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ARTICLE

The Skin Cancer Paradox

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ABSTRACT

Although the safety and efficacy of ultraviolet filters (sunscreens) is widely accepted by consumers and medical professionals, the scientific community has yet to validate this conclusion. This is evident based on multiple literature searches obtained from PubMed, Google Scholar, ScienceDirect, ResearchGate, sunscreen manufacturers and dermatologic organization websites. In the absences of definitive data, industry continues to promote the use of these products to prevent cancers, specifically a 40% reduction in squamous cell carcinoma and a 50% reduction in melanoma based on one confounded non-reproduced study with numerous design flaws. This causes consumers to be misinformed leading them to intentionally increase ultraviolet light exposure, increasing their risk of skin cancers. Until the scientific community can clearly demonstrate that these products reduce/eliminate skin cancers, consumers should follow sun avoidance measures.

Commentary

Many skin cancer groups and medical/skincare professionals have done an incredible job of educating consumers about identifying skin cancer(s) and even a better job at treating skin cancers saving numerous lives since the late 1970's. However, technology has changed and so has a great deal of the information we now know about sunscreens and skin cancers. Although not frequently mentioned by name anymore, the Australian "Nambour Study" was a pivotal study for the sunscreen industry that was conducted between 1992 and 2006[1,2]. The researchers concluded that the "Daily use of an SPF 15 or higher sunscreen reduces the risk of developing squamous cell carcinoma (SCC) by about 40 percent and melanoma by 50 percent". This study was never reproduced and although some statistical significance was noted for squamous cell carcinoma (SCC), no statistical significance was noted for the melanoma outcome or for basal cell carcinoma (BCC) reductions. Furthermore, not only are these claims unsubstantiated, but sunscreens as currently formulated (at least in the United Sates) with soluble organic ultraviolet filters (SOUVF) have little to no major skin cancer protecting ability because they simply do not absorb in the ultraviolet (UV) range above 370, which is more than likely the active spectrum associated with at least BCC and melanoma.

Although not many organizations still use this information, there are still a number of websites that share this data with consumers (see Table 1 for a few examples). These claims, which are not currently made by or supported by the sunscreen industry or the American Academy of Dermatology (via label/package copy, websites, print ads and/or radio/TV advertisements), lures the consumer into believing that they are protected from skin cancers while wearing sunscreen. This has never been scientifically proven or validated since the inception of sunscreens (see Table 2 for a few examples)[4-12]. Additionally, none of these organizations are the appropriate authority to assure anyone that sunscreens are safe and effective; consumers should be referred to the FDA who is the responsible organization for such determinations. Appendix I lists the current state of FDA safe and effective sunscreen actives.

Table 1: Websites Identifying Express and Implied Claims for Skin Cancers

Claim(s)	**Website Link (as of November 16, 2023)**
"SPF 15 or higher sunscreen applied daily reduces your risk of developing SCC or BCC by about 40 percent and 50 percent for melanoma."	https://www.atlantamedicaldermatology.com/skin-cancer-statistics-that-will-help-motivate-you-to-apply-sunscreen-this-summer/ - Last viewed November 16, 2023.
"Wearing sunscreen regularly can decrease the risk of skin pre-cancers and skin cancers. It reduces the risk of developing squamous cell carcinoma (SCC) by about 40 percent, and lowers the melanoma risk by 50 percent."	https://pdxderm.com/dermatology/sun-protection-and-sunscreen/ - Last viewed November 16, 2023.
"Regular daily use of an SPF 15 or higher sunscreen reduces the risk of developing squamous cell carcinoma by about 40 percent. AND Regular daily use of an SPF 15 or higher sunscreen reduces the risk of developing melanoma by 50 percent."	https://siegeldermatology.com/project/skin-cancer-melanoma/ - Last viewed November 16, 2023.
"And the Skin Cancer Foundation (SCF) reports that regular daily use of SPF 15 sunscreen can reduce your risk of developing squamous cell carcinoma (SCC) by about 40 percent, and lower your risk of melanoma, the most deadly form, by 50 percent."	https://www.genesisderm.com/2022/03/edible-sunscreens/ - Last viewed November 16, 2023.
"Studies that examine the effect of sunscreen use on skin cancer risk have consistently delivered encouraging results. One example is a rigorous study spanning the course of a decade that showed daily use of an SPF 15 or higher sunscreen reduces the risk of developing melanoma by 50 percent."	https://www.skincancer.org/press/sunscreen-101-how-to-get-the-most-out-of-your-sun-protection-products/ - Last viewed November 16, 2023.
"Skin cancer prevention starts with you … Regular daily use of SPF 15 or higher sunscreen reduces your risk of melanoma by 50%."	https://www.skincancer.org/wp-content/uploads/SCFSkinCancerPrevention.pdf - Last viewed November 16, 2023.

