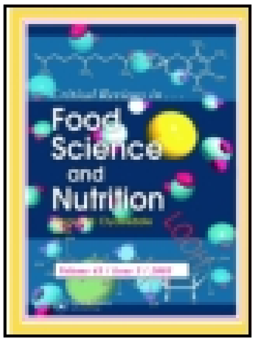

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Melatonin intake and effects on human health.

MELATONIN INTAKE AND POTENTIAL CHRONOBIOLOGICAL EFFECTS ON HUMAN HEALTH

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ABSTRACT

Melatonin is an indolamine with a recognized chronobiotic role. In turn, the supplementation of melatonin through capsules has been shown to be efficient in the modulation of inflammatory markers, oxidative stress, as well as in the control of hypertension and metabolic syndrome. However, the science of nutrition is interested in the study of the food sources of this hormone and its possible therapeutic effects. Thus, this review aimed to identify and present scientific papers that quantified melatonin in foods and evaluated its application in intervention studies. In total, 278 studies were found, of which 17 were included in this review. The results show that meats, fish, eggs, cereals, tubers, oilseeds, mushrooms, fruits, vegetables, alcoholic and non-alcoholic beverages and dairy products had some items analyzed for their melatonin concentrations. The concentrations reported presented considerable amplitude among different foods and even within the same species, possibly due to differences in cultivation and different hormonal dosing techniques. Also, different concentrations of melatonin can be presented for the same food when submitted to processes such as cooking, roasting or fermentation. The intervention studies presented positive results regarding the consumption of foods rich in melatonin and clinical-metabolic indicators. However, in order to guide nutritional behavior, it is necessary to consult a composition table that makes melatonin concentrations available and considers the processes involved in the preparation of the food. With this table, it will be possible to analyze the real effect of habitual consumption of melatonin from food on health.

Keywords

Food Analysis. Food Composition. Food Intake. Melatonin. Nutritional Sciences.

INTRODUCTION

In vertebrates, melatonin (N-acetyl-5-methoxytryptamine) is an indolaminergic hormone (molar mass 232.278 g/mol) synthesized mainly by the pineal gland, from the metabolism of tryptophan via serotonin after two enzymatic transformations that acetylate and replace the hydroxyl group by methoxy (Figure 1). Initially isolated by Aaron Lerner and colleagues at Yale University in 1958, the hormone can also be synthesized in the retina, appendix, bone marrow, lymphocytes, platelets and gastrointestinal tract (Aaron B. Lerner et al. 1958; Bubenik, 2008).

Melatonin is rapidly metabolized by the liver and its metabolite (6-sulfatoximelatonin – aMT6s), is identified in urine. This urinary melatonin, measured in the early hours of the morning, has a strong correlation with nocturnal production, and is often analyzed in scientific studies, which point to its inverse association with concentrations of uric acid and C-reactive protein (CRP), recognized metabolic and inflammatory markers, respectively (Cook et al. 2000; Masue et al. 2012).

In humans, its biosynthesis and secretion show a circadian pattern, with an increase between 6:00 p.m. and 8:00 p.m., peak at midnight and decline at 5:00 in the morning. This pattern is altered through aging, resulting in a reduction in the production of this hormone and consequent sleep disturbance (Benloucif et al. 2008).

In clinical practice, melatonin is used in the treatment of disorders such as insomnia, sleep-wake cycle with different periods of 24 hours, fragmentation, behavioral disorders of REM sleep, prolonged sleep latency and sleep corrections, especially in the elderly. Thus, it is seen as an important chronobiotic capable of synchronizing various functions of the organism(Pandi-Perumal et al. 2007).

In addition, it has anti-inflammatory, antioxidant and antiproliferative effects, modulates circadian rhythm, energy metabolism, improves glucose intolerance and lipid profile. Thus, studies are conducted aiming at evaluating the association between melatonin concentration and several cardiometabolic markers (Corbalán-Tutau et al. 2014).

By identifying this association and possible therapeutic effect, melatonin supplementation has emerged as a possible strategy in the treatment of obesity, hypertension and metabolic syndrome (Mesri Alamdari et al. 2015; Koziróg et al. 2011). In obese women, melatonin supplementation (6mg/day – 2 capsules of 3mg, 2 hours before sleep) indicated an improvement in inflammatory parameters such as tumor necrosis factor alpha (TNF-α) and interleukin-6 (IL-6) (Mesri Alamdari et al. 2015).

In patients with metabolic syndrome, supplementation (5 mg/day, 2 hours before sleep) for two months was able to improve antioxidant defense, verified by increased activity of the enzyme catalase (CAT) and the reduction of the concentrations of substances reactive to thiobarbituric acid (TBARS), LDL cholesterol and blood pressure (Koziróg et al. 2011).

To date, intervention studies have been conducted mostly with the supplementation of melatonin through capsules. Considering that food can act as a stimulus for the release of endogenous melatonin in addition to the dietary supplementation of this hormone, the nutrition science is interested in the study of food sources of melatonin and its possible therapeutic effects (Bubenik, 2002).

