TiO_2:Mn nanoparticles as enhanced UVA absorption, photostable sunscreen components

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ABSTRACT

Titanium oxide (TiO_2) nanoparticles are added to sunscreens as they have broad absorbance across the whole UV spectrum. Although photostable, TiO_2 nanoparticles can de-excite *via* surface states giving rise to reactive oxygen species (ROS) formation within the sunscreen formulation. An increased ROS load can degrade organic components within the sunscreen, such as UV absorbers or anti-oxidants, decreasing efficacy during topical use. Modifying the TiO_2 host lattice with manganese ions has three principal beneficial effects for application as a sunscreen component. Firstly, Mn-O states act as de-excitation centres for photoexcited charges. This almost completely eliminates production of free radicals via the particle surface. Secondly, manganese oxide associated with the particle surface acts to scavenge ROS generated in other formulation components, thus decreasing component degradation. Thirdly, Mn-O anti-bonding states increase the intrinsic UVA absorbance of TiO_2:Mn nanoparticles. The net result of these benefits is that sunscreens formulated with TiO_2:Mn nanoparticles show enhanced UVA absorption and extended photostability during topical use.

1 INTRODUCTION

Exposure to UV radiation in sunlight has damaging effects on the skin. The part of the UV spectrum that makes it through the earth's atmosphere and impacts the skin can be divided in to two regions, UVA (320-400nm) and UVB (290-320nm). UVB is considered more dangerous as it is strongly absorbed by DNA causing sunburn and chromosomal damage, which can lead to skin cancer[2], hence most commercial sunscreens focus on giving strong UVB absorption [1]. UVA is not directly absorbed by DNA, however DNA can be damaged by UVA via the formation of reactive oxygen species (ROS). The mechanism for this involves the absorption of UVA by skin chromaphores inducing cellular oxygen to generate free radicals such as hydroxyl radicals ($OH^{\bullet}$), singlet oxygen ($^1O_2$) and superoxide anions ($O_2^{\bullet}$). These radicals may go on to damage skin and cellular components, and hence can induce skin pathologies such as aging and carcinogenesis. The damaging effects of UVA have only recently been studied in depth, and sunscreens are still generally graded by their sun protection factor or SPF, which takes only UVB absorbance into account [3]. More recently UVA protection parameters such as Boots Star Rating [4] and PPD (persistent pigment darkening) are included on the consumer label, due to the growing awareness of the importance of UVA protection.

UV absorbing components in a sunscreen come in organic form and inorganic forms. Common organic UV absorbers used in commercial sunscreens are the UVA absorber butyl methoxydibenzoylmethane (BMDM) and the UVB absorber octyl methoxycinnamate (OMC). Using just organics in a sunscreen, without the addition of stabilising components, can lead to photoinduced decomposition post UV absorption [6], this is particularly an issue in the case of BMDM [7]. This can result in poor lifetime of sunscreen formulations. A common inorganic sunscreen active is TiO_2. At the correct particle size, TiO_2 exhibits good absorption across the whole UV spectrum, particularly boosting the UVB protection. It is photostable, that is it does not break down on exposure to UV, thus giving an extended lifetime to the sunscreen in topical application. Disadvantages of using TiO_2 alone are that high loadings are required which give a poor sensorial profile, give skin whitening and do not provide absorption at the far end of the UVA spectrum. Normally combinations of inorganic and organic materials are used to give best overall sunscreen performance.

Recent research into TiO_2 shows that the de-excitation mechanism post UV absorption produces a significant flux of free radicals. These can go on to attack the organic molecules present in the sunscreen, decreasing efficacy by destroying organic UV absorbers [8]. It has recently been demonstrated that the incorporation of manganese ions within the lattice of the TiO_2 and on the surface of the particles can reduce ROS concentration during solar exposure when such TiO_2:Mn nanoparticles are incorporated into a suitable sunscreen emulsion. The performance of the sunscreen is therefore significantly enhanced [9].

2 EXPERIMENTAL MATERIALS AND TECHNIQUES

2.1 Manganese Modified Titanium Oxide (TiO_2:Mn)

100% rutile TiO_2:Mn nanoparticles were used as supplied by Umicore. The Mn content was 0.67% wt and particle size 60nm.

