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Melatonin and Exercise: Their Effects on Malondialdehyde and Lipid Peroxidation

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Abstract

Melatonin as an omnipresent molecule is secreted by the pineal gland. It is a strong free radical scavenger, which reduces nitric oxide (NO) generation within mitochondria. Exercise has great impacts on many body's homeostatic systems. Most human's organisms display rhythms and have 24 hours environmental cycles, which are called circadian rhythm. Melatonin is one of the circadian rhythm generator in various physiological variables. Exercises could regulate plasma melatonin levels. Melatonin scavenges reactive oxygen species (ROS) and reactive nitrogen species (RNS) and acts as the antioxidant cascade. It not only decreases the exercise induced-oxidative stress in the muscles but also enhances muscle antioxidant enzymes, such as superoxide dismutase. Body lipids and unsaturated fatty acids are prone to oxidation, while the free radicals penetrate into bilayer membrane structure lipid peroxidation is going to happen. Malondialdehyde (MDA) is created by free radicals, and it is one of the most frequent marker of lipid peroxidation. Exercise, its duration, and time of the day have immediate and or delayed effects on melatonin secretion. The combination of aerobic exercise and melatonin reduces the exercise induced-free radicals agents. Melatonin supplementation, especially while it combined with aerobic training, could decrease the lipid peroxidation and malondialdehyde. Melatonin could impede exercise-induced ROS, increase body health, and exercise-related adaptation.

Keywords: exercise, health, lipid peroxidation, malondialdehyde, melatonin, reactive oxygen species

1. Introduction

Melatonin is an omnipresent molecule that has various functional activities in plants and animals [1]. It is possibly associated with longevity in which their dysfunction is what

initiates the aging process [2, 3]. Melatonin was secreted by pinecone-like gland that is deeply placed in the brain which is called the “pineal gland.” This gland has sympathetic innervation as its main sources due to its special location in the brain [2]. The pineal gland is a tranquilizing organ leading to a high melatonin production in response to darkness. Serotonin (made from tryptophan) through the cascade of enzymatic reactions produces melatonin with chemical name N-acetyl-5-methoxy tryptamine. This gland is located outside the blood–brain barrier (BBB) and has large uptake of tryptophan which produces high melatonin levels [2]. This hormone is mostly secreted at night and results in sleep regulation, signaling the time of the day that acts as chronological pacemaker, and participates in various physiological functions.

2. The melatonin advantages for the body

Melatonin is a strong free radical scavenger which reduces nitric oxide (NO) generation within mitochondria. NO strongly interferes with components of the respiratory chain in the mitochondria [4, 5]. Melatonin has two direct and indirect antioxidant capacities, which directly scavenges free radicals and indirectly regulates the activity of antioxidant enzymes. When melatonin interacts with the toxic reactants, several metabolites are generated which per se act as direct free radical scavengers such as N1-acetyl-N2-formyl-5-methoxykynuramine (AFMK) [6]. Melatonin impacts toxic radicals and breaks them down, eliminates reactive oxygen species-induced H_2O_2 (one of the most important reactive oxygen species or ROS), acts on uncoupling proteins (UCPs), and decreases body heat production [7, 8]. Moreover, as melatonin decreases NO generation, melatonin leads to mitochondria function development, and due to increase in the mitochondria respiration, the ATP production and electron transportation increase as well [5, 9, 10].

To have a glance at the other importance of melatonin, we pointed to neurodegenerative diseases. Melatonin production in aged individuals declines and is known as the primary contributing factor for aged-related neurodegenerative diseases. Also, hypoxia, hypoglycemia, viruses, drug neurotoxicity, radiation, or noxious substances all could produce neural damage. Through antioxidant effects of melatonin, it has been proposed as a neuroprotective agent. Over the melatonin therapeutic value, it is used as treatment of Alzheimer disease (AD), Parkinson disease (PD), amyotrophic lateral sclerosis (ALS), stroke, and brain trauma. Neurodegenerative disorders mostly happen due to free radical-mediated damage and mitochondria dysfunction as common pathophysiological mechanism [11].

3. What is exercise, and how does it affect the melatonin?

According to the Center for Disease Control and Prevention (CDC), exercise is a subcategory of physical activity that is planned, structured, repetitive, and purposive that improves or maintains one or more components of physical fitness. Physical activity also refers to any bodily movement which is produced by the skeletal muscle contraction that increases energy expenditure more than basal level and enhances health. Furthermore, health is a human

condition with three dimensions as physical, social, and psychological. To clarify the benefit of exercise and physical activity, we have to define the physical inactivity which refers to those physical activities less than what is required for optimal health and prevention of premature death [12, 13].

There are huge differences between physical activity and physical fitness which should not be interchangeably used. According to CDC physical fitness is the ability to carry out daily tasks without fatigue and of course with plenty of energy to enjoy leisure time and respond to emergencies. Physical fitness has a number of components consisting of cardiorespiratory endurance, skeletal muscle endurance, skeletal muscle strength, skeletal muscle power, flexibility, balance, speed of movement, reaction time, and body composition. Physical activity according to above definition refers to any bodily movement produced by skeletal muscle contraction [12, 13].

