



## DEMANDING SPF (SUN PROTECTION FACTOR): IN OUR DAY TO DAY GLOBAL WORMING LIFE

\*<sup>1</sup>Tanima Debnath Sarkar and <sup>2</sup>G. John Anbumani

<sup>1</sup>Department of Zoology of Annamalai University, <sup>2</sup>Department of Biochemistry and Biotechnology of Annamalai University, Annamalai Nagar-608002, Tamilnadu, India.

\*Corresponding Author: Tanima Debnath Sarkar

Department of Zoology of Annamalai University, Annamalai Nagar-608002, Tamilnadu, India.

Article Received on 12/05/2023

Article Revised on 01/06/2023

Article Accepted on 22/06/2023

### ABSTRACT

Scattering of Sunlight effectively or to absorb the erythema part of the sun's radiation is the main purpose of using sunscreen. Avobenzene, octisalate, octocrylene, homosalate etc. are chemical ingredients and zinc oxide, titanium are the mineral ingredients for protecting ultra violet (UV) radiation by physically reflecting or scattering the incident photons which is protecting of skin. Sunscreen and sun blocker are totally different because sunscreen absorbed the UV ray where as sun blocker literally blocks UV rays by forming of physical shield. But both are protected our skin from UV ray. Sunburn, leathery skin, wrinkles, skin cancer, skin sensitivity is protected by sunscreen because presence of tetracyclines, sulfa drugs, phenothiazines etc like chlorpromazine. Sunscreen is found in different format such as lotion, gel, spray, cream, stick, lip bum etc. Increasing of Ca, Mg, Na: lignosulfonate help to improvement quality value of SPF at tengkawang butter. Shoot up of SPF value has a friendly relationship with the chromophore compounds in lignin. Recreational sunbathing and artificial tanning are caused for risk factors of skin damage due to electromagnetic spectrum of UV. Pharmacological actions of sunscreen agents are broadly discuss in this review article.

**KEYWORDS:** Erythema, avobenzene, octisalate, octocrylene, homosalate, tetracycline, tengkawang butter.

**History of Sunscreen:** Using of sunscreen is a common factor from ancient time. Searching from history, we came to know that extract of rice bran, jasmine and lupine had applied as a sunscreen by Egyptians from 4000BC. Lupine lighten of the skin as a sun blocker, rice absorbs UV light where as jasmine repair DNA.<sup>[1]</sup> On 500BC In 'Charaka Samhita', an ancient Indian medical literature, the pushpanjan (Zinc oxide) was discovered which is employed in physical sunscreens nowadays.<sup>[2]</sup> In 1808, Johan Wilhelm Ritter first discovered UV radiation.<sup>[3]</sup> In 1944 Benjamin Green, a pharmacist, developed Coppertone suntan lotion, a more consumer-friendly formulation.<sup>[4]</sup> In 2018 Hawaii, octinoxate and oxybenzone were banned due to coral bleaching as most of the sunscreens had these two chemicals as an active ingredient.<sup>[5]</sup> In 2019, Matta and colleagues studied the plasma concentrations of four commonly available sunscreens (avobenzene, oxybenzone, octocrylene, and ecamsule) that exceeded the level established by the FDA.<sup>[6]</sup> In 2019 Sunburn alert stickers came into use which indicates when it is time to re-apply the sunscreen.<sup>[7]</sup> In 2020 Colourescience brush-on shield, the only powdered sunscreen, recommended by the skin cancer foundation for active use. It was recommended to use alone or over make-up with one application alone.<sup>[8]</sup>

**UV radiation:** Spectrum of ultra violet ray spread 40-400nm which is divided into Vacuum UV, Far UV, UVC, UVB and UVA. The amount of exposure to UVA usually remains constant, whereas UVB exposure occurs more in the summer.<sup>[9]</sup> The formation of matrix metalloproteinase (MMPs) enzymes which is regulates UVA up that degrade the matrix proteins elastin and collagen. If it is prevented for use then wrinkling will be increase. Both acute and chronic changes are occurred due to radiation of damage skins which is penetrating into the layer of skin and producing reactive oxygen. As a result induce polymorphous light eruptions (PMLE) insensitive skins.<sup>[10]</sup> Nuclear and mitochondrial DNA weaken, gene mutation and skin cancer, dysregulation of enzymatic chain reactions, immune suppression, lipid peroxidation or lipid membrane damage and photo allergic and photo toxic effects are occurred due to the radiation of UVA which is damage of antigen presenting cell activity (APC) of the epidermal cells. UVB radiation also impairs acute changes of pigmentation and sunburn and chronic changes of immune suppression and photocarcinogenesis. Sunburn is common in the United States with 34.4 percent of adults affected.<sup>[11]</sup> In Sweden, children are frequently affected, and use of sunscreen among children has been found to be protective.<sup>[12]</sup>

