

## Short Review

# Melatonin as a possible antidote to UV radiation induced cutaneous damages and immune-suppression: An overview

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## ABSTRACT

The sun rays brings along the ultraviolet radiations (UVRs) which prove deleterious for living organisms. The UVR is a known mutagen and is the prime cause of skin carcinomas. UVR causes acute oxidative stress and this in turn deteriorates other physiological functions. Inflammatory conditions and elevation of pro-inflammatory molecules are also associated with UVR mediated cellular damages. The inflammatory conditions can secondarily trigger the generation of free radicals and this act cumulatively in further deterioration of tissue homeostasis. Photoimmunologists have also related UVR to the suppression of not only cutaneous but also systemic immunity by different mechanisms. Some researchers have proposed the use of various plant products as antioxidants against UVR induced oxidative imbalances but Melatonin is gaining rapid interest as a product that can be utilized to delineate the pathological effects of UVR since it is an established antioxidant. Besides the antioxidative nature, the capacity of melatonin to attenuate apoptosis and more importantly the efficacy of its metabolites to further aid in the detoxification of free radicals have made it a key player to be utilized against UVR mediated aggravated conditions. However, there is need for further extensive investigation to speculate melatonin as an antidote to UVR. Although too early to prescribe melatonin as a clinical remedy, the hormone can be integrated into dermal formulations or oral supplements to prevent the ever increasing incidences of skin cancers due to the prevalence of the UVR on the surface of the earth. The present review focuses and substantiates the work by different photobiologists demonstrating the protective effects of melatonin and its metabolites against solar UVR – Melatonin as a possible antidote to UV radiation induced cutaneous damages and immune-suppression: an overview. *J Photochem Photobiol B.*

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## Contents

1. Introduction . . . . .	282
2. UV Radiation . . . . .	282
2.1. UVR Mediated Biological Damages . . . . .	282
2.1.1. UV Mediated Free Radical Damage and Apoptosis Induction . . . . .	283
2.1.2. The Immune Suppressive Actions of UVR . . . . .	283
3. Melatonin . . . . .	284
3.1. Biosynthesis and Metabolism . . . . .	284
3.2. Mechanism of Action . . . . .	284
3.3. Melatonin as an Antioxidant . . . . .	284
4. Melatonin as an Antidote to UV Radiation Mediated Damages . . . . .	285
5. Relevance of the Study of UV Radiation Incurred Damages in Tropical Rodents . . . . .	285
6. Conclusion . . . . .	286
Acknowledgment . . . . .	286
References . . . . .	286

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## 1. Introduction

The environment is a self-sustaining system of which we are only a part and the living systems get their life owing to the resources available and its proper utilization. Life on this planet started millions of years ago by the interaction of simple macromolecules under a harsh cover of toxic gases and heat. The interaction of the macromolecules gave rise to more complex chemical structures and ultimately life emerged in the form of single celled living organisms. Gradually the forces of evolution played its role as the guardian under whose strict vigilance life evolved adapting to the varying environmental conditions and wide plethora of natural disasters. We were not what we are today and could not have been so unless we got eventually adapted to the changing habitats. Of all the forces of nature that play a pivotal role in the evolution of life, the sun is one of most crucial abiotic factor. It provides both light as well as warmth to support the process of metabolism on which life solely depends. The autotrophs utilize the light energy to perform dissipation of electrons and through this complex process simple carbohydrate is formed from environmental oxygen and water. The heterotrophs depend on the plants for their food, higher heterotrophs depend on the lower ones and in such a well-tuned orchestration the food chain is sustained. A large number of such food chains build up an ecosystem sustained by the energy of the sun. The light that the sun provides also governs other complex processes like reproduction in higher animals who are entrained to seasonal and daily light dark cycles. However, like every other object the sun has its own demerits. A silent and deadly component lies hidden in the sun rays that causes serious damage to living organisms and the prevalence of the substance is ever increasing due to augmented levels of pollution owing to the rapid increase in urbanization during the last few decades. It is the ultraviolet radiation (UVR), a principal ingredient of sun rays which we cannot see or feel but it brings with it alarming consequences like skin malignancies, suppressed immune system and inflammatory responses of the body. Radiation which is one of the major immunotoxic agents suppress immunity in animals and humans and has gained interest in the past few decades because of the development in nuclear weapons and increase in number of personnel working with radiation. The overwhelming majority of chronic disease is not inherited, but resulted from environmental damage to cellular DNA or cellular processes. The primary root of all diseases is the increased amounts of oxidants and decline in antioxidants. Dietary antioxidant supplementation such as vitamins C, E, and glutathione counteract decreased immune function [1–2].

