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Melatonin Against Aging: Could We Stimulate Melatonin Secretion Through Tahajjud?

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Abstract

Background: Islamic instructions suggest waking up near dawn and praying to Allah. This is the time of maximum melatonin secretion, a hormone whose main function is regulating the circadian rhythm. Melatonin secretion declines with age, leading to different clinical consequences. This study investigated the melatonin levels among night vigil prayers, non-prayer late sleepers, and those with regular night sleep.

Methods: A questionnaire including information about age, gender, education, and occupation was used to collect the demographic information of the participants. Melatonin was measured with two blood draws (23:00 to 24:00 and 9:00 to 10:00). **Results:** There was a significant difference between the night vigil prayers' nocturnal and daily melatonin and the melatonin levels of the other two groups. There was no significant difference in the average daily serum melatonin levels between regular night sleepers and non-praying late sleepers (P=0.306). Moreover, a significant negative relationship was found between age and nocturnal melatonin (r=0.38, P<0.0001) and between age and daily melatonin (r=0.25, P=0.02).

Conclusion: Night vigil prayers had higher average nocturnal and daily serum melatonin levels than non-praying late sleepers and regular sleepers. Therefore, waking up at night accompanied by approaching Allah, prayer, supplication, and positive thoughts was related to release in melatonin.

Keywords: Prayer, Melatonin, Circadian rhythm, Night vigil prayers, Tahajjud

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Introduction

Melatonin (N-acetyl-5-methoxytryptamine) is a hormone produced by the pineal gland in the brain, and its main function is regulating the circadian rhythm, regulating the sleep-wake cycle (1), pubertal development, and seasonal adaptation (2). Melatonin distributes temporal cues to its receptors in different tissues, leading to their daily rhythmicity (3). Melatonin is secreted at night, and its secretion is suppressed by exposure to light (4). Its levels are also related to the length of the night, i.e., on long nights, there is a longer duration of secretion (5). Thus, melatonin secretion undergoes seasonal fluctuations according to the lengthening and shortening of the night's duration in winter and summer, sometimes leading to seasonal affective disorders (6).

On the other hand, melatonin can exert a protective role against age-induced conditions like skin aging (7), rheumatoid arthritis (8), and cardiac function (9). The antioxidant effects of melatonin protect the human body against cancer and aging by lowering free radicals (10-13). Melatonin, as a regulator of mitochondrial bioenergetic function and an autophagy regulator, is regarded as a



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potential treatment for chronic and neurodegenerative disorders such as Parkinson's disease or Alzheimer's disease, gastrointestinal diseases and metabolic and behavioral disorders, cancer, obesity, and viral infections. It could prevent the lethal effects of septic shock or ischemia-reperfusion (14-16). Extra-pineal melatonin plays an essential role in the homeostasis of organs and tissues. It is a first-line defense in organs exposed to the surrounding environment, avoiding the activation of the immunological system (17). Melatonin decreases sleep disorders, increases total sleep time, and improves sleep quality (18,19). It has also been used as an adjuvant therapy for cancer, effective in tumor remission and alleviating the side effects of radio-chemotherapy (20), nausea, vomiting, and hypotension (21). It significantly decreases the incidence of delirium in aged patients in medical wards (22). It has been used to manage pain and enhance preoperative and postoperative analgesia (23). Melatonin is helpful for the neuroprotection of the fetus in pregnant women (24). It has been negatively correlated with multiple sclerosis progression in human beings (25). Melatonin has also been used as an alternative medicine for COVID-19 (26). The influence of sleep duration on breast cancer risk is supposed to occur via its effect on melatonin levels (27), and the disruption of the molecular circadian clock has been reported in ovarian, endometrial, prostate, and hematological cancers (28).

Melatonin secretion declines with age, leading to insomnia and some clinical consequences (29). There are very low amounts of melatonin in meat, vegetables, beans, and other foods, but these are not enough to meet our bodily needs (5). Exogenous melatonin is used for therapeutic purposes in different health conditions (30).