Muscular strength is an essential factor for health and functional ability and consequently increases life quality. The importance of progressive resistance exercise had been clarified seen in World War II which was recommended for veteran rehabilitation. The important point of all resistance training is that the training must be “progressive” and progression is the act of advancing toward a specific goal which leads to continued improvement in muscle ability. Muscle development is under the effects of program variables such as exercise selection and order, number of sets and repetitions, and rest period length [14].

Physical activity and exercises are so important strategies to face chronic conditions, lower cancer risk, and synchronize the circadian system. Increasing physical activity and taking part in aerobic endurance activities, resistance training, and flexibility exercises have been shown to decrease the risk of several chronic diseases such as coronary heart disease, obesity, diabetes, low back pain, osteoporosis, and sarcopenia [12, 14–16]. Physical activities and exercises are nonphotic signals that entrain human circadian clock [16]. Physical activity could increase the melatonin levels, decrease estrogen production, and improve fat metabolism [15].

Cardiorespiratory fitness also is the capacity of the cardiovascular (both heart and vessels) and respiratory (lungs) systems to supply oxygen to the blood and consequently to the working skeletal muscles and the capacity of the muscles to use oxygen to produce energy for movement. The best test to determine the cardiorespiratory fitness is the maximum aerobic fitness; moreover in the human studies, length of time running or cycling in standardized test could examine the physiological/biochemical/psychological exhaustion [12].

Strength fitness is also another health component that is defined as the capacity of the skeletal muscle to move an external load. Balance is defined as the ability to control the body during the body movement, and flexibility is also defined as range of joint motion or range of motion (ROM) [12, 14].

To continue the importance of the combination of the exercise and melatonin on the body system, we have to deliberate some fundamental concepts of training. Overload as the first concept is the “gradual increase of stress placed upon the body during exercise training.” Specificity of training is that training should be specific to the body needs or both movement patterns and force-velocity characteristics. Also, the good training program should have

variation to support the training needs to remain optimal. In this case training periodization is defined as utilizes variation in training program design [14]. Exercise and physical activity can also act as preventer of chronic disease and regulate body systems. Regular activity and structured exercises are related to vast health benefits and body hormone regulation [12, 17, 18].

Exercise has great impacts on many body's homeostatic systems. Most human organisms display rhythms in their physiology and have 24 hour environmental cycle which is called circadian rhythm. Melatonin is one of the circadian rhythm generators in various physiological variables. Also, there are some voluntary rhythm modifiers such as activity or physical exercise; meal time can also act as circadian rhythm modifier signal [16]. Physical activity and exercise are nonphotic signals that regulate the human circadian clock and synchronize circadian system. Melatonin is one of the main signals of body clock that is commonly measured to report the effects of exercise on the circadian clock. Noteworthy almost different kinds of exercises and physical activities both acute and chronic could modify plasma melatonin levels. Meanwhile, endogenous profile of melatonin has different responses such as increase, decrease [19], or even unaffected to exercises that time of the day, and lighting condition is the most effective item on the melatonin secretion cycle even in response to exercises. As an overall consensus, those exercises which have been done at night or in the dark whether of moderate or high intensity result in delay in melatonin secretion. Indeed, the age does not influence the exercise-induced circadian rhythm of melatonin as nocturnal hormone. Besides the effects of exercises on the different phases of melatonin secretion, the exercises also transiently affect the melatonin levels. The mechanism of this transient changes in melatonin levels could be due to the circadian phase at that time exercise was undertaken. A bout of exercise increases the plasma melatonin levels, while regular training and exercises attenuate the melatonin [16]. There are several potent physiological factors that describe the melatonin changes. Melatonin acts as an antioxidant, and exercise especially strenuous exercise increases oxidative stress, hence melatonin which is secreted by the human body or even ingested capable of protecting against potential molecular damage [6]. It was reported that proximately after exercise melatonin levels increase and following 1 hour after physical activity, it returns to pre-exercise level [20]. Melatonin levels of trained individuals is higher in the morning compared to the evening, but in the following 3 weeks of hard training, the evening melatonin levels were higher than morning levels. Interestingly both morning and evening levels of melatonin decreased compared to pre-3 weeks of hard training. Well-trained individuals show an adaptive response to each training that they take part as their oxidative stress regulates and diurnal melatonin levels temporarily increase [16, 21]. Total mechanisms of the melatonin alteration following exercises remained unknown, but exercise-induced absolute rise in melatonin levels is more pronounced in the morning compared to the evening [22].

4. Exercises on the melatonin

4.1. Acute and strenuous exercises

Acute sport trainings and resistance exercises lead to change in the energy demands and are strong stimulation of muscle tissue. Intense exercises produce free radicals, inflammatory

responses, hormonal and biochemical disturbances, and metabolic and defensive changes [6]. Acute exercise increases oxygen consumption much more than rest time which makes muscles prone to oxidative stress. Oxygen molecule is a radical species per se and also results in generation of various free radicals, and those free radical species that are forming due to oxygen and nitrogen are the most important in the living organisms [23]. While subjects have routine life pattern, their energy demands and blood vessel contribution are balanced. During the acute or resistance exercise training, oxygen consumption of both striated and smooth muscles increases dramatically which leads to increase in reactive oxygen/nitrogen species that is called RONS. While exercise-derived RONS are generated, the body antioxidant defense system starts to work and protects cells and tissues against free radicals. The imbalance between body antioxidant defense system and RONS is called oxidative stress [24]. Low levels of ROS regulate muscle force through calcium release mechanism, and influencing myofilament structure creates adaptive response to training. However, high levels of ROS reduce force production and result in muscular fatigue [25].

