

مر الطين

فرآورده های ضد آفتاب و برنزه کننده Sunscreens دکتر شیوا گل محمدزاده استاد گروه فارماسیوتیکس دانشکده داروسازی مشهد



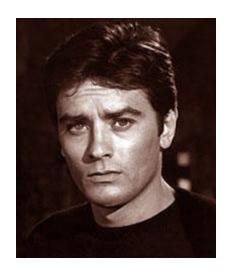
Sun light

- Sun Moderate exposure has beneficial effects on human health:
- It gives light, warmth, and energy, Antimicrobial, Antidepressant, peace of mind and general well-being. It also stimulates blood circulation, increases the formation of hemoglobin, and may also promote a reduction in blood pressure.
- It plays a critical role in producing vitamin D_3 which enhances the absorption of calcium.
- Finally by producing melanin and causing thickening of the horny layer of the skin, it plays an essential role in the formation of the body's natural protective against sunburn.



Adverse reactions to the sun UV rays

- Short-term inflammatory responses: dehydration, erythema, oedema, sunburn.
- Long-term effects: suppression of the immunological system, photosensitivity, skin cancers, thickening of the skin, loss of natural elasticity, laxity, roughness, dryness, irregular hyperpigmentation and cutaneous photoageing, deep wrinkles.



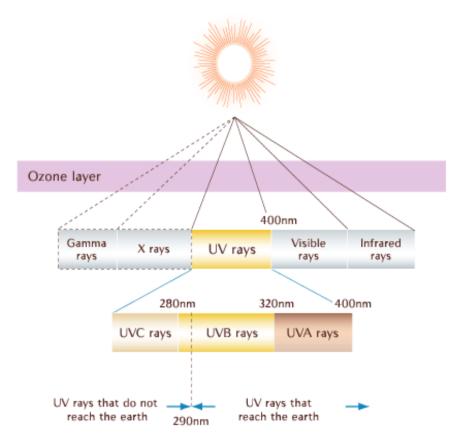




Ultraviolet radiation (UVR)

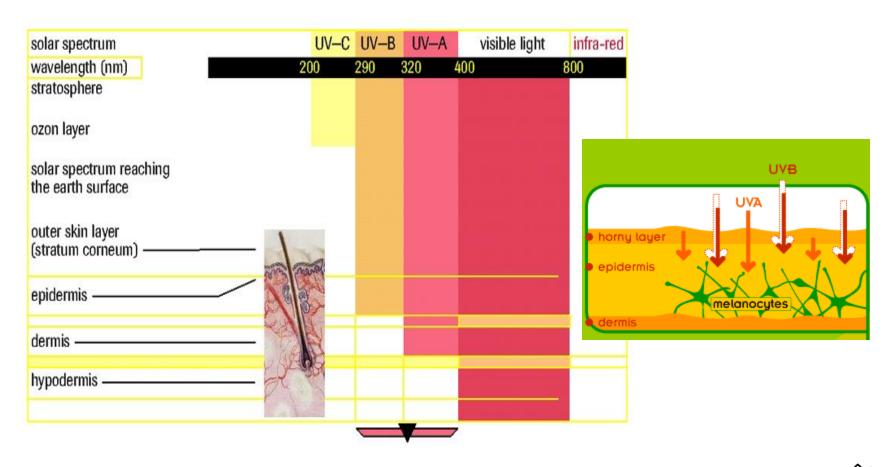


- UVC (200-290 nm)
- UVB (290-320 nm)
- UVA (320-400 nm)
- UVA II, 320 340nm
- UVA I, 340 400nm



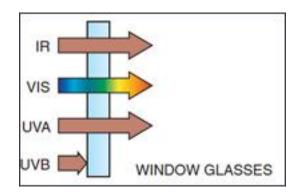


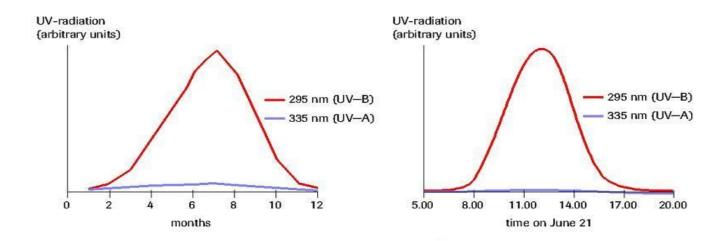
Solar spectrum wavelength and their penetration to the skin in different layers of the skin





