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COMMENTARY

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Sunscreen bans: Coral reefs and skin cancer

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Summary

What is known and objective: Hawaii recently enacted legislation that will ban the use of two major ingredients of the majority of commonly used sunscreens. The reason for the ban is the ingredients' putative deleterious impact on marine ecosystems, particularly coral reefs. But sunscreens also save lives by decreasing the risk of UV-induced skin cancers. We review both sides of the issue and potential implications for the healthcare system.

Comment: Coral reefs consist of organisms in delicate equilibria that are susceptible to small changes in their surroundings. Recent natural and man-made disruptions, direct or indirect, such as changes in ocean temperature and chemistry, ingress of invasive species, pathogens, pollution and deleterious fishing practices, have been blamed for the poor health, or even the outright destruction, of some coral reefs. The most popular sunscreen products contain two ingredients—oxybenzone and octinoxate—that have also been implicated in coral toxicity and will be banned. This creates a healthcare dilemma: Will the protection of coral reefs result in an increase in human skin cancers?

What is new and conclusion: Concentration estimates and mechanism studies support an association—direct or indirect (*via* promotion of viral infection)—of sunscreens with bleaching of coral reefs. A ban on the two most common sunscreen ingredients goes into effect in Hawaii on January 1, 2021. Proponents suggest that this is a trend, just the first of many such bans worldwide; opponents warn of a dire increase in human skin cancers. As a result, alternative sunscreen compounds are being sought.

KEYWORDS

coral reef, octinoxate, oxybenzone, skin cancer, sunscreen

1 | WHAT IS KNOWN AND OBJECTIVE

The legislature of the State of Hawaii of the United States touched off a firestorm of controversy with a decision to ban the two most commonly used sunscreen agents. The intent of the legislation is protection of coral reefs.[1] The ban goes into effect in Hawaii on January 1, 2021, but proponents predict that similar bans will soon spread to other areas of the world that have coral reefs (Figure 1). Opponents question the evidence and, more importantly, warn of potential latent increase in new cases of skin cancer. We review the evidence for claims of a deleterious effect (direct or indirect) of the ingredients on coral reef health, the potential for a rise in skin cancer incidence and solutions to the dilemma that are currently being investigated.

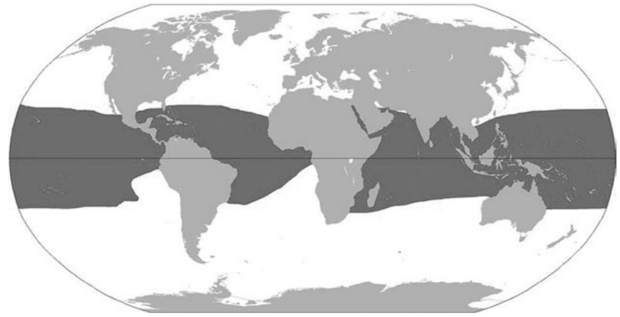

FIGURE 1 Coral reef locations worldwide. https://upload.wikimedia.org/wikipedia/commons/c/cb/Coral_reef_locations.jpg

FIGURE 2 Coral reef in Hawaii. https://commons.wikimedia.org/w/index.php?title=Special:Search&limit=50&offset=190&profile=default&search=hawaii+coral&searchToken=ep7kfakzpmmmhgmqmozhsxle2#/media/File:Heterocentrotus_trigonarius_in_Kona.jpg

2 | COMMENTARY

2.1 | Coral reefs and "bleaching"

Coral reefs are iconic biodiverse ecosystems comprised of colonies of diverse tiny animals found in marine waters that contain few nutrients. Unlike other species of the same phylum (such as anemones and jellyfish), corals secrete calcium carbonate, which holds the corals together and gives the reefs their crystalline texture (Figure 2). Extant coral reefs were formed after the last glacial period, thus are up to 10 000 years old. Because the bulk of a coral reef consists of coral skeletons from mostly intact coral colonies, chemical elements present within corals become incorporated into the calcium carbonate deposits, and shell fragments and remains of calcareous algae accumulate. Therefore, coral reefs have the ability to withstand damage from storms and other threats. However, they are extremely sensitive to changes in temperature and environmental insults. For example, small increases in the supply of nutrients can promote algal encroachment and enable algae to outcompete and kill coral.

