

Table S1. PRISMA checklist.

| Section/topic                      | #  | Checklist item  | Reported<br>on page # |
|------------------------------------|----|---|-----------------------|
| TITLE                              | •  |   |                       |
| Title                              | 1  | Identify the report as a systematic review, meta-analysis, or both.   | 1                     |
| ABSTRACT                           |    |   |                       |
| Structured summary                 | 2  | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 1                     |
| INTRODUCTION                       |    |   |                       |
| Rationale                          | 3  | Describe the rationale for the review in the context of what is already known.  | 1-2                   |
| Objectives                         | 4  | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).  | 2                     |
| METHODS                            |    |   |                       |
| Protocol and registration          | 5  | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.   | N/A                   |
| Eligibility criteria               | 6  | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.  | 2                     |
| Information sources                | 7  | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.  | 2                     |
| Search                             | 8  | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.   | 2                     |
| Study selection                    | 9  | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).   | 2                     |
| Data collection process            | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.  | 3                     |
| Data items                         | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.   | 3                     |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.  | N/A                   |
| Summary measures                   | 13 | State the principal summary measures (e.g., risk ratio, difference in means).   | N/A                   |
| Synthesis of results               | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I <sup>2</sup> ) for each meta-analysis.  | N/A                   |



## PRISMA 2009 Checklist

| Section/topic                 | #        | Checklist item   | Reported<br>on page # |
|-------------------------------|----------|--|-----------------------|
| Risk of bias across studies   | 15       | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).   | 3                     |
| Additional analyses           | 16       | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.   | N/A                   |
| RESULTS                       | ·        |  |                       |
| Study selection               | 17       | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.  | 3                     |
| Study characteristics         | 18       | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.   | 4-13                  |
| Risk of bias within studies   | 19       | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).  | N/A                   |
| Results of individual studies | 20       | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | 14-22                 |
| Synthesis of results          | 21       | Present results of each meta-analysis done, including confidence intervals and measures of consistency.  | N/A                   |
| Risk of bias across studies   | 22       | Present results of any assessment of risk of bias across studies (see Item 15).  | 22-23                 |
| Additional analysis           | 23       | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).  | N/A                   |
| DISCUSSION                    | <u> </u> |  |                       |
| Summary of evidence           | 24       | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).                     | 23-25                 |
| Limitations                   | 25       | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).  | 23-25                 |
| Conclusions                   | 26       | Provide a general interpretation of the results in the context of other evidence, and implications for future research.  | 25-26                 |
| FUNDING                       | I        |  |                       |
| Funding                       | 27       | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.   | 26                    |

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.

| Author<br>(vear)                               | Author Cohort<br>(year) allocation |  | Type of<br>disease/symptom                      |        | Inter | vention   |        | Comp  | arator  | Duration  | Blind            |
|--|------------------------------------|--|---|--------|-------|---|--------|-------|---|---|------------------|
| (),  |                                    |  |   | Number | M/F   | Dosage  | Number | M/F   | Dosage  | _   |                  |
| Bossi <i>et al.</i><br>(2017) [1]              | Italy                              | Randomized<br>controlled<br>trial              | Chemotherapy-<br>induced nausea<br>and vomiting | 121    | 83/38 | 40 mg of ginger<br>extract/cap, 4<br>capsules/day, bid                            | 123    | 77/46 | 4 placebo<br>capsules/day, bid                                | 42 to 56 days   | Double-<br>blind |
| Konmun <i>et</i><br>al. (2017) [2]             | Thailand                           | Randomized<br>controlled<br>trial              | Chemotherapy-<br>induced nausea<br>and vomiting | 40     | 4/36  | 5 mg of 6-gingerol<br>(1.4% w/w of ginger<br>extract)/cap, 4<br>capsules/day, bid | 41     | 2/39  | Capsule containing<br>diluents/binder, 4<br>capsules/day, bid | 12 weeks  | Double-<br>blind |
| Zeraati <i>et al.</i><br>(2016) [3]            | Iran                               | Randomized<br>controlled<br>trial              | Postoperative<br>nausea and<br>vomiting         | 46     | 0/46  | 25 drops of ginger<br>extract in 30 mL of<br>water                                | 46     | 0/46  | 30 mL of water  | 1 h before<br>surgery   | Double-<br>blind |
| Rad <i>et al.</i><br>(2018) [4]                | Iran                               | Crossover<br>randomized<br>controlled<br>trial | Primary<br>dysmenorrhea                         | 168    | 0/168 | 200 mg of powdered<br>ginger/cap, 4<br>capsules/day                               | 168    | 0/168 | 800 mg of<br>ibuprofen/cap, 4<br>capsules/day                 | Two<br>consecutive<br>cycles (at the<br>onset of pain)                                | Double-<br>blind |
| Shirvani <i>et</i><br><i>al.</i><br>(2017) [5] | Iran                               | Randomized<br>controlled<br>trial              | Primary<br>dysmenorrhea                         | 61     | 0/61  | 250 mg of powdered<br>ginger capsule  | 61     | 0/61  | Exercise  | 8 weeks (at the<br>onset of<br>menstruation<br>and every 6 h<br>until pain<br>relief) | Open-<br>label   |
| Mashak <i>et al.</i><br>(2018) [6]             | Iran                               | Randomized<br>controlled<br>trial              | Post-spinal<br>puncture<br>headache             | 80     | 0/80  | 250 mg of powdered<br>ginger/cap, 3<br>capsules/dose                              | 80     | 0/80  | No intervention   | Single-dose (24<br>h before the C-<br>section)  | Open-<br>label   |
| Hashemi <i>et</i><br><i>al.</i><br>(2019) [7]  | Iran                               | Randomized<br>controlled<br>trial              | Low back pain                                   | 40     | N/A   | Dose N/A (Ginger)   | 40     | N/A   | Dose N/A (Control)  | N/A   | Single-<br>blind |
|  | Iran                               | Randomized<br>controlled<br>trial              | Low back pain                                   | 40     | N/A   | Dose N/A (Ginger)   | 40     | N/A   | Dose N/A (vitamin<br>D)                                       | N/A   | Single-<br>blind |

Table S2. Study design and demographic description of the included studies with a quality score less than 10.

| Hasanvand<br><i>et al.</i><br>(2018) [8] | Iran | Randomized<br>controlled<br>trial | Chest pain by<br>percutaneous<br>transluminal<br>coronary<br>angioplasty                   | 17 | 9/8   | 250 mg of powdered<br>ginger/cap, 1<br>capsule/day          | 17 | 13/4  | 250 mg of<br>starch/cap, 1<br>capsule/day            | 7 days from 10<br>days before<br>angioplasty | Double-<br>blind |
|--|------|-----------------------------------|--|----|-------|---|----|-------|--|--|------------------|
| Azimi <i>et al.</i><br>(2016) [9]        | Iran | Randomized<br>controlled<br>trial | Type 2 diabetes<br>mellitus  | 41 | 15/26 | 3 g of powdered<br>ginger + black tea,<br>three times a day | 40 | 16/24 | 3 g of cinnamon +<br>black tea, three<br>times a day | 8 weeks                                      | Single-<br>blind |
|  | Iran | Randomized<br>controlled<br>trial | Type 2 diabetes<br>mellitus  | 41 | 15/26 | 3 g of powdered<br>ginger + black tea,<br>three times a day | 42 | 17/25 | 3 g of cardamom +<br>black tea, three<br>times a day | 8 weeks                                      | Single-<br>blind |
|  | Iran | Randomized<br>controlled<br>trial | Type 2 diabetes<br>mellitus  | 41 | 15/26 | 3 g of powdered<br>ginger + black tea,<br>three times a day | 42 | 16/26 | 1 g of saffron + black<br>tea, three times a<br>day  | 8 weeks                                      | Single-<br>blind |
|  | Iran | Randomized<br>controlled<br>trial | Type 2 diabetes<br>mellitus  | 41 | 15/26 | 3 g of powdered<br>ginger + black tea,<br>three times a day | 39 | 15/24 | Black tea, three<br>times a day                      | 8 weeks                                      | Single-<br>blind |
| bhidfar <i>et al.</i><br>(2015) [10]     | Iran | Randomized<br>controlled<br>trial | Type 2 diabetes<br>mellitus  | 22 | N/A   | 1 g of powdered<br>ginger/cap, 3<br>capsules/day            | 23 | N/A   | 1 g of lactose/cap, 3<br>capsules/day                | 3 months                                     | Double<br>blind  |
| Гаbibi <i>et al.</i><br>(2015) [11]      | Iran | Randomized<br>controlled<br>trial | Serum lipids and<br>lipoproteins levels<br>in peritoneal<br>dialysis patients<br>Metabolic | 18 | 11/7  | 250 mg of ginger/cap,<br>4 capsules/day                     | 18 | 10/8  | 250 mg of<br>starch/cap, 4<br>capsules/day           | 10 weeks                                     | Double<br>blind  |
| Karimi <i>et al.</i><br>(2015) [12]      | Iran | Randomized<br>controlled<br>trial | syndrome and<br>pro-inflammatory<br>markers of obese<br>women who have<br>diagnosed with   | 10 | 0/10  | 750 mg of powdered<br>ginger/cap, 4<br>capsules/day         | 10 | 0/10  | 1 g of starch/cap, 4<br>capsules/day                 | 7 days a week<br>and for 6<br>weeks.         | N/A              |
|  | Iran | Randomized<br>controlled<br>trial | breast neoplasms<br>Metabolic<br>syndrome and<br>pro-inflammatory                          | 10 | 0/10  | 750 mg of powdered<br>ginger/cap, 4                         | 10 | 0/10  | Exercise   | 6 weeks and 4<br>sessions at a<br>week       | N/A              |

