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Therapeutic Potential of Melatonin: Multifaceted Applications in Muscle Health, Metabolic Disorders and Cardiovascular Disease

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Abstract

Melatonin, a hormone primarily synthesized by the pineal gland, is traditionally associated with the regulation of circadian rhythms. However, recent research has unveiled its broad spectrum of biological effects, positioning it as a valuable therapeutic agent in diverse health contexts. Known for its potent antioxidant and anti-inflammatory properties, melatonin plays a crucial role in maintaining homeostasis and protecting cellular integrity. This review explores melatonin's therapeutic applications across multiple medical domains, including muscle health, metabolic disorders, chronic pain management, and cardiovascular health. In muscle health, melatonin facilitates muscle hypertrophy and regeneration by mitigating oxidative stress and enhancing the activity of satellite cells responsible for muscle repair. This action is particularly beneficial for individuals undergoing intense physical exertion, recovering from injuries, or combating age-related muscle. In metabolic disorders, such as type 2 diabetes, melatonin improves insulin sensitivity and reduces cellular oxidative damage, which supports beta-cell function and glucose regulation, potentially minimizing diabetes-related complications. Furthermore, in fibromyalgia - a condition marked by widespread pain and sleep disturbances - melatonin has demonstrated efficacy in alleviating pain and improving sleep quality, thus enhancing the overall quality of life for patients. In cardiovascular health, melatonin has shown promise in preventing and managing heart failure by reducing oxidative damage, modulating inflammatory pathways, and supporting endothelial function, which collectively contribute to improved cardiac health and reduced disease progression. This comprehensive review underscores melatonin's emerging role as an integrative therapeutic agent in modern medicine. By targeting key pathophysiological pathways, melatonin holds the potential to support health maintenance and therapeutic interventions across a spectrum of chronic conditions. Further clinical studies are needed to establish optimal dosing and long-term efficacy to fully harness melatonin's therapeutic potential.

Keywords: melatonin, melatonin therapy, muscle regeneration, heart failure prevention, fibromyalgia treatment, type 2 diabetes, oxidative stress reduction

Melatonin

Melatonin, a hormone predominantly synthesized in the pineal gland, plays a vital role in regulating the body's circadian rhythms, thus influencing sleep patterns and seasonal biological cycles. Beyond its traditional association with sleep regulation, melatonin is recognized for its extensive physiological functions, including potent antioxidant, anti-inflammatory, and immunomodulatory effects (1). These properties have spurred interest in melatonin's potential therapeutic applications across various medical fields, where it may serve as an adjunct treatment or even a primary therapeutic agent. Recent research has explored melatonin's role in muscle health, demonstrating its capacity to enhance muscle regeneration and hypertrophy, essential for athletes, aging populations, and individuals recovering from muscle injuries. Melatonin supports muscle recovery through its antioxidant properties, mitigating oxidative stress and promoting the activity of satellite cells crucial for muscle repair (2, 3). Its potential extends further into metabolic disorders, such as diabetes, where melatonin has been shown to improve insulin sensitivity, regulate glucose metabolism, and reduce oxidative stress, thereby supporting pancreatic function and glucose homeostasis (4-6).

In chronic pain conditions like fibromyalgia, melatonin's analgesic and sleep-regulating effects offer a novel approach to symptom management, improving patients' quality of life by reducing pain severity and enhancing sleep quality (7, 8). Moreover, in cardiovascular health, melatonin has shown promise in preventing and managing heart failure. By reducing oxidative stress and inflammation in cardiac tissues, melatonin provides cardioprotective effects, supporting vascular health and potentially mitigating disease progression (9, 10). This review aims to consolidate current knowledge on the diverse therapeutic applications of melatonin, focusing on its roles in muscle hypertrophy and regeneration, diabetes management, fibromyalgia treatment, and heart failure prevention. Through examining the molecular and clinical evidence, this publication seeks to elucidate melatonin's multifaceted benefits and its emerging importance in integrative healthcare strategies.