Muslims are encouraged to wake to pray sometime between midnight and dawn. This waking is termed "tahajjud" in the Holy Quran and other Islamic scripts. The night prayer or tahajjud prayer is an opportunity for Muslims to talk to their creator privately. Allah has promised extraordinary rewards for this prayer in the Holy Quran (31), "And during a part of the night, pray tahajjud beyond what is incumbent on you; maybe your Lord will raise you to a position of great glory" (The numbers in parentheses are respectively the number of Surah - chapter- and Ayah - verse; 17:79). The Holy Quran describes the noble servants of Allah as "the patient, and the truthful, and the obedient, and those who spend (benevolently) and those who ask forgiveness in the morning times" (3:17), And "they who pass the night prostrating themselves before their Lord and standing" (25:64), and "they used to sleep but little in the night" (51:17). In other verses, Allah glorifies dawn itself, when He swears to "the night when it departs" (81:17), and orders his prophet to "rise to pray in the night except a little" (73:2). Then Allah admires those who pray at nights, "Their sides draw away from (their) beds, they call upon their Lord in fear and in

hope, and they spend (benevolently) out of what We have given them; so no soul knows what is hidden for them of that which will refresh the eyes; a reward for what they did" (32:16-17).

Night prayer is a recurring suggestion by the Holy Prophet and his Holy Household, the infallible Muslim Imams. Those bound to this form of worship have been called "*the noblest of people*" in the words of Imams. Thus, tahajjud and waking for prayer, Quran recitation, and approaching Allah to deepen a relationship with Him have been traditionally adopted as a part of the lifestyle by great Muslim scholars and wise people. This worship could be helpful in spiritual enforcement, considering the spiritual needs (32) expected to be more critical among the elderly. Moreover, aged people experience a greater risk of cardiovascular disorders, heart attacks, and other diseases associated with melatonin shortage (33).

Regarding the Islamic instructions about tahajjud near dawn and its coincidence with the time of melatonin secretion and the vast effects of this hormone on health, it seemed that finding a relationship between the two could provide a cue for better and healthier aging. This study investigated melatonin levels among night vigil prayers, non-prayer late sleepers, and those with regular night sleep.

Methods

Design and setting

This was a descriptive and analytical cross-sectional study conducted in 2020 in Yazd, a central city of Iran.

Participants

Ninety people in three categories of night vigil prayers, non-prayer late sleepers, and those with regular night sleep participated in the study. Each group consisted of 30 persons.

Sampling

The convenience method was adopted for sampling. The general inclusion criteria were being above the age of puberty (9 for girls and 15 for boys), at which Muslims are required to fulfill their religious obligations and rituals, including prayers and being married. The specific criteria for each group of participants were as follows:

- The night vigil prayers made tahajjud an inseparable part of their lives, spending at least one hour from midnight to dawn praying.
- Non-prayer late sleepers were awake for at least one hour simultaneously without worship or praying.
- Those with regular night sleep were asleep from midnight to dawn.

The exclusion criteria were being on the night shift at work, being under medical treatment, being addicted, using night light during sleep, and sleeping in noisy environments. The groups were adjusted/matched in terms of the two variables of age and gender.

Data collection

To provide the data regarding the background variables, we used a questionnaire, including information about age, gender, education, and occupation.

Melatonin was measured with two blood draws (6,7) (from 23:00 to 24:00 and from 9:00 to 10:00). Blood sampling was done by a certified lab technician at work or at home with prior arrangement. In each session, 3 mL of blood was taken. Then, the serum of the blood samples was separated and frozen at zsssx-20 °C until the melatonin level was measured. We used the ELIZA method (Statfox 2100 Awareness Company USA) and Zell Bio GmbH (Germany) to measure the melatonin hormone. No. ZB-11013C-H9648 kits were used according to the manufacturing company's instructions and quality control after the dilution of solutions and reagents.

Data analysis

The data were analyzed by SPSS 21 using the one-sample Kolmogorov-Smirnov test, Pearson's chi-square, Pearson's correlation coefficient, and ANOVA. The significance level was set at 0.05.