|  |          |  | markers of obese<br>women who have<br>diagnosed with<br>breast neoplasms  |    |      | capsules/day +<br>exercise  |    |       |  |  |                  |
|--|----------|--|---|----|------|---|----|-------|--|--|------------------|
| Emrani <i>et al.</i><br>(2016) [13]              | Iran     | Randomized<br>controlled<br>trial              | Antituberculosis-<br>induced<br>gastrointestinal<br>adverse reactions   | 30 | 22/8 | 250 mg of powdered<br>ginger/cap, 2<br>capsules/day                       | 30 | 25/5  | 2 placebo<br>capsules/day                          | 4 weeks (at 30<br>min before<br>morning<br>antituberculosi<br>s medications) | Double-<br>blind |
| Kulkarni <i>et</i><br><i>al.</i><br>(2016) [14]  | India    | Randomized<br>controlled<br>trial              | Anti-<br>inflammatory and<br>antioxidant effect<br>in tuberculosis  | 34 | N/A  | 250 mg of ginger<br>extract/cap (1.5 g pure<br>powder), 2<br>capsules/day | 35 | N/A   | 250mg of starch/cap,<br>2 capsules/day             | 1 month  | N/A              |
| Miyamoto <i>et</i><br><i>al.</i><br>(2015) [15]  | Japan    | Crossover<br>randomized<br>controlled<br>trial | Thermoregulatory<br>function and fat<br>oxidation:<br>thermal balance,<br>T <sub>cor</sub> <sup>1</sup> , and blood<br>energy substrates<br>levels      | 5  | 5/0  | 250 mg of dried<br>ginger root<br>powder/cap, 4<br>capsules/dose          | 5  | 5/0   | 250 mg of<br>starch/cap, 4<br>capsules/dose        | Single dose  | N/A              |
|  | Japan    | Crossover<br>randomized<br>controlled<br>trial | Thermoregulatory<br>function and fat<br>oxidation:<br>threshold T <sub>cor</sub> <sup>1</sup><br>for skBF <sup>2</sup> and m <sub>sw</sub> <sup>3</sup> | 4  | 4/0  | 250 mg of dried<br>ginger root<br>powder/cap, 4<br>capsules/dose          | 4  | 4/0   | 250 mg of<br>starch/cap, 4<br>capsules/dose        | Single dose  | N/A              |
| Manusirivith<br>aya <i>et al.</i><br>(2004) [16] | Thailand | Crossover<br>randomized<br>controlled<br>trial | Chemotherapy-<br>induced nausea<br>and vomiting   | 43 | N/A  | 1 g of powdered<br>ginger root/day  | 43 | N/A   | Placebo (acute) and<br>metoclopramide<br>(delayed) | 5 days per<br>chemotherapy<br>cycle <sup>4</sup>                             | Double-<br>blind |
| Pillai <i>et al.</i><br>(2011) [17]              | India    | Randomized<br>controlled<br>trial              | Chemotherapy-<br>induced nausea<br>and vomiting   | 27 | N/A  | 1000 mg or 2000 mg<br>of powdered<br>ginger/day <sup>5</sup>              | 30 | 16/14 | 1000 mg and 2000<br>mg of starch<br>powder/day     | Day 1 to day 3<br>of<br>chemotherapy<br>cycle                                | Double-<br>blind |

| Panahi <i>et al.</i><br>(2012) [18]             | Iran   | Randomized<br>open-label<br>controlled<br>trial | Chemotherapy-<br>induced nausea<br>and vomiting | 37 | 0/37  | 500 mg of powdered<br>ginger and standard<br>antiemetic regimen <sup>6</sup>  | 41 | 0/41  | Standard antiemetic<br>regimen   | 4 days from<br>initiation of<br>chemotherapy             | Open-<br>label   |
|---|--------|---|---|----|-------|---|----|-------|--|--|------------------|
| Sontakke <i>et</i><br><i>al.</i><br>(2002) [19] | India  | Crossover<br>randomized<br>controlled<br>trial  | Chemotherapy-<br>induced nausea<br>and vomiting | 50 | 11/39 | 500 mg of powdered<br>ginger/cap, 2 ginger<br>capsules + 2 mL of<br>normal saline (i.v.) 20<br>min before<br>chemotherapy + 2<br>ginger capsules after<br>6 h | 50 | 11/39 | 2 lactulose capsules<br>+ metoclopramide<br>20 mg (i.v.) 20 min<br>before<br>chemotherapy + 2<br>capsules of 5 mg of<br>metoclopramide/cap | 3 cycle (21<br>days of<br>interval<br>between<br>cycles) | Double-<br>blind |
|   | India  | Crossover<br>randomized<br>controlled<br>trial  | Chemotherapy-<br>induced nausea<br>and vomiting | 50 | 11/39 | 500 mg of powdered<br>ginger/cap, 2 ginger<br>capsules + 2 mL of<br>normal saline (i.v.) 20<br>min before<br>chemotherapy + 2<br>ginger capsules after<br>6 h | 50 | 11/39 | 2 lactulose capsules<br>+ ondansetron 4 mg<br>(i.v.) 20 min before<br>chemotherapy + 2<br>capsules of 2 mg of<br>ondansetron/cap           | 3 cycle (21<br>days of<br>interval<br>between<br>cycles) | Double-<br>blind |
| Arslan <i>et al.</i><br>(2014) [20]             | Turkey | Randomized<br>controlled<br>trial               | Chemotherapy-<br>induced nausea<br>and vomiting | 30 | 30/0  | 500 mg of powdered<br>ginger mixed in<br>yogurt, twice/day  | 30 | 30/0  | No intervention  | 3 days   | Open<br>label    |
| Mohammad<br>beigi <i>et al.</i><br>(2011) [21]  | Iraq   | Randomized<br>controlled<br>trial               | Nausea and<br>vomiting of<br>pregnancy          | 34 | 0/34  | 200 mg of ginger<br>essence/cap, 3<br>capsules/day  | 34 | 0/34  | 10 mg of<br>metoclopramide/cap<br>, 3 capsules/day   | 5 days   | Double-<br>blind |
|   | Iraq   | Randomized<br>controlled<br>trial               | Nausea and<br>vomiting of<br>pregnancy          | 34 | 0/34  | 200 mg of ginger<br>essence/cap, 3<br>capsules/day  | 34 | 0/34  | 200 mg of flour/cap,<br>3 capsules/day   | 5 days   | Double-<br>blind |
| Ozgoli <i>et al.</i><br>(2009) [22]             | Iran   | Randomized<br>controlled<br>trial               | Nausea and<br>vomiting of<br>pregnancy          | 32 | 0/32  | 250 mg of powdered<br>ginger root/cap, 4<br>capsules/day  | 35 | 0/35  | 250 mg of<br>lactose/cap, 4<br>capsules/day  | 4 days   | Single-<br>blind |

| Keating et al.<br>(2002) [23]                   | United<br>States | Randomized<br>controlled<br>trial | Nausea and<br>vomiting of<br>pregnancy  | 13                         | 0/13  | 1 tablespoon of<br>commercially<br>prepared study syrup<br>(250 mg of ginger<br>with honey, water), 4<br>times daily | 11                          | 0/11  | 1 tablespoon of<br>commercially<br>prepared placebo<br>syrup (honey,<br>lemon oil, water), 4<br>times daily | 2 weeks   | Double-<br>blind |
|---|------------------|-----------------------------------|---|----------------------------|-------|--|-----------------------------|-------|---|---|------------------|
| Pongrojpaw<br><i>et al.</i><br>(2007) [24]      | Thailand         | Randomized<br>controlled<br>trial | Nausea and<br>vomiting of<br>pregnancy  | 85                         | 0/85  | 500 mg of powdered<br>ginger/cap, 2<br>capsules/day, bid   | 85                          | 0/85  | 50 mg of<br>dimenhydrinate/cap<br>, 2 capsules/day, bid   | 1 week  | Double-<br>blind |
| Saberi <i>et al.</i><br>(2013) [25]             | Iran             | Randomized<br>controlled<br>trial | Nausea and<br>vomiting of<br>pregnancy  | 37                         | 0/37  | 250 mg of powdered<br>ginger/cap, 3<br>capsules/day  | 36                          | 0/36  | 3 lactose<br>capsules/day<br>(Placebo)  | 4 days  | N/A              |
|   | Iran             | Randomized<br>controlled<br>trial | Nausea and<br>vomiting of<br>pregnancy  | 37                         | 0/37  | 250 mg of powdered<br>ginger/cap, 3<br>capsules/day  | 33                          | 0/33  | No intervention<br>(Control)  | 4 days  | N/A              |
| Javadi <i>et al.</i><br>(2013) [26]             | Iran             | Randomized<br>controlled<br>trial | Nausea and<br>vomiting of<br>pregnancy  | 47                         | 0/47  | 250 mg of powdered<br>ginger/cap, 4<br>capsules/day  | 48                          | 0/48  | 40 mg of vitamin<br>B6/tab, 2 tablets/day   | 4 days  | N/A              |
| Apariman <i>et</i><br><i>al.</i><br>(2006) [27] | Thailand         | Randomized<br>controlled<br>trial | Postoperative<br>nausea and<br>vomiting | 30                         | N/A   | 500 mg of powdered<br>ginger/cap, 3<br>capsules/day  | 30                          | N/A   | 3 capsules of placebo/day   | 1 h prior to the operation  | N/A              |
| Nanthakom<br>on <i>et al.</i><br>(2006) [28]    | Thailand         | Randomized<br>controlled<br>trial | Postoperative<br>nausea and<br>vomiting | 60                         | N/A   | 500 mg of powdered<br>ginger/cap, 2<br>capsules/dose   | 60                          | N/A   | 500 mg of<br>lactose/cap, 2<br>capsules/dose  | Single-dose<br>(one hour<br>before the<br>surgery)                          | Double-<br>blind |
| Kalava et al.<br>(2013) [29]                    | United<br>States | Randomized<br>controlled<br>trial | Postoperative<br>nausea and<br>vomiting | 116                        | 0/116 | 1 g of powdered<br>ginger/cap, 1<br>capsule/dose   | 123                         | 0/123 | 1 g of placebo/cap, 1<br>capsule/dose   | 30 min before<br>induction of<br>anesthesia and<br>2 hours after<br>surgery | Double-<br>blind |
| Visalyaputra<br><i>et al.</i><br>(1997) [30]    | Thailand         | Randomized<br>controlled<br>trial | Postoperative<br>nausea and<br>vomiting | Group 3<br>(ginger):<br>27 | 0/27  | 500 mg of ginger<br>root/cap, 2<br>capsules/dose + 0.5   | Group 1<br>(placebo):<br>28 | 0/28  | 500 mg of dried rice<br>starch/cap, 2<br>capsules/dose + 0.5  | 1 h before<br>induction of<br>anesthesia and                                | Triple-<br>blind |

