Research article

Study on the effect of Chamomile extract on melatonin hormone levels in subjects suffering from insomnia and anxiety

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ABSTRACT

Introduction and Aim: Insomnia and anxiety are the most common among the psychiatric disorders. These disorders have been associated to melatonin levels; an endocrine hormone produced by the pineal gland in brain. Melatonin has also been associated to several metabolic processes in the body. In this study we aimed to investigate into the effect of chamomile extract on serum melatonin levels as well as on various other blood parameters.

Materials and Methods: Fifty randomized subjects were orally treated with chamomile extract (15% w/v daily) for 8 weeks. Liver enzymes, urea, creatinine, and lipid profile were measured to see the effect of chamomile extract on the body.

Results: From the results, we found a significant increase in the melatonin levels after treatment with chamomile extract. We also did not observe any rise in the liver enzyme levels, blood urea and serum creatinine. Also we found decrease in cholesterol and triglyceride levels.

Conclusion: This study suggests that chamomile extract can be a natural and safe nutritional strategy for improving sleep duration and quality and in improving the lipids levels.

Keywords: Melatonin hormone; insomnia; anxiety; chamomile extract.

INTRODUCTION

Insomnia is a highly prevalent clinical illness that has negative health effects. The prevalence statistics for the problem range from 10-20% of the total adult population, while 35-50% of people in the population experience insomnia symptoms (1).

The Diagnostic Manual of Mental Disorders insomnia is described as "discontent with the quantity of sleep due to difficulty in commencement of sleep and maintaining it for a longer period, leading to significant health problems as well as impaired functioning'. The diagnostic scales for psychiatric disorders include symptoms of insomnia, and it is believed that those with insomnia are more likely to experience depression than people without insomnia (2).

The indolamine melatonin (N-acetyl-5-methoxy tryptamine), is a lipophilic hormone synthesized by the pineal gland in the brain and has been primarily associated with control of the sleep-wake cycle (3). In addition, this endocrine hormone has distant target sites throughout the body playing functionally diverse roles involved in controlling several vital physiological processes (4). In mammals, melatonin secretion by the pineal gland leads to photoperiodic information transmission, which in turn act on the neuroendocrine system and the brain affecting sleep by bringing about adaptive changes in physiology and endocrinology, immunology, reproduction, behavior and energy balance (5). Furthermore, Melatonin has been demonstrated to be a potent antioxidant and having both direct and indirect oncostatic capabilities, the effects being mediated via reproductive hormones (6).

Melatonin is also a natural product found in plants and animals. One of the most important medicinal herbs known to man is Chamomile (*Matricaria chamomilla* L.), whose role has been widely proven in the field of medicine. The dried chamomile flowers are considered medicinal in nature as they contain many chemical compounds, including flavonoids and terpenoids. Chamomile is commonly used to help people sleep or to ease anxiety. Further, clinical researches have demonstrated that chamomile powder can be used to relieve anxiety in people (8). It was discovered that chamomile pills greatly reduced anxiety symptoms in people. Animal studies have revealed that larger dosages of chamomile promote sleep, while lower amounts may alleviate anxiety (9).

Materials and Methods

Study subjects

A randomized study was conducted on 50 people (male and female) age 18- 60 years suffering from insomnia and anxiety disorders, samples were collected during the month of November 2021 through March 2022.

Ethical consideration

After describing the study purpose, a written informed consent was obtained from each participant prior to

data collection. Each patient was given the unrestricted right to withdraw at any moment. Throughout the trial, data confidentiality was ensured, and patients were promised that their information would only be used for research purpose.

Preparation of chamomile extract

Approximately 15.0 g of dried Chamomile (*Matricaria chamomilla* L.), grind the flowers into a powder and mixed in 100 ml of water. The mixture was heated up to 75°C for 35 minutes until the solution changed color. The extract was filtered and used in treatment studies (10).

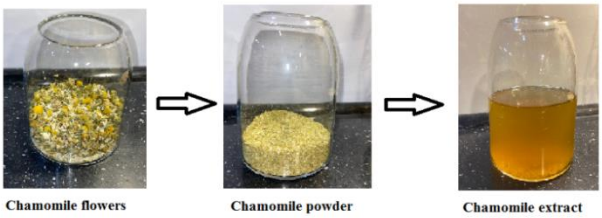

Fig.1: Chamomile extraction

Treatment and analysis

Patients included in the study were assigned to orally take 15 ml chamomile extract a day for a period of 60 days.