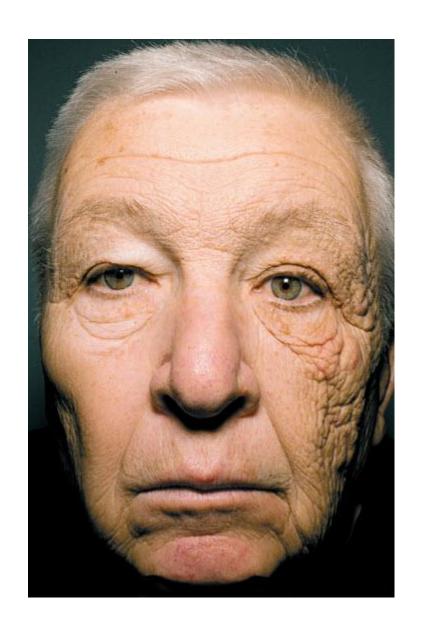






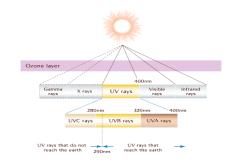
Hourly and monthly variation in amount of UVA and UVB radiations during a day and a year







IR Radiation



- IRR is inseparably linked to sunlight and perceived as heat. In the skin, heat is implicated in erythema and elastotic degeneration.
- IRA is responsible for accelerating skin aging by forming harmful free radicals in the dermis, diminishing skin's antioxidant capacity, and triggering further biological effects that result in wrinkles, loss of elasticity, and reduced firmness
- Sunscreen. UVA, UVB, IR

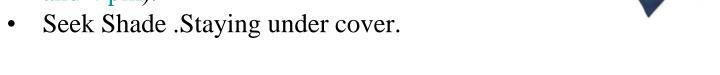
UV Reflection from different surfaces

- UV radiation can be reflected from snow (80% to 90%), water (up to 30%), grass (2.5% to 3%) and sand (20% to 30%).
- Pollutants, clouds, and fog can decrease the UVR reaching the earth's surface by scattering the radiation.



For Sun Protection

- Limit Time in the Midday Sun (between 10 am
- and 4 pm).



- Use Sunscreen .A broad spectrum sunscreen with a SPF of at least 15.
- Wear a Hat. Hat is good sun protection for your eyes, ears, face and the back of your neck.
- Wear Sunglasses. That Block 99 to 100 Percent of UVR.
- Watch for the UV Index (0-15). The UV index is an international standard measurement of how strong the UVR from the sun is at a particular place and day.
- Wear long sleeves and pants when playing or working outdoors. Darker colors and fabric with a tight weave provide the most protection.



Vitamin D

- Vitamin D is produced on the skin by UV light, particularly UVB rays.
- Vitamin D production is limited in fall and winter, as UVB are less intense.
- Adequate amounts of vitamin D₃ can be made in the skin after only ten to fifteen minutes of sun exposure at least two times per week to the face, arms, hands, or back without sunscreen. This should be done mid-morning or mid-afternoon. For strict sunscreen appliers DO MORE two times a week.
- Experts agree that too many people in the U.S don't get enough vitamin D in their daily lives.

Vitamin D

- People with very dark skin are more high risk.
- The pigment in skin (melanin) acts as a filter to (UVB) radiation and reduces synthesis of vitamin D.



Vitamin D

- The body can only absorb a certain amount of vitamin D at a time.
- Prolonged sun exposure does not result in your vitamin D levels increasing further, but does increase your risk of skin cancer.
- Short periods of sun exposure may be more efficient at producing vitamin D.
- Daily exercise will also assist your body to produce vitaming



"So what?" So what to do?



- There is no scientifically validated, safe threshold level of UV exposure from the sun that allows for maximal vitamin D synthesis without increasing skin cancer risk.
- The academy recommends increased intake of foods naturally rich in vitamin D, Vitamin D fortified foods like salmon, mushroom, milk and orange juice, eggs and vitamin D supplements.
- UV is both a major cause of skin cancer and the best natural source of vitamin D. We need to balance the risk of skin cancer from too much sun exposure with maintaining adequate vitamin D levels.
- Consult your physician to determine if you are at risk of vitamin D deficiency.
- If you are, you may need a blood test and regular or seasonal vitamin D supplementation.