|  |                   |                                   |   |  |       | mL of normal saline<br>(i.v.)   |                                 |       | mL of normal saline<br>(i.v.)   | 30 min before<br>discharge  |                  |
|--|-------------------|-----------------------------------|---|--|-------|---|---------------------------------|-------|---|---|------------------|
|  | Thailand          | Randomized<br>controlled<br>trial | Postoperative<br>nausea and<br>vomiting           | Group 4<br>(droperi<br>dol +<br>ginger):<br>27 | 0/27  | 500 mg of ginger<br>root/cap, 2<br>capsules/dose + 1.25<br>mg of droperidol in<br>0.5 mL of normal<br>saline (i.v.) | Group 2<br>(droperid<br>ol): 29 | 0/29  | 500 mg of rice<br>starch/cap, 2<br>capsules/dose + 1.25<br>mg of droperidol in<br>0.5 mL of normal<br>saline (i.v.) | 1 h before<br>induction of<br>anesthesia and<br>30 min before<br>discharge  | Triple-<br>blind |
| Phillips <i>et al.</i><br>(1993) [31]        | United<br>Kingdom | Randomized<br>controlled<br>trial | Postoperative<br>nausea and<br>vomiting           | 40   | 0/40  | 1 g of powdered<br>ginger root in 2<br>capsules   | 40                              | 0/40  | 5 mg of<br>metoclopramide/cap<br>, 2 capsules/dose  | Single-dose   | Double-<br>blind |
|  | United<br>Kingdom | Randomized<br>controlled<br>trial | Postoperative<br>nausea and<br>vomiting           | 40   | 0/40  | 1 g of powdered<br>ginger root in 2<br>capsules   | 40                              | 0/40  | 1 g of lactose in 2<br>capsules   | Single-dose   | Double-<br>blind |
| Bone <i>et al.</i><br>(1990) [32]            | United<br>Kingdom | Randomized<br>controlled<br>trial | Postoperative<br>nausea and<br>vomiting           | 20   | 0/20  | 500 mg of powdered<br>ginger root/cap and<br>injection of 2 mL of<br>sterile water                                  | 20                              | 0/20  | 500 mg of<br>lactulose/cap and<br>injection of 2 mL of<br>sterile water   | Single-dose   | Double-<br>blind |
|  | United<br>Kingdom | Randomized<br>controlled<br>trial | Postoperative<br>nausea and<br>vomiting           | 20   | 0/20  | 500 mg of powdered<br>ginger root/cap and<br>injection of 2 mL of<br>sterile water                                  | 20                              | 0/20  | 500 mg of<br>lactulose/cap and<br>injection of 10 mg of<br>metoclopramide   | Single-dose   | Double-<br>blind |
| Tavlan <i>et al.</i><br>(2006) [33]          | Turkey            | Randomized<br>controlled<br>trial | Postoperative<br>nausea and<br>vomiting           | 60   | 6/54  | Dexamethasone 150<br>μg/kg (i.v.) + 0.5 g of<br>ginger + 10 mg of oral<br>diazepam                                  | 60                              | 8/52  | Dexamethasone 150<br>μg/kg (i.v.) +<br>placebo + 10 mg of<br>oral diazepam  | Dexamethason<br>e: before the<br>induction of<br>anesthesia<br>Ginger,<br>placebo and<br>diazepam: 1 h<br>prior to<br>surgery | Double-<br>blind |
| Dabaghzade<br>h <i>et al.</i><br>(2014) [34] | Iran              | Randomized<br>controlled<br>trial | Antiretroviral-<br>induced nausea<br>and vomiting | 51   | 36/15 | 250 mg of powdered<br>ginger/cap, 4<br>capsules/day, bid  | 51                              | 34/17 | 250 mg of<br>starch/cap, 4<br>capsules/day, bid   | 14 days   | Double-<br>blind |

| Holtmann <i>et</i><br><i>al.</i><br>(1989) [35] | Germany          | Randomized<br>controlled<br>trial              | Emesis                   | 38  | 18/20    | One capsule<br>containing 1000 mg of<br>powdered ginger root   | 38   | 18/20  | One capsule<br>containing 100 mg<br>of dimenhydrinate  | N/A  | Double-<br>blind |
|---|------------------|--|--------------------------|---|----------|--|--|--|--|--|------------------|
| (1707) [33]                                     | Germany          | Randomized<br>controlled<br>trial              | Emesis                   | 38  | 18/20    | One capsule<br>containing 1000 mg of<br>powdered ginger root   | 38   | 18/20  | One capsule<br>containing lactose  | N/A  | Double-<br>blind |
| Grontved <i>et</i><br><i>al.</i><br>(1988) [36] | Denmark          | Randomized<br>controlled<br>trial              | Seasickness              | 40  | N/A      | 1 g of powdered ginger root  | 39   | N/A  | 1 g of lactose   | Single-dose  | Double-<br>blind |
| Grontved <i>et</i><br><i>al.</i><br>(1985) [37] | Denmark          | Crossover<br>randomized<br>controlled<br>trial | Vertigo and<br>nystagmus | 8   | N/A      | 1 g of powdered<br>ginger root/cap, 1<br>capsule/dose  | 8  | N/A  | 1 g of lactose/cap, 1<br>capsule/dose  | Single-dose  | Double-<br>blind |
| Mowrey <i>et</i><br><i>al.</i><br>(1982) [38]   | United<br>States | Randomized<br>controlled<br>trial              | Motion sickness          | 12  | 6/6      | 2 capsules of 940 mg<br>of powdered ginger   | Group 1:<br>12<br>Group 2:<br>12                   | Group 1:<br>6/6<br>Group 2:<br>6/6                           | Group 1: 100 mg of<br>dimenhydrinate<br>Group 2: 2<br>capsules of<br>powdered<br>chickweed herb<br>(placebo) | Single-dose  | N/A              |
| Stewart <i>et al.</i><br>(1990) [39]            | United<br>States | Randomized<br>controlled<br>trial              | Motion sickness          | Group<br>1: 8<br>Group<br>2: 8<br>Group<br>3: 8 | Group 1: | Group 1: 500 mg of<br>powdered ginger<br>Group 2: 1000 mg of<br>powdered ginger<br>Group 3: 1000 mg of<br>fresh ginger | Scopolami<br>ne group:<br>8<br>Control<br>group: 8 | Scopola<br>mine<br>group:<br>8/0<br>Control<br>group:<br>8/0 | Scopolamine group:<br>0.6 mg of<br>scopolamine<br>Control group:<br>lactose                                  | 1 h before the<br>test (ginger<br>and lactose)<br>and 30 min<br>before the test<br>(scopolamine) | N/A              |
| Jenabi <i>et al.</i><br>(2013) [40]             | Iran             | Randomized<br>controlled<br>trial              | Primary<br>dysmenorrhea  | 35  | 0/35     | 500 mg of powdered<br>ginger/cap, 3<br>capsules/day  | 34   | 0/34   | 3 capsules of<br>placebo/day   | First<br>menstruation<br>cycles for 3<br>days  | N/A              |
| Shirvani <i>et</i><br><i>al.</i> (2014)<br>[41] | Finland          | Randomized<br>controlled<br>trial              | Primary<br>dysmenorrhea  | 61  | 0/61     | 250 mg of powdered<br>ginger/cap, 4<br>capsules/day  | 61   | 0/61   | 250 mg of<br>mefenamic acid/cap,<br>3 capsules/day   | 2 cycles of<br>menstruation<br>(from the onset   | N/A              |

|   |                  |  |  |    |       |   |                             |                                    |  | of           |                  |
|---|------------------|--|--|----|-------|---|-----------------------------|------------------------------------|--|--------------|------------------|
|   |                  |  |  |    |       |   |                             |                                    |  | menstruation |                  |
|   |                  |  |  |    |       |   |                             |                                    |  | until pain   |                  |
|   |                  |  |  |    |       |   |                             |                                    |  | relief)      |                  |
| Black <i>et al.</i><br>(2008) [42]                            | United<br>States | Crossover<br>randomized<br>controlled<br>trial | Quadriceps<br>muscle pain<br>during moderate-<br>intensity cycling<br>exercise | 25 | 10/15 | Six capsules<br>containing 2 g of<br>ground ginger with<br>250 mL of water and 1<br>tablespoon of olive oil | 25                          | 10/15                              | Six capsules<br>containing 2 g of<br>placebo with 250<br>mL of water and 1<br>tablespoon of olive<br>oil             | Single-dose  | Double-<br>blind |
| Maghbooli <i>et</i><br><i>al.</i> (2014)<br>[43]              | Iran             | Randomized<br>controlled<br>trial              | Migraine   | 50 | 13/37 | 250 mg of powdered<br>ginger rhizome/cap, 1<br>capsule/onset of<br>migraine                                 | 50                          | 16/34                              | 50 mg powder of<br>sumatriptan/cap, 1<br>capsule/onset of<br>migraine  | Single-dose  | Double-<br>blind |
| Arablou <i>et</i><br><i>al.</i> (2013)<br>[44]                | Iran             | Randomized<br>controlled<br>trial              | Type 2 diabetes<br>mellitus  | 33 | 25/8  | 800 mg of powdered<br>ginger rhizome/cap, 2<br>capsules/day   | 30                          | 23/7                               | 800 mg of wheat<br>flour/cap, 2<br>capsules/day  | 12 weeks     | Double-<br>blind |
| Mozaffari-<br>Khosravi <i>et</i><br><i>al.</i> (2014)<br>[45] | Iran             | Randomized<br>controlled<br>trial              | Type 2 diabetes<br>mellitus  | 41 | 18/23 | 1 g of powdered<br>ginger/cap, 3<br>capsules/day  | 40                          | 13/27                              | 1 g of cellulose<br>microcrystalline/cap<br>, 3 capsules/day   | 8 weeks      | Double-<br>blind |
| Andallu <i>et</i><br><i>al.</i> (2001)<br>[46]                | India            | Randomized<br>controlled<br>trial              | Type 2 diabetes<br>mellitus  | 8  | 8/0   | 500 mg of powdered<br>ginger/cap, 2<br>capsules/day   | 8                           | 8/0                                | N/A (Control<br>group)   | 30 days      | N/A              |
|   | India            | Randomized<br>controlled<br>trial              | Hyperglycemia<br>and<br>hyperlipidemia   | 8  | 8/0   | 500 mg of powdered<br>ginger/cap, 2<br>capsules/day   | Group 1: 8<br>Group 2:<br>8 | Group 1:<br>8/0<br>Group 2:<br>8/0 | Group 1: 500 mg of<br>Ashwagandha/cap,<br>2 capsules/day<br>Group 2:<br>500 mg of<br>Mulberry/cap, 2<br>capsules/day | 30 days      | N/A              |
| Karimi <i>et al.</i><br>(2013) [47]                           | Iran             | Randomized<br>controlled<br>trial              | Obesity with breast cancer   | 10 | 0/10  | 750 mg of powdered<br>ginger rhizome/cap,<br>12 capsules/day, qid   | 10                          | 0/10                               | 1 g of starch<br>powder/cap, 12<br>capsules/day, qid   | 6 weeks      | Double-<br>blind |

