

Herbal Treatments for Hypothyroidism: An Evidence-Based Review

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SUPPLEMENTARY TABLES

Table 1: PICO.

Article reference	Population	Intervention	Comparator	Outcome variable	Study design
Lin, et al. [1]	60 patients with hypothyroidism (30 per group)	Jianpi Huatan Huoxue Decoction + levothyroxine sodium tablets	Levothyroxine sodium tablets alone	FT3, FT4, TSH, blood lipid indices (TC, TG, LDL-C, HDL-C), TCM symptom score	Randomized controlled trial
Chen, et al. [2]	80 patients with primary hypothyroidism	Jianpi Yishen Formula + levothyroxine	Levothyroxine alone	FT3, FT4, TSH, TCM symptom score	Randomized controlled trial

	with spleen-kidney yang deficiency syndrome (40 per group)				
Lu, et al. [3]	90 patients with subacute thyroiditis (46 treatment, 44 control)	Xiao Chaihu Decoction + Forsythia	Prednisone acetate	ESR, symptom relief time, recurrence rate, safety	Randomized controlled trial
Chen, et al. [4]	100 patients with hypothyroidism (50 per group)	Modified Zhenwu Decoction + Euthyrox	Euthyrox alone	FT3, FT4, TSH, TCM symptom score	Randomized controlled trial
Wang [5]	90 patients with hypothyroidism	Levothyroxine sodium + selenium yeast	Levothyroxine alone	FT3, FT4, TSH, adverse events, TPOAb, TGAAb	Randomized controlled trial
Guo [6]	120 hypothyroidism patients	Levothyroxine sodium + Tanshinone IIA injection	Levothyroxine alone	Thyroid hormones, IL-6, TNF- α , IFN- γ	Randomized controlled trial
Lou, et al. [7]	60 patients with hypothyroidism	Guipi Capsule + Levothyroxine sodium	Levothyroxine alone	FT3, FT4, TSH, symptom scores, safety	Randomized controlled trial
Guo and Fang [8]	82 patients with Hashimoto's thyroiditis	Danggui Lihuang Decoction + Western treatment	Western treatment alone	TCM symptom score, immune indices (IFN- γ , IL-6, TNF- α , IL-17A), adverse effects	Randomized controlled trial
Wang [5]	90 patients with hypothyroidism	Levothyroxine sodium + selenium yeast	Levothyroxine alone	FT3, FT4, TSH, adverse events, TPOAb, TGAAb	Randomized controlled trial

Lou, et al. [7]	60 patients with hypothyroidism	Guipi Capsule + Levothyroxine sodium	Levothyroxine alone	FT3, FT4, TSH, symptom scores, safety	Randomized controlled trial
Liu and Li [9]	60 patients with subclinical hypothyroidism	Acupuncture + Bupi Wenshen Paste	Bupi Wenshen Paste alone	TSH, FT3, FT4, TC, TG, HDL-C, LDL-C, total effective rate	Randomized controlled trial
Mo and Zhou [10]	62 patients with subacute thyroiditis	Chaihu Shengjiang Powder + conventional western treatment	Conventional western medicine alone (e.g., prednisone, beta-blockers)	VAS pain score, TCM symptom score, CRP, ESR, FT3, FT4, TSH	Randomized controlled trial
Teng [11]	68 patients with subclinical hypothyroidism and Qi-stagnation constitution	Chaixiang Jieyu Gao topical application + lifestyle guidance	Lifestyle guidance only	TSH, FT3, FT4, Hamilton Depression and Anxiety Scales (HAMD, HAMA)	Randomized controlled trial
Yu, et al. [12]	60 patients with Hashimoto's hypothyroidism (30 per group)	Erxian Xiaoying Decoction + levothyroxine (Euthyrox) for 12 weeks	Levothyroxine (Euthyrox) alone for 12 weeks	TT3, TT4, FT3, FT4, TSH, TGAb, TMAb, Euthyrox dosage, clinical symptoms	Randomized controlled trial
Ye, et al. [13]	56 patients with HT and either normal or subclinical thyroid function	Xiaoying Sanjie Prescription + Jinshuibao Capsule	Jinshuibao Capsule only	TPOAb, TGAb, IL-2, IL-6, TCM symptom score	Randomized controlled trial
Yang, et al. [14]	72 patients with Hashimoto's thyroiditis and spleen-kidney deficiency	Wenshen Jianpi Shugan Gao + Levothyroxine	Levothyroxine only	IL-4, IL-6, IL-10, TSH, FT4, FT3, symptom improvement	Randomized controlled trial