Results

Ninety people in three groups of night vigil prayers, nonprayer late sleepers, and those with regular night sleep participated in the study in groups matched in age and gender. Table 1 shows the demographic characteristics of the participants:

The data analysis showed a significant difference between the average nocturnal melatonin serum levels among the three groups of participants (Table 2 and Figure 1). The average daily melatonin serum level was not significantly different between the regular night sleepers and non-praying late sleepers groups (P=0.306). However, this difference was significant between the night vigil prayers and the other two groups (Table 2 and Figure 2). Moreover, an adverse significant relationship was found between age and nocturnal melatonin (r=0.38, P<0.0001) and between age and daily melatonin (r=0.25, P=0.02).

Discussion

This study examined blood melatonin levels among the three groups of night vigil prayers, non-praying late sleepers, and regular night sleepers. The results showed a significant relationship between age and the amount of melatonin secretion, both within and among different groups.

The research also showed a significant difference in the average nocturnal melatonin secretion among the three groups. Meanwhile, the average daily melatonin secretion in the vigil night prayers significantly differed from the non-praying late sleepers and the regular night sleepers. However, there was no significant difference between the non-praying late sleepers and regular night sleepers

Table 1. Demographic characteristics of the night vigil prayers, non-prayer late sleepers, and regular night sleeper participants

Variable		Night vigil prayers	Non-prayer late sleepers	Regular night sleepers	P value	
Age, Mean (SD)		44.10 (11.30)	41.57 (10.25)	44.60 (12.02)	0.535	
Gender, No. (%)	Male	19 (63.3)	20 (66.7)	19 (63.3)	0.447	
	Female	11 (36.7)	10 (33.3)	11 (36.7)		
	Sum	30	30	30		
	Illiterate	2 (6.7)	2 (6.7)	9 (30)		
Education, No. (%)	Under diploma	14 (4.7)	2 (6.7)	7 (23.3)		
	High-school diploma	8 (26.7)	2 (6.7)	0 (0)	0.021	
	Associate degree	0 (0)	1 (3.3)	0 (0)		
	Bachelor's	5 (16.7)	17 (56.7)	10 (33.3)		
	Master's	1 (3.3)	5 (16.7)	4 (13.3)		
	Seminary 1 or 2	0 (0)	1 (3.3)	0 (0)		
	Sum	30	30	30		
	Homemaker	9 (30)	13 (3.3)	4 (13.3)		
Occupation, No. (%)	Laborer	10 (33.3)	3 (10)	1 (3.3)		
	Government clerk	3 (10)	9 (90)	17 (56.7)		
	Clergyman	0 (0)	0 (0)	1 (3.3)	< 0.0001	
	Student	3 (10)	0 (0)	7 (23.3)		
	Self-employed	5 (16.7)	5 (16.7)	0 (0)		
	Sum	30	30	30		

Group	Nocturnal melatonin serum levels	P value	Daily melatonin serum levels	P value
Night vigil prayers	386.63 (66.87)		305.37 (77.65)	
Non-prayer late sleepers	335.03 (34.52)	< 0.0001	253.37 (51.25)	< 0.0001
Regular night sleepers	278.80 (44.92)		237.37 (47.19)	

Table 2. Comparison of daily and nocturnal serum melatonin levels (μ g/L) among the three groups: night vigil prayers, non-prayer late sleepers, and regular night sleepers





Figure 1. Means and error bars (95% Cl) of nocturnal serum melatonin levels. Comparison of daily and nocturnal serum melatonin levels (μ g/L) among the three groups: night vigil prayers, non-payer late sleepers, and regular night sleepers (P=0.0001)

regarding average melatonin secretion. This means that the average nocturnal and daily melatonin secretion in people awake at night for night prayers is higher than those awake at night without night prayers and those with regular night sleep. The difference between the two groups who were awake at night is worth consideration. However, the group performing night prayer showed a higher level of melatonin secretion, which can result from prayer, invocation, and goodwill. This is following the Islamic recommendations about the sleep-wake behavior of Muslims (34).