|  | Iran   | Randomized<br>controlled<br>trial | Obesity with breast cancer  | 10  | 0/10  | 750 mg of powdered<br>ginger rhizome/cap,<br>12 capsules/day, qid<br>+Water-based exercise<br>program | 10  | 0/10  | 1 g of starch<br>powder/cap, 12<br>capsules/day, qid +<br>Water-based<br>exercise program | 6 weeks   | Double-<br>blind |
|--|--------|-----------------------------------|---|-----|-------|---|-----|-------|---|---|------------------|
| Atashak <i>et</i><br><i>al.</i> (2011)<br>[48]   | Iran   | Randomized<br>controlled<br>trial | Obesity-related<br>cardiovascular<br>risk   | 8   | 8/0   | 250 mg of powdered<br>ginger/cap, 4<br>capsules/day   | 8   | 8/0   | 250 mg of<br>maltodextrin/cap, 4<br>capsules/day  | 10 weeks  | Double-<br>blind |
|  | Iran   | Randomized<br>controlled<br>trial | Obesity-related<br>cardiovascular<br>risk   | 8   | 8/0   | 250 mg of powdered<br>ginger/cap, 4<br>capsules/day with<br>resistance training                       | 8   | 8/0   | 250 mg of<br>maltodextrin/cap, 4<br>capsules/day with<br>resistance training              | 10 weeks  | Double-<br>blind |
| Alizadeh-<br>Navaei <i>et al.</i><br>(2008) [49] | Iran   | Randomized<br>controlled<br>trial | Hyperlipidemia  | 45  | 16/29 | 500 mg of powdered<br>ginger rhizome/cap, 6<br>capsules/day, tid                                      | 40  | 18/22 | 500 mg of<br>lactose/cap, 6<br>capsules/day, tid  | 45 days   | Double-<br>blind |
|  | Iran   | Randomized<br>controlled<br>trial | Metabolic<br>syndrome and<br>pro-inflammatory<br>markers of obese<br>women who have<br>diagnosed with<br>breast neoplasms | 10  | 0/10  | 750 mg of powdered<br>ginger/cap, 4<br>capsules/day +<br>exercise                                     | 10  | 0/10  | Exercise  | 6 weeks and 4<br>sessions at a<br>week                | N/A              |
| Imani <i>et al.</i><br>(2014) [50]               | Iran   | Randomized<br>controlled<br>trial | Serum glucose,<br>advanced<br>glycation end<br>products, and<br>inflammation in<br>peritoneal dialysis<br>patients        | 18  | 11/7  | 250 mg of ginger/cap,<br>4 capsules/day   | 18  | 10/8  | 250 mg of<br>starch/cap, 4<br>capsules/day  | 10 weeks  | Double-<br>blind |
| Hu <i>et al.</i><br>(2011) [51]                  | Taiwan | Randomized<br>controlled<br>trial | Functional<br>dyspepsia   | N/A | N/A   | 400 mg of powdered<br>ginger root/cap, 3<br>capsules/day  | N/A | N/A   | Placebo (starch)  | Two<br>afternoons,<br>separated by<br>at least 7 days | Double-<br>blind |

| Wu et al.<br>(2007) [52]                       | Taiwan           | Randomized<br>controlled<br>trial              | Gastric emptying<br>and motility in<br>healthy human   | 12  | 12/0 | 400 mg of powdered<br>ginger root/cap, 3<br>capsules/day  | 12   | 12/0 | 400 mg of<br>starch/cap, 3<br>capsules/day   | Two<br>afternoons,<br>separated by<br>at least 7 days  | Doub!<br>blind                      |
|--|------------------|--|--|---|------|---|--|------|--|--|-------------------------------------|
| Lien <i>et al.</i><br>(2002) [53]              | United<br>States | Crossover<br>randomized<br>controlled<br>trial | Motion sickness<br>and gastric slow-<br>wave<br>dysrhythmias<br>induced by<br>circular vection   | 13  | N/A  | 1 or 2 g of ginger in<br>capsules   | 13   | N/A  | Placebo (starch) in<br>capsules  | Single-dose at<br>1 hour before<br>circular<br>vection   | Doub<br>blin                        |
|  | United<br>States | Crossover<br>randomized<br>controlled<br>trial | Vasopressin-<br>evoked gastric<br>dysrhythmias and<br>nausea   | 4   | N/A  | 2 g of ginger in<br>capsule before the<br>infusion of<br>vasopressin at 0.1 and<br>0.2 U/min iv for 30<br>min                         | 4  | N/A  | The infusion of<br>vasopressin at 0.1<br>and 0.2 U/min IV for<br>30 min                                | Two separate<br>days, at least 3<br>days apart, 1<br>hour before<br>the basal EGG<br>recording | Doub<br>blin                        |
| Shariatpana<br>hi <i>et al.</i><br>(2009) [54] | Iran             | Randomized<br>controlled<br>trial              | Delayed gastric<br>emptying,<br>developing<br>ventilator-<br>associated<br>pneumonia,<br>clinical outcomes<br>in adult<br>respiratory<br>distress syndrome | 16  | 8/8  | 120 mg of ginger<br>extract added to tube<br>feeding/day, tid   | 16   | 8/8  | 1 g of coconut oil<br>added to tube<br>feeding/day, tid  | 21 days  | Doub<br>blin<br>(nur<br>unbli<br>ed |
| Gonlachanvi<br>t <i>et al.</i><br>(2003) [55]  | United<br>States | Randomized<br>controlled<br>trial              | Hyperglycemia-<br>evoked gastric<br>dysrhythmias   | Hypergl<br>ycemic<br>clampin<br>g<br>studies:<br>14 | N/A  | Hyperglycemic<br>clamping studies:<br>500 mg of powdered<br>ginger root/cap, 2<br>capsules/dose + 20%<br>dextrose (i.v.) <sup>7</sup> | hyperglyc<br>emic<br>clamping<br>studies: 14 | N/A  | Hyperglycemic<br>clamping studies:<br>2 placebo<br>capsules/dose + 20%<br>dextrose (i.v.) <sup>7</sup> | Single-dose  | Dout<br>blin                        |

|   | United<br>States | Randomized<br>controlled<br>trial               | Hyperglycemia-<br>evoked gastric<br>dysrhythmias             | Prostagl<br>andin<br>E1<br>(misopr<br>ostol)stu<br>dies: 11 | N/A                                  | Prostaglandin E1<br>(misoprostol) studies:<br>500 mg of powdered<br>ginger root/cap, 2<br>capsules/dose + 400<br>μg of misoprostol   | prostaglan<br>din E1<br>(misopros<br>tol)studies<br>: 11 | N/A              | Prostaglandin E1<br>(misoprostol)<br>studies: 2 placebo<br>capsules/dose + 400<br>μg of misoprostol | Single dose | Double-<br>blind |
|---|------------------|---|--|---|--------------------------------------|--|--|------------------|---|-------------|------------------|
| Haghighi <i>et</i><br><i>al.</i> (2005)<br>[56] | Iran             | Randomized<br>controlled<br>trial               | Osteoarthritis   | 40  | 29/11                                | 15 mg of ginger<br>extract/cap, 2<br>capsules/day  | 40   | 28/12            | 15 mg of<br>lactose/cap, 2<br>capsules/day  | 1 month     | Double-<br>blind |
|   | Iran             | Randomized<br>controlled<br>trial               | Osteoarthritis   | 40  | 29/11                                | 15 mg of ginger<br>extract/tab, 2<br>tablets/day   | 40   | 32/8             | 400 mg of<br>ibuprofen/cap, 3<br>capsules/day   | 1 month     | Double-<br>blind |
| Paramdeep<br><i>et al.</i><br>(2013) [57]       | India            | Randomized<br>open-label<br>controlled<br>trial | Osteoarthritis of<br>knee                                    | Group<br>2: 20<br>Group<br>3: 20                            | Group 2:<br>8/12<br>Group 3:<br>6/14 | Group 2: A capsule of<br>750 mg of powdered<br>ginger and a capsule<br>of placebo, twice/day<br>Group 3: A capsule<br>of 750 mg powdered<br>ginger and a tablet of<br>50 mg of diclofenac, | Group 1:<br>20   | Group 1:<br>6/14 | Group 1: A capsule<br>of placebo and a<br>tablet of 50 mg of<br>diclofenac,<br>twice/day            | 12 weeks    | Open-<br>label   |
| Drozdov <i>et</i><br><i>al.</i> (2012)<br>[58]  | Russia           | Randomized<br>controlled<br>trial               | Osteoarthritis of<br>the knee or hips                        | 21  | 4/17                                 | twice/day<br>100 mg of ginger<br>extract <sup>8</sup> + 500 mg of<br>glucosamine/cap, 2<br>capsules/day  | 22   | 4/18             | 100 mg of<br>diclofenac/tab, 1<br>tablet/day with 1000<br>mg of glucosamine                         | 4 weeks     | N/A              |
| Bliddal <i>et al.</i><br>(2000) [59]            | Denmark          | Crossover<br>randomized<br>controlled<br>trial  | Clinical<br>dysfunction and<br>pain due to<br>osteoarthritis | 56  | 15/41                                | 170 mg of ginger<br>extract  | 56   | 15/41            | Placebo   | 3 weeks     | Double-<br>blind |
|   | Denmark          | Crossover<br>randomized<br>controlled<br>trial  | Clinical<br>dysfunction and<br>pain due to<br>osteoarthritis | 56  | 15/41                                | 170 mg of ginger<br>extract  | 56   | 15/41            | 400 mg of ibuprofen   | 3 weeks     | Double-<br>blind |

| Gregersen <i>et</i><br><i>al.</i><br>(2013) [60] | Denmark          | Crossover<br>randomized<br>controlled<br>trial              | Diet-induced<br>thermogenesis  | 22 | 22/0 | 20 g of fine-chopped<br>ginger in the stewed<br>apples   | 22 | 22/0 | Placebo and other<br>pungent spices <sup>9</sup>      | Single-dose   | Single-<br>blind |
|--|------------------|---|--|----|------|--|----|------|---|---|------------------|
| Mansour <i>et</i><br><i>al.</i><br>(2012) [61]   | United<br>States | Crossover<br>randomized<br>controlled<br>trial              | Energy<br>expenditure,<br>feelings of<br>appetite and<br>satiety and<br>metabolic risk<br>factors in<br>overweight men | 10 | 10/0 | Breakfast meal with 2<br>g of powdered ginger<br>dissolved in hot water<br>beverage                        | 10 | 10/0 | Breakfast meal with<br>hot beverage<br>without ginger | Single-dose   | Open-<br>label   |
| Janssen <i>et al.</i><br>(1996) [62]             | Netherlan<br>ds  | Crossover<br>randomized<br>controlled<br>trial<br>Crossover | Anti-thrombotic<br>effect  | 18 | 9/9  | 125 g of vanilla<br>custard containing<br>15 g of Brazilian<br>ginger root<br>125 g of vanilla             | 18 | 9/9  | 125 g of vanilla<br>custard                           | 14 days   | Double-<br>blind |
|  | Netherlan<br>ds  | randomized<br>controlled                                    | Anti-thrombotic<br>effect  | 18 | 9/9  | custard containing<br>40 g of cooked stem  | 18 | 9/9  | 125 g of vanilla<br>custard                           | 14 days   | Double-<br>blind |
| Bordia <i>et al.</i><br>(1996) [63]              | N/A              | trial<br>Randomized<br>controlled<br>trial                  | Blood lipids,<br>blood sugar, and<br>platelet<br>aggregation<br>profiling<br>Pharmacokinetics                          | 10 | N/A  | ginger<br>4 g of powdered<br>ginger/day for 3<br>months and 10 g of<br>powdered ginger as a<br>single dose | 10 | N/A  | Placebo   | 3 months  | N/A              |
| Jiang <i>et al.</i><br>(2004) [64]               | Australia        | Crossover<br>randomized<br>controlled<br>trial              | and<br>pharmacodynamic<br>s of warfarin in<br>healthy subjects   | 12 | 12/0 | 400 mg of powdered<br>ginger rhizome/tab, 3<br>tablets/day   | 12 | 12/0 | No intervention                                       | 1 week after<br>warfarin<br>administration<br>(25 mg) | Open-<br>label   |
| Shariatpana<br>hi <i>et al.</i><br>(2013) [65]   | Iran             | Randomized<br>controlled<br>trial                           | Acute respiratory<br>distress syndrome   | 16 | 8/8  | 120 mg of ginger<br>extract  | 16 | 8/8  | 1 g of coconut oil                                    | 21 days   | Double-<br>blind |

| Rouhi et al. |      | Randomized |        |    |     | 20 drops of ginger             |    |     |         |          |     |
|--------------|------|------------|--------|----|-----|--------------------------------|----|-----|---------|----------|-----|
| (2006) [66]  | Iran | controlled | Asthma | 46 | N/A |                                | 46 | N/A | Placebo | 2 months | N/A |
| (2000) [00]  |      | trial      |        |    |     | solution/8 hours <sup>10</sup> |    |     |         |          |     |

1: Core body temperature

2: Finger skin blood flow

3: Sweating rates

4: Two capsules of ginger (placebo) at 30 min before and one capsule at 6 and 12 h after chemotherapy together with standard antiemetics in day 1. From day 2 to day 5, they received on capsule of ginger (or metoclopramide) four times a day.

