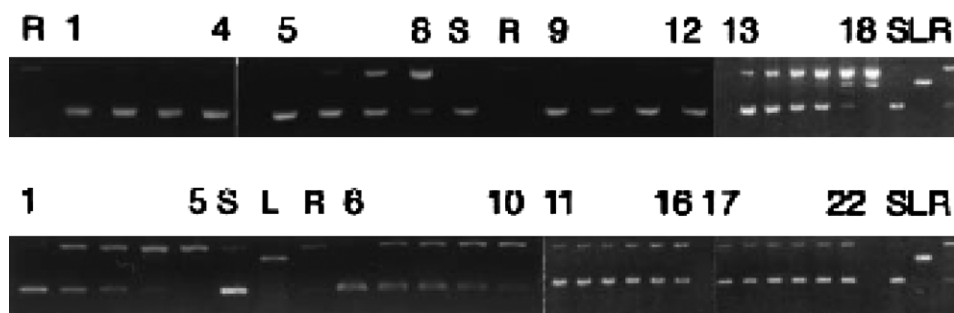


Fig. 2. Experimental results of plasmid nicking assays of pure (100%) anatase and rutile TiO₂, together with commercial sunscreens TiO₂ and ZnO. On the right hand side of both panels are reported the three forms of DNA detected by the electrophoretic technique: supercoiled (S), relaxed (R) and linear (L) forms. Reproduced from Ref. [30]. Copyright by Elsevier Science.

tobiology and photochemistry of sunscreens, the agency is not aware of any evidence at this time that demonstrates a safety concern from the use of *micronized TiO₂* in sunscreen products...". Yet, the FDA's own researchers showed in a 1997 report [38] that TiO₂ is *photocytotoxic* to human skin fibroblasts (18 h; 10 mg/cm²; UVA energy, 0.5 kJ/m²), and that RNA isolated from fibroblasts contained high levels of photooxidation products, namely hydroxylated guanine bases. Moreover, they found that TiO₂ photocatalyzed free radical formation, a point that we had emphasized at the 1996 public meeting [39].

To the extent that TiO₂ is photoactive and DNA damage on human skin follows from the photogenerated ·OH radicals, it became imperative to inactivate the TiO₂ physical sunscreen by a procedure that will be reported elsewhere [40]. Our strategy was to modify and then examine TiO₂ samples using a variety of *in vitro* and *in vivo* models. Our studies are part of an ongoing effort to prepare an OTC titanium dioxide sunscreen product that is photocatalytically inactive, but one that nonetheless provides protection against the damaging UV sunlight radiation. The photoactivity of the modified TiO₂ specimens was probed using the photooxidation of phenol as a screening test, along with damage (or lack thereof) to DNA plasmids *in vitro*, and to human cells and yeast cells (in cultures) [41]. The plasmid-nicking assay was employed to investigate the extent of the damage (if any) induced by the photo-inert TiO₂ by examining single-strand and/or double-strand breaks inflicted on naked DNA *in vitro*.

Fig. 3 reports the DNA plasmid nicking assays under conditions otherwise similar to those of Fig. 2 for various non-modified RXB and modified RXA TiO₂ specimens ($X = A1, 8, 19, 20, \text{ and } 22$). UV illumination of DNA alone caused some single-strand breaks that were accentuated in the presence of pure anatase and pure rutile TiO₂. For the anatase polymorph, all three forms of the DNA plasmids were observed. By contrast, the non-modified titania spec-

imens RXB caused severe and considerable damage to the DNA plasmids. In some cases, no supercoiled form remained (for R41B, R8B and R20B), and in the particular case of the R22B specimen no DNA strands were left after only 10 min of simulated sunlight UV irradiation. By comparison, the modified titanium dioxide specimens caused only minimal DNA damage.

The yeast *Saccharomyces cerevisiae* was also examined [41] to evaluate the possible (photocytotoxic or photogenotoxicity) of TiO₂ specimens to keratinocyte human skin cells when used to establish using comet assays whether any observed reaction on naked DNA occurs within the cellular environment. The results on yeast cells are illustrated in Fig. 4. Again, the non-modified R9B TiO₂ specimen caused far more kills of the yeast cells (Fig. 4b) than did the modified R9A specimen (Fig. 4c), which in fact showed a greater survival rate for the yeast cells relative to the survival in UV light alone (Fig. 4a). Remarkably, in the presence of Parsol 1789 (i.e., avobenzone) and Padimate-O chemical organic UV filters the survival rate of yeast cells has been severely compromised (Fig. 4d and e).

