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Review Article

Herbal remedies for hypothyroidism: A systematic review and meta-analysis

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Abstract

Background: Combination of various medical schools with modern medicine is one of the appropriate methods for diagnosing and treating diseases. Considering the expanded use of herbal remedies, this study aimed to investigate herbal remedies for hypothyroidism.

Methods: Keywords related to medicinal plants and hypothyroidism were searched among titles and abstracts of papers published on PubMed, Web of Science, and Scopus to find relevant papers published until the end of 2022. The quality of the extracted papers was assessed using JADAD scale. The data collected from the papers included general information, demographic characteristics of the participants, sample size in each group, type and duration of the intervention, doses of the herbs or extracts, side effects, and the effects of the intervention on thyroid function tests. The I^2 index was used to measure the heterogeneity of the papers; if I^2 statistic was above 50% or under 50%, the results of the papers were combined using random effect or fixed effect methods, respectively.

Results: Five of the 301 papers extracted from the abovementioned databases were selected for systematic review and 4 for meta-analysis. Three of the papers were about the properties of *Nigella sativa*. The meta-analysis results showed that herbal medicines used in these papers significantly changed level of T4 (SMD=0.86 CI95%: 0.47-1.24), T3 (SMD=0.50 CI95%: 0.13-0.87), and TSH (SMD=-1.19 CI95%: -1.82-0.56) compared to placebo.

Conclusions: Herbal medicines improved the results of thyroid function tests; their effects on TSH, T3, and T4 were strong, moderate, and mild, respectively.

Keywords: Herbal remedy, Extract, Hypothyroidism.

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Hypothyroidism is a common disease of the endocrine glands caused by insufficient secretion of thyroid hormone (1). Its worldwide prevalence ranges from 7.3% to 11% (2-4), and its prevalence in Iran is also on the rise (5). In addition, hypothyroidism is 6 times more common in women than in men (6). This disease can cause a variety of symptoms such as weight gain, lethargy, dry, rough skin, hair loss or Hertoghe's sign, loss of appetite, constipation, hypersomnia, depression, memory impairment, anemia, menstrual disorders in women such as polymenorrhea or hypermenorrhea, and fertility disorders (6-8). Animal thyroid or its extract was used to control the symptoms of hypothyroidism from the 6th century to the early 20th century (3). Currently, physicians commonly prescribe levothyroxine for patients with hypothyroidism. However, this treatment fails to bring satisfactory results for some patients because it cannot properly control some symptoms such as weight gain, lethargy, mood disorders, and memory impairment (3, 7, 9-15). The combination of various medical schools with modern medicine is currently one of the appropriate methods for diagnosing and treating diseases (16).

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Since the use of traditional and complementary medicine has considerably expanded around the world, the World Health Organization (WHO) has emphasized the revival of traditional medicine in different regions of the world over the last 3 decades (16). Researchers have examined the different types of complementary medicine such as biopsychosocial methods (9), acupuncture (17), traditional Chinese medicine (18, 19), yoga (20, 21), homeopathy (22, 23), and Ayurveda (24) to achieve the best treatment for patients with hypothyroidism. Considering the widespread use of herbal remedies and the paucity of comprehensive studies on herbal remedies for hypothyroidism, this systematic review and meta-analysis aimed to investigate herbal remedies for hypothyroidism.

Methods

This systematic review and meta-analysis investigated herbal remedies for hypothyroidism.

Strategy of search: The following keywords were searched among the titles and abstracts of papers published on PubMed, Web of Science, and Scopus to find the relevant papers published until October 22, 2023. (“herbal medicine” OR “herbal medicines” OR “plant extracts” OR" Plant Extract" OR plant OR plants OR "Chinese herbal medicines" OR "Chinese herbal medicine") AND (hypothyroidisms OR hypothyroidism OR "thyroid stimulating hormone deficiency" OR “TSH deficiency”)

Selection of papers: After the extracted papers were analyzed in EndNote, their abstracts and then full texts were reviewed by two independent and blinded persons. Any disagreement between the reviewers was settled by discussion to reach a consensus.