Chen and Qin [15]	60 patients with primary hypothyroidism	Wen Yang Yi Qi Decoction + Levothyroxine for 3 months	Levothyroxine alone	TSH, FT3, FT4, thyroid autoantibodies, symptom scores	Randomized controlled trial
Chen, et al. [16]	60 hypothyroid patients	Zhen Wu Decoction + Levothyroxine for 8 weeks	Levothyroxine alone	T3, T4, FT3, FT4, TSH, symptom scores, dosage reduction	Randomized controlled trial
Cao and Chen [17]	80 patients with Hashimoto's thyroiditis	Chinese herbal formula based on liver-spleen therapy + routine care	Routine care (Levothyroxine and general treatment)	Serum levels of TSH, T3, T4, TG-Ab, TPO-Ab, symptom improvement	Randomized controlled trial
Zhong, et al. [18]	76 Hashimoto's thyroiditis patients	Chinese herbal treatment for clearing liver heat + routine Western therapy	Routine Western therapy alone	Levels of TPO-Ab, TG-Ab, clinical symptoms, immune markers	Randomized controlled trial
Chen and Lou [19]	90 Hashimoto's thyroiditis patients with hypothyroidism	Liver detoxification + routine care for 12 weeks	Routine care	Changes in TG-Ab, TPO-Ab, TSH, thyroid hormones, symptom scores	Randomized controlled trial
Tao, et al. [20]	60 patients with Hashimoto's thyroiditis and hypothyroidism	Yinliu Ting granules + standard care	Standard care (control group)	Improvement in TCM symptoms and thyroid hormone levels	Randomized controlled trial
Tian, et al. [21]	60 patients with Hashimoto's thyroiditis	Bailing Capsule + standard western therapy	Standard western therapy only	TPO-Ab, TG-Ab levels; TCM syndrome improvement	Randomized controlled trial
Zhao, et al. [22]	80 pregnant women with early threatened abortion and	Yishen Jianpi formula + levothyroxine	Levothyroxine alone	TSH levels, abortion rate, symptom scores	Randomized controlled trial

	subclinical hypothyroidism				
Li, et al. [23]	72 patients with liver stagnation, spleen/kidney deficiency-type hypothyroidism	Yishen Xiaoyao Decoction + levothyroxine	Levothyroxine alone	TSH, FT4 levels, TCM scores	Randomized Controlled Trial
Fu, et al. [24]	66 patients with Hashimoto's thyroiditis and spleen/kidney yang deficiency	Zhenwu Tang + levothyroxine	Levothyroxine only	Serum 25(OH)D, lipids, TCM scores	Randomized controlled trial
Zhang, et al. [25]	80 patients with Graves' disease and elevated TRAb	Sodium selenite + ¹³¹ I therapy	¹³¹ I therapy alone	TRAb levels, FT3, FT4, TSH	Randomized controlled trial
Wang and Dong [26]	60 patients with Hashimoto's thyroiditis	Selenium + TCM (疏肝健脾法)	Selenium alone	T lymphocyte subsets, TPO-Ab, TG-Ab	Randomized controlled trial
Xu and Ke [27]	60 patients with primary hypothyroidism	Selenium yeast tablets + standard care	Standard care alone	TSH, FT3, FT4, inflammatory markers	Randomized controlled trial
Wang, et al. [28]	80 Hashimoto's patients with hypothyroidism	Selenium yeast + levothyroxine sodium	Levothyroxine alone	Serum selenium, TPO-Ab, TG-Ab	Randomized controlled trial
Li, et al. [29]	60 patients with hypothyroidism	Selenium yeast + levothyroxine sodium	Levothyroxine alone	FT3, FT4, TSH, clinical efficacy rate	Randomized controlled trial
Ding [30]	72 patients with Hashimoto's hypothyroidism	Selenium yeast + levothyroxine (Euthyrox)	Euthyrox alone	TSH, TPO-Ab, TG-Ab, clinical efficacy	Randomized controlled trial