Melatonin and its biological functions and clinical applications

Melatonin is a hormone produced primarily by the pineal gland, whose secretion is closely linked to the light-dark cycle, with peak levels occurring at night. This natural hormone regulates circadian rhythms, impacting sleep-wake cycles and helping the body adapt to daily changes. Beyond its role in sleep regulation, melatonin plays a series of essential roles in maintaining the body's homeostasis. First and foremost, it exhibits antioxidant properties, allowing it to neutralize free radicals and protect cells from oxidative stress, thereby reducing the risk of DNA and protein damage and slowing down cellular aging processes (1). Melatonin also influences immune system functions by strengthening the body's defense responses and modulating inflammatory reactions (8). Additionally, this hormone plays a role in regulating blood pressure and glucose levels, highlighting its potential importance in preventing metabolic diseases, such as type 2 diabetes, and cardiovascular diseases (2, 4, 5). Due to its broad range of effects, melatonin is used not only as a sleep aid but also as a substance with potential therapeutic applications in various medical conditions, especially where antioxidant protection and immune support are needed (11).

Impact of melatonin supplementation on muscle hypertrophy

Melatonin supplementation has been associated with various beneficial effects on muscle physiology. Several research studies have explored the relationship between melatonin supplementation and muscle growth, with findings suggesting a positive correlation between melatonin intake and muscle fiber hypertrophy demonstrated that melatonin supplementation could promote skeletal muscle growth, improve mitochondrial function, and reduce fat deposition in muscle tissue (12). Studies have shown that melatonin can mitigate mitochondrial malfunction by scavenging reactive oxygen and nitrogen species generated within the mitochondria. Furthermore, melatonin has been demonstrated to enhance antioxidant action against lipid peroxidation in mitochondria, indicating its protective role in maintaining mitochondrial health (13, 14). In the context of fat deposition, melatonin has been shown to suppress milk fat synthesis by inhibiting the mTOR signaling pathway, thereby affecting key genes involved in fat synthesis (15). Additionally, melatonin has been found to induce browning of white adipose tissue, promoting thermogenesis and altering gene expression related to fat metabolism (16).

Moreover, the effects of melatonin on exercise performance have also been investigated, showing promising results highlighted that melatonin supplementation could lead to increased glucose levels in muscles, reduced body mass, decreased muscle oxidative stress, prolonged muscle strength, and better adaptation to physical effort, all of which are factors that can contribute to improved exercise performance (17). In addition to its effects on muscle growth, melatonin has been studied for its role in mitigating cardiac hypertrophy. Research by Khatoon (2023) indicated that melatonin can suppress pro-inflammatory cytokines and markers associated with cardiac hypertrophy, suggesting a cardioprotective potential of melatonin against hypertrophic changes in the heart (18). Furthermore, the impact of melatonin on muscle atrophy has been a subject of interest in various studies. Lee et al. (2012) demonstrated that melatonin administration could have prophylactic and therapeutic effects on muscle atrophy through different signaling pathways, such as MuRF1/MAFbx and IGF-1-mediated pathways, in a stroke animal model. This suggests that melatonin supplementation may help prevent muscle wasting and promote muscle maintenance, which are essential factors in supporting muscle hypertrophy (19). Moreover, the potential of melatonin to prevent muscle atrophy and promote muscle health has been highlighted in studies involving aging animals. Mendes et al. (2013) showed that melatonin supplementation, in conjunction with aerobic physical training, increased glycogen stores in the liver and skeletal muscle, indicating the importance of melatonin in metabolic adaptations to exercise, particularly in aging animals. This suggests that melatonin may play a crucial role in maintaining muscle integrity and function, which are essential for supporting muscle hypertrophy, especially in aging individuals (20). Additionally, the effects of melatonin on energy metabolism and obesity have been investigated in various studies. Xu et al. (2022) found that melatonin supplementation could attenuate weight gain, insulin resistance, adipocyte hypertrophy, inflammation, and hepatic steatosis induced by a high-fat diet, indicating its potential in combating obesity-related changes. These findings suggest that melatonin may influence energy expenditure and lipid metabolism, factors that can impact muscle hypertrophy indirectly by regulating overall body composition and metabolic health (21). In conclusion, the existing body of research provides compelling evidence for the potential benefits of melatonin supplementation in promoting muscle hypertrophy (12, 17). From enhancing muscle fiber growth and reducing fat deposition to improving exercise performance and mitigating cardiac hypertrophy, melatonin appears to have a multifaceted impact on muscle health (17, 18). Moreover, its role in preventing muscle atrophy, supporting metabolic adaptations to exercise, and influencing energy metabolism underscores its potential significance in the context of muscle hypertrophy (12-14). Overall, the findings suggest that melatonin supplementation may be a promising avenue to explore for individuals looking to enhance muscle growth and overall muscle health (17).

