Safer Sunscreens

Nature’s Approach to UV Protection

Partnered with Method

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Greener Solutions

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Executive Summary

Current sunscreen formulations are effective UVA/UVB blockers but pose significant health and ecological hazards. Recent research describing the extent of negative human health and environmental impacts demands the development of safer alternatives. Three classes of compounds - colorless carotenoids, mycosporine-like amino acids (MAAs), and select antioxidants, were evaluated as potential alternatives. UV absorption spectra of these compounds reveal that colorless carotenoids and MAAs are likely to be superior UV blockers than currently used compounds. There is also evidence to suggest that the antioxidants vitamins C and E may mitigate tissue damage from UV radiation. Despite limited toxicological exposure information, the ubiquitous nature of carotenoids and vitamins C and E in our diets, specifically in food associated with positive health outcomes, suggest that they may be safer than currently used compounds. We propose that these compounds, or possible synthetic variants, may be useful additives or alternatives to existing UV blockers, reducing or eliminating compounds known to be harmful to humans and the environment.
Introduction

Humans have used sunscreens of various kinds for at least two thousand years. In ancient times, these took the form of plant oils and gels such as aloe vera. It was not until the 20th century that sunscreen, as we think of it today, was developed. In 1928, benzyl salicylate and benzyl cinnamate came on the market as the first chemical sunscreens. The exact compounds used as sunscreen have changed over the years, but the fundamental need for them has not. Ultraviolet (UV) radiation exposure continues to be a significant and ever-present human health hazard, particularly in its connection to skin cancer. Almost 100,000 cases of skin cancer occur in the U.S. annually, with melanoma rates steadily increasing over the past twenty years. Despite modern developments in cancer treatment, approximately 9% of those diagnosed with melanoma will die from it. The connection between UV damage and melanoma is significant: one recent study showed that just five bad sunburns early in life, can increase melanoma risk by 80%.

Skin damage from UV radiation occurs through two mechanisms, each related to a different range of wavelengths (Figure 1). UV radiation consists of three different bands: UVA, UVB, and UVC. UVA consists of light with wavelengths between 315-400 nm. This light passes directly through the Earth’s ozone layer and damages skin primarily through the production of reactive oxygen species (ROS), which in turn can damage cellular tissues including DNA. UVB consists of
light with wavelengths between 280-315 nm. It is partially blocked by the ozone layer, but the light that gets through is of sufficiently high energy to damage DNA directly. UVA is present year-round, and its intensity is not dependent on season or weather conditions unlike UVB, which is strongest in the summertime during a four-hour period around solar noon and clear skies.\textsuperscript{4} UVB is the form of UV radiation that is primarily associated with skin erythemal response (e.g. sunburn), whereas UVA is typically associated with skin darkening (e.g. tanning). UVC, with wavelengths between 100-280 nm, is the highest energy of three but is blocked almost entirely by the ozone layer (Figure 2).

\textbf{Figure 2.} Illustration of the skin penetration depths and health hazards related to UVA, UVB, and UVC radiation.
There are currently 16 organic UV blockers and two mineral (inorganic) UV blockers approved for use in the U.S., eight of which are used in most available sunscreen formulations (Figure 3). These UV blockers address UVA and UVB radiation through two primary mechanisms. Organic UV blockers absorb UV radiation and dissipate it as heat, preventing that radiation from being absorbed by skin tissues. Inorganic UV blockers can work either through this first mechanism or by reflecting UV light, depending on the exact formulation used.

**Figure 3.** Organic (left) and mineral (right) UV blockers currently sold and used in the U.S.

The current regulatory environment provides a hurdle to the implementation of new UV blockers. Because UV blockers in the U.S. are regulated as over-the-counter medications, the adoption of new compounds is exceptionally difficult. In fact, no new UV blockers have been approved in the U.S. for more than 20 years and many of the ones currently in use were grandfathered into the system rather than making their way through the current regulatory structure. Although there are many regulatory difficulties, there is a need to use a health and ecologically conscious design to move towards a new generation of sunscreens.
Health and Environmental Hazards of Current Organic UV Blockers

Despite the benefits of preventing skin damage and subsequent cancer, existing UV blockers approved for use in the U.S. possess a number of health and ecological hazards. In particular, oxybenzone and related compounds are endocrine disruptors and have been directly linked to coral reef bleaching.

Chemical UV blockers can impact marine ecosystems by disrupting endocrine systems, decreasing coral larvae activity, increasing coral morphological deformities, causing phototoxicity impacts, damaging DNA. Benzophenones can cause several types of damage to genetic material including oxidative damage to DNA, the formation of cyclobutane pyrimidine dimers, single-strand DNA breaks, cross-linking of DNA to proteins, and an increase in the formation of DNA abasic sites. Chemical UV blocker can also bioaccumulate in fish causing more harm to humans, as humans tend to eat fish that are higher up on the food chain. These aforementioned negative effects of chemical UV blockers exacerbate similar mechanisms imposed by increasing sea-surface temperatures.

The factors leading to coral bleaching are complex and no single chemical mechanism has been attributed to a coral bleaching event. Regardless, current chemical products cause coral to become stressed, perhaps through the action of several concurrent mechanisms. Eventually corals expel their symbiotic algae, zooxanthellae. Figure 4 (below) depicts these species’ symbiotic relationship. Zoxanthellae give coral its color; therefore, its expulsion leads to the loss of color resulting in bleached coral. Oxybenzone and octinoxate induced coral bleaching is also exacerbated by light exposure in addition to chemical UV blocker compounds.

Figure 4. Symbiotic relationship between algae and coral.
Coral reef bleaching has been steadily increasing globally over the past twenty years (Figure 5). Due to their link to coral bleaching events, Hawaii became the first state to ban the distribution of sunscreens containing the chemicals oxybenzone and octinoxate in May of 2018. The phaseout must be completed by 2021. Also, in November 2018, the Pacific Island of Palau passed a similar law, to come into effect in 2020.

Recent research has found that current products are not only endocrine disruptors in marine organisms such as fish and coral but also in humans and other mammals. One study conducted an extensive review of chemical UV absorbers’ mechanism of action as endocrine disruptors. A simplified table can be found below summarizing the mechanisms of various UV filters.