Inclusion criterion: Clinical trials in English language about the use of herbs or their extract for the treatment of hypothyroidism were included in this study.

Quality assessment: The quality of the selected papers was assessed using the JADAD scale, which is a three-question checklist scored on a 5-point scale. The questions are as follows:

- Was the study described as randomized?
- Was the study described as double-blind?
- Was there any explanation concerning withdrawals or dropouts?

A score of 2 was assigned to each question if the paper described the method of randomization and blinding and that method was considered appropriate. If the method of randomization or blinding described in the paper was inappropriate, a score of 1 was given to each question. In addition, a score of 1 was assigned to papers that explained both the number and reasons for withdrawals and dropouts (25).

Data extraction: Two blinded persons independently extracted the required data from the papers and recorded them on a form designed for this purpose. Any disagreement between the reviewers was settled through discussion to reach a consensus. The extracted data included general information in the paper (title and authors), age and gender of participants, sample size in each group, type and duration of the intervention, doses of the herbs or extracts, side effects, and the effects of the intervention on thyroid function tests.

Data analysis: The data were statistically analyzed in Comprehensive Meta-Analysis Software (version 2.0). The I^2 index was used to measure the heterogeneity of papers; if the I^2 statistic was above 50% or under 50%, the results of papers were combined using random effect or fixed effect methods, respectively. In addition, a funnel chart was drawn to measure the publication bias.

Results

Five of the 301 extracted papers were entered into the systematic review (4 of them into the meta-analysis) (figure 1). Table 1 shows that 3 of the 5 clinical trials selected for the systematic review were about the properties of *Nigella sativa*. The drugs were administered in doses from 0.6 to 4 g per day, and the duration of most studies was 8 weeks. The papers reported no serious side effects and the mild side effects included nausea, fever, and headache. In addition, the quality assessment of the papers indicated that most of them received an acceptable score in terms of randomization and report of withdrawals or dropouts (figure 2). The metal-analysis results demonstrated that the herbal medicines used in these papers significantly increased the T4 level compared to the placebo (SMD=0.86 CI95%: 0.47-1.24) (figure 3). In addition, the funnel chart indicated no publication bias (figure 4). The metal-analysis results also showed that the herbal medicines significantly increased the T3 level compared to the placebo (SMD=0.50 CI95%: 0.13-0.87) (figure 5). The funnel chart indicated no publication bias (figure 6). The metal-analysis results also demonstrated that the herbal medicines significantly reduced the TSH level compared to the placebo (SMD=-1.19 CI95%: -1.82-0.56) (figure 7). The funnel chart indicated no publication bias (figure 8).