Effect of melatonin supplementation on regeneration of damaged muscles

Research indicates that melatonin plays a crucial role in muscle regeneration by reducing oxidative stress and inflammation, which are significant contributors to muscle damage and impaired recovery. For instance, melatonin has been shown to normalize plasma pro-inflammatory cytokines and markers of muscle injury in conditions such as Duchenne muscular dystrophy, suggesting its protective role against muscle degeneration (22).

Additionally, melatonin treatment has been associated with increased expression of Pax7, a transcription factor critical for satellite cell activation and muscle differentiation, thereby enhancing muscle recovery (23). In experimental models, melatonin administration has demonstrated a protective effect against muscle atrophy induced by various stressors. For example, in a study involving reserpine-induced myalgia in rats, melatonin supplementation resulted in significant increases in muscle weight and myotube diameter, indicating its role in counteracting muscle atrophy (24). Melatonin has been shown to ameliorate TNF-α-induced muscle atrophy by enhancing antioxidant enzyme activity, which suggests a mechanism through which melatonin protects muscle cells from oxidative damage (25). Melatonin's influence on mitochondrial function is noteworthy. It has been reported that melatonin can prevent mitochondrial dysfunction and improve bioenergetics in skeletal muscle, which is vital for muscle recovery and regeneration (26).The regenerative effects of melatonin are also linked to its ability to modulate signaling pathways involved in muscle repair. For instance, melatonin has been shown to inhibit the NF-κB inflammatory pathway, which is activated during muscle injury and contributes to muscle degeneration (27). In summary, melatonin supplementation appears to facilitate muscle regeneration through its antioxidant properties, reduction of inflammation, enhancement of myogenic differentiation, and improvement of mitochondrial function. These findings underscore the potential of melatonin as a therapeutic agent for promoting recovery in damaged muscle tissues (24, 26, 27).

The Impact of Melatonin on Diabetes

Melatonin has shown promise as a modulator of metabolic health, particularly in the context of diabetes management. Its effects on glucose metabolism and insulin regulation stem primarily from its antioxidant and anti-inflammatory properties, which play crucial roles in mitigating the oxidative stress and chronic inflammation commonly associated with diabetes (28). Studies have demonstrated that melatonin enhances insulin sensitivity by reducing reactive oxygen species (ROS) in the pancreas, which protects pancreatic beta cells responsible for insulin production. This effect is particularly relevant in type 2 diabetes, where beta-cell dysfunction and insulin resistance are predominant issues (5). Furthermore, melatonin’s influence on circadian rhythms helps regulate insulin release patterns and improve metabolic stability, underscoring its potential to address metabolic dysregulation linked to disrupted sleep-wake cycles, which are often seen in diabetic patients (29). In experimental studies, melatonin has shown protective effects on diabetic complications in various organs, including the liver and kidneys, by decreasing oxidative stress and reducing inflammation, mechanisms essential in preventing complications such as diabetic nephropathy and retinopathy (4). Research supports melatonin’s antioxidative defense role in maintaining cellular integrity, suggesting it may prevent long-term organ damage caused by hyperglycemia (30). Additionally, clinical studies indicate that melatonin can support insulin sensitivity and glycemic control, positioning it as a potential adjunctive therapy for improving blood glucose management in diabetic patients (5). Melatonin may also counteract inflammation-driven insulin resistance by modulating pro-inflammatory pathways, which are known to contribute to insulin resistance in type 2 diabetes. This anti-inflammatory effect highlights melatonin’s potential to reduce insulin resistance through cytokine regulation and improve metabolic homeostasis (31).