<table>
<thead>
<tr>
<th>UV blocker</th>
<th>Chemical group</th>
<th>Mechanism of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzophenones</td>
<td></td>
<td>Activate ER and block estradiol; Antagonize AR and inhibit testosterone formation; interfere with THR</td>
</tr>
<tr>
<td>Camphor</td>
<td></td>
<td>Activate ER and block estradiol; Antagonize AR and inhibit testosterone formation; Antagonize PR</td>
</tr>
<tr>
<td>Cinnamate</td>
<td></td>
<td>Decrease T4 levels; Antagonize PR and AR</td>
</tr>
</tbody>
</table>

Table 1. Summary of endocrine disruption effects of different classes of chemical UV blockers. ER: estrogen receptor alpha; AR: androgen receptor; THR: thyroid hormone receptor; PR: progesterone receptor; T4: thyroxine

Figure 5: The number and severity of unbleached coral locations are dramatically decreasing (blue line). The cumulative number and severity of bleaching events are dramatically increasing (red line)
Organic UV blockers have been used in the U.S. for decades, but their health hazards and ecological toxicity towards algae and coral were not known until recently. These chemical blockers have been used in formulations because they are effective, cheap, U.S. FDA (United States’ Food and Drug Administration) approved and have robust toxicological profiles. Despite this, research is emerging indicating that chemical UV blockers are persistent, toxic to marine ecosystems, skin sensitizers, and endocrine disruptors. Only now have the negative impacts of these chemicals begun to outweigh their efficacy and economic viability. This new toxicity information and political pushes from Hawaii and Palau have highlighted the need for new research evaluating the downsides of current formulations. With an estimate of 14,000 tons of sunscreen ending up in the ocean annually and reaching uninhabited ecosystems (such as the Arctic), the demand for an innovative alternative formulation is critical.
Health and Environmental Hazards of Current Inorganic UV Blockers

Mineral or inorganic sunscreens also pose a threat to human and environmental health. Mineral sunscreens, which often include nanoparticle components of zinc oxide and titanium dioxide, work by reflecting UV light. Mineral UV blockers are incorporated into formulations as nanoparticles to avoid a streaky white appearance of sunscreen upon application onto the skin. Mineral sunscreens are considered safer by the Environmental Working Groups (EWG), but inorganic sunscreens pose a carcinogenic hazard to industrial workers via inhalation and have multiple points of exposure and environmental release (Figure 6, below). Furthermore, zinc and titanium oxide have also been shown to increase absorption of other contaminants such as pesticides, adding additional concern due to all the health hazards other contaminants themselves pose.

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>Group I Human</th>
<th>Group II and III Human</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Carcinogenicity</td>
<td>Mutagenicity</td>
</tr>
<tr>
<td>Zinc Oxide</td>
<td>L</td>
<td>M*</td>
</tr>
<tr>
<td>Titanium Dioxide</td>
<td>H*</td>
<td>-</td>
</tr>
</tbody>
</table>

Figure 6. Human health and environmental endpoints for titanium dioxide and zinc oxide.

There are additional drawbacks to these nanoparticle formulations of inorganic UV blockers. In these formulations, nanoparticles have a protective coating, often alumina or silica, that breaks down in marine environments. The products of this breakdown pose a hazard through reactive oxygen species (ROS) generation. Lastly, these mineral nanoparticles are also chemosensitizers, which increases the toxicity of other chemicals. Currently, there is no regulation specifically on nanoparticle formulations, in part because they are difficult and expensive to characterize.
We considered several criteria in order to develop an alternative sunscreen formulation that is high performing, compatible, and safe.

The first set of criteria that we implemented to gauge the overall effectiveness of the new formulation was technical performance standards. Multifunctional UV-blockers represent the most attractive chemicals for use in a new sunscreen formulation because they may confer other benefits in addition to their capacity to directly absorb and dissipate UV light. The most important technical properties for UV-blockers under consideration are the following:

1. **UVB/UVA molar absorptivity** is the capacity of a particular chemical to absorb light in the UV spectrum on a per mole basis normalized by pathlength.

2. **Antioxidant capacity** is important because much of the skin damage associated with UVA light is due to the formation of ROS. Antioxidants quench ROS, which may otherwise damage DNA, cause lipid peroxidation, etc.

3. **Chemical stability** protects the chemical structure, especially the portion conferring UV absorbance, from a rapid loss to side reactions.

4. **Skin permeability** should be minimal for ideal UV-blocking chemicals so that exposure to exogenous chemicals is low.

5. **Water resistance** increases the longevity of a UV-blocker on the skin, especially when used while swimming or interacting with water.

6. **Emollience** adds a soft touch or soothing feeling when applying a cream formulation.

**Technical Performance Criteria**

(1) UVA/UVB molar absorptivity:

The ability of a UV-blocker to absorb UV light is the most fundamental of the technical performance criteria. Absorbance is a measure of how much light of a particular wavelength passes through a controlled volume containing a fluid and is given by the Beer-Lambert Law:

\[ A = \log \left( \frac{I_0}{I} \right) = \varepsilon \cdot c \cdot l \]
Absorbance ($A$) is the decrease in light intensity ($I$) after passing through a substance with a given molar absorptivity or molar extinction coefficient, $\varepsilon$ (cm$^{-1}$ M$^{-1}$), at a concentration, $c$ (M), over a path length, $l$ (cm). An absorbance spectrum gives the absorbance of a chemical or mixture over a range of wavelengths. Absorbance is dependent on concentration and path length, whereas molar absorptivity is independent of these variables. In order to compare various chemicals, it is therefore important to convert absorbance spectra to molar absorptivity spectrum, which is the absorptivity of a chemical over a range of light wavelengths (Figure 7).

![Figure 7. Example UV absorption spectrum demonstrating the difference in molar absorptivity between oxybenzone and an ideal alternative.](image)

New chemical considerations need to have a large UVA and UVB absorbance range. The graph above illustrates the molar extinction coefficient or how strongly a substance absorbs light. A strong absorbance or high molar extinction coefficient suggests the relative quantity of the compound necessary to absorb light. A broad UVA/UVB spectrum absorbance is important to protect against cellular damage.

(2) Antioxidant Capacity:

ROSs generated by the absorbance of UV light can cause significant skin damage. This is the main mechanism by which UVA light damages skin cells without the typical sunburn erythemal response. In addition, ROS may oxidize active ingredients, decreasing their performance over time. Antioxidants react with radicals to form oxidized products or by dissipating the energy of singlet

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oxygen as heat.\textsuperscript{15} How the absorbance spectra of proposed alternatives change upon oxidation and any toxicities of potential oxidation products will need to be considered.