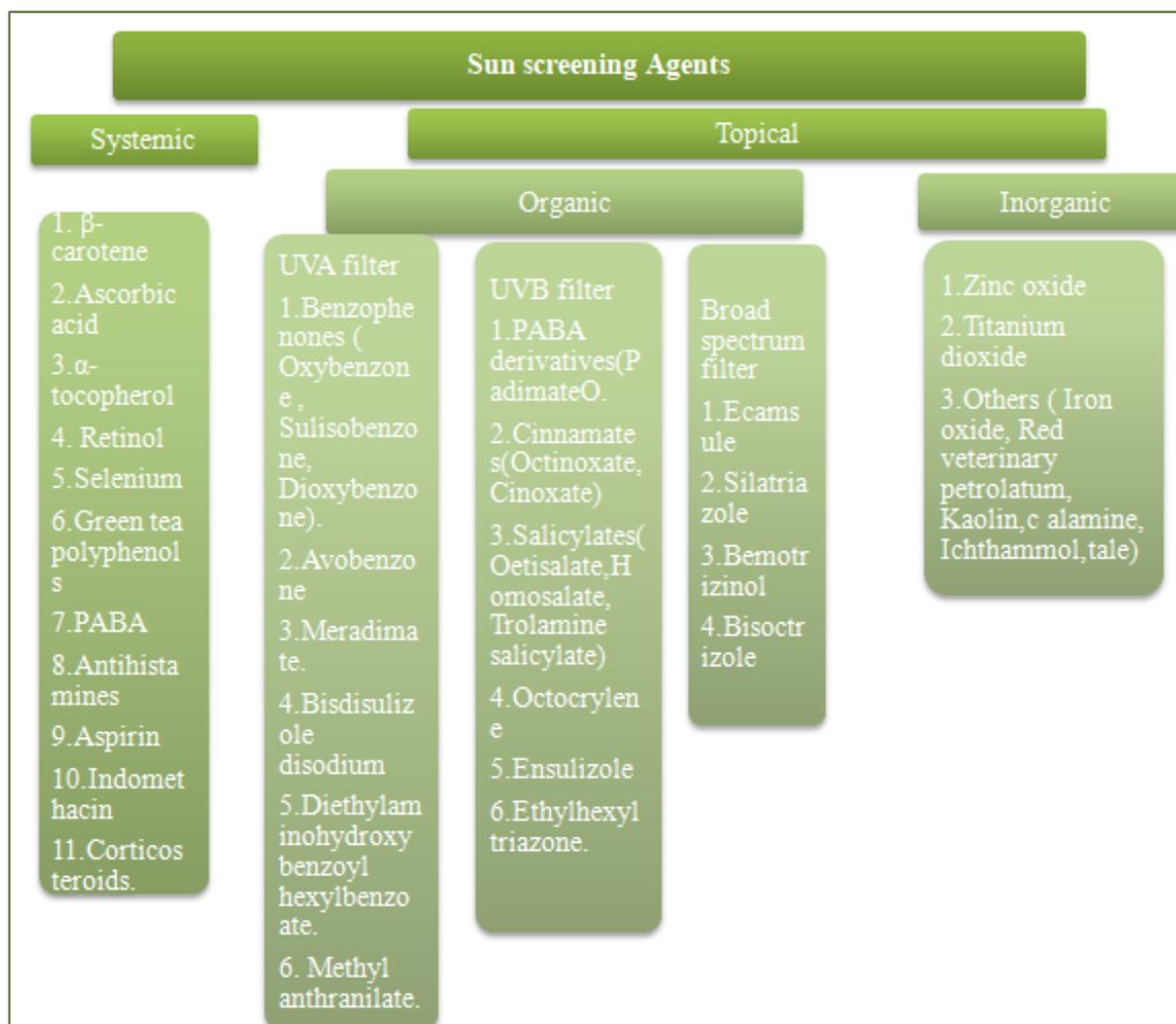


Figure 1:- Classification of sun screening agents.

**In modern age:** Among cosmic ray, gamma ray, X-ray, micro waves, radio waves, UV ray only UV ray does not filtered out. Due to different UV wavelength causing apart sun filters the components of sunscreen work in the same pathway. Active ingredient which is filtered

the sun is generally 20% and formulation of stabilizers is 55% are found in sunscreen. Benzene ring compounds such as avobenzone, homosalate, octinoxate like components which are using agent of sunscreen absorb the photon, and convert light energy to heat energy.

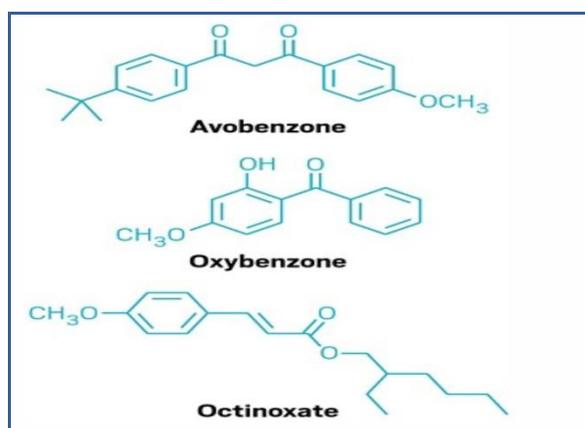


Figure:-2- Main benzene compounds used as a sunscreen.

