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Melatonin Milk; A Milk of Intrinsic Health Benefit: A Review

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ABSTRACT

The aim of this theme is to highlight the important points related to melatonin. It is a hormone secreted in pineal glands and helps in the induction of sleep in human beings. Melatonin is a naturally occurring compound in animals, plants and microbes. It is responsible for the regulation of circadian rhythms for several biological functions. It is sensitive to the light and its concentration in the milk varies with the intensity of light. The basic functions of this hormone include antioxidant property, in correction of sleeping disorders, in alleviation of jet lag and in prevention of cancers. Besides these major functions, it also has some associated functions like protection of skin damage from ultraviolet light. Generally, <0.3 mg melatonin is required per day for human beings for usual induction of sleep and relaxation.

Key words: Melatonin, milk, sleeps sickness, health, darkness, pineal gland, hormone

INTRODUCTION

Melatonin is one of the important hormones primarily secreted by the pineal gland. The secondary sources for this hormone are retina, gut, skin, platelets, bone marrow and possibly other structures. It is naturally present in animal products like milk and is responsible for regulation of body clock in human beings (Altun and Ugur-Altun, 2007). The level of melatonin varies in the human body with every step within the time of 24 h as well as in the whole life span. Milk is an important natural source of melatonin as compared to the other sources (Caniato *et al.*, 2003; Paredes *et al.*, 2009; Turek and Gillette, 2004). Today's synthetic melatonin's are also available but they are not as good as natural melatonin in respect to induction of sleep and healthfulness (Richardson, 2005; Perreau-Lenz *et al.*, 2004). The routine intake of melatonin should be on fixed time for better results. Light has the key role in secretion of melatonin in milk (Brainard *et al.*, 2001; Kayumov *et al.*, 2005). It is also reported that the concentration of melatonin is much more in the milk of cow's who put down on milking early in the morning before sunrise (Challet, 2007).

In modern era when lifestyle is changing in a faster pace, most of the population suffers from insomnia. It is a sleep disorder which can be treated by the melatonin milk. On the advancement of age, level of the melatonin decreases. The effect of heat treatment on milk supplementary enhances the melatonin effect in the body. As a result, the problems like insomnia and sleeping

disorders can be treated by a cup of night milk. The drinking of milk during night not only helps in correction of diseases but it is also helpful in stimulation of dynamism in humans during day time (Fonteh *et al.*, 2005; Midau *et al.*, 2010).

Melatonin hormone is commonly known as “the hormone of darkness” because the production of melatonin by the pineal gland is prevented by light and permitted by darkness. The inception of melatonin in animal products each evening is called the Dim-Light Melatonin Onset (DLMO). It is a hormone principally responsible for circadian rhythms and is secreted by mainly pineal glands of mammals and some other tissues. Production of melatonin and its intensity in the blood is on top in the mid of the night and step by step falls throughout the succeeding half of the night. The typical variations can be seen in the timings according to the person’s chronotype. The release of melatonin is three to four times higher in milk which is let down before sunrise than in the milk which is obtained during day time (Brainard *et al.*, 2001; Kayumov *et al.*, 2005). The resources of melatonin are both animals as well as plants (Bhat and Bhat, 2011; Singh and Sachan, 2011a). It acts as a potent antioxidant (Hamad *et al.*, 2011; Okonkwo, 2011; Tan *et al.*, 2007) and is useful in improving sleeping disorders (Buscemi *et al.*, 2006). Melatonin is also known as the terminal (suicidal) antioxidant (Tan *et al.*, 2000) because it can produce stable end products in the reaction with free radicals and on oxidation it cannot be reduced further in its previous state. This hormone is also useful in alleviation of jet lag disease (Buscemi *et al.*, 2006; Hardeland, 2005). It is an excellent therapy for lifestyle-related diseases and can be used in prevention of cancers (Mohammad and El-Zubeir, 2011; Okonkwo, 2011). So, to highlight the salient features regarding melatonin and its positive effects on the body system is the aim of this manuscript.