History

Table 2	History of Photoprotection
Year	Advances
1887	Veiel started using tannin as photoprotector
1891	Hammer studied various topical photoprotective agents
Early 1900s	Zinc oxide, magnesium salts, bismuth were used as photoprotective agents
1928	First commercial sunscreen with benzyl salicylate and benzyl cinnamate became available (United States)
1943	PABA patented
1944	Green developed red veterinary petrolatum, used by soldiers during World War II as sunscreen
1948	PABA esters became available
1962	First UVA filter, a benzophenone, was introduced
1974	Greiter popularized "SPF," which was first proposed by Schulze in 1956
1977	First waterproof sunscreen became available
1978	FDA published guidelines on sunscreens, and adapted SPF method to assess sunscreens
1979	Long UVA filter, dibenzoylmethane derivatives, became available
1989– 1992	Micronized inorganic filters became available (titanium dioxide in 1989, zinc oxide in 1992)
Abbreviati	ons: PABA, para-aminobenzoic acid; SPF, sun protection factor; FDA, Food and Drug

Abbreviations: PABA, para-aminobenzoic acid; SPF, sun protection factor; FDA, Food and Drug Administration.



Sunscreen products

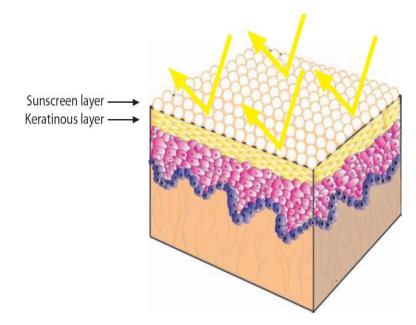
- Sunscreen products in the United States and Australia are regulated by the FDA as over-the-counter (OTC) drugs.
- In Europe, sunscreen products are considered to be cosmetics, their function being to protect the skin from sunburn.
- In Japan, sunscreens are classified as cosmetics.





Sunscreens

- Physical sunscreens
- Scatter UV; include titanium dioxide, zinc oxide, talc, kaolin, calamine, barium sulfate, magnesium oxide, iron oxide and red petrolatum jelly.
- microfine and nano sized zinc oxide and titanium dioxide (TiO2)
- Microfine and coated Tio2 is better





Mode of action of a physical sunscreen that reflects radiation.

Physical sunscreens

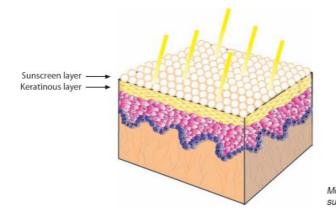
- Physical blockers have the advantage of lowered skin irritancy and penetrating and photostability. IR, UVR
- Titanium Dioxide (TiO2): UVA and UVB
- TiO2 was the first micropigment extensively used. Advantages include a broad spectrum of protection and inability to cause contact dermatitis.
- Microfine TiO2 at an equal concentration offers somewhat more protection in the UVB range.

Physical sunscreens

- Particle size needs to be less than 200 nm to achieve transparency.
- Zinc Oxide (UVA and UVB)
- ZnO has a refractive index of 1.9, as opposed to 2.6 for TiO2, and therefore causes less whitening than TiO2.
- ZnO attenuates UVR more effectively in the UVA I range.