Table 2 below, identifies multiple researchers that question the validity of sunscreens to protect against skin cancers dating back to 1973. The World Health Organization (WHO)[3] appears to have summarized it best "The working group concluded that the topical use of sunscreens reduces the risk of sunburn in humans and that sunscreens probably prevent squamous-cell carcinoma of the skin when used mainly during UNINTENTIONAL sun exposure. No conclusion can be drawn about the cancer-preventive activity of topical use of sunscreens against basal cell carcinoma and cutaneous melanoma. Use of sunscreens can extend the duration of intentional sun exposure, such as sunbathing. Such an extension may increase the risk for cutaneous melanoma. The working group warned against relying solely on sunscreens for protection from UV radiation."

Table 2: Published Research Questioning Sunscreen Efficacy

Year	Lead Author	Conclusion
1973	Emmett[4]	"The preparations are all designed to protect against the acute effects of ultraviolet, namely sunburn. Because of their effectiveness in this regard, they are often assumed to protect against ultraviolet carcinogenesis. In most cases, however, there is little or no published evidence that they do so and the relationship is inferential."
1994	Wolf[5]	"In summary, the results of this study indicate that inflammation and enhanced melanoma growth are different effects of UV radiation involving different mechanisms and have different sensitivities for sunscreen protection. Furthermore, protection against sunburn does not necessarily imply prevention of other possible UV radiation effects, such as enhanced melanoma growth. In fact, sunscreen protection against UV radiation-induced inflammation may actually encourage prolonged exposure to UV radiation and thereby increase the risk of development of cutaneous melanoma."
2000	Vainio[3]	"No conclusion can be drawn about the cancer-preventive activity of topical use of sun-screens against basal-cell carcinoma and cutaneous melanoma. Use of sunscreens can extend the duration of intentional sun exposure, such as sunbathing. Such an extension may increase the risk for cutaneous melanoma. The working group warned against relying solely on sunscreens for protection from UV radiation."
2006	Environmental Protection Agency (EPA)[6]	"Although a sunscreen with an SPF of 15 or higher offers protection from sunburn, it does not block all of the sun's damaging rays. In fact, there is no evidence that sunscreens protect you from malignant melanoma, the deadliest form of skin cancer, even though sunburns have been linked with the development of melanoma."
2011	Planta[7]	"Despite the availability and promotion of sunscreen for decades, the incidence of CMM (cutaneous malignant melanoma) continues to increase in the U.S. at a rate of 3% per year. There currently is little evidence that sunscreens are protective against CMM."
2018	Saes da Silva[8]	"The strength of the association between risk of skin cancer and sunscreen use has constantly decreased since the early 1980s, and the association was no longer statistically significant from the early 1990s. While the current evidence suggests no increased risk of skin cancer related to sunscreen use, this systematic review does not confirm the expected protective benefits of sunscreen against skin cancer in the general population."
2019	Waldman[9]	"Sunscreen is a multibillion-dollar industry, and its efficacy in the prevention of skin cancer are often taken as fact. Despite this, there are only 4 prospective studies that examine sunscreen's role in preventing skin cancer, and none of these studies examine the efficacy of sunscreen in preventing skin cancer in otherwise healthy individuals"
2021	Godar[10]	"From this analyzed data and published data in the literature, the major risk factors of CMM appear to be light hair color, especially red and white hair (reactive oxygen species and UVA; 320–400 nm), low cutaneous vitamin D3 levels, and HPV after 1960, while there was no apparent risk from exposure to UVB (290–320 nm) or sunburns."
2021	Serpone[11]	"So to come back to the question: have we made any progress in the last two decades? Evidently, much remains to be done on three fronts: first and foremost are (a) the safety issues of sunscreen ingredients, (b) the photostability of sunscreens, especially the photostability of the UVA filters remains an important issue, and (c) the direct cause-effect relationship between sunscreen usage and skin cancers remains to be demonstrated unambiguously."