2.2 Test Formulations

Formulations containing UV absorbers at the following loading, 5% OMC, 3% BMDM and 5% TiO_2 (or TiO_2:Mn), were made according to the following protocol. The formulation is an oil in water (O/W) emulsion. The oil phase contains 10% Crodasperse, 4% Crodafos CS20 Acid, 0.75% Volpo S20, 0.5% Volpo S2. The UV absorbers are added to a heated water phase of 70.5% water and 1% Veegum and 0.25% Xanthan Gum and stirred vigorously. This is left to cool and used in sunscreen photostability testing.

2.3 Experimental Techniques

a) Sunscreen photostability Testing.

Formulation samples are applied to 6.5 x 7 cm rectangles of Vitro-Skin^{TM} substrate (purchased from IMS Testing Group) with a gloved finger, at a surface loading of 2 mg/cm2. (The films are hydrated in a chamber containing 15%w/v glycerol at room temperature for 16-24 hours prior to application). The films were left to dry for 10 min. Immediately after drying, UV absorption measurements were taken using a Labsphere UV-1000S across a wavelength range of 290-400nm. The films were then exposed to UV radiation in a Spectral Energy xenon arc solar simulator equipped with a Schott WG320 filter for a total of four hours. The power output of the solar simulator was $7mW.cm^{-2}$ (equivalent to Southern Mediterranean sunlight). Samples of sunscreen on skin were run as duplicates and UV absorption readings were taken using the Labsphere UV-1000S at t=30, 60, 120, 180, 240, 360 and 480 minutes. Results for each sample were averaged over five readings and the relative losses in absorbance calculated.

b) DPPH Scavenging Assay.

DPPH is a stable free radical which absorbs strongly at 520nm. Samples containing 1,1-diphenyl-2-picrylhydrazyl (DPPH) (120µl, 1mM, MeOH) and TiO_2 suspension (300µl, 3mg/ml, MeOH) were made up to 3ml with methanol in a 15 ml eppendorf tube. These were placed on a shaker (all the time in the dark) for a total of 60 mins. (NB. One sample was kept blank i.e. no TiO_2). At t=30 and t=60 1ml samples were pipetted from each tube into a 1.5ml eppendorf lid. These were centrifuged for 10 mins to separate the particles from the solution. 120µl was pipetted from the surface into a UV cuvette. Absorption readings were taken at 520nm on the U-4100 Hitachi Spectrophotometer. Any loss in absorption when compared to the blank sample would indicate free radical scavenging had occurred. [10,11,12]

c) Coumarin ROS Generation Assay.

In the presence of ROS, coumarin is converted into the highly fluorescent species 7-hydroxycoumarin. Formation of the oxidised product can be monitored by measuring the increase in fluorescence at 460nm.

Samples containing coumarin solution (8ml, 10mM) and TiO_2 suspension (1ml, 5mg/ml, pH7.5 phosphate buffer) were placed in a 30ml UV vial and exposed to UV radiation in a Spectral Energy xenon arc solar simulator equipped with a Schott WG320 filter for a total of three hours. Every 30 mins, 1ml samples were pipetted from each vial into a 1.5ml eppendorf lid. These were centrifuged for 10 mins to separate the particles from the solution. 50ml was pipetted from the surface into a fluorescence cuvette. Fluorescence readings were taken at 460nm on the F4500 Fluorometer. Any increase in fluorescence indicates free radical scavenging generation by the nanoparticles. [13]

3 RESULTS AND DISCUSSION

3.1 Properties of Manganese Modified Titania

The ROS scavenging properties of two standard cosmetic grade nanoparticle TiO_2 samples are compared against TiO_2:Mn using the DPPH assay described previously and the results are given in Figure 1. It is clear that manganese modification significantly increased the free radical scavenging ability of TiO_2 nanoparticles.

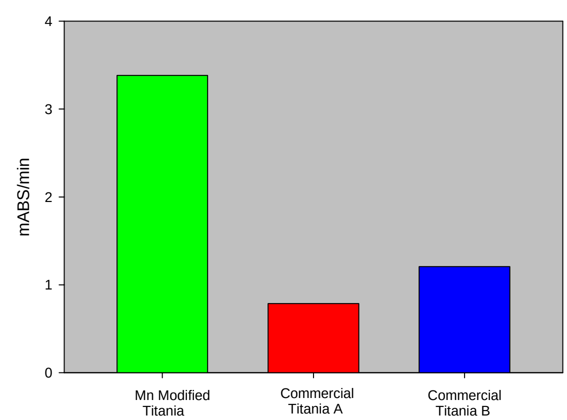

Fig. 1 DPPH scavenging abilities of TiO_2 and TiO_2:Mn nanoparticles

The ROS generation rates of TiO_2 and TiO_2:Mn are given in Figure 2, against a blank coumarin control line. The rate of ROS production is reduced by 97-100% by the introduction of Mn ions in to the titania lattice in comparison with a standard commercial grade of TiO_2.