Qi, Du [31]	60 patients with Hashimoto's thyroiditis	Selenium yeast + Euthyrox	Euthyrox alone	Thyroid function, antibody levels, symptom relief	Randomized controlled trial
Zhang and Zhang [32]	Literature review; elderly hypothyroidism patients	Various Chinese-Western combined therapies	Western medicine alone (conceptual)	Comparative summary of efficacy	Literature Review (Narrative)
Fan, et al. [33]	60 CKD Stage 3–4 patients with hypothyroidism (Qi deficiency + blood stasis)	Modified Shenshuai Decoction	Routine western treatment	eGFR, serum creatinine, FT3, FT4, TSH	Randomized controlled trial
Chen, et al. [34]	100 patients with chronic lymphocytic thyroiditis (HT)	Astragalus and Sea Gall-eliminating Soup + levothyroxine sodium	Levothyroxine sodium alone	Total effective rate, thyroid function (T3, T4, FT3, FT4, TSH), TGAb, TPOAb, thyroid size/nodules	Randomized controlled trial
Weng, et al. [35]	100 elderly patients with chronic heart failure and subclinical hypothyroidism (Qi deficiency and blood stasis type)	Qi Hong Yi Qi and Blood Formula + conventional Western medicine	Conventional Western medicine alone	Cardiac function (Lee's score, 6-minute walk test, left ventricular ejection fraction), thyroid function (TSH, FT3, FT4)	Randomized controlled trial
Xing, et al. [36]	116 hypothyroidism patients (aged 18–60; 58 in each group)	Modified Shuyu Pills + levothyroxine sodium tablets	Levothyroxine sodium tablets alone (standard dosing)	Primary: Thyroid function (TSH, FT3, FT4) Secondary: Blood lipids (TC, TG, HDL-C, LDL-C), TCM symptom scores, adverse reactions	Randomized Controlled Trial (RCT)

		(individualized dosing)			
Kou, et al. [37]	144 patients with kidney-yang deficiency type of preeclampsia combined with hypothyroidism	Bushen Yangxue Antaitang (补肾养血安胎汤) + Euthyrox (levothyroxine)	Euthyrox (levothyroxine) alone	Total effective rate, thyroid function (TT3, TT4, FT3, FT4, TSH), pregnancy hormones (E2, P, HCG), cytokines (IL-2, IL-10)	Randomized controlled trial
Zhu, et al. [38]	94 pregnant patients with hypothyroidism	Bushen Yangxue Antai Tang (TCM) + levothyroxine sodium tablets	Levothyroxine sodium tablets alone	Thyroid function (FT3, FT4, TSH), pregnancy hormones (HCG, P, E2), blood lipids (TC, TG, LDL-C, HDL-C), total effective rate	Randomized controlled trial
Zhang, et al. [39]	80 patients with subacute thyroiditis (heat-toxin congestion syndrome)	Jiedu Xiaoying Decoction (TCM) + prednisone acetate tablets	Prednisone acetate tablets alone	Thyroid function (FT3, FT4, TSH), inflammatory markers (ESR, CRP, TNF- α , IL-6), symptom scores, recurrence rate, hypothyroidism incidence	Randomized controlled trial
Tian, et al. [40]	136 patients with simple goiter	Xiaoyao Powder + Haizao Yuhu Decoction (TCM) + levothyroxine sodium tablets	Levothyroxine sodium tablets alone	Thyroid function (FT3, FT4, TSH), TCM symptom scores, hyper/hypothyroidism incidence, adverse reactions	Randomized controlled trial
Zheng, et al. [41]	90 patients with Yang-deficiency type Subclinical Hypothyroidism (SCH)	Jin Gui Ren Qi Wan (TCM group) or Eugenol (Western medicine group)	Dietary education and intervention (control group)	TSH, TCHO, TG, LDL, HDL levels; clinical efficacy	Randomized controlled trial