Melatonin due to its scavenging ability could directly interact with a variety of oxygen- and nitrogen-based radicals. It is an antioxidant that regulates the activities of other antioxidant enzymes [6, 25]. Strenuous sport activities lead to acute muscle injuries that are indicated by muscle soreness, prolong loss of muscle function, and leakage of muscle proteins. Acute exercise-induced muscle injuries consist of 30–67% of athletic injuries, while exercise-induced severe muscle injuries could impede the athletic progression. Muscle damages result in multidimensional changes in muscle tissue such as inflammation that per se encourage the free radical production and muscle atrophy [26, 27]. This condition could be reduced with optimal nutrition mostly by increasing dietary content of nutritional antioxidant. Melatonin as one of the body-secreted natural antioxidants could cross all barriers and reduce the oxidative damage in almost every environment in the body. Intensive exercises cause abundant changes in immunity and also change the carbohydrate and lipid metabolism that make athletes vulnerable to infection. In this case melatonin protects heart muscle cells and other body parts from exercise-induced inflammation [6, 27]. As previously mentioned, strenuous exercise muscle injuries lead to protein degradation that encourages muscle injury. Whenever exercise-induced protein degradation and consequent muscle atrophy are limited, the extent of muscle injuries could be blunted. Melatonin is one of the most effective factors that could limit muscle injuries. It was shown that melatonin inhibited the nuclear factor kappa-B (NFκB) activation that prevents the cytokine-induced atrophy and thus muscle injury. Melatonin also decreases proinflammatory cytokines, tumor necrosis factor-α (TNF-α), and interleukin-6 (IL-6) expression within the muscle. Also, muscle atrophy F-box (MAF_{bx}) and muscle RING finger 1 (MURF-1) are inhibited by melatonin. MAF_{bx} is a muscle-specific ubiquitin ligase that mediates the degradation of muscle-specific transcription factor MyoD. MURF-1 also is a member of ubiquitin ligase family which interacts with the giant protein titin in the muscle and is called titin-associated protein that expert antihypertrophic activity [28, 29]. In this case melatonin through the elevation of the expression of the muscle Akt could reduce the ratio of the MAF_{bx}/MURF-1 and inhibits the breakdown of the structural muscle protein such as myosin heavy chain (**Figure 1**). The functional role of the melatonin and strenuous muscle injury prevention is not fully understood, but the melatonin effects on the muscle cytokines, NFκB activation, muscle Akt elevation, and consequent decline in the MAF_{bx}/MURF-1 could open new points of view to the melatonin protection mechanism [26].

