

Melatonin; from pineal gland to healthy foods

Melatonin; pineal bezden sağlıklı yiyeceklere

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ABSTRACT

Obviously, the human diet has become progressively more divergent from those of our ancestors. This maladaptive change became apparent with the Industrial Revolution and has been accelerating in recent decades. In conjunction with this discordance between our ancient, genetically determined biology and the nutritional pattern, in contemporary Western populations, many of the so-called diseases of civilization such as cardiovascular diseases, cancer, and diabetes have emerged. Despite remarkable pharmacological and technological advances, the pandemic of civilization-related diseases continues. Because of this situation, in the last three decades, functional foods, officinal plants are becoming of progressive public and scientific interest and a variety of biologically active compounds have been found in plants. One of them is melatonin; a ubiquitous molecule in nature including most of the edible plants with a variety of health benefits. This paper provides a brief outline about melatonin in functional foods and officinal plants.

Keywords: Diet, Disease of civilization, Officinal plants, Melatonin

ÖZET

Aşık bir şekilde, insanoğlunun diyeti dereceli olarak atalarınınkinden daha farklı olmaya başlamıştır. Bu uyumsuz değişiklik Endüstri Devrimi ile belirgin hale geldi ve geçen on yıllar içinde hızlandı. Eski ile aramızdaki bu uyumsuzlukla birlikte, genetik olarak belirlenmiş biyoloji ve beslenme modeli, çağdaş Batı toplumlarında kardiyovasküler hastalıklar, kanser ve diyabet gibi uygarlık hastalıklarının çoğunu ortaya çıkarmıştır. Kayda değer farmakolojik ve teknolojik gelişmelere rağmen, uygarlık ile bağlantılı hastalıkların yayılımı devam etmektedir. Bu durumdan dolayı, geçen 30 yıl içinde, fonksiyonel yiyecekler, şifalı bitkiler zaman geçtikçe toplum ve bilimsel ilgiyi kendine çekmiş ve bitkilerde çok sayıda biyolojik olarak aktif bileşikler bulunmuştur. Bunlardan birisi de, çok çeşitli sağlık yararları olan yenilebilir bitkiler çoğu dahil olmak üzere doğada yaygın olarak bulunan bir molekül olan melatonindir. Bu yazı, fonksiyonel yiyecekler ve şifalı bitkilerde bulunan melatonin hakkında özet bilgi sağlamaktadır.

Anahtar Kelimeler: Diyet, Uygarlık hastalıkları, Şifalı bitkiler, Melatonin

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INTRODUCTION

It is well known that melatonin (N-acetyl-5-methoxytryptamine) occurs ubiquitously in nature and its actions are thought to represent one of the most phylogenetically ancient of all biological signaling mechanisms. It has been identified in all major taxa of organisms (including bacteria, unicellular eukaryotes and macroalgae), in different parts of plants (including the roots, stems, flowers and seeds) and in invertebrate and vertebrate species.

Although Rene Descartes (1596-1650) maintained that the pineal gland is the part of the body with which the soul is most immediately associated, the pineal gland was considered as a rudimentary organ for centuries. Lerner et al. in late 1950s opened a new era of investigation when they discovered the main product of this almost forgotten organ; this product was found to be melatonin [1-3]. Another important discovery that followed soon thereafter is that melatonin synthesis in the pineal is much higher at night than during the day; thus it is often referred to as the chemical expression of darkness.

After its discovery, for years melatonin was generally considered as a pineal product which is basically related to its ability to mediate seasonal changes in reproductive competence in photoperiodically-dependent seasonal breeders. The functional diversity of melatonin, however, extends well beyond its control of annual cycles of sexual physiology in photoperiodic animals. The circadian rhythm of melatonin has been unequivocally linked to biological rhythmicity, sleep, immune function, blood pressure, anti-aging, body weight regulation, diabetes, neurodegenerative diseases, ischemia/reperfusion injury, cell physiology and cancer inhibition among others. The data in reference to efficacy of melatonin on a variety of diseases and conditions are not only derived from experimental studies but most of them are also clinically well founded [4]. It is now also both experimentally and clinically well established that not only melatonin but its metabolites can function as endogenous free-radical scavengers and broad-spectrum antioxidants [5, 6]. Although enormous amount of data have accumulated related to melatonin and the pineal gland, currently melatonin has still been mostly known to correct insomnia and jet lag.

Mammalian pineal gland produces progressively less melatonin in advanced age and the incidence of disorders mentioned above again increases as humans become older. Therefore, it has become popular in western countries to take additional (exogenous) melatonin via either in pharmacological form or in

particular plant-based foods which themselves contain melatonin. Since melatonin is found throughout both the plant and animal kingdoms, if not all plants contain melatonin. Melatonin has been detected in the roots, leaves, fruits, and seeds of a considerable variety of plant species [7]. Some plants have surprisingly high melatonin content in their edible parts (Table 1).