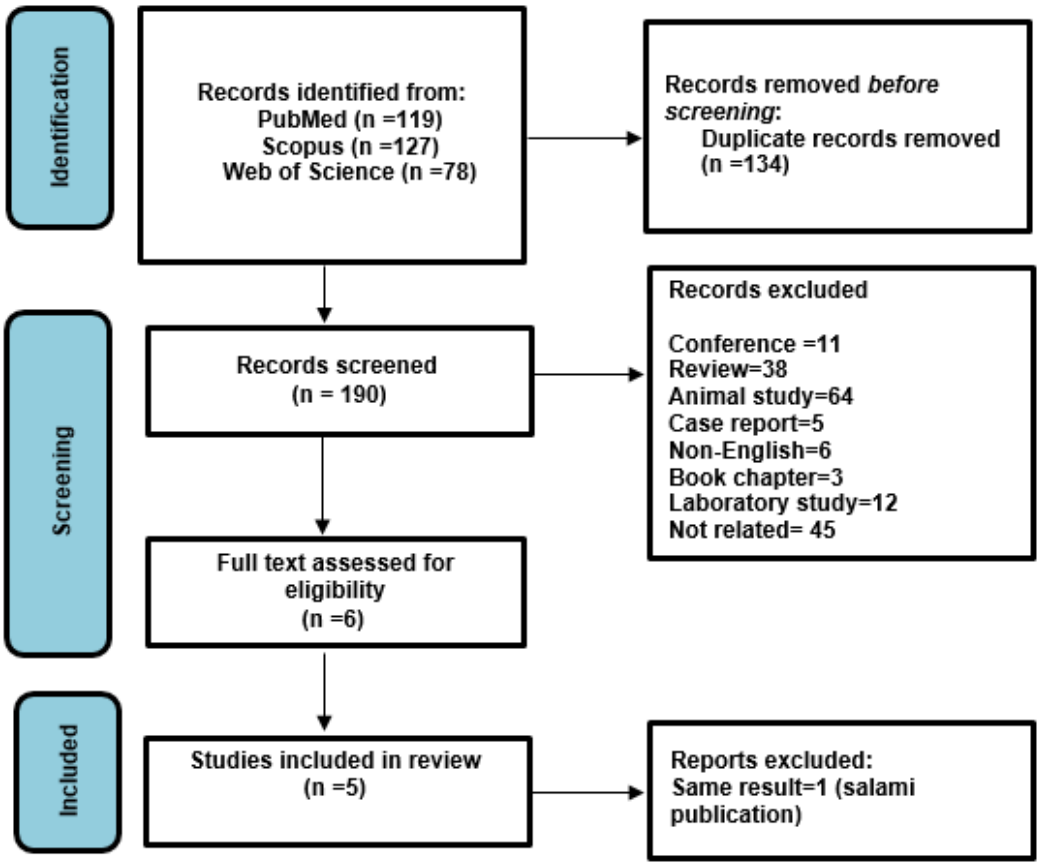

Figure 1. The PRISMA flowchart of the papers selected for the systematic review and meta-analysis

Table 1. Characteristics of the papers selected for the systematic review

Author	Year	Plant (Part)	Sample size in intervention group	Sample size in placebo group	Side effect	Duration (week)	Dose (g/day)	Mean (SD) age in intervention group	Mean (SD) age in placebo group	Quality Assessment score
Tekieh, M. F. (a*) (26)	2019	Nigella sativa (Seeds)	7	3	not reported	8	4	46 (9.87)	40.67 (12.42)	3
Tekieh, M. F. (b*) (26)	2019	Nigella sativa (Seeds)	11	9	not reported	8	4	43.42 (10.24)	42.7 (11.33)	3
Sharma, A. K. (27)	2018	Ashwagandha (Root)	25	25	fever, asthenia, cough, headache	8	0.6	35.56 (7.95)	35.08 (9.56)	5
Tajmiri, S. (28)	2016	Nigella Sativa (Seeds)	20	20	itching and nausea	8	2	35.7 (8.18)	33.95 (8.72)	4
Ashraf, H. (29)	2022	Ginger (Rhizome)	27	26	no	4	1	42.44 (8.48)	38.42 (7.86)	5
Alam, M. A. (30)	2021	Moringa oleifera Lam (leaf)	8	-	no	6	10	33.5 (11.77)	-	1

a: Anti-TPO levels < 40 UI/mL, b: Anti-TPO levels > 40 UI/mL.