Venous blood (5 ml) was drawn from these subjects in two phases, before (G1, control) and after treatment (G2) with chamomile extract. Blood drawn was centrifuged at 4,000 x g for 10 minutes. The serum obtained was used immediately to determine AST, ALT, ALP, urea, creatinine and lipid levels based on the Kit method (11,12), and analyzed in an automated machine (Roche Cobas C111 Analyzer, Germany). Melatonin hormone levels were measured based on ELISA technique.

Results obtained were represented as mean ± SEM. Statistical test for assessment of the significance of the difference between G1 and G2 phases was performed using the paired t-test was. P-value calculated was considered significant (P≤0.05) or non-significant (P≥0.05).

RESULTS

Table 1 shows serum melatonin levels of control subjects (G1) and after treatment by chamomile extract (G2), A significant elevation in serum blood melatonin levels (P≤0.05) was observed in G2 as compared to G1.

Table 1: Serum melatonin levels in G1 and G2

Parameters	G1 phase Control	G2 (Chamomile extract treatment)	T-Test (P-value)
Melatonin (ng/ml)	0.173 ± 0.105	0.55 ± 0.478	≤0.05*

Table 2 shows the results for liver enzymes, urea, and creatinine in G1 and G2. The values in Table show that the levels of AST, ALT, ALP, urea, and creatinine are statistically non-significant between G1 and G2.

The results obtained for cholesterol, triglyceride, HDL, LDL, and VLDL levels in phases G1 and G2 are presented in Table 3. Table 3 shows that, other from HDL-c, the levels of the lipid profile significantly decreased following chamomile administration (G2) as compared to G1 level.

Table 2: Blood biochemical parameters for control and treatment groups

Parameters	G1 (Control)	G2 (Chamomile extract treatment)	T-Test G1 vs G2 (P-value)
AST (U/l)	11.22± 10.458	12.08± 9.558	≥0.05 *
ALT (U/l)	13.28± 8.758	14.00± 7.651	≥0.05 *
ALP (U/l)	65.97± 25.237	63.99± 27.331	≥0.05 *
Urea (mg/dl)	25.71 ± 12.209	24.91 ± 10.333	≥0.05 *
Creatinine (mg/dl)	0.72 ± 0.288	0.75 ± 0.10	≥0.05 *

Table 3: Levels of lipid profile for control and treatment groups

Parameters	G1 (control)	G2 (Chamomile extract treatment)	T-Test (P-value)
TC (mg/dL)	145.79±10.01	105.01±15.11	≤0.05 *
TG (mg/dL)	135.04±20.11	90.79±4.01	≤0.05 *
HDL-c (mg/dL)	41.166±4.44	53.476±5.0	≤0.05 *
LDL-c (mg/dL)	82.2±14.37	55.13±16.37	≤0.05 *
VLDL-c (mg/dL)	21.0±4.02	18.158±0.8	≤0.05 *

DISCUSSION

The chamomile plant has been used primarily for medicinal purposes as an anti-inflammatory, antiseptic, antioxidant, effects in wound-healing and antispasmodic (13). To our knowledge, animal studies have demonstrated anti-diabetic effects of chamomile aqueous extract. Based on literature review, this study is the first to report the effect of chamomile extract on melatonin levels in people with insomnia and anxiety.

Our findings showed intake of chamomile extract significantly increased the level of melatonin in the blood in group 2 (G2) compared to the control group (G1) which indicates that chamomile extract could be used to treat insomnia and anxiety. Similarly, our study found that daily and regular consumption of chamomile extract significantly reduced blood levels of total cholesterol, triglycerides, low-density lipoproteins, and very low density lipoproteins. This finding supports and agrees with earlier studies that found lower serum lipid profile levels in diabetic mice (14), lower serum total cholesterol levels in Wistar rats (15) and reduced total cholesterol levels in chamomile diet-induced rats (16). As a result of the information that has been provided thus far, we recommend that chamomile extract be evaluated for use in biological chemistry as well as a variety of medicinal applications, including the treatment of cancer may be recommended to treat CML (17), Adenocarcinoma (18), and the prevention of a wide range of pathogenic bacteria, viruses, and parasites such as *Clostridium perfringens* (19), *Brucella melitensis* (20), *Proteus vulgaris* (21), *Staphylococcus aureus* (22), *Pseudomonas aeruginosa* (23), and *Toxoplasma spp* (24,25), SARS-Cov-2 (26).