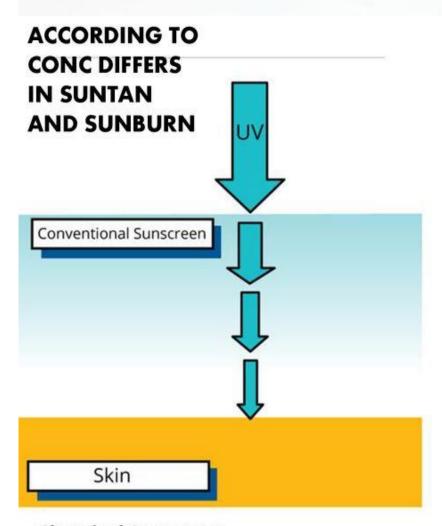


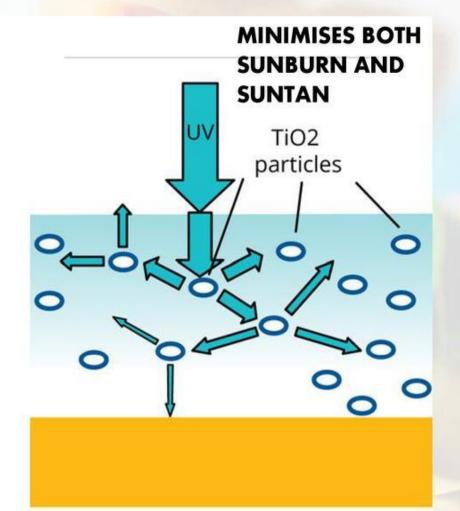


- Chemical sunscreens
- Absorb UV; benzophenone derivatives, salicylic acid derivatives, cinnamates, para-amino benzoic acid derivatives, anthranilates, dibenzoylmethanes, some camphor, Sulfonic Acid and Triazone derivatives and a few miscellaneous chemicals.
- There are some oils which can absorb UVR. Olive oil, avocado oil, coconut oil, cotton oil, almond oil and sesame oil.
- The degree of absorption depends on the substance and its concentration.



MECHANISMS OF OPERATION OF SUNSCREENING AGENTS





Chemical Sunscreen

UV light is absorbed as it passes through the film



Mineral Sunscreen

UV light is mostly scattered by TiO2 particles

- PABA derivatives; UVB absorber, high penetration, color, water soluble compound PABA (padimate O), ...
- Cinnamates; Potent UVB absorbers, replaced PABA derivatives, less water resistant. Octinoxate (octyl methoxycinnamate) is most frequently used.
- Cinoxate (ethoxy-ethyl-p-methoxycinnamate), Isoamyl p-methoxycinnamate,....
- Octocrylene: is cinnamates. It can be used to boost SPF and improve water resistance in a given formulation. Octocrylene is photostabile and can improve the photostability of other sunscreens. It is expensive and can present difficulties in formulation.



Camphor Derivatives

UVB absorber, Except Tetraphtalydine dicamphor sulfonic acid (Mexoryl SX) (UVA absorber) .Not approved by the FDA in the US but not in Europe.

- Phenylbenzimadazole Sulfonic Acid (Ensulizole) (PSA)
- It is a water-soluble UVB absorber, allowing for a less-greasy, more aesthetically pleasing formulation such as a daily use moisturizer containing sunscreen. **Ensulizole** boosts the SPF of organic and inorganic sunscreens. It can also be used in clear gels owing to its water solubility.





Salicylates

Salicylates are weaker UVB absorbers.

Octyl salicylate, homosalate (homomenthyl salicylate).

Trolamine (triethanolamine salicylate) has good water solubility.





- Menthyl Anthranilate
- Meradimate (menthyl anthranilate) is a weak UVB filter, UVA II.
- It is less less widely used.





- **Triazones** No irritation
- Tinosorb M (Bisoctrizol): UVA, UVB.
- Tinosorb S (Bemotrizinol): UVA, UVB.





Benzophenones

- Oxybenzone (benzophenone-3); UVB, UVA II. It boosts SPF values in combination with other UVB absorbers. Has poor solubility in water.
- Sulisobenzone (benzophenone-4) UVB, UVA II. is water soluble, somewhat unstable, and used with less frequency.
- Irritation
- Penetration
- No permitted in children





- Avobenzone
- Avobenzone (Butyl methoxydibenzoylmethane, Parsol 1789) UVAI
 , UVB. Better than benzophenone.
- EU no. ...Parsol 1789, Eusolex
- Irritation



List of US Food and Drug Administration-approved ultraviolet (UV) filters, their maximum allowable concentration, and UV absorbance