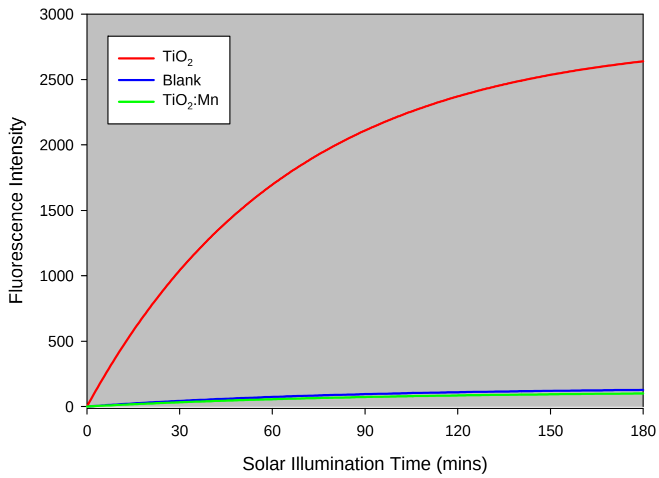

Fig. 2 ROS generation of TiO_2 and TiO_2:Mn nanoparticles during 180 mins solar exposure

3.2 Photostability of Formulations Containing TiO_2:Mn and Commercial Sunscreens

The photostability of TiO_2:Mn nanoparticle containing sunscreen formulations over eight hour exposure to simulated solar radiation in given in Fig. 3 as a function of variation of UVA:UVB ratio. The test emulsion is compared to two commercially available formulations with similar SPF ratings and a similar mixture of UV screening components (BMDM, OMC, TiO_2). The UVB absorbance is due to the presence of the OMC and TiO_2 or TiO_2:Mn. The UVA absorbance is mainly due to the presence of BMDM, with a contribution by TiO_2 or TiO_2:Mn. BMDM is less stable in the presence of ROS than OMC thus will break more rapidly. Reduction in UVA:UVB ratio is primarily due to a loss of UVA protection caused when BMDM breaks down, either by photoinduced decomposition or by attack from ROS, which may be produced by the de-excitation of TiO_2 nanoparticles. Lower sunscreen ROS loading during solar exposure will result in a reduction, or elimination, in variations to the sunscreen UVA:UVB ratio. The UVA:UVB ratio is therefore an efficient method of measuring the efficacy of the sunscreen. The Boots Star Rating System is used in consumer products in the form of a 0-5 star rating, in which a ratio of 0.9 and above gives a 5 star rating, 0.8-0.9 a 4 star rating, 0.6-0.8 a 3 star rating, 0.4-0.6 a 2 star rating, 0.2-0.4 a 1 star rating and below 0.2 a 0 star rating. Figure 3 shows that large losses in UVA:UVB ratio of the two commercial TiO_2 samples occurs rapidly during solar exposure, giving 1 star rated performance after 4 hours. The sunscreen containing TiO_2:Mn maintains 5 star rated performance during solar exposure. This directly relates to the reduction in ROS load demonstrated by Figures 2 and 3. The reduction in ROS load within the sunscreen results in a corresponding reduction in photoinduced breakdown of BMDM, the primary organic UVA absorber, and therefore a stabilization of the UVA:UVB ratio during solar exposure.

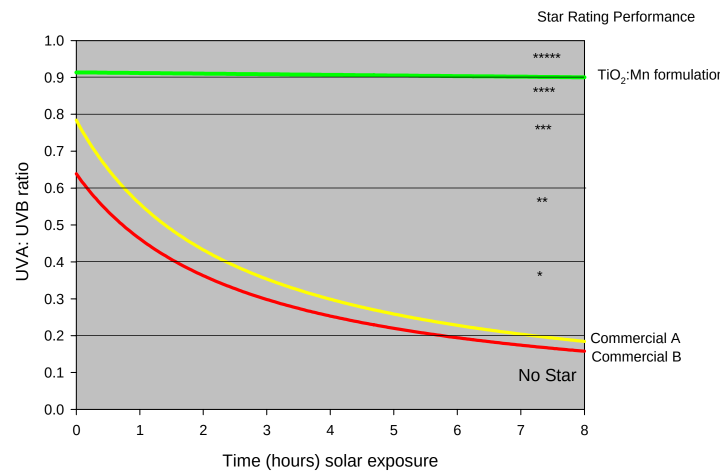

Fig. 3 Photostability of TiO_2:Mn containing sunscreens and two commercial products during full day solar exposure.