STRUCTURE AND PROCESS OF MELATONIN FORMATION

The chemical structure of the melatonin is N-acetyl-5 methoxytryptamine. The secretion of melatonin in pinealocytes of pineal gland (located in the brain) is stimulated by darkness and suppressed by sunlight. For its stimulation retina gets information from light and darkness. The precursor for melatonin formation is tryptophan (Reiter, 1991). It is synthesized from serotonin with the help of 5-hydroxyindole-O-methyltransferase enzyme. The suprachiasmatic nuclei of the hypothalamus in the brain are a location of melatonin receptors. These receptors are responsible for control of circadian rhythms and have direct action on the nuclei in this regard. The melatonin metabolism is taken place in liver in presence of microsomal enzyme. The main excretory product in this reaction is 6-sulphatoxy-melatonin and the intermediate product is 6-hydroxy-melatonin. The quantity of its secretion can easily be measured in the children’s as compared to the adults.

Circadian rhythms from this indole hormone are produced by clock gene expression in the suprachiasmatic nuclei by closed-loop negative feedback. The cyclic production and metabolism of melatonin is controlled by an enzyme N-acetyl transferase and hydroxyl indole-O-methyl transferase (Eriksson *et al.*, 1998). It is well understood that melatonin is rapidly released in blood vascular system and can cross the entire morpho-physiological barriers such as Blood-Brain Barrier (BBB) and placenta, respectively. The secretory activity of melatonin varies between 18-40 pg mL⁻¹ among different persons at night. The half-life of melatonin is reported less than 30 min. The secretion of melatonin in different individuals varies according to their age, gender, seasons and in certain diseases condition. The level of melatonin decreases with the advancement of age of an

individual although its secretion is higher in older women than elderly men. The concentration of melatonin varies with the seasonal variations (Fonteh *et al.*, 2005; Midau *et al.*, 2010). The concentration of melatonin is reported higher in winters as compared to summers. The concentration of melatonin also varies with the type of milk in fashion of conjugated linoleic acid in different milks (Singh and Sachan, 2011b).

SOURCES OF MELATONIN AND THEIR MODE OF ACTION

Banana and milk are the natural sources of melatonin therefore, the intake of these foods commonly support good quality sleep. The intake of banana and milk simultaneously exerts synergistic action on sleep initiation and also in prevention of lethargic effect in human beings. Among them Banana is a good source of melatonin because it contains good source of L-tryptophan. L-tryptophan is an amino acid which acts as a precursor molecule for the synthesis of melatonin and gets transformed to 5HTP in the brain. The formation of melatonin is a series of reactions in which 5HTP gets converted into serotonin and ultimately produces melatonin. Serotonin is a calming neurotransmitter whereas melatonin is a natural controller of hormonal rhythms in the body, especially in sleep.

L-Tryptophan (precursor molecule) → 5-HTP → Serotonin → NAS (Nor melatonin)

The reaction of melatonin in human body is of various types. In one instance L-tryptophan can cross only blood-brain barrier. In other instance drinking of milk by human beings releases insulin which pushes most amino acids from blood into storage (Tamarin *et al.*, 1985). The melatonin milk also contains calcium which is a calming agent (Singh and Sachan, 2011a) and warm milk is a good source of L-tryptophan.

Tryptophan is a vital compound (Singh and Sachan, 2011b) that is responsible for conversion of serotonin to melatonin. Among these hormones melatonin is responsible for induction of sleep while serotonin keeps our body relaxed and happy (Brown *et al.*, 1997). However, intake of too much tryptophan can disturb the sleep. So, always prefer to drink milk or eat tryptophan rich foods instead of supplementation (Singh and Sachan, 2011c, d). The conversion of serotonin to melatonin is depending on the availability of nor-epinephrine (nor-adrenaline). So, the drinking of green tea in daytime can further influence the conversion process. This effect can further be improved by the use of caffeine free green tea extracts at night.