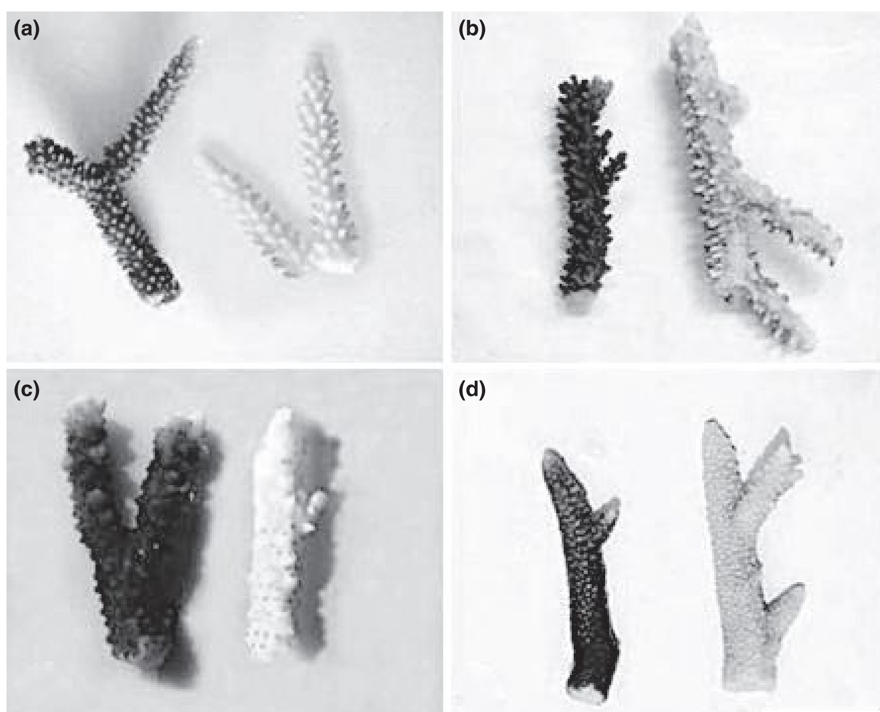

FIGURE 3 Impact of sunscreen addition on nubbins of *Acropora*. Untreated (brown) and treated (bleached) nubbins of (a) *Acropora cervicornis*(Caribbean Sea, Mexico); (b) *Acropora divaricata* (Celebes Sea, Indonesia); (c) *Acropora* sp. (Red Sea, Egypt); and (d) *Acropora intermedia*(Andaman Sea, Thailand). Images were taken within 62 h of the start of sunscreen incubations. Scale bar = 2 cm. From Donovaro et al. (2008) Environment Health Perspect 116:441-447. US government publication in the public domain

Unfortunately, it is estimated that over half of all coral reefs worldwide are currently threatened.[2,3] And damage or death of coral reefs has a multiplicative negative domino impact on other life forms, because coral reefs either directly or indirectly support a large variety of animals, including fish, seabirds, sponges, jellyfish, worms, shrimp, lobsters, crabs, molluscs, starfish, sea urchins, sea cucumbers, turtles and snakes.

A telltale sign of distress in coral reefs is "bleaching" (Figure 3). Corals "bleach," that is turn white, when they are under stress and expel the algae (zooxanthellae) living in their tissues. Coral is not necessarily dead when bleached, corals can survive a bleaching event, but bleaching is a clear indication that the coral is under stress and is in danger of dying. The dramatic increase in coral bleaching has been observed worldwide over the past 20 years, and it has raised concern and alarms about the future viability of coral reefs, the life forms dependent on them and their economic value (estimated to be $30-375 billion US dollars).[4] As an indication of the magnitude of the problem, in 2005, the United States lost half of its coral reefs in the Caribbean due to a massive bleaching event.[5] The phenomenon of bleaching is exacerbated when ocean temperatures rise, in the presence of excess ultraviolet (UV) radiation and in the presence of bacterial pathogens and pollutants.[6–9] It is also exacerbated when the coral is exposed to certain chemicals.

