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Effects of chamomile (*Matricaria chamomilla* L.) on sleep: A systematic review and meta-analysis of clinical trials

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ABSTRACT

Objective: We aimed to investigate the effects of chamomile (*Matricaria chamomilla* L.) on sleep in this systematic review and meta-analysis of clinical trials.

Methods: PubMed, Scopus, Web of Science, and Cochrane Library were searched until August 2023. All clinical trials that investigated the effects of chamomile on sleep, either in healthy or diseased adults, were eligible to enter the study. The quality of studies was assessed using the Cochrane tool. Random-effects meta-analysis was used to pool weighted mean differences (WMD) and 95 % CI for the outcomes assessed by at least three studies with relatively consistent participants.

Results: The systematic review included ten studies (772 participants). Meta-analysis was conducted for the Pittsburgh Sleep Quality Index (PSQI) score and sleep length. A significant reduction in PSQI score (WMD: −1.88, 95 %CI: −3.46, −0.31, I2: 88.4 %, n = 5) was found. For other outcomes, meta-analysis was not conducted. Sleep onset latency or ease of getting to sleep were improved in three of the four studies. Daytime functioning measures, including fatigue severity index or postpartum fatigue scale, did not change in all three studies. Sleep efficiency did not change in two studies and deteriorated in one. The number of awakenings after sleep or staying asleep was improved in two of the three studies. No adverse events were reported in any of the studies although passive surveillance was used to assess adverse effects except in one study. Only one study surveyed the blinding success and tested the purity and/or potency of the used products.

Conclusion: Chamomile improved sleep, especially the number of awakenings after sleep or staying asleep; however, it did not lead to an improvement in the duration of sleep, percentage of sleep efficiency, and daytime functioning measures. Future studies are suggested to assess objective measures.

1. Introduction

Sleep is a fundamental physiological process that is vital for overall health and well-being.[1,2] However, sleep disorders and insufficient sleep have become increasingly prevalent, affecting a significant portion of the population worldwide.[3,4] Individuals suffering from sleep disorders encounter notable distress and disruption in their daily activities and responsibilities.[5,6] Numerous studies have documented various conditions associated with insomnia, encompassing psychiatric disorders, substance abuse and dependence, medical ailments, and neurological complications. Additionally, enduring sleep disorders was linked to an array of unfavorable consequences, including an elevated risk of mortality.[7,8]

Various treatment approaches exist for sleep disorders, including psychotherapeutic methods and pharmacotherapy.[9–11] However, these strategies face significant challenges such as limited availability, costs,

Abbreviations: CI, confidence interval; CKD, chronic kidney disease; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; OSA, Oguri sleep survey sheet; PSQI, Pittsburgh Sleep Quality Index; SD, standard deviation; WMD, weighted mean differences,.

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insufficient evidence, and potential dependency.[12,13] Furthermore, it is noteworthy that over two-thirds of individuals with insomnia do not seek medical assistance and instead resort to over-the-counter medications or self-treatment.[14] As a result, there has been growing interest in exploring complementary and alternative medicine (CAM) approaches to improve sleep quality and duration, including the use of herbal remedies.[15–18]

Chamomile, derived from the German chamomile, *Matricaria chamomilla* L. (Asteraceae), has a long history of traditional use as a medicinal herb, particularly for its calming and sedative properties.[19–21] The most important part of chamomile used for its therapeutic properties is its flower. It contains various bioactive compounds, such as flavonoids (e.g., apigenin, luteolin, and quercetin[19,22]) and terpenoids (e.g., chamazulene, bisabolol, and bisabolol oxide [23,24]) which are believed to contribute to its potential sleep-enhancing effects.[25,26] Chamomile is commonly consumed as a tea or in the form of dietary supplements. While traditional medicine perspectives, including traditional Persian medicine, suggest that chamomile may enhance sleep quality, the current evidence-based support for its efficacy remains inconclusive. Previous studies investigating the effect of chamomile on sleep have yielded mixed results, with some reporting positive effects, while others find no significant improvements.[27–30]