Li [42]	92 elderly patients with SCH and coronary artery disease	Jin Gui Ren Qi Wan + Levothyroxine Tablets	Levothyroxine Tablets alone	Thyroid function (TSH, FT3, FT4), lipid levels (TG, TC, LDL-C, HDL-C), NO, CRP, MPO levels, clinical efficacy	Randomized controlled trial
Zheng and Yang [43]	60 patients with Hashimoto's thyroiditis and hypothyroidism	Jin Gui Ren Qi Wan + Levothyroxine Sodium Tablets	Levothyroxine Sodium Tablets alone	Thyroid function (TSH, FT3, FT4, TPOAb, TgAb), lipid levels (TC, TG, LDL-C, HDL-C), clinical efficacy	Randomized controlled trial
Liu, et al. [44]	100 AIT patients (aged 20–65) with elevated TGAAb/TPOAb but normal thyroid function	Jinshuibao capsule (3 capsules, 3x/day) + conventional therapy	Conventional therapy (low iodine diet)	TGAAb, TPOAb levels; thyroid size (ultrasound); FT3, FT4, TSH	Randomized controlled trial
Zeng, et al. [45]	68 patients with subacute thyroiditis	Yin Qiao Ma Bo San + Shengjiang Powder (oral decoction, 2x/day)	Indomethacin enteric-coated tablets (25 mg, 3x/day)	TCM symptom scores; FT3, FT4, TSH; ESR, CRP; recurrence rate	Randomized controlled trial
Zhang, et al. [46]	Patients with hypothyroidism (Yang deficiency type)	Traditional Chinese Medicine (TCM) treatments (e.g., herbal prescriptions, acupuncture, dietary therapy, combined TCM-Western medicine)	Western medicine (lifelong hormone replacement therapy)	Improvement in clinical symptoms (fatigue, cold intolerance, edema), thyroid function levels (TSH, FT3, FT4), quality of life	Review article (summarizing clinical studies and trials)

Lyu [47]	84 patients with early coronary heart disease and cardiac decompensation	Atorvastatin (20 mg/day) + coenzyme Q10 (30 mg, 3 times/day) for 1 month	Atorvastatin (20 mg/day) alone for 1 month	Cardiac function indices (LVESD, LVEDD, LVEF), treatment efficacy (significant/effective/ineffective), adverse reactions	Randomized controlled trial
Guo and Mao [48]	120 hypothyroid patients (Yang deficiency type)	Fugui Dihuangwan (TCM) + Euthyrox (levothyroxine sodium)	Euthyrox alone	Thyroid function (FT3, FT4, TSH), TCM symptom scores, blood lipids (TC, TG, LDL-C), clinical efficacy	Randomized controlled trial
Xie et al. [49]	100 HT patients with hypothyroidism	Xiangyuan Mixture (TCM) + levothyroxine sodium	Levothyroxine sodium alone	Thyroid volume, thyroid antibodies (TgAb, TPOAb, TRAb), TSH, FT3, FT4, ESR, CRP	Randomized controlled trial
Xu et al. [50]	84 pregnant patients with subclinical hypothyroidism	High-iodine TCM (e.g., seaweed, kombu) + levothyroxine sodium	Levothyroxine sodium alone	Serum VB12, Hcy, TSH, FT3, FT4, blood lipids (TG, TC, LDL-C), clinical efficacy	Randomized controlled trial
Farhangi et al. [51]	Patients with Hashimoto's thyroiditis aged 20-50 years	Daily administration of 2g of Nigella sativa powder for 8 weeks.	Daily administration of 2g of starch powder (placebo) for 8 weeks.	Changes in thyroid function (TSH, T3, T4, anti-TPO). Changes in serum VEGF and Nesfatin-1 concentrations. Changes in anthropometric features (body weight, BMI, waist	Randomized, double-blind, placebo-controlled trial

				circumference, hip circumference, WHR).	
An et al. [52]	Hypothyroid patients on levothyroxine treatment who still experienced fatigue (FSS score ≥ 36)	L-carnitine supplementation (990 mg L-carnitine twice daily) for 12 weeks.	Placebo for 12 weeks.	Fatigue-related symptoms measured by the Fatigue Severity Scale (FSS), Physical Fatigue Score (PFS), and Mental Fatigue Score (MFS).	Randomized, double-blind, placebo-controlled trial.
Hoang et al. [53]	Patients (n=70, age 18-65 years) diagnosed with primary hypothyroidism on a stable dose of L-T4 for 6 months	Patients were randomized to either desiccated thyroid extract (DTE) or L-T4 for 16 weeks	L-T4.	Biochemical and neurocognitive tests at baseline and at the end of each treatment period.	Randomized, double-blind, crossover study.
Ma et al. [54]	Mildly iodine deficient adults (n=112) aged 18-40 years	Participants were supplemented with 150 μ g of iodine as potassium iodate daily for 24 weeks	Placebo daily for 24 weeks	Change in thyroglobulin (Tg) concentration	Randomized, double-blind, placebo-controlled, clinical trial
Gautam et al. [55]	A 30-year-old female patient with subclinical hypothyroidism (SCH).	Treatment with 3 gm of Trikatu Powder twice a day for 4 months.	There is no comparison group.	Reduction in serum TSH level, weight loss, and improvement in associated symptoms.	Case report
Zhao et al. [56]	NHANES study design: Participants aged	Coffee consumption.	NHANES study design: Different levels	Thyroid function indicators: Serum TT4, TT3, FT4, FT3, and TSH concentrations.	MR study design