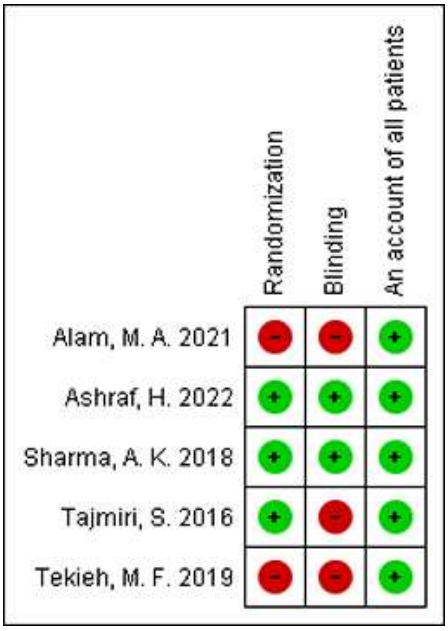

Figure 2. Quality of the papers selected for the systematic review

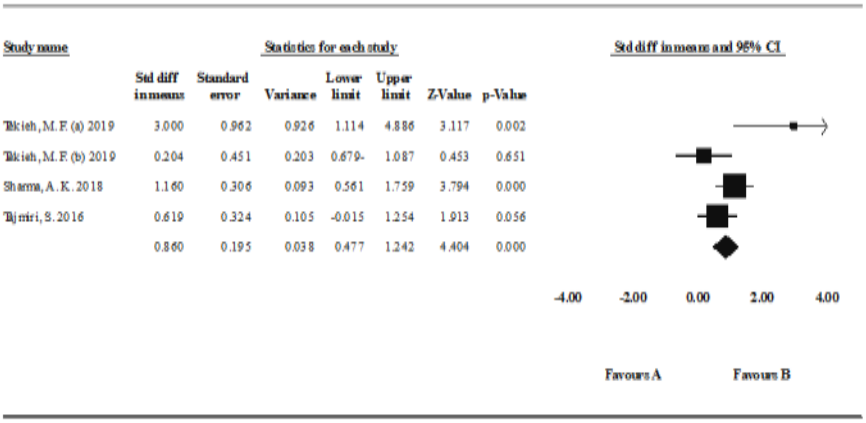

Figure 3. Forest plot of the effects of the herbal medicines on FT4 level in patients with hypothyroidism

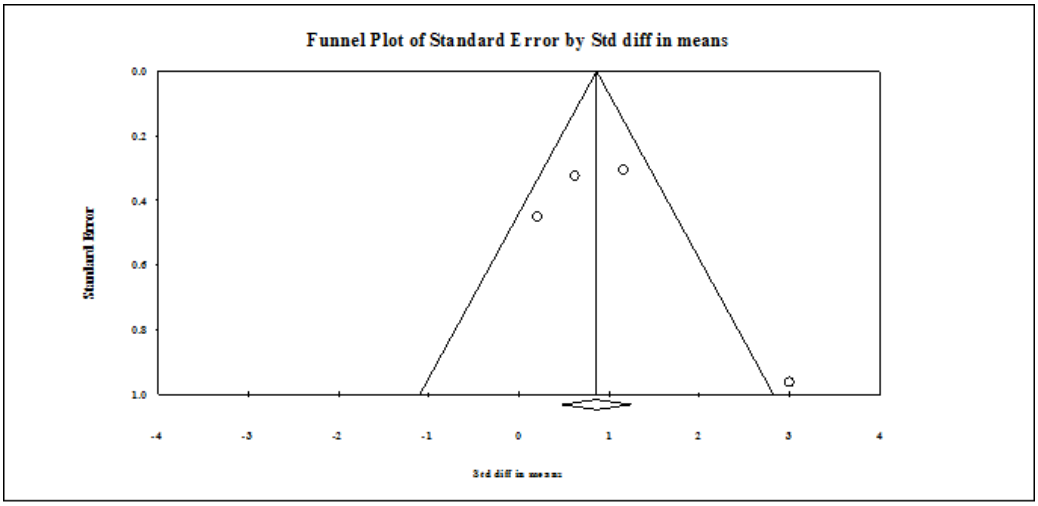

Figure 4. Publication bias chart of the effects of the herbal medicines on FT4 level in patients with hypothyroidism