4. Photostability of sunscreen lotions

Personal observations on several beaches in Italy and southern France indicate that beach lovers and suntan lovers apply sunscreen lotions perhaps once or twice daily and go to the beach at a time of day when the UV index is at its greatest, namely between 10:00 and 16:00 h. This is precisely the time period that the American Cancer Society recommends that beach goers limit their Sun exposure and to use a sunscreen with an SPF index greater than 15 so as to minimize the potential for skin cancer [http://www.cancer.org/docroot/CRI/content/CRI_2_4_2X_Can_skin_cancer_be_prevented_51.asp].

For an appropriate protection against the Sun's UV radiation it is imperative, therefore, that the applied sun-

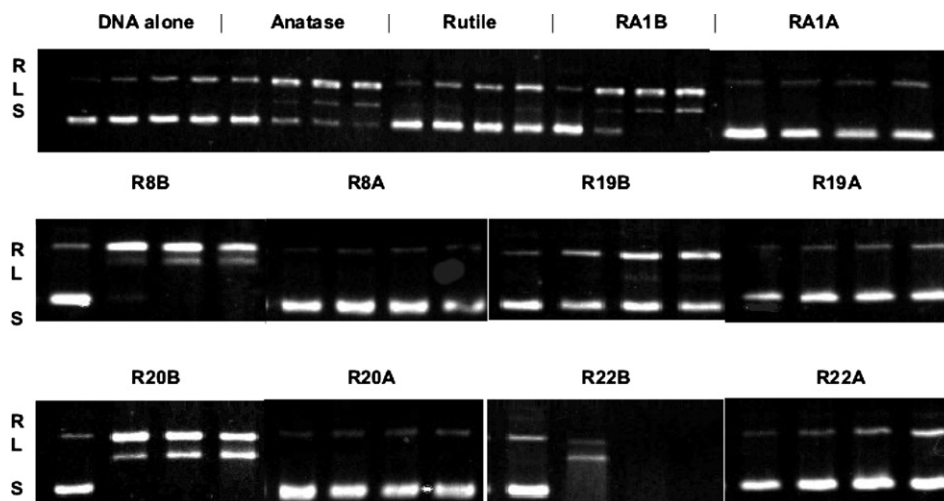


Fig. 3. Relaxation and migration of S, R, and L forms of DNA plasmids caused by various RXB and RXA TiO₂ specimens before and after modification. Irradiation times were: 0, 10, 20, and 30 min. Reproduced from Ref. [41]. Copyright by Elsevier Science.