Studies further suggest that melatonin receptors, especially MT2, play a critical role in enhancing insulin receptor sensitivity, promoting glucose uptake in peripheral tissues, and ultimately supporting improved glycemic control (30). As research continues to explore melatonin's broader effects on metabolic pathways, it becomes evident that this hormone holds substantial promise in reducing both the onset and progression of diabetes-related complications.

Application of Melatonin in the Treatment of Fibromyalgia

Melatonin, known for its role in regulating sleep and circadian rhythms, has shown promising potential in treating fibromyalgia, a chronic condition marked by widespread pain, sleep disturbances, and fatigue. The therapeutic effects of melatonin on fibromyalgia appear to be multifaceted, primarily due to its antioxidative and anti-inflammatory properties. Melatonin is believed to counteract the elevated levels of oxidative stress and inflammation observed in fibromyalgia patients, which contributes to pain and tissue damage (8). Studies suggest that melatonin’s antioxidant action can mitigate the oxidative damage in muscle tissues, thereby alleviating pain and improving muscle function in fibromyalgia patients (32). Another key benefit of melatonin in fibromyalgia management lies in its impact on sleep quality. Sleep disorders are a common complaint among fibromyalgia patients, often exacerbating their symptoms. Melatonin supplementation has been found to improve sleep quality and duration, which in turn reduces daytime fatigue and enhances the patients' overall quality of life (33). Research highlights that melatonin not only aids in regulating sleep cycles but also positively influences mood and reduces the severity of depression and anxiety, which are prevalent comorbidities in fibromyalgia patients (7). Furthermore, melatonin may interact with pain-modulating systems in the brain, enhancing the efficacy of conventional pain treatments. In a randomized study, melatonin used in combination with fluoxetine was shown to significantly improve pain relief outcomes, suggesting that melatonin could potentiate the effects of other analgesic therapies (34). Melatonin’s effects on mitochondrial function have also been noted, as it helps to stabilize mitochondrial activity and reduce cellular stress, factors that are often compromised in fibromyalgia and contribute to muscle fatigue and discomfort (35). The cumulative evidence suggests that melatonin could serve as a valuable adjunct treatment for fibromyalgia, offering a combination of antioxidant, anti-inflammatory, and sleep-enhancing effects that directly target several core symptoms of the condition. These findings underscore the need for further large-scale clinical trials to fully establish melatonin’s efficacy and optimal dosages in fibromyalgia treatment (36).

The Role of Melatonin in the Prevention and Therapy of Heart Failure

Melatonin, a potent antioxidant, has garnered attention for its protective role against cardiovascular diseases, particularly in the context of heart failure. Studies have shown that melatonin reduces oxidative stress within cardiac tissues by scavenging reactive oxygen species (ROS), which are associated with myocardial damage and heart failure progression (37). By neutralizing ROS, melatonin helps prevent oxidative damage to heart cells, a key factor in preserving myocardial function and reducing the risk of heart failure. Additionally, melatonin inhibits lipid peroxidation and supports mitochondrial function, crucial for maintaining energy production in heart cells and minimizing ischemia-reperfusion injury (9).

One of the essential mechanisms through which melatonin exerts its cardioprotective effects is by modulating inflammatory pathways. Heart failure is often accompanied by chronic inflammation, which exacerbates myocardial remodeling and fibrosis. Melatonin has been observed to downregulate pro-inflammatory cytokines, such as TNF-α and IL-6, reducing inflammation and slowing the progression of heart failure (10). Furthermore, melatonin improves endothelial function, enhancing vascular relaxation and reducing hypertension—a significant risk factor for heart failure (38). By improving blood vessel health, melatonin reduces the workload on the heart, aiding in the management of conditions associated with cardiac insufficiency.

