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Use of herbal to reduce nausea and vomiting in pregnancy: a systematic review

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ABSTRACT
Nausea and vomiting in pregnancy are discomforts that are estimated to occur in 70-80% of pregnant women. Some pregnant women usually avoid chemical or conventional drugs as far as possible due to concerns about potential teratogenic effects, so there is an increasing trend towards alternative treatments. The use of herbal medicines is often not reported to health professionals and health professionals rarely question the use of herbal medicines. Lack of knowledge about potential toxicities and ability to interact with conventional treatments may impact the mother and fetus . This article discusses herbs that have the potential to relieve symptoms of nausea and vomiting using a systematic review method by searching, collecting, filtering and reviewing related articles that meet the inclusion and exclusion criteria. This article uses two databases, namely Pubmed and Sciencedirect. It can be concluded that ginger, peppermint, lemon, quince, pomegranate, chamomile and cardamom can be used as alternative herbal choices to reduce nausea and vomiting and are safe for consumption by pregnant women at the appropriate dose.

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INTRODUCTION

Pregnancy is a physiological process in a woman's life. During the development process of pregnancy, some women will feel a lot of discomfort which will affect the quality of their life. In the first trimester there are three complaints that are most frequently complained of by pregnant women, namely: nausea, vomiting, fatigue and breast pain, while complaints in the second and third trimesters are: polyuria, fatigue and heart burn (Nazik & Eryilmaz, 2013) . Some women feel psychologically suffering and some decide to terminate their pregnancies rather than tolerate severe symptoms (RN, Caroline Maltepe Rada Boskovic, Koren, & Gideon (2007) corrected by CFP (2019). (Ellilä, Laitinen, Nurmi, Rautava, & Koivisto, 2018) stated that overall 88.0% of women reported some level of nausea and vomiting, of which 6.4% were severe, 52.2% were moderate and 29.4% light.

There is still a lot of research to find out the unclear etiology of nausea and vomiting in pregnancy , there are many logical theories that have been proposed, including hormones that experience changes such as the Human Chorionic Gonadotropin (hCG) hormone

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and increased estradiol levels, evolutionary adaptation, psychological predisposition (ACOG). , 2018) , lower circulating levels of vitamin B6 (Wibowo, Purwosunu, Sekizawa, & Farina, 2012) , Helicobacter pylori infection (Ng et al., 2017) , significant changes in olfactory performance (Simsek & Bayar, 2014) and other causes.

The use of herbal medicines is an increasing trend throughout the world (DA Kennedy, Lupattelli, Koren, & Nordeng, 2016) . The sale of herbal products on the market gives women greater freedom in their health care choices (Adams, Sibbritt, & Lui, 2011) . The prevalence of herbal medicine or herbal use varies significantly during pregnancy, depending on geographic location, ethnicity, cultural traditions, and socioeconomic status (Illamola et al., 2019) . According to multinational research, 28.9% of women reported using herbal medicine during pregnancy (Deborah A Kennedy, Lupattelli, Koren, & Nordeng, 2013) .

METHODS

This article uses a systematic review method by searching, collecting, filtering and reviewing related articles using 2 databases, namely *Pubmed* and *Scientdirect,* with *the keyword " Herbal Medicine OR Natural Medicine AND Pregnancy AND NVP OR Hyperemesis Gravidarum* OR *Emesis Gravidarum"* , 163 articles were identified. A total of 79 articles came from *Pubmed* , and 84 articles came from *Scientdirect.* There were 10 duplicate articles found. Filtering was carried out according to the inclusion and exclusion criteria so that 14 articles were obtained. Then further filtering of articles was carried out to look for appropriate and complete references regarding herbal medicine interventions for pregnant women who experience nausea and vomiting, and 12 suitable articles were obtained, which will be used for the *Systematic Review .*

