REVIEW ARTICLE

Sunscreen in the Spotlight: A Comprehensive Review of Over-the-Counter SPF Drug Products for Sun Protection

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In 2012, the Food and Drug Administration revised their guidelines on sunscreen in an attempt to cease the misleading and unsubstantiated claims commonly published on sunscreen product labels. Skin cancer is the most frequently diagnosed form of cancer in the United States with cases of skin cancer increasing worldwide. Despite these statistics, misconceptions among both consumer patients and health care practitioners, regarding sun protection factor, ultraviolet radiation, sunscreen efficacy, and application remain prevalent. For these reasons, it is imperative that practitioners have a fundamental understanding of sunscreen formularies in order to provide evidence based skin cancer prevention recommendations to their patients. This article aims at providing practitioners with a simplified yet comprehensive review of over-the-counter sunscreen drug products and the most recent FDA sunscreen monograph.

INTRODUCTION

Skin cancer is the most frequently diagnosed form of cancer in the United States. According to the most recent Center for Disease Control (CDC) statistics, in 2011, there were nearly 71,000 people diagnosed with melanoma and over 12,000 melanoma related deaths in the US alone.[1] This is a steep rise from one year earlier when the CDC reported 61,000 new diagnoses and 9,000 deaths.[1] As if a 33% rise in melanoma deaths over a one year period wasn't concerning enough, studies have found that children born today have a one in 33 risk of developing melanoma, a drastic upsurge from the one in 1,500 risk calculated in 1935.[2] Despite these alarming statistics, medical students receive minimal education in over-the-counter SPF drug products and physicians report that that skin cancer prevention counseling is not a priority. According to a survey of over 1600 American Academy of Pediatrics physicians, over 90% of pediatricians acknowledge the necessity for counseling patients on sun safety measures, however most admitted to rarely following through due to time constraints.[2] Furthermore, common misconceptions regarding sun protection factor (SPF), ultraviolet radiation (UVR), and the mechanism of action of SPF drug ingredients remain prevalent among healthcare providers.

The Food and Drug Administration (FDA) has produced several monographs on sunscreen since 1978, with significant activity in 2011. This article aims at providing practitioners with a simplified yet comprehensive review of over-the-counter (OTC) sunscreen drug products and the most recent FDA sunscreen monograph. In addition, the authors have addressed common misconceptions about SPF, such as measured efficacy and areas of debate requiring the provider's clinical judgment on a case-by-case basis.

ULTRAVIOLET RADIATION

The light emitted by the sun's rays, as classified by its wavelength on the electromagnetic spectrum, ranges from the longer wavelengths of visible light to the shorter wavelengths of ultraviolet (UV) light. Ultraviolet light is further subdivided into three potentially skin-damaging subcategories: UVA (315-400nm), UVB (290-315nm), and UVC (270-290nm).[3] Although sources slightly differ on cutoff endpoints, wavelengths shorter than 300nm typically do not result in skin damage because they are absorbed by the earth's ozone layer.[3] Therefore humans have minimal radiation exposure to UVC light.

Ultraviolet radiation, through the depletion of antioxidants and initiation of DNA damage, activates a complex cascade that leads to immunosuppression, inflammation, and free radical generation. The resultants of these cumulative processes are reactive oxygen species (ROS) that create oxidative damage to proteins, lipids and carbohydrates. These broken down molecules accumulate in the dermal and epidermal layers of the skin and aid in the process of photoaging.[4]

Both UVA and UVB radiation are known causes of cellular damage, which may result in cutaneous changes such as aging and skin cancer. However, due to their respective wavelength spectrums, their primary effect on the skin differs. As a general rule of thumb, the longer wavelengths of UVA light penetrate through the epidermis and into the dermis, producing a delayed tanning effect as well as alterations in dermal collagen,