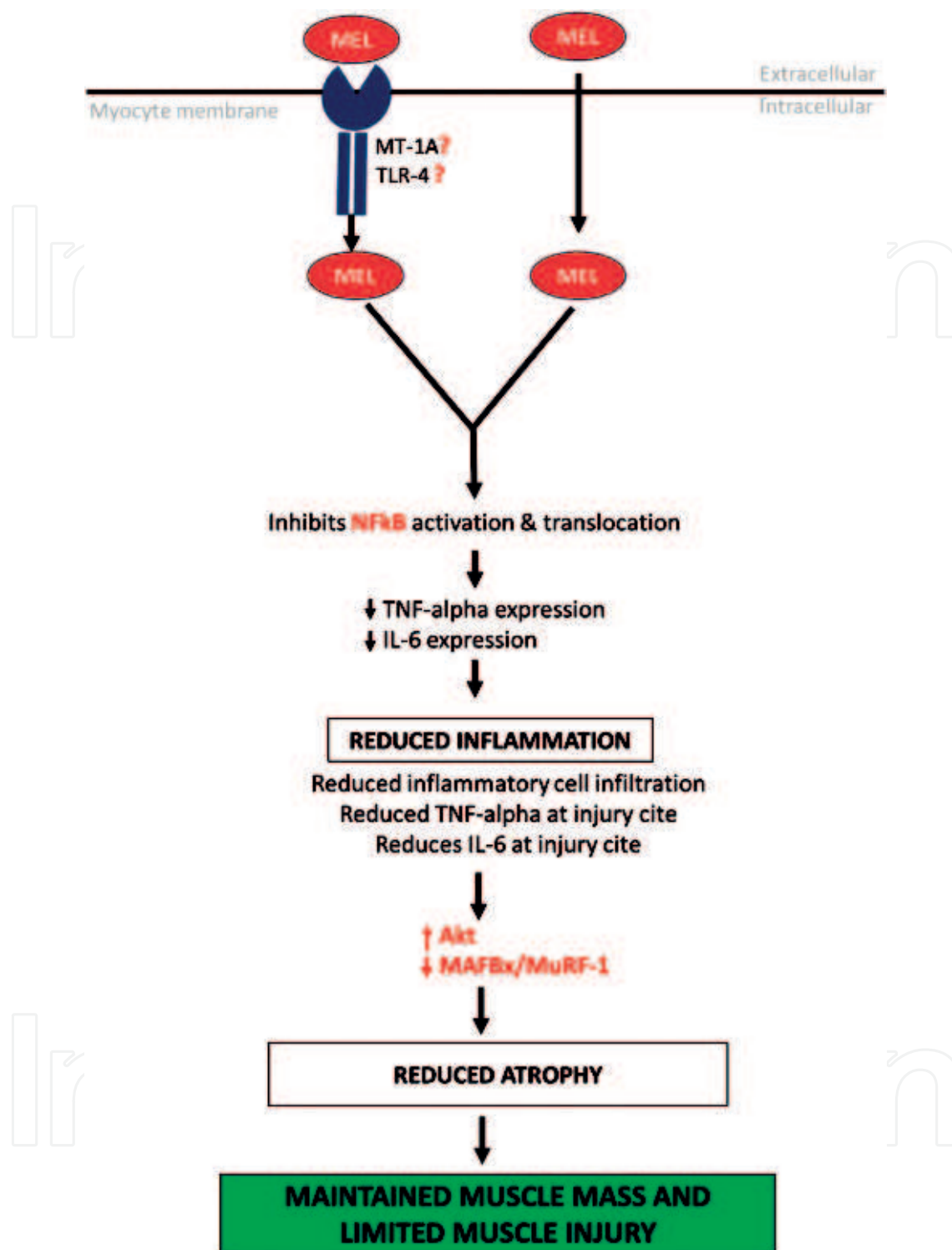


Figure 1. Advantages of melatonin on the muscle injury that contribute to the strenuous exercise. Melatonin inhibits the activation of the nuclear factor kappa-light-chain-enhancer of activated B cells (NFκB) and translocates it that reduces the expression of tumor necrosis factor-α or TNF-α and interleukin-6 or IL-6 in exercise-induced injured muscle. Consequently melatonin could limit inflammation and increase the activation of the protein kinase B also known as Akt to control protein deprivation and downregulate the atrophy via NFκB/MAFBX/MURF-1/Akt pathway during injury. NF-κB, nuclear factor kappa-B; TNF-α, tumor necrosis factor-α; IL-6, interleukin-6; Akt, serine/threonine kinase; MAFBX, muscle atrophy F-box; and MuRF-1, muscle RING finger 1 [26].

Melatonin and all its metabolites could scavenge ROS and reactive nitrogen species (RNS) and act as the antioxidant cascade. Melatonin not only decreases the exercise-induced oxidative stress in the muscles but also enhances muscle antioxidant enzymes such as superoxide dismutase. Moreover, melatonin reduces muscle inflammatory factors such as IL-6 and TNF- α [25–27]. Melatonin could successfully manage the strenuous exercise-induced muscle damage through several ways. It increases the strength of injured muscle, reduces severity of the injury, increases number of satellite cells, inhibits NF- κ B activation/translocation, causes TNF- α and IL-6 to decline, and increases muscle Akt and thus decreases MAFBX/MuRF-1 ratio. Due to its broad-spectrum antioxidant, it could protect DNA, proteins, and biological membrane lipids from the effects of ROS and other oxidative stress [6, 24, 26].

4.2. Aerobic training

Physical exercise is performing some activities to keep healthy weight, building and conserving healthy bone, muscle, and joints to develop physiological health. Exercise also promotes the immune system. Immune system responses to exercise are directly dependent on the intensity, duration, and body adaptive responses. It has been suggested that moderate exercise through endocrine hormone elevation could reverse immunosenescence. Moderate exercise training modulates exercise-induced ROS and DNA damage and regulates cytokine levels [30].

Aerobic training and regular physical activity are highly associated with vast beneficial health issues including limiting cardiovascular disease (CVD), diabetes type 2, and age-related mortality. Aerobic training also induces vast acute and chronic adaptation in various physiological systems. Furthermore, physical inactivity is one of the four main causes of premature mortality. Although the aerobic physical activity increases in the current society, the level of the physical inactivity is still high [17, 31]. It was shown that physical activity could elevate melatonin levels, decrease estrogen production, improve fat metabolism, and reduce cancer risk as well. It has been reported that short- or even long-term physical activity has no substantial effects on the melatonin levels [15]. Moderate exercise, in another study, could modulate ROS, cytokines, and hormone levels that all affect apoptosis. Melatonin as one of this regulating hormones has diverse physiological aspects that it can counteract the immune depression following acute stress or aging and also upregulate TNF [30]. Exercise has immediate and/or delayed effects on melatonin secretion, in which duration, type of exercise, time of the day, fitness status, and age have also been identified as intervening factors in exercise-induced changes in the melatonin levels (**Figure 2**).