## 2. UV Radiation

Ultraviolet radiation is one of the constituents of the solar spectrum along with the visible light and the infra-red rays. The range of UVR is 200–400 nm that is just below the visible light spectrum. The UV is further classified as UVA (320–400 nm), UVB (280–320 nm) and UVC (<280 nm) depending upon the wavelengths and energy that it possesses. The different UV rays have different penetrance and are associated with varying pathogenesis in altering the body homeostasis. The UVC barely reaches the earth as it is completely blocked by the ozone layer while the UVB and UVA do penetrate the atmosphere and reach the earth to induce the varying types of cellular damages. The ozone is a very important gas that acts as an UV shield and is primarily present in the stratosphere (90%) and is present in highest concentrations at altitudes of 20–25 km [3]. However, the increased urbanization and its associated consequences have proved deleterious for the sustenance of the ozone layer. According to the British Antarctic Survey (BAS) the ozone layer has decreased each September and October since 1977 at a rate of 40% [4]. This is an alarming sign as the complete destruction of the ozone layer will cause all the UVRs to enter the earth surface and that will be a catastrophe. The principal cause of depletion of the ozone layer is the chlorofluorocarbons (CFCs) that are released from

air conditioning devices, sprays etc. BAS measurements indicated unexpected ozone depletion in the Antarctic region so severe that computers receiving satellite data often rejected ozone amounts as technical errors. Thus, the increased pollution levels pose a serious threat to the protective ozone layer and it should be controlled to avoid getting in contact with the toxic UVR. One can also get exposed to UVR from artificial sources like the sun-beds, electric-arc lamps, and artificial lighting systems [5]. Thus there exist many ways of getting an UVR exposure and the consequence is not just a skin tan but a more severe pathological condition. The UVR mediated damages are due to the interaction of photons directly with cellular DNA causing mutations and oxidation of nitrogenous bases, generation of toxic and highly reactive free radicals that incur serious biological anomalies and also the generation of pro-inflammatory molecules that induce the physiological generation of reactive oxygen species (ROS) [6]. All these taken together trigger complex pathological symptoms that are truly deleterious for the normal body *milieu*.

### 2.1. UVR Mediated Biological Damages

The skin is the organ of the body that primarily is bombarded with harmful effects from various stressors and thus is suitably equipped to deal with those. The skin synthesizes a variety of different hormones and peptides and thus these are respectively linked to the action of skin against stressors [7]. The UVC barely reaches the upper dermis of the skin (Fig. 1) while UVB penetrates the epidermis and part of it reaches the dermis. The UVA is the most penetrative and easily penetrates the dermis and also reaches the underlying sub-cutaneous tissues [8]. Since UVR induces oxidative stress the body should possess substantial defense mechanism to counteract the stressor else every single person would suffer from skin carcinoma which is not the scenario. The regulation of stress (psychological, chemical or oxidative) is under the control of the Hypothalamo–Pituitary–Adrenal axis (HPA axis) which defends against the perturbation of homeostasis under the effect of stressors [9]. Interestingly, the skin which is the largest and an integral part of innate immune system possesses all the machinery to counteract disruption of local homeostasis [10–11]. In other words research has shown that the skin expresses a local HPA axis including all the components like CRH, POMC, ACTH,  $\beta$ -endorphin and their respective receptors to counterbalance the effect of stressors including UV radiation to maintain local homeostasis [10–13]. It has been extensively demonstrated by both immuno-cytochemical localization and expression pattern via Western blotting that these peptides are stimulated under the influence of UVR depending on the wavelength and intensity [12]. The local production of corticosterone and cortisol further strengthens the speculation that the skin tries to maintain local homeostasis to stabilize central homeostasis when challenged by environmental stressors like UVR [14–17]. UVR stimulates the production of CRF locally which in turn stimulates ACTH in a similar way to what occurs in the central HPA axis depending on the wavelength of radiation and it is only in case of a very high intensity of UVR or in instances of stress induction more than that the local stress management system can endure, that the skin activates the central HPA axis as in case of irradiation by UVB [18–19] ultimately signaling a critical situation involving all the machinery to counterbalance the deleterious condition and maintaining the

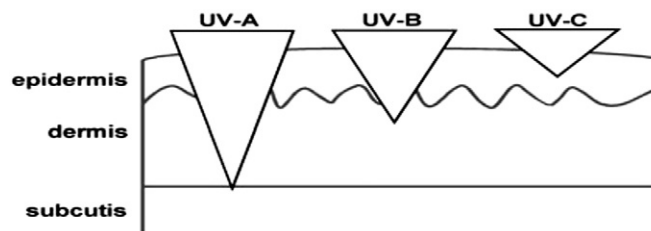


Fig. 1. The penetrance of UVR components (UVA, UVB and UVC) [Adapted from Ref. [8]].

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