



Ginger for health care: An overview of systematic reviews

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ABSTRACT

Objectives: To summarize the evidence from systematic reviews (SRs) and meta-analyses that evaluated the efficacy of ginger in treating any conditions and critically assess the quality of these evidence.

Methods: A systematic search of the literature was conducted from inception until February 28, 2019 using the PubMed, EMBASE, Web of science, Cochrane library, and four Chinese databases. Literature selection and data extraction were conducted by two independent reviewers. The quality of SRs was evaluated using the AMSTAR-2 tool. The GRADE system was used to assess the quality of evidence.

Results: Twenty-seven SRs were included. The number of included studies were various, range from 3 to 27. The condition with the most included SRs was nausea and vomiting (n = 12, 44.4%). Many SRs showed a promising efficacy of ginger, including nausea and vomiting, metabolic syndrome and pain, while the effect of ginger for platelet aggregation failed to draw a certain conclusion. The quality of SRs was heterogeneous. All of included SRs well complied with the Item 1 (“research questions included the components of PICO”) and Item 3 (“explained selection of the study designs for inclusion”). Twenty review failed to provide registration information. Only one SR reported the sources of funding for studies included.

Conclusions: In our overview, most of SRs suggest ginger is a promising herbal medicine for health care, which is beneficial for nausea and vomiting, metabolic syndrome and pain. However, considering the limited quality of included evidence and heterogeneity of different clinical trials, more well-design studies are required to confirm the conclusion further.

1. Introduction

Ginger (*Zingiber officinale* Roscoe) is a monocotyledonous in the family Zingiberaceae originating from southeast Asia.¹ The main components of ginger include starch, lipids, proteins, and inorganic compounds.² It is widely used around the world as a flavoring or fragrance in foods, but also in traditional oriental medicine since ancestral times.³ For centuries, ginger has been an integral part of the various traditional and folk systems of medicine in China and India for the treatment of different diseases, such as headaches, colds, osteoarthritis, muscle pains, nervous diseases, gingivitis, toothache, and asthma.^{3–8} Currently,

there are many studies that devoted to specific aspects of ginger's actions. For example, Stoilova et al studied the antioxidant effect of ginger extract.⁹ Yogeshwer Shukla et al reviewed the evidence of ginger as a inhibitors of the carcinogenic process.¹⁰ Lantz, RC explored the anti-inflammatory activity of compounds isolated from ginger.¹¹ Besides, ginger has also shown anticarcinogenic, immune modulatory, anti-bacterial, antifungal, anti-hyperglycemic, and antiatherosclerotic activity.

There is promising evidence about the health-promoting properties of ginger nowadays, which has been consumed in more and more countries. Ginger is especially used in significant amounts in Asian food

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products. In Europe countries, it is estimated the apparent consumption of ginger amounted to 58,000 tons in 2014.¹² Due to its abundance, low cost and safety in consumption, ginger has been the subject of intensive scientific research and much knowledge on the health beneficial biological activities of ginger and its bioactive constituents have been found in the recent decade.¹³

Several systematic reviews (SRs) or meta-analysis have investigated the efficacy and safety of ginger for treating certain condition, such as for chemotherapy-induced nausea and vomiting,¹⁴ osteoarthritis¹⁵ and dysmenorrhea.¹⁶ However, the results of SRs are not consistent, and the methodological quality of SRs is unknown. There is no overview that focused on the efficacy and safety of ginger for use in health care. The aim of this study was to summarize the evidence from SRs and meta-analyses that evaluated the effectiveness of ginger in treating any conditions and critically assess the quality of the evidence.

2. Materials and methods

2.1. Literature search

A systematic search of the literature was conducted from inception until February 28, 2019 using the PubMed, EMBASE, Web of science, Cochrane library, and four Chinese databases, which including Chinese Biomedical Databases (CBM), China National Knowledge Infrastructure (CNKI), Wanfang and VIP. No language, publication date or publication status restrictions were used. The English search terms were used the following terminology: (“ginger” OR “ginger*” OR “zingiber officinale” OR “zingiber” OR “zingiber*”) AND (“systematic review” OR “meta analysis” OR “meta-analysis”). In addition, the references of all eligible studies were manually retrieved to ensure the comprehensiveness of the search. The detailed search strategies for PubMed were presented in Appendix A.

2.2. Inclusion criteria

SRs were considered for inclusion that systematically evaluated the effectiveness and/or safety of any type of ginger as a treatment for any condition. The detailed criteria following “PICOS” principle (P: Participants, I: Intervention, C: Control, O: Outcomes, S: Study designs) were showed in Table 1. And comments, reply, non-systematic review, non-English or non-Chinese language articles, conference abstracts, and repeated publication were excluded.

2.3. Literature selection and data extraction

The retrieved records were imported into the EndNote X7 software and the duplicate publications were excluded. Two reviewers (LMX and YL) independently read the titles and abstracts of all identified records to exclude those that were clearly not relevant. Then the full texts of the articles retained were reviewed to further determine their suitability. The excluded reasons for full texts were list in Appendix B. Differences opinions were resolved by consensus.

The data were extracted by two reviewers (LMX and YL) independently using a pre-defined form. The following characteristics of

Table 1
The inclusion criteria.

Category	Inclusion criteria
Population	People without any condition, country or ages restriction
Intervention	Ginger (any dosage, type or duration)
Comparator	Placebo or active drug or treatment as usual another
Outcome	Measure(s) (about the efficacy and/or safety of the ginger)
Study design	Systematic review or meta-analysis (with detailed methodology, including systematic research strategy and explicit inclusion/exclusion criteria)

the guidelines were collected: the first author, publication year, country, number of included studies, sample size, search databases, search time, quality assessment methods for included studies and key finding. Any discrepancies were resolved by consensus.