In view of the above, the present review aimed to identify and present scientific papers that quantified melatonin in foods and evaluated its application in intervention studies.

METHODOLOGY

Searches were held in electronic databases, PubMed / Medline and Scopus, with no limitation to year of publication. The following descriptors were used: Melatonin, Food Composition, Food Analysis, Food Intake and Vegetables. The search was restricted to studies published in English.

Interventional, longitudinal and transverse studies with men and /or women aged 18 years or older who used melatonin in some specific situation or only underwent their chemical analysis were included. We excluded studies that had other outcome or explanatory variables other than those previously mentioned; those that included other age groups and did not present differentiated results between them. Qualitative studies were excluded as well as tutorials, editorials, news, letters, comments, reviews, expert opinions, narrative and systematic reviews, meta-analyzes, case studies or conference proceedings.

In total, 278 studies were found but 75 studies were pre-selected after reading the titles, excluding the narrative and systematic reviews, meta-analyzes, case studies, original studies with different themes of interest and repetitions.

Subsequently, the abstracts were read and 67 studies were selected. Finally, after reading the whole studies, 17 studies were included in the present review (Figure 2).

RESULTS AND DISCUSSION

MELATONIN IN FOOD

Meat, fish and eggs

To date, only one study has been conducted with the objective of quantifying the concentration of melatonin in meat and meat by-products. The hormone was detected in all the samples evaluated, as in chicken heart and liver blend (1.1 ± 0.01 ng/g), chicken meat with skin

(2.3 ± 0.23 ng/g), lamb (1.6 ± 0.14 ng/g), beef (2.1 ± 0.13 ng/g), pork (2.5 ± 0.18 ng/g), salmon 3.7 ± 0.21 ng/g) and dried egg powder (6.1 ± 0.95 ng/g) (Table 1) (Tan et al. 2014).

Taking into consideration the presence of melatonin in meat, a study based on two cohorts The Nurses' Health Study (NHS; n = 585) and NHS II (n = 413), assessed the association of nutrients, dietary factors and food groups with the concentration of creatinine-adjusted 6-sulfatoximelatonin in healthy women. It was found that a high consumption of red meat was associated with a lower concentration of aMT6s excreted. Thus, although some nutrients are associated with melatonin, certain foods such as red meat, may increase the risk of diseases such as cancer, and promote the reduction of the concentration of urinary melatonin (Schernhammer et al. 2009).

Cereals and tubers

In cereals grown in Egypt, melatonin concentrations were detected in corn (187.8 ng/100g), rice (149.8 ng/100g), ginger (142.3 ng/100g) and barley grains (87.3 ng/100g) (Badria, 2002). Once harvested, barley can be germinated and transformed into malt and thus assigned to brewing. The concentration of melatonin differs according to the production stage, showing peaks at the beginning (339 ± 9 pg/mL) and after the second fermentation (333 ± 7 pg/mL). Moreover, the amount of melatonin in the beverage is proportional to its alcohol content (Garcia-Moreno, Calvo, and Maldonado, 2013).

Oilseeds

The walnut tree (*Juglans regia*) is native to Europe and Asia and its fruits, nuts, are consumed as part of the Mediterranean diet. When comparing four distinct cultivators (*Serr*, *Hartley*, *Chandler* and *Howard*) melatonin concentrations by fresh weight were found to be 1.02 ± 0.06 ng/g; 1.77 ± 0.14 ng/g; 1.37 ± 0.17 ng/g; 1.9 ± 0.4 ng/g, respectively (Tapia et al. 2013).

The basis of the Moroccan diet, argan oil, has high concentrations of linoleic and oleic acid (mean of 38 and 45%, respectively), polyphenols and tocopherols. A study revealed that the concentration of melatonin in argan oil is on the average 60.5 ± 51.2 ng/kg of oil, higher values than those found in extra virgin olive oil (30.8 ± 12.9 ng/kg). In addition, it has been identified that the hormonal concentration varies according to the method of extraction, traditional or industrialized, and the oils extracted by the traditional method have the highest concentrations (Venegas et al. 2011).

In Spain, researchers found melatonin concentrations in virgin olive oil (71 ± 15.1 and 119 ± 2.93 pg/mL), refined olive oil (53 ± 5.6 and 75 ± 6.92 pg/mL) and sunflower oil (50 ± 12.2 pg/mL) (de la Puerta et al. 2007).

Mushrooms

Several species of mushrooms are consumed by virtue of their known nutritional value, tonic and medicinal properties, in addition to their versatile use in cooking. Among the world’s leading producers of mushrooms is Poland, a central European country. A study carried out with species cultivated in that country analyzed indole compounds, including melatonin, in *Boletus edulis*, *Suillus luteus* and *Pleurotus Ostreatus* species (acquired from a local shop). The hormone was identified in two species, *B. edulis* (0.68 mg/100g) and *S. luteus* (0.71 mg/100g), respectively (Muszynska, Sulkowska-Ziaja, and Ekiert 2011).