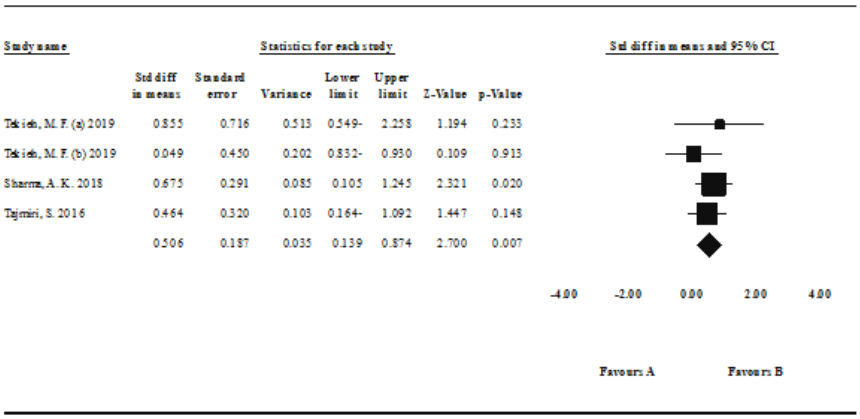

Figure 5. Forest plot of the effects of the herbal medicines on FT3 level in patients with hypothyroidism

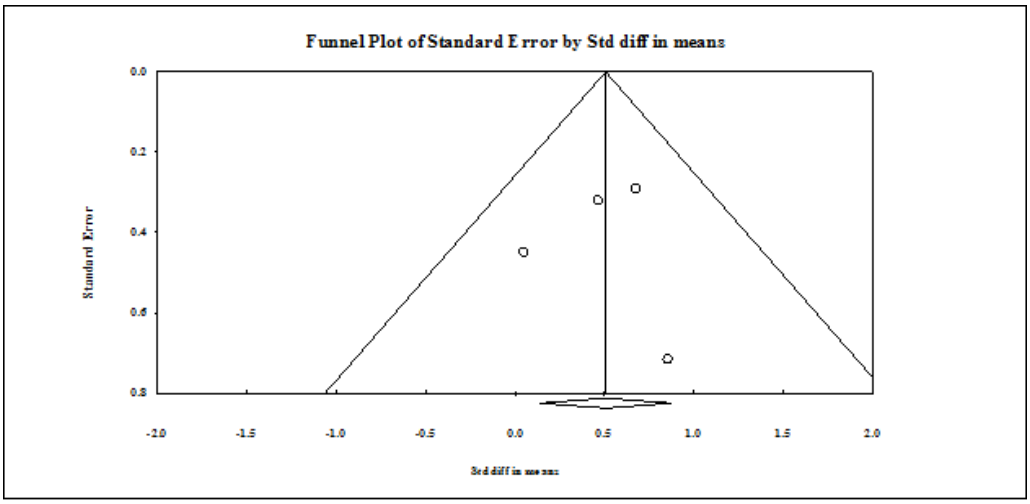

Figure 6. Publication bias chart of the effects of the herbal medicines on FT3 level in patients with hypothyroidism

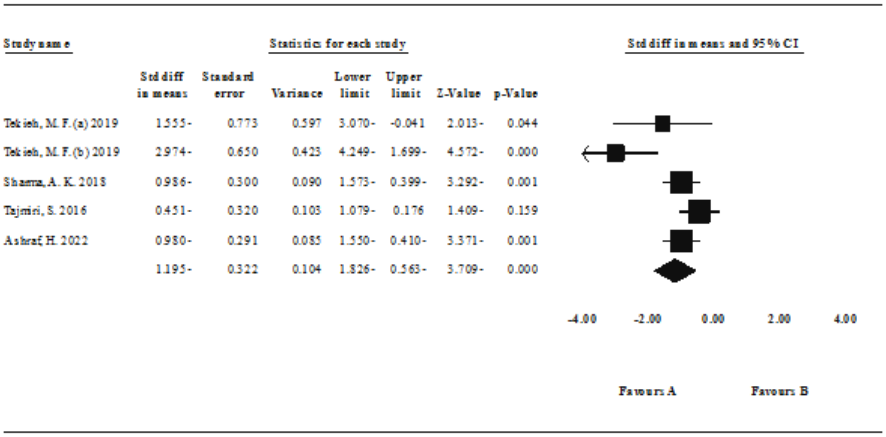

Figure 7. Forest plot of the effects of the herbal medicines on TSH level in patients with hypothyroidism