CONCLUSION

The results of the current study suggested that those who experience sleeplessness and anxiety may benefit from using chamomile extract to help regulate their levels of melatonin and serum lipids. As a result, our findings imply that chamomile extract may be employed as a safe and natural herb for enhancing the quality of sleep as well as the lipid levels.

CONFLICT OF INTEREST

There is no conflict of interest for the study.

REFERENCES

1. Mirchandaney, R., Barete, R., Asarnow, L.D. Moderators of cognitive behavioral treatment for insomnia on depression and anxiety outcomes. Current Psychiatry Reports.2022; (24):1-8.
2. Blake, M.J., Trinder, J.A., Allen, N.B. Mechanisms underlying the association between insomnia, anxiety, and depression in adolescence: implications for behavioral sleep interventions. Clinical Psychology Review.2018; 63(1):25-40.
3. Gandolfi, J.V., Di Bernardo, A.P.A., Chanes, D.A.V., Martin, D.F., Joles, V.B., Amendola, C.P., *et al.*, The effects of melatonin supplementation on sleep quality and assessment of the serum melatonin in ICU patients: a randomized controlled trial. Critical Care Medicine. 2020; 8(12): e1286-e1293.
4. Reiter R.J., Tan, D.X., Fuentes-Broto, L. Melatonin: a multitasking molecule. Prog Brain Res. 2010;181:127-51.
5. Hardeland R, Cardinali DP, Srinivasan V, Spence DW, Brown GM, Pandi-Perumal SR. Melatonin--a pleiotropic, orchestrating regulator molecule. Prog Neurobiol. 2011; 93(3):350-384.
6. Macchi MM, Bruce JN. Human pineal physiology and functional significance of melatonin. Front Neuroendocrinol. 2004;25(3-4):177-195.
7. De Almeida, E.A., Di Mascio, P., Harumi, T., Warren Spence, D., Moscovitch, A., Hardeland, R., *et al.*, Measurement of melatonin in body fluids: standards, protocols, and procedures. Child's Nervous System. 2011; 27(6):879-891.
8. Amsterdam, J.D., Shults, J., Soeller, I., Mao, J.J., Rockwell, K., Newberg, A.B. Chamomile (*Matricaria recutita)* may have antidepressant activity in anxious depressed humans-an exploratory study. Alternative Therapies in Health and Medicine. 2012; 18(5):44-49.
9. Amsterdam, J.D., Li, Y., Soeller, I., Rockwell, K., Mao, J.J., Shults, J. A randomized, double-blind, placebo-controlled trial of oral *Matricaria recutita* (Chamomile) extract therapy of generalized anxiety disorder. Journal of Clinical Psychopharmacology. 2009; 29(4):378-382.
10. Veisi, H., Zohrabi, A., Kamangar, S.A., Karmakar, B., Saremi, S.G., Varmira, K., *et al.*, Green synthesis of Pd/Fe3O4 nanoparticles using Chamomile extract as highly active and recyclable catalyst for Suzuki coupling reaction. Journal of Organometallic Chemistry. 2021; 951:122005.
11. Ali, R.J., Ali, D.R., Ahmed, Z.I., Ahmed, A.A., Hassen, D.S., Tahir, R.M. Comparison of deferasirox and deferoxamine effect on liver enzyme activities and ferritin level in patients with beta-thalassemia. Zanco Journal of Medical Sciences. 2020; 24(3):354-359.
12. Hasan, S.M., Mohammed, A.K. and Taha, A.M. Measurement of paraoxonase-1, visfatin levels in Iraqi diabetic and diabetic with hypothyroidism. Biomedicine. 2022; *42*(1):165-168.
13. Rafraf, M., Zemestani, M., Asghari-Jafarabadi, M. Effectiveness of Chamomile tea on glycemic control and serum lipid profile in patients with type 2 diabetes. Journal of Endocrinological Investigation. 2015; 38(2): 163-170.