2.4. Quality assessment

The methodological quality of included SRs/MAs was appraised by the AMSTAR-2 (Assessing the Methodological Quality of Systematic Reviews 2),¹⁷ which was a reliable and validated tool for critically appraising SRs of randomized controlled clinical trials (RCTs), or non-randomised studies, or both. It consisted of 16 domains. Each item was evaluated three evaluation option, “Yes”, “Partial Yes” and “No”. If the domain specific questions in AMSTAR 2 was framed, a “Yes” answer was rated. If no information was provided to rate an item, the item was rated as a “No”. A “partial Yes” was rated in some instances where we considered it worthwhile to identify partial adherence to the standard. Two reviewers (LMX and YL) independently assessed the quality of the evidence derived from included SRs. Disagreements were resolved by discussion. The GRADE system (the Grading of Recommendations Assessment Development and Evaluation) was used to assess the quality of evidence associated with specific outcomes from five aspects: limitations, inconsistencies, indirectness, inaccuracy, and publication bias.^{18,19}

3. Results

3.1. Search results

Initially, 488 potentially relevant records were retrieved. After screening titles and abstracts, 312 records were excluded and the remaining 50 records were considered potentially eligible for full-text screening. Finally, 27 SRs^{15,20–45} were included in this overview (Fig. 1).

3.2. Description of included SRs

Twenty-seven SRs were published in period from 2000 to 2018. Fig. 2 showed the number of SRs was gradually increasing since the first SRs published in 2000,⁴³ demonstrated the types of ginger included

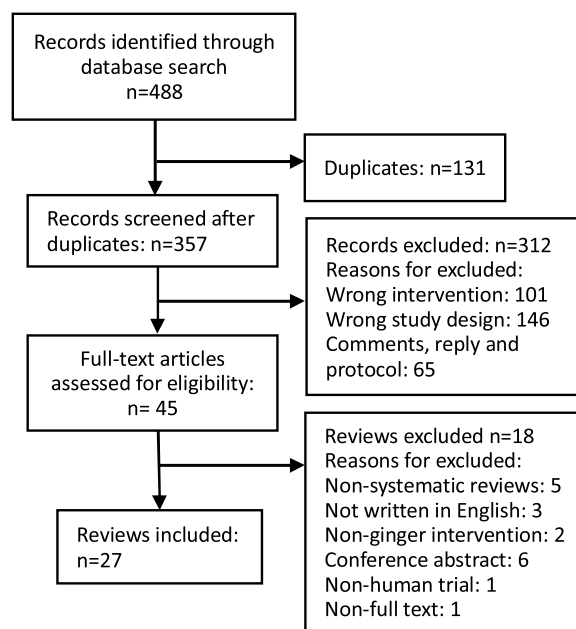


Fig. 1. Flow diagram outlining the selection process.

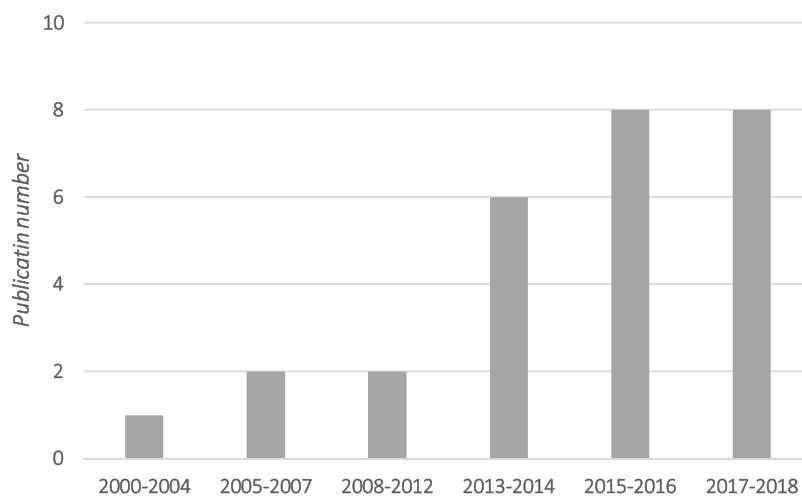


Fig. 2. The number of included SRs published between 2000 and 2018.

ginger powder capsules, ginger syrup, ginger biscuits, ginger essence capsules, and ginger extract capsules, one³³ including any orally monopreparation of ginger root, one⁴³ including any form of ginger (fresh root, dried root, powder, tablets, capsules, liquid extract, and tea), one³² for ginger capsules contained Javanese ginger extract, rhizome extract, and curcuminoids, one²¹ for ginger preparations obtained from fresh ginger root and ginger syrup, one²⁸ for ginger powder. Of the 27 reviews, 16 SRs (59.3%) conducted meta-analysis while the remaining SRs (40.7%) did not. There were 11 from Asia, six (22.2%) from Europe, five (18.5%) from Australia, four (14.8%) from the North America and 1 (3.7%) from the South Africa. Table 2 summarizes the key characteristics of all SRs. The effect sizes for main outcomes in included SRs were summarized in Table 3.