5: Patient  $\geq$  20 kg and < 40 kg: 6 capsules/day containing 167 mg ginger powder (total dose: 1,000 mg/day); patient  $\geq$  40 kg and < 60 kg: 5 capsules/day containing 400 mg ginger powder (total dose: 2,000 mg/day)

6: Granisetron plus dexamethasone

7: To achieve a plasma glucose concentration between 250 and 290 mg/dL

8: Corresponds to 2000 mg of dry ginger rhizome

9: 8.3 g of shredded horseradish, 21 g of Dijon mustard, 1.3 g of black pepper

10: 150 mg as powdered ginger in 25 drops of solution

| Author (year)                         | Evaluation outcome system   | Main result  | Adverse<br>effect |
|---------------------------------------|---|--|-------------------|
| Bossi <i>et al.</i> (2017)<br>[1]     | Incidence and intensity of nausea (VAS), impact of<br>nausea on daily life (FLIE questionnaire), nausea and<br>vomiting domain scores, impact of fatigue (BFI<br>questionnaire) | Cancer patients receiving highly emetogenic chemotherapy did not show<br>beneficial effect of ginger treatment regarding the reduction of CINV (delayed,<br>intercycle, and anticipatory).   | No                |
| Konmun <i>et al.</i><br>(2017) [2]    | Complete response, intensity of nausea and appetite<br>(by Intensity of nausea and appetite), quality of life<br>(by Functional Assessment of Cancer Therapy-<br>General)       | In addition to highly emetogenic chemotherapy using ondansetron,<br>metoclopramide, dexamethasone, 6-gingerol has reduced complete response<br>rate significantly in both acute and delayed CINV.  | No                |
| Zeraati <i>et al.</i> (2016)<br>[3]   | Severity of nausea (by VAS), retching incidents   | Ginger extract showed improvement in terms of reducing the incidence and mean severity score of nausea and vomiting during the cesarean section.   | No                |
| Rad et al. (2018) [4]                 | PVAS, multidimensional verbal rating scale (MVRS),<br>and pictorial, blood loss assessment chart (PBAC)<br>Pain intensity (by VAS), pain duration, and                          | Ginger is as effective as mefenamic acid in relieving pain with primary dysmenorrhea.  | No                |
| Shirvani <i>et al.</i><br>(2017) [5]  | menstruation characteristics (menstrual cycle<br>duration, duration on menstruation, severity of<br>dysmenorrhea, bleeding)   | Instead of taking ginger for reducing pain and dysmenorrhea, stretching exercise is safer, low-cost treatment to effectively relieve the pain.   | No                |
| Mashak <i>et al.</i> (2018)<br>[6]    | Mean arterial pressure, heart rate, arterial oxygen saturation, cesarean duration, VAS  | There is significant difference in mean score of post-spinal puncture headache between ginger treatment and control group except 12 hours after C-section.   | No                |
| Hashemi <i>et al.</i><br>(2019) [7]   | Pain (by VAS), IL-6, CRP  | There is no significant difference in levels of VAS and IL-6 when comparing ginger group and vitamin B6 group, however, level of CRP in ginger group significantly decreased.  | No                |
| Hasanvand <i>et al.</i><br>(2018) [8] | Serum troponin I level, chest pain (by numeric rating scale)  | Chest pain occurred during coronary angioplasty could be reduced by taking ginger. Also, as taking ginger is better regarding convenience and no significant complication, it could be a better choice for therapeutic agents in reducing chest pain during angioplasty. | No                |
| Azimi <i>et al.</i> (2016)<br>[9]     | sICAM-1, systolic blood pressure, diastolic blood pressure, anthropometric measures   | In within-group comparison, ginger intake significantly reduced the concentration of sICAM-1 and affected systolic blood pressure.   | No                |
| Shidfar <i>et al.</i> (2015)<br>[10]  | Serum concentration of glucose, insulin, hs-CRP, paraoxonase-1, TAC, MDA, HbA1c, HOMA-IR  | Serum glucose, HbA1c, insulin, insulin resistance, hs-CRP significantly decreased while paraoxonase-1, TAC and MDA significantly increased by supplementation of ginger in T2DM patients.  | No                |
| Tabibi <i>et al.</i> (2015)<br>[11]   | Triglyceride, total cholesterol, LDL-C, HDL-C, lipoprotein (a), IL-6  | Administrating 1000mg ginger daily reduces serum triglyceride concentration<br>in peritoneal dialysis patients.  | No                |

## **Table S3.** Evaluation system and key finding of the included studies with a quality score less than 10

| Karimi <i>et al.</i> (2015)<br>[12]               | IL-10, hs-CRP, insulin, insulin resistance, glucose, TG,<br>TC, LDL-Cholesterol, HDL- Cholesterol, HDL/LDL-<br>Cholesterol         | The ginger treatment and the water-base exercise reduced the hs-CRP, IL-10,<br>insulin, glucose, insulin resistance, LDL- Cholesterol, TG levels but increased<br>the HDL- Cholesterol and HDL-Cholesterol /LDL- Cholesterol. The<br>combination showed a better effect than alone supplementation.           | No  |
|---|--|---|-----|
| Emrani <i>et al.</i> (2016)<br>[13]               | Nausea (VAS score), number of vomiting, anti-TB-<br>induced hepatotoxicity, time to onset of anti-TB-<br>induced hepatotoxicity    | Ginger can be considered as a potential additional therapy to prevent<br>gastrointestinal adverse reactions including hepatotoxicity, which was induced<br>by antituberculosis.   | Yes |
| Kulkarni <i>et al.</i><br>(2016) [14]             | TNF-alpha, ferritin, MDA   | Ginger supplementation significantly reduced the levels of TNF alpha, ferritin<br>and MDA in ginger supplemented group in comparison to baseline. Ginger<br>supplementation with antitubercular treatment significantly lowered TNF<br>alpha, ferritin and MDA concentrations in comparison to control group. | No  |
| Miyamoto <i>et al.</i><br>(2015) [15]             | Thermal sensation and thermal comfort, oxygen<br>consumption, CO2 production, respiratory exchange<br>ratio, serum-free fatty acid | The effect of treating ginger seems to has no effect in peripheral and central thermoregulatory function. However, treating ginger can affect fat utilization and the treating time also can affect fat utilization.  | No  |
| Manusirivithaya et<br>al. (2004) [16]             | Nausea score, number of days of nausea   | The addition of ginger to standard antiemetic regimen has no advantage in<br>reducing nausea or vomiting in acute phase of cisplatin-induced emesis. In<br>delayed phase, ginger and metoclopramide have no statistically significant<br>difference in efficacy.  | No  |
| Pillai <i>et al.</i><br>(2011) [17]               | ESAS   | Ginger root powder was effective in reducing severity of acute and delayed<br>CINV as additional therapy to ondansetron and dexamethasone in patients<br>receiving high emetogenic chemotherapy.  | No  |
| Panahi <i>et al.</i> (2012)<br>[18]               | The modified form of RINVR   | Standard antiemetic therapy with ginger significantly reduced prevalence of nausea 6 to 24 h post-chemotherapy. However, there is no other advantage in reducing prevalence or severity of CINV.  | No  |
| Sontakke <i>et al.</i><br>(2002) [19]             | Control of nausea and vomiting   | Efficacy of ginger in term of antiemetic was as effective as metoclopramide in cancer patients who used lose dose cyclophosphamide with cytotoxics causing mild emesis  | No  |
| Arslan <i>et al.</i> (2014)<br>[20]               | Nausea intensity, nausea, vomiting and, retching episodes  | In the first 3 days of chemotherapy, administering ginger powder could be effective in reducing the severity of CINV in breast cancer patients who received anthracycline-based chemotherapy.   | No  |
| Mohammadbeigi <i>et</i><br><i>al.</i> (2011) [21] | Vomiting, Nausea, Rhodes index   | Ginger and metoclopramide groups had no significant effect, however, there<br>was a significant difference in reducing vomiting and nausea caused by<br>pregnancy compared to placebo group.  | No  |
| Ozgoli <i>et al.</i> (2009)<br>[22]               | Nausea intensity and vomiting episodes   | Ginger treatment significantly decreased nausea intensity and vomiting episodes in pregnancy.   | No  |
| Keating <i>et al.</i> (2002)<br>[23]              | Degree of nausea and vomiting, number of vomiting episodes, daily functioning related to symptoms.                                 | It was good option for early pregnancy to take 1g of ginger in syrup or capsules daily as antiemetics.  | Yes |