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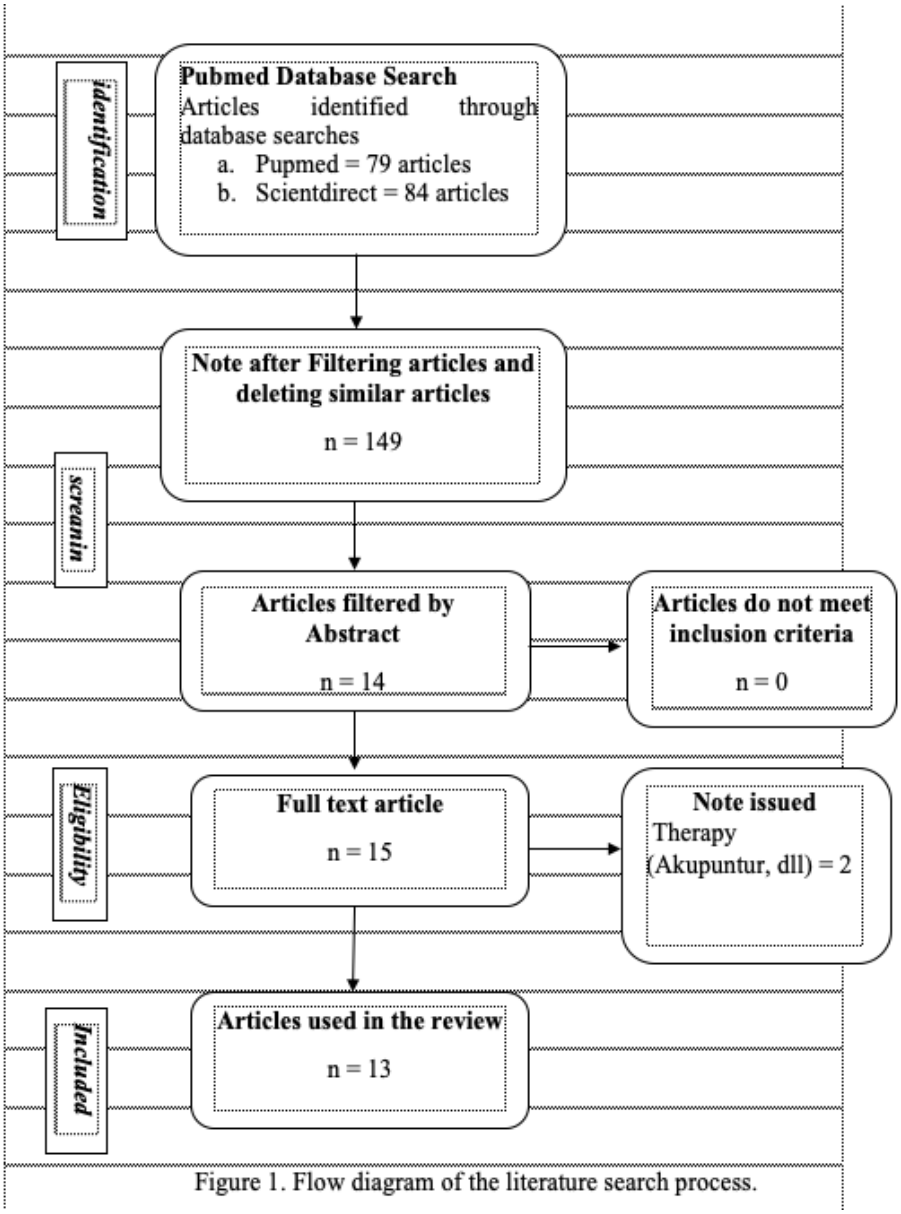

Figure 1. Flow diagram of the literature search process.