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leading to signs of photoaging. Light from UVB, on the other hand, does not penetrate beyond the epidermis and has been shown to produce primarily a sunburn reaction.[5] Until recently, it was believed that only UVB rays produced skin cancer.[6] In comparison to the shorter wavelengths of UVB, UVA is able to penetrate through glass and reach the deeper layers of the skin. It has been found that 90-95% of UVA light and 5-10% of UVB light emitted by the sun will penetrate the skin, and that 20-50% of UVA light and 9-15% of UVB light will reach melanocytes.[7]

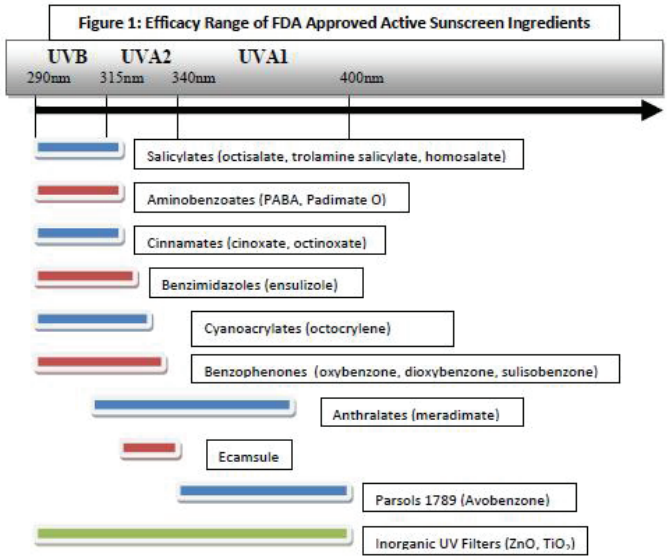
For these reasons, it is essential to use a sunscreen that provides both UVA and UVB protection, such as broad spectrum sunscreen discussed in greater detail below.

THE ACTIVE INGREDIENTS IN SUNSCREEN

There are two categories of sunscreen ingredients: organic UV filters, commonly known as chemical blockers, and inorganic UV filters, often referred to as physical blockers. Organic UV filters contain chromophores that absorb a range of UV wavelengths, triggering a series of molecular changes that ultimately result in a conversion of the absorbed energy into heat, which is transepidermally eliminated. Essentially, the chemical change that occurs from UV light interacting with chromophores prevents radiation from penetrating the skin.[6] The current FDA approved organic UV filter ingredients are: Parsol 1789 (avobenzone), dioxybenzone, oxybenzone, sulisobenzone, para-aminobenzoic acid (PABA), padimate O, ecamsule (Mexoryl SX), meradimate, cinoxate, octinoxate, octisalate, trolamine salicylate, homosalate, ensulizole, and octocrylene.[8] The chromophores within organic filters are composed of π-electron systems resulting in greatest effectiveness against the shorter wavelengths of UVB light.[3] Most of these ingredients are either ineffective or minimally effective against UVA light, however, ecamsule, which is capable of absorbing short UVA wavelengths (320-340nm), and Parsol 1789, which protects against longer UVA wavelengths (340-400nm), may be utilized for broad spectrum chemical protection (see Figure 1).[6]

Inorganic UV filters, the second category of sunscreens, are metal oxide powders that reflect UV radiation (UVR) away from the skin, thereby acting as a physical protective barrier.[6] The current FDA approved inorganic UV filters are: titanium dioxide (TiO2) and zinc oxide (ZnO). These ingredients are capable of diffusing wavelengths larger than 370nm and, therefore provide protection against UVA and a portion of UVB radiation.[6] The primary disadvantage of these ingredients is that they appear thick and chalky on the skin, making them aesthetically unappealing to consumers.

The majority of OTC sunscreen products consist of a combination of organic and inorganic UV filter ingredients.



