

# “High Melatonin Milk”- Milk with Intrinsic Health Benefit

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## **Abstract**

Melatonin  $C_{13}H_{16}N_2O_2$  (molecular weight: 232) or N-acetyl-5-methoxytryptamine, is chemically an indoleamine and derived from the essential amino acid tryptophan. It is a hormone and due to secretion from pineal gland, it is also called as active pineal factor. Its IUPAC name is N-[2-(5-methoxy-1H-indol-3-yl)ethyl] acetamide. The indole ring acts as the chromophore showing maximum absorbance at 223 nm, and the functional groups contribute to its fluorescence property. Lerner et al. 1959 reported that extract from beef pineal gland are able to lighten frog's skin by reversing the darkening effect of melanocyte stimulating hormone and therefore, named this compound as “melatonin” since it caused aggregation of melanin granules. Melatonin hormone is more effective and active when compared to other hormones like adrenaline and nor-adrenaline (100 times), triiodothyronine (200 times), and serotonin (5000 times) in preventing darkening of frog skin by contracting melanophores. It is a white powder having melting point of 117°C. It is an amphiphilic molecule (having solubility in both water and lipid) which facilitates its movement across the cell membrane and various body fluids and makes melatonin a prominent molecule in almost all tissues of mammals.

**Keywords:** Melatonin, tryptophan, hormone of darkness

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## **INTRODUCTION**

### **The Hormone of Darkness**

Normally, the presence of light inhibits and darkness promotes the production of melatonin by the pineal gland. In 24 h a day, during night hours the synthesis and secretion of melatonin increases to its maximum value at midnight. After that its synthesis and secretion decrease to its lower value of day time. For this reason melatonin has been called hormone of darkness.

### **Biosynthesis of Melatonin**

Melatonin is synthesised from tryptophan in a four step pathway. First, tryptophan is converted to 5-hydroxytryptophan by the action of tryptophan 5-hydroxylase enzyme. Then, Aromatic-L -amino acid decarboxylase catalyses the conversion of 5-hydroxytryptophan to serotonin (5-hydroxytryptamine). Serotonin -n acetyl transferase acetylates serotonin to n-acetylserotonin. This is the immediate precursor of melatonin. This process takes place mainly in the pineal gland, where

Serotonin -n acetyltransferase is expressed. The last step in this biosynthetic pathway is catalysed by hydroxyindol-o-methyltransferase, which leads to the formation of melatonin. The production and secretion of melatonin depends upon the environment (presence of light or dark). Only during darkness at night pineal gland produce melatonin in abundance.

### **Why there is a Need for Melatonin Supplementation to Body**

Melatonin is regular hormone that is produced in body and regulates sleep and wake process of human beings. But as the age proceeds the level of melatonin decreases and it often causes sleeping disorders in older people. People with low melatonin will eventually begin to show signs of anxiety, hyperirritability and hypersensitivity. The symptoms of melatonin deficiency include complaints of insomnia or frequent waking, un-refreshing sleep and fatigue.

### How to Increase Melatonin Secretion in Human Body

It is always possible to solve problems of any deficiency by just taking a pill but hormone-containing pills should always be used judiciously. Besides taking pills there are many strategies for increasing melatonin levels like; sleeping in a dark room, the temperature at which you sleep as sleeping in too warm or too cold environments will impair melatonin production, by manipulating the diet rich in fruits such as; bananas, vegetables such as; corn and tomatoes, grains such as; rice and oats and milk will enhance melatonin synthesis.

Avoid drinking of coffee and alcohol before sleeping as it may decrease melatonin

secretion and certainly contribute to sleep disturbance.

### Enhancement of Food that will Provide More Melatonin

1. **Intake of food rich in tryptophan:** as tryptophan is a precursor for melatonin synthesis, intake of high tryptophan will increase melatonin synthesis but there are some constraints (Table 1).
  - a. Firstly tryptophan will use to complete amino acid requirement, after that it will be used for melatonin synthesis.
  - b. Vitamin B<sub>6</sub> and calcium are also needed to synthesize serotonin from tryptophan.
  - c. Stress, Intake of Caffeine, alcohol and tobacco will decrease the melatonin synthesis.

**Table 1: Foods are Naturally Rich in Tryptophan.**

Food	P g/100 g food	Tryp g/100 g food	Tryp/P%
Milk	3.22	0.08	2.34
Sesame seed	17.00	0.37	2.17
Sunflower seed	17.20	0.30	1.74
Pumpkin seed	33.08	0.57	1.72
Soybeans, raw	36.49	0.59	1.62
Cheese, parmesan	37.90	0.56	1.47
Cashew	17.00	0.25	1.47

2. **Fortify foods with melatonin as food additive** to increase melatonin content of food: But melatonin is not permitted as food additive by FDA and also do not have GRAS status.
3. **Naturally enhance the melatonin content of milk:** Melatonin has been found in human, bovine and goat milk [1,2] at a low concentration (5–25 pgmL<sup>-1</sup>). Its concentration is maximum at midnight and minimum at noon, which parallels that of serum to some extent. Synthesized by pineal gland and secreted in milk by blood through an active transport within the mammary gland. It has been suggested that night-time milk could serve as source of melatonin to improve sleep and diurnal activity in elderly people [3] (Table 2).

