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Failure to Protect: Do Sunscreens Prevent Skin Cancer in Humans?

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Abstract

According to the Food and Drug Administration, the current scientific literature does not support the safety of organic sunscreen actives currently approved for use in the United States. Furthermore, the International Agency for Research on Cancer cannot find definitive proof that sunscreens prevent skin cancers. The concept that sunscreens prevent skin cancer is predicated on the observation that they inhibit the occurrence of sunburn and that one or two blistering sunburns can lead to skin cancer. Although the latter part of this statement may be true, the prevention statement is not and questions the efficaciousness of current sunscreen technologies in preventing melanoma and carcinomas period. We posit the thesis that current sunscreen technologies fail to protect against the threat of skin cancers when applied in common-occurrence situation(s). Therefore, before any local or global regulatory body approves old or new actives for human use, it is essential that 1) sunscreen actives demonstrate that they have the ability, alone or in combination, to sufficiently absorb/block the entire ultraviolet spectrum, 2) validated models based on demonstrated toxicologic and exposure-delivery principles need to be developed to evaluate a product's efficacy to inhibit keratinocyte cancers or melanoma, and 3) safety testing as outlined in the Food and Drug Administration's Sunscreen Innovation Act of 2014 or similar tenets must be completed to assure human safety.

Keywords: Sunburn ; Basal cell carcinoma ; Melanoma ; Dermal irritation

Introduction

The Food and Drug Administration (FDA) approved all but one of the 14 organic sunscreen actives (avobenzone was approved in 1997) used today in Sun Protection Factor (SPF) products in 1978, based on a review of the safety/efficacy data submitted by companies already selling products containing these actives. The data and claims stated in the 1978 FDA Sunscreen monograph were unsubstantiated or misleading, as well as arguably frivolous. For example, information supplied for ethylhexyl p–methoxycinnamate, also known as octinoxate, was substantiated based on "… a line of products where the ingredient ethylhexyl p–methoxycinnamate was combined with a benzophenone, over 8 million units were sold, 38 complaints of skin irritation were received by the manufacturer, but not a single case of skin irritation could be clearly related to the use of the products. Over 209 tons of ethylhexyl p–methoxycinnamate were sold in 27 countries in 2 year." [1].

A primary critique in the area of irritant/allergic contact dermatitis posits that without specifically testing the 38 individuals in question to each ingredient used in the product(s) noted, it is impossible to determine the causative agent(s) that evoked the response. A second critique is based on the fact that "209 tons were sold in 27 countries" is also a meaningless value since there is no way of knowing how the tonnage was used; sunscreen is not the only use for this chemical. A third critique should be noted that in 1978, this type of "post–marketing surveillance" in addition to acute toxicity testing (animal ocular irritation, dermal irritation, and oral toxicity), perhaps a few human skin-irritation, allergy, and SPF studies were considered "state–of–the–art toxicology" when determining human safety. It should also be noted that efficacy testing consisted of only SPF determination measuring only short wave ultraviolet (UVB) protection and very little was understood about the impact of long wave ultraviolet (UVA), or its role in skin cancer. (Table 1) compares the requirements for safety/efficacy testing used in 1978 to the 2014 Sunscreen Innovation Act currently required for new sunscreen drug actives by the FDA.

In 1978, FDA also allowed manufacturers of these products to claim "Overexposure to the sun may lead to premature aging of the skin and skin cancer. The liberal and regular use over the years of this product may help reduce the chance of premature aging of the skin and skin cancer." Over time this statement was modified to "if used as directed with other sun protection measures decreases the risk of skin cancer and early skin aging caused by the sun." To again point-out this fallacious argument, the lack of data to substantiate sunscreen benefits does not justify the statement that "sun protection measures" are a necessary factor in reducing the risk to skin cancer. Regardless, this statement both launched the propaganda campaign for the "sunscreen revolution to prevent skin cancer", but it also created the anti–aging skin care market; both of which are now worth well over $10 billion each in the current global marketplace. Until this time, the only legal way to say "prevents aging" was through the use of appearance or puffery claims that suggested that moisturizers can help prevent "premature skin aging" or "the appearance of fine lines and wrinkles".

Sunscreen compounds also found their way into hyper–pigmentation products meant to minimize age spots, melasma, and other forms of skin discoloration. As noted in a recent industry trade magazine article exploring consumer perception of SPF products "Preventing skin cancer is the top motivation among sunscreen wearers (71%), followed by preventing the appearance of aging skin (46%), and preventing sun spots (43%)"[2]. The word "preventing" has many definitions, such as "stop, avert, foil, thwart, preclude, inhibit, counteract, block … etc."; none of which are puffery in nature, but are definitive claims, especially in the consumer's mind. Based on

these specious claims, this paper explores the "preventative" ability that these U.S.–approved sunscreen actives have in preventing skin cancer as reported in the scientific literature.

