ARTICLE

Sunscreens

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SUMMARY

Sunburn is caused by ultraviolet B radiation, but ultraviolet A may be more damaging to the skin. Sunscreens should ideally block both wavebands.

The sun protection factor of a sunscreen is mainly based on blocking ultraviolet B. It does not measure the effectiveness against blocking ultraviolet A.

Sunscreens may be organic or inorganic chemicals. The cosmetic acceptability of metal oxide sunscreens may be improved if they are formulated as nanoparticles.

The absorption of organic sunscreens and nanoparticles does not appear to cause significant systemic effects.

Regular use of sunscreen significantly reduces the development of actinic keratosis, squamous cell carcinoma and melanoma.

Introduction

Sunscreens were originally developed to prevent sunburn from excessive exposure to sunlight. These products were designed to block the ultraviolet B (UVB) rays that cause sunburn but had little effect on ultraviolet A rays (UVA). We now know that UVA causes damage to cells under the dermis which may lead to premature ageing of the skin as well as some types of skin cancers. There are currently sunscreens which block both wavebands. Sunscreens are now used daily by many people and form a component of many 'anti-ageing' moisturising creams, lipsticks and other beauty products.

The solar spectrum and skin damage

Sunlight reaching the earth's surface consists of ultraviolet (290–400 nanometres), visible (400–760 nanometres) and infrared (greater than 760 nanometres) wavelengths. The ultraviolet wavebands are further subdivided into UVB (290–320 nanometres), UVA2 (320–340 nanometres) and UVA1 (340–400 nanometres).

Terrestrial UV radiation consists of 5% UVB which is mostly absorbed by the epidermis and 95% UVA which can penetrate below the dermis (Fig. 1). UVB is higher energy and is responsible for sunburn and direct damage to DNA. More recently identified is the role of lower energy UVA radiation in causing direct[1] and indirect DNA damage by free radical generation, photoageing, immune suppression and photocarcinogenesis.[2]

Sunscreens

Currently there are 33 active ingredients approved by the Therapeutic Goods Administration (TGA) as sunscreens in Australia.[3] These ingredients are divided into organic (consisting of synthetic organic chemicals) and inorganic sunscreens (see Table 1 online with this article at www.australianprescriber.com/magazine/35/5/148/51).

Organic sunscreens

Certain organic chemicals can absorb UV radiation. This radiation provides the energy for a photo-induced tautomerisation or isomerisation of the chemical to a higher energy state. The chemical then returns from the less stable excited state to its original form releasing the excess energy as heat or longer wave, lower energy visible light.[4]