	20 years and older from the NHANES 2007-2012 database.		of coffee consumption (0, <2, 2-4, and >4 cups/day). MR study design: Regular vs. infrequent coffee consumers.	Thyroid disorders: Hyperthyroidism and hypothyroidism	
Bellipanni et al. [57]	Perimenopausal and menopausal women aged 42 to 62 years.	3 mg of melatonin administered at bedtime	Placebo administered at bedtime	Hormone levels: Thyroid hormones (T3 and T4), Luteinizing Hormone (LH), Follicle-Stimulating Hormone (FSH). Menstrual cyclicality. Perimenopausal symptoms: mood, depression, and other symptoms recorded <i>via</i> questionnaire.	Randomized placebo controlled study
Shimomura et al. [58]	Hypothyroid patients aged 20 to 45 years and healthy volunteers aged 20-45.	Administration of 300mg of γ -oryzanol	Single-dose study: TSH levels before and after γ -oryzanol administration, and with and without γ -oryzanol administration. Chronic treatment study: TSH levels	Serum TSH, Thyroxine-iodine (T4-I), and Triiodothyronine (T3) concentrations.	Interventional study design

			before and after 7 days of γ -oryzanol treatment, and comparison between hypothyroid patients and normal subjects		
Sharma et al. [59]	Subjects with subclinical hypothyroidism, aged 18 to 50 years, with elevated serum thyroid stimulating hormone (TSH) levels (4.5-10 μ IU/L) and normal serum triiodothyronine (T3) and thyroxine (T4) levels.	Ashwagandha root extract.	Placebo (starch).	Serum TSH, T3, and T4 levels	Double-Blind, Randomized Placebo-Controlled Trial

The risk of bias was assessed using the Cochrane risk of bias 2.0 (ROB2) tool, with detailed results presented in the supplementary Table 2.

Table 2: ROB.

Article reference	Randomization	Allocation concealment	Blinding of participants/personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
Lin, et al. [1]	Low risk	Unclear risk	High risk (no blinding reported)	Unclear risk	Low risk	Low risk	Low risk
Chen, et al. [2]	Low risk	Unclear risk	High risk (no blinding)	Unclear risk	Low risk	Low risk	Low risk
Lu, et al. [3]	Low risk	Unclear risk	High risk	Unclear risk	Low risk	Low risk	Low risk
Chen, et al. [4]	Low risk	Unclear risk	High risk	Unclear risk	Low risk	Low risk	Low risk
Wang [5]	Low risk	Unclear risk	High risk (no blinding mentioned)	Unclear risk	Low risk	Low risk	Low risk
Guo [6]	Low risk	Unclear risk	High risk	Unclear risk	Low risk	Low risk	Low risk
Lou, et al. [7]	Low risk	Unclear risk	High risk	Unclear risk	Low risk	Low risk	Low risk
Wang [5]	Low risk	Unclear risk	High risk	Unclear risk	Low risk	Low risk	Low risk
Lou, et al. [7]	Low risk	Unclear risk	High risk	Unclear risk	Low risk	Low risk	Low risk
Liu and Li [9]	Low risk	Unclear risk	High risk	Unclear risk	Low risk	Low risk	Low risk
Mo and Zhou [10]	Low risk	Unclear risk	High risk (no blinding due to herbal intervention)	Unclear risk	Low risk	Low risk	Low risk
Teng [11]	Low risk	Unclear risk	High risk (topical intervention not blinded)	Unclear risk	Low risk	Low risk	Low risk
Yu, et al. [12]	Low risk	Unclear risk	High risk (no participant blinding)	Unclear risk	Low risk	Low risk	Low risk