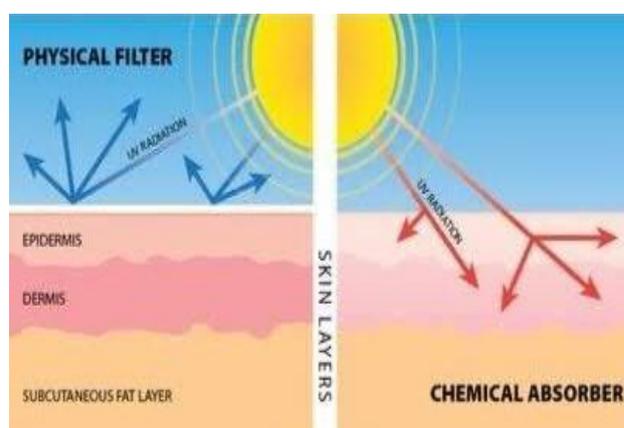


Figure:-3- Both pathway physical filters and chemical absorber is working into our skin.

Due to flavor of PABA (4-aminobenzoic acid or p-aminobenzoic acid) people sometimes developed a skin allergy. Sun screen base must be stable and spread easily and evenly on the skin. A 2021 law in Hawaii bans where oxybenzone and octinoxate are using in as a coral reef sunscreen because of bleaching components causes diseases. Maximum time water is used as a solvent sometimes oil may be used as a solvent in the component of sunscreen. Using phenoxyethanol and tocopherol help for preservation. Also emulsifiers, chelating agents, pH – balancing agents, antioxidants also found as an ingredients of sunscreen. Sometimes extra reagent is used for protected from pollution or blue light.

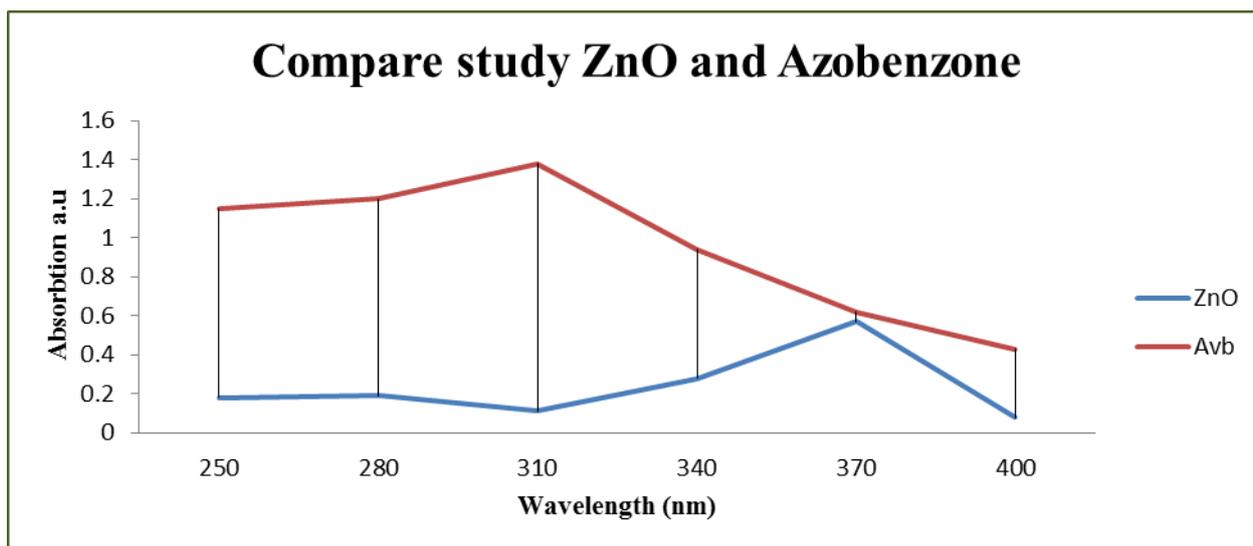
The efficiency of sunscreens in protecting the skin from the dangers of the sun is expressed in terms of the sun protection value (SPF), which is defined as the UV energy needed to produce a minimum erythema dose (MED) on protected skin divided by the UV energy needed to produce MED on unprotected skin.<sup>[13]</sup> MED was defined as the shortest time for the onset of erythema due to UV radiation.<sup>[14, 15]</sup> Titanium dioxide (TiO<sub>2</sub>) which acts as a physical blocker, recently announce by the International Agency for Research on Cancer (IARC), which states that this substance is a carcinogenic group that can trigger cancer in the body.<sup>[16]</sup> Lycopene, phenolic, cinnamic acid and myristic acid are main ingredients of natural SPF's. These natural ingredients are found e tomatoes, green tea, shea butter and jojoba oil.<sup>[17]</sup> Additionally extraction from Shea nuts, Tengkawang nuts, Cocoa butter is the good sources of

SPF. Lignin, a natural adhesive plant component, presence of phenolic compound to bond with ketones and intermolecular oxygen to protect against UV rays. Kaolin, talc, zinc oxide (ZnO), calcium carbonate, and magnesium oxide are physical blockers also.

**Mechanism of action:** Depending upon action of blocking, reflecting and scattering of sunlight the composition and mechanism of sunscreen are varying. Physical blockers reflect or scatter light and chemical blockers absorb high energy UV rays. Bemotrizinol, avobenzone, bisoctizole, benzophenone-3 (BZ3, oxybenzone), and octocrylene, are broad-spectrum agents and Ecamsule (terephthalydene dicamphor sulphonic acid), dometrizole trisiloxane, bemotrizinol, and bisoctizole are considered organic UVA sunscreens agents also.