Therefore, a comprehensive evaluation of the available evidence is needed to determine the overall impact of chamomile on sleep quality and duration. A systematic review and meta-analysis of relevant clinical trials can provide a robust and objective assessment of the effects of chamomile on sleep outcomes. The objective of this study is to conduct a systematic review and meta-analysis of clinical trials to investigate the effects of chamomile on sleep. We aim to assess the available evidence, evaluate the methodological quality of the included studies, and determine the overall impact of chamomile on subjective and objective measures of sleep. By elucidating the potential benefits of chamomile on sleep, this study can contribute to the growing body of literature on CAM options for sleep improvement. Furthermore, a comprehensive analysis of the available evidence can guide healthcare professionals and individuals seeking natural remedies for sleep problems, providing them with evidence-based information to make informed decisions regarding chamomile supplementation.

2. Methods

We registered the protocol in the International Prospective Register of Systematic Reviews (PROSPERO; www.crd.york.ac.uk/prospero/index.asp; identifier CRD42023448497) and used Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist in reporting of this systematic review.

2.1. Search strategy

PubMed, Scopus, Web of Science, and Cochrane Library were searched from inception until August 2023, with no language restriction. Reference lists of the included articles were also scanned to ensure no eligible studies were missed. The following search terms were used: Chamomile, *Matricaria chamomilla*, *Matricaria recutita*, insomnia sleeplessness, and sleep quality. The complete search strategy used to find original article for inclusion in our systematic review is presented in Supplementary Text 1.

2.2. Study selection

Two authors (PE, AK) initially screened the title and abstract of all studies. Then, the full texts of studies that could not be decided to be excluded in the previous phase were scanned. All controlled trials that investigated the effect of chamomile (oral, aromatherapy, etc.) on sleep, either in healthy people or subjects with disease conditions aged $\geq$ 18 years were eligible to be included in our systematic review. We excluded the studies that assessed the effect of chamomile in combination with other herbal remedies, did not have a control or placebo group, and studied the participants aged under 18 years.

2.3. Data extraction and risk of bias assessment

Two authors (PE, SS) independently extracted data from the included studies. Any discrepancies were resolved by the third author (AK). The following data was extracted: the first author's name, publication year, study characteristic (study design, location, and follow-up duration), participants' characteristics (age, sex, and health condition), form and dosage of chamomile, method of sleep assessment, number of participants in the chamomile and control or placebo groups, and mean and standard deviation (SD) of sleep indicators before and after the intervention (or their change) in both groups.

The risk of bias in studies was assessed using the Cochrane Risk of Bias Tool for Randomized Controlled Trials [31] by two researchers (SS and AK). Based on this tool, seven domains of study implementation and methodology could be assessed: 1) random sequence generation; 2) allocation concealment; 3) blinding of participants and researchers; 4) blinding of outcome assessors; 5) incomplete outcome data (missing bias); 6) selective reporting; 7) other biases (we considered it as excluding subjects who had used opioids, analgesics, or hypnotic drugs).

2.4. Data synthesis and statistical analysis

We conducted a meta-analysis for the outcomes that were assessed by at least three studies with relatively consistent participants. The random-effects model was used to calculate the summary mean difference. The mean difference in Pittsburgh Sleep Quality Index (PSQI) score change and their corresponding standard deviations (SD) between the intervention and control or placebo groups were used as the effect size for analysis. For the studies that did not report the mean change, the difference between groups and SD was estimated using the 0.5 correlation coefficient. The weighted mean difference (WMD) and its corresponding SE were calculated using the DerSimonian and Laird method.[32] The Cochrane Chi-squared test was used to explore the heterogeneity. We conducted sensitivity analyses by excluding one study at a time and re-estimating the WMD.

3. Results

A total of 370 publications were obtained from the initial search; 89 were duplicates, so they were removed. Of the 281 papers that remained, 258 were excluded after being determined to be irrelevant based on title and abstract screening. The remaining were considered for full text examination, and 13 of them were excluded due to lack of control or placebo groups; combination of chamomile with other medical herbs; lack of reporting the required outcomes; or non-clinical design of study. Finally, 10 publications with 772 participants were included in the systematic review.[33–42] The PRISMA flowchart of the selection procedure is illustrated in Fig. 1.

