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Broad spectrum UV protection by crystalline organic microrod sunscreens

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ABSTRACT

Ultraviolet (UV) light has the potential to cause many adverse effects on the body including causing the cancers melanoma and squamous cell carcinoma. The use of sunscreens to protect against these harmful effects has become common practice. However, many of the sunscreens currently being used have the ability to cross the skin barrier and enter the body. These components can produce reactive oxygen species inside the body which can cause damage to cells. We have developed a sunscreen product that contains organic particles that are too large to diffuse into the skin. These particles are formed from four FDA approved UV blocking molecules that are solids at room temperature. The components are first mixed together, melted, and then emulsified in water and allowed to cool. Once cooled, the particles slowly crystallize in the solution forming sphere to rod-like particles about one micron wide and one to tens of microns in length. SPF measurements of the samples showed comparable results to two commercially available sunscreens with SPFs of 50. The particles were shown to maintain their excellent UV blocking properties after exposure to UV light and show great promise as possible sunscreens.

1. Introduction

It is well known that ultraviolet (UV) light can cause a number of ailments to the skin and other parts of the body after extended exposure including skin cancer and photo aging of the skin (World Health Organization, 2014). Studies have shown that prolonged exposure to the sun increases the risk for the cancers melanoma and squamous cell carcinoma (Burnett and Wang, 2011). The public has been well educated on many of these dangers, and it is now a much more common practice for people to take precautions when doing outdoor activities and apply sunscreen. Regular application of sunscreen has been shown to reduce many of the risks involved in skin exposure to sunlight (Hayden et al., 1997), but surprisingly the increased use of sunscreens has coincided with an increase in the occurrence of melanoma (Hanson et al., 2006). This has prompted several researchers to explore correlations and causal links between the use of sunscreens and cancer. Researchers have suggested that chemicals used in sunscreens could potentially diffuse into the skin and further exposure to the UV light results in generation of reactive oxygen species that can cause significant damage to the cells (Hayden et al., 1997; Treffel and Gabad, 1996). The penetration of UV blocking chemicals found in common sunscreens has been proven in several cases (Hayden et al., 1997; Wissing and Müller, 2002). In a study conducted by Hayden et al. (1997), a sunscreen formulation containing oxybenzone 6% (w/v), octyl methoxycinnamate 7.5% (w/v), octyl salicylate 5% (w/v) and octocrylene 7% (w/v) was applied at a surface density of about 12.4 mg/cm^2, which is about 6 times the recommended application density. The sunscreen was washed off after 12 h and urine samples were collected periodically for about 2 days after the application of the sunscreen. It was estimated that about 1–2% of the applied oxybenzone at the increased surface density was absorbed into the skin. The fraction absorbed could be estimated to be higher than 10% if the application density was consistent with the recommended dose of 2 mg/cm^2, assuming the diffusion rate remained constant at the lower application density. These results are supported by in vitro studies which showed significant uptake of oxybenzone, 2-ethylhexyl 4-methoxycinnamate, and 2-ethylhexylsalicylate into the skin and also transport across the skin mounted in a diffusion cell (Treffel and Gabad, 1996). In another study 25 subjects applied a sunscreen containing 4% benzophenone-3 twice a day for 5 days. Analysis of urine samples collected

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during the 5 days of application and 5 days afterwards showed that 1.2–8.7% (mean 3.7%) of the total amount of applied benzophenone was excreted in urine (Gonzalez et al., 2006). The absorbed components of the sunscreens could cause systemic toxicity but more importantly it has been shown that the penetrated octocrylene, octyl methoxycinnamate, or benzophenone-3 generate highly reactive oxygen species in the cytoplasm of the nucleated keratinocytes in the epidermis (Hanson et al., 2006). These studies suggest that further research is needed to explore the transport of various sunscreen components into the skin and the potential for toxicity from the reactive species generated in the skin. Additionally it would be prudent to develop novel sunscreens that prevent or minimize the transport of the UV absorbing components into the skin.