The French philosopher Rene Descartes described the pineal gland as "the seat of the soul" (35). Considering the vital role of melatonin as a product of the pineal gland, this implied that the soul and spiritual conditions affect physical health. However, the mechanism of this effect was not clear. The remarkable research findings about the role of melatonin in health may be seen as clues to how these effects are exerted. Melatonin is a biological modulator of mood, sleep, sexual behavior, reproductive alterations, immunologic function, and circadian rhythms (35). Previous studies have indicated the relationship between melatonin and different health conditions, including cancer (36), metabolic and cardiovascular disorders, gastrointestinal conditions, neonatology and pediatrics, neurodegenerative disorders, mental disorders, pain syndromes, reproductive functions, sleep disorders, and traumatic injuries (37). The close relationship between melatonin and the circadian rhythm and the relationship between circadian rhythms and psychological disorders like depression (38) are among the major findings aligned with this study's aims.

Figure 2. Means and error bars (95% CI) of nocturnal serum melatonin levels. Comparison of the melatonin serum level day and night (μ g/L) among the three groups: daily and nocturnal (P=0.0001)

Because of the determining effect of melatonin on different aspects of health, including its high potential in detoxifying free radicals and protecting cellular systems (39), its role in regulating both inflammation and motility in the gastrointestinal tract (40), and its protective effect against neurodegenerative diseases such as stroke, Alzheimer's disease, Parkinson's disease, Huntington's disease, and amyotrophic lateral sclerosis (41), it seems that we have sufficient scientific evidence to convince us to investigate exact ways to increase the amount of melatonin in those who are subject to its decline. The findings of this study regarding the significant relationship between night prayer and melatonin level, accompanied by the empirical findings on the significant role of melatonin on health, could provide valuable hints to correct healthy lifestyles. Islamic instructions have pointed out the physical health outcomes of night prayer and its spiritual and otherworldly rewards. Imam Reza (PBUH), in a hadith, has mentioned the role of night prayer in the longevity of life (42).

The issue of melatonin and attempting to compensate for its decline is very important in the elderly. Decreased melatonin secretion is amplified with a smaller intake of foods that may contain small quantities of melatonin. Aging, along with dementia, psychiatric disorders, and sleep disorders, are among the factors altering melatonin secretion levels (43). Thus, exogenous melatonin is used to treat insomnia in the elderly with nocturnal melatonin deficiency or experience an abnormality in melatonin secretion (44).

The findings of this study are important because of the significant effect of melatonin on different aspects of health, including its cytoprotective effects on tissues and, accordingly, against aging, neurodegenerative diseases, immunomodulation, and cancer (45). Because of the effects of melatonin on the circadian rhythm and its other health outcomes, it has been considered a sleeping aid for elderly people (46). Apart from melatonin therapy, alternative and complementary solutions have been adopted to increase melatonin secretion and reduce insomnia and other related disorders (47). However, according to this study's findings, we could think of other non-medical solutions. This needs further investigation, but we could think of other religious and spiritual indicators like moral virtues, religious attitude, and piety as effective on melatonin secretion and its subsequent outcomes.

The study's main limitation was the existence of confounding variables such as sleep cycle, nutrition style, urban or rural lifestyle, underlying disease, etc, and it was not possible to eliminate the effect of all these confounding variables in this research.

Conclusion

This study showed that the average nocturnal and daily melatonin levels in the night vigil prayers were higher compared to the non-praying late sleepers and regular night sleepers. Therefore, waking up at night to approach Allah and engage in prayer, supplication, and positive thoughts is associated with the release of the melatonin hormone and can be considered in regulating sleep and improving physical and mental health. However, cohort studies and studies with more accurate control of confounding factors are suggested to understand this relationship further.

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Competing Interests

The authors declare that they have no conflict of interest.

Ethical Approval

This study was conducted with the approval of the ethics committee in biomedical research of Qom University of Medical Sciences (Code IR.MUQ.REC.1399.172). The participants received adequate information about the aims and nature of the study. They entered the study after providing written informed consent. All the data were treated anonymously, and the confidentiality of the participants was completely observed. All the stages of the study were performed following guidelines and regulations.