Melatonin's influence extends to circadian rhythm regulation, a factor increasingly recognized in cardiovascular health. Patients with disrupted circadian rhythms often exhibit poorer heart function and a higher incidence of heart disease. Melatonin helps restore circadian alignment, which may lead to improvements in blood pressure control, heart rate variability, and overall cardiac health (39). In clinical settings, melatonin supplementation has shown promising results in improving symptoms in heart failure patients, including reduced fatigue and enhanced exercise tolerance, suggesting it could serve as an adjunct to conventional heart failure therapies (40). The combined antioxidative, anti-inflammatory, and circadian regulatory effects of melatonin underscore its potential as a therapeutic option for heart failure. However, further large-scale trials are necessary to define optimal dosages and assess long-term efficacy in heart failure patients.

Conclusions

Melatonin, primarily known for its role in regulating circadian rhythms, holds considerable therapeutic potential across multiple health domains. Its antioxidant and anti-inflammatory properties make it a valuable agent in muscle health, where it supports hypertrophy and regeneration, particularly beneficial for athletes and aging populations facing muscle degeneration (2, 3). Furthermore, in metabolic disorders such as diabetes, melatonin has demonstrated efficacy in improving insulin sensitivity, reducing oxidative stress, and protecting pancreatic beta cells, highlighting its promise in managing type 2 diabetes and its complications (4, 5). In the treatment of fibromyalgia, melatonin’s ability to enhance sleep quality and reduce pain severity has been shown to improve the quality of life for patients, pointing to its therapeutic relevance in chronic pain management (7, 8). In cardiovascular health, melatonin offers protective effects against heart failure by reducing oxidative damage and inflammation within cardiac tissue, thus supporting vascular health and potentially slowing disease progression (9, 10). These findings suggest that melatonin could serve as a valuable adjunctive therapy in various clinical contexts, with benefits extending to antioxidative protection, circadian regulation, and metabolic support. Given its wide-ranging benefits, melatonin is emerging as an integrative therapeutic option in modern medicine. However, further large-scale clinical studies are necessary to determine optimal dosing and evaluate its long-term efficacy and safety across different conditions.

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References

1. Favero G, Franco C, Stacchiotti A, Rodella LF, Rezzani R. Sirtuin1 Role in the Melatonin Protective Effects Against Obesity-Related Heart Injury. Front Physiol. 2020;11:103.
2. Chen B, You W, Shan T. The regulatory role of melatonin in skeletal muscle. J Muscle Res Cell Motil. 2020;41(2-3):191-8.
3. Jin H, Xie W, Hu P, Tang K, Wang X, Wu Y, et al. The role of melatonin in sarcopenia: Advances and application prospects. Exp Gerontol. 2021;149:111319.
4. Cipolla-Neto J, Amaral FG, Afeche SC, Tan DX, Reiter RJ. Melatonin, energy metabolism, and obesity: a review. J Pineal Res. 2014;56(4):371-81.
5. Garaulet M, Qian J, Florez JC, Arendt J, Saxena R, Scheer F. Melatonin Effects on Glucose Metabolism: Time To Unlock the Controversy. Trends Endocrinol Metab. 2020;31(3):192-204.
6. Lauritzen ES, Kampmann U, Smedegaard SB, Støy J. Effects of daily administration of melatonin before bedtime on fasting insulin, glucose and insulin sensitivity in healthy adults and patients with metabolic diseases. A systematic review and meta-analysis. Clinical Endocrinology. 2021;95(5):691-701.
7. Caumo W, Hidalgo MP, Souza A, Torres ILS, Antunes LC. Melatonin is a biomarker of circadian dysregulation and is correlated with major depression and fibromyalgia symptom severity. J Pain Res. 2019;12:545-56.
8. Reiter RJ, Acuna-Castroviejo D, Tan DX. Melatonin therapy in fibromyalgia. Curr Pain Headache Rep. 2007;11(5):339-42.
9. Pourhanifeh MH, Dehdashtian E, Hosseinzadeh A, Sezavar SH, Mehrzadi S. Clinical Application of Melatonin in the Treatment of Cardiovascular Diseases: Current Evidence and New Insights into the Cardioprotective and Cardiotherapeutic Properties. Cardiovasc Drugs Ther. 2022;36(1):131-55.