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RESULTS AND DISCUSSION

Data Extraction

No	Title/ author/ years/ grade	Aim	Type of research	Participants/sample size	Group		Measure	Results	Jadad score
					Intervention	Controls			
1	A comparison between the effects of ginger, pyridoxine (vitamin B6) and placebo for the treatment of the first trimester nausea and vomiting of pregnancy (NVP) (Sharifzadeh et al., 2018) (Iran)	The aim of this study was to compare the effects of ginger, pyridoxine (vitamin B6) and placebo for the treatment of nausea and vomiting in pregnancy (NVP).	Quantitative A triple blind clinical trial	77 pregnant women	1st group : Ginger 2nd group : Pyridoxine (Vitamin B_6)	Placebo	Rhodes	Ginger was more effective than placebo for the treatment of mild to moderate NVP and was comparable to vitamin B_6 with P = 0.039 and P = 0.007, respectively.	5
2	Comparing the Effectiveness of Vitamin B6 and Ginger in Treatment of Pregnancy-Induced Nausea and Vomiting (Haji, Javadi, Salehi, & Mashrabi, 2013) (Iran)	Comparing the effectiveness of vitamin B_6 (40mg twice daily) and ginger (250mg four times daily) in the treatment of nausea in pregnancy.	Quantitative _ Double - blinded clinical trial	102 pregnant women	Ginger (250mgx4 a day)	Vitamin B_6 (40mgx 2 a day)	MPUQE	Ginger and B6 were effective in reducing NVP and had no significant difference (P = 0.172).	3

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N	Title/ author/	Aim	Type of re-	Partici-	Group		Meas-	Results	Jadad
3	Comparison of ginger with vitamin B6 in relieving nausea and vomiting during pregnancy (Omidvar, Firouzbakht, Nikpour, & Jamali, 2014) (Iran)	To investigate the effect of ginger on nausea and vomiting during pregnancy compared with vitamin B_6 and placebo.	Quantitative _ Randomized and double - blind clinical trial	120 pregnant women	1st group : – Ginger (250mg) 2nd group : – Vitamin B_6 (40mg) One capsule every 6 hours a day for 4 consecutive days	Placebo: Sugar (40mg)	VASE	There were significant differences between groups in the severity of nausea and frequency of vomiting ($P < 0.001$). Ginger was as effective as vitamin B_6 in reducing nausea and vomiting compared to placebo.	5
4	Comparison of the effects of powdered ginger and fresh root on nausea and vomiting in pregnancy (Narenji F * 1 , Delarvar M 2, 2013) (Iran)	To compare the effects of ginger powder with fresh ginger root on nausea and vomiting in pregnancy.	Quantitative _ Clinical trials	100 pregnant women	1 teaspoon ginger syrup (fresh ginger root)	250 mg ginger powder	VASE	The results of the study showed that fresh ginger root compared to ginger powder was equally effective in reducing nausea and vomiting.	3
5	Effect of ginger on relieving nausea and vomiting in pregnancy: A Randomized, Placebo-Controlled Trial (Saberi, Sadat, Kalahroudi, & Taebi, 2014)	This study was conducted to assess the effectiveness of ginger in treating nausea and vomiting in pregnancy	Quantitative A Randomized, Placebo-Controlled Trial	120 pregnant women	1st group : – Ginger capsules (250 mg) 2nd group : – Placebo (lactose capsules) 3 capsules/day for 4 days	Control group	Rhodes	Ginger is effective for alleviating mild and moderate NVP ($P = 0.001$)	4

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N	Title/ author/ (Iran)	Aim	Type of re-	Partici-	Group		Meas-	Results	Jadad
6	Comparing the effects of ginger and metoclopramide on the treatment of pregnancy nausea (Mohammadbeigi, R., Shahgeibi, S., Soufizadeh, N., Rezaiie, M., Farhadifar, 2011) (Pakistan)	To examine the effect of ginger on nausea and vomiting due to pregnancy and compare it with the drug metoclopramide.	Quantitative A double blind controlled trial	120 pregnant women	1st group : metoclopramide (10 mg) 2nd group : ginger (200 mg) Given 3x a day	Placebo (under 200 mg)	Rhodes	The trend in changes in the severity of nausea decreased in the three groups but there was a slight increase in the metoclopramide group on the fourth day. The observed difference between the severity of nausea on the second to fifth days of intervention compared with the first day was statistically significant (p = 0.006); So the trend of change between the two groups of ginger (p = 0.046) and metoclopramide (p = 0.018) had a statistically significant difference with the placebo group.	5
7	Effect of Aromatherapy with Peppermint	To determine the effect of	Quantitative _	56 pregnant women	Peppermint oil	Placebo (pepper	PUQE	The severity of NVP in each group decreased	3