(3) Chemical stability:

An ideal UV blocker should persist on the skin surface over a couple of hours in order to preserve the UV-blocking integrity of the formulation. However, the UV blocker should not be overly persistent especially in the aquatic environment or in wastewater treatment plants in order to minimize potential biological effects of exposure to the chemical. The time scale of oxidation of alternative products should be considered before use of these compounds as active ingredients in sunscreen. These products should be UV-stable long enough to maintain their efficacy. Sunscreen formulations should also be stable over a wide temperature range, as these products will be used in a wide variety of climates.

(4) Skin permeability and water resistance:

In order to prevent unnecessary systemic exposure to UV-blockers, the skin permeability of the blocker should be relatively low. The skin permeability of a chemical can be described quantitatively using the permeability coefficient, $K_p$ (cm/s). The skin permeability coefficient is related to several chemical properties and can be determined using quantitative structure-activity relationships (QSARs).\textsuperscript{16} The permeability coefficient is most directly related to the molecular weight and hydrophobicity of the chemical.\textsuperscript{17} Higher molecular weights diffuse more slowly into inner layers of the skin, whereas more lipophilic molecules are attracted to cell membranes and diffuse more quickly into skin cells. Potts and Guy published a widely used QSAR for the empirical relationship between molecular weight, hydrophobicity and skin permeability coefficients given by the equation below:\textsuperscript{17}

$$\log K_p = 0.71\log K_{ow} - 0.0061MW - 6.3$$

$K_p$ is the permeability coefficient, $K_{ow}$ is the octanol-water partition coefficient, a measure of how hydrophobic a chemical is, and $MW$ is the molecular weight. From this relationship, we have calculated $K_p$ values for traditional UV blockers and our proposed alternatives.

(5) Emollience:

Emollience provides the smooth on-skin feel as sunscreens are applied to the body. Certain structural components of compounds are associated with emollience such as saturated
hydrocarbons, unsaturated hydrocarbons, and alcohols (Figure 8, below). They are often derived from petrochemical or natural sources, such as vegetable oils and fats, such as coconut oil. Their hydrophobicity and viscosity add to their “soft touch” and perceived “spreadability”.

Emollients act as a barrier on the skin to lock in moisture, either by preventing water evaporation from the skin or by holding moisture in the upper layers of the skin. Consumers need emollient components in a sunscreen formulation in order to ensure a soft, on skin feel.

**Human and Environmental Toxicity Criteria:**

Safer sunscreen formulations must consider human health criteria. This criterion is critical to ensure alternative products. Alternatives should not confer negative health impacts such as endocrine disruption, acting as carcinogens, and acting as skin sensitizers. A sunscreen formulation alternative will ideally pose little risk to human health in all aspects.

We also assessed how alternatives will affect the environment. Marine environments are sensitive to the chemicals found in current sunscreen formulations. Therefore, an improved formulation should pose little to no toxicity to aquatic life. An alternative compound should biodegrade and should not bioaccumulate. Furthermore, an alternative should not break down into more harmful compounds that could pose a secondary environmental or health concern.

In order to assess the human and environmental toxicities, associated with current products and alternatives, we conducted an extensive search of authoritative using the platform Data Commons. Our hope was to use this data to build a toxicological profile (the absorption, distribution, metabolism, and excretion in an organism), which is crucial in understanding how chemicals will behave within an organism. We also hope to gain information about multiple toxicity endpoints that such as carcinogenicity, endocrine disruption, genotoxicity, etc. However, very little data was found for our proposed alternatives and we identified a significant data gap in safety testing that needs to be addressed (Figure 9, below).
We, therefore, laid out our hypothesis based on a detailed literature review and a comprehensive analysis of currently utilized chemicals. From the primary literature search, we compared structural analogs of currently used and documented as safe compounds, to our proposed alternatives. Our proposed alternatives were carotenoids, mycosporine-like amino acids (MAAs), and antioxidants. We then generated a health and environmental process by which we searched for four important aspects associated with our alternatives and structural analogs. The first was endocrine disruption which was based on the safety information available about the alternative compounds, the safety of structural analogs, and hormone structure comparisons. The second aspect of the health and environmental criteria process was assessing the carcinogenicity of the alternative compounds to structural analogs. The third criteria analyzed the skin sensitization of the alternative compounds to structural analogs. The fourth criterion was assessing the biodegradability of the alternative compounds in relation to the structural analogs. We assessed whether the alternative compounds were broken down by enzymes and were common in biosynthetic pathways.

**Figure 9:** Human health and environmental endpoints for the identified alternatives. Many areas lack research indicating more studies need to be conducted.

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There are criteria that were not considered in the final evaluation for the sunscreen formulation. These include cost, manufacturing hazards, and regulatory oversight. Cost was not considered because, as it pertains to the vitality of the project and the expertise of the group, cost beyond the final scope of the evaluation. Manufacturing was not considered because hazards have not been clearly identified for the manufacturing process. Lastly, this investigatory evaluation did not consider the cost of multiple entities (for example research and development), manufacturing technicalities, or regulatory introduction (for examples: Food and Drug Administration (FDA) approval). However, they have been brought to the attention of the partner firm and are being evaluated by the appropriate personnel.
Evaluation of Alternative 1: Colorless Carotenoids

Plants have evolved to be efficient photosynthesizers, yet also employ mechanisms to protect themselves from the harmful effects of UV exposure. The main chemical strategy employed by plants as photoprotection is the production of carotenoids. Carotenoids are found in the chloroplasts of plants; their primary function is to extend the visible light region from which energy can be absorbed to drive photosynthesis. Their secondary, protective function is to act as quenchers to prevent triplet-state molecules from generating ROS. This can be accomplished by quenching triplet chlorophyll back to the ground state, or quenching the photosystem reactive centers themselves, which can become overexcited in bright light. Without this quenching mechanism, any generated ROS could interfere with the photosynthetic pathway and production of chlorophyll.

Carotenoids encompass over six hundred naturally occurring compounds, marked by their fat-soluble properties imparted by their tetraterpenoid-based structure. They are ubiquitous in nature, as they can be synthesized by plants, algae, yeast, fungi, and photosynthetic bacteria. They are generally classified into two distinct classes, carotenes and xanthophylls, which are oxygenated derivatives of carotenes. Both are involved in the photoprotection mechanism in the chloroplasts. Some of the most commonly studied carotenoids as they pertain to human health are beta-carotene, lycopene, lutein, and zeaxanthin, which have been shown to have protective effects against certain cancers and eye disease. This is mainly attributed to their antioxidant properties.