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References

- Arendt J. Melatonin, circadian rhythms, and sleep. N Engl J Med. 2000;343(15):1114-6. doi: 10.1056/ nejm200010123431510.
- Pandi-Perumal SR, Trakht I, Srinivasan V, Spence DW, Maestroni GJ, Zisapel N, et al. Physiological effects of melatonin: role of melatonin receptors and signal transduction pathways. Prog Neurobiol. 2008;85(3):335-53. doi: 10.1016/j.pneurobio.2008.04.001.
- Pévet P. The internal time-giver role of melatonin. A key for our health. Rev Neurol (Paris). 2014;170(11):646-52. doi: 10.1016/j.neurol.2014.05.008.
- Higuchi S, Motohashi Y, Ishibashi K, Maeda T. Less exposure to daily ambient light in winter increases sensitivity of melatonin to light suppression. Chronobiol Int. 2007;24(1):31-43. doi: 10.1080/07420520601139805.
- Zhdanova IV, Tucci V. Melatonin, circadian rhythms, and sleep. Curr Treat Options Neurol. 2003;5(3):225-9. doi: 10.1007/s11940-003-0013-0.
- Wehr TA, Duncan WC Jr, Sher L, Aeschbach D, Schwartz PJ, Turner EH, et al. A circadian signal of change of season in patients with seasonal affective disorder. Arch Gen Psychiatry. 2001;58(12):1108-14. doi: 10.1001/archpsyc.58.12.1108.
- Bocheva G, Slominski RM, Janjetovic Z, Kim TK, Böhm M, Steinbrink K, et al. Protective role of melatonin and its metabolites in skin aging. Int J Mol Sci. 2022;23(3):1238. doi: 10.3390/ijms23031238.
- MacDonald IJ, Huang CC, Liu SC, Tang CH. Reconsidering the role of melatonin in rheumatoid arthritis. Int J Mol Sci. 2020;21(8):2877. doi: 10.3390/ijms21082877.
- Segovia-Roldan M, Diez ER, Pueyo E. Melatonin to rescue the aged heart: antiarrhythmic and antioxidant benefits. Oxid Med Cell Longev. 2021;2021:8876792. doi: 10.1155/2021/8876792.
- Bonnefont-Rousselot D, Collin F. Melatonin: action as antioxidant and potential applications in human disease and aging. Toxicology. 2010;278(1):55-67. doi: 10.1016/j. tox.2010.04.008.
- Anisimov VN, Popovich IG, Zabezhinski MA, Anisimov SV, Vesnushkin GM, Vinogradova IA. Melatonin as antioxidant, geroprotector and anticarcinogen. Biochim Biophys Acta. 2006;1757(5-6):573-89. doi: 10.1016/j.bbabio.2006.03.012.
- Rodriguez C, Mayo JC, Sainz RM, Antolín I, Herrera F, Martín V, et al. Regulation of antioxidant enzymes: a significant role for melatonin. J Pineal Res. 2004;36(1):1-9. doi: 10.1046/j.1600-079x.2003.00092.x.
- 13. Reiter RJ, Mayo JC, Tan DX, Sainz RM, Alatorre-Jimenez

M, Qin L. Melatonin as an antioxidant: under promises but over delivers. J Pineal Res. 2016;61(3):253-78. doi: 10.1111/jpi.12360.