4 DISCUSSION AND CONCLUSIONS

The introduction of manganese into the TiO_2 lattice results in Mn^{3+} ions sitting on Ti^{4+} lattice site acting as a Mn^{3+} + hole, p-type dopant. The Mn-O energy level, and hole associated with it, lie almost exactly in the middle of the band gap giving a level for any photogenerated charges to de-excite. This reduces free radical generation by >95%.

The results from the DPPH demonstrate that the TiO_2:Mn is superior to TiO_2 at scavenging for free radicals. This is likely to be the outcome of surface Mn-O whereby there is a redox reaction as the Mn switches between a 2+ and 3+ oxidation states and scavenges for free radicals.

The absorbance within the UVA part of the spectrum is increased and this is probably due to the Mn-O antibonding state that sits at the bottom of the conduction band and aids to increase the density of states of the material.

The net result of this is that sunscreens formulated with TiO_2:Mn nanoparticles instead of standard TiO_2 show enhanced UVA absorption and extended photostability during topical use. Enhanced photostability allows continued high levels of protection throughout exposure to UV.

REFERENCES

[1] H. Yasui and H. Sakurai, "Chemiluminescencent detection and imaging of reactive oxygen species in live mouse skin exposed to UVA", Biochem. Biophys. Res. Commun., 2000, 269, 131-136

[2] Y. Matusmara and H.N. Ananthaswamy, "Toxic effects of ultraviolet radiation on the skin", Toxicol. Appl. Pharmacol., 2004, 195, 298-308

[3] M. Toyoshima, K. Hosoda, M. Hanamura, K.Okamoto, H. Kobayashi and T. Negishi, "Alternative methods to evaluate the protective ability of sunscreen against photo-genotoxicity", J. Photochem. Photobiol. B: Biol., 2004, 73, 59-66

[4] The revised guidelines to the practical measurement of UVA:UVB ratios according to the Boots star rating system, The Boots Co PLC

[5] D. Moyal, A. Chardon and N. Kollias, "Determination of UVA protection factors using persistent pigment darkening (PPD) as the end point", Photodermatology. Photoimmunology. Photomedicine, 2000, 16,245-249

[6] P. Perugine, S. Simeoni, S. Scalia, I. Genta, T. Modena, B. Conti and F. Pavanetto, "Effect of nanoparticle encapsulation on the photostability of the sunscreen agent 2-ethylhexyl-*p*-methoxycinnamate", Int. J. Pharma., 2002, 246, 37-45

[7] D.N. Biloti, M.M. dos Reis, M.M.C. Ferreira and F.B.T. Pessine, "Photochemical behaviour under UVA radiation of β-cyclodextrin included Parsol® 1789 with a chemometric approach" J. Mol. Struct., 1999, 480-481, 557-561

[8] A. Ricci, M.N. Chrétien, L. Maretti and J.C. Scaiano, "TiO_2 promoted mineralization of organic sunscreen in water suspension and sodium dodecyl sulphate micelles", Photochem. Photobiol. Sci., 2003, 2, 487-492

[9] G. Wakefield, M. Green. S. Lipscomb and B. Flutter, "Modified titania nanomaterials for sunscreen applications: reducing free radical generation and DNA damage", Mater. Sci. Tech., 2004 in press

[10] L. Magalhaes, M. Segundo, S. Reis and J. Lima, "Automatic method for determination of total antioxidant capacity using 2,2-diphenyl-1-picrylhyrazyl assay", Analytica Chimica Acta, 2006, 558, 310-318

[11] S. Hussain and S.F. Ali, "Manganese scavenges superoxide and hydroxyl radicals: an in vitro study in rats", Neurosci. Lett., 1999, 261, 21-24

[12] C. Sanchez-Moreno, "Review: methods used to evaluate the free radical scavenging activity in foods and biological systems", Food Sci. Tech. Int., 2002, 8, 121-137

[13] G. M. Makrigiorgos, J. Baranowska-Kortylewicz, E. Bump, S. K. Sahu, R. M. Berman and A. I. Kassis, "A method for detection of hydroxyl radicals in the vicinity of biomolecules using radiation-induced fluorescence of coumarin