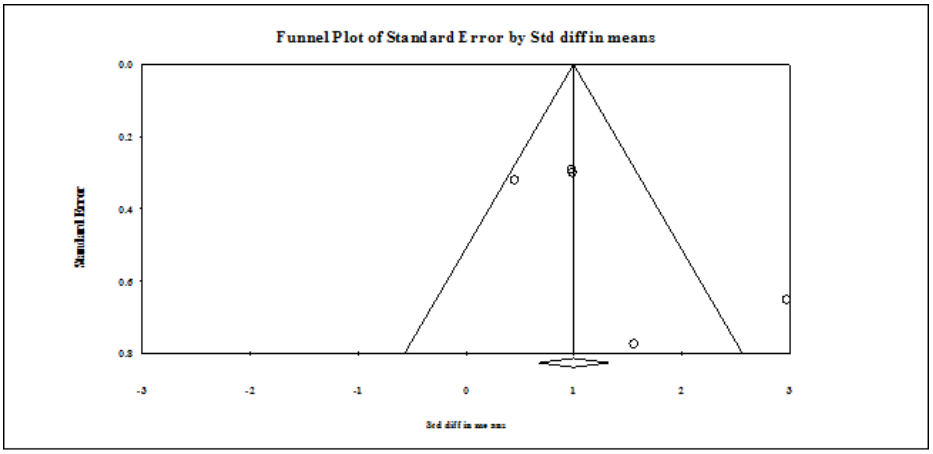

Figure 8. Publication bias chart of the effects of the herbal medicines on TSH level in patients with hypothyroidism

Discussion

This systematic review and meta-analysis investigated the herbal remedies used in the clinical trials for treating hypothyroidism. The meta-analysis results showed that the herbal medicines used in the reviewed papers significantly increased the T4 level compared to the placebo. Considering the SMD value, it can be stated that the effect size was medium. Although many studies have employed existing resources or even animal models to investigate the effects of herbal medicines on hypothyroidism, few studies have measured these effects in clinical trials. The results also indicated that the herbal medicines significantly reduced the TSH level compared to the placebo. Considering the SMD value, it can be concluded that the effect size was large. Nigella sativa was the most common plant used in the reviewed clinical trials; the positive effects of this plant can be attributed to the presence of thymoquinone, which has antioxidant properties (31) that protect the endocrine tissue against free radical species and contribute to hormonal rebalance (32).

In the same vein, and in confirmation of the role played by Nigella sativa, animal models have also proven the protective role of Nigella sativa in reversing hypothyroidism and improving oxidative stress and thyroid cell damage in hypothyroidism caused by propylthiouracil in rats (31, 33). The study results also demonstrated that the herbal medicines significantly reduced the T3 level compared to the placebo. Considering the SMD value, it can be concluded that the effect size was small. In similar systematic review and meta-analysis by Luo et al. (34) they have been shown that Chinese Herbal Medicine combined with Western Medicine in Hashimoto's thyroiditis had more effective than Western Medicine alone and there were positive effects on FT3 (SMD = 0.59; 95% CI (0.48, 0.71)), FT4 (SMD = 0.59; 95% CI (0.48, 0.71)), TSH (SMD = -0.97; 95% CI (-1.35, -0.58)). This result is similar to the present study findings. Extensive animal studies, limited clinical trials and one systematic review for Chinese Herbal Medicine, which reported acceptable results in our meta-analysis (especially regarding TSH and T4), can suggest the therapeutic effects and properties of Nigella sativa for hypothyroidism. Nevertheless, more studies on technological innovations that can improve the bioavailability and penetrability of the ingredients of this plant will be very helpful. The exact mechanism by which herbal medicine affects hypothyroidism is not fully understood, but it seems that Nigella sativa (35), ginger (36) and Moringa oleifera Lam (37) may have antioxidant activity and reduce oxidative stress in the thyroid or Ashwagandha have endocrine-stimulating properties that can suppress cortisol levels and boost thyroid function (27). The limitations of this study included the limited number of studies on this subject and the small sample size in the reviewed studies. The present study showed that herbal medicines improved the results of thyroid function tests; their effects on TSH, T3, and T4 were strong, moderate, and mild, respectively.

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