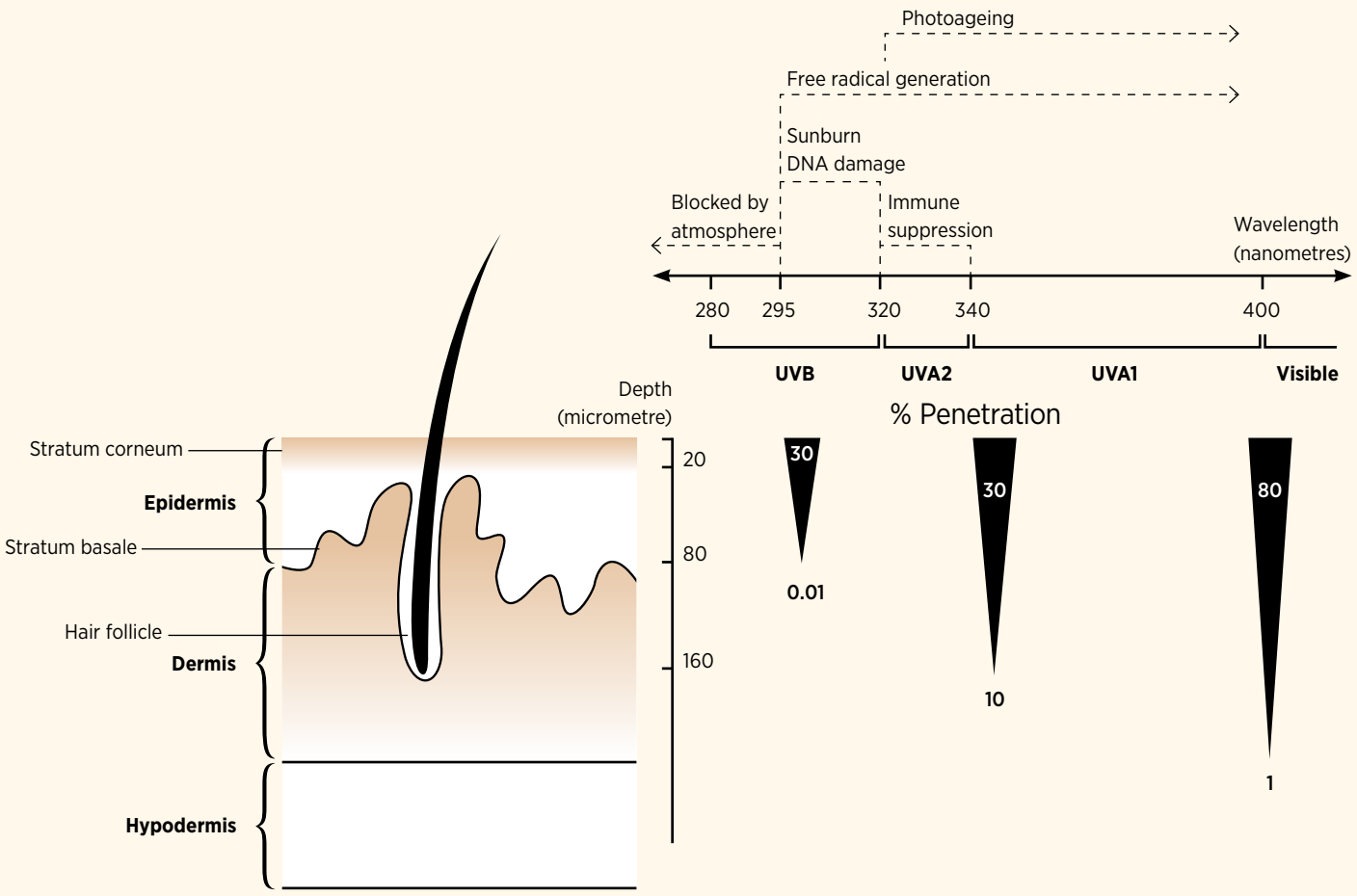
Safety

Most active sunscreen ingredients have been used globally for more than 15–30 years and are considered to be safe in humans. In Australia sunscreens are classified as drugs and all active ingredients undergo stringent approval processes including acute and chronic phototoxicological assessments.

Minor stinging and skin irritations are the most common complaints from sunscreen use. True allergy to sunscreens is uncommon, however adverse reactions from sunscreen use include allergic and irritant contact dermatitis, phototoxic and photoallergic reactions. Sunscreens are becoming one of the most important causes of photoallergy due to their increasing use. Although many suspected sunscreen allergies arise from non-active ingredients in the formulation, the most common sunscreen photoallergens are para-aminobenzoic acid (now rarely used), benzophenones and butyl methoxy dibenzoylmethane.[5]

Concerns have been raised about the oestrogenic effects of some sunscreen ingredients, especially benzophenones, which have a high topical bioavailability, and 4-methylbenzylidene camphor (4-MBC) and octyl methoxycinnamate (OMC), which have shown weak oestrogenic effects in vitro.