Melatonin also plays an important role in the exercise-induced metabolic adaptation. Pinealectomized animals do not show adaptive metabolic changes due to aerobic training. Melatonin acts as a mediator between environment situation and physiological regulatory manner. Besides melatonin effects on the blood pressure and endocrine regulation, it also acts on the GLUT 4 (glucose transporter) gene expression (31). In this case aerobic training is coworker of melatonin in which both of them stimulate glucose uptake through

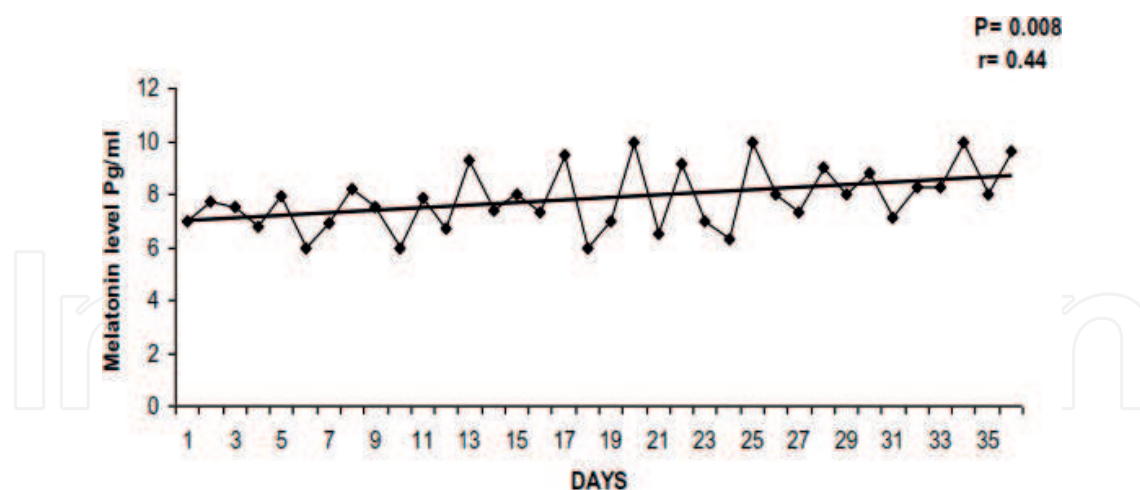


Figure 2. The effects of exercise time duration on the melatonin levels [30].

insulin-independent process and increase GLUT 4 protein expression. It was reported that those pinealectomized rats that undergo aerobic training did not show any metabolic development. So melatonin plays key role in metabolic adaptation in both adipose and muscle tissues. As it was mentioned, melatonin has circadian rhythm and regulates body clock; it also regulates energy metabolism circadian timing in which period of activity and adaptation to activity affect this timing [16, 31]. In one study the effects of melatonin supplementation on the aerobic exercise-induced adaptation were examined. For this purpose male wistar rats are divided into four groups: sedentary control, trained control, sedentary treated with melatonin, and trained treated with melatonin. Glucose tolerance, physical capacity, citrate synthesis, phosphatidylinositol 3-kinase (PI3K), mitogen-activated protein kinase (MAPK), and GLUT4 were examined. Following the 8-week aerobic exercise training on treadmill, those trained animals that treated with melatonin showed better results in their measured parameters that are mentioned above. Briefly, melatonin supplementation plus aerobic training creates great metabolic adaptation and improves metabolism efficiency [31]. The combination of aerobic exercise and melatonin, also, reduces the exercise-induced free radical agents. Low to moderate levels of free radicals have regulatory roles, but their high levels create cellular damages and induce oxidative stress [24]. Melatonin elevation or melatonin supplementation especially while it is combined with aerobic training could decrease the lipid peroxidation and malondialdehyde—lipid peroxidation most frequent marker—in sedentary individuals [18]. Long-term aerobic training could manage the lipid profile of sedentary individuals. Meanwhile when combined with melatonin, the protective effects of aerobic training against free radicals advance, and the body antioxidant defense system improves [18].

Two central and direct ways guide the melatonin effects on the brown adipose tissue to increase exercise-energy expenditure. The nervous system is the central way that controls the melatonin through the sympathetic system. Sympathetic nerve-secreted norepinephrine controls the daily variation in melatonin synthesis [16]. Also, exercise leads to high increase in the activity of the sympathetic nervous system and catecholamine secretion which could modulate melatonin secretion [16]. Melatonin acts as antioxidant [6]. Its secretion is affected by daytime and especially the nervous system. Exercise training stimulates sympathetic