COMPOUNDS RESPONSIBLE FOR SLEEP AND RELAXATION

Melatonin is one of the known compound for the induction of sleep and serotonin for relaxation of human body. Insufficient quantities of these compounds can prevent proper sleep and relaxation. Due to this reason serotonin imbalance depression sufferers often have sleep disturbances. The deficiency of melatonin in the body can be corrected either by the natural sources or by the synthetic means. In all way it is synthesized by the body via tryptophan. The primary function of tryptophan is to synthesize protein (Sachan and Singh, 2010). In its excess production body can store and/or convert it to serotonin and melatonin. The excess amount reaches to the human body through the excess ingestion of tryptophan diet. It is true particularly in ingestion of dairy products because dairy products are extremely high in tryptophan-protein ratio (Sachan and Singh, 2011; Singh and Sachan, 2011a). These two components serotonin and melatonin is responsible for sleep induction and relaxation but this effect is less physiological and more towards psychological effect.

Webb and Puig-Domingo (1995) reported that synthetic melatonin or supplemental melatonin is a little stronger than average glass of milk in induction of sleep. Melatonin has no precipitation property and has very less side effects during sleep induction because it is naturally found in the human body (Karbownik *et al.*, 2001). Another precursor of melatonin is 5HTP but it is not a well established drug for sleep induction. It is also a good alternative for the generation of melatonin. However, it is not as effective as tryptophan but it may be used for the correction of insomnia like diseases.

FUNCTIONS OF MELATONIN IN RELATION TO HUMAN HEALTH

- Melatonin helps in the recovery of certain diseases such as Jet leg, delayed sleep phase syndrome, insomnia in the elders and sleep disturbances related to neuro-psychiatric disorders in children (Garfinkel *et al.*, 1995)
- Melatonin is also important for induction of sleep in healthy people and helps in curing of bipolar disorders or sleep disturbance. Other benefits of melatonin include sleep latency reduction, enhancement of alertness and reduce daytime fatigue
- Melatonin also helps in recovery from delayed sleep phase syndrome
- Melatonin can be utilized in children suffering from various neuro-psychiatric disorders such as mental retardation, autism, psychiatric disorders, visual impairment, or epilepsy. The way of its therapeutic use in above mentioned disease is not well established
- It acts as an antioxidant or free radical scavenger in oxidative damage conditions
- Melatonin is a good remade for attention deficit hyperactivity disorder in children
- Ravindra *et al.* (2006) reported that melatonin is a useful drug in malignancies such as brain, breast, colorectal, gastric, liver, lung, pancreatic and testicular cancer. They also recommended the use of melatonin in conditions like lymphoma, melanoma, renal cell carcinoma and soft-tissue sarcoma. The use of melatonins lowers the side effects of drugs in cancer treatment
- The use of melatonin can correct the *Circadian rhythm* especially in blind persons
- Melatonin is a good therapy for the patients having depression particularly associated with sleep disturbances
- Melatonin milk is a good drug for glaucoma because it reduces intraocular pressure in eyes
- It helps in prevention of headache associated with migraine, cluster and tension (Tan *et al.*, 1993; Al-Baarri *et al.*, 2011; Foda *et al.*, 2009)
- Hypertension can also be reduced with the use of melatonin
- It is also suggested that melatonin helps in the recovery of inflammatory bowel disease
- It is a good therapy for the sleep latency and insomnia conditions of unknown origin in old age peoples
- Melatonin can be used for preoperative sedation or anxiolysis prior to magnetic resonance imaging (MRI)
- Some evidences suggest melatonin helps in minimizing Rett syndrome conditions
- The chances of development of diseases such as Alzheimer's, Parkinson's and Schizophrenia can be reduced by the use this compound
- Melatonin can be used in correction of sleep disturbances in young people having damaged pineal gland by tumors or surgery
- It helps in induction of sleep in asthma patients
- It may reduce tendency of smoking

- It helps in increasing platelet production in individuals suffering from thrombocytopenia particularly in cancer therapies
- It helps in protection of skin from ultraviolet light due to its antioxidant properties

CONCLUSION

On the basis of above facts it is concluded that melatonin, a naturally occurring hormone in the cow milk especially may serve, the purpose of recovery from sleep disturbances. The other sources like pills of melatonin and 5 HTP may be used for sleep induction. They are more effective but unlike other chemicals they also have some side effects. So, the naturally occurring melatonin should be preferred over them. The doses of melatonin should be <0.3 mg per day because this much melatonin is required by the human body in a day for normal induction of sleep and good relaxation.

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