Drug Name (Active ingredient)		Concentration (%)		Absorbance
Para Aminobenzoic acid		Up to 15		UV-B
Padimate O (Octyl dimethyl	Up to 8		UV-B	
Octinoxate (Octyl methoxyc	arsol MCX)	Up to 7.5	UV-B	
Cinoxate	Up to 3		UV-B	
Octysalate (Octyl salicylate)		Up to 5		UV-B
Homosalate (Homomenthyl	Up to 15		UV-B	
Trolamine salicylate	Up to 12		UV-B	
Octocrylene	Up to 10		UV-B	
Ensulizole(Phenylbenzimida	UV-B			
Oxybenzone (Benzophenone	Up to 6		UV-B, UV-A II	
Sulisobenzone (Benzopheno	Up to 10		UV-B, UV-A II	
Dioxybenzone (Benzopheno	Up to 3		UV-B, UV-A II	
Padimate O7 (Octyl dimethy	Up to 8		UV-B	
Butyl methoxydibenzoyl me	B UV-A I			
Meradimate (Menthyl anthra	Up to 5	, ,	UV-A II	
Titanium dioxide	2-25	Physical		
Zinc oxide 2-20		Physical		



"Hybrid" formulations

• "Hybrid" formulations employing a combination of chemical absorbers with inorganic particulates may represent a practical compromise.



New active substances

- Pongamol is an active ingredient derived from Karanja Pongamia Extract which enhances UVA protection.
- The Karanja Tree grows in India and Australia.
- Its round brown seeds are rich in oil, which is widely used for personal care, herbal medicine and agriculture.





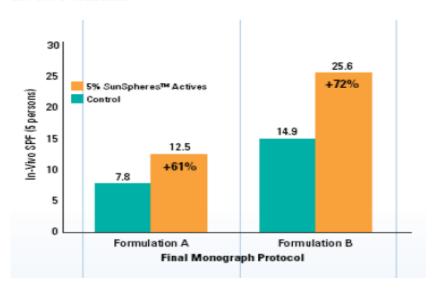


SunSpheresTM SPF Boosters

- SunSpheresTM SPF Booster uses a unique hollow sphere technology to improve the UVB and UVA protection of organic and inorganic sunscreen filters by reflecting UVR.
- Hollow styrene/acrylic copolymer spheres approximately 300-400 nm for enhancing UV protection. They are nearly invisible and cannot be felt.
- When manufactured, the spheres are filled with water, and remain so until the sunscreen is applied to the skin, when the water migrates out to leave a voided sphere in the product film.

SunSpheresTM SPF Boosters

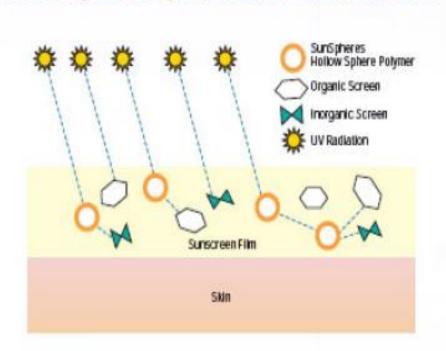
Screening Formulations: In Vivo Results



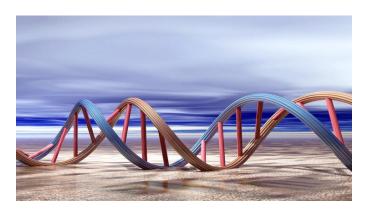


SunSpheresTM SPF Boosters

Model for UV Scattering by the SUNSPHERES Hollow Sphere Polymer Within a Sunscreen Film







فرآورده های جدید ضد آفتاب

- محققین دانشگاه بینگهمپتون آمریکا محصول ضد آفتاب جدیدی را معرفی کردند که ترکیبی از DNAبدست آمده از ماهی آزاد است که پس از قرار گرفتن روی پوست یک لایه شفاف و درخشان تشکیل میدهد.
 - این لایه نازک DNAبه عنوان لایه به اصطلاح فداکار در روی پوست استفاده شود تا از آسیب به سلولهای موجود در پوست جلوگیری شود.
- این فیلمها تا ۹۰ درصد طول موجهای UVB و تا ۲۰ درصد طول موجهای ۹۰ را مسدود کردند و مانع رسیدن آنها به پوست بدن شدند. در واقع این سپرهای DNA قوی تر از کرمهای ضد آفتاب امروزی عمل کردند و جالب تر اینجاست که نور خورشید تک تک مولکولهای DNA این فیلمها را به گونهای تغییر می دهد که به میرور زمان نور بیشتری را جذب می کنند.