Researchers are postulating that the generation of sunlight-induced free radicals causes changes in skin; use of sunscreens reduces these free radicals on the skin, suggesting the antioxidant property.<sup>[18]</sup> Broad-spectrum agents have been found to prevent UVA radiation-induced gene expression in vitro in reconstructed skin and in human skin in vivo.<sup>[19]</sup>

There are two keys for using Zinc is better than avobenzone. Because Zinc can UV spectrum coverage and photostability is proven by FDA monograph.<sup>[20,21,22,23]</sup>



**Figure:4-** The Zinc curve is greater than the area under the avobenzone curve which is indicating Zn is better UV protection.

Photostability means how long sunscreen will act after using. Avobenzone is not inherently photostable. It needs additional chemical for photostability. Some source of news it may concluded that (1) A 2008 study, 96.8% of 2,517 urine samples prove all common sunscreens penetrated the stratum corneum but only oxybenzone.<sup>[21]</sup> (2) A 2001 German study, pregnant or breastfeeding

woman should not use oxybenzone containing sunscreen.<sup>[22]</sup> Initial research suggested that some form of toxicity might be present as a result of oxybenzone absorption.<sup>[21,22]</sup> A 2001 UK study found oxybenzone to have a much higher rate of reactions compared with other UV protectors.<sup>[23]</sup>

The constructions of visible light controlled molecular systems tetra-ortho-fluoro azobenzenes are a class of photo switches which can be used to achieve spatio-temporal control over the properties of chosen biocompatibility. A photochemical property of tetra fluoro azobenzene has photochromic system such as high photostationary state distribution and long half lives in both organic and water soluble whose functionization trehalose group to enable the uptake of the photo switch in microbacteria which isolated total lipid extract, attachment handles and water solubilizing groups, has a chemical properties.

Molecular photoswitches are powerful tools to both manipulate and study biological systems.<sup>[24,25,26,27,28]</sup> Among those, azobenzenes are the most widely used photochromic molecules, in particular due to the large change in geometry and polarity they undergo upon photoswitching.<sup>[28,29,30,31,32]</sup> Using UV light for photoswitching of the stable trans isomer to the metastable cis isomer is one of the disadvantage of the classical azobenzene photochromes. UV light is not optimal for biological applications since it causes damage to living cells and has a low penetration

depth.<sup>[33,34,35,36]</sup> After a long adaptation the azobenzene switch with visible light by separating the  $n-\pi^*$  absorption bands of the two isomers.<sup>[37,38,39,40,41]</sup> Furthermore, the introduction of substituents in all orthopositions to the azo-bond, such as methoxy, chloro, or fluoro groups, results in  $n-\pi^*$  band separation.<sup>[37,40,42,43]</sup> Both for the tetra-ortho-methoxy<sup>[37,40]</sup> and the tetra-ortho-chloro system.<sup>[38,44,45]</sup> the band shift is caused by geometry distortion (nonplanar conformation) of the trans isomer.

Due to the favorable photochemical properties of tetra-ortho-fluoro azobenzenes, it comes as no surprise that this system has been most widely applied for various biological targets, both as freely diffusing effectors<sup>[46,47,48,49,50]</sup>, as well as through incorporation into proteins.<sup>[51,52,53]</sup> Bioactive molecules containing the fluorinated azobenzene were used to reversibly modulate the circadian rhythm<sup>[54]</sup>, regulate the activity of the carbonic anhydrase enzyme *in vivo*<sup>[49]</sup>, control the activity of muscarinic acetylcholine receptors<sup>[48]</sup>, photoregulate transmembrane transport<sup>[47]</sup>, as well as to intercalate DNA.<sup>[46]</sup>

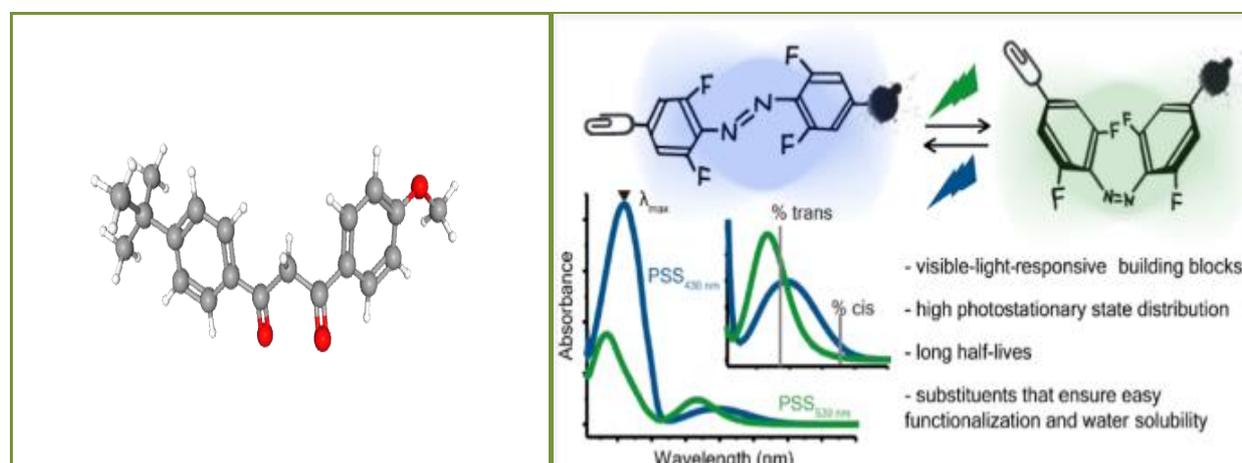


Figure-5: Molecular docking of Avobenzene.