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N	Title/ author/	Aim	Type of re-	Partici-	Group		Meas-	Results	Jadad
	Oil on the Severity of Nausea and Vomiting in Pregnancy: A Single-blind, Randomized, Placebo-controlled trial (Joulaeerad, Ozgoli, Hajimehdipoor, Ghasemi, & Salehimoghaddam, 2018) (Iran)	aromatherapy with peppermint oil on the severity of nausea and vomiting in pregnancy (NVP).	A Single-blind, Randomized, Placebo-controlled trial		essential oil)			significantly ($p<0.001$). Comparison of the severity of NVP during the study period and the end of the study period was not statistically significant between the placebo and peppermint oil groups ($p = 0.227$)	
					The intervention was carried out for 4 days (3x a day)				
8	Study of the Effect of Mint Oil on Nausea and Vomiting During Pregnancy (Pasha, Behmanesh, Mohsenzadeh, Hajahmadi, & Moghadamnia, 2012) (Iran)	To evaluate the effect of mint on nausea and vomiting during pregnancy.	Quantitative Double blind RCT	60 pregnant women	Mint essential oil	Normal saline solution	VASE	The results showed that the severity of nausea and vomiting did not differ between the two groups in the 7 days before and after the intervention using repeated measurement tests. But during the intervention, the severity of nausea showed a decreasing trend (especially on the 4th night) in mint and an increas-	4
					4 nights in a row				

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N	Title/ author/	Aim	Type of re-	Partici-	Group		Meas-	Results	Jadad
								ing trend in the control group. The severity of nausea in the 7 days after the intervention had a tendency to decrease in both groups; However, the intensity was lower in the mint than the salt group but was not statistically significant . No significant association was detected during and after the intervention for vomiting intensity.	
9	The Effect of Lemon Inhalation Aromatherapy on Nausea and Vomiting of Pregnancy: A Double-Blinded, Randomized, Controlled Clinical Trial (Kia, Safajou, Shahnazi, & Nazemiyeh, 2014)	The aim of this study was to determine the effect of lemon inhalation aromatherapy on nausea and vomiting during pregnancy.	Quantitative _ A Double-Blinded, Randomized, Controlled Clinical Trial .	100 pregnant women	Essential oils (lemon zest + almond oil)	Placebo (carrot water+almond oil)	PUQE-24	There was a statistically significant difference between the two groups in the mean scores of nausea and vomiting on the second and fourth days (P = 0.017 and P = 0.039). The average intensity of nausea	5
					When participants felt nauseous, they had to drip 2 drops of the solution onto a cotton swab, and then breathe deeply 3 times				

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N	Title/ author/ (Iran)	Aim	Type of re-	Partici-	Group		Meas-	Results	Jadad
					through their nose, with the cotton swab 3 cm away from their nose.			and vomiting on the second and fourth days in the intervention group was significantly lower than the control group. Moreover, in intragroup comparisons by ANOVA with repeated measures, nausea and vomiting in five intervals, showed statistically significant differences in each group (P < 0.001 and P = 0.049).	
10	Comparison of quince with vitamin B6 for treatment of nausea and vomiting in pregnancy: a randomized clinical trial (Jafari-Dehkordi et al., 2017) (Iran)	The aim of this trial was to compare the effects of quince with vitamin B_6 to relieve nausea and vomiting in pregnancy.	Quantitative _ A randomized clinical trial	110 pregnant women	Quince syrup (1 spoon)	Vitamin B_6 (20 mg pills)	PUQE-24 & VAS	Quince fruit was proven to be more effective in reducing nausea and vomiting than vitamin B_6 (p = 0.001).	4
					3x a day before meals for 7 days.				
11	Effects of Pome-	The aim of this	Quantitative	74 pregnant wom-	Pomegranate	Vitamin	PUQE-	A large decrease in	4