Sunscreen formulations of large particles of zinc oxide and titanium dioxide will not penetrate the skin. These particles were successfully developed a long time back but application of these products results in a chalky appearance due to scattering of the visible light. The zinc and titanium dioxide particles act as UV blockers by reflection and absorption of the UV radiation. To minimize the visible light scattering, newer formulations were developed with nanosized particles and so the formulations were not opaque (Morabito et al., 2011). However, TiO_2 particles ingested by rats have been shown to have an impact on liver and nervous system functions (Duan et al., 2010; Hu et al., 2010) and zinc oxide nanoparticles have been shown to further the carcinogenesis process in mammalian cells (Ng et al., 2011). Some benefits of using the chemical blockers over the metal oxide components include reducing the visibility of the sunscreen. Also, the inorganic formulations are comparatively difficult to spread on the skin, which tends to cause decreased application rates of these types of sunscreen (Diffey and Grice, 1997). Finally, the inorganic components are prone to producing free radicals on exposure to light (Dunford et al., 1997)

Here we propose to develop a novel sunscreen by crystallization of commonly used organic sunscreen agents. By using chemicals that have a high melting point in solutions that they are not soluble in, crystallization of the material results in particles that are too large to go into the skin while still maintaining high UV blocking. By crystallizing the UV blocking molecules into the particles, we reduce the potential for transport of the chemicals into the skin. Since the particles can utilize highly effective UV absorbers, the particle based formulations will achieve similar (sun protection factor) SPF values for inorganic formulations. The lower refractive index of the particles compared to zinc oxide will keep the particle based formulations more transparent. Essentially our approach will retain many of the benefits of using zinc oxide particles but eliminate some of the disadvantages. Here we focus on incorporation of benzophenones in the particles because it is known to permeate into the skin, but it is used in several commercial formulations due to the excellent UV blocking properties.

2. Materials and methods

2.1. Materials

Oxybenzone (OB) was obtained from Acros Organics, avobenzone (AB) was obtained from Spectrum chemicals, dioxybenzone

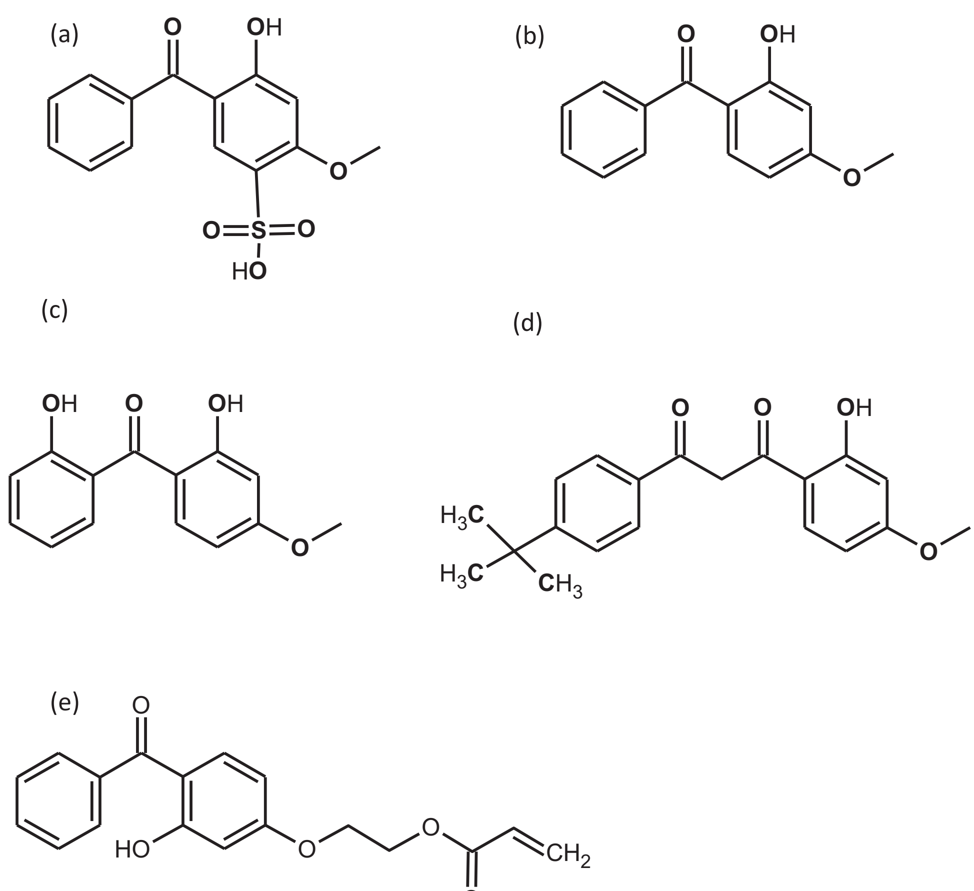

Fig. 1. Molecular structures of UV blocking components: (a) sulizobenzone, (b) oxybenzone, (c) dioxybenzone, (d) avobenzone, and (e) (4-benzoyl-3-hydroxyphenoxy)ethyl acrylate.