Mushrooms are usually consumed by the population after being subjected to heat treatment. Considering this, extracts from six species of edible mushrooms were analyzed before and after treatment. Of the six species, melatonin was not detected in two species – *Pleurotus ostreatus* and *Armillaria mellea*. *Cantharellus cibarius* species had a mean melatonin content of 0.14 ± 0.011 mg/100g before thermal processing and increased after cooking, 4.40 ± 0.05mg/100g. Also, melatonin was not identified in the raw sample of the *Boletus badius* species, however after cooking it had a concentration of 0.71 ± 0.02 mg/100g. A reduction in melatonin concentration after cooking was observed in *Boletus edulis* species (before treatment 0.68 ± 0.006 mg/100g) and *Lactarius deliciosus* species (before treatment 1.29 ± 0.077mg/100g) (Muszyńska and Sułkowska-Ziaja 2012).

In summary, subjecting various species of mushrooms to a heat treatment may alter their indolic content, due to their instability when subjected to high temperatures.

Fruits and beverages

Several studies have been conducted with the aim of quantifying melatonin concentrations in fruits and vegetables. Among them, the concentration of melatonin was measured in eight different species of cherries grown in the Jerte Valley, located in the Province of Cáceres, Spain. The respective concentrations identified according to species were *Burlat* (22.4 ± 1.2 ng/100g), *Navalinda* (2.7 ± 2.4 ng/100g), *Van* (1.4 ± 0.9 ng/100g), *Pico limon negro* (0.6 ± 0.7 ng/100g), *Sweetheart* (6.0 ± 2.0 ng/100g), *Pico negro* (11.5 ± 3.3 ng/100g), *Pico Colorado* 4.8 ± 2.2 ng/100g) and *Ambrune* (not detected) (González-Gómez et al. 2009).

Two fruits are commonly consumed in several countries, tomato (*Lycopersicon esculentum*) and strawberry (*Fragaria ananassa*). Melatonin in strawberries presented a variation of 1.38 to 11.26 ng/g (fresh weight), on the other hand for tomato cultivars, the concentration range was 4.11 ng/g to 114.52 ng/g (fresh weight) (Stürtz et al. 2011).

Recurring in the Mediterranean diet, grape and its by-products are also rich in melatonin. A study in Italy quantified melatonin concentrations in red, white and dessert wines, grape juices and Modena balsamic vinegar. The highest concentration of melatonin was detected in Melag red wine (0.62 ± 0.04 ng/mL) where concentrations in red wines were higher than those found in dessert wines. In the vinegar, melatonin concentration was low (0.13 ± 0.03 ng/mL) and was not detected in the grape juices (Vitalini et al. 2013).

In the evaluation of extracts of eight different *Vitis vinifera* cultivars, the following concentrations of melatonin were identified: *Nebbiolo* (0.965 ng/g), *Croatina* (0.870 ng/g), *Sangiovese* (0.332 ng/g), *Merlot* ((0,264 ng/g), *Marzemino* (0.031 ng/g), *Cabernet Franc* (0.005 ng/g), *Cabernet Sauvignon* (0.422 ng/g) and *Barbera* (0.633 ng/g) (Iriti, Rossoni, and Faoro 2006).

Considering that the fermentation process may increase the concentration of melatonin in beverage, different researches have been conducted in this area. Among them, a wine produced from two cultivars of pomegranates was developed and its content analyzed. The wine produced with the cultivar *Wonderful* presented a melatonin concentration of 5.50 ng/mL and the cultivar *Mollar de Elche*, 0.54 ng/mL (Mena et al. 2012). Lastly, a study analyzed the content of orange wine and the oscillations of melatonin concentration during its manufacture. Melatonin concentration increased from the start of the process (2.49 ± 0.03 ng/mL) until the 15th day of fermentation (20.0 ± 2.02 ng/ mL) (Fernández-Pachõn et al. 2014). Based on the expressive content of melatonin in the new fermented beverages and the interest of the industry in its production, studies should be conducted with the purpose of evaluating the possible effects of the consumption of these beverages on the cycle of melatonin in healthy and sick individuals.

Coffee

Coffee is a beverage made from the roasted beans from the coffee fruit and is present in the routine of a large portion of the world's population. Besides containing high concentration of caffeine, which promotes alertness and prolonged attention, it has antioxidant compounds and consequent health benefits to consumers.

Originally from West Africa, *Coffea canephora* (robusta) is considered one of the most consumed coffee species in the world and, combined with *Coffea arabica* (arabica), they are used in the production of soluble and expresso coffees. With regard to its composition, *C. canephora* tissues were tested and a high melatonin content (115.25 ± 6μ/g) was found in the green bean after 9 months of cultivation (Ramakrishna et al. 2012a).

Considering the roasting, milling and infusion processes of coffee, Ramakrishna et al. (2011) quantified the concentration of the hormone in green, roasted grains and in the infusion of *C.canephora* and *C. arabica*. Melatonin was detected in green beans (5.8 ± 0.8 μg/g), roasted beans (8.0 ± 0.9 μg/g) and the infusion of *C. canephora species* (3.0 ± 0.6 μg/50 mL). In the *C. arabica* species, the concentrations found were 6.8 ± 0.4 μ/g in the green beans, 9.6 ± 0.8 μ/g in the roasted beans and 3.9 ± 0.2 μ /50 mL in the prepared beverage (Ramakrishna et al. 2012b).