**Table 2: List of Hormone shows Range of Bovine Milk.**

Hormone	Ranges reported in bovine milk
Estrogen	5–10 pg mL <sup>-1</sup>
Progesterone	2–20 ng mL <sup>-1</sup>
Androgens	0–50 pg mL <sup>-1</sup>
Prolactin	5–200 ng mL <sup>-1</sup>
Growth hormone	0–1 ng mL <sup>-1</sup>
Insulin	5–40 ng mL <sup>-1</sup>
Calcitonin	700 ng mL <sup>-1</sup>
Melatonin	5–25 pg mL <sup>-1</sup>

4. **Production of milk rich in melatonin:** Melatonin is a natural compound found in milk. Concentration of melatonin exhibits a marked daily rhythm, with increasing concentrations in milk produced at night. This phenomenon seems to be universal amongst mammals. The cows' night-time milking contains 100 times the melatonin as normal milk. If the daily cycle of mammals is divided into one light and one

dark period and animals are milked at the end of the dark phase, they will secrete more melatonin in their milk. Different brands of melatonin rich milk are available all over the world. They have 20–25 times more melatonin compare to normal milk and their cost is also 20–30 times more than available regular milk.

marketed in crystalline form to be mixed with milk or yogurt.

### Coolattin Cheddar Cheese

In Ireland, the Coolattin cheddar is a special type of cheese, which aids relaxation and sleep because it is prepared from milk high in melatonin (Figure 1).

### Natchmilch kristalle (Night milk Crystals)

The German firm milchkristalle has developed a way to produce melatonin-rich milk that can be marketed as a natural crystalline source of the “sleep hormone” that helps regulate the body’s sleep cycles. They produce milk powder with 100 times more melatonin than normal. After milking from cows under night time, the milk is freeze-dried, packed and

Country	Brand Name
Finland	Maito
United kingdom	Slumber bed time milk, Night time milk
Ireland	Ardrahan lullaby milk
Germany	Nocturnal milk
Japan	Anti-stress milk
South Korea	Good night milk
Thailand	Bedtime milk
New Zealand	Synlait Night Milk



Fig. 1: Different Brands of Melatonin Rich Milk Available in World Market.

### Bioavailability of Exogenous Melatonin

Melatonin being an amphiphilic molecule is readily absorbed in the gastrointestinal tract when taken orally in pure form, and influences the blood plasma concentration. The oral consumption of melatonin rich food is reported to increase the serum melatonin concentration. Its absolute bioavailability is reported to be 15%. It is a short lived molecule with an average life of about 20 to 40 min, depending upon the conditions. Inactivation of melatonin occurs mainly in liver where it is converted into 6-hydroxymelatonin.

### Processing of Melatonin Rich Milk

Melatonin rich milk needs to be processed in the normal way to give all the familiar milk products. The hormone melatonin is bound to protein molecules in the milk and is not destroyed by pressure, heat or freeze treatment. On reducing the fat and lactose in milk, there is a relative increase in proportion of melatonin.

### Factors Affecting Melatonin Content in Bovine Milk

Factors that affect melatonin content in milk include presence of light during milking, age of cow, lactation, season, and diet. Night-time milk, winter milk and late lactation have a greater ability to accumulate melatonin in milk [1].

### Therapeutic Potential of Melatonin Rich Milk

The product “melatonin rich milk” joins a growing international market that is creating a profitable new segment of the dairy sector. With so much attention directed at foods that can combat cholesterol, diabetes, osteoporosis and other diseases it is often overlooked that the most successful nutritional products are not the ones that fight disease but those that address lifestyle issues – health problems that reduce people’s quality of life but aren’t life-

threatening diseases. Sleeplessness is one such lifestyle issue and it's an important issue for a significant percentage of consumers over the age 45 - almost a quarter of women aged over 45 regularly have difficulty getting to sleep at night. The problem affects a further 50% to a lesser degree. The clutch of high-melatonin milk brands that have surfaced in recent years are an excellent example of how consumers are willing to pay premium prices for products that will improve their lifestyle.

Melatonin is a natural sleeping aid and used for natural treatment of insomnia. Melatonin is a multi-functional hormone that is produced naturally by the human body, but it is not just about sleep-wake cycles. It's been shown to:

- Help regulate the female reproductive cycle and may also control the onset of puberty.
- Children who take melatonin can suffer a delay in sexual development.
- Role in regulating blood flow, specifically in constricting coronary arteries.

#### Melatonin and Aging

Melatonin plasma levels in mammals decline considerably with aging after early childhood, which might be a factor in the greater vulnerability of elderly people to deficits and diseases associated with aging. People over age 60 may show no increase in melatonin production at night. In children, nocturnal melatonin production decreases significantly at puberty. The decrease is more strongly associated with the stage of puberty than with chronological age [4].

#### Anti-oxidant Actions

Melatonin is a very powerful anti-oxidant. Unlike vitamin C or glutathione, which are only active in aqueous (watery) phase and vitamin E, which is only active in lipid (oily) phase, melatonin is effective in both aqueous and lipid phases. Unlike vitamin E and vitamin C, which cannot readily cross the blood-brain barrier, melatonin easily crosses the blood-brain barrier [5]. The chief metabolite of melatonin, 6-hydroxymelatonin (formed in the liver) has as much anti-oxidant activity as melatonin [6]. Vitamin C can become a toxic pro-oxidant when exposed to free iron, and most anti-oxidants become weak

free radicals after having neutralized a free radical. But melatonin's anti-oxidant action involves donation of two electrons, not one electron, thereby ensuring that melatonin does not become a free radical. Melatonin administration leads to increased expression of the anti-oxidant enzymes superoxide dismutase and glutathione peroxidase [7].

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