Combination formularies are often preferable due to the fact that they offer protection against a larger UVR wavelength spectrum. Another benefit to combination products is increased durability. Organic UV filters have limited photostability under normal environmental conditions; therefore inorganic UV filters are typically added for their durability throughout prolonged periods of sun exposure.[6, 8-9]

Two proprietary sunscreens have been approved by the FDA: Helioplex, produced by Johnson & Johnson Neutrogena, and Mexoryl SX (La Roche-Posay), created by L'Oreal Paris. Both products utilize the broad spectrum, yet photo-unstable, azobenzone and combine it with oxybenzone to enhance resiliency. These proprietary sunscreens are advantageous in that they are broad spectrum, photostable and non-irritating.[2]

SUNSCREEN EFFICACY

Efficacy of sunscreen drug products is measured by two key components: sun protection factor (SPF) and UVA protection profile. The SPF of a sunscreen is measured by in vivo laboratory testing. Volunteers with Fitzpatrick skin types I-III skin types receive a sunscreen density of 2mg/cm^2 and are subsequently administered increasing doses of UVR.[3,9] The "minimal erythema dose" (MED) is defined as the least amount of UVR required for visible erythematous skin changes with distinct and clear borders 16-24 hours following UV introduction.[3] In theory, the MED correlates to the amount of time the sunscreen product protects the skin against the reddening effects of UVB, as opposed to the amount of time that erythema would occur without protection.[10] For instance, if your patient normally sunburns after 10 minutes in the sun, applying SPF 15 with an appropriate application thickness (2mg/cm^2) will protect an individual from sunburn for 150 minutes (2.5 hours). It is essential to note that SPF specifically refers to UVB protection alone, and that this testing model has many limitations such as inter-laboratory variability and

genetic or sensitivity variability of the volunteers.[11]

The method of measuring the second component of sunscreen efficacy, UVA protection profile, varies worldwide. In the United States, the FDA included in their most recent monograph a mandate for in vitro critical wavelength assessment. In this test, the product being evaluated is placed at a density of 0.75 mg/cm^2 in polymethylmethacrylate plates.[3] Ultraviolet doses starting at 290nm are then administered until the sum of the product's total absorbance reaches 90% of that product's total absorbance in the UVA spectrum (290-400 nm).[3,11] A sunscreen's critical wavelength is thus a measurement of the product's range of UVA protection.

THE NEW FDA MONOGRAPH FOR OTC SUNSCREEN PRODUCTS

The U.S. FDA recently published guidelines for over-the-counter sunscreen labels with a compliance deadline of December 2012.[8] According to these guidelines sunscreen products that adequately provide both UVA and UVB protection may garnish the label "broad spectrum." Adequate UVB protection has been defined as a minimum SPF of 15, whereas, satisfactory UVA protection, according to the FDA, has 90% of its absorbance at the critical wavelength of 370nm or greater.[8-9,12]

On sunscreens that have been deemed broad spectrum, the FDA now allows manufacturers to add the following claim to their product: "if used as directed with other sun protection measures…decreases the risk of skin cancer and early skin aging caused by the sun."[8] In the same light, sunscreens that do not meet the critical UVA wavelength and/or have an SPF of less than 15 are now required to print the following warning: "Skin Cancer/Skin Aging Alert: Spending time in the sun increases your risk of skin cancer and early skin aging. This product has been shown only to help prevent sunburn, not skin cancer or skin aging."[13]

Prior to the FDA guidelines, there was an epidemic of uncorroborated claims regarding length of protection and durability of sunscreen products in high moisture environments. Now, claims such as "all-day protection", "waterproof" and "sweat-proof" are replaced with strict time limitations of either 40 or 80 minutes. For instance, sunscreens that have proven resiliency against water for 40 minutes following application, now state on the bottle "water resistant (40 minutes)."[14]

In addition to the new monograph, the FDA proposed a regulation that, if finalized, limits SPF to 50+. Advocates of the proposal argue that higher SPF values increase exposure to potentially irritating chemicals while providing minimal additional UVB protection.[12] The claim that little benefit is gained from SPF values greater than 30 stems from the absorbance equation, A=1-1/SPF, which demonstrates a logarithmic curve with UVB absorbance plateauing at SPF 30 (see Figure 2).[9]