While most carotenoids are intensely colored, there are a few that are colorless and absorb light in the UVA/UVB range, making them candidates for sunscreen formulations. Two of these known carotenoids, phytoene and phytofluene (formed by a desaturation reaction of phytoene), can be found in tomatoes, carrots, watermelon, apricots, among other ubiquitous dietary sources. Phytoene and phytofluene are the products of the initial stages of carotenoid biosynthesis, produced from the condensation of two geranyl-geranyl diphosphate (GGDP) molecules. Further downstream, lycopene, alpha- and beta-carotene, and zeaxanthin are synthesized. Levels of carotenoids in plants depend on the plants’ developmental stage, its environment, as well as environmental stressors. Given that production of phytoene is the first step of the pathway, it is viewed as the limiting step in carotenoid biosynthesis. Ideally, we can identify the most practical sources and extraction methods to harness the UV absorptive capacity and antioxidant properties of phytoene and phytofluene in safer, more effective sunscreen formulations.
Figure 10. The biosynthesis pathway of carotenoids. Phytoene is the first product of the pathway; phytofluene can form via a desaturation reaction of phytoene.
Technical Performance of Colorless Carotenoids

UVA/UVB Molar Absorptivity

In order to assess the effectiveness of colorless carotenoids as UVB and UVA blockers, their molar absorptivity spectra were plotted together with currently used UV-blocking active ingredients. Figure 11 (below) shows that the colorless carotenoids phytoene and phytofluene are both more effective UVA and UVB blockers than the compound oxybenzone. In addition, phytofluene absorbs particularly in the UVA spectrum which suggests it may be useful in broad-spectrum formulations.

Antioxidant Capacity

Phytoene and phytofluene may act as antioxidants by reacting with radicals to form oxidized products or by dissipating the energy of singlet oxygen as heat. The portions of phytoene and phytofluene that are most likely to react with ROS are the electron-rich double bond regions.

Figure 11. Molar extinction coefficient (molar absorptivity) spectra for phytoene, phytofluene, and oxybenzone. UVB range is highlighted from 290-320 nm and UVA range is highlighted from 320-400 nm.
Chemical Stability

Phytofluene is known to degrade abiotically in the presence of oxygen\textsuperscript{17}. To combat this, other compounds that can combat this degradation should be considered as potential additives to a formulation. However, interaction data will need to be thoroughly investigated. Alternatively, synthetics with slight alterations can also be considered. Similarly, any synthetics will need to be toxicologically assessed.

Skin Permeability and Water Resistance

$K_p$ values for traditional UV blockers (blue, left) and colorless carotenoids (green, right) were calculated using the aforementioned formula (Figure 12).

![Figure 12. Permeability coefficients for traditional UV-blockers vs colorless carotenoids.](image)

Figure 12 shows that phytoene and phytofluene have permeability coefficients orders of magnitude higher than traditional UV blockers. This means that they are expected to have significantly more skin penetration and potential exposure in sunscreen formulations compared to other UV blockers. In addition, highly hydrophobic, linear compounds are shown to enhance the skin penetration of other chemicals in contact with the skin by disrupting highly ordered lipid bilayers of cell membranes.\textsuperscript{29,30} These effects should especially be considered when evaluating phytoene and phytofluene as additives to formulas containing other active ingredients. This effect may warrant synthetic alteration to these structures to limit their hydrophobicity.

UV-blockers should stay on the skin for an adequate amount of time especially when interacting with water (e.g. swimming, sweating). The high hydrophobicity (log$K_{ow}$~15) of phytoene and phytofluene suggest that they should stay on the skin surface. However, as previously
mentioned, this characteristic will increase skin penetration and potential exposure to other exogenous chemicals.

**Emollience**

Phytoene and phytofluene are both similar to common emollients, especially the saturated isoprenoid compounds squalene and squalane (*Figure 13*). These structural similarities suggest that phytoene and phytofluene may also contribute to and be compatible with the emollience of a cream formulation.

![Figure 13. The molecular structures of squalene, squalane, and phytoene.](image)

**Health and Environmental Performance of Colorless Carotenoids**

The alternatives, phytoene, and phytofluene, are anticipated to have a much lower impact on human and environmental health than existing chemical formulations including oxybenzone and avobenzone. From our literature review we compared carotenoids to the current chemical UV blocker, oxybenzone, and based on structural differences it is likely that the carotenoids will not antagonize the androgen receptor within human cells. More safety research is needed to confirm the overall toxicological performance of carotenoids.

Colorless carotenoids are ubiquitous in the human diet, especially in foods associated with positive health outcomes, and therefore the potential health risks are likely to be of low concern. However, little research has been done to create a toxicological profile for these compounds. Structural analogs offer some insight into the potential toxicity of colorless carotenoids. Further research needs to be done to understand if these chemicals are absorbed through the skin, where colorless carotenoids are distributed in the body, how they are metabolized if they are readily excretable and if there is any risk for creation of bioactive metabolites that may be harmful. Thus far, research has focused on exposure through oral consumption of colorless carotenoids. Studies on oral consumption of colorless carotenoids have not reported any health risks. Alternatively,
studies have reported antitumor activity of colorless carotenoids in a variety of cancers including skin, breast, prostate cancer as well as leukemia.32

A current concern with products on the market is that they are endocrine disruptors predominantly due to the benzophenone group antagonizing common hormone receptors such as progesterone, androgen, and estrogen.11 As shown in Figure 14, colorless carotenoids are very different in structure to current products and therefore are less likely to behave in a similar matter. However, endocrine disruption encompasses many different mechanisms that are not all understood and therefore further research should be conducted to determine whether colorless carotenoids could be endocrine disruptors through other mechanisms.