Fig. 1 **Schematic cross section of skin showing dermal penetration and biological effects of different wavelengths of UV radiation** *



* modified from reference 2

However, a European review found they did not exert oestrogen-like effects in people, estimating that currently approved sunscreens would need to be 100 000 times more potent before they showed any hormonal effect.[6] Newer ingredients such as ethylhexyl triazone, drometrizole trisiloxane and terephthalylidene dicamphor sulfonic acid have been specifically designed with a high molecular weight to decrease skin penetration, so they are considered safe.[4]

Inorganic metal oxide sunscreens

The metal oxides, zinc oxide (ZnO) and titanium dioxide (TiO_2), were previously referred to as physical sunscreens. Zinc oxide offers true broad spectrum UV protection, although titanium dioxide has better UVB protection. Both oxides have been used in sunscreens for many years, but were originally micro-sized particles (200–500 nanometres) and required a thick application to provide a barrier to reflect and scatter UV rays. This made them cosmetically unacceptable due to the opaque white layer on the skin.

The use of nanoparticles (20–100 nanometres) has improved the cosmetic acceptability of inorganic sunscreens and microfine titanium dioxide has been used in sunscreens since the early 1990s.[7] Microfine or nanoparticles of titanium dioxide and zinc oxide absorb and reflect/scatter UV radiation. They are transparent on the skin.

Safety

Sunscreens containing only inorganic agents have often been recommended for children. However, widespread use of nanoparticles has led to health concerns regarding their safety. There are now some products containing zinc oxide that promote the fact that they do not contain nano-sized particles. In relation to sunscreens, these concerns are focused on whether nanoparticles can penetrate the skin and enter the body and whether nanoparticles generate free radicals.

In 2009, the TGA reviewed the scientific literature about nanoparticles in sunscreens. The vast majority of well-conducted scientific studies found that

during normal use on intact skin nanoparticles do not penetrate below the stratum corneum, but may travel down the hair follicle. However, it is likely that nanoparticles do penetrate through damaged skin.[8]

Titanium dioxide nanoparticles exposed to UV radiation can generate hydroxyl radicals that can damage the DNA of viable cells. However, titanium dioxide nanoparticles in sunscreens are coated with dimethicone or silica to prevent particle agglomeration and these coatings also inhibit free radical generation. The TGA concluded that as nanoparticles do not penetrate into viable skin, concerns relating to systemic toxicity are greatly diminished.[8]

Sun protection ratings

The sun protection factor (SPF) of a sunscreen is determined by a highly regulated clinical test using lamps that simulate solar radiation on human volunteers. It measures the time taken for a minimal erythema to appear when sunscreen is applied compared to the minimal erythemal dose (MED) without sunscreen. An SPF of 15 means that if it takes 10 minutes for skin to start to burn without sunscreen it will take 150 minutes with that sunscreen.

$$\text{SPF} = \frac{\text{MED with sunscreen}}{\text{MED without sunscreen}}$$

The Australian/New Zealand standard 'Sunscreen products – Evaluation and classification' was reviewed in 2011 and the new standard AS/NZS 2604:2012, published in May 2012, permits SPF ratings of 4–50+ (Table 2).[9] The previous edition of the standard permitted SPF ratings of 2–30+.[10] The measurement of SPF uses the biologically relevant endpoint of erythema, however the SPF is biased towards UVB and only measures how effective a sunscreen is at preventing sunburn. It does not measure how effective a sunscreen is at blocking UVA rays.

Previously, the standards for measuring UVA protection were less well defined in Australia.[10] However, the new AS/NZS 2604:2012 aligned the standard for UVA protection with ISO 24443. This requires the monochromatic protection factor at 380 nanometres (MPF380) to be calculated from the in vitro transmission at 380 nanometres. If the SPF is 15 or higher and the SPF/MPF ratio is less than three, then the sunscreen may be identified as broad spectrum.[9]

Sunscreens that have identical SPF ratings will have equal protection against UVB rays under the controlled conditions that are used to determine the SPF. However, the effectiveness of a sunscreen is determined by a number of factors. These include the age of the product and expiry date, the specific ingredients, overall formulation, water resistance, the amount of time that the sunscreen has been exposed to the sun and the amount applied.

The SPF of a sunscreen is measured with a standard application of 2 mg/cm^2 and applying less will not give the same protection.[9] For an average sized adult this means full body coverage requires approximately 30 mL of sunscreen. Current guidelines recommend that to achieve the maximum protection, sunscreen should be applied 20–30 minutes before going outside and then reapplied at least every two hours, especially after swimming. The water resistance of a sunscreen must also be determined using a standardised protocol of repeated 20 minute immersions followed by SPF measurement.[9]

Do sunscreens prevent skin cancer?