| Pongrojpaw <i>et al.</i><br>(2007) [24]   | Visual analogue nausea scores (VANS) and vomiting times   | Ginger showed similar effect with dimenhydrinate 3-7 days after the treatment.<br>Therefore, taking ginger can be an alternative choice for the treatment of<br>nausea and vomiting for pregnant women.  | Yes |
|---|---|--|-----|
| Saberi <i>et al.</i> (2009)<br>[25]       | Nausea, vomiting, and retching (by Rhodes Index<br>Score)   | At less than 16 weeks gestation, ginger was an effective treatment for the relieving in mild to moderate nausea and vomiting in pregnant women.  | No  |
| Javadi et al. (2013)<br>[26]              | Nausea and vomiting (by MPUQE score)  | There was no significant difference in efficacy of ginger and Vitamin B6 regarding reduction of symptoms of pregnancy-induced nausea.  | No  |
| Apariman <i>et al.</i><br>(2006) [27]     | VAS, presences of vomiting at 0-2/2-6 hour postoperation  | VAS in ginger group was significantly lower than placebo group at 6 hour postoperation, but there were no statistically significant differences in any other indexes.  | No  |
| Nanthakomon <i>et al.</i><br>(2006) [28]  | Frequency of vomiting, nausea (by VAS)  | Ginger treatment showed a significant effect in preventing nausea and vomiting of post major gynecologic surgery   | No  |
| Kalava <i>et al.</i> (2013)<br>[28]       | The intraoperative incidence of nausea, the number of<br>episodes of intraoperative nausea, the incidence of<br>intraoperative vomiting, the number of episodes of<br>vomiting in the first 24 h after surgery, severity of<br>nausea postoperatively | The frequency of episodes of intraoperative nausea was significantly reduced<br>in ginger group comparing with placebo group. However, frequency of nausea,<br>vomiting, and pain during and after an elective cesarean section was not<br>affected by ginger. | Yes |
| Visalyaputra <i>et al.</i><br>(1997) [30] | Incidence and severity of PONV (nausea score and vomiting frequency)  | Incidence of PONV after gynecological laparoscopy was not reduced by taking 2 g of ginger, 1.25 mg of droperidol or both.  | No  |
| Phillips <i>et al.</i> (1993)<br>[31]     | Nausea (number of complaints), vomiting (number of episodes), postoperative analgesic   | Ginger was useful as a promising antiemetic, especially for day case surgery.  | No  |
| Bone <i>et al.</i> (1990)<br>[32]         | Incidences of nausea, vomiting, retching, sedation,<br>abnormal movements, pain, itching and eye<br>disturbances at the four assessment times, nausea and<br>pain grade, postoperative use of analgesia   | The antiemetics effectiveness of ginger group was significantly better than placebo group, and other antiemetic groups in patients after receiving the major gynecological surgery.  | No  |
| Tavlan <i>et al.</i> (2006)<br>[33]       | Nausea (mild, moderate, severe), retching, episode of vomiting, rescue antiemetics  | Ginger treatment combination with dexamethasone for reducing postoperative<br>nausea and vomiting did not have significant result compared with the result<br>when using dexamethasone alone.  | No  |
| Dabaghzadeh <i>et al.</i><br>(2014) [34]  | Nausea (by VAS), number of vomiting episodes  | Ginger was useful to prevent nausea and vomiting-induced by antiretroviral regimens.   | No  |
| Holtmann <i>et al.</i><br>(1989) [34]     | Optokinetic nystagmus, caloric response, postrotatory<br>nystagmus  | Ginger had little effect on the vestibular or the oculomotor system.   | No  |
| Grontved <i>et al.</i><br>(1988) [36]     | Seasickness (nausea, vertigo, vomiting, and cold sweating scores)   | Ginger is effective in reducing vomiting and cold sweating when compared with placebo.   | No  |
| Grontved <i>et al.</i><br>(1985) [37]     | Vertigo score, nystagmus duration, maximum slow<br>phase velocity of nystagmus  | Motion sickness symptoms such as vertigo, nausea, vomiting, cold sweat are reduced better by taking ginger root than placebo group.  | No  |

| Mowrey <i>et al.</i><br>(1982) [38]                 | Times in revolving chair and power functions for<br>magnitude estimations   | Ginger treatment showed higher effect in reducing the gastrointestinal distress<br>in motion sickness compared to demenhydrinate and placebo treatment.   | No  |
|---|---|---|-----|
| Stewart <i>et al.</i> (1990)<br>[39]                | Head movements, gastric emptying,<br>electrogastrography  | Ginger did not have anti-motion sickness activity and had no function of altering gastric function during motion sickness.  | Yes |
| Jenabi (2013) [40]                                  | Pain (by VAS)   | Ginger treatment significantly reduced VAS of post-therapy pain compared with placebo group.  | No  |
| Shirvani <i>et al.</i><br>(2014) [41]               | Severity of dysmenorrhea 100mm visual analog scale<br>( by VAS), severity of dysmenorrhea, pain duration,<br>cycle duration and bleeding volume | There was no significant difference in terms of pain intensity, severity of dysmenorrhea, pain duration, cycle duration and bleeding volume between two groups. The menstrual days were longer in ginger group in first and second cycle.   | No  |
| Black <i>et al.</i> (2008)<br>[42]                  | Heart rate, oxygen consumption, work rate,<br>quadriceps muscle pain, ratings of perceived exertion,<br>values for total mood disturbance       | Compared with placebo, ginger had no clinically meaningful or statistically<br>significant effect on perceptions of muscle pain, ratings of perceived exertion,<br>work rate, heart rate, or oxygen uptake during exercise. Recovery of oxygen<br>uptake and heart rate after the 30 min exercise followed a similar time course in<br>the ginger and placebo conditions. | No  |
| Maghbooli <i>et al.</i><br>(2014) [43]              | Time of headache onset, severity, and response self-<br>assessments   | Ginger showed similar effect to sumatriptan when patients relieved migraine attack.   | No  |
| Arablou <i>et al.</i> (2013)<br>[44]                | Anthropometric indices <sup>1</sup> , glycemic and lipid profile  | There were significant differences between ginger intervention group and placebo group in serum FPG, HbA1c, Insulin, HOMA, TG, TC, CRP, PGE <sub>2</sub> while there were no significant differences in HDL, LDL and TNF-alpha.   | No  |
| Mozaffari-<br>Khosravi <i>et al.</i><br>(2014) [45] | FBS, HbA1c, fructosamine, QUICKI, BMI, fasting<br>insulin, HOMA-IR, insulin sensitivity, beta-cell<br>function                                  | FBS decreased 10.5% in ginger intake group while it increased 21% in placebo<br>group. There is significant difference in fasting insulin level, insulin sensitivity,<br>HOMA-IR, QUICKI more increased in ginger group significantly.  | No  |
| Andallu <i>et al.</i> (2001)<br>[46]                | Body weight, blood glucose, total cholesterol,<br>triglycerides, HDL cholesterol, LDL cholesterol, VLDL<br>cholesterol                          | Ginger treatment may be helpful in reducing blood glucose and serum lipid levels in diabetic or hypercholesterolemic people.  | No  |
| Karimi <i>et al.</i> (2013)<br>[47]                 | Adiponectin, glutathione peroxidase, nitric oxide,<br>MDA   | It was concluded that ginger could reduce oxidative stress in obese women who were diagnosed with breast cancer.  | No  |
| Atashak <i>et al.</i> (2011)<br>[48]                | CRP, HOMA-IR, Insulin, blood lipids (total<br>cholesterol, LDL-C, HDL-C, TG), anthropometric<br>measurements                                    | This study showed that treating ginger supplements alone or combination may reduce chronic inflammation.  | No  |
| Alizadeh-Navaei et<br>al. (2008) [49]               | Lipid levels (fasting serum TG, cholesterol, HDL, LDL,<br>and VLDL), fasting lipoprotein-α, fasting<br>homocysteine                             | The mean change level of triglyceride and cholesterol was significantly higher<br>in ginger group than control group. In addition, the significant reduction of TC,<br>cholesterol, LDL, VLDL, lipoprotein- $\alpha$ and homocysteine were observed when<br>comparing the before and after ginger treatment.  | No  |

| Imani <i>et al.</i> (2014)<br>[50]         | Serum fasting glucose, carboxymethyl lysine,<br>pentosidine, MDA, hs-CRP, sICAM-1, sVCAM-1, sE-<br>selectin  | Administrating 1000 mg ginger daily reduced serum fasting glucose in patients undergoing peritoneal dialysis.  | No  |
|--|--|--|-----|
| Hu et al. (2011) [51]                      | Antral area, antral contractions, fundic area and diameter, and gastric half-emptying time (T50)   | Gastric half-emptying time was more rapid in ginger treatment group than placebo group. There is no significant difference in any other parameters.  | No  |
| Wu et al. (2007) [52]                      | Antral area, antral contraction, gastric half-emptying<br>time, fundic area and diameter, gastrointestinal<br>sensations score (by VAS)  | In ginger treatment group, the antral area and gastric half-emptying time were decreased more rapidly while the frequency of antral contractions was increased.  | No  |
|  | Vection-induced gastric dysrhythmias (EGG), vection-   |  |     |
| Lien <i>et al.</i> (2002)                  | induced elevation of plasma vasopressin, vasopressin-  | Ginger treatment has the effect in reducing the severity of nausea, tachygastric   | No  |
| [52]                                       | evoked nausea, vasopressin-evoked gastric<br>dysrhythmias  | activity, and vasopressin release.   |     |
| Shariatpanahi <i>et al.</i><br>(2009) [54] | Mean nutritional intake on first 48 h, Mean nutritional<br>intake on total period of study, ICU free days,<br>ventilator-free days, mortality, nosocomial pneumonia  | Reducing delayed gastric emptying, eliminating the use of transpyloric feeding<br>and preventing the development of nosocomial pneumonia can be achieved by<br>gastric feeding with ginger extract.                                  | No  |
| Gonlachanvit <i>et al.</i><br>(2003) [55]  | Plasma glucose level, electrogastrography,<br>hyperglycemic clamping technique   | Ginger root could prevent slow-wave dysrhythmias evoked by acute<br>hyperglycemia. However, no influence was recorded on dysrhythmias induced<br>by a prostaglandin E1 analog.   | No  |
| Haghighi <i>et al.</i><br>(2005) [56]      | Severity of pain, gelling pain score, joint swelling score, joint motion slope score   | Regarding relieving symptoms of osteoarthritis, the ginger and ibuprofen<br>groups were significantly more affected than the placebo group, however, there<br>was no significant difference between the ginger and ibuprofen groups. | No  |
| Paramdeep <i>et al.</i><br>(2013) [57]     | WOMAC index, pain (by VAS)   | this study indicates that ginger added additional effect regarding analgesic and anti-inflammatory effect in patients of Osteoarthritis.   | Yes |
| Drozdov <i>et al.</i><br>(2012) [58]       | PGE1, PGE2, PGF2α, PGI2, serum gastrin-17 levels<br>severity of dyspepsia assessment form, arthritic pain<br>(by VAS)  | Treatment combination of ginger and glucosamine was as effective as NSAID in OA patients and may have an additional gastro protective effect.  | No  |
| Bliddal <i>et al.</i> (2000)<br>[59]       | Pain assessment (by VAS), Lequesne-index for either hip or knee, range of motion   | The result suggested that the treating ginger to deal with the pain and dysfunction of osteoarthritis of the hip or knee is more effective than placebo but less effective than ibuprofen.   | No  |
| Gregersen <i>et al.</i><br>(2013) [60]     | Diet-induced thermogenesis, respiratory quotient, and<br>substrate oxidation, catecholamines, hemodynamic<br>factors, ad libitum energy intake, appetite measures,<br>energy balance, blood parameters                 | At palatable levels in food, ginger had no significant effects on any of the primary or secondary outcome measures relating to energy metabolism, appetite or food intake.   | No  |
| Mansour <i>et al.</i><br>(2012) [61]       | Increase of Thermic Effect of Food (difference between<br>post-prandial energy expenditure and resting<br>metabolic rate), AUC for Thermic Effect of Food, post-<br>prandial energy expenditure, respiratory quotient, | Ginger may have a potential effect on weight management by enhancing thermogenesis and reducing feelings of hunger.  | No  |