Due to this known concentration of melatonin in coffee, a clinical study evaluated the impact of caffeinated beverage consumption on the quality and quantity of sleep in adults and it identified a reduction in the excretion of the melatonin metabolite in morning urine. Thus, although it contains melatonin, coffee consumption should be avoided at night because of its stimulating ability and possible influence on melatonin cycle (Shilo et al. 2002).

Dairy products

Milk and its derivatives are a group of foods with great nutritional value and have widespread consumption around the world. With the support of health professionals, breastfeeding is a practice that is stimulated by its various benefits. Among them, it offers the child considerable amounts of the hormone melatonin through breast milk (Engler et al. 2012). In this context, indolamine concentrations in breast milk may vary within 24 hours, being undetectable during the day, elevated overnight and reaching a peak at 3:00 am, then its concentration is attenuated. The same researchers evaluated melatonin concentrations in artificial formulas, but their values were not detected (Engler et al. 2012).

In relation to cow milk, when comparing different types of milk processing, a mean concentration of 13.6 pg/mL was found in raw milk and the values vary between the animals (1.3 to 25 pg/mL). Raw milk and milk powder enriched with melatonin had the highest concentrations of the hormone, while UHT (ultra high temperature) milk had the lowest concentrations (Schaper, Koethe, and Braun 2015).

IMPLICATIONS OF MELATONIN CONSUMPTION ON HEALTH: INTERVENTION STUDIES

Considering the high concentration of melatonin in foods, research has been carried out in order to evaluate the consumption of these foods and their impact on the health of healthy and sick individuals.

Among them, a study carried out in Japan evaluated the effect of the consumption of six vegetables (sweet corn, goya-bitter gourd, kaiware-Japanese radish sprout, shungiku-garland chrysanthemum, shimeji mushroom, and shiitake mushroom) on the concentrations of melatonin metabolite (aMT6s) in healthy women. The individuals were allocated in two groups, the intervention group being oriented to consume a large amount (350 g/day) of the vegetables for 65 days, and the control group to avoid the consumption of these same vegetables in the same period. At the end of the intervention, the mean daily melatonin intake in the control group was 5.3 ng and 1288 ng in the intervention group. In this latter group, the mean aMT6 concentration changed from 48.1 ng/mg to 49.6 ng/mg, adjusted for creatinine concentrations. In the control group, the mean concentration of aMT6s ranged from 55.5 ng/mg to 50.8 ng/mg. Comparing the groups, these concentrations showed statistical significance (p = 0.03) (Oba et al. 2008).

In conclusion, the authors suggest that increased consumption of vegetables rich in melatonin increases the circulatory concentrations of this hormone (Oba et al. 2008). In fact, this effect was observed, however, one should consider the high consumption of vegetables that was necessary to cause an increase in the excretion of aMT6s. It is emphasized that certain individuals may not tolerate this consumption pattern.

For the fruit group, one study evaluated the consumption of six fruits (orange, mango, pineapple, banana, papaya and pawpaw) individually in 30 healthy individuals (15 men and 15 women). The fruits were processed according to the daily consumption tolerance (juice or unit) and were consumed in the evening after meal, between 6 pm and 6:30 pm. An increase in aMT6s urinary concentration was observed after the intake of pineapple (266%, p = 0.004), banana (180%, p = 0.001), and orange (47%, p = 0.007) (Johns et al. 2013). With this, consumption of these fruits can be stimulated close to bedtime.

Likewise, a study evaluated the consumption of fruits and fruit juices containing melatonin and its possible influence on the antioxidant profile of twelve healthy male volunteers. The participants ingested juice extracted from a kilo of orange / pineapple or two whole bananas, with an interval of one week between fruit juices or fruit. The highest concentration of melatonin in the serum was observed 120 minutes after fruit consumption, being the values significantly increased after consumption of pineapple (146 versus 48 pg/mL, p = 0.002), orange (151 versus 40 pg/mL, P = 0.005), and banana (140 versus 32 pg/mL, p = 0.008) (Sae-Teaw et al. 2013).

The positive correlation between serum melatonin concentration and antioxidant capacity after fruit consumption was identified. There was an increase in the ferric reducing antioxidant power (FRAP) (increase of 7--14%, p = 0.004) and oxygen radical absorption capacity (ORAC) (increase of 6--9%, p = 0.002). These findings suggest that tropical fruit consumption increases the concentrations of melatonin in the serum, as well as improves antioxidant capacity (Sae-Teaw et al. 2013).

Suggestion that the consumption of cherry (*tart cherry*) is able to increase the concentration of aMT6s in adults and promote improved sleep, a placebo-controlled study was conducted with twenty volunteers for seven days. Juice intake – 30 mL of concentrated juice (90-100 cherries) diluted in 200 mL of water – increased total excreted melatonin concentration and the total sleep time of the participants (Howatson et al. 2012).

