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Frontiers in Molecular Medicine and Therapeutics

EDITORIAL

Melatonin in molecular medicine and therapy: A frontier ally in health and disease

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Nowadays, diagnosis, treatment and overall, prevention of disease, are pointed out as pivotal challenges for the society. Majorly, neurodegenerative diseases and cancer are increasing their presence in a little-by-little aging society. The etiology of these diseases is under intense study. However, their complexity and the fact that they might be derived from a variety of factors which, among others, include genetic and environmental factors, has led the scientists to pay attention to disease at the molecular and genetic level, in order to develop medicine on the basis of prompt detection and application of proper therapy.

As mentioned, genetic and environmental factors, including diet and lifestyle, contribute to illnesses, among which cancer and neurodegenerative diseases represent major causes of morbidity and mortality. Research supports the assumption that disbalance of redox state can lead to neuroinflammation and to damage of a certain tissue and has been considered the basis of disease. Accordingly, oxidative damage markers have been found in tissues obtained from patients affected by metabolic or neurodegenerative diseases and cancer. In this line, the effects of antioxidants against oxidative stress and their role in cellular physiology have highlighted their putative role to prevent or heal disease. A wide variety of compounds, either natural or synthetic, are available to be used in the treatment of disease. Every year new compounds are added to the list. These drugs must enter the body to exert their effects. But, what if one of those compounds was already inside the body?

Melatonin (N-acetyl-5-methoxytryptamine) is a neurohormone that is mainly produced by the pineal gland and reaches highest levels in plasma during the night. Impairment of melatonin secretion could occur due to disturbance of sleep-wake cycle, due to insomnia, nightshift work, or others and, hence, set the basis of imbalance of cellular functions that, at long term, could end in disease. But melatonin is produced not only in the pineal gland. In addition, melatonin is found in other tissues like retina, gastrointestinal tract, skin, leukocytes, testis or bone marrow. In these locations, melatonin acts as a paracrine or autocrine agent. Interestingly, melatonin and/or its precursors are also present in fruits and vegetables; i.e., availability is additionally present out of the body. The latter has given the industry the potential to prepare supplements that can be used in the treatment of different disorders, mainly, sleep disorders.

Melatonin can act on target cells via specific high affinity receptors located at the cellular membrane, termed MT1/MT2. Moreover, melatonin also can bind to intracellular receptors. In this group, researchers have signalled to calmodulin, hydroquinone or RZR/ROR nuclear receptors. These receptors count with widespread presence in different organs and tissues. However, not all cells express receptors for melatonin, especially membrane receptors. Nevertheless, these cells have exhibited responses to melatonin what makes us think that melatonin might exert direct effects, i.e., actions not mediated through its membrane receptors. Hence, melatonin has the ability to play pleiotropic activities in the human body. In general, melatonin regulates circadian functions. In addition, it also regulates inflammatory and immune processes. Moreover, it exhibits potent antioxidant ability and allows scavenging of oxidative stress. Furthermore, anticancer effects have also been suggested. In this line, it has been shown that melatonin induces death of malignant cells, whereas healthy cells might be protected. In other words, depending on the cellular status, melatonin sets decisions that will direct cell fate. Therefore, we could argue that melatonin could act as a guard, a keeper or caretaker of cellular physiology.

To date, it seems clear that most diseases have, although not exclusively, an oxidative stress link. Moreover, withing a certain organ or tissue, cells respond differentially to oxidative stress, in part due to the fact that some cells resist better oxidative stress in comparison with their neighbors. It is well known that the probability of cancer development increases in people with night shift working. In addition, blood levels of melatonin are lower in elderly, a stage in life in which probability of cancer and neurodegeneration development increases. This is the reason why the availability of antioxidants within the body might represent a powerful tool to prevent damage that, if not sorted out, could evolve towards disease. If not available to a certain level within the body, entry of antioxidants with diet can help metabolic machinery in creating a barrier against the noxious actions of oxidative stress.

Summarizing, in view of the close relationship between oxidative stress and bad habits in today´s society, which include smoking, sedentarism, alcohol consumption, unbalanced diet and/or sleep rhythm disturbance among others, we could conclude that melatonin arises as insider ally that exhibits an interesting and potential role in health and, when impaired, in medicine and therapy.

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