2.2 | Skin cancer protection

2.2.1 | Solar radiation and Ultraviolet Spectrum

Solar radiation is a general term for the electromagnetic radiation emitted by the sun. The radiation encompasses a broad range of wavelengths (or the inverse, frequencies), which is collectively called the electromagnetic spectrum. Energy levels vary across the continuous electromagnetic spectrum according to the fundamental principle that energy is inversely proportional to wavelength. That is, shorter wavelengths (eg, ultraviolet through X-rays and gamma rays) are higher energy; longer wavelengths (eg, infrared through radio waves) are lower energy. Ultraviolet radiation (UVR) is a specific range of wavelengths (Figure 4) that interact with living tissue and cause biochemical and physiological changes in exposed tissue. The unprotected exposure to UVR can cause sunburn, premature ageing and increased risk of skin cancers.

UVR has been subdivided into three wavelength ranges: UVA (320-400 nm), UVB (290-320 nm) and UVC (200-290 nm).[10] The UVA range (longer wavelengths) is associated with the lowest energies, the UVB range (intermediate wavelengths) with intermediate energies and the UVC range (shorter wavelengths) with highest energies. Approximately 80%-90% of UVA reaches the earth's surface, only 1%-10% of UVB is able to reach the surface, and UVC radiation

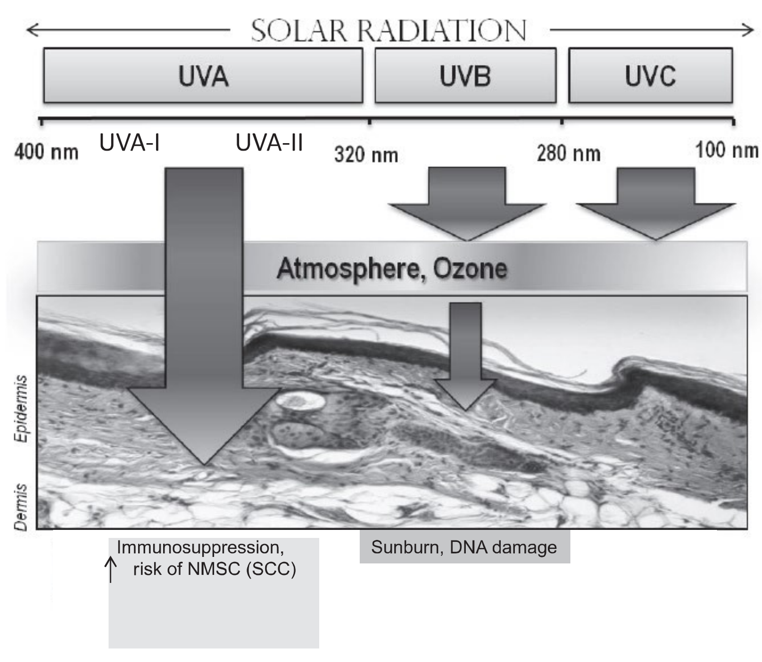

FIGURE 4 The three subdivisions of the UV radiation spectrum (100-400 nm) are depicted along with their interaction with skin tissue. The shortest wavelength, highest energy UVC radiation, is completely blocked by earth's atmosphere from reaching earth's surface. The UVB radiation is partially blocked by the atmosphere and only 1%-10% reaches the earth and is able to penetrate the upper layers of the epidermis, primarily causing sunburn. UVA radiation is the most dangerous to tissue since 80%-90% of the radiation reaches the surface and is capable of penetrating deeper layers of the skin, initiating biochemical changes that can potentially lead to skin cancers. Modified from https://www.researchgate.net/figure/Electromagnetic-spectrum-of-visible-and-UV-radiation-and-biologic-effects-on-the-skin_fig3_237095045

is completely screened out by the earth's atmosphere and does not reach the surface.[11] All three forms of UVR have been shown to cause various types of tissue damage.

2.2.2 | UVR, Sunburn and skin cancer

The relationship between UVR and damaging effects on DNA has been known since the 1960s.[12,13] It is now well established that UVR exposure causes numerous changes in the skin that can result in actinic keratoses, which is thought to be a precursor of certain types of non-melanoma skin cancer (NMSC), and squamous cell carcinoma (SCC). NMSC is the most common malignancy in the United States.[14] Both conditions are generally attributed to UVA radiation, likely because UVA penetrates into deeper skin layers than does UVB,[15] but UVB also plays a role.[16,17] Other common risk factors for developing skin cancer include the amount of solar exposure in early childhood, genetic factors, skin type, pigmentation and ageing.[18]