The incidence of skin cancers (particularly melanomas) has continued to increase in Australia despite 30 years of 'Slip, slop, slap'. This has been used as an argument against the use of sunscreen.[11] However, it is only since the mid-1990s that broad spectrum sunscreens have been widely available. The use of UVB-only sunscreens may have provided a false sense of security, encouraging people to stay in the sun even longer and therefore increasing their exposure to harmful UVA rays. The long latency between sun exposure and the appearance of skin cancers also means that the efficacy of broad spectrum sunscreens in preventing skin cancer may not become really apparent for another 25 years or more when the population born in the 1990s reach the age when most skin cancers begin to appear.

Table 2 **Current and previous category descriptions for sunscreens** *

Category description	Tested sun protection factor (SPF) (from 2012)	Tested sun protection factor (before 2012)
Very low protection sunscreen	-	2 < 4
Low protection sunscreen	4 < 15	4 < 8
Medium or moderate protection sunscreen	15 < 30†	8 < 15
High protection sunscreen	30 < 50††	15 < 30
	50 < 60††	
Very high protection sunscreen	60 (labelled 50+)††	30+

The sun protection factors are ranges, for example 2 < 4 means at least 2 but less than 4

* The new Australian/New Zealand standard 2604:2012 was published in May 2012

† If the SPF/monochromatic protection factor ratio is less than 3, these sunscreens may be identified as broad spectrum

†† Must also meet broad spectrum requirements

The largest and most comprehensive clinical trial was the five-year randomised controlled Nambour Skin Cancer Prevention Trial. This compared the development of new skin cancers in adults who applied broad spectrum SPF 16 sunscreen daily to face, neck, arms and hands (reapplied if necessary) with a control group who applied sunscreen at their discretion. Follow-up after five and eight years found a significant reduction in the number of precancerous actinic keratoses[11] and squamous cell carcinomas.[12] After 10 years there was a significant reduction in the number of new melanomas.[13] This long-term study clearly shows that regular use of sunscreen can prevent the development of skin cancers. While basal cell carcinomas did decrease, the results were not statistically significant. This may be because basal cell carcinomas result from damage caused early in life and this study only looked at adults.

Sunscreens and vitamin D deficiency

Although vitamin D deficiency is believed to be common in Australia,[14] several prospective clinical or population-based studies have not shown a correlation between vitamin D deficiency and sunscreen use.[15] In Australia, sufficient vitamin D synthesis in healthy active people can usually be gained from 5–15 minutes sun exposure 4–6 times a week (outside the hours of 10 am–2 pm).[14] However, people who may be at risk of vitamin D deficiency should discuss with their doctor sunscreen use, sun exposure and use of vitamin D supplements.

New developments

Recent advances include methods for encapsulating chemical sunscreen ingredients in inert tetraethoxysilane polymers. This microencapsulation improves sunscreen stability, decreases or prevents systemic absorption, increases formulation possibilities and diminishes allergic reactions.[16]

Another approach is the addition of hollow styrene/acrylate polymer beads to the active ingredients. Although the beads do not absorb UV irradiation, they scatter the UV rays increasing the probability of contact with the active ingredients. They work with both organic and inorganic sunscreens to enhance their effectiveness across the whole UV spectrum, making it possible to reduce the amount of active sunscreen ingredients.[17]

Conclusion

Sunscreens have been found to be a safe and effective way of protecting the skin from UV radiation. Despite possible concerns about long-term safety, the benefits outweigh the harms. Sunscreens should only form one part of a sun protection strategy. Staying out of the sun and covering exposed parts of the body with photoprotective clothing remain priorities. If sun exposure cannot be avoided, then the use of a broad spectrum high SPF sunscreen, applied according to directions to protect against sunburn, photoageing and photocarcinogenesis is essential. ◀

Conflict of interest: none declared

Q:

SELF-TEST QUESTIONS

True or false?