![Figure 14. Carotenoids do not contain the benzophenone moiety. A) colorless carotenoids: phytoene and phytofluene. B) two common benzophenone chemical blockers: oxybenzone and octocrylene.](image)

Other safety information that pertains to phytoene and phytofluene was found in a study where an intervention of a tomato-based drink provided protective effects against UVB damage.31

Safety information related to structural analogs suggests that colorless carotenoids may be safer than currently used ingredients. In fact, many of these analogs are beneficial to humans. Table 2 (below) shows a variety of compounds, their structures, and their health benefits.
## Structural Analogues

<table>
<thead>
<tr>
<th>Compound</th>
<th>Structure</th>
<th>Health benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Squalane</td>
<td><img src="#" alt="Structure" /></td>
<td>Anti-oxidant and anti-cancer properties</td>
</tr>
<tr>
<td>Squalene</td>
<td><img src="#" alt="Structure" /></td>
<td>Anti-oxidant and anti-cancer properties</td>
</tr>
<tr>
<td>Lycopene</td>
<td><img src="#" alt="Structure" /></td>
<td>Anti-cancer properties</td>
</tr>
<tr>
<td>Beta-carotene</td>
<td><img src="#" alt="Structure" /></td>
<td>Variety of health benefits, for example: vision and immune system</td>
</tr>
</tbody>
</table>

Table 2. The table illustrates five analog compounds that confer health benefits. These compounds include squalane, squalene, lycopene, and beta-carotene. The health benefits of these compounds include anti-cancer properties and vision and skin health benefits.⁶³⁷
Squalane and squalene, similar in structure to phytoene and phytofluene, are currently used in many applications on the market including in daily moisturizers and flu vaccines. Additionally, both the Environmental Working Group (EWG) and the World Health Organization (WHO) have identified squalene and squalane as safe. These chemicals would also be expected to be biodegradable because phytoene and phytofluene are broken down by enzymes into other carotenoids. Phytoene and phytofluene are considered to be the precursor to all carotenoids.

For environmental exposure, phytoene and phytofluene are important to the carotenoid biosynthetic pathway because they serve as the precursors for photosynthesis in plants. Increased influx of these chemicals into the marine ecosystems could have a positive environmental impact on plants and algae. However, too much of these compounds could be detrimental. While phytoene and phytofluene serve as the precursors to all other carotenoids there are other regulatory mechanisms that are independent of this breakdown process that helps mitigate carotenoid toxicity due to high doses; for example, in humans, retinol controls the amount of vitamin A converted from beta-carotene. However, specific studies aimed at high doses for an extended period of times should be considered to determine if there are any negative health effects or impacts on marine ecosystems. The toxicity of more hydrophilic oxidation products is still unknown, and more research needs to be conducted in this area.

Some unknowns still exist with the synthetic and natural processing of phytoene and phytofluene. For synthetic processing reagents, phytoene is the first C40 intermediate in the biogenesis of carotenoids. It is formed by two enzyme activities, catalyzing the coupling of two molecules geranylgeranyl diphosphate to yield prephytoene diphosphate and the conversion of prephytoene diphosphate into phytoene. For synthetic processing catalysts, phytoene synthase is a necessary enzyme in the synthetic processing of phytoene and has Km values for geranylgeranyl diphosphate and prephytoene diphosphate at 0.30, M and 0.27, uM. Mn²⁺ is a critical divalent cation that is needed for reactions with phytoene synthase. Further research needs to be conducted in order to better assess the natural extraction process of phytoene and phytofluene.
Evaluation of Alternative 2: Mycosporine-like Amin o Acids (MAAs)

MAAs are UV absorbing compounds produced primarily by marine algae. Recent research has discovered MAA production in multicellular marine organisms as well, such as fish and scallops. While there are over thirty different MAAs, they all share the same core structure: a cyclohexenimine chromophore with a nitrogen substituent (Figure 15). Due to their structure, MAAs absorb in the 310-360 nm range.

Currently, MAAs are mostly extracted from algae, which poses a limitation on large-scale production. Recently, a group found a variety of yeast that produces MAAs; however, this is a recent discovery and further research needs to be done to fully understand the mechanism and upscale potential.\(^{35}\) The complex biosynthetic pathway of MAAs is another challenge. The pathway is not specific for each organism but depends on many abiotic conditions that influence synthesis.\(^{36}\) Due to this extrinsic control factor, mimicking the pathway is very difficult and poorly understood. In addition, the chiral centers of MAA structures make synthetic production very complex and costly. The exact chirality will not affect the UV-vis absorption spectrum of these compounds, so provided the various stereoisomers are safe, enantiomeric mixtures could be used, simplifying synthetic routes. One further alternative is to design MAA-like compounds that would be simpler in structure and therefore easier to manufacture on a large-scale basis and more economical.

One MAA-based product that is already on the market, Helioguard 365, is composed of MAAs from red algae *Porphyra umbilicalis*. While Helioguard-365 is promising to get more MAA-based products approved, the MAAs in Helioguard-365, Porphyra-334, and Shinorine, only absorb in the UVA region with minimal protection against UVB rays. Another challenge with Helioguard-365 is its thermostability. There is strong MAA stability at 4 °C over an extended period of time, but stability decreases at higher temperatures over time.\(^{37}\) This limitation may be overcome through the design of synthetic variants.
Technical Performance of MAAs

UVA/UVB Molar Absorptivity

MAAs are notable alternatives for chemical UV blockers based on their technical performance. MAAs absorb UV rays more effectively than current products. The graph below (Figure 16) shows two MAAs: palythine and asteria 330. MAAs have a broader molecular extinction coefficient, particularly in the UVA range, compared to oxybenzone (Figure 16). This indicates that they are likely to absorb UVA and UVB rays better than oxybenzone when used in combination and could offer greater protection against these rays.

![Graph showing UVA and UVB absorbance capacities of MAAs compared to oxybenzone, a chemical UV blocker.](image)

Antioxidant Capacity

MAAs are strong antioxidants as shown by Coba et al. who compared the overall antioxidant capacity of MAAs in relation to known antioxidants, such as vitamin C. Coba compared the micromolar concentrations of each compound that will inhibit the reaction with a radical indicator. The IC50 is the concentration of an inhibitor where the response, or binding, is reduced by half. If the IC50 is 100%, that means that no inhibitor function occurred, and the chemical does not have a good antioxidant capacity. The IC50 is also a measure of how much a chemical prevents decolorization of a selected cationic radical, or ABTS (2,2'-azino-bis) a commonly used radical in
biochemistry reaction kinetics. From the chart below (Figure 17), it is evident that some MAAs have a strong antioxidant capacity.

Figure 17. The IC50 is the concentration (uM) needed to inhibit 50% of a reaction with a radical indicator, which quantifies the antioxidant capacity of a chemical.

**Chemical Stability**

As mentioned above, there is strong MMA stability at 4 °C over an extended period of time, but stability decreases at higher temperatures over time.\(^{37}\) This limitation may be overcome through the design of synthetic variants.