Factors influencing the SPF

• Silicones in Sunscreens



- Dimethicone is listed in the FDA monograph for Skin Protectants. Because of their hydrophobicity, provide a water resistant barrier against waterborne contaminants. Better spreading, Recent studies indicate that cyclomethicone and dimethicone may also prevent irritation caused by sunscreen agents.
- Alkyl methicones can enhance the SPF of products containing either organic or inorganic sunscreens, stearyl dimethicone, cetyl dimethicone.



Photostability



- The ability of a molecule to remain intact with irradiation.
- Photostability is potentially a problem with all UV filters.
- This issue been raised specifically with avobenzone.
- Octocrylene and Tinosorb M, S stabilized avobenzone.



The use of sunscreen in childhood



The use of sunscreen in childhood

- In a study demonstrated regular use of sunscreen with an SPF 7.5 for the first 18 years of life could reduce the lifetime incidence of nonmelanoma skin cancers by 78%.
- The 1999 FDA Final Monograph recommends that physicians should be consulted for the use of sunscreen in children under 6 months of age, because their physiologic systems for metabolism and excretion of absorbed agents may not be fully developed.





ضد آفتابهای مناسب کودکان

• از محصولاتی که روی آنهابر چسبهای" بدون مواد تحریک non-irritating "کننده" ایا" بدون عطرمواد خوش بو کننده" fragrance free یا" ضد حساسیت" hypoallergenic



• بدون مواد بنزوفنون، پابا





Sun Protection Factor (SPF)

• Sun Protection Factor (SPF) of a sunscreen represents the effectiveness of the sunscreen in protecting against UVR-induced erythema. The sunscreen is spread on the skin which is then exposed to UV. The SPF is the ratio between the UV dose required or time to produce the minimal erythematous reaction while using sunscreen and the UV dose or time needed to produce the same reaction without the sunscreen, after the application of 2 mg/cm² of the sunscreen product.

• In this equation: $SPF = \frac{MED(PS)}{MED(US)}$

MED(PS): Minimum erythemal dose for protected skin

MED(US): Minimum erythemal dose for unprotected skin



Sunscreen potency assessment by the FDA, based on sun protection factor (SPF)

SPF

- *Minimal* 2 12
- *Moderate* 12 30
- $High \ge 30$



SPF determination



- SPF determination by in vivo methods
- SPF determination by in vitro methods

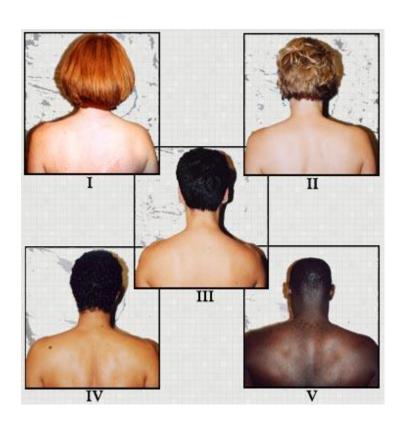
• *In vivo* SPF testing is carried out on the skin of the backs of human volunteers having skin type's I - III. There are some differences between FDA, Australia/New Zealand and COLIPA standards.



Skin type and sunburn and tanning history

- I. Always burns easily; never tans.
- II. Burns easily; tans minimally.
- III. Burns moderately; tans gradually.
- IV. Burns minimally; always tans well.
- V. Rarely burns; tans profusely.
- VI. Never burns; deeply pigmented







SPF determination according to Australian standard by *in vivo* method

- 10 subjects: male or female without a history of abnormal response to medication and UVR
- No allergies to topically cosmetics.
- Shouldn't take photosensitizing medications.
- Skin type shall be type I III.
- Darker skin are not suitable because of the long time. The results obtained from any skin type are similar, only the exposure times will differ.
- The test site is located on the subject's back without hair. Test sites have a minimum area of 30 cm².