The claims noted in Table 1, related to SCC and melanoma reductions, are all based on the results of one non-reproducible randomized, controlled human clinical study that was conducted in Nambour Australia[1,2] (a region that had and still has the highest rate of skin cancers in the world). The Nambour Study, is the only human study that tested the hypothesis or examined if there was a correlation between sunscreen use and a reduction in melanoma incidence. The authors concluded that a 50% reduction in melanoma and a 40% reduction in SCC was observed. This conclusion has been the crux of the justification for sunscreen use, and has been used as the case study for advocating the use of sunscreens. Unfortunately, this study exhibited a number of experimental design flaws that prevent a sound logical inference to make such a conclusion. The main concerns are noted below in Table 3.

Table 3: Critique of the Nambour Study Data

Methodological, Experimental Design and Analysis Concerns	**Observations**
Sunscreen Actives	The group showing a reduction in skin cancers were given a sunscreen containing 2% avobenzone and 8% octinoxate, a formula combination that is known to be photo-unstable (see Table 4) and, therefore, was highly unlikely to protect from any significant UV exposure present in Nambour.
Panel Selection	Although no statistical differences were noted between the groups, the group not given sunscreen had twice as many people enrolled that had predispositions for skin cancer (history of skin cancer, burned more readily, work outdoors more … etc.).
Sample Distribution	From 1992 to 1996 one group was given free sunscreen products to use while the other group was told they could use a sunscreen product if desired. A follow-up of the study was conducted from 1996 to 2006 – no sunscreens were given to either group for this time-period. However, the panelists were split into various subgroups to study the effects of beta-carotene. Making it unclear if any of the benefits observed were from sunscreen use for the 4 ½ years that sunscreens were given-out and the 10 years no sunscreens was given to panelist; or was it the beta-carotene; or a combination of 4 ½ years of sunscreen use and 10 years of beta-carotene use without sunscreens; or did the observations simply occur randomly or simply because the panelist were made aware of the damaging effects of the sun and practice sun-avoidance? Moreover, during the 4 ½ years of sunscreen use and throughout the follow-up period there was no data collected/presented that demonstrated that the panelists used the product(s) giving to them or used any sunscreen product(s) during the time of beta-carotene testing.
Adverse Reactions	The study also had a total of 173 unexplained deaths out 1,621 participants with more deaths occurring in the group showing a reduction in melanoma (87 vs. 86 deaths). Additionally, no causes of death were noted?
Proposed Benefits	The statistics applied to the data demonstrated a significance difference between the groups for SCC, but not for melanoma or BCC. More importantly, there was no change in the melanoma rate in Nambour either before or during the 15–year study period (initial melanoma rate = 71/100,000 people) nor was there a change observed 21 years after study completion (current melanoma rate = 72/100,000 people). It is also unclear what the value of a 50% reduction in melanoma and a 40% reduction in SCC is in a region that demonstrates no change in the incidence of skin cancer over two decades. If reducing the melanoma rate by 50% was achieved by simply using a sunscreen, numerous Nations would have adopted (especially Australia) the use of such a product and the level of skin cancers would be decreasing, not increasing.
Extrapolation of Data Across all Sunscreen Products	Even if there was some benefit that actually occurred during the Nambour study, the product used to substantiate skin cancer prevention, does not represent what is currently available for consumers to buy/use today (not all products work the same way). What is available today are products with 35% to 45% different active combinations and different inactive ingredients with different textures/feels that have not been proven effective against anything. It is not logical to indiscriminately tell people to use any sunscreen drug – based on formulation esthetics - to protect against a variety of different types of skin cancers (SCC, BCC, melanoma, merkel cell carcinoma … etc.). These skin cancers all have different mechanisms of action and impacts. One does not allow a patient to pick a drug because they like the way it feels or looks, one prescribes it because it has been proven to be effective at treating the disease in question.

To further add to the lack of data integrity of the Nambour Study, the following research is being provided to demonstrate that the 2 actives, avobenzone and octinoxate used in the study, are not stable when used together in a product or in many cases when used with other sunscreen actives (see Table 4)[11-28]. The studies noted below were published after the Nambour study started in 1992 and in some cases after the study was published in 2011. Avobenzone was not approved for use in the United States (US) until 1996 and instability data started being published in 1998 and is still being published in 2023. These papers are from independent researchers, academic researchers, and/or from industry itself. It is no surprise to anyone that these actives are unstable in a product. We know this now, but did not know this in 1992 when the study was conducted. Therefore, the integrity issue is not with the scientists that conducted the study, but rather with the industry who presumedly link their sunscreen products with protection from skin cancer. The Nambour data has been and continues to be miscommunicated to consumers and more importantly to medical practitioners that have been force-fed this confounded conclusion and who continue to tell everyone to use ANY type of sunscreen with an SPF 15, 30 or greater.