3.2.1. Ginger for nausea and vomiting

Twelve reviews^{21–23,26,28,29,34,36,39,41–43} examined the efficacy of ginger as an intervention for nausea and vomiting. Five reviews^{21,26,39,41,43} assessed effectiveness and safety of ginger for nausea and vomiting of pregnancy (NVP). The newest review was by Stanisiere J et al which included 14 RCTs and 3 prospective clinical studies. The results demonstrated that ginger was a safe and effective treatment for NVP. Besides, it was needed that medical supervision and the quality assurance of ginger when ginger was recommended for NVP in early pregnancy. Three reviews^{23,34,36} investigated the potential use of ginger as a prophylactic or treatment for chemotherapy-induced nausea and vomiting (CINV). The review by Chang W P et al²³ included the most studies (10 RCTs) and indicated that ginger was significantly effective for CINV (OR: 0.71, 95% CI: 0.54–0.94), particularly acute vomiting (OR: 0.58, 95% CI: 0.37–0.94). However, author simultaneously emphasized ginger wasn't a complete alternative for antiemetic drugs. Three reviews^{22,29,42} evaluated the efficacy of ginger on postoperative nausea and vomiting (PONV). Results from all three reviews showed that there was a positive effect. The newest review⁴² included ten RCTs and the meta-analysis results supported that ginger could decrease the severity of PONV. One prior review by Ernst E et al²⁸ assessed the efficacy of ginger for clinical nausea and vomiting, which included four different clinical conditions: seasickness, morning sickness, chemotherapy-induced nausea and postoperative nausea. Only six RCTs were included and the review failed to draw firm conclusions.

3.2.2. Ginger for metabolic syndrome

Six reviews^{20,30,31,37,38,45} studied the ginger for the metabolic syndrome, including obesity, diabetes and metabolic profile. Two reviews^{20,31} investigated the use of ginger for weight loss. However, there was some inconsistencies. Ebrahimzadeh Attari V et al²⁰ reviewed 27 articles (6 in vitro, 17 animal, and 4 human studies). They found effect

of ginger for weight lowering may be positive in obese animal models, whereas there were no changes or slight changes of anthropometric measurements and body composition in human studies. Instead, meta-analysis by Jugran A K et al³¹ demonstrated that ginger could decreased body weight (BW), waist-to-hip ratio (WHR), hip ratio (HR), fasting glucose and insulin resistance index and HDL-cholesterol levels. One review by Pourmasoumi M et al³⁸ reported that ginger had a favorable effect on triacylglycerol (TAG) and low density lipoprotein cholesterol (LDL-C). Also, the result revealed that low dose of ginger (≤ 2 g/day) had greater lowering impact on TAG and total cholesterol (TC). There were three reviews^{30,37,45} reported the relationship between ginger and type 2 diabetes mellitus. The meta-analysis by Zhu J et al⁴⁵ revealed that ginger could significantly reduce fasting blood glucose and glycosylated hemoglobin (HbA1c). However, the heterogeneity couldn't be ignored. Besides, other two reviews^{30,37} also indicated that ginger had a positive effect for controlling blood glucose and lipid profile.

3.2.3. Ginger for pain

Five reviews^{24,25,32,40,44} focused on pain. Two reviews^{24,25} evaluated the efficacy of ginger for treating dysmenorrhea. They included similar studies, which one review²⁴ included six RCTs, while another review²⁵ added an additional RCT. They drew a consistent conclusion that ginger could be an effective treatment for menstrual pain in dysmenorrhea. One review⁴⁴ assessed the evidence for ginger as an analgesic and ergogenic aid for exercise training and sport. Sixteen studies were included, which seven for analgesic, nine for ergogenic aid. Despite meta-analysis was not conducted, the review drew a conclusion that ginger as a dietary supplement in exercise training and indicated ginger may modestly reduce muscle pain stemming but no clear ergogenic benefit oxygen use, heart rate, metabolic rate and body composition. Two reviews^{32,40} without disease restrictions evaluated the effect of ginger for any type pain. One of them⁴⁰ included the studies of ginger as analgesic for osteoarthritis pain, dysmenorrhea, and acute muscle pain. This review was unable to draw any firm conclusions due to without high-quality evidence. Another review³² focused on chronic pain and included 18 RCTs, which indicated that Zingiberaceae extracts could offer effective relief and the dose-dependent effect identified implied that higher doses may potentially increase the effect further.

3.2.4. Ginger for osteoarthritis

Two reviews^{15,33} focused on the osteoarthritis (OA). The newest review included five RCTs and meta-analysis results showed that ginger was modestly efficacious and reasonably safe for reducing pain and disability in OA.

Table 2
The characteristics of included SRs.