Studies on red wine are well documented in the literature. Twelve volunteers were asked to consume red wine (125 mL) or a capsule of red wine extract (300 mg) or water (125 mL) and thereby evaluate possible effects on salivary antioxidant activity. After the study, it was concluded that consuming wine was not able to improve antioxidant activity, unlike the wine extract administered in capsules (Varoni et al. 2013).

Rich in antioxidant compounds, beer is one of the most consumed beverages worldwide. Different brands sold in Spain were analyzed for the content of melatonin and it was verified that the greater the alcohol content of the beer, the greater the concentration of melatonin. In the same study, it was suggested that moderate consumption of beer has an effect on total antioxidant capacity (TAC) in the serum of seven volunteers (Maldonado, Moreno, and Calvo 2009). Thus, moderate beer consumption can improve diet quality in relation to melatonin in healthy adults.

The study, *postmenopausal Women's Alcohol*, assessed alcohol consumption and excretion of aMT6s in post-menopausal women who did follow hormone replacement therapy. In this study, the women consumed a controlled diet and followed treatments (non-alcoholic beverage, 15g alcohol/day and 30g alcohol /day) for a period of 8 weeks for each treatment, with 2 to 5 weeks of washout (no alcohol). The aMT6s were dosed in 3 moments: Start, 4 weeks and 8 weeks of consumption. At the end, it was observed that, after adjusting body mass index, hours of sleep, hours of the day and aMT6s baseline, alcohol consumption in no treatment was able to modify the excretion of urinary aMT6s (Hartman et al. 2012).

The consumption of alcoholic beverages before bedtime should be investigated in studies that take into account not only the increase in melatonin excretion but also the quality and cycle of sleep as a consequence of the acute and chronic consumption of different doses and beverages.

FINAL CONSIDERATIONS

The presence of the hormone melatonin was detected in foods belonging to several food groups of habitual consumption in various populations. Reported concentrations presented considerable amplitude (pg/g-μg/g of food) among different foods and even within the same species, possibly due to crop differences in cultivation (soil type, climate and solar incidence) or different hormonal dosage techniques.

A relevant alteration was also identified in the concentrations of melatonin in foods after processes such as cooking, roasting or fermentation, thus food preparation should be considered for the supply of melatonin from food.

In this context, the disparity in relation to the information on the content of melatonin makes it necessary to consult a table that makes available melatonin/g concentrations in food which also considers the processes involved in its preparation. With this table, it will be possible to analyze the real effect of melatonin consumption on the health of individuals.

Finally, the intervention studies presented positive results regarding the consumption of foods rich in melatonin, clinical parameters and metabolic parameters, however, it is necessary to consider the volume of food ingested to promote a change in these parameters and to evaluate whether this quantity is consistent with daily intake capacity.

Footnotes

The authors declare that they have no conflict of interest.

Author Contributions

Study conception and design, critical revisions of manuscript, data collection and analysis – Bressan, J.; Hermsdorff, H.H.M, and Domingos, A.L.G.

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Table 1. Concentration of melatonin in food, dosage technique and country of cultivation/production

Food	Melatonin concentration (Mean ± standard deviation)	Dosage technique	Country	Reference
Meat/Fish/Egg				
Chicken heart and liver blend	1.1 ± 0.01 ng/g	HPLC	USA	(Tan et al. 2014)
Chicken meat with skin	2.3 ± 0.23 ng/g	HPLC	USA	(Tan et al. 2014)
Lamb	1.6 ± 0.14 ng/g	HPLC	USA	(Tan et al. 2014)
Beef	2.1 ± 0.13 ng/g	HPLC	USA	(Tan et al. 2014)
Pork	2.5 ± 0.18 ng/g	HPLC	USA	(Tan et al. 2014)
Salmon	3.7 ± 0.21 ng/g	HPLC	USA	(Tan et al. 2014)
Dried egg powder	6.1 ± 0.95 ng/g	HPLC	USA	(Tan et al. 2014)
Cereals/Tubers				
Corn *(Zea mays)*	187.8 ng/100g	GC/MS	Egypt	(Badria, 2002)
Rice *(Oryza sativum)*	149.8 ng/100g	GC/MS	Egypt	(Badria, 2002)
Ginger *(Zingiber officinale)*	142.3 ng/100g	GC/MS	Egypt	(Badria, 2002)
Carrot *(Daucus carota)*	49.4 ng/100g	GC/MS	Egypt	(Badria, 2002)
Potato *(Solanum tuberosum)*	ND	GC/MS	Egypt	(Badria, 2002)
Barley *(Hordeum vulagare)*	87.3 ng/100g	GC/MS	Egypt	(Badria, 2002)
Oleaginosas Oilseeds				
Walnut (cultivar *Serr*)	1.02 ± 0.06 ng/g	HPLC/MS	Spain	(Tapia et al. 2013)
Walnut (cultivar *Hartley*)	1.77 ± 0.14 ng/g	HPLC/MS	Spain	(Tapia et al. 2013)
Walnut (cultivar *Chandler*)	1.37 ± 0.17 ng/g	HPLC/MS	Spain	(Tapia et al. 2013)
Walnut (cultivar *Howard*)	1.9 ± 0.4 ng/g	HPLC/MS	Spain	(Tapia et al. 2013)
Argan Oil	60,5 ± 51,2 ng/kg	HPLC	Spain	(Venegas et al. 2011)
Extra virgin olive oil	30,8 ± 12,9 ng/kg	HPLC	Spain	(Venegas et al. 2011)
Virgin olive oil	71 ± 15.1 to 119 ± 2.93 pg/mL	ELISA	Spain	(de la Puerta et al. 2007)
Refined olive oil	53 ± 5.6 to 75 ± 6.92 pg/mL	ELISA	Spain	(de la Puerta et al. 2007)
Sunflower oil	50 ± 12.2 pg/mL	ELISA	Spain	(de la Puerta et al.