Conclusion:

In summary, promoting unsubstantiated claims that are misleading and confusing to consumers and skincare professionals based on a clinical study that has never been reproduced and that is plagued with significant scientific flaws is wrong. No individual sunscreen company markets a sunscreen product using a 40% reduction in SCC and a 50% reduction in melanoma claim because it would be identified as a misbranded drug under the Food, Drug & Cosmetic Act and subject to regulatory intervention. This association between sunscreen use and protection against skin cancer is not only false and misleading, but it puts the consumer at significant risk by intentionally over-exposing themselves to the sun, which according to the WHO leads to skin cancers.

The data from the Nambour Study is significantly flawed and shouldn't be used to substantiate prevention or protection claims against skin cancer. Einstein is attributed with saying "the definition of insanity is doing the same thing over and over again, but expecting different results". Telling people for over 50 years to use unstable drug actives that do not absorb in the correct UV wavelengths known to cause specific skin cancers, that have been shown to demonstrate numerous types of toxicities in humans/animals[29], that have not been scientifically proven to prevent skin cancers and expecting less skin cancer rates/deaths would appear to fit Einstein's adage. It is time to re-educate consumers that the best way to prevent skin cancers are to practice sun avoidance (not abstinence) mainly between solar peak hours (10:00 AM and 4:00 PM); when at the beach/pool seek shade or use a large umbrella or cabana; wear protective clothing including a hat/sunglasses; and until more effective/less toxic sunscreen products become available, only use a mineral (zinc oxide or titanium dioxide) sunscreen when going outside in the sun.

Note: This commentary is being published on behalf of the 400,159 individual Americans who have died from causes associated with skin cancer between the years 1975 - 2017 (Appendix II) based on data from the American Cancer Society, plus the 59,130 additional skin cancer deaths projected/reported between 2018 – 2023[30-35], plus the 40% of organ transplant recipients that will develop a skin cancer on partially sun-exposed or sun-protected areas[36], and the 4.9 million people, between 2007 – 2011, that have had one or more BCC or SCC at a cost of $8.1 billion each year as reported by the Center for Disease Control[3]

Table 4: Publications identifying instability of avobenzone and octinoxate combinations

Year	Lead Author	Conclusion
2023	Gholap[12]	"Investigators tested the impact of Tinosorb S in sunscreens with this UV filter mixture because it has been found that AVB (AKA: Avobenzone) destabilizes ethylhexyl methoxycinnamate or EHM (AKA: Octinoxate)."
2021	Serpone[11]	"Within this context, the US Federal Register on OTC drugs discourages the simultaneous presence of these two representatives in sunscreen formulations because of their inherent photo-instability that could produce some undesirable photoadducts formed between octinoxate and photogenerated fragments of avobenzone."
2020	Garbe[13]	"In the reference sunscreen formula S2 as well as in the two different sunscreen products, especially long-wave radiation (>400 nm) had an effect on photostability, (the effect was a negative effect … formula S2 contained a mixture of Octinoxate, Avobenzone and Octocrylene)"
2020	Lebedev[14]	"Avobenzone is a widely used UV filter. In its pure form it is known to undergo several transformations including photo-isomerisation, photodegradation, and halogenation."
2020	Herzog[15]	"However, photostabilization may also be caused by quenching mechanisms, such as singlet–singlet or triplet– triplet energy transfer. Investigation of butyl methoxy dibenzoylmethane (Avobenzone) and ethylhexyl methoxycinnamate (Octinoxate) as photolabile sunscreens in the presence of either octocrylene …."
2019	Yuan[16]	"The Benesi-Hildebrand's method showed that avobenzone formed 1:2 stoichiometric inclusion complex with 2-HP-β-CD. The solubility, thermal stability and the photostability of avobenzone were all improved after encapsulating by the 2-HP-β-CD."
2018	People4Ocean Sun Care[18]	"In sunscreen formulations, octinoxate can react with avobenzone (another chemical filter) reducing the overall sun protection factor of the product, leading to photo-instability and an increase risk of sunburn"
2015	Prospector[19]	"Perhaps the best approach to stabilizing avobenzone is to incorporate octocrylene (EU) in the formulation to help prevent the formation of the triplet state. … This approach can help you formulate avobenzone with octinoxate, which can react with avobenzone …"
2015	Stylecaster[20]	"Before you go applying sunscreens or products with SPF, take a look at the ingredients. Octinoxate will actually degrade Avobenzone, making your sunscreen unstable and offering you less protection."
2011	Hojerová[21]	"The most photoinstability showed sunscreens S1 (EHMC is "Octinoxate", BMBM is "Avobenzone" and phenylbenzimidazole sulphonic acid) and S6 (EHMC is "Octinoxate", BMBM is "Avobenzone", phenylbenzimidazole sulphonic acid and ethylhexyl triazone)"
2010	Beasley[22]	"To sustain its absorption capacity within a sunscreen film during UVR exposure, avobenzone needs to be formulated into sunscreen products using sound formulation strategies …"
2009	Paris[23]	"Avobenzone is one of the most frequently employed sunscreen ingredients, but it has been reported to partially decompose after irradiation."
2007	Gonzalez[24]	"Sunscreens 1, 2 and 3 are unstable (Note: all three sunscreens contained Octinoxate and Avobenzone)"
2005	Sayre[25]	"We report the concomitant photolysis of avobenzone and octinoxate that predominates over expected E/Z photoisomerization …"
2001	Chatelain[26]	"Since AVB (AKA: Avobenzone) was shown to destabilize ethylhexyl methoxycinnamate (AKA: Octinoxate) …"
2001	Scribd[27]	"Avobenzone has been reported to be unstable when contained in formulations with physical sunscreens."
1998	Bredholt[28]	"Considerable breakdown of most filters was observed after doses of irradiation equivalent to moderate sun exposure."