The permeability constants for three common MAAs: shinorine, gadusol, and palythine are all lower than the conventional chemical UV blockers (Figure 18, below). This is beneficial as a low permeability constant indicates that a compound is less likely to penetrate the skin. Additionally, their mid-molecular weight, less than 400 g/mol, also gives some support that they will be less likely to penetrate the skin. However, MAAs are highly hydrophilic and polar, indicating that the MAAs will wash-off of the skin quite easily. MAAs capacity to easily wash-off the skin hinders the overall technical performance of the MAAs in a sunscreen formulation. One group of researchers, Torres et al., suggests replacing the amino acid or amino alcohol moieties with alkylamino groups to improve the hydrophilic properties.\(^{41}\) However, this will require new performance studies as well as human and environmental toxicological studies.
Our extensive literature review determined that MAAs have an unknown emollience. Their behavior in formulation will have to be further explored.

**Emollience**

From a human health standpoint, there is currently little information available as to the toxicological profile of MAAs. However, the one MAA product currently on the market, Helioguard 365, has been studied *in vitro* and *in vivo*. These studies have shown protection from lipid peroxidation, increased skin firmness and smoothness, and reductions in DNA damage in skin cells. Other MAAs have also shown a variety of health benefits and no adverse outcomes both *in vitro* and *in vivo*. For example, Ryu et al. tested the MAA porphyra-334 *in vitro* and found with increasing doses, there was no change in cell viability. Another study found that two MAAs, Porphyra-334 and shinorine, protected against UV-induced skin damage in mice and did not report any adverse skin reactions. Given the structural similarities of many of the MAAs, we believe that other specific structures would also show these human health benefits and make them safe formulations. However, more toxicity testing needs to be done across a variety of MAAs to fully understand the toxicological profile. Further caution should also be given to the similarities that exist between the biosynthesis process of MAAs and marine toxins.

**Figure 18.** The permeability constants for conventional UV blockers and MAAs.
The technical performance analysis of MAAs suggests that they may be excellent compounds for sunscreen formulations; however, the biggest hurdle in their use is the remaining human and environmental safety data gaps. This recommendation is based on some initial inferences. Notably, MAAs are found in many marine species as well as terrestrial plants, suggesting their biocompatibility in the environment. This does not guarantee that increased usage of these compounds would be harmless nor that their extraction from natural sources might have its own environmental consequences. These compounds would have to be more formally evaluated looking at their lifecycle and routes for extraction and/or synthesis. This evaluation would spark interest in making them widely available for toxicological studies. However, given their excellent molar absorptivity lower concentrations would be required for their formulation, minimizing any potential negative environmental or human health impacts.
Evaluation of Alternative 3: Antioxidants

While sunburn is a visible effect of UV damage, it is not the only cellular damage that occurs. UVB (290-320 nm) rays, which are higher in energy than UVA (320-400 nm) rays, are the main cause of sunburn. Upon penetrating the epidermis, they cause direct DNA damage in cells and produce an inflammatory response associated with the redness of a sunburn, known as erythema. UVA rays, while lower in energy, have a longer wavelength and can penetrate through the second layer of the skin or dermis layer. They promote ROS generation, which causes oxidative stress in the body and leads to cell aging processes. While UVB damage is best combated by a UV blocking or absorbing mechanism, we propose combating the harmful effects of UVA damage by an intracellular mechanism.

Antioxidants are naturally used in plant and human cells to prevent oxidative damage. In plants, structural components called chromoplasts are responsible for carotenoid synthesis. Carotenoids are a class of antioxidants that function by quenching high energy, excited state species that are produced during photosynthesis. These species primarily include excited state chlorophyll and ROS species produced by excited state chlorophyll. In humans, cells use vitamins as antioxidants to prevent ROS damage thereby promoting cellular longevity. Recently, chemopreventive research has focused on the role of antioxidants in our diets. Additionally, there has been an increasing interest in using antioxidants in skin care formulations to counteract cell aging processes such as collagen degradation, which is caused by ROS damage.

Technical Performance of Antioxidants & Implied Health Impacts

Using our technical performance criteria, we identified the following antioxidants as beneficial additives in a sunscreen formulation: vitamin C, vitamin E, and the flavonoids epigallocatechin gallate and anthocyanin. We chose these antioxidants because they are commonly found in nature and abundant in our diets, as well as known for their many positive health benefits and anti-aging, anti-cancer properties.
**Vitamin C:** Vitamin C, or ascorbic acid, is a plentiful antioxidant found in human tissues and skin. Humans cannot synthesize vitamin C due to the lack of an enzyme required by the biosynthetic pathway, so we must obtain it from dietary sources. Vitamin C acts as the primary aqueous phase antioxidant in the body, meaning it is responsible for chemical reduction processes including quenching of radical oxygen species in aqueous environments. In its natural form, vitamin C has an acid dissociation constant of 4.2, meaning that it will be primarily deprotonated and negatively charged around a neutral cellular pH (~7.0-7.4) (Figure 19).

![Figure 19. The deprotonation process of vitamin C.](image)

**Figure 19.** The deprotonation process of vitamin C.

![Figure 20. The permeability constants on conventional UV blockers and antioxidant alternatives.](image)

**Figure 20.** The permeability constants on conventional UV blockers and antioxidant alternatives.
In order to be dermally absorbed, vitamin C must cross the outer layer of the skin (stratum corneum) which is composed of fatty acids and cholesterol. In its charged, hydrophilic form, it cannot pass through this layer. However, by designing an acidic formulation or using a different chemical form, vitamin C can be made dermally available. One way this can be accomplished is by incorporating ferulic acid, a plant-derived antioxidant, into the formulation. Ferulic acid acts to lower the formulation pH and stabilize vitamin C, making it viable for skin application and dermal absorption. Vitamin C can also be made more stable and lipophilic via chemical esterification to ascorbyl-6-palmitate and magnesium ascorbyl-phosphate, however, the efficacy of dermal absorption of these forms is still unclear. Although the dermal absorption of the vitamin C formulations is unclear, it is known that Vitamin C does not easily penetrate the skin due to the low $K_p$ value.

Numerous studies have shown that vitamin C can prevent photoaging, premature aging of the skin caused by repeated exposure to ultraviolet radiation (UV), and photodamage, changes in the skin that occur after prolonged exposure to solar irradiation. It can prevent collagen degradation, immunosuppression, and photocarcinogenesis by quenching reactive species that damage or alter protein transcription processes in the cells. Additionally, vitamin C reduces lipid peroxidation, limits the release of pro-inflammatory proteins, and protects against cell death. Given its abundance in our diets and these established benefits, vitamin C is a promising additive for sunscreen formulations.