3. The sun protection factor of a sunscreen is a measure of its effectiveness in blocking ultraviolet A radiation.

4. There is no evidence that the regular use of sunscreen prevents the development of melanoma.

Answers on page 171

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Table 1 **Active ingredients approved for use in Australian sunscreens**

Organic sunscreens				
Ultraviolet wavelengths (nanometres)		**Australian approved name**	**Synonyms/abbreviations/brand names**	**Notes on usage and safety**
UVB		**Cinnamates**		
	290-330	Isoamyl methoxycinnamate	Isoamyl p-methoxycinnamate, IMC, Neo Heliopan E1000, Amiloxate	Octyl methoxycinnamate is the most common UVB filter, used in 90% of sunscreens globally. It has little topical absorption and a favourable human safety profile, based on acute and repeat dose toxicity studies.
	280-310	Octyl methoxycinnamate	Ethylhexyl methoxycinnamate, OMC	
	270-328	Cinoxate	2-Ethoxyethyl 3-(4-methoxyphenyl)propenoate	
		Paraminobenzoic acid	**PABA**	
	260-313	Aminobenzoic acid	4-Aminobenzoic acid	PABA derivatives were some of the first widely used chemical sunscreens. They are strongly UVB absorbing, but associated with a number of adverse reactions, particularly photoallergy, and are now rarely used. They have been largely replaced by cinnamates, particularly OMC.
	290-315	Padimate O	2-Ethylhexyl-4-dimethylaminobenzoate, Octyl dimethyl PABA	
		Ethoxylated ethyl 4-aminobenzoic acid	PEG25 PABA	
		Salicylates		
	260-310	Octyl salicylate	2-Ethylhexyl salicylate	The two most commonly used salicylates, octyl salicylate and homosalate, are oil-soluble, weakly absorbing UVB filters with limited dermal absorption. They are photostable and have good safety profiles. Octyl salicylate is often used as a solvent for other UV filters, especially avobenzone.
	290-315	Homosalate	Homomethylsalicylate, HMS	
		Isopropylbenzyl salicylate	4-Isopropylbenzyl salicylate	
	269-320	Triethanolamine salicylate	Trolamine salicylate	
	269-320	Salicylic acid salts (potassium, sodium and triethanolamine)		
		Camphor based		
	280-315	alpha-(2-oxoborn-3-ylidene)toluene-4-sulfonic acid and its salts	Benzylidene camphor sulfonic acid	Generally considered photostable and not to be dermal irritants or sensitisers
	280-315	N,N,N-Trimethyl-4-(oxoborn-3-ylidenemethyl)anilinium methyl sulfate	Camphor benzalkonium methosulfate	
	270-335	4-Methylbenzylidene camphor	3-(4-Methylbenzylidene)-d-1 camphor, 4-MBC	
		Miscellaneous		
	290-340	Phenylbenzimidazole sulfonic acid	2-Phenylbenzimidazole-5-sulfonic acid and its potassium, sodium and triethanolamine salts, ensulizole	Considered photostable and not to be a dermal irritant or sensitiser
	280-340	Polysilicone-15	Dimethicodiethylbenzalmalonate, Parsol SLX	Photostable, high molecular weight polymer with limited dermal penetration and good safety profile. Often used in hair care products.
	280-330	Octyl triazone	2,4,6-Trianalino-(p-carbo-2'-ethylhexyl-1'oxy)1,3,5-triazine, ethyl hexyl triazone, EHT	Photostable, strong UV absorber. Low dermal absorption.