Studies	Country	No. of primary studies	Databases Source	Search Time	Registration Number	Quality Assessment	Meta-analysis	Condition	Adverse effects	Key Finding
Leach M 2008 ³¹	Australia	3 RCTs	AARP Ageline, AMED, AMI, BioMed central gateway, CAM on PubMed, CENTRAL, CINAHL, Cochrane library, DARE, Dissertations Abstract International, EMBASE, Health Source Nursing/Academic edition, International Pharmaceutical Abstract, MEDLINE, Natural medicines comprehensive database and TRIP	Jan-07	NR	Joanna Briggs Institute (JBI) critical appraisal of evidence of effectiveness' tool	N	Osteoarthritis	Heartburn, bad taste, dyspepsia, changes in stools, nausea and conjunctivitis	Current evidence is weak for the use of Ginger in adults with OA of the knee and/or hip.
Ding M 2013 ²⁵	Australia	4 Studies (3 RCTs and 1 non-RCTs)	CAM on PubMed, CINAHL, Google Scholar, MEDLINE, National Library of Australia, Cochrane Library, TRIP	1980-2010	NR	NR	N	Any conditions	No	Evidence is insufficient to draw any conclusions about the safety and effectiveness of topical ginger.
Terry R 2011 ³⁸	UK	8 Studies	AMED, CINAHL, Cochrane Library, EMBASE, Medline, Web of Knowledge	Sep-10	NR	Jadad scale	N	Pain	Heartburn	Evidence of the efficacy of ginger to treat pain remains insufficient.
Marx W 2015 ³³	Australia	10 Studies (8 clinical trials and 2 observational studies)	Web of Knowledge, Embase, Cochrane Library	May-14	NR	Cochrane risk of bias tool	N	Platelet aggregation	No	Ginger affects platelet aggregation and coagulation is equivocal.
Lee J 2013 ²²	South Korea	5 RCTs	PubMed	Apr-15	NR	Jadad scale	Y	Chemotherapy-induced nausea and vomiting	Diarrhea and dizziness, heartburn, bruising, flushing, rash, drowsiness, sleepiness, dry mouth, thirst, heartburn, or restlessness	Ginger did not contribute to control of the incidence of acute nausea and vomiting or of the severity of acute nausea.
Pourmasoumi 2018 ³⁵	Iran	14 Trials	PubMed, Scopus, Science Direct, ISI Web of Science and Google Scholar	May-17	CRD42017054682	Jadad scale	Y	Lipid profile	NR	Ginger had a favorable effect on TAG and LDL-C.
Bartels E 2015 ¹⁵	Denmark	5 RCTs	PubMed, EMBASE, CINAHL, Web of Science, Scifinder	24-Apr-14	CRD42011001777	Self-making tool	Y	Osteoarthritis	NR	Ginger has a superior effect on OA pain and disability to placebo, and apparently without serious adverse events.
Jugran 2018 ²⁹	Iran	14 RCTs	MEDLINE, EMBASE, Web of Science, and Cochrane Central Register of Controlled Trials, Databases of International Standard Randomized Controlled Trial Number Register and Meta-register for RCTs	Nov-17	NR	Cochrane risk of bias tool	Y	Obesity and metabolic profiles	NR	Ginger intake reduced BW, WHR, HR, fasting glucose and HDLcholesterol, but did not affect insulin, BMI, triglycerides, total- and LDL-cholesterol levels
Ernst E 2000 ²⁶	UK	6 RCTs	Medline, Embase, Biosis, CISCOM Cochrane Library	Nov-97	NR	Jadad scale	N	Nausea and vomiting	No	Ginger is a promising antiemetic herbal remedy.
Stanisiere J 2018	France	18 Studies	PubMed	Dec-17	NR	NR	N	Pregnancy-induced nausea and vomiting	NR	Ginger is a safe and effective treatment for NVP.

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Table 2 (continued)

Studies	Country	No. of primary studies	Databases Source	Search Time	Registration Number	Quality Assessment	Meta-analysis	Condition	Adverse effects	Key Finding
Ding M 2013 ²⁴	Australia	4 RCTs	CINAHL, Cochrane Library, MEDLINE, RIP	2000-2009	NR	Critical Appraisal Skills Programme (CASP) tool	N	Pregnancy-induced nausea and vomiting	Burning sensations, belching, retching, vomiting	Ginger is a safe and effective treatment for PNV.
Thomson 2014 ³⁹	Canada	6 RCTs	PubMed, EMBASE, CINAHL, Cochrane Library, and all evidence-based medicine reviews using the OVID Portal of Queen's University, Kingston, Ontario	NR	NR	Cochrane risk of bias tool	Y	Pregnancy-induced nausea and vomiting	Reflux, heartburn	Ginger is an effective nonpharmacological option for treating NVEP.
Zhang G 2015 ²⁷	China	8 RCTs	Pubmed, Web of science, Google scholar	May-15	NR	Jadad scale	Y	Postoperative nausea and vomiting	NR	Ginger is safe and effective in preventing postoperative nausea and vomiting.
Tóth B 2018 ⁴⁰	America	10 RCTs	PubMed, Embase, Cochrane Central Register of Controlled Trials, Web of Science	26-Feb-18	CRD42017064278	Cochrane risk of bias tool	Y	Postoperative nausea and vomiting	NR	Ginger is safe and well tolerated, and decreases the severity of PONV, and may lower the incidence of postoperative nausea and vomiting.
Chang WP 2018 ²¹	China, Taiwan	10 RCTs	PubMed, ProQuest, MEDLINE, Cochrane Library	2000 - 2017	NR	Cochrane risk of bias tool	Y	Chemotherapy-induced nausea and vomiting	NR	Ginger is significantly effective in controlling acute CINV but not effective in controlling DNV
Wilson P 2015 ⁴²	Hungary	16 RCTs	PubMed	Apr-15	NR	NR	N	Analgesic and Ergogenic Aid	Heartburn	Ginger may accelerate recovery of maximal strength after eccentric resistance exercise and reduce the inflammatory response to cardiorespiratory exercise.
Zhu J 2018 ⁴³	China	10 RCTs	PubMed, Embase, Cochrane Library, Chinese Biomedical Database (CBM), China National Knowledge Infrastructure (CNKI), Wanfang Database	19-May-17	CRD42017069241	Cochrane risk of bias tool	Y	Type 2 Diabetes Mellitus and Components of the Metabolic Syndrome	NR	Ginger may be a promising adjuvant therapy for T2DM and MeTS.
Borrelli F 2005 ¹⁹	UK	7 Studies (6 RCTs and 1 prospective observational cohort study)	MEDLINE, EMBASE, and Cochrane Library	Jun-04	NR	Jadad scale	N	Pregnancy-induced nausea and vomiting.	Heartburn, bruising or flushing, rash, and gastrointestinal discomfort	Ginger may be an effective treatment for nausea and vomiting in pregnancy.
Marx W 2013 ³⁴	Australia	7 RCTs	PubMed, Cochrane Library, CINAHL	Apr-12	NR	American Dietetic Association's quality criteria checklist	N	Chemotherapy-induced nausea and vomiting	Heartburn, bruising or flushing, rash, and gastrointestinal discomfort	Ginger may be useful for some patients but also that care needs to be taken in its application.
Jafarnejad 2017 ²⁸	Iran	9 RCTs	PubMed, Scopus	30-Oct-16	NR	Jadad scale	Y	Blood glucose and lipid concentrations in diabetic and hyperlipidemic subjects	NR	Ginger supplementation (tablet, capsules, powder or rhizomes) significantly reduced FBG, TC and TG and significantly increased HDL-C.
Mazidi M 2016 ³⁵	China	9 RCTs	PubMed, Web of Science, Cochrane Database, and Google Scholar	Jul-16	CRD42016035973	Cochrane risk of bias tool	Y	Serum C-reactive protein, lipid profile and glycaemia	NR	Ginger supplementation significantly reduces serum CRP and improves glycaemia indexes and lipid profile.