				2007)
Mushrooms				
Raw mushroom (*Suillus luteus*)	0.71 ± 0.077 mg/100g	HPLC	Poland	(Muszynska, Sulkowska-Ziaja, and Ekiert, 2011)
Raw mushroom *(Pleurotus ostreatus)*	ND	HPLC	Poland	(Muszyńska and Sułkowska-Ziaja, 2012)
Cooked mushroom *(Pleurotus ostreatus)*	< 0.001 mg/100 g	HPLC	Poland	(Muszyńska and Sułkowska-Ziaja, 2012)
Raw mushroom *(Armillaria mellea)*	< 0.001 mg/100 g	HPLC	Poland	(Muszyńska and Sułkowska-Ziaja, 2012)
Cooked mushroom *(Armillaria mellea)*	< 0.001 mg/100 g	HPLC	Poland	(Muszyńska and Sułkowska-Ziaja, 2012)
Raw mushroom *(Cantharellus cibarius)*	0.14 ± 0.011 mg/100g	HPLC	Poland	(Muszyńska and Sułkowska-Ziaja, 2012)
Cooked mushroom *(Cantharellus cibarius)*	4.40 ± 0.05 mg/100g	HPLC	Poland	(Muszyńska and Sułkowska-Ziaja, 2012)
Raw mushroom *(Boletus badius)*	< 0.001 mg/100 g	HPLC	Poland	(Muszyńska and Sułkowska-Ziaja, 2012)
Cooked mushroom (*Boletus badius)*	0.71 ± 0.02 mg/100g	HPLC	Poland	(Muszyńska and Sułkowska-Ziaja, 2012)
Raw mushroom (*Boletus edulis)*	0.68 ± 0.006 mg/100g	HPLC	Poland	(Muszyńska and Sułkowska-Ziaja, 2012)
Cooked mushroom (*Boletus edulis)*	< 0.001 mg/100g	HPLC	Poland	(Muszyńska and Sułkowska-Ziaja, 2012)
Raw mushroom *(Lactarius deliciosus)*	1.29 ± 0.077 mg/100g	HPLC	Poland	(Muszyńska and Sułkowska-Ziaja, 2012)
Cooked mushroom *(Lactarius deliciosus)*	< 0.001 mg/100g	HPLC	Poland	(Muszyńska and Sułkowska-Ziaja, 2012)
Fruits/Beverages				
Cherry *Burlat*	22.4 ± 1.2 ng/100g	HPLC	Spain	(González-Gómez et al. 2009)
Cherry *Navalinda*	2.7 ± 2.4 ng/100g	HPLC	Spain	(González-Gómez et al. 2009)
Cherry *Van*	1.4 ± 0.9 ng/100g	HPLC	Spain	(González-Gómez et