- Srinivasan V, Spence DW, Pandi-Perumal SR, Brown GM, Cardinali DP. Melatonin in mitochondrial dysfunction and related disorders. Int J Alzheimers Dis. 2011;2011:326320. doi: 10.4061/2011/326320.
- Farhud D, Tahavorgar A. Melatonin hormone, metabolism and its clinical effects: a review. Iran J Endocrinol Metab. 2013;15(2):211-23. [Persian].
- Boga JA, Caballero B, Potes Y, Perez-Martinez Z, Reiter RJ, Vega-Naredo I, et al. Therapeutic potential of melatonin related to its role as an autophagy regulator: a review. J Pineal Res. 2019;66(1):e12534. doi: 10.1111/jpi.12534.
- Markus RP, Sousa KS, da Silveira Cruz-Machado S, Fernandes PA, Ferreira ZS. Possible role of pineal and extra-pineal melatonin in surveillance, immunity, and first-line defense. Int J Mol Sci. 2021;22(22). doi: 10.3390/ijms222212143.
- Ferracioli-Oda E, Qawasmi A, Bloch MH. Meta-analysis: melatonin for the treatment of primary sleep disorders. PLoS One. 2013;8(5):e63773. doi: 10.1371/journal.pone.0063773.
- Andersen LP, Werner MU, Rosenberg J, Gögenur I. A systematic review of peri-operative melatonin. Anaesthesia. 2014;69(10):1163-71. doi: 10.1111/anae.12717.
- Wang YM, Jin BZ, Ai F, Duan CH, Lu YZ, Dong TF, et al. The efficacy and safety of melatonin in concurrent chemotherapy or radiotherapy for solid tumors: a meta-analysis of randomized controlled trials. Cancer Chemother Pharmacol. 2012;69(5):1213-20. doi: 10.1007/s00280-012-1828-8.
- 21. Seely D, Wu P, Fritz H, Kennedy DA, Tsui T, Seely AJ, et al. Melatonin as adjuvant cancer care with and without chemotherapy: a systematic review and meta-analysis of randomized trials. Integr Cancer Ther. 2012;11(4):293-303. doi: 10.1177/1534735411425484.
- Chen S, Shi L, Liang F, Xu L, Desislava D, Wu Q, et al. Exogenous melatonin for delirium prevention: a metaanalysis of randomized controlled trials. Mol Neurobiol. 2016;53(6):4046-53. doi: 10.1007/s12035-015-9350-8.
- Srinivasan V, Lauterbach EC, Ho KY, Acuña-Castroviejo D, Zakaria R, Brzezinski A. Melatonin in antinociception: its therapeutic applications. Curr Neuropharmacol. 2012;10(2):167-78. doi: 10.2174/157015912800604489.
- Wilkinson D, Shepherd E, Wallace EM. Melatonin for women in pregnancy for neuroprotection of the fetus. Cochrane Database Syst Rev. 2016;3(3):CD010527. doi: 10.1002/14651858.CD010527.pub2.
- Farez MF, Mascanfroni ID, Méndez-Huergo SP, Yeste A, Murugaiyan G, Garo LP, et al. Melatonin contributes to the seasonality of multiple sclerosis relapses. Cell. 2015;162(6):1338-52. doi: 10.1016/j.cell.2015.08.025.
- Mukti GI, Hilmi IL, Salman S. Literature review: clinical trial on the effectiveness of melatonin as an alternative medicine for COVID-19. Jurnal EduHealth. 2022;13(2):1158-63.
- 27. Wu AH, Wang R, Koh WP, Stanczyk FZ, Lee HP, Yu MC. Sleep duration, melatonin and breast cancer among Chinese women in Singapore. Carcinogenesis. 2008;29(6):1244-8. doi: 10.1093/carcin/bgn100.
- Rana S, Mahmood S. Circadian rhythm and its role in malignancy. J Circadian Rhythms. 2010;8:3. doi: 10.1186/1740-3391-8-3.
- Wurtman RJ. Age-related decreases in melatonin secretionclinical consequences. J Clin Endocrinol Metab. 2000;85(6):2135-6. doi: 10.1210/jcem.85.6.6660.
- Lim S, Park S, Koyanagi A, Yang JW, Jacob L, Yon DK, et al. Effects of exogenous melatonin supplementation on health outcomes: an umbrella review of meta-analyses

based on randomized controlled trials. Pharmacol Res. 2022;176:106052. doi: 10.1016/j.phrs.2021.106052.