Ye, et al. [13]	Low risk	Unclear risk	High risk (herbal+oral therapy, no blinding)	Unclear risk	Low risk	Low risk	Low risk
Yang, et al. [14]	Low risk	Unclear risk	High risk (herbal topical paste not blinded)	Unclear risk	Low risk	Low risk	Low risk
Chen and Qin [15]	Low risk	Unclear risk	High risk (no blinding reported)	Unclear risk	Low risk	Low risk	Low risk
Chen, et al. [16]	Low risk	Unclear risk	High risk (open-label design)	Unclear risk	Low risk	Low risk	Low risk
Cao and Chen [17]	Low risk	Unclear risk	High risk (unblinded)	Unclear risk	Low risk	Low risk	Low risk
Zhong, et al. [18]	Low risk	Unclear risk	High risk (intervention visible)	Unclear risk	Low risk	Low risk	Low risk
Chen and Lou [19]	Low risk	Unclear risk	High risk (no blinding)	Unclear risk	Low risk	Low risk	Low risk
Tao, et al. [20]	Low risk	Unclear risk	High risk (no blinding)	Unclear risk	Low risk	Low risk	Low risk
Tian, et al. [21]	Low risk	Unclear risk	High risk	Unclear risk	Low risk	Low risk	Low risk
Zhao, et al. [22]	Low risk	Low risk	High risk	Unclear risk	Low risk	Low risk	Low risk
Li, et al. [23]	Low risk	Unclear risk	High risk	Unclear risk	Low risk	Low risk	Low risk
Fu, et al. [24]	Low risk	Unclear risk	High risk	Unclear risk	Low risk	Low risk	Low risk
Zhang, et al. [25]	Low risk	Unclear risk	High risk (no blinding reported)	Unclear risk	Low risk	Low risk	Low risk
Wang and Dong [26]	Low risk	Unclear risk	High risk	Unclear risk	Low risk	Low risk	Low risk
Xu and Ke [27]	Low risk	Unclear risk	High risk	Unclear risk	Low risk	Low risk	Low risk
Wang, et al. [28]	Low risk	Unclear risk	High risk	Unclear risk	Low risk	Low risk	Low risk

Li, et al. [29]	Low risk	Unclear risk	High risk	Unclear risk	Low risk	Low risk	Low risk
Ding [30]	Low risk	Unclear risk	High risk	Unclear risk	Low risk	Low risk	Low risk
Qi and Du [31]	Low risk	Unclear risk	High risk	Unclear risk	Low risk	Low risk	Low risk
Zhang and Zhang [32]	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	High risk (narrative review bias)
Fan, et al. [33]	Low risk	Unclear risk	High risk	Unclear risk	Low risk	Low risk	Low risk
Chen, et al. [34]	Low risk (randomized)	Unclear risk (not described)	High risk (no blinding reported)	Unclear risk (not described)	Low risk (no dropouts mentioned)	Low risk (all outcomes reported)	Low risk
Weng, et al. [35]	Low risk (randomized numerical table)	Unclear risk (not described)	High risk (no blinding reported)	Unclear risk (not described)	Low risk (all completed study)	Low risk (all outcomes reported)	Low risk
Xing, et al. [36]	Low risk (Random number table used)	Unclear risk (Not explicitly stated)	High risk (No blinding for TCM intervention)	Unclear risk (Not reported)	Low risk (No attrition mentioned)	Low risk (All outcomes reported)	Low risk (Baseline characteristics balanced)
Kou, et al. [37]	Low risk (random number table used)	Unclear risk (not explicitly stated)	High risk (no blinding reported)	Unclear risk (not explicitly stated)	Low risk (no cases shed)	Low risk (all outcomes reported)	Low risk (funding declared, no conflicts reported)
Zhu, et al. [38]	Low risk (random number table)	Unclear risk (not stated)	High risk (no blinding reported)	Unclear risk (not stated)	Low risk (no dropouts)	Low risk (all outcomes reported)	Low risk (funding declared)