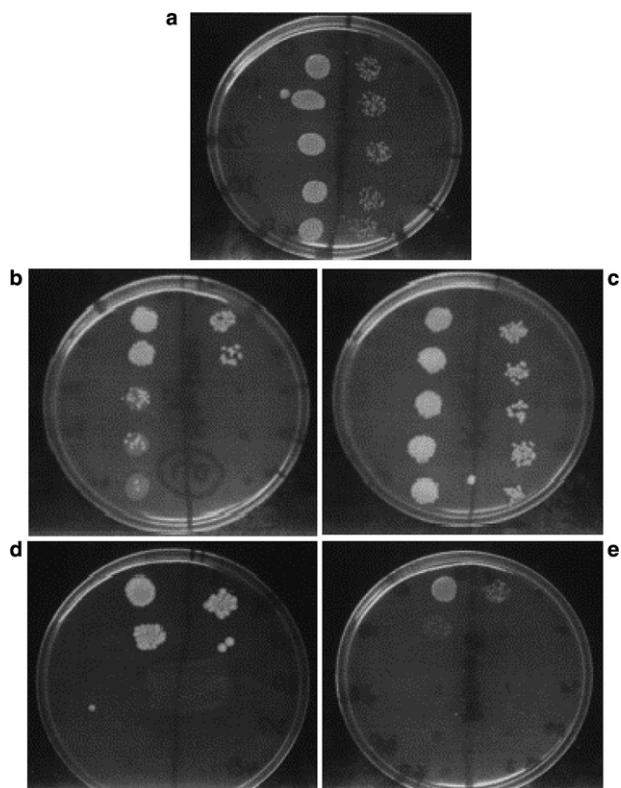


Fig. 4. Survival of *Saccharomyces Cerevisiae* yeast cells on UV illumination for 0, 10, 20, 30, and 40 min for (a) yeast cells alone, and in the presence of (b) R9B titanium dioxide, (c) R9A titanium dioxide, (d) Parsol 1789, and (e) Padimate-O. Experiments were repeated twice. Note that the population of yeast cells on the left hand side is 2× the yeast cell population on the right. Reproduced from Ref. [41]. Copyright by Elsevier Science.

screen lotions be photostable so as to provide the consumer the kind of protection implied by the value of the SPF factor, which is specific only to UVB radiation and not to UVA radiation. Accordingly, it is relevant to query whether sunscreen active agents are photostable when subjected to sunlight UV radiation (simulated or natural). Despite some early claims, they are not photostable [10]. After all, a molecule that absorbs UV (or any other type) radiation must dissipate or convert the absorbed energy. Three pathways are available, namely radiative decay (emission), non-radiative decay (heat), and photochemistry (i.e., an excited molecule undergoes photochemical changes that may lead to its breakdown, and generate photoproducts that may no longer provide protection and that may cause allergies or photoallergies).

The lack of photostability of *chemical* organic UV filters is now recognized as a common problem for UV organic absorbers [42], which become inactivated by UV radiation [43], thus losing their photoprotective characteristics [44], and even becoming photooxidizing agents [45]. The photostability of some *chemical* filters can even be enhanced when two or more organic sunscreen agents are combined in a formulation [46]. In this regard, the FDA monograph [1] on OTC sunscreen products provides a list of permitted combinations of approved active agents and gives the

maximal concentration of each ingredient in sunscreens. In effect, the efficiency of a sunscreen is usually tested more with respect to its macroscopic ability to prevent skin erythema and sunburns, than at the molecular and cellular level to ascertain protection against the risk of skin cancer.

Fig. 5 displays the changes in absorption with irradiation time when the active ingredient Padimate-O in a polar (water) and non-polar solvent (neat hexane) is subjected to simulated sunlight UV radiation. After only 20 min, this UVB chemical filter has lost all its potential UVB protection. More relevant is the question whether the active agents in actual sunscreen lotions are photostable?

Fig. 6 shows the histograms displaying the photostability (or lack thereof) of two well known commercial sunscreen lotions (conditions: solar simulator; 295–400 nm; 27 mW/cm²). After only 2 h of simulated sunlight UV illumination, nearly 50% protection is lost [47]. Similar findings were reported recently by Sayre and coworkers [48]