10. Zhou H, Ma Q, Zhu P, Ren J, Reiter RJ, Chen Y. Protective role of melatonin in cardiac ischemia-reperfusion injury: From pathogenesis to targeted therapy. J Pineal Res. 2018;64(3).
11. Hardeland R. Melatonin and inflammation-Story of a double-edged blade. J Pineal Res. 2018;65(4):e12525.
12. Stacchiotti A, Favero G, Rodella LF. Impact of Melatonin on Skeletal Muscle and Exercise. Cells. 2020;9(2).
13. León J, Acuña-Castroviejo D, Escames G, Tan DX, Reiter RJ. Melatonin mitigates mitochondrial malfunction. J Pineal Res. 2005;38(1):1-9.
14. Milczarek R, Hallmann A, Sokołowska E, Kaletha K, Klimek J. Melatonin enhances antioxidant action of alpha-tocopherol and ascorbate against NADPH- and iron-dependent lipid peroxidation in human placental mitochondria. J Pineal Res. 2010;49(2):149-55.
15. Wang Y, Guo W, Xu H, Tang K, Zan L, Yang W. Melatonin suppresses milk fat synthesis by inhibiting the mTOR signaling pathway via the MT1 receptor in bovine mammary epithelial cells. J Pineal Res. 2019;67(3):e12593.
16. Jiménez-Aranda A, Fernández-Vázquez G, Campos D, Tassi M, Velasco-Perez L, Tan DX, et al. Melatonin induces browning of inguinal white adipose tissue in Zucker diabetic fatty rats. J Pineal Res. 2013;55(4):416-23.
17. Almendros-Ruiz A, Lopez-Moro A, Conde-Pipò J, Santalla A, Requena B, Mariscal-Arcas M. The Effects of Melatonin Supplementation on Professional Football Player Performance: A Systematic Review. Nutrients. 2023;15(20).
18. Khatoon R, Sarkar, S., Chattopadhyay, A., Bandyopadhyay, D. The cardioprotective potential of melatonin on cardiac hypertrophy: A mechanistic overview. Melatonin Research 2023.
19. Lee S, Shin J, Hong Y, Lee M, Kim K, Lee SR, et al. Beneficial effects of melatonin on stroke-induced muscle atrophy in focal cerebral ischemic rats. Lab Anim Res. 2012;28(1):47-54.
20. Mendes C, Lopes AM, do Amaral FG, Peliciari-Garcia RA, Turati Ade O, Hirabara SM, et al. Adaptations of the aging animal to exercise: role of daily supplementation with melatonin. J Pineal Res. 2013;55(3):229-39.
21. Xu L, Li D, Li H, Zhang O, Huang Y, Shao H, et al. Suppression of obesity by melatonin through increasing energy expenditure and accelerating lipolysis in mice fed a high-fat diet. Nutr Diabetes. 2022;12(1):42.
22. Chahbouni M, Escames G, Venegas C, Sevilla B, García JA, López LC, et al. Melatonin treatment normalizes plasma pro-inflammatory cytokines and nitrosative/oxidative stress in patients suffering from Duchenne muscular dystrophy. J Pineal Res. 2010;48(3):282-9.
23. Su CM, Tsai CH, Chen HT, Wu YS, Chang JW, Yang SF, et al. Melatonin improves muscle injury and differentiation by increasing Pax7 expression. Int J Biol Sci. 2023;19(4):1049-62.
24. Favero G, Trapletti V, Bonomini F, Stacchiotti A, Lavazza A, Rodella LF, et al. Oral Supplementation of Melatonin Protects against Fibromyalgia-Related Skeletal Muscle Alterations in Reserpine-Induced Myalgia Rats. Int J Mol Sci. 2017;18(7).
25. Park JH, Chung EJ, Kwon HJ, Im SS, Lim JG, Song DK. Protective effect of melatonin on TNF-α-induced muscle atrophy in L6 myotubes. J Pineal Res. 2013;54(4):417-25.