Characteristics of the included studies are presented in Table 1. Two studies were conducted on postmenopausal women,[33,39] two on elderly subjects,[34,35] one on subjects with poor sleep,[40] one on sleep-disrupted postnatal women,[41] one on adolescents with dysmenorrhea,[38] one on patients with heart failure,[42] and one on patients with chronic kidney disease.[37] All of the studies except one were conducted in Asia [Iran (n = 5), Indonesia (n = 1), Pakistan (n = 1), Taiwan (n = 1), and USA (n = 1)]. The duration and sample sizes of the studies ranged from two days to one month and 34 to 110, respectively. Seven studies used the PSQI questionnaire, one Postpartum Sleep Quality Scale, one St. Mary's Hospital Standard Sleep Quality Index, and one Oguri sleep survey sheet (OSA) to assess the quality of sleep.

Table 2 presents pharmacologicaldetails of the studies. No adverse events were reported in any of the studies although passive surveillance

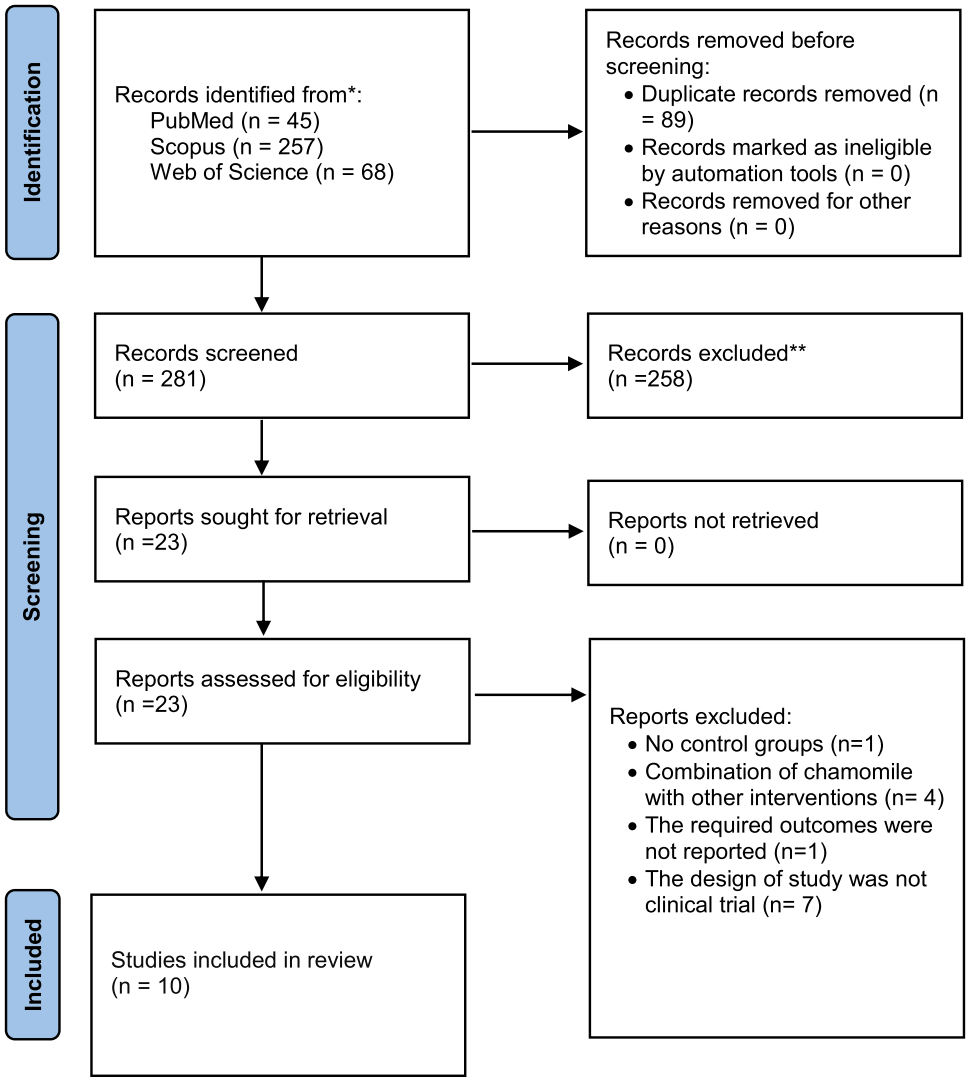

Fig. 1. PRISMA flow diagram for study selection process.

was used to assess adverse effects except in one study.[40] Only one study surveyed the blinding success and tested the purity and/or potency of the used products.[40]

We conducted a meta-analysis for outcomes assessed by at least three studies with relatively consistent participants, which was applied to the PSQI score with five studies and sleep time length, a component of PSQI. For other PSQI components, including sleep onset latency and sleep efficiency, although assessed by three studies, we did not conduct the meta-analysis as the summary WMD changed by excluding the Adib-hajbaghery et al.'s study.