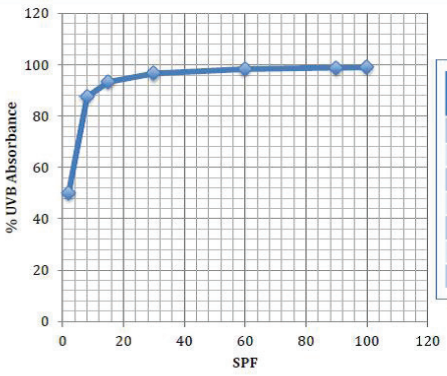
Opponents of the FDA's proposed SPF limit argue that the measurement of 'minimal erythema' utilized in the determination of SPF only evaluates for a visible erythematous response and does not take into consideration potential damage on the cellular or molecular level.[10] The ability for UVR doses below the minimal erythema level to cause long-term skin damage such as aging, immunosuppression, and skin cancer, has been well documented in the literature.[10] Furthermore a study, by Cole et al, found that a photostable SPF 55 offered cellular and molecular protection proportional to the SPF level.[10] However, this study compared the cellular changes of unprotected skin exposed to UVR to SPF 55 protected skin exposed to UVR. Despite these findings, there remains a lack of research comparing the cellular and molecular changes of UVR-exposed skin with SPF levels of 30 to that of higher SPF levels. A second counterargument to the FDA proposed SPF cap is that consumers average a sunscreen application thickness of 25-50% of the FDA recommended 2mg/cm^2 application density, thus resulting in actual SPF protection values significantly lower than labeled.[15-16] A recent study by Ou-Yang, et al that compared the actual SPF value of six sunscreens (with varying labeled SPF values between 30-100) at four application densities, found that broad spectrum SPF > 70 products were required when applying at a low application density of 0.5 mg/cm^2 in order to provide the FDA's minimal required protection for broad spectrum of SPF 15.[15] The FDA has not yet published guidelines for high SPF sunscreen and has stated that it will continue to review submitted data on sunscreens with SPF > 50.

CLINICAL CONSIDERATIONS & RECOMMENDATIONS

The new FDA monograph does not pertain to all forms of over-the counter sunscreens. Only oils, creams, lotions, gels, butters, pastes, ointments, sticks and sprays are considered eligible for inclusion. All other formularies, such as body washes, towelettes, powders, shampoos, etc., must apply for consideration from the FDA on a case-by-case basis.[12-13]

Regarding spray products, the FDA has requested additional information on their effectiveness and they plan to further investigate potential health consequences secondary to incidental inhalation.[13] A study by McKinney et al detected cardiovascular and pulmonary damage secondary to inhalation of spray TiO2 particles.[17] Therefore, spray sunscreen products are of particular concern in patients, particularly children, with known respiratory disease as asthma exacerbations may occur. Additional drawbacks to

Figure 2: Absorbance of UVB radiation as related to SPF level



SPF Level	UVB Absorbance
2	50%
8	87.5%
15	93.33%
30	96.67%
60	98.33%
90	98.89%
100	99%

using spray products include the requirement of manually rubbing in the product for complete coverage. Consumers are unable to safely assume that spraying the product and walking away will provide adequate sun protection coverage. Healthcare professionals should keep the above information in mind, along with their clinical judgment, when providing recommendations regarding sunscreen formularies to their consumer patients.

For patients of all age groups, long sleeve shirts, sunglasses, and wide brim hats in concert with careful avoidance of sunlight during the peak hours of 10am-2pm should be the mainstay of photoprotection methodology.[3] In adults, a broad spectrum sunscreen with SPF > 30 applied to sun exposed skin every two hours during periods of sun exposure is recommended.[18]

Unfortunately, due to limited research, pediatric guidelines are not as straightforward. Pediatrics, particularly infants, have a significantly larger body surface area to volume ratio than adults lending to the potential for increased chemical absorption when applied topically. For this reason, sunscreen drug products should be avoided in infants < 6 months of age and parents must be counseled on proper sun avoidance techniques.[16] The FDA determined in the new monograph that sunscreen is now considered safe in patients > 6 months old.[9] However, only inorganic UV filters are advised for children between 6 months and 2 years of age due to the fact that they are less irritating to the skin and less readily absorbed.[2,9,16] Keep in mind that inorganic filters do not provide the same range of UVB protection as combination sunscreens, thus further necessitating limited sun exposure along with protective clothing as the primary methods of UVR protection.