1978 Sunscreen Monograph*	2014 Sunscreen innovation act**
Animal/Human irritation/sensitization studies	Human irritation/sensitization studies
Animal/Human photosafety studies	Human photosafety studies
X	Human absorption studies/maximal usage trial
	Pediatric considerations
	Nonclinical safety testing
	Carcinogenicity studies: dermal and systemic
	Developmental and reproductive toxicity studies
	Toxicokinetics
Postmarketing safety data	Postmarketing safety data
Effectiveness testing (shortwave-ultraviolet)	Effectiveness testing (shortwave-ultraviolet)
Longwave–ultraviolet testing started in 1990's	Anticipated final formulation testing (Longwave-ultraviolet, Water resistant … etc.)

Table 1: Comparison of required Safety/Efficacy Testing for Sunscreens.

Data Source:

* 1978 Sunscreen Monograph pages 38206–69: https://tile.loc.gov/storage–services/service/ll/fedreg/fr043/fr043166/fr043166.pdf#page=204. Accessed January 23, 2021

** 2014 Sunscreen Innovation Act: https://www.fda.gov/media/94513/download. Accessed January 23, 2021

Search strategy and selection criteria

Data for this Review were identified by references from relevant articles. Abstracts and reports from meetings were included only when they related directly to previously published work. Only articles published in English between 1973 and 2020 were included.

Sunburn (SPF Protection)

FDA states that sunscreens, when used correctly (2 mg/cm2 applied 15 minutes before sun exposure and reapply every 40, 80, or 120 minutes), can minimize sunburn that can lead to skin cancer [1]. With that said, consumers trust that if they wear a sunscreen when intentionally exposing themselves to long periods of UV (sunbathing, gardening, outdoor activities … etc.) they will not become sunburned and will avert skin cancer. The latter point has never been definitively proven. Furthermore, it is often implied that the higher the SPF value used, the more protection from UV exposure is achieved and the longer one can safely stay in the sun [3]. The International Agency for Research on Cancer (IARC) has termed these behaviors "sunscreen abuse" [4]. IARC also conducted an international evaluation of the cancer–preventive potential of sunscreens concluding "… 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 [5]".

The observation that sunscreens inhibit sunburn is an effect of suppressing the mechanisms that cause erythema and not the prevention of the underlining biochemical impact that is occurring. The confusion between these two mechanisms needs to be addressed when evaluating the efficacy of these actives. For instance, one may not get sunburned, but still have several unwanted effects occurring in the skin. The sunscreen actives oxybenzone, octocrylene, octinoxate, PABA, and the European 4–methylbenzyliden camphor have been reported to induce free radicals [6] known to cause caspase enzymes to be produced that are linked to adverse reactions like photosensitization [7], stimulation of melanoma tumor growth[8], and neurotoxicity [8-12] to name just a few. Therefore, it appears that the subversion of sunburn by sunscreen use is not free of the unseen consequences that can lead to the future development of skin cancers and toxicities.

Cutaneous Squamous Cell Carcinoma (cSCC)

As noted above by IARC "sunscreens probably prevent squamous–cell carcinoma of the skin when used mainly during unintentional sun exposure". There appear to be no valid or compelling scientific data in humans that demonstrate sunscreen use and prevention of cSCC. Waldman [13] evaluated the only four prospective human studies that relate sunscreen use with skin cancer prevention, two of which relate to cSCCs. First, the Nambour Study [14] which did demonstrate a 40% reduction in cSCC, however, the validity of the study is in questionable since the product used an unstable mixture of sunscreen actives (avobenzone and octinoxate) [15] which more than likely provided little to no protection from UV exposure. The second study reviewed, evaluated cSCC in transplant patients [16] for which no significant differences were observed. The review of the four studies led the authors to ask a very important and common question "Could it be that the nearly universal recommendation of dermatologists and professional societies to use sunscreen to prevent skin cancer is unfounded?"

There have been a few cSCC studies conducted in mice. Kligman [17] observed that the topical administration of an SPF 2 containing 2% octyl dimethyl PABA (Padimate O) reduced cSCC formation by 50% and an SPF [15] (7% Padimate O and 3% oxybenzone) completely prevented tumor formation. More recently, Bode [18] evaluated eight commonly used FDA sunscreen actives, alone and in combination, using a prevention therapy and intermittent dosing treatment against regrowth of cSCC. The data presented in (Table 2) represents a modification of the published data to include the percent reduction from baseline values for the categories evaluated. The data shows that zinc oxide (approved by FDA in 1998) was the most effective (second only to no UV exposure) demonstrating a 93.3% reduction in tumor formation. Additionally, Hacker etal [19] found that zinc oxide and titanium dioxide combination sunscreen when applied to the skin before exposure to twice the minimal erythemal dose of UV completely blocked the effects of DNA damage, p53 tumor protein induction, and cellular proliferation in both melanocytes and keratinocytes. These findings would suggest that the wavelength responsible for cSCC formation lies outside the protective absorption

spectra of most of the petrochemical (organic chemical) actives, including avobenzone.