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Table 2 (continued)

Studies	Country	No. of primary studies	Databases Source	Search Time	Registration Number	Quality Assessment	Meta-analysis	Condition	Adverse effects	Key Finding
Daily JW 2015 ²³	South Korea	7 RCTs	PubMed, EMBASE, Cochrane Library, Korean databases, Chinese medical databases, Indian scientific database	NR	NR	Cochrane risk of bias tool	Y	Dysmenorrhea	NR	The results provide suggestive evidence for the effectiveness of ginger in treating primary dysmenorrhea.
Ebrahimzadeh 2018 ¹⁶	Iran	27 Trials (6 in vitro, 17 animal, and 4 human studies)	PubMed, Scopus, Google scholar, Science Direct	1995-May 2017	NR	Cochrane Collaboration's tool for RCTs, SYRCL's risk of bias tool for animal studies, vitro studies for Checklist for Reporting in vitro Studies guideline	N	Obesity	NR	This review article provides some convincing evidence to support the efficacy of ginger in obesity management.
Viljoen E 2014 ⁴¹	South Africa	12 RCTs	Pubmed, EBSCO host, Academic Search Premier, CINAHL, CAB abstracts, CENTRAL, Science Direct, ISI Web of Science, ISAP, Proquest, Scopus Abstracts, Africa Wide, SABINET, Current Controlled Trials Clinical trials.gov	1966-12 July 2013	CRD42011001237	Cochrane risk of bias tool	Y	Pregnancy-induced nausea and vomiting	No	This review suggests potential benefits of ginger in reducing nausea symptoms in pregnancy.
Chen CX 2016 ²²	America	6 RCTs	PubMed, EMBASE, Cochrane Library, CINAHL, Web of Science, PsycINFO, AMED, LILACS, International Pharmaceutical Abstracts, Biological Abstracts, Websites of clinical trial registries	May-15	CRD42015016744	Cochrane risk of bias tool	Y	Dysmenorrhea	NR	This review suggests potential benefits of oral ginger in managing dysmenorrhea pain.
Chaiyakunapruk 2006 ³⁰	Thailand	5 RCTs	Medline, IPA, CINAHL, Cochrane CENTRAL, HealthStar	NR	NR	Jadad scale	Y	Postoperative nausea and vomiting	Abdominal discomfort	Use of ginger is an effective means for reducing postoperative nausea and vomiting Zingiberaceae extracts are clinically effective hypoalgesic agents and the available data show a better safety profile than non-steroidal anti-inflammatory drugs.
Lakhan S 2015 ³⁰	Canada	18 RCTs	PubMed, ScienceDirect, and Cochrane Library	Dec-14	NR	NR	Y	Pain	NR	

*RCT: randomized controlled trials; NR: not report; N: no; Y: Yes.
 OA: Osteoarthritis; TAG: triacylglycerol; LDL-C: low density lipoprotein cholesterol; BW: body weight; WHR: waist-to-hip ratio; HR: hip ratio; HOMA-IR: insulin resistance index; NVP: nausea and vomiting of pregnancy (NVP); PNV: pregnancy-induced nausea and vomiting; NVEP: Nausea and vomiting in early pregnancy; PONV: Postoperative nausea and vomiting; CINV: chemotherapy-induced nausea and vomiting; DNV delayed nausea and vomiting; T2DM: type 2 diabetes mellitus; Mets: metabolic syndrome; FBG: fasting blood-glucose; TC: total cholesterol; TG: triglyceride; HDL-C: high density lipoprotein cholesterol; GRP: C-reactive protein.

Table 3
The summary of effect size of main outcomes from included meta-analysis.