26. Potes Y, Díaz-Luis A, Bermejo-Millo JC, Pérez-Martínez Z, de Luxán-Delgado B, Rubio-González A, et al. Melatonin Alleviates the Impairment of Muscle Bioenergetics and Protein Quality Control Systems in Leptin-Deficiency-Induced Obesity. Antioxidants (Basel). 2023;12(11).
27. Li SJ, Cheng WL, Kao YH, Chung CC, Trang NN, Chen YJ. Melatonin Inhibits NF-κB/CREB/Runx2 Signaling and Alleviates Aortic Valve Calcification. Front Cardiovasc Med. 2022;9:885293.
28. Peschke E. Melatonin, endocrine pancreas and diabetes. J Pineal Res. 2008;44(1):26-40.
29. McMullan CJ, Curhan GC, Schernhammer ES, Forman JP. Association of nocturnal melatonin secretion with insulin resistance in nondiabetic young women. Am J Epidemiol. 2013;178(2):231-8.
30. García JA, Volt H, Venegas C, Doerrier C, Escames G, López LC, et al. Disruption of the NF-κB/NLRP3 connection by melatonin requires retinoid-related orphan receptor-α and blocks the septic response in mice. Faseb j. 2015;29(9):3863-75.
31. Cipolla-Neto J, Amaral FGD. Melatonin as a Hormone: New Physiological and Clinical Insights. Endocr Rev. 2018;39(6):990-1028.
32. González-Flores D, López-Pingarrón L, Castaño MY, Gómez M, Rodríguez AB, García JJ, et al. Melatonin as a Coadjuvant in the Treatment of Patients with Fibromyalgia. Biomedicines. 2023;11(7).
33. Hemati K, Amini Kadijani A, Sayehmiri F, Mehrzadi S, Zabihiyeganeh M, Hosseinzadeh A, et al. Melatonin in the treatment of fibromyalgia symptoms: A systematic review. Complement Ther Clin Pract. 2020;38:101072.
34. Hussain SA, Al K, II, Jasim NA, Gorial FI. Adjuvant use of melatonin for treatment of fibromyalgia. J Pineal Res. 2011;50(3):267-71.
35. Fusco R, Siracusa R, D'Amico R, Peritore AF, Cordaro M, Gugliandolo E, et al. Melatonin Plus Folic Acid Treatment Ameliorates Reserpine-Induced Fibromyalgia: An Evaluation of Pain, Oxidative Stress, and Inflammation. Antioxidants (Basel). 2019;8(12).
36. Lawson K. Is there a role for melatonin in fibromyalgia? AIMS Molecular Science. 2019;6.
37. Reiter RJ, Tan DX. Melatonin: a novel protective agent against oxidative injury of the ischemic/reperfused heart. Cardiovasc Res. 2003;58(1):10-9.
38. Tengattini S, Reiter RJ, Tan DX, Terron MP, Rodella LF, Rezzani R. Cardiovascular diseases: protective effects of melatonin. J Pineal Res. 2008;44(1):16-25.
39. Korkmaz A, Reiter RJ, Topal T, Manchester LC, Oter S, Tan DX. Melatonin: an established antioxidant worthy of use in clinical trials. Mol Med. 2009;15(1-2):43-50.
40. Altun A, Ugur-Altun B. Melatonin: therapeutic and clinical utilization. Int J Clin Pract. 2007;61(5):835-45.