Test agent	% Reduction of mice with tumors1	% Reduction in average tumor number2	% Reduction in tumor volume3
Solar Simulated Light Only (SSL)	0·00%	0·00%	0·00%
SSL+lotion only (Vehicle=V)	0·00%	9·0%	0·00%
SSL+V + 12% Titanium Dioxide	0·00%	61·2%	71·4%
SSL+V + 5% Octisalate	0·00%	61·2%	88·6%
SSL+V +3% Avobenzone	6·70%	44·8%	68·6%
SSL+V +6% Oxybenzone	13·7%	65·7%	82·8%
SSL+V +10% Homosalate	20·0%	61·2%	91·1%
SSL+V +7·5% Octinoxate/5% Octisalate	20·0%	71·6%	93·6%
SSL+ V+7·5% Octinoxate	20·0%	79·1%	89·8%
SSL+V +10% Octocrylene	33·3%	74·6%	89·2%
SSL+V +3% Avobenzone/7·5% Octinoxate	46·7%	80·6%	95·3%
SSL+V +3% Avobenzone/7% Octocrylene/6% Titanium Dioxide	80·0%	97·0%	99·3%
SSL+V +7% Octocrylene/6·9% Zinc Oxide	86·7%	98·1%	99·6%
SSL+V +20% Zinc Oxide – Only	93·3%	98·1%	99·5%
No SSL	100·0%	100·0%	100·0%

Table 2: Cutaneous squamous cell Carcinoma in Mice.

Data Source: Bode AM, Roh E. FDA–Approved Sunscreen Components Effective in Preventing Solar UV–Induced Skin Cancer? Cells 2020; 9: 1674.

Note: Data order is from highest (only SSL) to lowest (no SSL) level of % Reduction of Mice with Tumors

1) The percentage of reduction in the number of mice with tumors was determined as 100 x [(SSL − SSL with sunscreen treated group)/ SSL].

2) The percentage of reduction in the average (or total) tumor number was determined as 100 x [(SSL − SSL sunscreen treated group)/ SSL].

3) The percentage of reduction in the average (or total) tumor volume was determined as 100 x [(SSL − SSL sunscreen treated group)/ SSL]

Basal Cell Carcinoma (BCC)

The same two authors [14,16] that reported on cSCC also studied BCC incidence. Neither study found a statistically significant response to sunscreen use and basal cell carcinoma occurrence.

Melanoma

What is often referred to as "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 [14]. The authors concluded that a 50% reduction in melanoma and a 40% reduction in cSCC 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 methodological and experimental design flaws that prevent a sound logical inference to make such a conclusion.

Faulty methodological, experimental design and analysis examples include:

(A) 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 [15] and, therefore, was highly unlikely to protect from any UV exposure.

(B) 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.).

(C) There was no change in the melanoma rate in Nambour either before or during the 15–year study period (71/100,000 people) nor was there a change to date observed 13–years after study completion (72/100,000 people) [20]. If reducing the melanoma rate by 50% was achieved by simply using a sunscreen, numerous nations would have reported such benefits. Unfortunately, IRAC has reported just the opposite trend in the cancer incidence in five continents [21].

(D) 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). It is unclear what the value of a 50% reduction in melanoma and a 40% reduction in cSCC is in a region that demonstrates no change in the incidence of melanoma over time.

Discussion

With respect to the general safety concerns of these chemicals, FDA summarized it best when they concluded that the "public record does not support the safety of these chemicals" [22], which is the reason why they removed organic sunscreen actives from the category Generally Recognized As Safe and Effective (GRASE) to either "not safe for human use" (PABA and Trolamine Salicylate) or additional data needed to prove GRASE status (the remaining 12 organic actives approved for use in the US). FDA further explains: "For example, the available literature includes studies indicating that oxybenzone is absorbed through the skin to a greater extent than previously understood and can lead to significant systemic exposure, as well as data showing the presence of oxybenzone in human breast milk,

amniotic fluid, urine, and blood plasma. The significant systemic availability of oxybenzone, coupled with a lack of data evaluating the full extent of its absorption potential, is a concern, among other reasons, because of questions raised in the published literature regarding the potential for endocrine activity in connection with systemic oxybenzone exposure. Nearly all of these sunscreen active ingredients also have limited or no data characterizing their absorption." This is why FDA requested industry to conduct a variety of testing, such as, but not limited to, carcinogenicity and reproductive toxicity prior to reinstating them into the GRASE category.