3.1. Risk of bias

Some methodological domains of risk of bias were not met according to the Cochrane criteria in nine studies, so they were rated as high risk of bias (Fig. 2). Only one study met all the Cochrane's standards for quality research designs.[40] Domains that were not met in most of the studies were allocation concealment, blinding of participants and researchers, other risks of bias, and blinding of outcome assessors. Allocation concealment and blinding of participants and researchers were not performed in six and two studies, respectively. In six studies, the subjects who consumed opioids, analgesics, or hypnotic drugs were not excluded. Blinding of outcome assessors was unclear in seven studies and was not performed in one study. Attrition bias was low in all of the studies, and random sequence generation and selective reporting were low in most of the studies.

3.2. PSQI score

Among the studies which had reported the PSQI score, two were conducted on elderly subjects,[34,35] two on postmenopausal women,[33,39] one on subjects with insomnia,[40] one on chronic kidney disease (CKD) patients,[37] and one on adolescents with dysmenorrhea.[38] Meta-analysis of studies conducted on the elderly, postmenopausal women, and subjects with insomnia showed a significant reduction of 1.88 in PSQI score (WMD: −1.88, 95 %CI: −3.46, −0.31, I^2: 88.4 %; Fig. 3). Sequential removal of studies did not change the direction or magnitude of the pooled WMD (WMD range= −1.42- −2.33). The studies in CKD patients and adolescents with dysmenorrhea were not included in the analysis because of heterogeneous study participants. Results of these studies also indicated a significant reduction in PSQI scores following chamomile consumption.

Components of PSQI and OSA were assessed by three[35,39,40] and one studies,[36] respectively:

Meta-analysis of the three studies that assessed sleep time length [35, 39,40] failed to show a significant change (WMD: 0.20, 95 %CI: −0.62, 1.02, I^2: 95.9 %; Fig. 3). Meta-analysis was not conducted for other outcomes. Sleep onset latency improved in two [35,39] out of the three [35,

Table 1
Characteristics of the studies which investigated the effects of chamomile on sleep indicators.