It was reported by the Hecht group that the introduction of an electron-donating group to the ortho-fluorinated azobenzene in the para positions negatively influenced the photochemical properties as the  $n-\pi^*$  band separation was smaller when compared to the unsubstituted parent azobenzene.<sup>[55,56]</sup> However, ortho-fluorination lowers the energy of the  $n$ -orbital only for the cis isomer, which causes the separation of the two  $n-\pi^*$  transitions. Larger overlap of the  $n-\pi^*$  bands of each isomer results in a lower photostationary state distribution (PSD) upon irradiation. Electron-withdrawing groups (EWGs) on the other hand have the opposite effect as they help to lower the energy of the trans isomer, thus resulting in a larger band separation.<sup>[55,56]</sup> Often, fluorinated azobenzenes feature impressively long half-lives, likely due to the stabilization effect of the EWG fluoro substituents in the cis isomer.<sup>[55,56]</sup> From here, come to know the following points:- (1)Effect of Functional Substituents on

Photochemical Properties.<sup>[57]</sup> (2)Building Blocks with Two Functional Moieties.<sup>[57]</sup> (3)Photochemical Properties in Water.<sup>[57]</sup> (4) Incorporation of Azobenzene-Modified Trehalose in Mycobacteria.<sup>[57]</sup>

**Factors Determining Efficacy:** The contribute to effectiveness of sunscreen factors are determining SPF and substantivity. UVB protection is measured by a product's SPF, which theoretically indicates that products with high SPFs provide more protection against hazardous effects of sunlight than those with low SPFs.<sup>[58]</sup>

SPF = MED of protected skin/MED of unprotected skin [MED = minimal erythemal dose].

[If a product with SPF 50 is applied, it will protect the skin until it is exposed to 50 times more UVB radiation than that is required to burn the unprotected skin.]

There was a reduction in SPF of 38 and 41 percent after four hours and of 55 and 58 percent after eight hours of application of organic and inorganic sunscreen, respectively.<sup>[59]</sup> Immediate pigment darkening response is calculated as the dose of UVA required to produce the effect with the sunscening agent to that produced without an agent.<sup>[60]</sup>

**Pharmacokinetics:** It was observed that lipid microparticles loaded with ethylhexyl methoxycinnamate (EHMC), which filters UVB, and butyl methoxydibenzoylmethane (BMDBM), which filters UVA, had reduced skin penetration, thus preserving the UV filter efficacy and limiting potential toxicological risks.<sup>[61]</sup> Gonzalez et al<sup>[62]</sup> studied the percutaneous absorption of BZ-3 after repeated whole-body applications, with and without UV irradiation in 25 volunteers. They observed that large amounts of BZ-3 is absorbed, accumulated in the body, and excreted, even after five days after the last application.<sup>[62]</sup> In another study, after 48 hours, the average amount of BZ-3 excreted in urine was 11mg (median=9.8mg). In some volunteers, BZ-3 was excreted even after 48 hours. This study showed that BZ-3 undergoes conjugation and converts to a water-soluble compound. The age at which liver attains maturity and is able to metabolize these chemicals and conjugate is unknown. Therefore, it is recommended that physical filters (i.e., zinc oxide, titanium dioxide, ferrous oxide) be used in children.<sup>[63]</sup> BZ-3 is FDA approved for use in children above six months of age. Janjua et al<sup>[64]</sup> studied the absorption of sunscreens BZ-3, octyl-methoxycinnamate (OMC), and 3-(4-methylbenzylidene) camphor (4-MBC) from topical application and their effects on the endogenous reproductive hormones in 32 healthy volunteers. After two-week, whole-body application, there was no change in follicle-stimulating hormone (FSH) levels or luteinizing hormone (LH) levels, but there was a minor difference in testosterone levels. In men, a minor difference in serum estradiol and inhibin B levels was observed.<sup>[64]</sup>

Sunscreens are generally available in cream, gel, lotion, ointments, pastes, oils, butters, sticks, and sprays form. Spray or gel-based sunscreens are preferred in oily skin and acne. New sunscreens with microfine particles are found to be safe and effective in patients with acne and rosacea. Sunscreen filters are also added to hair care products, such as shampoo, to minimize sun damage to hair.<sup>[65]</sup>

## CONCLUSION

A significant protection to fibroblast cells against UVA radiation has shown bacterial derived melanin. Benefit of the use sunscreen to minimize occurrence of skin cancer in people with fair skin. New technologies enhancing sunscreen product designing and efficacy which embraced as regulatory authorities reassign the classification of sunscreen from cosmetics to therapeutic drugs.