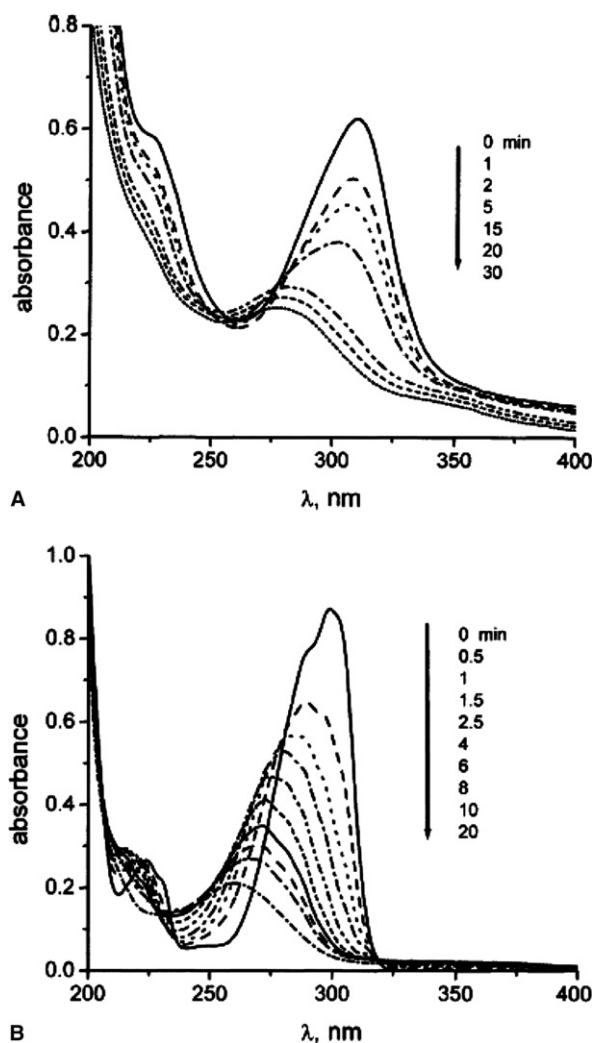


Fig. 5. Temporal changes in the absorption spectra of Padimate-O in (A) water and (B) in hexane. Other active agents have also been shown to be photounstable under similar conditions and in other solvents from non-polar hexane to polar H₂O. Reproduced from Ref. [10]. Copyright by the Royal Society of Chemistry.

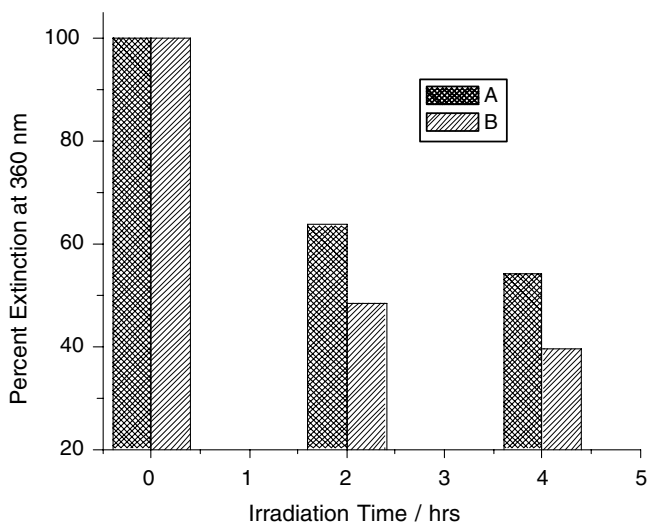


Fig. 6. Histograms displaying the photostability (or lack thereof) of two well known commercial sunscreen products (identified only as A and B) using thin films of the emulsions.

for a sunscreen lotion containing the organic UV filters avobenzone (Parsol 1789), octinoxate (OMC), and oxybenzone. Some of the initial all-*trans*-OMC isomer was converted to the *cis*-isomer during UV exposure. Octinoxate and Parsol 1789 were both not photostable relative to oxybenzone losing 60% absorption after about 2 MEDs of UVA exposure (1 MED $\sim 80 \text{ J/m}^2$ for skin type II). Under these conditions then, can sunscreens protect the skin from UV radiation damage, as they are claimed they can? Germane to this question, Green and coworkers [49] have reported an extensive 5-year skin cancer study that involved 1621 residents of the town Nambour in Queensland, Australia. They showed that the incidence of basal-cell and squamous-cell carcinomas was experimentally similar (scheme in Fig. 7), if not identical, whether or not

the residents were given a sunscreen (and betacarotene or a placebo). Evidently, betacarotene also played no role in suppressing the generation of skin cancer. Related to these findings, a recent article in the Italian *La Repubblica Magazine* of May 2005 noted that the incidence of melanoma has increased three-to-fourfold in the last 10 years in Italy alone (<http://www.skincancerday.it>), and that there are annually some 65 000 new cases of skin carcinomas (about 1.5–2 million such cases in the United States [50]), despite the increased use of sunscreen lotions. A similar report by Miller and Weinstock in 1994 [51] also reported an alarming increase in the incidence of skin cancers even then. Clearly, something does not square away. Consequently, either the consumers are not using the sunscreen lotions properly, or else the sunscreen lotions are not performing as they are claimed to perform. Maybe it is a bit of both. In the former case, consumers do not apply the sunscreens properly as the effective SPF protection is about a third of the sunscreen's labeled SPF on application and because several spots of the bare skin are not covered by the sunscreen [52]. In the latter case, we have seen that many of the organic UV sunscreens are simply not photostable [10,48].

