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PROTECTION

The sunscreen pill

A tablet that protects against sunburn is an attractive idea, but the science is patchy.

BY ERIN BIBA

It sounds like a lazy sunbather's dream come true: a pill that has all the protective properties of sunscreen without the bother of slathering yourself in lotion or remembering to re-apply it. Over the years, research into such a pill[1] has yielded a slew of over-the-counter supplements that claim to fight sun damage to the skin, mostly based on the fact that they contain antioxidants. But the US Food and Drug Administration (FDA) doesn't regulate supplements, so none of these products have needed to prove their effectiveness. Despite much research and a plethora of claims by manufacturers, the problems of moving antioxidants through the human body make it tricky to develop a pill that can replace sunscreen lotion.

Many of the current pills are based on an antioxidant-rich extract from the tropical fern *Polypodium leucotomos*, although a UK researcher is trying to patent an extract from algae found on coral. And there are reasons to suppose that antioxidants might help. Exposing the skin to ultraviolet radiation triggers the formation of certain reactive oxygen species known as free radicals that damage skin cells and can ultimately lead to malignancy. Antioxidants are known to destroy free radicals in the body and on the skin. The hard part is getting the antioxidants from the stomach to the skin.

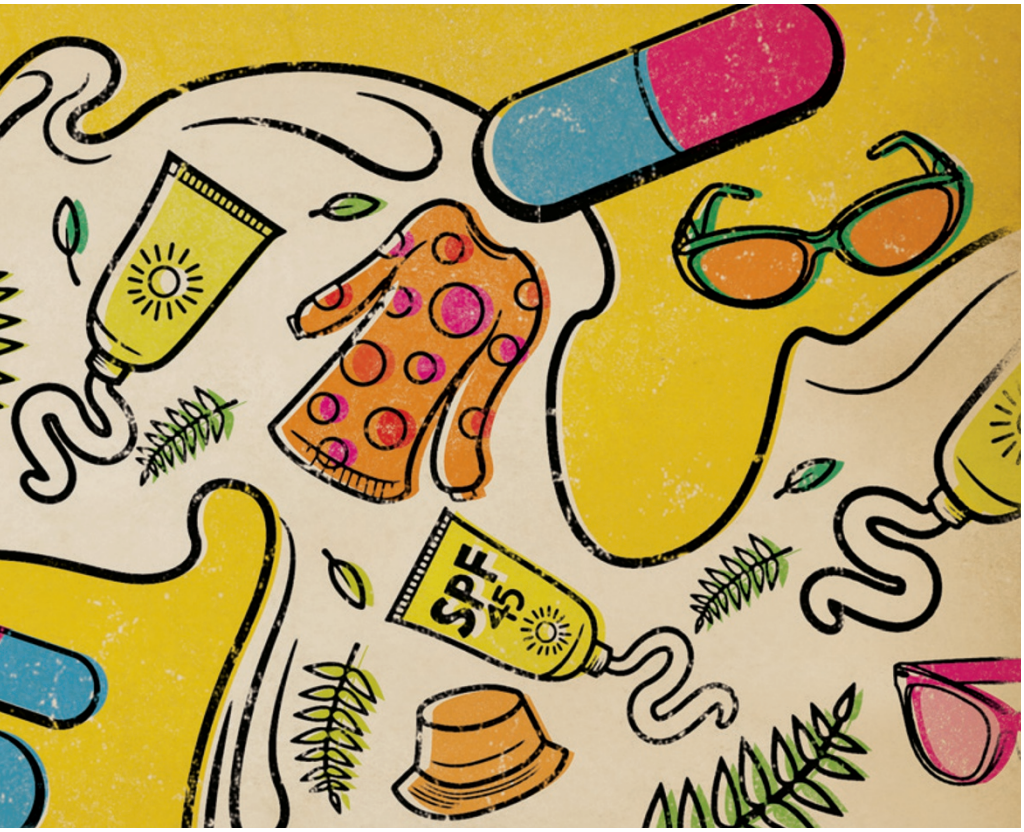
Salvador González, a dermatologist based in Madrid, Spain, who works as a consultant with the Memorial Sloan Kettering Cancer Center in New York, has been studying the fern extract since the early 1990s. But making it work effectively in pill form is difficult, he says.

LESS RADICAL

Scientists have tested the extract against various diseases and disorders such as skin cancer. They have injected it, applied it topically to the skin, and given it to patients in pill form. All these methods revealed at least some reduction in the amount of free radicals on the skin[2]. But pills were the least beneficial route, largely because of the way the body's metabolism interacts with the extract.

"If you think about taking a pill by mouth, it has to go through multiple steps," explains Henry Lim, a dermatologist at the Henry Ford Hospital in Detroit, Michigan. "It has to be absorbed, go through the blood and then through the liver before it gets to the skin." This is especially problematic for an antioxidant-based sunscreen pill because antioxidants, by their very nature, are unstable and tend to break down before they reach the target.