## REFERENCES

1. Aldahan AS, Shah VV, Mlacker S, Nouri K. The history of sunscreen. *JAMA Dermatol*, 2015; 151: 1316.
2. Craddock PT. 2000 Years of Zinc and Brass. British Museum, 1998.
3. Urbach F. The historical aspects of sunscreens. *J Photochem Photobiol B*, 2001; 64: 99–104.
4. Coppertone Owes its Success to a Pharmacist. *Pharmacy Times*. Accessed January 19, 2022. <https://www.pharmacytimes.com/view/coppertone-owes-its-success-to-a-pharmacist>.
5. Downs CA, Kramarsky-Winter E, Segal R, Fauth J, Knutson S, Bronstein O, et al. Toxicopathological effects of the sunscreen UV filter, Oxybenzone (Benzophenone-3), on coral planulae and cultured Primary cells and its environmental contamination in Hawaii and the U.S. Virgin Islands. *Arch Environ Contam Toxicol*, 2016; 70: 265–88.
6. Matta MK, Zusterzeel R, Pilli NR, Patel V, Volpe DA, Florian J, et al. Effect of sunscreen application under maximal use conditions on plasma concentration of sunscreen active ingredients: A randomized clinical trial. *JAMA*, 2019; 321: 2082–91.
7. Sakkaravarthi, Vinupriya. "History of sunscreen." *Cosmoderma 2* (2022).
8. Sunforgettable® Total Protection™ Brush-On Shield SPF 50 | Colorescience. Accessed January 19, 2022. <https://www.colorescience.com/products/sunforgettable-total-protection-brush-on-shield-spf-5>.
9. DeBuys HV, Levy SB, Murray JC, et al. Modern approaches to photoprotection. *Dermatol Clin*, 2000; 18: 577–590.
10. Ortel B, Tanew A, Wolff K, Hönigsmann H. Polymorphous light eruption: action spectrum and photoprotection. *J Am Acad Dermatol*, 1986; 14: 748–753.
11. Buller DB, Cokkinides V, Hall HI, et al. Prevalence of sunburn, sun protection, and indoor tanning behaviors among Americans: review from national surveys and case studies of 3 states. *J Am Acad Dermatol*, 2011; 65: S114–S123.
12. Rodvall YE, Wahlgren CF, Ullén HT, Wiklund KE. Factors related to being sunburnt in 7-year-old children in Sweden. *Eur J Cancer*, 2010; 46: 566–572.
13. Darmawan, Muhammad Arif, et al. "Natural sunscreen formulation with a high sun protection factor (SPF) from tengkawang butter and lignin." *Industrial Crops and Products*, 2022; 177: 114466.
14. Wolf, R., Wolf, D., Morganti, P., Ruocco, V., 2001. Sunscreens. *Clin. Dermatol*, 19: 452–459.
15. Wood, C., Murphy, E., 2000. Sunscreen efficacy: a burning issue. *Glob. Cosmet. Ind*, 167: 38–44.
16. IARC 2009. Identification of research needs to resolve the carcinogenicity of high priority IARC carcinogens In: *CANCER*, I. A. F. R. O. (ed.). Lyon,