UVA causes the formation of reactive oxygen species, which can indirectly cause DNA damage by creating breaks in the tertiary structure.[11] UVB is absorbed by DNA and causes structural damage. In addition, UVR exposure causes mutations in p53 tumour suppressor genes which play an important role in DNA repair and cellular death (apoptosis) in cells that have sustained DNA damage. Analysis of p53 gene mutations induced by UVR has shown that there is a connection between UVR exposure, DNA damage and skin carcinogenesis.[19]

2.2.3 | Effect of UVB and UVA radiation on the skin and role of the SPF

It is now well established that the sunburn that results from exposure of skin to solar radiation is primarily due to the UVB portion of the spectrum. The SPF (sun protection factor) that is associated with sunscreen products refers only to the ability to protect skin against sunburn, and this has been shown not to be related to the potential for developing skin cancers caused by exposure to both UVA and UVB portions of the spectrum.[17,20] By definition, SPF is a measure of how much solar energy (UVB radiation) is required to produce sunburn on protected skin (*i.e.*, in the presence of sunscreen) relative to the amount of solar energy required to produce sunburn on unprotected skin. The larger the SPF value, the greater the sunburn protection. The SPF is not related to protection against UVA-induced damage. Poon *et al*[20] conducted studies in humans that showed that a separate factor, immune protection factor (IPF), was a better predictor of protection against UVA. These authors also found that there was no correlation between IPF and SPF.[20] In general, clinical evidence has shown that broad-spectrum sunscreens, when properly used, are able to decrease the rate of new precancerous lesions, result in significantly fewer actinic keratoses and result in fewer SCCs.[21] However, there is little evidence to show that sunscreen use can protect against basal cell skin cancers and melanomas.[21]

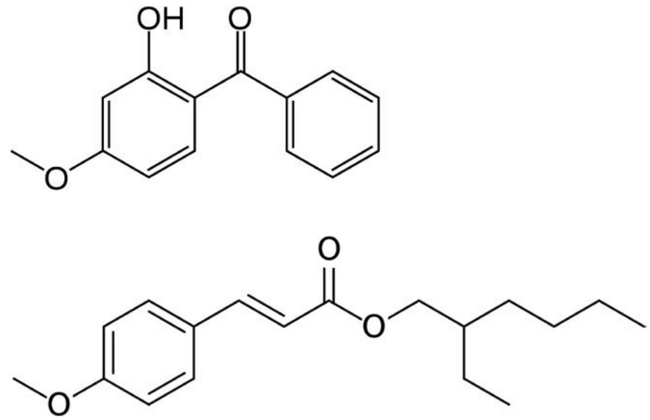

FIGURE 5 Chemical structures of oxybenzone (top) and octinoxate (bottom)

2.3 | Oxybenzone and octinoxate

Two ingredients of sunscreens that are to be banned in Hawaii are oxybenzone and octinoxate (Figure 5). They are the main active ingredients in an estimated 70%-80% of sunscreens. Oxybenzone (BP-3; benzophenone-3; 2-hydroxy-4-methoxyphenyl-phenylmethanone; 2-hydroxy-4-methoxybenzophenone; CAS No. 131-57-7) and octinoxate (OMC; ethylhexyl-4-methoxycinnamate; *trans*-octyl methoxycinnamate; ethylhexylmethoxycinnamate; CAS No. 5466-77-3) are widely used in sunscreen lotions and in a host of personal-care products (such as body fragrances, hair-styling products, shampoos, conditioners, skin care products, body creams and lotions, insect repellents, cosmetics and soaps). Both have been studied for their potential ability to harm coral.

Oxybenzone has a molecular weight of 290.4 and absorbs UVB (UV_{max} = 288 nm) and UVA-II radiation (UV_{max} = 326 nm), resulting in a photochemical excitation and absorption of energy. After the molecule has absorbed energy, it returns to the ground state by emitting at a longer wavelength radiation thereby decreasing the skin penetration of radiation which then reduces the risk of DNA damage.[22] Because oxybenzone absorbs both UVA and UVB radiation, it is considered a broad-spectrum UV filter. Octinoxate has a molecular weight of 228.2 and filters UVB radiation with a UV_{max} = 310 nm.[23]

2.4 | Testing

Three representative studies that have reported an association of sunscreens with cell or coral toxicity are summarized below:

- Stein *et al*[24] isolated and characterized the cellular toxicities of the major products of UV-induced photolysis of octinoxate. They reported that the parent compound and two cyclodimer photoproducts are toxic to cells (NIH/3T3).
- Danovaro *et al*[25] conducted several independent in situ studies on several species of coral in different areas of the world. At all sampling sites sunscreens, including oxybenzone and octinoxate

produced dose-related (as low as 10 μL/L) and temperature-related (greater at 30°C vs 28°C) bleaching.
- Downs et al.[26] examined the effects of oxybenzone on the larval form (planula) of one species of coral and in vitro toxicity of six additional species of coral. The LC_{50} values (median lethal concentration) for oxybenzone-exposed planulae ranged from 139 to 779 μg/L at 24 hours. The values for coral cells (4 hours, in the light) ranged from 8 to 340 μg/L.

2.5 | Mechanism

In addition to a possible direct toxic effect on coral by ingredients of sunscreens, an alternative indirect mechanism has been proposed. The alternative might be even more serious. Sunscreens can significantly enhance viral production in seawater by inducing the lytic cycle in prokaryotes with the equivalent to latent infection in eukaryotes (known as lysogenic infection in prokaryotes).[27]

2.6 | Environmental load

Danovaro et al.[25] proposes that the global release of sunscreen in areas containing coral reefs can be roughly estimated as follows:

- an average dose application of 2 mg/cm^2 of sunscreen (the amount that is recommended by the US FDA) applied to a full body surface of 1 m^2, which yields an average usage of 20 g per application.[28]
- two applications per tourist per day for an average of 5 days, times 78 million tourists per year in coral reef-containing locales (10% of world tourists).
- 10 000 tons of sunscreen produced annually, with 25% of applied sunscreen washed off while in the water [sample test] = 4000 to 6000 tons/y in reef-containing areas.[25] Some put the estimate significantly higher.

Similar results were obtained from a few direct measurements. The concentrations of oxybenzone are said to be 0.8-19.2 μg/L at Hawaiian sites and 75-1400 μg/L in the US Virgin Islands. Thus, sunscreens are likely present at, or above, levels that can be toxic to coral reefs at a significant number of locations.

2.7 | Dissenting point of view

It should be stated that not everyone agrees that sunscreens should be implicated in damage to coral reefs. For example, the Hawaii Medical Association and Skin Cancer Coalition cite an absence of peer-reviewed evidence demonstrating causality and characterize studies that suggest that sunscreens cause a decline in the health of coral flawed because they were conducted in laboratory settings under artificial conditions and not in actual marine environments.[1] Others suggest that sunscreen is a relatively minor contributor to coral reef damage.[29]

2.8 | The search for replacements

A recent review describes efforts to come up with alternatives to oxybenzone and octinoxate.[30] Potential sources include the following:

- marine organisms (eg, compounds that contain a cyclohexene ring or a cyclohexenone ring, plus various functional groups)
- red algae (eg, palythine, 2-[[3-amino-5-hydroxy-5-(hydroxymethyl)-2-methoxycyclohex-2-en-1-ylidene]amino]acetic acid, and shinorine, (2*S*)-2-[[3-(carboxymethylimino)-5-hydroxy-5-(hydroxymethyl)-2-methoxycyclohexen-1-yl]amino]-3-hydroxypropanoic acid), both of which are UV filters.
- zebrafish (eg, gadusol, 3,4,5-trihydroxy-5-(hydroxymethyl)-2-methoxycyclohex-2-en-1-one).
- Plants (eg, derivatives of glucolimnanthin in the wildflower meadowfoam)

3 | WHAT IS NEW AND CONCLUSION

Coral reefs are experiencing serious damage as a consequence of a variety of man-made and natural threats. Sunscreens are chemicals of emerging concern[31] and are suspected of contributing to coral reef damage. And the damage is exacerbated by global warming. Sunscreens are washed off into ocean waters directly or indirectly during washing. Because sunscreen components are lipophilic, they can accumulate in aquatic animals. In response to the real or perceived magnitude of the threat, Hawaii has initiated the first ban of two common ingredients of sunscreens. Others may follow.

It would seem an easy decision to ban components of sunscreens, whether or not the link to coral reef damage is definitive. However, sunscreens protect wearers from getting skin cancers. The question thus becomes coral reefs vs skin cancers: What balance? Fortunately, some sunscreens still considered safe for coral reefs, such as zinc oxide, titanium oxide and several others are currently available, and new substances are being investigated.

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