				al. 2009)
Cherry *Pico Limón Negro*	0.6 ± 0.7 ng/100g	HPLC	Spain	(González-Gómez et al. 2009)
Cherry *Sweetheart*	6.0 ± 2.0 ng/100g	HPLC	Spain	(González-Gómez et al. 2009)
Cherry *Pico Negro*	11.5 ± 3.3 ng/100g	HPLC	Spain	(González-Gómez et al. 2009)
Cherry *Pico Colorado*	4.8 ± 2.2 ng/100g	HPLC	Spain	(González-Gómez et al. 2009)
Cherry *Ambruné*	ND	HPLC	Spain	(González-Gómez et al. 2009)
Tomato *(Lycopersicon esculentum Bond)*	23.87 ± 2.02 ng/g	HPLC	Spain	(Stürtz et al. 2011)
Tomato *(Lycopersicon esculentum Marbone)*	114.5 ± 3.7 ng/g	HPLC	Spain	(Stürtz et al. 2011)
Strawberry *(Fragaria ananassa Camarosa)*	1.4 ± 0.6 ng/g	HPLC	Spain	(Stürtz et al. 2011)
Strawberry *(Fragaria ananassa Primoris)*	4.2 ± 0.7 ng/g	HPLC	Spain	(Stürtz et al. 2011)
Orange *(Citrus reticulata)*	150 ± 4 pg/g	HPLC	Thailand	(Sae-Teaw et al. 2013)
Pineapple *(Ananus comosus Merr.)*	302 ± 27 pg/g	HPLC	Thailand	(Sae-Teaw et al. 2013)
Banana *(Musa sapientum Linn.)*	8.9 ± 0.3 pg/g	HPLC	Thailand	(Sae-Teaw et al., 2013)
Mango	699 ± 75 pg/g	HPLC	Thailand	(Johns et al. 2013)
Pawpaw	241 ± 14 pg/g	HPLC	Thailand	(Johns et al. 2013)
Papaya	ND	HPLC	Thailand	(Johns et al. 2013)
Melag red wine	0.62 ± 0.04 ng/mL	HPLC	Italy	(Vitalini et al. 2013)
Dessert wine	0.17 ± 0.11 ng/mL	HPLC	Italy	(Vitalini et al. 2013)
Grape juice	ND	HPLC	Italy	(Vitalini et al. 2013)
Modena Balsamic vinegar	0.13 ± 0.03 ng/mL	HPLC	Italy	(Vitalini et al. 2013)
Grape (*Vitis vinífera Nebbiolo)*	0.965 ng/g	HPLC/ELISA	Italy	(Iriti, Rossoni, and Faoro, 2006)
Grape (*Vitis vinífera Croatina)*	0.870 ng/g	HPLC/ELISA	Italy	(Iriti, Rossoni, and Faoro, 2006)
Grape (*Vitis vinífera Sangiovese)*	0.332 ng/g	HPLC/ELISA	Italy	(Iriti, Rossoni, and Faoro, 2006)
Grape *(Vitis vinífera Merlot)*	0.264 ng/g	HPLC/ELISA	Italy	(Iriti, Rossoni, and Faoro, 2006)
Grape (*Vitis vinífera Marzemino)*	0.031 ng/g	HPLC/ELISA	Italy	(Iriti, Rossoni, and Faoro, 2006)
Grape *(Vitis vinífera Cabernet Franc)*	0.005 ng/g	HPLC/ELISA	Italy	(Iriti, Rossoni, and Faoro, 2006)

Grape (*Vitis vinífera Cabernet Sauvignon)*	0.422 ng/g	HPLC/ELISA	Italy	(Iriti, Rossoni, and Faoro, 2006)
Grape *(Vitis vinífera Barbera)*	0.633 ng/g	HPLC/ELISA	Italy	(Iriti, Rossoni, and Faoro, 2006)
Pomegranate wine (cultivar *Wonderful)*	5.50 ng/mL	LC-ESI MS/MS	Spain	(Mena et al. 2012)
Pomegranate wine (*Mollar de Elche)*	0.54 ng/mL	LC-ESI-MS/MS	Spain	(Mena et al. 2012)
Orange wine (beginning of fermentation)	2.49 ± 0.03 ng/mL	HPLC	Spain	(Fernández-Pachõn et al. 2014)
Orange wine (15 days of fermentation)	20.0 ± 2.02 ng/mL	HPLC	Spain	(Fernández-Pachõn et al. 2014)
Coffee				
Coffee *Coffea canephora* (green bean)	5.8 ± 0.8 µ/g	HPLC	India	(Ramakrishna et al. 2012)
Coffee *Coffea canephora* (roasted bean)	8.0 ± 0.9 µ/g	HPLC	India	(Ramakrishna et al. 2012)
Coffee *Coffea canephora* (infusion)	3.0 ± 0.6 µ/50 mL	HPLC	India	(Ramakrishna et al. 2012)
Coffee *Coffea arabica* (green bean)	6.8 ± 0.4µ/g	HPLC	India	(Ramakrishna et al. 2012)
Coffee *Coffea arabica* (roasted bean)	9.6 ± 0.8 µ/g	HPLC	India	(Ramakrishna et al. 2012)
Coffee *Coffea arabica* (infusion)	3.9 ± 0.2 µ/50 mL	HPLC	India	(Ramakrishna et al. 2012)
Dairy products				
Raw cow milk	13.6 ± 6.3 pg/mL	ELISA	Germany	(Schaper, Koethe, and Braun, 2015)
Powdered milk enriched with melatonin	12.4 ± 2.8 pg/mL	ELISA	Germany	(Schaper, Koethe, and Braun, 2015)
UHT milk	4.5 ± 1.7 pg/mL	ELISA	Germany	(Schaper, Koethe, and Braun, 2015)

ND: Not detected; MS: Mass spectrometry, HPLC: High-performance liquid chromatography, GS/MS: Gas chromatography–mass spectrometry.