Author, year	Design	Country	Population characteristics	Gender (n)	Duration (days)	Age (mean, median, or range)	Sleep assessment	Results	Survey on the success of blinding
Kakuta et al., 2007	RCT	Japan	Healthy men and women subjects, 30 to 48 years of age	F & M (40)	NM but assessed the acute effect	37.7	OSA sleep survey sheet	Significant improvement in sleep quality.	No
Zick et al., 2011	RCT Double blind	USA	Men and women aged 18 to 65 years of age who met DSM-IV criteria for primary insomnia ≥ 6 months	F (25), M (9)	28	Intervention (42.2), placebo (40.8)	Sleep diary, PSQI, ISI, FSS, BDI, STAI-T	PSQI, ISI, FSS, BDI, STAI-T did not improve.	Yes
Abdullahzadeh et al., 2014	RCT	Iran	Patients ≥ 60 y hospitalized in nursing homes	F (41), M (36)	28	74.3	PSQI	Sleep quality (PSQI) was improved.	No
Moeini et al., 2015	RCT Triple blinded	Iran	CKD patients aged 18 −65 y who had routine hemodialysis for at least 6 months, PSQI> 5	F (51), M (59)	30	Intervention (57.0), placebo (53.8)	PSQI	Sleep quality (PSQI) significantly improved.	No
Abbasinia et al., 2016	RCT Double blinded	Iran	Menopause women aged 50 −60, PSQI≥ 5	F (109)	14	Intervention (54.7), control (52.2)	PSQI	Sleep quality (PSQI) was improved.	No
Chang et al., 2016	RCT Single blind	Taiwan	Women in their sixth postpartum week with poor sleep quality (PSQS≥16)	F (73)	28	Intervention (33.2), control (32.7)	PSQS, Edinburgh Postnatal Depression Scale, and Postpartum Fatigue Scale	Sleep quality and mental health significantly improved	No
Adib-hajbaghery et al., 2017	RCT Single blind	Iran	People aged ≥ 60 y and lived in Kahrizak day care, PSQI≥ 5	F (41), M (19)	28	Intervention (69.4), placebo (70.7)	PSQI, sleep duration, use of sleep medications, subjective sleep quality, sleep disturbances, daytime dysfunction, habitual sleep efficiency, sleep latency	Sleep quality significantly improved	No
Rasool et al., 2019	RCT	Pakistan	Post-menopausal women who presented to the Gynecology outdoor patients department with any type of sleep disturbance	F (106)	28	Intervention (51.1), placebo (49.7)	PSQI, STAI-T, Sleep latency, time of awakening after sleep, number of awakenings, total sleep time, sleep quality, sleep efficiency, BDI, FSS	significantly improved sleep latency, time of waking after sleep onset, number of awakenings, STAI-T and total sleep time. But PSQI, FSS, BDI did not show improvement.	No
Rashidi et al., 2020	RCT double-blind	Iran	Patients aged 40–70 y with heart failure, no severe and disturbing pain, with various degrees of sleep disorders		7	Intervention (40- 65), placebo (41-67)	Questionnaire of St. Mary's Hospital Standard Sleep Quality Index	Sleep disorders improved.	No
Nurbayanti et al., 2022	RCT	Indonesia	Adolescents (17 −21 y) with dysmenorrhea, there was no cut off for PSQI as an inclusion criterion	F (54)	2	Intervention (19.0), control (18.8)	Modified PSQI	Sleep quality improved.	No

Abbreviations: BDI, beck depression inventory; CKD, chronic kidney disease; EPDS, Edinburgh postnatal depression scale; FSS, fatigue severity scale; ISI, insomnia severity index; MHSQ, St. Mary's Hospital Standard Sleep Quality; OSA, Oguri sleep survey assessment; PSQI, Pittsburgh sleep quality index; PSQS, postpartum sleep quality scale; RCT, randomized controlled trial; STAI-T, State Trait Anxiety Inventory- trait subscale;

[39, 40]studies that used PSQI for assessment. The small sample size in this study may have contributed to the lack of statistical significance in the observed change, with 17 individuals in each group. The effect size of 0.61 was within the range of intermediate effect. The ease of getting to sleep, as assessed by OSA in one study and could be equal to sleep onset latency, was also improved.[36] The percentage of sleep efficiency (total sleep time/time in bed*100) did not change in two studies and deteriorated in one study. The number of awakenings after sleep or staying asleep improved in two [36,39] out of the three[36] studies. Subjective sleep quality was reduced in one study[35] and did not change in another one.[40] Daytime sleep time was another outcome we aimed to investigate; however, it was not reported by any study.

3.3. Other outcomes

Daytime functioning measures, including the fatigue severity index or postpartum fatigue scale, did not change in three studies. Depression improved in postpartum women but not in elderly subjects and

Table 2
Pharmacological details of studies investigating the effects of chamomile on sleep indicators.