• 3 Days:

- First day the MEDUPS is determined;
- Skin type I, MED or exposure time is probably ≤9 sec.
- Skin type II is ≥ 9 seconds and ≤ 13 sec.
- Skin type III is ≥ 14 seconds.
- The day after, 16-24 h after exposure MED shall be observed.
- The observer shall select the subsite estimated to be the first one to show a minimal redness perceptible to the eye, when corrected for normal vision.
- The test site shall be divided into at least 5 subsites to avoid overlap of radiation.
- The product and reference applied 2.0 ± 0.1 mg/cm². The product has to spread with uniform thickness with finger-stall.



- Dry for 15 min.
- Each subsite exposes to controlled amounts of simulated sunlight using a solar simulator. From one to the next, the exposure time should increase by a constant ratio.
- If the estimated SPF is less than 25, increments between subsequent exposures will be not greater than 1.25 times and for estimated SPF more than 25 this will be 1.1 times.
- For example if the MED of a person is 6 seconds and the estimated SPF is 15, the exposure time is 57, 72, 90, 112 and 140 sec.
- In third day: MED will observe.
- The FDA Homosalate Standard (SPF= 4 5) and P3 Standard with SPF (12.5 18.5) is used as references.

The MED observed 20 h after UV exposure from UV source of solar simulator to a subject with the skin type II. The forth erythema from right is MED.





Adverse effects of sunscreens

- The most common skin reaction with sunscreen is irritation, which may include an itchy rash that may lead to eczema and pruritus.
- It may cause a non-allergic inflammatory response that is frequently observed in the eye area. Allergic reactions have been observed and more frequently with perfumes, preservatives and other ingredients.
- PABA and its derivatives, benzophenone, avonenzone and fragrances are among the most allergenic ingredients in sunscreens.
- Systemic absorption of some chemical sunscreens like benzophenone-3 (oxybenzone) after topical application to human has recently reported.
- Physical sunscreens, generally do not cause skin reactions



Adverse effects of sunscreens

Eye irritation

- Stinging of the eyes is a common side effect experienced after applying a sunscreen. This is most commonly related to irritation of the eyes from the fumes and some chemicals of the preparation.
- People who encounter this problem should change to a different sunscreen (preferably a physical sunscreen).
- Water-resistant sunscreens tend to be less runny, and are recommended for the area around the eyes.



Sun protection

Protect the Lips

• A sunscreen should be used on the lips. Tumors on the lips are more common in men than in women. The difference was attributed to the widespread use of lipstick by women. The lipstick acts as a filter for the sun's rays because of the dyes it contains, which function as a physical sunscreen and prevent penetration of the rays to the skin.

Protect the Neck

• It would be advisable to wear clothing that covers the neck and the upper chest. Excessive sun exposure to these areas causes characteristic features of sun damage with wrinkling.

Common Irritating Ingredients

Alcohol	Lanolin & Derivatives
Fragrances	Some essential oils
Preservatives (Parabens, imidazolidinyl Urea,	PG and PEG
Colors and Pigments	TEA
Tocopheryl acetate Capric and Caprilic acid	Mineral oils and PAH in vaseline cocamide DEA



Comedogenic Ingredients

5	4
Isopropyl isostearate	Cetearyl alcohol
Isopropyl myristate Isopropyl Palmitate Laureth-4 Myristyl myristate	Cocoa butter Coconut oil
Oleth 3 Agea extract SLS Wheat germ oil	Lanolin drivatives Octyl Palmitate



PA system

- The Protection Grade of UVA (PA).
- According to the Japan Cosmetic Industry
 Association PA+ corresponds to a UVA protection
 factor between two and four, PA++ between four and
 eight, and PA+++ more than eight.



Evaluation of UVA radiation

- Boots star rating system (UK):
- *In vitro* measurement of the ratio of a product's UVA (320-400 nm) absorbance over its UVB (290-320 nm) absorbance is used to calculate its Boots star rating.
- Products with better UVA absorbance have a higher Boots star rating.



BOOTS STAR RATING SYSTEM

The Boots guideline for star rating

The Boots star rating is based on the average of UVA/UVB ratio. A different rating is given to a range of values as shown below. Rating levels differ for different wavelength sampling intervals.