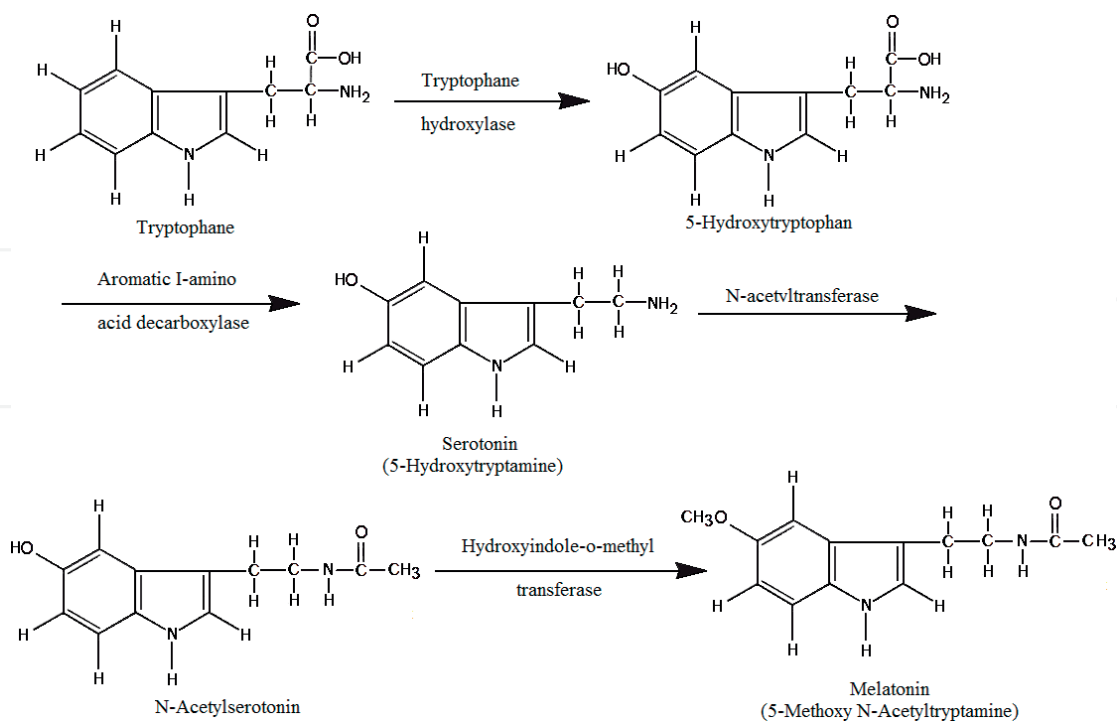


Figure 3. Tryptophan to melatonin cascade process. Tryptophan is the precursor of serotonin and melatonin [32].

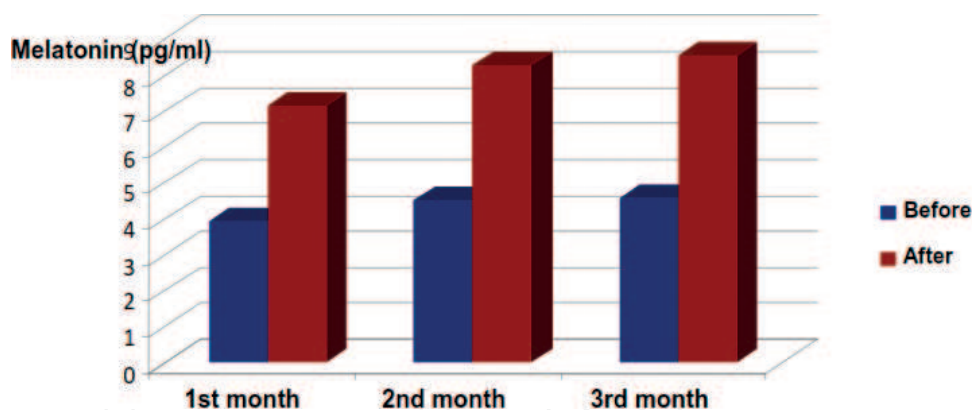


Figure 4. Direct positive correlation between melatonin levels and exercise duration. As the training days progress, the melatonin levels increase [30].

nervous system and releases noradrenaline. Noradrenaline increases the tryptophan levels [30]. Tryptophan is uptaken by the pineal gland and decarboxylated to form serotonin (or 5-hydroxytryptamine). Serotonin during the daylight is stored in the pineal gland. Darkness causes noradrenaline to activate the enzymes (serotonin-N-acetyltransferase) and finally convert serotonin into melatonin (**Figure 3**) [32].

Also, in the direct way, protein kinase C (PKC) pathway leads to increase growth factor and mitochondria biogenesis [33]. Melatonin also could increase LDL receptor and inhibit cholesterol synthesis which is even useful for control obesity [33].

Regarding long-term endurance training, the melatonin hormone reaches steady state. Furthermore, there is direct positive correlation between melatonin levels and exercise

duration (**Figure 4**) [30]. Following exercise melatonin gradually increases, and due to endurance training which should last for about 3 months, the melatonin reaches to steady state [30]. It was reported that the low-intensity aerobic training has better adaptation and lipid peroxidation prevention in sedentary individuals. Melatonin supplementation for about 2 months improves dyslipidemia, decreases LDL, and improves lipid metabolism [25].