**Vitamin E:** Vitamin E is a combination of eight different chemical compounds, known as tocopherols and tocotrienols. These compounds are composed of long hydrocarbon chains making them very lipophilic, enabling them to act as the primary lipid phase antioxidant in the body. One of these forms, alpha-tocopherol, is the only form of vitamin E required by humans. It is selectively re-secreted by the liver and has the highest blood and cellular concentrations compared to the other forms.

Vitamin E acts as a ROS scavenger, particularly for the peroxyl radical, which can cause damage to membranes via radical chain reactions. Like vitamin C, topical vitamin E can prevent lipid oxidation and photoaging in addition to photocarcinogenesis. Most interesting for our application, there have been some studies done showing the synergistic effect of vitamin C and vitamin E in topical formulations which have shown very promising effects for preventing sunburn and cell damage. Lin et al. found that a combination of 15% ascorbic acid and 1% alpha-tocopherol
provided a 4-fold damage against UV induced erythema, aerythema andthymine dimer formation which can lead to DNA damage.

In a later study, Lin et al. found that ferulic acid was also an effective stabilizing agent in vitamin C/vitamin E formulations. This combinatorial approach to antioxidant additives is an effective and safe strategy for preventing not only UVA-induced damage but also UVB induced erythema with a topical formulation.

Figure 21. Prevention of UV induced erythema due to vitamin C and vitamin E topical formulation use.

Plant-Derived Flavonoids: Plant-derived flavonoids are one class of antioxidants that have been extensively studied for their anti-cancer properties. Two of the most potent compounds with well-established health benefits are epigallocatechin gallate and anthocyanin. Epigallocatechin gallate (ECGC) is found primarily in tea leaves and scavenges ROS species in vitro and in vivo by generating more stable phenolic radicals. ECGC induces cell death in multiple cancer cell lines including melanoma cells and can modulate the growth and viability of cancer cells. However, not much has been established as to its efficacy or safety in a topical application, as most studies have been based on injection in animal models or dietary/oral delivery. While we believe it would be a good candidate for preventing UVA damage, further studies should be done to determine its properties in a topical formulation.

Anthocyanins are also well-known for their ability to prevent cellular oxidative damage. They have anti-inflammatory properties, making them an ideal candidate for skin care applications. Shih et al. proposed that anthocyanins act to elevate the expression of phase II and antioxidant enzymes, acting to alleviate oxidative stress causing cell damage and cell death. While most of the dosages studied in vitro are not equivalent to those present in vivo, it is still likely that anthocyanins demonstrate a chemopreventive effect and should be further analyzed for efficacy.

Although there is a lack of toxicological data, there are minimal adverse health effects associated with vitamin C, vitamin E, and flavonoids. Figure 22 below summarizes some of the potential adverse antioxidant health effects that merit further research.
Several antioxidants have limited or minor adverse health effects, which supports the use of these alternatives in a sunscreen formulation.
Conclusions

Recent attention has been given to sunscreens due to the heightened human and ecological toxicity of the active ingredients. Regulatory action has taken place in Hawaii and Palau to eliminate chemical UV blockers that are causing coral bleaching and associated with human health endpoints, such as carcinogenicity and endocrine disruption. The need to create a safer UV-blocking formulation is becoming apparent for industry, and Method is at the forefront of safer consumer product design. Method is a certified B corporation, focusing on the social and environmental impacts of their products as well as the entire life cycle of their products.

From our research, it was evident that current chemical UV blockers have many ecological and human health issues. These include coral bleaching, persistence in the environment, human endocrine disruption, and skin sensitization. Mineral UV blockers likewise have ecological, human health issues as well as formulation issues. Zinc oxide and titanium dioxide, common mineral UV blockers, form ROS, are persistent in the environment and have protective coatings made of silica and alumina that breakdown in the environment. Mineral UV blockers are also carcinogenic upon inhalation during workplace formulation and require high concentrations of nanoparticles to decrease the white-streaky appearance in topical application.

To determine our new sunscreen formulation we considered four performance criteria. These criteria included: broad-spectrum UV absorbance, antioxidant capacity, skin compatibility, and emollience. We also considered human and environmental health criteria: non-toxic to humans, non-toxic to aquatic life, and biodegradable. Based on these two sets of criteria, we selected and evaluated three categories of alternatives. The first alternative was colorless carotenoids, which are produced by plants, do not absorb in the visible range, and protect cells against radical and UV damage. The second alternative was mycosporine-like amino acids, derived from algae, which protect plants against UV and radical damage. The third alternative was antioxidants, such as vitamin C & E, which quench free radicals, have known health benefits, and protect against UVB-induced inflammation and UVA-induced cell damage. The overall technical performance of the solutions is summarized below in Table 3 (below).
Technical Performance

<table>
<thead>
<tr>
<th>Colorless Carotenoids</th>
<th>Mycosporine-like Amino Acids</th>
<th>Antioxidants</th>
</tr>
</thead>
<tbody>
<tr>
<td>-Absorb UVB more effectively than oxybenzone</td>
<td>-Absorb UVB more effectively than oxybenzone</td>
<td>-Used for radical quenching capacity</td>
</tr>
<tr>
<td>-Known antioxidants</td>
<td>-Known, high performing antioxidants</td>
<td>-Varied skin penetration characteristics</td>
</tr>
<tr>
<td>-Will penetrate readily into the skin</td>
<td>-Will NOT penetrate readily into the skin, may wash off</td>
<td>-Vitamin E is similar in structure to widely used emollients</td>
</tr>
<tr>
<td>-Similar in structure to widely used emollients</td>
<td>-Unknown emollience</td>
<td></td>
</tr>
</tbody>
</table>

**Table 3.** The overall technical performance for carotenoids, MAAs, and antioxidants is summarized.

**Figure 23** (below) evidently shows that colorless carotenoids, phytoene and phytofluene, and MAAs, palythine, absorb UVB light more effectively than oxybenzone.

![Figure 23](image)

**Figure 23.** The molar extinction coefficient spectra for colorless carotenoids (phytoene & phytofluene), MAA’s (asteria 330 & palythine), and a chemical UV blocker (oxybenzone).
The skin compatibility performance was also compared based on the $K_p$ values of the conventional UV blockers and our proposed alternatives (Figure 24). As there was limited data from authoritative lists regarding the human and environmental health hazards associated with our alternatives, a series of steps was utilized to determine the safety of the alternatives. For our hazard assessment process, we conducted an in-depth literature review, compared our alternative chemicals to structural analogs, and then employed a health and environmental framework. This framework analyzed the endocrine disruption, the safety of related structures, environmental fate, and positive health impacts of the proposed solutions.