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N	Title/ author/	Aim	Type of re-	Partici-	Group		Meas-	Results	Jadad
	granate and Spear-mint Syrup on Nau-sea and Vomiting During Pregnancy: A Randomized Con-trolled Clinical Trial (Abdolhosseini, Hashem-Dabaghian, Mokaberinejad, Sadeghpour, & Mehrabani, 2017) (Iran)	experiment was to evaluate the effectiveness of pomegranate with spearmint syrup on NVP	_ A Random-ized Con-trolled Clin-ical Trial	en	syrup + spear-mint (5 cc/ TDS) + vitamin B_6	$B_{6\ tablets}$ (20 mg/TDS)	24	PUQE-24 scores was observed in both groups, indicating the syrup group was more significant (p = 0.001). On the 7th day and 14th day, the syrup group also showed a significantly lower PUQE-24 score com-pared to the control group (p= 0.02).	
					3x a day for 1 week				
12	Effect of Ginger and Chamomile capsules on nausea and vom-iting in pregnancy (Modares M, Besharat S, Rahimi Kian F, Besharat S, Mahmoudi M, 2012) (Iran)	This research was conducted to determine the effect of Ginger and Chamomile capsules on nausea and vomiting in pregnancy.	Quantitative _ Triple - blinded clinical trial	105 pregnant women	1st group : Gin-ger capsules 2nd group : Chamomile capsules	Placebo (sugar capsule)	Rhode s	The mean Rhodes in-dex after intervention in the placebo, Ginger and Chamomile groups was 11.47 ± 6.43, 7.28 ± 3.74 and 5.73 ± 4.32, respec-tively (P < 0.05). Bon-ferroni test showed that there was no dif-ference regarding changes in scores (af-ter and before) be-tween Ginger and Chamomile and Gin-	5
					2x a day for 1 week				

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N	Title/ author/	Aim	Type of re-	Partici-	Group	Meas-	Results	Jadad
							ger and placebo, but this difference was significant between Chamomile and placebo groups (P < 0.05). This study shows that Chamomile capsules are more effective in nausea and vomiting during pregnancy compared to Ginger.	
13	Cardamom powder effect on nausea and vomiting during pregnancy (Gharyagh Zandi M, Ozgoli G, Nazem Ekbatani N, Alavi majd H, 2015) (Iran)	The aim of this study was to determine the effect of cardamom powder on the severity of nausea and vomiting in pregnant women	Quantitative _ Double blinded randomized clinical trial	120 pregnant women	Cardamom capsules (500 mg) placebo 3 times a day, for 4 days	PUQE	Findings showed that the frequency and duration of nausea and frequency of vomiting decreased significantly in the Cardamom or Cardamom powder group (p < 0.0001).	5

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RESULTS AND DISCUSSION

A search was carried out in 2 databases according to the predetermined inclusion criteria and 163 articles were obtained. Then filtering was carried out according to the inclusion and exclusion criteria and 15 articles were obtained. 2 articles were excluded because they used acupuncture methods as therapy. The final results after screening were 13 articles, then the author reviewed and extracted the articles obtained and carried out a final review. Of these, 4 RCTs were classified as having high bias due to lack of blinding. A total of 7 articles trialed ginger as an intervention, 2 articles used peppermint, 1 article used lemon, 1 article used quince, 1 article used pomegranate, and 1 article used cardamom as an intervention in clinical trials to relieve nausea and vomiting.

The article in this research is quantitative research with an *RCT design.* A total of 13 articles discussed different interventions and trials to compare the effectiveness of each herb in alleviating nausea and vomiting in pregnancy. Among them are:

1. Ginger
   Ginger *(Zingiber officinale)* is available in several preparations, such as capsules, fresh roots, powder, tablets and others. The antiemetic properties of ginger were first described in traditional Chinese medicine (Thomson, Corbin, & Leung, 2014) . A total of 6 articles compared ginger with other drugs and placebo, all studies reporting improvements in symptoms of nausea and vomiting.
2. Peppermint
   Two RCTs tested peppermint aroma therapy to reduce symptoms of nausea and vomiting. Ozgoli et al., 2018 (n = 56) and Pasha et al., 2011 (n = 60) compared peppermint aroma therapy oil with placebo and reported that there was no significant difference between therapy aroma oil and placebo.
3. Lemons
   Kia et al., (2014) examined the effect of aromatherapy for nausea and vomiting. The results of the study reported that there was a statistically significant difference on the second and fourth days (P = 0.017 and P = 0.039) . The average intensity of nausea and vomiting on the second and fourth days in the intervention group was significantly lower than the control group. Moreover, in intragroup comparisons by ANOVA with repeated measures, nausea and vomiting in five intervals, showed statistically significant differences in each group (P < 0.001 and P = 0.049).
4. Quinces
   Jafari-Dehkordi et al., 2017 (n = 110) from Iran conducted an experiment to prove the effect of quince on nausea and vomiting in pregnancy. The experiment was carried out to compare the effects of quince with vitamin B6 using the A randomized clinical trial method. PUQE scores at baseline and 7 and 14 days after intervention showed a significant reduction in nausea and vomiting scores in both groups compared to before and after treatment .
5. Pomegranate
   Abdolhosseini et al., 2017 (n = 74) conducted an experiment to evaluate the effectiveness of pomegranate with spearmint syrup on NVP. The PUQE-24 scale is used to

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assess NVP in the last 24 hours, then followed by evaluating the severity of nausea using VAS.

The decrease in PUQE-24 scores from baseline to day 7 and day 14 decreased significantly, based on the results of the Friedman test (P <0.001). The decrease in PUQE-24 scores was 4.7 ± 2 vs 2.5 ± 2.7 in the syrup group and in the control group on days 0 - 7 (P = 0.005) and 4.5 ± 2.8 vs 2.3 ± 2.6 on days 0-14 (P = 0.001) in each group. A slight increase was reported in PUQE-24 scores on days 7 to 14 in both groups (0.2 ± 2.5 vs. 0.16 ± 2.0; P = 0.2). However, there was no significant difference between the 2 groups.

6. Chamomile

Modares et al., 2012 (n = 105) conducted research to determine and compare the effect of ginger capsules, placebo and chamomile on NVP. This randomized triple-blind placebo-controlled trial was conducted on 105 pregnant women within 6-16 weeks of gestation with mild to moderate nausea and vomiting, who were referred to the prenatal care clinic at Dezyani, Gorgan, Northern hospital and health center. Iran during 2009-2010. The Rhodes index questionnaire was given to all participants to complete before bedtime for two weeks. In the first week no intervention was carried out and capsule prescription was started the following week. Subjects were divided randomly into 3 groups: In group 1, ginger capsules were consumed twice a day for one week, in group 2; twice daily chamomile capsules and in the placebo group, glucose capsules were prescribed. Scores were calculated and all data were entered into SPSS-16 software, analysis was carried out using analysis of variance, Will-Cockson.

The mean Rhodes index before intervention in the placebo, ginger and chamomile groups was 12.71 ± 5.88, 10.42 ± 0.76 and 11.19 ± 5.51, respectively. In addition, the average Rhodes index after intervention in the placebo, ginger and chamomile groups was 11.47 ± 6.43, 7.28 ± 3.74 and 5.73 ± 4.32, respectively (P < 0.05). The Bonferroni test showed that there was no difference in change scores (after and before) between ginger and chamomile and ginger and placebo, but this difference was significant between the chamomile and placebo groups (P <0.05). This study shows that Chamomile capsules are more effective in nausea and vomiting during pregnancy compared to Ginger.

7. Cardamom

Gharyagh et al., 2015 (n = 120) conducted this study to determine the effect of cardamom powder on the severity of nausea and vomiting in pregnant women. The intervention given was a capsule containing 500 mg of cardamom compared to placebo with a dose of 3 times a day for 4 days. The results of this study showed that the frequency and duration of nausea and the frequency of vomiting decreased significantly in the Cardamom or Cardamom powder group with (p <0.0001).

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