Studies	The effect sizes of main outcomes	Quality of evidence*
Chang WP 2018 ²³	CINV, OR: 0.71, 95% CI: 0.54, 0.94 Acute CINV, OR: 0.60, 95% CI: 0.42, 0.86	⊕⊕⊕○ ⊕⊕⊕○
Chen CX 2016 ²⁴	Acute vomiting, OR, 0.58, 95% CI: 0.37, 0.94 Pain severity in dysmenorrhea (comparing with placebo), MD: -1.55, 95% CI: -2.43, -0.68	⊕⊕⊕○ ⊕⊕○○
Daily JW 2015 ²⁵	Pain severity in dysmenorrhea (comparing with NSAID), SMD: 0.00, 95% CI: -0.40, 0.41	⊕⊕○○
Jafarnejad S 2017 ³⁰	Pain severity in dysmenorrhea, MD: -1.85, 95% CI: -2.87, -0.84 Triglyceride, MD: -8.84; 95% CI: -11.95, -5.73	⊕⊕⊕○ ⊕⊕○○
Jugran A 2018 ³¹	Total cholesterol, MD: -4.42; 95% CI: -8.70, -0.13 LDL-C, MD: -5.07; 95% CI: -10.45, 0.30 HDL-C, MD: 2.87; 95% CI: 0.88, -4.86 FBG, MD: -14.93; 95% CI: -19.83, -10.04	⊕⊕○○ ⊕⊕○○ ⊕⊕○○ ⊕○○○
	Body weight, SMD: -0.66; 95% CI, -1.31, -0.01 Waist-to-hip ratio, SMD: -0.49, 95% CI: -0.82, -0.17 Hip ratio, SMD: -0.42, 95% CI: -0.77, -0.08 Fasting glucose, SMD: -0.68, 95% CI, -1.23, -0.05 Insulin resistance index, SMD: -1.67, 95% CI: -2.86, -0.48	⊕○○○ ⊕○○○ ⊕○○○ ⊕○○○
Chaiyakunapruk 2006 ²²	HDL-C, SMD: 0.40, 95% CI: 0.10, 0.70 PONV, RR: 0.65, 95% CI: 0.51, 0.84	⊕⊕○○ ⊕⊕⊕○
Mazidi M 2016 ³⁷	POV, RR: 0.62, 95% CI: 0.46, 0.84 Serum C-reactive protein, MD: -0.84, 95% CI: -1.38, -0.31 Fasting blood glucose, MD: -1.35, 95% CI: -2.04, -0.58	⊕⊕⊕○ ⊕⊕○○ ⊕⊕○○
	High-density lipoprotein, MD: 1.16, 95% CI: 0.52, 1.08 Low-density lipoprotein, MD: -1.33, 95% CI: -2.54, -0.11 Triglyceride, MD: -1.63, 95% CI: -3.10, -0.17	⊕⊕○○ ⊕⊕○○ ⊕○○○
Pourmasoumi 2018 ³⁸	HbA1c, MD: -1.01, 95% CI: -1.28, -0.72 Triacylglycerol, MD: -17.59, 95% CI: -29.32, -5.87 Total cholesterol, MD: -5.13, 95% CI: -11.05, 0.78	⊕○○○ ⊕○○○ ⊕○○○
	LDL-C, MD: -4.90, 95% CI: -22.30, -6.17 HDL-C, MD: 2.18, 95% CI: -0.08, 4.45	⊕○○○ ⊕⊕○○
Thomson 2014 ⁴¹	NVP, OR: 4.89, 95% CI: 1.88, 12.73	⊕○○○
Tóth B 2018 ⁴²	The severity of PONV, SMD: -0.247, 95% CI: -0.455, -0.040 PON, SMD: -0.151, 95% CI: -0.351, 0.048	⊕⊕⊕○ ⊕○○○
	POV, SMD: -0.194, 95% CI: -0.492, 0.104	⊕⊕○○
Viljoen E 2014 ⁴³	Nausea of pregnancy, MD: 1.20, 95% CI: 0.56, 1.84 Vomiting of pregnancy, MD: 0.72, 95% CI: -0.03, 1.4	⊕⊕⊕○ ⊕⊕○○
Zhu J 2018 ⁴⁵	HbA1c, MD: -1.00, 95% CI: -1.56, -0.44 Fasting insulin, MD: -1.62, 95% CI: -2.20, -1.05	⊕⊕○○ ⊕⊕⊕○
	HOMA-IR, MD: -0.59, 95% CI: -1.01, -0.17	⊕⊕○○
Zhang G 2015 ²⁹	POV, RR: 0.73, 95% CI: 0.58, 0.92	⊕⊕⊕○
	PONV, RR: 0.78, 95% CI: 0.68, 0.89	⊕⊕⊕○
Bartels E 2015 ¹⁵	Pain, SMD: -0.30, 95% CI: -0.50, -0.09 Disability, SMD: -0.22, 95% CI: -0.39, -0.04	⊕⊕⊕○ ⊕⊕⊕○
Lakhan S 2015 ³²	Chronic pain, SMD: -0.67; 95% CI: -1.13, -0.21	⊕⊕○○
Lee J 2013 ³⁴	The delayed vomiting, RR: 1.22, 95% CI: 0.44, 3.43	⊕○○○

RR: risk ratio; OR: Odds Ratio; SMD: standardized mean difference; High: ⊕⊕⊕⊕; Moderate: ⊕⊕⊕○; Low: ⊕⊕○○; Very low: ⊕○○○; *Factors of decreasing quality of evidence: Risk of Bias, Inconsistency, Indirectness, Imprecision, and Publication bias.

CINV: Chemotherapy-induced nausea and vomiting; PONV: Postoperative nausea and vomiting; POV: Postoperative vomiting; NSAID: Nonsteroidal anti-inflammatory drug; LDL-C: Low density lipoprotein cholesterol; HDL-C: High density lipoprotein cholesterol; FBG: Fasting blood-glucose; HbA1c: Glycosylated hemoglobin; HOMA-IR: homeostasis model assessment-insulin resistance index; NVP: Nausea and vomiting of pregnancy.