**Figure 24.** Skin permeability coefficients ($K_p$) for some chemicals and proposed solutions. A higher $K_p$ value indicates more skin penetration.
Proposed solution: Short-term

From this analysis of proposed solutions, we suggested one short-term and one long-term solution. The short-term solution combined the alternative chemicals and their positive functional uses to lower the active ingredient concentrations of the current chemical UV blockers. Table 4 shows the positive functional uses of each proposed alternative in bold. The bolded functional uses are used in structurally similar compound formulations or in the listed chemicals. The unbolded functional uses are based on structural inferences from proposed chemical classes. The compounds marker with an asterisk is currently used in cosmetics.

<table>
<thead>
<tr>
<th>Proposed Solution 1 (Short-term): Use alternatives directly as multipurpose additives in order to lower required active ingredient concentrations.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Strategy</strong> (<em>currently used in cosmetics</em>)</td>
</tr>
</tbody>
</table>
| Colorless Carotenoids | 1. Emollient  
2. Chemical Stabilizer/Antioxidant  
3. UV Absorber |
|  • Phytoene  
• Phytofluene | |
| Mycosporine-like Amino Acids | 1. Chemical Stabilizer/Antioxidant  
2. Antimicrobial  
3. UV Absorber |
|  • Mycosporine glycine*  
• Shinorine*  
• Porphyra 334*  
• Palythine  
• Gadusol  
• Asteria 330 | |
| Antioxidants | 1. Chemical Stabilizer/Antioxidant  
2. Skin Conditioner  
3. Antimicrobial  
4. Indirect UV Absorber |
|  • Vitamin E*  
• Vitamin C* | |

Table 4: A list of proposed strategies and functional uses. The bolded functional uses are current uses of the alternatives or very structurally similar chemicals, in the case of carotenoids.
Proposed solution: Long-term

The long-term solution would combine the positive qualities and performance criteria of the proposed alternative chemicals. For example, to decrease the skin permeability of colorless carotenoids, hydrophilic groups should be added to the chemical chain to decrease the high natural hydrophobicity of the carotenoid chemical structure. This resolution would add hydrophilic groups to the end of the carotenoid hydrocarbon chain to preserve the UV-absorbing conjugated pi-system. Likewise, another long-term solution alteration would be improving the low hydrophobicity of MAAs. To preserve the UV-absorbing properties of the MAAs, the conjugated pi-system could be untouched. Hydrophobic R-groups, including CO₂H, could be added to the MAA structure to increase the hydrophobicity. By increasing the hydrophobicity of MAAs, the sunscreen formulation would be less likely to easily wash off the skin.

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Issue</th>
<th>Resolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorless Carotenoids</td>
<td>Skin permeability is too high due to high hydrophobicity</td>
<td>Add hydrophilic moieties</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Preserve UV-absorbing properties</td>
</tr>
<tr>
<td></td>
<td></td>
<td><img src="image1.png" alt="Image" /></td>
</tr>
<tr>
<td>Mycosporine-like Amino Acids</td>
<td>Will easily wash off of skin due to low hydrophobicity</td>
<td>Replace hydrophilic moieties with hydrophobic groups</td>
</tr>
<tr>
<td></td>
<td></td>
<td><img src="image2.png" alt="Image" /></td>
</tr>
</tbody>
</table>

Table 5. The proposed long-term solution considers synthetically modifying colorless carotenoids or MAAs with alternative functional groups. This will impart a formulation with desired skin permeability and stability.
Remaining Knowledge Gaps

Although there are many positive attributes of our strategies, there are data and knowledge gaps that could not be addressed within the scope of the project. Considering our new solutions there are three knowledge gap categories. The first category is technical information. Further technical questions include determining the rate of dermal absorption of colorless carotenoids. Another technical question includes determining the persistence of MAAs on human skin. Other technical questions are the thermal and photostability of the proposed formulations and the formulation benefits of including antioxidants in sunscreen. These questions persist as they are key to determining the performance and health hazards associated with the proposed solutions. Due to a lack of safety and toxicological data, these questions could not be properly addressed.

The second knowledge gap category was related to safety data. From our research, it was clear that there was generally a limited amount of toxicological data and research. Another remaining question was if the colorless carotenoids influence the dermal penetration of other ingredients in the formulation. Other safety data gap questions are the associated workplace hazards with manufacturing once the formulations are set to a large-scale production model. The third knowledge gap category is the need for future research. This includes further toxicity testing, sourcing of raw materials, and assessing the cost feasibility of the solutions. Likewise, although our proposed solutions are suggested for a safer sunscreen, the ideal formulation would still need to be calculated out to determine the exact formulation. Lastly, by adding new compounds to the market, it is unclear how these compounds would fare in a regulatory environment. Although there are many data and knowledge gaps, the proposed solutions fare far better for human and environmental health than the current chemical UV blocker formulations.
Appendix

About the Authors

Our team consists of UC Berkeley graduate students with diverse skill-set ranging from chemistry to public health:

**Amanda Keller, MS** is a third year Ph.D. candidate in the Molecular Toxicology program at UC Berkeley. She received her MS in global health from UCSF. She currently studies environmental toxicant-induced metabolic disorders, namely in the liver. For this project, she will be contributing to the hazard assessment of current and potential formulations.

**Angela Perantoni** is entering the 3rd year of her Ph.D. in Environmental Engineering. She studies the fate and transformation of waste-water derived pharmaceuticals and personal care products in a constructed wetland. Angela will evaluate the environmental impacts and biodegradability of alternative sunscreen formulations.

**Sophia Steffens** is in her second year in the Chemistry Ph.D. program. She is interested in groundwater purification, particularly as it relates to remediation and reuse of agricultural wastewater. She previously worked at an agro-materials startup called Apeel Sciences and enjoyed working with Method to experience the interface between academia and industry research.

**Steven Lyle** is a 5th year Ph.D. candidate in Chemistry. He currently works on the synthesis and design of porous crystalline polymeric materials for use in gas storage, gas separations, and catalysis. For the purposes of this work, he will be focusing on the development of potential new UV blockers, and an understanding of their mechanisms in achieving this end.

**Tessa Oliaro** is a 2nd year Master candidate in Public Health with an emphasis in Industrial Hygiene. She has an interest in health and safety within workplaces and spent a summer conducting hazard analyses of garment factories in Mekelle Ethiopia this past summer. After graduation, she hopes to apply for jobs working with a CIH in New Haven, Connecticut.
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