Table 1. Selected examples for edible and officinal sources of melatonin (data collected from the references 7,8,15,19,22)

Dietary source	Tissue	Melatonin (pg/g)
Alfalfa	Seed	16000 ^a
Almond	Seed	39000 ^a
Apple	Fruit	48
Barley	Grain	378
Black mustard	Seed	129000 ^a
Celery	Seed	7000 ^a
Flax	Seed	12000 ^a
Fennel	Seed	28000 ^a
Fenugreek	Seed	43000 ^a
Feverfew	Leaf	7.000.000 ^a
Grape berries	Skin	5-965
Ginger	Tuber	584
Milk thistle	Seed	2000 ^a
Mint	Young plant	16000
Oat	Grain	90-1796
Olive oil	Extra virgin	71-119 ^b
Poppy	Seed	6000 ^a
Red radish	Root tuber	600
Rice	Grain	1006
St. John's wort	Leaf	1.750.000
St. John's wort	Flower	4.000.000
Sunflower	Seed	29000 ^a
Tart cherry	Fruit	2.000-18.000
Tomato	Fruit	500-1399
Turmeric	Tuber	120.000 ^a
Walnuts	Fruit	3500
Wheat	Grain	125
White mustard	Seed	189.000 ^a

^apg/g dry tissue, ^bpg/mL

Melatonin in the world

In several countries, melatonin is sold over the counter; in others its free sale is prohibited. The usefulness of melatonin as a food additive continues to be a matter of debate. In Turkey, melatonin is now sold only a sleep aid without prescription. Because of its health benefits, it is important to know about the melatonin content of foods. One can conclude that relevant quantities of melatonin are present in most vegetables, fruit, nuts and cereals. In particular, interest can be given to some foods which are commonly consumed in Turkey or in Mediterranean diets. Most prominent foods rich in melatonin in Mediterranean diets are nuts, grapes, cherries, tomato

berries, species, olive-based products (black or green olive, olive oil) and a variety of grains. Currently, it is believed that some of the health benefits from Mediterranean diets are derived from their phytochemicals including phenylpropanoids (or phenolic compounds), isoprenoids, alkaloids and melatonin [8]. Below two examples will be given regarding to putative melatonin efficacy in one functional food (walnut) and in one officinal plant (St. John's wort).

Melatonin in walnuts

Walnuts (*Juglans regia* L.) are becoming of interest as a healthy foodstuff because their regular consumption has been reported to decrease the risk of heart disease [9, 10]. In a recent meta-analysis, thirteen studies representing 365 participants were included and authors found that high-walnut-enriched diets significantly decreased total and LDL cholesterol for the duration of the short-term trials [11]. According to the food composition database published by the US Department of Agriculture, 100 g of walnuts contain 15.2 g protein, 65.2 g fat, and 6.7 g dietary fiber. Whereas most nuts are high in monounsaturated fatty acids, walnuts are composed largely of polyunsaturated fatty acids (47.2 g), especially alpha-linolenic acid (18:3n3; 9.1 g) and linoleic acid (18:2n6; 38.1 g) [12]. The health benefits of walnuts are usually attributed to their high content of ω -3 fatty acids and, to a lesser degree, to the amount of vitamin E they contain. It was recently reported that melatonin is also present in walnuts and, when eaten, their consumption increases blood melatonin concentrations [13]. The rise in blood melatonin levels correlates with an increased antioxidative capacity of this fluid. This increment may also be protective against cardiovascular damage and cancer initiation and growth.

The influence of walnut consumption on cancer growth has also been investigated. Hardman et al. [14] injected human breast cancer cells into mice. They fed the animals with two different diets which were isocaloric, isonutrient and relevant to human consumption. The walnut diet for the mice was formulated to provide 18% of calories from walnuts. The results of this study demonstrated that the addition of walnuts to the diet slowed the cancer growth. In our laboratory, we are already investigating the efficacy of walnuts in human prostate cancer growth in mice. From the preliminary results of this ongoing study, we can conclude that walnut diet has also inhibits prostate tumor growth in this experimental model.

Melatonin in St. John's wort (*hypericum perforatum* L.)

St. John's wort is a yellow-flowering, perennial herb native to Europe, West Asia, and North Africa, which has been naturalized to North and South America. It has been used for centuries as an antibiotic, antiviral, antioxidant, anti-inflammatory, sedating and antidepressant for a variety of diseases [15]. By far the most pharmacological research has been done to investigate the antidepressant activity of St. John's wort extracts and clinical benefits has been reported [16].

Although major beneficial effects of St. John's wort are believed to derive from its active compounds such as hypericin and hyperforin still, 30–50% of its compounds are as yet not structurally defined and some of these might well contribute to its beneficial clinical effects [17]. We believe that one of its active compounds is melatonin (table 1) [18, 19]. Melatonin might contribute virtually all the beneficial effects of St. John's wort. Melatonin is a well established antibiotic [20], antiviral [21], a powerful and multi-tasking antioxidant [22], a strong anti-inflammatory [23], and a very useful sedating and analgesic agent [24, 25].

A crucial and encouraging coincidence for melatonin and efficacy of St. John's wort is in the reduction of depression. Although one early study reported negative results, several subsequent studies found that melatonin significantly reduced depression ratings in patients with winter depression [26] or seasonal affective disorder [27]. Because the clinical usage of melatonin was not approved by FDA, physicians are generally reluctant to design clinical trials to identify the efficacy of melatonin as an antidepressant.

Although the results of the clinical trials on the possible antidepressant effects of melatonin are not yet sufficient or conclusive, it is noteworthy that within the last decade, a pure melatonin receptor agonist, agomelatine, has been commercialized as a potent antidepressant drug [28] and has exhibited remarkable clinical success [29].

Within the European Community, St. John's wort products are available both as food supplements and as drugs (and among the drugs, both in the categories 'well-established use' and 'traditional use'). In the United States, St. John's wort also is available as a dietary supplement and is therefore not subject to stringent drug regulations. In our country, it is sold as a food supplement.

In conclusion, a variety of chronic diseases such as metabolic, neurologic, and mood among others seem to occupy the bulk of the health problems in

developed and developing countries. It also seems that functional foods and officinal plants have definitely a future in 21th century medicine and one reason may relate to the melatonin they contain.

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