14. Najla, O.A., Olfat, A.K., Kholoud, S.R., Enas, N.D., Hanan, S.A. Hypoglycemic and biochemical effects of *Matricaria chamomilla* leave extract in streptozotocin-induced diabetic rats. Journal of Health Sciences. 2012; 2(5):43-48.
15. Al-Jubouri, H.H.F., Al-Jalil, B.H., Farid, I., Jasim, F., Wehbi, S. The effect of chamomile on hyperlipidemias in rats. Journal of the Faculty of Medicine (Baghdad). 1990; 32(1): 5-11.
16. Weidner, C., Wowro, S.J., Rousseau, M., Freiwald, A., Kodelja, V., Abdel-Aziz, H., Kelber, O., *et al.*, Antidiabetic effects of Chamomile flowers extract in obese mice through transcriptional stimulation of nutrient sensors of the peroxisome proliferator-activated receptor (PPAR) family. PloS one. 2013; 8(11): e80335.
17. Ahmed, A.A., Khaleel, K.J., Fadhel, A.A., Al-Rubaii, B.A.L. Chronic Myeloid Leukemia: A retrospective study of clinical and pathological features. Bionatura, 2022, 7(3), 41. DOI. 10.21931/RB/2022.07.03.41.
18. Ali, S.M., Lafta, B.A., Al-Shammary, A.M., Salih, H.S. In vivo oncolytic activity of non-virulent newcastle disease virus Iraqi strain against mouse mammary adenocarcinoma. AIP Conference Proceedings, 2021, 2372, 030010.
19. Hashim, S.T., Fakhry, S.S., Rasoul, L.M., Saleh, T.H. ,Alrubaii, B.A.L. Genotyping toxins of Clostridium perfringens strains of rabbit and other animal origins. Tropical Journal of Natural Product Research.2021; 5(4):613-616.
20. Abdulkaliq Awadh, H., Hammed, Z.N., Hamzah, S.S., Saleh, T.H., AL-Rubaii, B.A.L. Molecular identification of intracellular survival related Brucella melitensis virulence factors. Biomedicine.2022; 42(4):761-765.
21. kadhim AL-Imam, M.J.,AL-Rubaii, B.A.L.The influence of some amino acids, vitamins and anti-inflammatory drugs on activity of chondroitinase produced by Proteus vulgaris caused urinary tract infection. Iraqi Journal of Science.2016; 57 (4A):2412-2421.
22. Sabah Fakhry, S., Noori Hammed, Z., Abdul-elah Bakir, W.,Abdullah Laftaah ALRubaii, B. Identification of methicillin-resistant strains of Staphylococcus aureus isolated from humans and food sources by use mecA 1 and mecA 2 genes in Pulsed-field gel electrophoresis technique. Bionatura.2022; 7(2), 44. http://dx.doi.org/10.21931/RB/2022.07.02.44.
23. Shehab, Z.H., AL-Rubaii, B.A.L. Effect of D-mannose on gene expression of neuraminidase produced from different clinical isolates of Pseudomonas aeruginosa. Baghdad Science Journal.2019; 16(2):291–298.

24. Abdulla, L., Ismael, M.K., Salih, T.A., Malik, S.N.,Al-Rubaii, B.A.L. Genotyping and evaluation of interleukin-10 and soluble HLA-G in abortion due to toxoplasmosis and HSV-2 infections. Annals of parasitology.2022; 68(2):385-390.
25. Jiad, A.L., Ismael, M.K., Muhsin, S.S., Al-Rubaii, B.A.L. ND2 Gene Sequencing of Sub fertile Patients Recovered from COVID-19 in Association with Toxoplasmosis. Bionatura.2022; 7(3), 45. http://dx.doi.org/10.21931/RB/2022.07.03.45.
26. Rasoul, L.M., Nsaif, M.M., Al-Tameemi, M.T., Al-Rubaii, B.A.L. Estimation of primer efficiency in multiplex PCR for detecting SARS-Cov-2 variants. Bionatura, 2022, 7(3), 48. http://dx.doi.org/10.21931/RB/2022.07.03.49