- France: International Agency for Research on Cancer.
17. Goswami, P.K., Samant, M., Srivastava, R., 2013. Natural sunscreen agents: a review. *Sch. Acad. J. Pharm*, 2: 458–463.
  18. Meinke MC, Haag SF, Schanzer S, et al. Radical protection by sunscreens in the infrared spectral range. *Photochem Photobiol*, 2011; 87: 452–456.
  19. Marionnet C, Grether-Beck S, Seité S, et al. A broad-spectrum sunscreen prevents UVA radiation-induced gene expression in reconstructed skin in vitro and in human skin in vivo. *Exp Dermatol*, 2011; 20: 477–482.
  20. Zano 10 and Xperse, excellent broad-band UV protection from mineral UV filters in personal care and sunscreen formulations, Measurements done in O/W emulsion to 4MEDs (5.7cm<sup>2</sup> TUV per MED), McBride, pg 16, 7/26/2010.
  21. Concentrations of Sunscreen Agent Benzophenone-3 in Residents of the United States: National Health and Nutrition Examination Survey 2003-2004, Antonio M. Calafat; Lee-Yang Wong; Xiaoyun Ye; John A. Reidy; Larry L. Needham, Posted: 08/11/2008; *Environmental Health Perspectives*. 2008; 116(7): 893-897. 2008 National Institute of Environmental Health Sciences.
  22. Nachweis von UV-Filtersubstanzen in Muttermilch = Detection of sunscreen agents in human breast milk, Hany, J., Nagel, R., Henrich-Heine- Univ. Dusseldorf, medizinisches Inst. Umwelthyg., 40225 Dusseldorf Allemagne.
  23. Photoallergic contact dermatitis is uncommon., Darvay A, White IR, Rycroft RJ, Jones AB, Hawk JL, McFadden JP., Department of Environmental Dermatology, St. John's Institute of Dermatology, St. Thomas' Hospital, Lambeth Palace Road, London SE1 7EH, UK.
  24. Szymanski, W.; Beierle, J. M.; Kistemaker, H. A. V.; Velema, W. A.; Feringa, B. L. Reversible Photocontrol of Biological Systems by the Incorporation of Molecular Photoswitches. *Chem. Rev*, 2013; 113: 6114–78.
  25. Lerch, M. M.; Hansen, M. J.; Velema, W. A.; Szymanski, W.; Feringa, B. L. Orthogonal Photoswitching in a Multifunctional Molecular System. *Nat. Commun*, 2016; 7: 12054.
  26. Fuchter, M. J. On the Promise of Photopharmacology Using Photoswitches: A Medicinal Chemist's Perspective. *J. Med. Chem*, 2020; 63: 11436–11447.
  27. Hüll, K.; Morstein, J.; Trauner, D. In Vivo Photopharmacology. *Chem. Rev*, 2018; 118: 10710–10747.
  28. Volarić, J.; Szymanski, W.; Simeth, N. A.; Feringa, B. L. Molecular Photoswitches in Aqueous Environments. *Chem. Soc. Rev*, 2021; 50: 12377–12449.
  29. Pianowski, Z. L. Recent Implementations of Molecular Photoswitches into Smart Materials and Biological Systems. *Chemistry*, 2019; 25: 5128–5144.
  30. Beharry, A. A.; Woolley, G. A. Azobenzene Photoswitches for Biomolecules. *Chem. Soc. Rev*, 2011; 40: 4422–4437.
  31. Mart, R. J.; Allemann, R. K. Azobenzene Photocontrol of Peptides and Proteins. *Chem. Commun*, 2016; 52: 12262–12277.
  32. Küllmer, F.; Gregor, L.; Arndt, H.-D. Systematic Modifications of Substitution Patterns for Property Tuning of Photoswitchable Asymmetric Azobenzenes. *Org. Biomol. Chem*, 2022; 20: 4204–4214.
  33. Cheong, W. F.; Prah, S. A.; Welch, A. J. A Review of the Optical Properties of Biological Tissues. *IEEE J. Quantum Electron*, 1990; 26: 2166–2185.
  34. Banerjee, G.; Gupta, N.; Kapoor, A.; Raman, G. UV Induced Bystander Signaling Leading to Apoptosis. *Cancer Lett*, 2005; 223: 275–284.
  35. Kamarajan, P.; Chao, C. C.-K. UV-Induced Apoptosis in Resistant HeLa Cells. *Biosci. Rep*, 2000; 20: 99–108.
  36. Bachelor, M. A.; Bowden, G. T. UVA-Mediated Activation of Signaling Pathways Involved in Skin Tumor Promotion and Progression. *Semin. Cancer Biol*, 2004; 14: 131–138.
  37. Beharry, A. A.; Sadovski, O.; Woolley, G. A. Azobenzene Photoswitching without Ultraviolet Light. *J. Am. Chem. Soc*, 2011; 133: 19684–19687.
  38. Samanta, S.; Beharry, A. A.; Sadovski, O.; McCormick, T. M.; Babalhavaeji, A.; Tropepe, V.; Woolley, G. A. Photoswitching Azo Compounds in Vivo with Red Light. *J. Am. Chem. Soc*, 2013; 135: 9777–9784.
  39. Wang, H.; Bisoyi, H.; Zhang, X.; Hassan, F.; Li, Q. Visible Light-Driven Molecular Switches and Motors: Recent Developments and Applications. *Chem.-Eur. J*, 2021; 28: No. e202103906.
  40. Dong, M.; Babalhavaeji, A.; Samanta, S.; Beharry, A. A.; Woolley, G. A. Red-Shifting Azobenzene Photoswitches for in Vivo Use. *Acc. Chem. Res*, 2015; 48: 2662–2670.
  41. Wegener, M.; Hansen, M. J.; Driessen, A. J. M.; Szymanski, W.; Feringa, B. L. Photocontrol of Antibacterial Activity: Shifting from UV to Red Light Activation. *J. Am. Chem. Soc*, 2017; 139: 17979–17986.
  42. Dong, M.; Babalhavaeji, A.; Collins, C. V.; Jarrah, K.; Sadovski, O.; Dai, Q.; Woolley, G. A. Near-Infrared Photoswitching of Azobenzenes under Physiological Conditions. *J. Am. Chem. Soc*, 2017; 139: 13483–13486.
  43. Hansen, M. J.; Lerch, M. M.; Szymanski, W.; Feringa, B. L. Direct and Versatile Synthesis of Red-Shifted Azobenzenes. *Angew. Chem., Int. Ed*, 2016; 55: 13514–13518.
  44. Lameijer, L. N.; Budzak, S.; Simeth, N. A.; Hansen, M. J.; Feringa, B. L.; Jacquemin, D.; Szymanski, W. General Principles for the Design of Visible-Light-Responsive Photoswitches: Tetra- ortho -Chloro-