LC-ESI-MS/MS: Liquid chromatography-electrospray ionization-tandem mass spectrometry

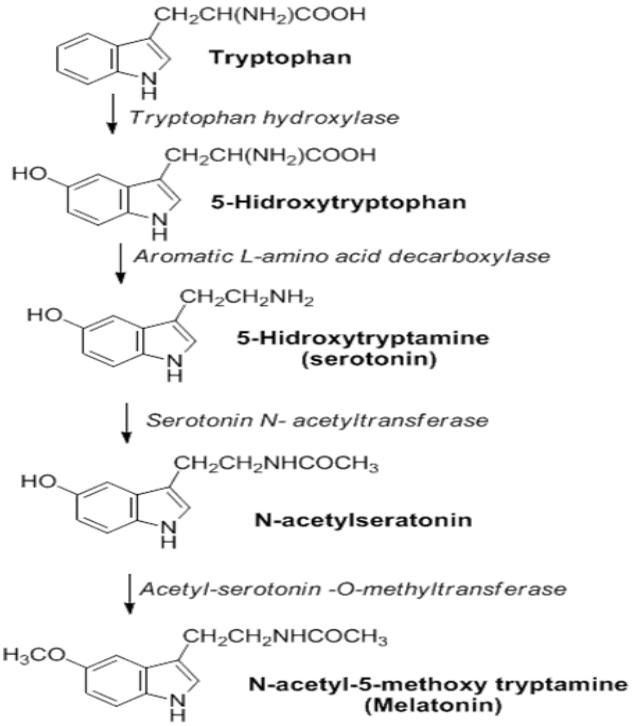

Fig 1. Melatonin biosynthesis.

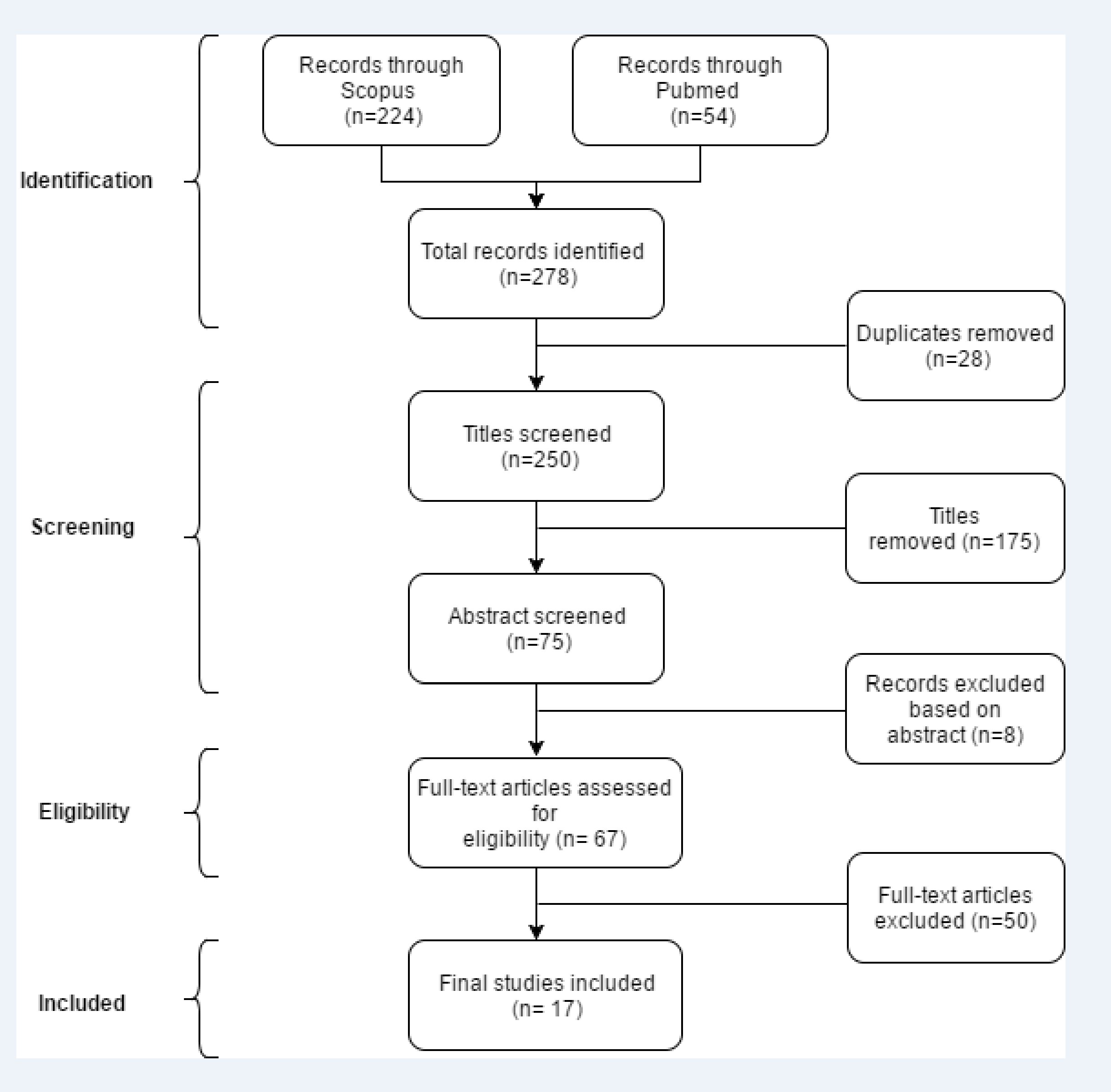

Fig 2. Flowchart of the steps followed to obtain the articles selected for this review.