Zhang, et al. [39]	Low risk (randomized numerical table)	Unclear risk (not stated)	High risk (no blinding reported)	Unclear risk (not stated)	Low risk (1 dropout in control group)	Low risk (all outcomes reported)	Low risk (no conflicts)
Tian, et al. [40]	Low risk (random number method)	Unclear risk (not stated)	High risk (no blinding reported)	Unclear risk (not stated)	Low risk (no dropouts)	Low risk (all outcomes reported)	Low risk (no conflicts)
Zheng, et al. [41]	Unclear risk (method not specified)	Unclear risk	High risk (no blinding reported)	Unclear risk	Low risk (complete data)	Low risk	Low risk
Li [42]	Unclear risk (randomized but method not detailed)	Unclear risk	High risk (no blinding reported)	Unclear risk	Low risk (complete data)	Low risk	Low risk
Zheng and Yang [43]	Unclear risk (randomized but method not detailed)	Unclear risk	High risk (no blinding reported)	Unclear risk	Low risk (complete data)	Low risk	Low risk
Liu, et al. [44]	Unclear risk (method not specified)	Unclear risk	High risk (no blinding reported)	Unclear risk	Low risk (complete data)	Low risk	Low risk
Zeng, et al. [45]	Unclear risk (randomized numerical table used)	Unclear risk	High risk (no blinding reported)	Unclear risk	Low risk (complete data)	Low risk	Low risk
Zhang, et al. [46]	Not applicable (review article)	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Potential bias in study selection (narrative review)

Lyu. [47]	Low risk (randomly divided)	Unclear risk (not described)	High risk (no blinding reported)	Unclear risk (not described)	Low risk (all patients accounted for)	Low risk (all outcomes reported)	Low risk (baseline characteristics comparable)
Guo and Mao [48]	Low risk (random number table)	Unclear risk (not described)	High risk (no blinding)	Unclear risk (not described)	Low risk (all accounted for)	Low risk (all outcomes reported)	Low risk (baseline comparable)
Xie et al. [49]	Low risk (random number table)	Unclear risk (not described)	High risk (no blinding)	Unclear risk (not described)	Low risk (92/100 completed)	Low risk (all outcomes reported)	Low risk (baseline comparable)
Xu et al. [50]	Low risk (randomized numerical table)	Unclear risk (not described)	High risk (no blinding)	Unclear risk (not described)	Low risk (no dropouts reported)	Low risk (all outcomes reported)	Low risk (baseline comparable)
Farhangi et al. [51]	Low risk- Random permuted block procedure with allocation by computer- generated numbers in sealed envelopes.	Low risk- Double-blind design with placebo similar in appearance to intervention.	Low risk-Loss to follow-up reported and reasons provided; balanced attrition between groups.	Low risk- Primary outcomes clearly defined and study registered.	Low Risk	Low Risk	Low risk
An et al. [52]	Low risk-The allocation sequence was determined using Random Allocation	Low risk- This was a double- blind, placebo- controlled trial.	Low risk-Loss to follow-up was reported, and the number of participants who completed the study in each group was provided.	Low risk- The study protocol was registered	Low risk	Low risk	Low risk

	Software with a block size of 4.						
Hoang et al. [53]	Low risk- Patients were randomized using a computer-generated random number table, stratified in blocks.	Low risk- The study was double-blinded; both participants and investigators were blinded.	Low risk- The study reported the number of patients enrolled and those who completed the study.	Low risk- The primary outcome measures were clearly defined.	Low risk	Low risk	Low risk
Ma et al. [54]	Unclear risk- Participants were block randomized, but the method of sequence generation is not described in detail.	Low risk- Double-blind design, reducing the risk of bias affecting both participants and researchers.	Low risk- Loss to follow-up was reported and accounted for in the analysis.	Low risk- Primary outcome was clearly defined.	Low risk	Low risk	Low risk
Zhao et al. [56]	N/A - NHANES is an observational study design without randomization	High risk- Neither study design involved blinding	Unclear- It is unclear if the exclusion of participants with missing data led to attrition bias	Unclear- It is unclear if the study protocol registered	High risk	High risk	High risk
Bellipanni et al. [57]	Low risk- The study used a randomized design to assign participants to	Low risk- The study was double-blinded, meaning that neither the	Unclear- The study mentioned variations in participant numbers due to "minor failure of some determinations," but the extent and	Unclear- The study did not state whether the study	Moderate risk	Moderate risk	Moderate risk

	the melatonin or placebo group.	participants nor the researchers knew who was receiving the melatonin or the placebo.	reasons for attrition are not clearly reported.	protocol was pre-registered			
Shimomura et al. [58]	Unclear-The study does not explicitly mention the method of randomization.	Unclear-The study does not mention whether blinding was used.	Unclear-The study does not provide information about participant dropout.	Unclear-It is unclear if the study protocol was pre-registered.	Unclear risk	Unclear risk	High risk
Sharma et al. [59]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk

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