5. Concluding remarks

The role of sunlight UV radiation as an initiator of cancer and as a promoter of cancer is no longer in question [53]. Perhaps the most interesting and relevant new findings are from the recent work of Chiang and coworkers [54] who noted that "...sunscreens may prevent skin redness partly by UV absorption and partly by inhibiting the skin's inflammatory response. As such, sunscreens *might promote* instead of protecting against melanoma".

If this were not disconcerting enough, a study done at the University of Zurich study (2001) reported that some

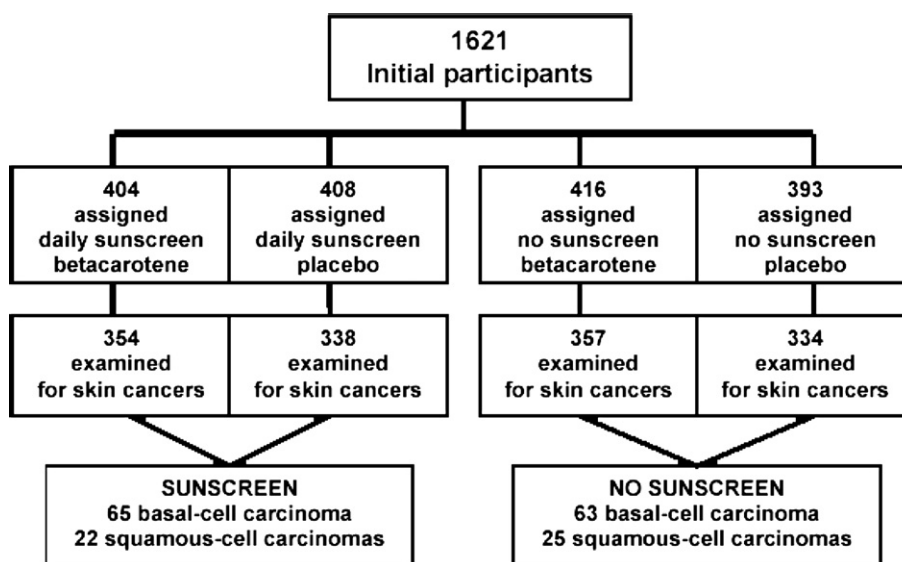


Fig. 7. Results of a 5-year skin cancer study in Queensland, Australia. Adapted from the data reported in Ref. [49].

sunscreen active agents are endocrine disruptors [55]. Other studies found that components of sunscreen lotions also display or otherwise acquire estrogenic activity [56]. Clearly, further studies are necessitated by these new findings that if confirmed are the cause of some concern.

In conclusion then, when consumers are advised to use high SPF sunscreens for protection against the Sun's UV radiation and for acquiring a suntan, we are reminded of a statement by the French epidemiologist Jean François Doré of Lyon,³ who in 1998 was quoted as saying "... Donner cette information, c'est participer à la notion qu'une crème permet de rester plus longtemps au soleil. Les gens utilisent une crème pour bronzer sans rougir et c'est en prolongeant l'exposition qu'ils reçoivent des doses UV qui déclenchent les effets biologiques néfastes... Quant aux crèmes, il s'agit d'un dispositif de sécurité qui est mal employé. Il faudrait les utiliser...oui...(mais) à l'ombre".⁴ In this regard, in a recent rather informative article ("New-Wave Sunscreens", *Chem. & Eng. News*, April 11, 2005) Mark S. Reisch reported that American consumers have no idea of how effective a sunscreen product is in protecting them against the cancer-causing rays of the Sun. Clearly, much remains to be done to better educate the consumers about the hazards and the risks connected with long exposure to the Sun's UV radiation, and the formulators of sunscreens and skincare products to provide safer and more photostable products.

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³ Quoted in T. Souccar, "Alerte aux Crèmes Solaires", *Sciences et Avenir*, August 1998.

⁴ "...To give this information is to propagate the notion that a sunscreen lotion allows one to stay exposed longer to the sun. People use a sunscreen to get a suntan without getting a sunburn and it is on being exposed longer to the sun that they receive UV doses that have deleterious biological effects... As for the sunscreen lotions, they are but a safety item that is badly employed. They should be used...yes...(but) in the shade".

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