5. What is lipid peroxidation, and what is malondialdehyde?

Free radicals are those species that are created as a result of cellular oxygen consumption and are mediator of lipid peroxidation. Different elements and situations affect the lipid peroxidation such as heat, oxygen, and enzymes. Free radicals have one or even more than one free electron(s). All of these ingredients could damage the molecules' organisms and create oxidative stress. Body natural defense system impedes the oxidative stress; whenever an imbalance occurs between the free radical production and antioxidant defense system effectiveness, the oxidative stress happens [18, 34]. Lipids are one of the important agents either in food or body's biological system. Body lipids are prone to oxidation, and it would happen during several stages as food storage process or even in physiological/pathological conditions. Unsaturated fatty acids are prone to oxidation; while the free radicals penetrate into bilayer membrane structure, lipid peroxidation is going to happen [18, 35]. Oxygen and free radicals damage the unsaturated fatty acids under lipoperoxide formation. This compound is unstable and could break down into wide range of reactive species which bind to free amino groups and decrease the proteolytic degradation [34]. Free radical-induced lipid peroxidation happens in three stages: initiation, propagation, and termination [35]. In the first stage, free

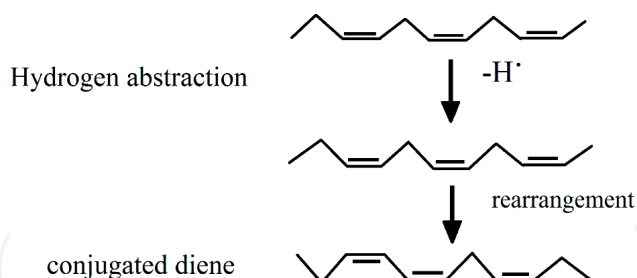


Figure 5. The first stage (initiation stage) of lipid peroxidation process [36].

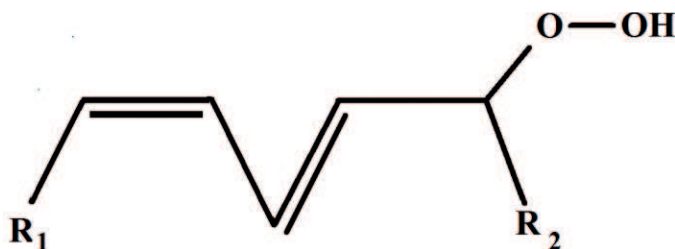


Figure 6. Structural formula of conjugated diene during lipid peroxidation [34].

radicals attack fatty acid molecule which detach hydrogen ion and create fatty acid radical. Due to reordering of double bond, two double bonds between carbon atoms contain and create conjugated diene. The diene structure reacts with oxygen molecule and creates lipoperoxyl radical (Figures 5 and 6).