Author, year	Chamomile (dose, and form)	Characterization of preparations	Placebo composition	Testing for purity and/or potency	Adverse events	Surveillance of adverse events
Kakuta et al., 2007	*Matricaria chamomilla*, chamomile jelly (10 gr dried chamomile)	The formulation involved steeping 10 g of dried chamomile flowers in 1 L of freshly boiled water for one minute, similar to preparing chamomile tea. Subsequently, gellan gum and sugar were incorporated into the extract to achieve a Brix sugar level of 14, and 75 g portions of jelly were prepared. These jellies were then filled into plastic containers, sealed, and subjected to sterilization at 85 °C for ten minutes.	Chamomile-free jelly was made with the same composition excluding the presence of chamomile extracts.	No	Not mentioned	Not mentioned
Zick et al., 2011	*Matricaria chamomilla*, 540 mg/day capsule	Chamomile extract from the flowering tops was formulated at a concentration of 6:1 (volume to volume) using an extraction solvent consisting of 70 % ethanol and 30 % water. This extract was standardized to contain a minimum of 2.5 mg of (-)-a-bisabolol and at least 2.5 mg of apigenin per tablet. Analysis using high-performance liquid chromatography (HPLC) and gas chromatography-mass spectrometry (GC-MS) revealed that 90 mg of chamomile extract contained 3.9 mg of apigenin and 1.8 mg of (-)-a-bisabolol.	Not mentioned	Yes	There were no significant differences in total adverse events between treatment groups. All adverse events were mild and transient.	Active
Abdullahzadeh et al., 2014	*Matricaria chamomilla*, 800 mg/day capsule	*Matricaria chamomilla*'s dry extract was injected into jelly capsule.	No placebo	No	No adverse events	Passive
Moeini et al., 2015	*Matricaria chamomilla*, 400 mg/day syrup	Maceration circulation was utilized for a 48-hour extraction process involving 25 kg of chamomile, a 25-liter water solution, and 50 % alcohol. The resulting extract underwent filtration using cloth and cellulose filters, followed by the evaporation of alcohol in a rotary vacuum distiller. Sweetener saccharin was incorporated to enhance taste and mitigate the flavor of chamomile.	Water + Saccharin	No	Not mentioned	Not mentioned
Abbasinia et al., 2016	Not mentioned, 800 mg/day capsule	Not mentioned	No placebo	No	No adverse events	Passive
Chang et al., 2016	*Matricaria chamomilla*, 1 cup/day chamomile tea (2 gr of dried flowers in hot water)	Not mentioned	No placebo	No	No adverse events	Passive
Adib-hajbaghery et al., 2017	*Matricaria chamomilla*, 400 mg/day (extract) capsule	The plant material was ground and immersed in 70 % ethanol. Subsequently, an extraction procedure was carried out over a week, and the resulting extract was concentrated under vacuum. Following this, the concentrated solution was dried into chamomile extract powder using a spray dryer.	Wheat flour	No	No adverse effect	Passive
Rasool et al., 2019	*Matricaria chamomilla*, 60 drops/day, oral	No explanation	Not mentioned	No	No adverse effect	Not mentioned
Rashidi et al., 2020	Whole chamomile extract with chamazulene versus placebo with chamazulene, 30 oral drops/day (1 cc)	Not mentioned	Not mentioned	No	No adverse effect	Passive
Nurbayanti et al., 2022	Not mentioned, 2 glass/day Warm chamomile	Not mentioned	No placebo	No	Not mentioned	Not mentioned