Mean UVA/UVB Ratio	Star Rating Category	Star Rating Designation
0 to 0.2	-	No claim
0.21 to 0.4	*	Minimum
0.41 to 0.6	**	Moderate
0.61 to 0.8	***	Good
0.81 to 0.9	***	Superior
0.91 and above	***	Ultra



Evaluation of UVA radiation

- You may see the phrases 'multi spectrum', 'broad spectrum' or 'UVA/UVB protection' on sunscreen labels, and these all indicate that some UVA protection is provided.
- However, because there is no consensus on how much protection these terms indicate, such phrases may not be entirely meaningful.

How to apply the sunscreen

- Sunscreen, daily and all seasons to all over the skin, 15 30 min before going outdoors, even on cloudy days (up to 80 % of UVR still reach the earth's surface).
- Reapply every 2 or 3 h, or after swimming, sweating and rubbing or towel. Reapply all sunscreens even if the label says waterproof (3 to 4 h).
- Sunscreen reapplication can maintenance an adequate thickness. It does not extend the period of protection or double the SPF.
- Consumers apply between 0.5 and 1.5 mg/cm², then an effective SPF is between 20% and 50% of expected from the product label.
- Sunscreen needs to be applied liberally and generously.
- Apply even at home.



- سطح پوست صورت ۶۰۰ سانتی متر مربع
- نیم گرم برای پوشاندن صورت معادل یک بند انگشت

2FTU: 1g •





The thickness of a sunscreen

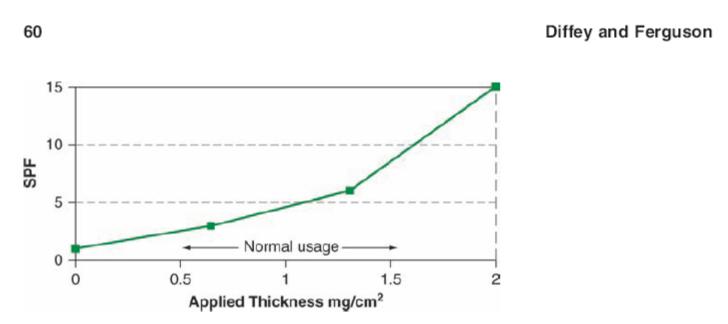


Figure 2 The variation of delivered SPF with application thickness for a sunscreen of nominal SPF 15 (41). *Abbreviation*: SPF, sun protection factor.



How to apply the sunscreen

- The accepted recommendation is to apply the sunscreen 15 to 30 minutes before going out into the sun (so that it has time to penetrate into the keratinous layer of the skin) and then once again, 15 to 30 minutes following exposure to the sun.
- It has been shown that most people use inadequate quantities of sunscreen and apply it unevenly, leaving unprotected areas of skin. As the surface of the skin is nonuniform, applying two coats.
- Apply chemical sunscreens that need to be absorbed first, barriers (like moisturizers, makeup, and physical block sunscreens) last.

Note: No sunscreen is 100% effective. The term "sunblock" is prohibited.



كرمهاى BB و CC

- Blemish Balmیا بالم لک است
- کرم بی بی علاوه بر خاصیت پوشانندگی (مثل یک کرم پودر سبک) حاوی SPFو آنتی اکسیدان نیز هستند و بدینوسیله مراقبت از پوست را نیز انجام میدهند. این محصولات از کرم پودر سبکتر بوده و نسبت به مرطوب کنندههای رنگی سنگین ترند.

کرمهای BB و CC

- کرمهای color corrective CCبه معنای تصحیح کننده رنگ است، درست همان مزایایی را که کرمهای بی بی دارند، ارائه میدهند با این تفاوت که پوشش این محصولات قوی تر و بیشتر است. از بی بی کرمها سبکتر هستند.
- بدین معنا که بیشتر هدف آنها پوشش لکه های قرمز، زرد و خالهای ریز و لکه ها و نواقص رنگی میپردازند.





ضد آفتابهای چند منظوره

- برخی ضد آفتابها چند منظوره ضد آفتاب با عصاره شیرین بیان (گلبریدین)
- کرم ضد آفتاب با مواد ضد چروک و یا مواد ضد آکنه











Water Resistance Property

• A water-resistant product maintains its SPF (loss less than 25%) level after 40 min of water immersion, and a very water-resistant (waterproof) product maintains the SPF (loss less than 25%) level after 80 min of water immersion.