- Azobenzenes. *Angew. Chem., Int. Ed*, 2020; 59: 21663–21670.
45. Konrad, D. B.; Savasci, G.; Allmendinger, L.; Trauner, D.; Ochsenfeld, C.; Ali, A. M. Computational Design and Synthesis of a Deeply Red-Shifted and Bistable Azobenzene. *J. Am. Chem. Soc*, 2020; 142: 6538–6547.
46. Heinrich, B.; Bouazoune, K.; Wojcik, M.; Bakowsky, U.; Vázquez, O. ortho-Fluoroazobenzene derivatives as DNA intercalators for photocontrol of DNA and nucleosome binding by visible light. *Org. Biomol. Chem*, 2019; 17: 1827–1833.
47. Kerckhoffs, A.; Bo, Z.; Penty, S. E.; Duarte, F.; Langton, M. J. Red-shifted tetra-ortho-haloazobenzenes for photo-regulated transmembrane anion transport. *Org. Biomol. Chem*, 2021; 19: 9058–9067.
48. Agnetta, L.; Bermudez, M.; Riefolo, F.; Matera, C.; Claro, E.; Messerer, R.; Littmann, T.; Wolber, G.; Holzgrabe, U.; Decker, M. Fluorination of Photoswitchable Muscarinic Agonists Tunes Receptor Pharmacology and Photochromic Properties. *J. Med. Chem*, 2019; 62: 3009–3020.
49. Aggarwal, K.; Kuka, T. P.; Banik, M.; Medellin, B. P.; Ngo, C. Q.; Xie, D.; Fernandes, Y.; Dangerfield, T. L.; Ye, E.; Bouley, B.; Johnson, K. A.; Zhang, Y. J.; Eberhart, J. K.; Que, E. L. Visible Light Mediated Bidirectional Control over Carbonic Anhydrase Activity in Cells and in Vivo Using Azobenzenesulfonamides. *J. Am. Chem. Soc*, 2020; 142: 14522–14531.
50. Zhang, L.; Zhang, H.; Gao, F.; Peng, H.; Ruan, Y.; Xu, Y.; Weng, W. Host-guest interaction between fluoro-substituted azobenzene derivative and cyclodextrins. *RSC Adv*, 2015; 5: 12007–12014.
51. Luo, J.; Samanta, S.; Convertino, M.; Dokholyan, N. V.; Deiters, A. Reversible and Tunable Photoswitching of Protein Function through Genetic Encoding of Azobenzene Amino Acids in Mammalian Cells. *ChemBioChem* 2018; 19: 2178–2185.
52. Hoppmann, C.; Maslennikov, I.; Choe, S.; Wang, L. In Situ Formation of an Azo Bridge on Proteins Controllable by Visible Light. *J. Am. Chem. Soc*, 2015; 137: 11218–11221.
53. Albert, L.; Peñalver, A.; Djokovic, N.; Werel, L.; Hoffarth, M.; Ruzic, D.; Xu, J.; Essen, L. O.; Nikolic, K.; Dou, Y.; Vázquez, O. Modulating Protein-Protein Interactions with Visible-Light-Responsive Peptide Backbone Photoswitches. *ChemBioChem*, 2019; 20: 1417–1429.
54. Kolarski, D.; Miró-Vinyals, C.; Sugiyama, A.; Srivastava, A.; Ono, D.; Nagai, Y.; Iida, M.; Itami, K.; Tama, F.; Szymanski, W.; Hirota, T.; Feringa, B. L. Reversible Modulation of Circadian Time with Chronopharmacology. *Nat. Commun*, 2021; 12: 3164.
55. Bléger, D.; Schwarz, J.; Brouwer, A. M.; Hecht, S. oFluoroazobenzenes as Readily Synthesized Photoswitches Offering Nearly Quantitative Two-Way Isomerization with Visible Light. *J. Am. Chem. Soc*, 2012; 134: 20597–20600.
56. Knie, C.; Utecht, M.; Zhao, F.; Kulla, H.; Kovalenko, S.; Brouwer, A. M.; Saalfrank, P.; Hecht, S.; Bléger, D. orthoFluoroazobenzenes: Visible Light Switches with Very Long-LivedZIsomers. *Chem.-Eur. J*, 2014; 20: 16492–16501.
57. Volarić, Jana, et al. "Design and Synthesis of Visible-Light-Responsive Azobenzene Building Blocks for Chemical Biology." *The Journal of Organic Chemistry*, 2022; 87.21: 14319-14333.
58. Singhal M, Khanna S, Nasa A. Cosmeceuticals for the skin: an overview. *Asian J Pharm Clin Res*, 2011; 4: 16.
59. Bodekaer M, Faurshou A, Philipsen PA, Wulf HC. Sun protection factor persistence during a day with physical activity and bathing. *Photodermatol Photoimmunol Photomed*, 2008; 24: 296–300.
60. Kaidbey K, Barnes A. Determination of WA protection factors by means of immediate pigment darkening in normal skin. *J Am Acad Dermatol*, 1991; 25: 262–266.
61. Scalia S, Mezzena M, Ramaccini D. Encapsulation of the UV filters ethylhexyl methoxycinnamate and butyl methoxydibenzoylmethane in lipid microparticles: effect on in vivo human skin permeation. *Skin Pharmacol Physiol*, 2011; 24: 182–189.
62. Gonzalez H, Farbroth A, Larkö O, Wennberg AM. Percutaneous absorption of the sunscreen benzophenone-3 after repeated whole-body applications, with and without ultraviolet irradiation. *Br J Dermatol*, 2006; 154: 337–340.
63. Gustavsson GH, Farbroth A, Larkö O. Percutaneous absorption of benzophenone-3, a common component of topical sunscreens. *Clin Exp Dermatol*, 2002; 27: 691–694.
64. Janjua NR, Mogensen B, Andersson AM, et al. Systemic absorption of the sunscreens benzophenone-3, octylmethoxycinnamate, and 3-(4-methyl-benzylidene) camphor after whole-body topical application and reproductive hormone levels in humans. *J Invest Dermatol*, 2004; 123: 57–61.
65. M.S.Latha, MD; Jacintha Martis,MD; Shobha V, MD; Rutuja Sham Shinde; Sudhakar Bangera,MD;Binny Krishnankutty,MD;Shantala Bellary, BDS; Sunoj Varughese; Prabhakar Rao; B.R.Naveen Kumar,MBBS; Sunscreening Agents, a literature review, *The Journal of Clinical Aesthetic Dermatology*, January 2013; 6(1).