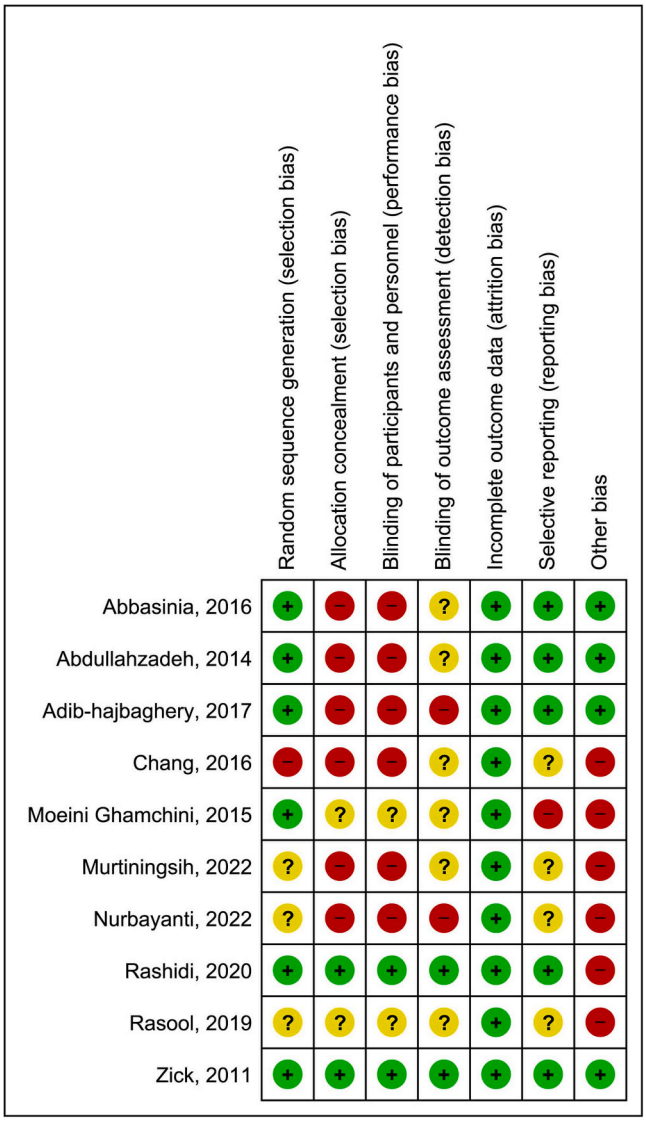

Fig. 2. Risk of bias assessment based on Cochrane's ROBINS-I tool (Cochrane Risk of bias in Non-randomized Studies of Interventions). Green, red, and yellow circles represent low, high, and unknown risk of bias, respectively.

postmenopausal women, and anxiety did not change in two studies. Sleep disorder, which was assessed by the St. Mary's Hospital Standard Sleep Quality Index, improved in heart failure patients.

4. Discussion

This systematic review and meta-analysis aimed to evaluate the efficacy of chamomile in improving sleep among different populations. The meta-analysis results showed a significant reduction in the PSQI score; however, no significant changes were observed in sleep time length. For other outcomes, we identified two to three studies and did not conduct a meta-analysis. Nonetheless, an improvement was observed in sleep onset latency and the number of awakenings after sleep or staying asleep in these studies, whereas daytime functioning measures were not changed.

Our study provided scientific support that chamomile may be a useful adjunctive therapy for improving sleep, especially improvement in sleep onset latency and the number of awakenings after sleep or staying asleep.

Poor sleep quality is associated with a higher risk of obesity,[43] diabetes,[44] metabolic syndrome,[45] and hypertension.[46] Additionally, sleep quality has a direct relationship with happiness, life satisfaction, and overall quality of life.[47] As a result, many individuals with sleep disturbances seek agents, particularly natural products to improve their sleep. Chamomile has been used as a mild sedative and anti-anxiety herb that is believed to have benefits for sleep problems.[48,49] However, the scientific data on this topic was limited and conflicting. The findings of this study suggest that chamomile may be an effective and safe treatment for improving sleep quality in various populations, especially through improvement in sleep onset latency and the number of awakenings after sleep or staying asleep.

The results of this study are consistent with a previous meta-analysis that has shown the efficacy of chamomile in improving sleep quality. However, they had assessed studies conducted until November 2017, including those in which chamomile was combined with other herbs, so a complex effect was assessed; finally, studies with different health conditions and sleep assessment tools were pooled in the analysis.[30]

The effects of chamomile on sleep are believed to be due to its binding to benzodiazepine and gamma-aminobutyric acid (GABA) receptors, which have hypnotic effects on sleep-wake cycles. Additionally, chamomile infusion contains high melatonin content, which is crucial for promoting sleep. Its antidepressant and anxiolytic activities may also contribute to its beneficial effects on sleep quality. The antioxidant properties of chamomile may contribute to its sleep-promoting effects since chronic oxidative stress is reported to disrupt key mechanisms in the regulation of circadian rhythms and sleep homeostasis.[48]

There is limited evidence available regarding the potential side effects and toxicity of chamomile.[49] None of the studies included in this systematic review reported significant adverse events. Rarely reported side effects included dizziness, nausea, disturbances in the menstrual cycle, and some allergic reactions such as contact dermatitis and hypersensitivity. Additionally, chamomile may have interactions with sedative, anticoagulant, and antiplatelet drugs.[50,51] However, it should be noted that some of the included studies did not consider these interactions in their methodology. Furthermore, chamomile has been identified as a possible carrier of Clostridium botulinum spores.[52] Studies have also reported the genotoxicity of chamomile in mice using the ultra-viable micronucleus assay of reticulocytes.[53] However, it has been noted that the aqueous and alcohol extracts of chamomile are considered safe for mice, as reported by Wang et al. The maximum tolerated dose of the aqueous and alcohol extracts has been documented as 535 and 425 times higher than the typical adult clinical dose.[54]

