

## Review of Retinoid Biology: Part 2

Mariana Phillips, MD. (Updated July 2015\*)

Photobiology	
UVA	UVA1: 340-400 nm UVA2: 315-340 nm Responsible for photoaging; >95% of sun's UV radiation reaching Earth's surface Penetrates glass Predominately UVA sunblocks: anthranilates, oxybenzone, avobenzone
UVB	UVB: 290-315 nm Most important in photocarcinogenesis; wavelengths most responsible for sunburn Vitamin D synthesis: 7-dehydrocholesterol pre-vitamin D3 Predominately UVB sunblocks: PABA, cinnamates, salicylates, Padimate O
UVC	UVC: 200-290 nm Absorbed by ozone in the atmosphere
Acute tanning	"Immediate pigment darkening" due to oxidation and redistribution of existing melanin Most prominent with UVA
Delayed tanning	Peaks 3 days after light exposure and may last 10 days, primarily due to UVB Increased number and size of melanocytes, increased tyrosinase activity (melanin synthesis), and increased melanocyte dendrites
Sunburn	UVB
Thymidine dimer photoproducts	Occurs in DNA following excitation with short wave UVB "UV signature mutations" Results in transition mutations during DNA transcription Occurs due to covalent linkage between two pyrimidines Most common: T-T > C-T > T-C > C-C
Pyrimidine- pyrimidone photoproducts	Same as above with thymidine dimers Most common: T-C > C-C and T-T
8-hydroxyguanosine photoproduct	Characteristic DNA damage generated by UVA Generates G:C to T:A transversion mutations during transcription
Sunless Tanning	Dihydroxyacetone binds stratum corneum and produces tanned appearance Provides SPF 2-3
Sunscreens	
SPF (Sun Protection Factor)	Measures protection in the UVB spectrum, max labeling allowed by FDA is 50+
Water resistant	Maintains SPF while swimming/sweating: 40 min and 80 min labeling permitted only
Waterproof/Sweatproof	No longer permitted labeling per the FDA
Timing and amount	Apply sunscreen 20 minutes before sun exposure 1 oz of sunscreen to cover entire body (2 mg/ cm <sup>2</sup> )
Physical (inorganic) sunscreens	Titanium dioxide (Ti) and Zinc oxide (Zn) Reflects sunlight Low incidence of contact sensitivity UVA and UVB protection (Zn broader than Ti)
Oxybenzone (AKA: benzophenone)	Broad spectrum UVA & UVB, photo-stabilizer in Helioplex (stabilizes Avobenzone) #1 sunscreen used, but controversy over hormonal and photoallergenic effects Most common cause of sunscreen allergy or photoallergy
Avobenzone (trade name: Parsol 1789)	UVA protection; derivative of dibenzoylmethane; in Helioplex (Avobenzone + Oxybenzone); Photo-stability unreliable when combined with cinnamates
Cinnamates (trade name: Parsol MCX)	UVB protection Cross-reacts with Balsam of Peru Frequent cause of allergic reactions
Octocrylene	Photo-stabilizer
Ecamsule and Drometrizole trisiloxane (trade name: Mexoryl)	UVA->UVB absorber (290-390 nm) Photo-stabilizer
Cross reactivity with PABA	Sulfa drugs, Benzocaine (ester anesthetic), Paraphenylenediamine, Azo/Aniline dyes



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Cosmeceuticals	
Vitamin C	L-ascorbic acid is the predominant antioxidant in the skin Essential for collagen biosynthesis, a co-factor for collagen transcription Increases collagen I and III mRNAs Increases tissue inhibitors of matrix metalloproteinases (MMPs) Reduces solar elastosis Inhibits tyrosinase, thus decreasing pigment synthesis Improves epidermal barrier function by stimulating ceramide production
Vitamin E (tocopherol)	Body's major lipid phase antioxidant Protects against cytotoxic effects of UVB Major function is to prevent lipid peroxidation Inhibits melanogenesis and has activity against tyrosinase Inhibits thymidine dimer formation Topical use may lead to allergic contact dermatitis (#2 allergen in sunscreens)
Niacinamide (nicotinamide)	Important in energy related cellular metabolic functions (increases NADPH) Increases synthesis of collagen, filaggrin, and keratin Improves epidermal barrier function by stimulating ceramide production Decreases pigmentation by suppressing melanosome transfer to keratinocytes
Retinoids	Thickens the nucleated epidermis, promotes differentiation, increased keratohyaline granules, Odland body secretion, increased filaggrin Thins the stratum corneum Increases collagen I fibers in the dermis Increases inhibitors of tissue MMPs Increases production of hyaluronic acid and fibronectin
Hydroxy-acids	Keratolytic Increases type I procollagen mRNA Stimulates TGF-beta expression due to acidic pH
Ferulic acid (N <sup>6</sup> -fufuryladenine)	AKA: kinetin Plant growth factor Acts as an antioxidant, retards aging of fibroblasts in culture
Soy	Most plentiful isoflavones in soy: genistein, daidzein May have collagen stimulating effects Reduces pigmentation by inhibition of tyrosinase kinase Potent antioxidant and inhibitor of UV induced immunosuppression
Alpha-lipoic acid (ALA)	Potent lipid and water soluble antioxidant Strong intracellular free radical scavenging abilities
Coenzyme Q10	AKA: ubiquinone-10, serves as a coenzyme for energy production within cells Antioxidant that protects cells from UVA damage Reduces expression of UVA induced MMPs
Copper peptides	Known cofactors in antioxidant reactions Used to promote healing in diabetic foot ulcers, surgical wounds, and post-follicular unit hair transplants Stimulates glycosaminoglycan synthesis
Camellia sinensis (green tea)	Polyphenols (antioxidants) that remove reactive oxygen species (created by UVR)
Resveratrol (grapes, nuts)	Antioxidant, reduces UVB-induced edema
Silybum marianum (milk thistle)	Flavonoid, antioxidant
Curcuma longa (turmeric)	Anti-inflammatory, antioxidant

### References:

1. Bologna J, Jorizzo J, Rapini R, et al. *Dermatology*. Elsevier Limited; 2012.
2. Kockaert M and Neumann, M. Skin Rejuvenation: Systemic and topical drugs for aging skin. *Drugs in Dermatol* 2003; 2:435-441.
3. Pinnell, SR. Cutaneous photodamage, oxidative stress, and topical antioxidant protection. *J Am Acad Dermatol*;48:1-19.
4. Sadick, NS. Cosmeceuticals: Their role in dermatology practice. *J Drugs in Dermatol* 2003; 2:529-537.
5. Wolverton, SE. *Comprehensive Dermatologic Drug Therapy*, 2nd edition. W.B. Saunders Company; 2007.

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