|                                      | AUC of VAS ratings of hunger, AUC for VAS ratings                  |  |                 |  |
|--------------------------------------|--|--|-----------------|--|
|                                      | of food intake, AUC for VAS ratings of greater                     |  |                 |  |
|                                      | fullness, glucose, insulin, lipids, or inflammatory                |  |                 |  |
|                                      | markers  |  |                 |  |
| Janssen <i>et al.</i> (1996)<br>[62] | Maximum ex vivo platelet thromboxane B2 production                 | It was concluded that ginger intake had no significant effect on anti-thrombotic.      | No              |  |
| Bordia, et al. (1996)                | Adenosine diphosphate-induced platelet aggregation,                | A 4 g daily of ginger intake showed no effect on adenosine diphosphate- and            |                 |  |
| [63]                                 | epinephrine-induced platelet aggregation, blood                    | epinephrine-induced platelet aggregation, blood lipid, and blood sugar. 10 g of        | No              |  |
| [05]                                 | lipids, blood sugar  | single dose after 4 h had a significant effect in reducing platelet aggregation.       |                 |  |
| Jiang <i>et al.</i> (2004)           | Pharmacokinetic parameters, pharmacodynamic                        | Ginger did not show significant effect on the pharmacokinetics or                      | No              |  |
| [64]                                 | parameters Platelet aggregation                                    | pharmacodynamics of warfarin and clotting status.                                      | INO             |  |
|                                      |  | Patients consumed ginger have a significant lower level of IL-1, IL-6, and TNF         |                 |  |
| Shariatpanahi et al.                 | IL-1, IL-6, TNF-alpha, LTB4, red blood cell                        | alpha but significant higher level of red blood cell glutathione. Ginger               | No              |  |
| (2013) [65]                          | glutathione, organ failure-free days                               | treatment group has less duration of mechanical ventilation and length of              | 110             |  |
|                                      |  | intensive care unit stay.  |                 |  |
| Rouhi <i>et al.</i> (2006)           | Dyspnea, wheezing, chest tightness, stage of                       | This study showed that 1-4 g of ginger is effective in reducing asthmatic              |                 |  |
| [66]                                 | disease, nocturnal cough, spray dosage, dyspnea                    | symptoms, but ineffective in spirometry findings and changing the stage of the         | No              |  |
| [00]                                 | attack, FEF25-75, FEV1, FVC  | disease.   |                 |  |
| 1: Body weight, BMI,                 | serum FPG, HbA1c, Insulin, HOMA, TG, TC, HDL, LDL,                 | CRP, TNF-alpha, PGE2   |                 |  |
| CINV: chemotherapy-                  | -induced nausea and vomiting; CRP: C-reactive protein; I           | FBS: fasting blood sugar; FLIE-5DR: functional living index emesis 5 day recall; hs-CR | P: high-sensiti |  |
| C-reactive protein; HO               | DMA-IR: homeostasis model assessment of insulin resista            | nce; HDL-C: high density lipoprotein-cholesterol; HbA1c: Hemoglobin A1c; IL: inter     | leukin; LDL-C   |  |
| density lipoprotein-ch               | olesterol; MDA: malondialdehyde; PVAS: pain visual an              | alog scale; QUICKI: quantitative insulin sensitivity check index; RINVR: Rhodes Inve   | entory of Naus  |  |
| Vomiting and Retchin                 | g; TNF- $\alpha$ : tumor necrosis factor alpha; TAC: total antioxi | dant capacity; VAS: visual analog scale; ESAS: edmonton's symptom assessment scal      | e; PG:          |  |
| prostaglandins; sICAN                | M-1: soluble intercellular adhesion molecule type 1; sVCA          | AM-1: soluble vascular cell adhesion molecule type 1; WOMAC: Western Ontario and       | McMaster        |  |
| Universities osteoarth               | ritis  |  |                 |  |

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Table S4. Types of adverse effect, incidence rate, and dosage from 17 trials.

| Reference                          | <b>Reported adverse effect</b> | Reported case                      | Dosage (per day)         |
|------------------------------------|--------------------------------|------------------------------------|--------------------------|
|                                    | Headache                       | 2.17%                              |                          |
| Kashefi <i>et al.</i> (2013)       | Diarrhea                       | 0%                                 | 750 mg                   |
|                                    | Heartburn                      | 3.26%                              |                          |
|                                    | Heartburn                      | 2.17%                              |                          |
| Kashefi <i>et al.</i> (2015)       | Abdominal pain                 | 2.17%                              | 750 mg                   |
|                                    | Diarrhea                       | 2.17%                              |                          |
| Aryaeian <i>et al.</i> (2019)      | Heartburn                      | 3.03%                              | 1500 mg                  |
| Mahluji <i>et al.</i> (2013)       | Heartburn                      | 3.57%                              | 2000 mg                  |
|                                    | Bloating                       |                                    |                          |
| —<br>—                             | Gas                            |                                    | ••••                     |
| Citronberg <i>et al</i> . (2013) — | Nausea                         | — Overall, 70%                     | 2000 mg                  |
|                                    | Heartburn                      |                                    |                          |
| Wigler <i>et al</i> . (2003)       | Heartburn                      | 6.90%                              | 1000 mg                  |
|                                    | Nausea                         | 10.00%                             |                          |
| Paramdeep <i>et al</i> . (2013)    | Epigastric distress            | 10.00%                             | 750 mg                   |
|                                    | Heartburn                      | 10.00%                             |                          |
|                                    | Heartburn                      | 7.00%                              |                          |
| Kalava <i>et al.</i> (2013)        | Diarrhea                       | 4.00%                              | 1000 mg                  |
|                                    | Mouth irritation               | 1.00%                              |                          |
|                                    | Heartburn                      | N/A                                |                          |
| Ryan <i>et al.</i> (2012)          | Bruising/flushing              | N/A                                | 250 mg, 500 mg or 750 mg |
|                                    | Rash                           | N/A                                |                          |
|                                    | Flu-like symptom               | 1.69% (300 mg/d), 1.75% (600 mg/d) |                          |
| Eberhart <i>et al</i> . (2003) —   | Heartburn                      | 1.69% (300 mg/d), 3.51% (600 mg/d) | 300 mg or 600 mg         |
|                                    | Cardiovascular symptom         | 0% (300 mg/d), 3.51% (600 mg/d)    | Soo mg or ooo mg         |
|                                    | Respiratory symptom            | 3.39% (300 mg/d), 0% (600 mg/d)    |                          |

|  | Infection  | 5.08% (300 mg/d), 0% (600 mg/d)                           |                    |  |
|--|--|---|--------------------|--|
| Emrani <i>et al</i> . (2016)           | Heartburn  | 10.00%  | 500 mg             |  |
| Tilburg <i>et al.</i> (2014)           | Not sure about the ginger's side effect <sup>1</sup> | N/A   | 1000 mg or 2000 mg |  |
| Zick <i>et al.</i> (2014)              | Not sure about the ginger's side effect <sup>2</sup> | N/A   | 2000 mg            |  |
| $P_{\text{opposition}}$ at $a1$ (2007) | Drowsiness   | 5.88%   | 1000 mg            |  |
| Pongrojpaw <i>et al</i> . (2007)       | Heartburn  | 15.29%  | 1000 mg            |  |
|  | Abdominal pain                                       |   |                    |  |
| irouzbakht <i>et al</i> . (2014)       | Nausea   | 10.20%  | 1000 mg            |  |
|  | Heartburn  |   |                    |  |
|  | Gastric burning                                      | 37.50%  | <b>F</b> 00        |  |
| Stewart <i>et al</i> . (1990)          | Intense urge to urinate                              | 25.00%  | 500 mg or 1000 mg  |  |
| Yekta <i>et al</i> . (2012)            | Heartburn  | 10.00% (anticipatory), 12.50% (acute),<br>5.00% (delayed) | 1000 mg            |  |

| Author<br>(year)                        | Random<br>sequence<br>generation | Allocation<br>concealment | Blinding of<br>participants<br>and<br>personnel* | Blinding of<br>outcome<br>assessment* | Incomplete<br>outcome<br>data* | Selective<br>reporting | Other bias | QA score (L=2,<br>U=1, H=0) |
|---|----------------------------------|---------------------------|--|---------------------------------------|--------------------------------|------------------------|------------|-----------------------------|
| Black <i>et al.</i><br>(2010)           | L                                | L                         | L  | Н                                     | L                              | L                      | L          | 12                          |
| Black <i>et al.</i><br>(2008)           | U                                | L                         | L  | Н                                     | L                              | L                      | Н          | 9                           |
| Gregersen <i>et al.</i><br>(2013)       | L                                | Н                         | U  | L                                     | L                              | L                      | Н          | 9                           |
| Manusirivithaya <i>et al.</i><br>(2004) | U                                | Н                         | L  | Н                                     | L                              | L                      | Н          | 7                           |
| Pillai <i>et al.</i><br>(2011)          | L                                | Н                         | L  | Н                                     | L                              | L                      | U          | 9                           |
| Kulkarni <i>et al.</i><br>(2016)        | U                                | Н                         | U  | Н                                     | L                              | L                      | Н          | 6                           |
| Holtmann <i>et al.</i><br>(1989)        | U                                | Н                         | L  | Н                                     | L                              | L                      | Н          | 7                           |
| Karimi <i>et al.</i><br>(2013)          | U                                | Н                         | U  | Н                                     | L                              | L                      | Н          | 6                           |
| Attari <i>,et al.</i><br>(2016)         | U                                | L                         | L  | Н                                     | L                              | L                      | L          | 11                          |
| Ensiyeh <i>et al.</i><br>(2009)         | L                                | L                         | L  | Н                                     | L                              | L                      | L          | 12                          |
| Hashemi <i>et al.</i><br>(2019)         | U                                | L                         | L  | Н                                     | U                              | L                      | Н          | 8                           |

 Table S5. Quality assessment outcomes and quality assessment scores of the included studies.