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Appendix I

Fda fact sheet
Fda proposed rule: sunscreen drug products for over-the-counter-human use; proposal to amend and lift stay on monograph
(available at https://www.fda.gov/media/124655/download - last view on november 16, 2023)

1. Proposed GRASE Status of Active Ingredients Listed in the Stayed 1999 Final Monograph
FDA has proposed the following categories for the 16 sunscreen monograph ingredients.

GRASE* for use in sunscreens	**Not GRASE** for use in sunscreen**	***Insufficient data for use in sunscreens**
Zinc oxide and titanium dioxide	Aminobenzoic acid (PABA) and trolamine salicylate	Cinoxate, dioxybenzone, ensulizole, homosalate, meradimate, octinoxate, octisalate, octocrylene, padimate O, sulisobenzone, oxybenzone, avobenzone

*GRASE= Generally Recognized as Safe and Effective **These ingredients are not currently marketed. ***For those ingredients in the "insufficient data" category, FDA proposes that it needs additional data to determine that sunscreens with these ingredients would be GRASE.

Appendix II

As published in DiNardo and Downs "Failure to Protect: Do Sunscreens Prevent Skin Cancer in Humans?" Toxicol: Open Access 2021, 7:3-8. Available at https://www.omicsonline.org/open-access/failure-to-protect-do-sunscreens-prevent-skin-cancer-in-humans.pdf. Last view on November 16, 2023

Table 4: Annual malignant skin cancer deaths, 1975-2017

Year of death	Skin cancer deaths	US Population (in millions)*	Deaths/Million People
1975	5,256	219	24
1976	5,697		
1977	5,904		
1978	6,035		
1979	6,155		
1980	6,151	229	27
1981	6,444		
1982	6,774		
1983	7,048		
1984	7,282		
1985	7,595	240	32
1986	7,925		
1987	7,943		
1988	8,078		
1989	8,350		
1990	8,589	252	34
1991	8,658		
1992	8,816		
1993	8,893		
1994	8,826		
1995	8,976	265	34
1996	9,363		
1997	9,316		
1998	9,490		
1999	9,572		
2000	9,734	282	35
2001	10,032		
2002	9,958		
2003	10,269		
2004	10,349		
2005	10,845	295	37
2006	11,109		
2007	11,279		
2008	11,385		
2009	12,172		
2010	12,125	309	39
2011	12,263		
2012	12,516		
2013	12,807		
2014	13,116		
2015	12,868	321	40
2016	12,098	323	37
2017	12,098	325	37
	Total Deaths: 400,159		**54% Increase in Deaths****

Data source: American Cancer Society/National Center for Health Statistics, 2019.
* Population Data obtained from https://www.populationpyramid.net/united-states-of-america/1975/ Accessed January 23, 2021
** % Increase in deaths calculated by: 2017 deaths/million people (minus) 1975 deaths/million people (divided by) 1975 deaths/million people (times) 100.