Organic sunscreens				
Ultraviolet wavelengths (nanometres)		**Australian approved name**	**Synonyms/abbreviations/brand names**	**Notes on usage and safety**
UVB + UVA-2		**Benzophenones**		
	270-360	Benzophenone		Benzophenones are commonly used UVB absorbers, with the highest bioavailability of any sunscreen ingredient after topical application (up to 10%). Potential endocrine effects were reported from in vitro and animal studies, however, clinical studies did not demonstrate biologically significant hormonal disruption with topical application of oxybenzone in humans. Relatively high incidence of photoallergy (particularly oxybenzone).
	280-390	Benzophenone-2	Bis(2,4-dihydroxyphenyl)methanone	
	206-380	Dioxybenzone	Benzophenone 8	
	270-350	Oxybenzone	Benzophenone 3	
	250-380	Sulisobenzone	Benzophenone 4	
		Sulisobenzone sodium	Benzophenone 5	
		Benzotriazoles		
	280-380	Bemotrizinol	Tinosorb S	Relatively new broad spectrum sunscreen ingredients, no endocrine effects, large molecules therefore not dermally absorbed, photostable and also stabilise other UV absorbers. Tinosorb S is for oil-phase sun-care formulations. Tinosorb M consists of microfine organic particles that are dispersed in the sunscreen emulsion. They scatter, reflect and absorb UV rays, combining the benefits of organic filters with those of inorganic filters.
	280-380	Methylene bis-benzotriazolyl tetramethylbutyl phenol	Tinosorb M 2,2'-Methylene-bis-6-(2H-benzotriazol-2-yl)-4-(tetramethyl-butyl)-1,1,3,3-phenol	
		Miscellaneous		
	290-360	Drometrizole trisiloxane	Mexoryl XL Phenol,2-(2H-benzotriazol-2-yl)-4-methyl-6[2-methyl-3-[1,3,3,3-tetramethyl-1-[(trimethylsilyl)oxy]disiloxanyl] propyl	Photostable and oil-soluble. Used synergistically with Mexoryl SX.
	287-323	Octocrylene	2-Cyano-3,3-diphenyl acrylic acid, 2-Ethylhexyl ester, 2-Ethylhexyl-2-cyano-3,3-diphenylacrylate	Photostable, broad spectrum absorber, often used to stabilise avobenzone. Octocrylene is not irritating to skin and lacks phototoxicity and photoallergenicity potential, but may increase skin's photosensitivity to sun.
UVA-2	310-400	Butyl methoxy dibenzoylmethane	1-(4-tert-butylphenyl)-3(4-methoxyphenyl)propane-1,3-dione, avobenzone, BMDM, 4-tert-butyl-4-methoxy dibenzoylmethane	First organic UVA absorber, low systemic bioavailability, extensive toxicological evaluation with favourable profile, most noted effect is photoallergy. Photo-unstable resulting in rapidly decreasing UVA efficiency after sun exposure, but formulation with other UV absorbers such as oxybenzone and octocrylene reduces this photodegradation. Combined with oxybenzone for stability in Helioplex.
	300-380	Menthyl anthranilate	Meradimate	
	295-390	Ecampsule	Terephthalylidene dicamphor sulfonic acid, Mexoryl SX	Photostable and water-soluble. Used synergistically with Mexoryl XL.
	300-370	Disodium phenyl dibenzimidazole tetrasulfonate	Bisdisulizole disodium, Bisimidazylate, Neoheliopan AP, 2,2'-(1,4-Phenylene) bis-(1-H-benzimidazole-4,6-disulfonic acid, monosodium salt)	Relatively new photostable sunscreen ingredient. High molecular weight with limited dermal absorption.

Inorganic metal oxides				
Ultraviolet wavelengths (nanometres)		**Australian approved name**	**Synonyms/abbreviations/brand names**	**Notes on usage and safety**
UVB, UVA-2	290-350	Titanium dioxide	TiO_2	Less likely to cause skin irritation than organic sunscreens. ZnO has a very long history of use as a soothing topical agent. Photostable and unlikely to cause skin irritation. Both TiO_2 and ZnO may cause skin to appear white, however this is less of a problem in newer formulations and those using nanoparticles that have been coated to prevent particle agglomeration and improve photostability. Nanoparticles of TiO_2 and ZnO are not believed to penetrate healthy intact skin and are therefore considered safe to use.
UVB, UVA-2, UVA-1	290-400	Zinc oxide	ZnO	