There is some evidence that antioxidants do reach the skin, however. A small 2004 study in which people were given oral doses of the fern extract after exposure to ultraviolet light found that their skin was less red and had fewer sunburnt cells than subjects not given the extract[3,4]. And a 1997 study looked for markers of cell damage caused by exposure to ultraviolet light in ten volunteers who ingested the fern extract[5]. The extract boosted the ability of the immune system to repair the damage caused by sunlight, and reduced the reaction of the skin cells to ultraviolet that results in sunburn. They also exposed subjects to twice the threshold of ultraviolet needed to cause sunburn and found that damage in those given the fern extract decreased by 84%, whereas it increased by 217% in subjects not given the extract. The results were not statistically significant, but the researchers suggested that larger studies may



show that the fern extract protects the skin.

Despite these data, Lim — who has worked as a consultant to Ferndale Healthcare, a supplement manufacturer in Detroit that makes a fern-based sunscreen pill — says no dermatologist would currently recommend using a pill instead of sun lotion. "None of the pills at this moment are 100% successful," he says.

LOOSE REGULATION

One problem in assessing the pills currently on the market is that they are deemed to be supplements, not medicines, so they are not regulated by the FDA. As long as the manufacturer makes no false or misleading claims, and there is no immediate health threat, the makers can sell whatever supplements they want — it's up to the consumer to decide whether they are worthwhile or not.

In the United States, supplements are regulated more loosely than sunscreen lotion, which is viewed as both a cosmetic and a drug. Cosmetics are regarded as anything that is applied to the body for cleansing or beautifying, and a drug is something intended for treatment or prevention. Because sunscreen lotion is both, it must follow the regulations for each type of product. Cosmetics don't require FDA approval, but drugs do, so sunscreen lotion is held to a higher standard than normal moisturizer — and also higher than supplements.

In August 2013, the American Academy of Dermatology released a statement on oral sunscreens declaring that there is "no scientific evidence that oral supplements alone can provide an adequate level of protection from the sun's damaging ultraviolet rays."

Dermatologists say that a pill may well be a reasonable addition to a cream-based sun protection regimen, which should also include wearing long clothing and a hat, and staying in the shade. In a series of studies González has conducted over the years, he was able to achieve a sun protection factor (SPF) of just 2 from the fern-based pill, compared with SPFs ranging from 15 to 50 for sun creams on the market in the United States. "Increasing the amount of antioxidants in a pill to a level that could robustly block sun damage would probably cause unwanted side effects," he says.

MAKE TAN

The most promising example of a non-topical sunscreen is a prescription drug created by the company Clinuvel Pharmaceuticals based in Melbourne, Australia. Known as Scenesse (afamelanotide), and currently awaiting FDA approval for marketing in the United States, it is a chemical analogue of a naturally occurring hormone, α-melanocyte-stimulating hormone, that is released into the body on exposure to ultraviolet radiation. The hormone — and the drug — triggers skin cells to release the dark pigment melanin, as they do to create a tan when skin is exposed to the sun.

Tanning creates a natural shield against ultraviolet radiation. The melanin acts as a filter, screening out some of the wavelengths of sunlight that induce the formation of dangerous free radicals. Lim, who consulted with Clinuvel while they were developing the drug, says that anyone who takes Scenesse would eventually become very tanned and, as a result, would be much less likely to burn.

But Scenesse is not marketed at general consumers — the FDA approval would be for use as a prescription drug to treat people with diseases such as vitiligo that make them extremely photosensitive. Clinuvel hopes the drug can also be used to treat people with photodermatosis, a disorder that causes mild-to-severe skin rashes after exposure to ultraviolet radiation.

If approved, Scenesse will not be administered as an oral pill, but as an implant the size of a grain of rice that is injected under the skin. Tanning from the injection will start within two days and lasts up to two months before another injection is needed. However, because it is injected, and is only indicated for severe photosensitivity disorders, it is impractical as an everyday treatment for people who lack sun-sensitivity diseases. The injection would protect patients from severe sun damage, but Clinuvel actively discourages people from thinking of the drug as a sunscreen pill.

Another lead in the search for a pill to prevent sun damage comes from Paul Long's lab at King's College London — and it's based on compounds made by algae that live on coral. Over the past five years, Long has been studying mycosporine-like amino acids (MAAs), which are naturally occurring sunscreens produced by organisms that live in clear, shallow water and so are exposed to high levels of ultraviolet radiation. Long discovered that the algae living inside coral produce MAAs and pass them to the coral they live on. Both organisms, and the fish that eventually feed on them, are protected by the MAAs, which absorb ultraviolet radiation before it can damage them. By sequencing the coral's genome, Long identified the genes that encode the pathway that allows the coral to take up and use the MAAs.

Long is trying to patent the ingredient for use in pills, but it's already proving effective in other products. In 2012, King's College London entered into partnership with Aethic, a UK skincare company, to commercialize the use of MAAs in sunscreen lotions.

González says the research is promising but that MAAs will be one of many sun-protective compounds derived from nature, none of which is fully effective in blocking the sun. So in the end, any sun-protection regimen will still have to include lotion and a good hat. ■

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