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Commentary

The molecular basis of UV-induced mutagenicity of sunscreens

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Knowland et al. recently described sunlight induced mutagenicity of a common sunscreen ingredient (padimate-O) [1]. In addition, they showed direct evidence for DNA damage using alkaline agarose gel electrophoresis of DNA which had been irradiated in vitro in the presence of Padimate-O. Earlier we [2] and others [3] demonstrated that the prototypical sunscreen, para-aminobenzoic acid, underwent several different photochemical reactions. Photoproducts resulting from dimerization as well as photoaddition to the common DNA bases have been characterized after exposure to ultraviolet B radiation. Although the photochemical reactions of other sunscreens have not been as well characterized, the in vitro formation of similar photoadducts in cells exposed to sunscreens and ultraviolet radiation could explain the observed mutagenic effects of these agents.

The first law of photochemistry states that in order for a photochemical reaction to occur, a photon must first be absorbed [4]. The ultraviolet absorbing ability of sunscreens make them excellent candidates for photoactivation and hence enhances the likelihood of photoreactions with biological molecules. In addition, the effect of irradiating wavelength must be considered. Many older studies used light sources producing mainly UVB, with relatively little UVA and longer wavelengths. However, it is important to note that productive photochemistry can also occur with photons far from the wavelengths maximally absorbed by the sunscreen. For these reasons, studies on the photochemistry of sunscreens should be conducted using solar simulators, which produce not only UVA and UVB but also the longer wavelength radiation present in sunlight. For example, Sutherland reported the absorption characteristics of DNA at wavelengths extending into the visible range [5]. Even though DNA photoadducts have not been directly ascribed to irradiation at these wavelengths, the effects of these longer wavelengths on cells has been demonstrated [6]. On the other hand, the use of visible light to activate 8-methoxypsoralen (a commonly used photochemotherapeutic agent) has been recently reported. Gasparro et al. measured 8-MOP extinction coefficients well into the visible (~450 nm) and showed that the irradiation of either DNA or cells in the presence of 8-MOP led to the formation of psoralen photoadducts with a surprising level of efficiency [7]. It was suggested that this efficiency might have resulted from a reduction in the secondary reactions typical of bifunctional psoralen compounds. These studies with visible light suggest that some of the observed effects of sunscreens on skin (and in skin cells) could arise from their exposure to photons of wavelengths far from their absorption maxima.

Although Knowland et al. did not characterize the actual photochemical events it is reasonable to assume that padimate-O will have photochemical properties similar to PABA. Others have shown that a film of medium protection sunscreen containing 3–4% padimate-O transmits all photons greater than 350 nm [8]. At shorter wavelengths the absorptive properties of the sunscreen drastically reduce the amount of transmitted radiation. Knowland et al. pointed out that although the UVA activation of padimate-O appeared to be less efficient, this route may operate in sunbathers who use UVB-filtering sunscreens to eliminate the burning wavelengths and, as a consequence of prolonged exposure to sunlight, receive heavy doses of longer wavelength radiation (UVA and visible).

Another issue to be considered is the indirect photosensitization of DNA damage. In this case light absorbed by the sunscreen can lead to DNA base damage. Recently the photosensitized induced formation of thymine dimers was described [9]. Similar results had been described earlier for several other photosensitizers including some with structures very similar to several common sunscreen ingredients [10].

Knowland et al. cited studies showing that skin tumor induction in sunscreen protected hairless mice required a greater UVB dose (17 vs. 11 J/cm^2) to observe tumor induction. These data indicate a protective effect for the sunscreen. In hairless mice, tumorigenesis is reduced when sunscreen-treated mice receive the same does of

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light as controls [11]. Superficially, such results indicate that sunscreens are protective. However, by virtue of their prevention of sunburn, sunscreens encourage longer exposure to the sun. Thus, it may be more relevant to compare the effect of a given exposure in untreated animals with a longer exposure in treated mice. Here, it appears that sunscreens delay tumorigenesis, but it is not certain that they prevent it. Furthermore, as Knowland et al. emphasized, it may be difficult to distinguish between the protective effects of surface sunscreen as opposed to the DNA-damaging effects of intracellular sunscreen molecules once exposed to UV light. The two-edge behavior of sunscreens, viz., skin-protective (anti-sunburn) and mutagenic may confound experimentalists for a long time to come. However, more realistic studies on the photoinduced sunscreen-damage of DNA (especially in vivo) could further our understanding of these widely used compounds.

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