3.2.5. Ginger for other conditions

One review³⁵ assessed the effect on ginger for platelet aggregation. However, meta-analysis wasn't available due to the heterogeneity of included studies. The qualitative synthesis demonstrated it was equivocal that ginger affect platelet aggregation and coagulation.

3.3. Quality of included SRs

The quality of SRs was heterogeneous. The quality assessment results using AMSTAR-2 were given in Table 4. All of SRs (27, 100%) complied with the Item 1 ("research questions included the components of PICO") and Item 3 ("explained selection of the study designs for inclusion"). Eighteen SRs (66.7%) reported the potential sources of conflict of interest (Item 16). Fourteen SRs (51.9%) was performed study selection (Item 5) in duplicate. Thirteen SRs (48.1%) reported data extraction (Item 6) was performed in duplicate. Only one SR (3.7%) described the sources of funding for the studies included (Item 10). Seven SRs (25.7%) provided registration information (Item 2). Twenty-two SRs (81.5%) did not provide a list of excluded studies and

justify the exclusions (Item 7). The GRADE system was used to classify the evidence quality of the included sixteen SRs that conducted meta-analysis. Forty-four outcomes were evaluated and 14 (31.8%) outcomes were evaluated moderate quality (Table 3).

4. Discussion

Many reviews have been published on ginger effects and there is no systematic overview in the literature, which simultaneously covers all these of condition. In this overview, we identify 27 SRs published from 2000 to 2018. The number of SRs is raising with time. This indicates that the scientific interest on this therapy is increasing. The condition with the most included SRs is nausea and vomiting (12/27, 44.4%). The newest research hot is metabolic syndrome, which four SRs are published in 2018. The top three countries with the highest number of SRs published are Australia (5/27, 18.5%), China (4/27, 14.8%) and Iran (4/27, 14.8%). The majority of SRs show a promising efficacy of ginger, including for nausea and vomiting, metabolic syndrome and pain, while ginger for platelet aggregation fail to draw a certain conclusion.

Table 4
The quality assessment results of SRs included using the AMSTAR 2 tool.

Studies	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Item 12	Item 13	Item 14	Item 15	Item 16	Overall rating
Bartels E 2015 ¹⁵	Y	Y	Y	PY	Y	Y	N	Y	Y	N	Y	Y	Y	Y	N	Y	CL
Borrelli F 2005 ²¹	Y	N	Y	PY	Y	Y	N	Y	PY	N	NM	NM	Y	N	NM	N	CL
Chaiyakunapruk 2006 ²²	Y	N	Y	PY	N	Y	Y	Y	PY	N	Y	N	N	Y	N	N	CL
Chang WP 2018 ²³	Y	N	Y	PY	N	N	N	PY	Y	N	Y	N	N	Y	Y	Y	CL
Chen CX 2016 ²⁴	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	N	Y	CL
Daily JW 2015 ²⁵	Y	N	Y	PY	Y	Y	Y	Y	Y	N	Y	N	Y	N	Y	Y	L
Ding M 2013 ²⁷	Y	N	Y	PY	N	N	N	PY	N	N	NM	NM	N	N	NM	N	CL
Ding M 2013 ²⁶	Y	N	Y	PY	N	N	N	Y	PY	N	NM	NM	Y	N	NM	N	CL
Ebrahimzadeh 2018 ²⁰	Y	N	Y	PY	Y	Y	N	Y	Y	N	NM	NM	Y	N	NM	Y	CL
Ernst E 2000 ²⁸	Y	N	Y	PY	Y	Y	N	Y	PY	N	NM	NM	N	N	NM	N	CL
Jafarnejad S 2017 ³⁰	Y	N	Y	PY	N	Y	Y	PY	PY	N	Y	Y	Y	Y	Y	N	L
Jugran A 2018 ³¹	Y	N	Y	PY	Y	Y	N	PY	Y	N	Y	N	N	N	Y	Y	CL
Lakhan S 2015 ³²	Y	N	Y	PY	N	N	N	PY	N	N	Y	N	N	Y	Y	Y	CL
Leach M 2008 ³³	Y	N	Y	PY	Y	N	Y	Y	PY	N	NM	NM	Y	Y	NM	N	L
Lee J 2013 ³⁴	Y	N	Y	PY	N	N	N	PY	PY	N	Y	Y	Y	Y	N	N	CL
Marx W 2015 ³⁵	Y	N	Y	PY	N	N	N	Y	Y	N	NM	NM	N	N	NM	Y	CL
Marx W 2013 ³⁶	Y	N	Y	PY	N	N	N	PY	PY	N	NM	NM	Y	N	NM	Y	CL
Mazidi M 2016 ³⁷	Y	Y	Y	PY	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	M
Pourmasoumi 2018 ³⁸	Y	Y	Y	PY	Y	N	Y	Y	PY	N	Y	Y	N	Y	Y	Y	L
Stanisiere J 2018 ³⁹	Y	N	Y	N	N	N	N	N	N	N	NM	NM	N	N	NM	Y	CL
Terry R 2011 ⁴⁰	Y	N	Y	PY	N	Y	N	Y	PY	N	NM	NM	Y	N	NM	Y	CL
Thomson 2014 ⁴¹	Y	N	Y	PY	Y	N	N	Y	Y	N	Y	N	N	Y	N	Y	CL
Tóth B 2018 ⁴²	Y	Y	Y	PY	Y	Y	Y	PY	Y	N	Y	Y	Y	Y	Y	Y	M
Viljoen E 2014 ⁴³	Y	Y	Y	PY	Y	N	N	Y	Y	N	Y	Y	N	Y	N	Y	CL
Wilson P 2015 ⁴⁴	Y	N	Y	N	N	N	N	Y	N	N	NM	NM	N	N	NM	Y	CL
Zhang G 2015 ²⁹	Y	N	Y	PY	N	N	N	PY	PY	N	Y	N	Y	Y	Y	N	CL
Zhu J 2018 ⁴⁵	Y	Y	Y	PY	Y	Y	N	Y	Y	N	Y	N	Y	Y	Y	Y	L

*Y: yes; N: no; PY: partial Y; NM: N meta-analysis; CL: Critically low; L: Low; M: Moderate; H: High.