PATIENT EDUCATION

It is imperative to educate patients on the importance of purchasing broad-spectrum sunscreens. Sunscreens than do not don the "broad spectrum" label do not offer protection while driving or sitting near windows due to their lack of UVA absorbance. Although SPF 15 is eligible to be considered broad spectrum by the FDA, the American Academy of Dermatology (AAD) maintains a recommendation of SPF 30, reapplied every two hours when outdoors.[18] Furthermore, the FDA conducts SPF testing with a standard application of 2 mg/cm^2 of sunscreen product to the skin. According to previous studies, consumers average an application thickness less than 50% of that amount.[4,19-20] This suggests that, without proper physician instruction, consumers are often not receiving full SPF protection despite the use of sunscreen. A simple method physicians may use for patient education is to instruct their patients to squeeze a golf ball sized amount of sunscreen product into the palm of their hand and then thoroughly rub all of that product evenly onto exposed skin.

Another necessary topic for patient education is sunscreen shelf life. Current FDA regulations do not mandate the publication of expiration dates on OTC drug products without dosage limitations that are stable for a minimum of three years.[13] Nevertheless, it is commonly advised that sunscreen products be discarded after three years of use. Moreover, products purchased prior to the December 2012 FDA compliance deadline may not provide substantiated evidence regarding UVA protection, durability, and water resistance.

Lastly, since peek daylight hours and outdoor activities often go hand in hand, it is important to discuss the topic of combining bug repellants and SPF drug products with your patients. N,N-diethyl-m-toluamide (DEET), the most frequently used active ingredient in bug repellents, is estimated to decrease the SPF of a sunscreen by approximately 33%.[21] Therefore, in order to obtain the same degree of sun protection, sunscreen must be reapplied even more frequently and in greater amounts. Another health concern that arises with the topical co-administration of sunscreen and insect repellants is resulting higher transdermal absorption of the repellant product.[22] Currently, the CDC recommends that consumers apply SPF and insect repellants separately and that insect repellants be reserved for patients over 2 months of age.[23]

ON THE HORIZON

As consumers are becoming increasingly more conscious of the harmful effects of UVR, technological advancements in photoprotection are rapidly enhancing our ability to prevent skin cancer. One of the newest technologies developed is nanoparticle polymer spheres, ZnO and TiO2 particles reduced to sizes less than 100nm diameter.[5] The nanoparticles are easily incorporated into makeup and clothing for a multitude of potential uses without leaving the characteristic chalky residue of their larger sized counterparts. However, these particles are easily absorbed resulting in controversy regarding their safety.[5]

Heliocare, Fernblock and Sunpill are oral supplements containing polypodium leuctomos, an extract that has demonstrated modest evidence of antioxidant, immunomodulating, and photoprotection properties.[5] However, the sample sizes studied were small and the products are not intended to replace sunscreens, but instead to work in concert with topical SPF 30 products. The FDA has not provided their recommendations on these new products. Still, some are available to consumer patients, potentially prompting them to seek the advice of their physician.

CONCLUSION

In 2012, the FDA revised their guidelines on sunscreen in an attempt to cease the misleading and unsubstantiated claims commonly published on sunscreen product labels. The new guidelines deem products providing a minimum of SPF 15 and UVA protection as "broad spectrum." However, clinicians should be conscious that the AAD upholds their SPF 30 recommendation.

Under application, failure to reapply sunscreen every two hours, and misconceptions regarding the meaning of SPF are common reasons for sunscreen failure. Due to the increased incidence in skin cancer worldwide, physicians should educate consumer patients on the method of application in order to reduce the damaging cutaneous effects of UVR. Additionally, physicians should be familiar with the sunscreen formularies and active ingredients in order to provide evidence based recommendations to their consumer patients.

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