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Melatonin: From Tadpoles to Humans

In 1917, Carey Pratt McCord and Floyd Pierpont Allen working at Johns Hopkins University in Baltimore, Maryland, observed that a substance contained in the pineal gland was able to bleach the amphibian skin. They crushed the pineal gland and added it to water in which tadpoles were growing. The tadpoles became lighter in color. This was a curious phenomenon that defied explanation at that time. Melatonin was named by American physician Aaron B. Lerner in 1958 who was an expert on skin pigmentation disorders. He named it melatonin on analogy to its effect on amphibian skin. Melatonin is actually a chemically modified version of serotonin and is stored together with norepinephrine in nerve terminals and is released at a later time. Finally, in 1964, working with Solomon H. Snyder, Axelrod proved that serotonin was necessary for maintaining the sleep cycles and thus melatonin was found to be essential for maintaining the sleep/wake cycle.

Melatonin is produced in smaller quantities by the retina, gastrointestinal tract, skin, bone marrow, and lymphocytes. It is centrally involved in sleep regulation and is in control of other circadian rhythms. Melatonin is also produced in smaller quantities by the cerebral cortex, cerebellum, and hypothalamus. It influences various functions such as thermoregulation, circadian rhythms, sleep, and mood regulation. Melatonin also plays a role in mood disorders, depression, and cancer. It is currently being studied for its potential use in treating sleep disorders, jet lag, and other circadian rhythm disorders.

Melatonin is a wonder molecule that not only controls the body clock but also has several other useful functions to perform.
Serotonin-N-acetyltransferase

Tryptophan Serotonin N-acetyl serotonin Melatonin

The circadian clock in mammals is situated in the suprachiasmatic nucleus (SCN), a distinct group of cells in the hypothalamus. The SCN contains the "biological clock". The pineal gland that resembles the epiphysis organ of lower vertebrates synthesizes melatonin from its precursor tryptophan via sequential transformation of L-tryptophan to serotonin and then melatonin by activities of tryptophan hydroxylase, serotonin N-acetyl-transferase and hydroxyindole-o-methyltransferase.

Serotonin as an Antioxidant

Aerobic organisms generate free radicals like superoxide anion radicals, hydrogen peroxide and highly toxic hydroxyl radicals as by-products of their normal metabolic processes. These free radicals are deleterious and can induce decay in neurons, proteins and DNA, which can lead to cell damage. To prevent this, the body must have a defense system to protect the cells from these radical-induced damage.

How Melatonin Shows its Effects

Melatonin, whether administered orally or intraperitoneally, has been shown to possess antioxidant properties. Melatonin has been reported to possess antioxidant properties that work to reduce free radicals and protect the body from radical-induced damage.

Melatonin as an Antioxidant

Melatonin interacts with antioxidants like superoxide dismutase and glutathione peroxidase by means of the N-acetyltransferase pathway involving the spinal cord and the sympathetic nervous system. The SCN takes photic information about day length from the retina, interprets it and passes it on the circadian clock via a multi-synaptic pathway involving the spinal cord and the sympathetic nervous system.

Melatonin and Circadian Rhythm

The circadian rhythms or biological clocks that operate in all organisms help to coordinate the various physiological processes of the organism. The circadian rhythms are controlled by a master clock located in the suprachiasmatic nucleus of the hypothalamus. The SCN is the body's "biological clock".

Role in Human Aging

Aging is a complex phenomenon characterized by a series of changes that occur in the body over time. One of the most important changes that occur during aging is the increased incidence of cancer, infectious and degenerative diseases. In humans, plasma melatonin levels begin to increase steadily after 1900 hr to 2300 hr to attain peak value around 0200-0400 hr. In presence of light or during the day this melatonin changes into serotonin is converted back to melatonin. Thus circadian rhythm or day-night cycle under the influence of high dietary tryptophan levels.

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It has been observed that the broad-spectrum antioxidant and free radical scavenger melatonin plays a critical role in reducing the age-promoting free radicals. Melatonin also enhances immune function in aged individuals by affecting G protein-cAMP (cyclic adenosine monophosphate) signal pathway and by regulating intracellular glutathione, which is a naturally occurring antioxidant inside the cell.

Melatonin in Skin Physiology and Pathology
In our busy life, daily we are exposed to stressors like solar and radiation energy, biochemical agents and other environmental pollutants that may cause serious damage to the skin. To fight the deleterious effects of these stressors, the skin has evolved specific signals that integrate into a stress-response neuroendocrine system. This system produces melatonin that plays a very important role in skin physiology and related pathology.

Melatonin is implicated in skin functions such as hair growth cycling, fur pigmentation and melanoma control. Melatonin is also able to suppress radiation-induced damage to skin cells via its strong antioxidant activity. It buffers external or internal stressors to preserve the vital integrity of the organs and to maintain homeostasis.

Melatonin and Hair
Studies with a human hair organ culture model showed that melatonin had bimodal effects on hair elongation consisting of stimulation as well as inhibition. Positive effects of melatonin in human hair growth suggest that it could be a potential target for hair growth regulation. Melatonin increases cell viability in UV-irradiated fibroblasts by countering the formation of polyamines and the accumulation of malondialdehyde (lipid peroxidation product) while reducing apoptosis (autodestruction) of cells.

Immune Booster
The body has a unique ability to resist infections and toxins that tend to damage tissues and organs. Studies have confirmed that a dose of melatonin stimulates the immune system. It increases the production of interferon and stimulates the release of cytokines and other immune mediators. Immune modulation also plays a role in the pathogenesis of autoimmune disorders and in the regulation of allergic and chronic inflammatory reactions.

Fighting Against Cancer
Melatonin is known to influence a variety of biologic processes including circadian rhythms, neuroendocrine, confundulator, skin pathology and immune functions as well as in hormone regulation.

Cure for Jet lag
People who travel across time zones often suffer jet lag. Jet lag is a sleep disorder characterized by a constellation of symptoms including poor nighttime sleep, increased daytime sleepiness, decreased alertness, impaired performance, fatigue, irritability, depressed mood and gastrointestinal distress. It is caused by a temporary misalignment between the endogenous circadian clock and the desired destination circadian sleep-wake schedule. Melatonin has been found to be effective in treating jet lag. It has been observed that taking melatonin close to the target bed time of the destination can alleviate symptoms. Melatonin realigns the circadian clock to a new environment.

The rhythmic pattern of melatonin secretion is important because it provides information to organisms to do a specific physiological function at a specific time. In comparison to other signaling molecules, the numerous actions that have been attributed to melatonin are exceptional. The versatile nature of melatonin from starting of life to the end, from direct interference to indirect, shows its effect in almost full body physiology. No doubt this molecule of darkness lights our day.

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