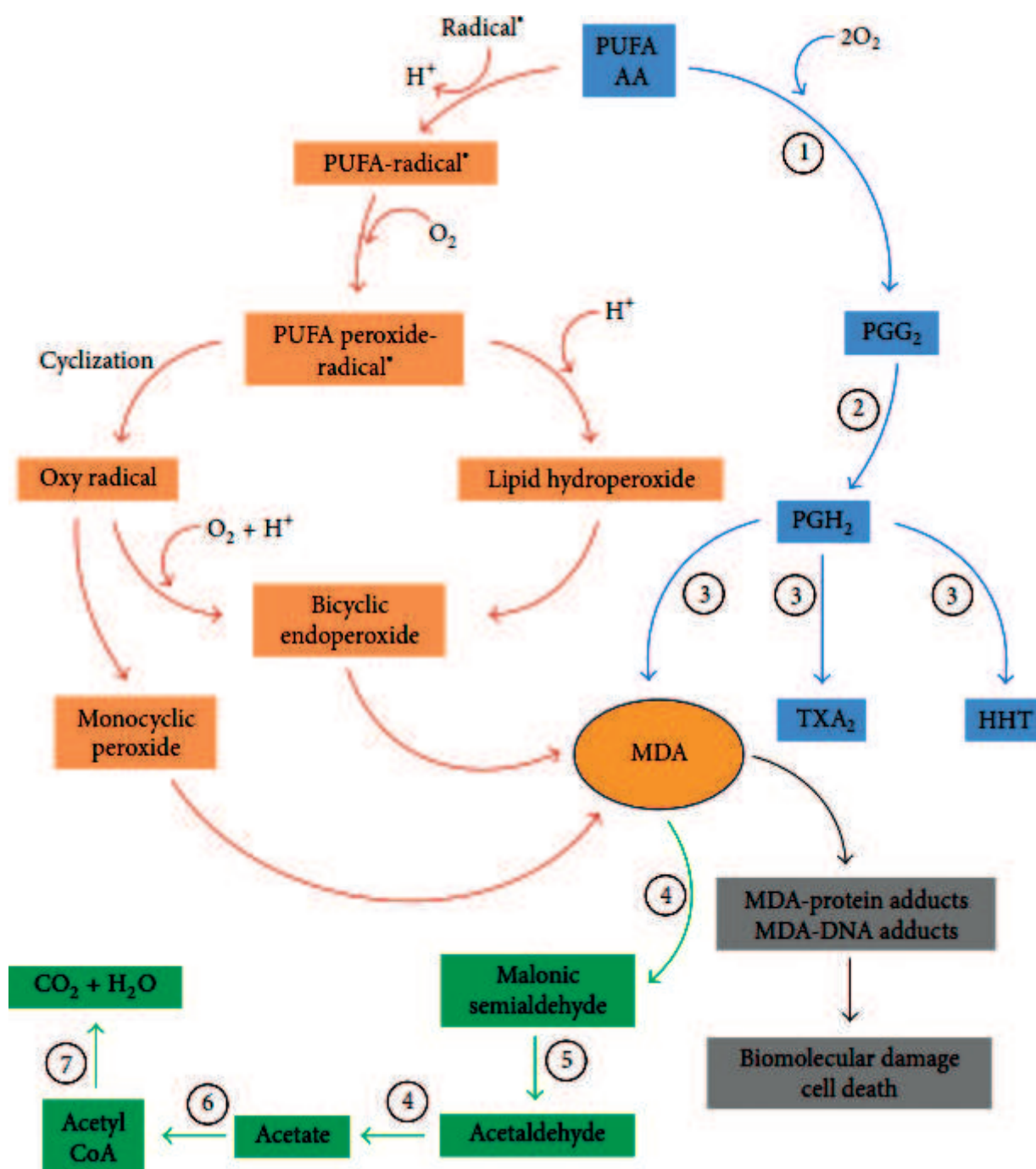


Figure 7. Malondialdehyde formation and metabolism process. Decomposition of arachidonic acid (AA) and PUFAs as side products of enzymatic process during the biosynthesis of thromboxane A_2 (TXA $_2$) and 12-l-hydroxy-5,8,10-hepadecatrienoic acid (HHT) (blue pathway) or nonenzymatic process by lipid peroxidation-induced bicyclic endoperoxides (red pathway) generates malondialdehyde. Malondialdehyde could enzymatically be metabolized (green pathway); those key enzymes in both malondialdehyde formation and metabolism are cyclooxygenase [1], prostacyclin hydroperoxidase [2], thromboxane synthase [3], aldehyde dehydrogenase [4], decarboxylase [5], acetyl CoA synthase [6], and tricarboxylic acid cycle [7] [38].

In the second phase named propagation, the lipoperoxyl radical, the first phase product, reacts with other fatty acid molecules. Further this reaction a hydrogen atom detaches due to lipid hydroperoxide formation. Following propagation the last stage which is called termination occurs. In this phase enzymatic lipid peroxidation which catalyzes cyclooxygenase and lipoxygenase enzymes happens [34, 36].

Lipid peroxidation leads to two results as structural damage into membrane and creates secondary products. Broken fatty acyl chains and lipid-lipid or even lipid-protein cross-links could damage membrane and affect biological systems and impair membrane function and enzymatic inactivation [36]. Malondialdehyde, which is known as MDA, is a three-carbon molecule that is created by free radicals, and it is not only a secondary product but also the most frequent marker of lipid peroxidation [18, 37]. MDA is generated by decomposition of arachidonic acid and polyunsaturated fatty acids (PUFAs) (**Figure 7**). MDA is stable and membrane permeable which may act as signaling messenger [38]. MDA is one the most popular oxidative stress markers, and due to its toxicity, it becomes very relevant to biomedical condition, and several technologies are used to determine MDA such as liquid chromatography-mass spectrometry (LC-MS) and several derivatization-based strategies [38].

There are multiple methods to prevent lipid peroxidation and MDA harmful effects that among them antioxidant usage is the most effective and suitable approach [39]. Antioxidants scavenge free radicals and inactivate peroxides and other ROS consequently could prevent or even delay oxidation process. The chemical structure, concentration, temperature, and type of oxidation substrate determine the efficiency of antioxidants. It means that to select the best antioxidant, we have to consider many points of view and take many factors into account [39]. Antioxidant defense system helps organism to battle with oxidative stress. This system has three lines of defense. In the first stage, ROS overproduction impedes. The second defense line is mainly created by enzymes, and in the third line of defense, molecules should scavenge ROS [24].

6. Conclusion

Melatonin as pineal gland hormone is secreted according to circadian rhythm. Melatonin is also a strong antioxidant that could cross physiological barrier due to its amphiphilic feature, thereby decreasing oxidative damage. Melatonin has direct (direct scavenging of free radical and activate DNA repair enzymes) and indirect (support superoxide dismutase or SOD) antioxidant capacities [24]. Amphiphilic feature of melatonin makes it strong scavenging factor that increases the efficiency of melatonin's radical scavenging which could pass between lipidic and aqueous phases. Melatonin also neutralizes singlet oxygen, peroxyxynitrite anion, and nitric oxide [24]. A wide range of biological systems such as linoleate model system or LDL contributes in melatonin antioxidant properties [39, 40]. Melatonin supplementation decreases the MDA and also lipid peroxidation [18]. In an experimental study, it was shown that melatonin supplementation during long-term aerobic exercise could diminish the exercise-induced lipid peroxidation and also malondialdehyde [18]. Exercise training generates almost twofold elevation in oxygen species, lipid peroxidation, and MDA levels [41]. Another report represented that melatonin administration 30 min before the exercise impressively

decreases triglyceride and MDA [6]. Four-week melatonin supplementation followed by single exercise that lasts about 30 min decreases oxidative stress and MDA as well [42].

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Conflict of interest

There is no conflict of interest for all authors.

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