| Haghighi <i>et al.</i><br>(2005)                | U | Н | L | Н | L | L | Н | 7  |
|---|---|---|---|---|---|---|---|----|
| Mohammadbeigi <i>et</i><br><i>al.</i><br>(2011) | L | Н | L | Н | L | L | Н | 8  |
| Sharifzadeh <i>et al.</i><br>(2018)             | L | L | L | L | L | L | Н | 12 |
| Maghbooli <i>et al.</i><br>(2014)               | U | L | L | Н | L | L | Н | 9  |
| Ozgoli <i>et al.</i><br>(2009)                  | Н | L | L | L | L | L | L | 12 |
| Kashefi <i>et al.</i><br>(2013)                 | L | L | L | L | Н | Н | L | 10 |
| Janssen <i>et al.</i><br>(1996)                 | U | L | U | Н | L | L | Н | 8  |
| Martins <i>et al.</i><br>(2018)                 | L | Н | L | L | L | L | L | 12 |
| Arfeen <i>et al.</i><br>(1995)                  | U | L | L | L | L | L | Н | 11 |
| Willetts <i>et al.</i><br>(2003)                | L | L | L | L | L | L | Н | 12 |
| Marx <i>et al</i> .<br>(2017)                   | L | Н | L | L | L | L | L | 12 |
| Azimi <i>et al.</i><br>(2016)                   | U | Н | L | Н | L | L | L | 9  |
| Shariatpanahi <i>et al.</i><br>(2013)           | U | Н | L | L | L | L | Н | 9  |

| Bordia <i>et al.</i><br>(1997)                       | U | Н | U | Н | L | L | Н | 6  |
|--|---|---|---|---|---|---|---|----|
| Shidfar <i>et al.</i><br>(2015)                      | U | U | L | U | L | L | Н | 9  |
| Kashefi <i>et al.</i><br>(2015)                      | L | L | L | L | L | L | L | 14 |
| Sanaati <i>et al.</i><br>(2016)                      | L | L | L | L | L | L | L | 14 |
| Rad <i>et al.</i><br>(2018)                          | U | Н | L | Н | L | L | L | 9  |
| Arablou <i>et al.</i><br>(2013)                      | U | Н | L | Н | L | L | Н | 7  |
| Jenabi<br>(2013)                                     | L | L | U | Н | Н | L | Н | 7  |
| Panahi <i>et al.</i><br>(2012)                       | Н | Н | Н | Н | L | Н | L | 4  |
| Paritakul <i>et al.</i><br>(2016)                    | L | L | L | L | L | L | L | 14 |
| Hu <i>et al.</i><br>(2011)                           | U | Н | L | Н | L | L | L | 9  |
| Mashak <i>et al.</i><br>(2018)                       | U | L | Н | Н | L | L | L | 9  |
| Mozaffari-Khosravi <i>et</i><br><i>al.</i><br>(2014) | L | Н | L | Н | L | Н | L | 8  |
| Jiang <i>et al.</i><br>(2013)                        | L | L | L | L | L | L | L | 14 |

| Aozaffari-Khosravi <i>et</i><br><i>al.</i><br>(2016) | L | Н | L | L | L | L | L | 12 |
|--|---|---|---|---|---|---|---|----|
| Aryaeian <i>et al.</i><br>(2019)                     | L | L | L | L | L | L | U | 13 |
| Jiang <i>et al.</i><br>(2004)                        | U | Н | Н | Н | L | L | Н | 5  |
| Shirvani <i>et al.</i><br>(2014)                     | U | Н | U | Н | L | Н | L | 6  |
| Rahnama <i>et al.</i><br>(2012)                      | L | L | L | L | L | L | L | 14 |
| Attari <i>et al.</i><br>(2015)                       | L | L | L | Н | L | L | L | 12 |
| Apariman <i>et al.</i><br>(2006)                     | L | Н | U | Н | L | L | L | 9  |
| Mahluji <i>et al.</i><br>(2013)                      | U | L | L | L | L | L | U | 12 |
| Ozgoli <i>et al.</i><br>(2009)                       | U | Н | L | Н | L | L | L | 9  |
| Wu <i>et al.</i><br>(2007)                           | U | Н | L | Н | L | L | U | 8  |
| Lien <i>et al.</i><br>(2002)                         | U | Н | L | Н | L | L | Н | 7  |
| Imani <i>et al.</i><br>(2014)                        | L | Н | L | Н | L | L | Н | 8  |
| Tabibi <i>et al.</i><br>(2015)                       | L | Н | L | Н | L | L | Н | 8  |
| Rouhi <i>et al.</i><br>(2006)                        | U | Н | U | Н | L | L | Н | 6  |

| Citronberg <i>et al.</i><br>(2013)   | L | Н | L | L | L | L | L | 12 |
|--------------------------------------|---|---|---|---|---|---|---|----|
| Matsumura <i>et al.</i><br>(2015)    | L | Н | L | U | U | L | L | 10 |
| Wigler <i>et al.</i><br>(2003)       | L | L | L | L | L | L | L | 14 |
| Paramdeep<br>(2013)                  | U | Н | Н | Н | L | L | Н | 5  |
| Thamlikitkul <i>et al.</i><br>(2016) | L | Н | L | L | L | L | U | 11 |
| Li <i>et al.</i><br>(2017)           | L | L | L | L | L | L | L | 14 |
| Ansari <i>et al.</i><br>(2016)       | U | U | L | L | L | L | Н | 10 |
| Nanthakomon <i>et al.</i><br>(2006)  | U | U | L | Н | L | L | Н | 8  |
| Kalava <i>et al.</i><br>(2013)       | U | Н | L | Н | L | L | L | 9  |
| Visalyaputra <i>et al.</i><br>(1997) | U | Н | L | L | L | L | Н | 9  |
| Phillips <i>et al.</i><br>(1993)     | U | Н | L | Н | L | L | Н | 7  |
| Ryan <i>et al.</i><br>(2012)         | L | Н | L | Н | L | L | L | 10 |
| Black <i>et al.</i><br>(2009)        | L | Н | L | L | L | L | Н | 10 |

| Sontakke <i>et al.</i><br>(2002)      | U | Н | L | Н | L | L | Н | 7  |
|---------------------------------------|---|---|---|---|---|---|---|----|
| Mansour <i>et al.</i><br>(2012)       | U | Н | Н | Н | L | L | L | 7  |
| Eberhart <i>et al.</i><br>(2003)      | L | L | L | L | L | L | Н | 12 |
| Shariatpanahi <i>et al.</i><br>(2009) | U | Н | L | Н | L | L | Н | 7  |
| Vutyavanich <i>et al.</i><br>(2001)   | U | L | L | Н | L | L | U | 10 |
| Dabaghzadeh <i>et al.</i><br>(2014)   | U | Н | L | Н | L | L | L | 9  |
| Emrani <i>et al.</i><br>(2016)        | U | Н | L | Н | L | L | L | 9  |
| Bossi <i>et al</i> . (2017)           | L | Н | L | Н | L | Н | Н | 6  |
| Gonlachanvit <i>et al.</i><br>(2003)  | U | Н | L | Н | L | L | Н | 7  |
| Grontved <i>et al.</i><br>(1988)      | U | L | L | Н | L | L | Н | 9  |
| Bone <i>et al.</i><br>(1990)          | U | Н | L | Н | L | Н | Н | 5  |
| Keating <i>et al.</i><br>(2002)       | L | Н | L | Н | L | L | U | 9  |

| Fischer-Rasmussen <i>et</i><br><i>al.</i><br>(1990) | U | L | L | L | L | L | Н | 11 |
|---|---|---|---|---|---|---|---|----|
| Drozdov <i>et al.</i><br>(2012)                     | L | Н | U | Н | L | L | Н | 7  |
| Alizadeh-Navaei <i>et</i><br>al.<br>(2008)          | U | Н | L | Н | L | L | U | 8  |
| Tilburg <i>et al.</i><br>(2014)                     | L | L | L | Н | L | L | L | 12 |
| Atashak <i>et al.</i><br>(2011)                     | U | Н | L | Н | L | L | Н | 7  |
| Miyamoto <i>et al.</i><br>(2015)                    | U | Н | U | Н | L | L | Н | 6  |
| Arslan <i>et al.</i><br>(2014)                      | L | Н | Н | Н | L | L | Н | 6  |
| Konmun <i>et al.</i><br>(2017)                      | U | Н | L | Н | L | L | Н | 7  |
| Zick <i>et al.</i><br>(2011)                        | L | L | L | L | L | L | Н | 12 |
| Zick <i>et al.</i><br>(2008)                        | L | L | L | L | L | L | L | 14 |
| Suzanna <i>et al.</i><br>(2014)                     | L | L | L | Н | L | L | L | 12 |
| Tavlan <i>et al.</i><br>(2006)                      | L | U | L | Н | L | L | Н | 9  |

| Pongrojpaw <i>et al.</i><br>(2007)  | U | Н | L | Н | L | L | Н | 7  |
|-------------------------------------|---|---|---|---|---|---|---|----|
| Smith <i>et al.</i><br>(2004)       | L | U | L | L | L | L | Н | 11 |
| Bliddal <i>et al.</i><br>(2000)     | U | Н | L | L | L | L | Н | 9  |
| Shirvani <i>et al.</i><br>(2017)    | L | Н | U | Н | L | L | L | 9  |
| Grontved <i>et al.</i><br>(1985)    | U | Н | L | Н | U | L | Н | 6  |
| Phillips <i>et al.</i><br>(1992)    | L | L | L | Н | L | L | Н | 10 |
| Hasanvand <i>et al.</i><br>(2018)   | U | Н | L | Н | L | L | Н | 7  |
| Biswas <i>et al.</i><br>(2011)      | L | L | L | Н | L | L | L | 12 |
| Saberi <i>et al.</i><br>(2009)      | L | Н | U | Н | L | L | U | 8  |
| Andallu <i>et al.</i><br>(2001)     | Н | Н | U | Н | U | L | Н | 4  |
| Karimi <i>et al.</i><br>(2015)      | U | Н | U | Н | L | L | Н | 6  |
| Firouzbakht <i>et al.</i><br>(2014) | L | L | L | Н | L | L | Н | 10 |
| Javadi <i>et al.</i><br>(2013)      | U | Н | U | Н | Н | L | Н | 4  |

| Fahimi <i>et al.</i><br>(2010)    | U | U | L | Н | L | L | L | 10 |
|-----------------------------------|---|---|---|---|---|---|---|----|
| Mandal <i>et al.</i><br>(2014)    | L | U | L | Н | L | L | L | 11 |
| Zeraati <i>et al.</i><br>(2016)   | U | Н | L | Н | L | L | Н | 7  |
| Mowrey <i>et al.</i><br>(1982)    | U | U | U | Н | L | L | Н | 7  |
| Stewart <i>et al.</i><br>(1990)   | L | Н | U | Н | Н | L | Н | 5  |
| Yekta <i>et al.</i><br>(2012)     | L | U | L | L | L | L | L | 13 |
| Arzati <i>et al.</i><br>(2017)    | U | U | L | Н | L | L | L | 10 |
| Khandouzi <i>et al.</i><br>(2013) | L | L | L | Н | L | L | L | 12 |