Our study has some limitations. Firstly, the characteristics of the participants were not similar across studies, and sleep quality was not assessed using the same questionnaire. Therefore, we could not include all the studies in the meta-analysis. Secondly, most of the included studies were at high risk of bias, indicating the need for further high-quality studies in the future. Moreover, there was a high heterogeneity in the meta-analyses of PSQI, which was the primary outcome. However, the trend of the associations in all the studies included in the analyses was consistent. One explanation for this high percentage of heterogeneity may be the variety of the preparations used, many of which were not adequately described in the studies (Table 2). Additionally, the lack of sufficient characterization of the used preparations should be considered an important limitation of the included study. Therefore, the large heterogeneity in the data is primarily due to differences in the magnitude of the study-specific WMD. Finally, the results of our study are based on subjective measures. Future studies are suggested to assess objective measures.

5. Conclusion

In conclusion, chamomile was found to improve sleep, especially the number of awakenings after sleep or staying asleep, but it did not lead to an improvement in the duration of sleep, percentage of sleep efficiency, and daytime functioning measures. However, further well-designed clinical trials that meet the standard quality of research design and

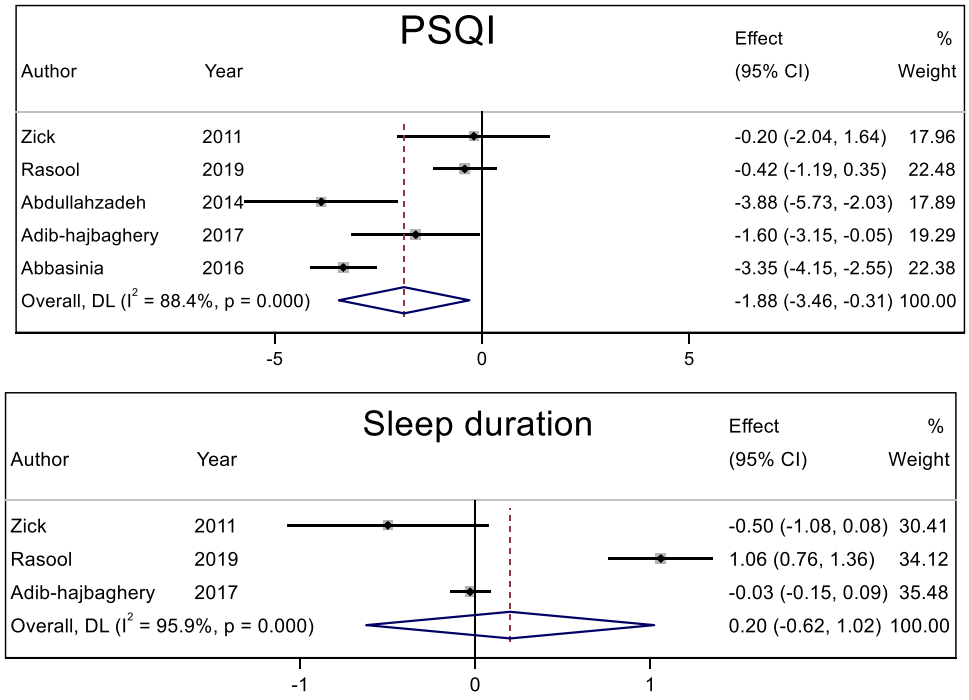

Fig. 3. Forest plot of clinical trials illustrating weighted mean differences in Pittsburgh sleep quality index (PSQI) and sleep duration between chamomile and control groups.

assess objective measures are required to confirm the results. Moreover, future studies are recommended to explore the potential mechanisms by which chamomile improves the sleep.

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CRediT authorship contribution statement

Mohammad Hashem Hashempur: Writing – review & editing, Methodology, Conceptualization. **Parham Eskandarzadeh:** Writing – review & editing, Methodology. **Sara Shojaei-Zarghani:** Writing – review & editing, Methodology. **Asma Kazemi:** Writing – original draft, Methodology, Investigation, Formal analysis, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data Availability

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ctim.2024.103071.

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