Item 1: Did the research questions and inclusion criteria for the review include the components of PICO?; Item 2: Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?; Item 3: Did the review authors explain their selection of the study designs for inclusion in the review?; Item 4: Did the review authors use a comprehensive literature search strategy?; Item 5: Did the review authors perform study selection in duplicate?; Item 6: Did the review authors perform data extraction in duplicate?; Item 7: Did the review authors provide a list of excluded studies and justify the exclusions?; Item 8: Did the review authors describe the included studies in adequate detail?; Item 9: Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?; Item 10: Did the review authors report on the sources of funding for the studies included in the review?; Item 11: If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?; Item 12: If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?; Item 13: Did the review authors account for RoB in individual studies when interpreting/discussing the results of the review?; Item 14: Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?; Item 15: If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?; Item 16: Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?.

The quality of included SRs was needed to improve. The key factors affecting the quality of the literature include item 2 (“explicit statement that the review methods were established prior to the conduct of the review”), item 7 (“providing a list of excluded studies and justify the exclusions”) and item 10 (“reporting on the sources of funding for the studies included in the review”). Thus, it is suggested that future studies should comply with the AMSTAR 2 to improve the methodology quality of SRs, especially focusing on these three items.^{46–48} Besides, the results of the evidence grade evaluation using the GRADE methods indicated the current quality of evidence was not satisfying and still needed to improved.^{49–51}

In this overview, five SRs^{27,33–35,40} did not conclude positive findings. Of them, four SRs^{27,33,34,40} were published before in 2013, which meaning the available evidence may be lacking during that period. Instead, some later SRs drew a positive result about the efficacy of ginger, likely nausea and vomiting, metabolic syndrome and pain. The adverse events with the use of ginger as an intervention were scarcely reported. Most of them did not come to a definite conclusion.

Few included SRs demonstrated the types of ginger. However,

chemistries of different forms ginger are not the same and some of the indications are slightly different, which might affect the treatment effect. It is suggested that the type of ginger should be reported specifically both in the original studies and systematic reviews. There were eleven SRs conducted qualitative analysis. Most stated that due to considerably clinical discrepancy and methodological heterogeneity, meta-analysis could not be conducted. Among studies, different types of ginger were used, such as ginger extract, dry ginger, ginger powder, or ginger capsule. The treatment dose and duration of ginger among studies were also various. Moreover, most trials studied the effect of ginger compared with placebo, while it was still unknown whether ginger could be an alternative therapy to routine drugs.

Regarding the mechanism of action, some studies had been reported. One review by Wolfgang Marx et al⁵² outlined proposed mechanisms of ginger in CINV and stated ginger contained a wide array of bioactive compounds that could potentially act on multiple pathways involved in the physiology of CINV. The possible pathways included the modulation of relevant neuropeptides, vasopressin release, and gastrointestinal motility as well as redox and anti-inflammatory signaling.

Yogeshwar Shukla et al.⁵³ reviewed relevant laboratory, animal and in vitro studies that explored the anticancer effect of ginger, and provided substantial evidences that ginger and its organic pungent vallinoid compounds were effective inhibitors of the carcinogenic process. Review by Attari V E²⁰ summarized potential possible mechanisms of the anti-obesity action of ginger, including increasing thermogenesis and energy expenditure, increasing lipolysis, suppression of lipogenesis and lipid accumulation, inhibition of intestinal absorption of dietary fat and controlling appetite.

There were several limitations. Firstly, we tried to collect all relevant eligible articles as far as possible and eight databases were searched. But there were still other databases were not been searched and non-English and non-Chinese language articles were not included. Secondly, our overview did not retrieve individual RCTs and primary information from RCTs were not collected. Thirdly, the quality was evaluated by two trained reviewers, but there still existed some discrepancies. Moreover, this study failed to preregister and protocol was not published in advance.

5. Conclusions

Our overview indicates ginger is a promising herbal medicine for health care, which is beneficial for nausea and vomiting, metabolic syndrome and pain. However, considering the limited quality of included evidence and heterogeneity of different clinical trials, more well-design studies are required to confirm the conclusion further. We recommend that future SRs comply with the AMSTAR 2 as possible as to improve the quality of SRs. Future studies should focus on intensity and treatment duration of ginger therapy and pay more attention to adverse effects. Moreover, the mechanism studies of ginger active are need to help researchers and clinical professionals to understand the mode of functional.

Authors' contributions

The authors contributed the following: Kehu Yang and Xingrong Liu: developed review protocol. Huijuan Li: developed, edited and critically reviewed the manuscript. Meixuan Li and Liang Yao: conducted selected articles, data extraction, quality assessment of included SRs. Peijing Yan and Dan Luo: designing the review methodology. Yuzhen Ma and Jie Zhang: critically reviewed the manuscript.

Competing interests

None declared.

Provenance and peer review

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Transparency document

The [Transparency document](#) associated with this article can be found in the online version.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.ctim.2019.06.002>.

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