The data summarized in this paper clearly demonstrates the failure of sunscreens to protect against skin cancers. This point is further supported by the many researchers and regulators that have published similar conclusions over the last several decades (Figure 1) (Table 3). Despite this, there is an agenda to support propaganda that sunscreens are necessary to prevent skin cancers. For example, Mancuso etal [23] states "While several controversies regarding sunscreen exist, the data to support the regular use of sunscreen far outweigh the limited data regarding its possible side effects." These statements are simply not based on the published science or deductive reasoning, but purely on irrationally–derived opinion. This is especially true when one looks at the actual number of deaths in the United States occurring from skin cancers (Table 4) which identifies that 400,159 deaths have occurred from malignant skin cancers between 1975 – 2017 representing a 54% increase, adjusting for population growth, since the major push to use sunscreens. Additionally, it is approximated that at least 10,000 people a year will continue to die from skin cancers [24]. Sunscreen's failure to protect are jeopardizing public lives and inflicting rising costs to health care in what should be a straightforward and effective management to public health.

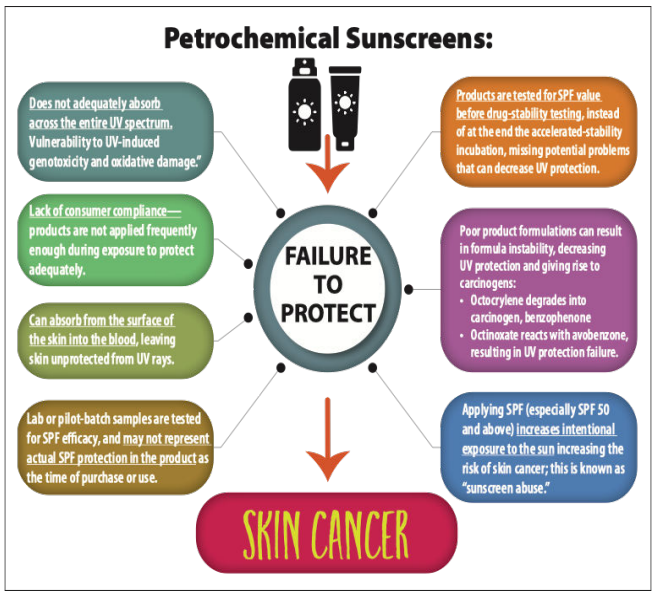

Figure 1: Failure to Protect

Year published	Lead author	Conclusion
1973	Emmett	"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	"In summary, the results of this study indicate that inflammation and enhanced melanoma growth are different effects of UV radiation involving diferent 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."
2006	EPA	"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	"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 sun -screens are protec- tive against CMM."

2018	Saes da Silva	"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."
2021	Serpone	"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."

Table 3: Published research questioning sunscreen efficacy.

Information Source:

1) 1973 – Emmett EA. Ultraviolet radiation as a cause of skin tumors. CRC Crit Rev Toxicol 1973; 2: 211–55.

2) 1994 – Wolf P, Donawho CK, Kripke ML. Effect of sunscreens on UV radiation–induced enhancement of melanoma growth in mice. J Natl Cancer Inst 1994; 86: 99–105.

3) 2006 – EPA: Sunscreen the burning facts 2006. Is sunscreen fail–safe (pg6). https://www.epa.gov/sites/production/files/documents/sunscreen.pdf. Accessed January 22, 2021.

4) 2011 – Planta MB. Sunscreen and melanoma: is our prevention message correct? J Am Board Fam Med 2011; 24: 735–9.

5) 2018 – Saes da Silva et al. Use of sunscreen and risk of melanoma and non–melanoma skin cancer: a systematic review and meta–analysis. Eur J Dermatol 2018; 28: 186–201.

6) 2021 – Serpone N. Sunscreens and their usefulness: have we made any progress in the last two decades. Photochem Photobiol Sci 2021; 20: 189–244.

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		54% Increase in deaths**
	400,159		

Table 4: Annual malignant skin cancer deaths, 1975–2017.

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.

Conclusion

Based on the data in the scientific literature, sunscreens do not prevent skin cancers associated with intentional sun exposure. Furthermore, in light of the current safety issues, it would appear that the risks associated are outweighed by the lack of benefits observed. Those wishing to still partake in intentional sun exposure should practice sun avoidance measures when possible, especially during peak hours of UV exposure (10 AM – 3 PM), wear protective clothing including a broad–brimmed hat with sunglasses, and/or use an oversized umbrella/cabana when at the beach or pool. If sunscreen is desired, use a non–nano particle - sized mineral- based zinc oxide or titanium dioxide sunscreen, which are currently considered safe and effective for human use, until adequate actives become commercially available that demonstrate safety and efficacy.

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