- 31. Shakir MH. The Holy Quran: Arabic Text and English Translation. Houston: R.A. Juma; 1974.
- 32. Chodijah S. The concept of tahajud prayer through psychotherapy approach in relationship with psychological health. In: Proceedings of the 1st International Conference on Innovative Pedagogy (ICIP 2017). Banda Aceh, Indonesia: STKIP Bina Bangsa Getsempena; 2017.
- Tobeiha M, Jafari A, Fadaei S, Mirazimi SM, Dashti F, Amiri A, et al. Evidence for the benefits of melatonin in cardiovascular disease. Front Cardiovasc Med. 2022;9:888319. doi: 10.3389/ fcvm.2022.888319.
- Nor ZM, Yusoff NN, Razi FR, Sanusi NA. A good night's sleep: a narrative review from Islamic perspectives in relation to modern sciences. Med J Malays. 2018;17(2):117-22. doi: 10.31436/imjm.v17i2.933.
- Beyer CE, Steketee JD, Saphier D. Antioxidant properties of melatonin--an emerging mystery. Biochem Pharmacol. 1998;56(10):1265-72. doi: 10.1016/s0006-2952(98)00180-4.
- Mills E, Wu P, Seely D, Guyatt G. Melatonin in the treatment of cancer: a systematic review of randomized controlled trials and meta-analysis. J Pineal Res. 2005;39(4):360-6. doi: 10.1111/j.1600-079X.2005.00258.x.
- Posadzki PP, Bajpai R, Kyaw BM, Roberts NJ, Brzezinski A, Christopoulos GI, et al. Melatonin and health: an umbrella review of health outcomes and biological mechanisms of action. BMC Med. 2018;16(1):18. doi: 10.1186/s12916-017-1000-8.
- Boyce P, Barriball E. Circadian rhythms and depression. Aust Fam Physician. 2010;39(5):307-10.
- 39. Vielma JR, Bonilla E, Chacín-Bonilla L, Mora M, Medina-Leendertz S, Bravo Y. Effects of melatonin on oxidative stress, and resistance to bacterial, parasitic, and viral infections: a review. Acta Trop. 2014;137:31-8. doi: 10.1016/j. actatropica.2014.04.021.
- 40. Terry PD, Villinger F, Bubenik GA, Sitaraman SV. Melatonin and ulcerative colitis: evidence, biological mechanisms, and future research. Inflamm Bowel Dis. 2009;15(1):134-40. doi: 10.1002/ibd.20527.
- Wang X. The antiapoptotic activity of melatonin in neurodegenerative diseases. CNS Neurosci Ther. 2009;15(4):345-57. doi: 10.1111/j.1755-5949.2009.00105.x.
- 42. Majlesi MB. Bihar- al- Anvar. Dar Ehya- al-Torath- al-Arabic; 1983, Beirut, Lebanon.
- Scholtens RM, van Munster BC, van Kempen MF, de Rooij SE. Physiological melatonin levels in healthy older people: a systematic review. J Psychosom Res. 2016;86:20-7. doi: 10.1016/j.jpsychores.2016.05.005.
- 44. Brzezinski A, Vangel MG, Wurtman RJ, Norrie G, Zhdanova I, Ben-Shushan A, et al. Effects of exogenous melatonin on sleep: a meta-analysis. Sleep Med Rev. 2005;9(1):41-50. doi: 10.1016/j.smrv.2004.06.004.
- Mayo JC, Sainz RM, González Menéndez P, Cepas V, Tan DX, Reiter RJ. Melatonin and sirtuins: a "not-so unexpected" relationship. J Pineal Res. 2017;62(2):e12391. doi: 10.1111/ jpi.12391.
- Papillon-Ferland L, Mallet L. Should melatonin be used as a sleeping aid for elderly people? Can J Hosp Pharm. 2019;72(4):327-30. doi: 10.4212/cjhp.v72i4.2920.
- Spence DW, Kayumov L, Chen A, Lowe A, Jain U, Katzman MA, et al. Acupuncture increases nocturnal melatonin secretion and reduces insomnia and anxiety: a preliminary report. J Neuropsychiatry Clin Neurosci. 2004;16(1):19-28. doi: 10.1176/jnp.16.1.19.