Use of lipid-lowering medicinal herbs during pregnancy: A systematic review on safety and dosage

Hojjat Rouhi-Boroujeni(1), Esfandiar Heidarian(2), Hamid Rouhi-Boroujeni(3), Minasadat Khoddami(4), Mojgan Gharipour(5), Mahmoud Rafieian-Kopaei(6)

Abstract

BACKGROUND: Hyperlipidemia is one of the important diseases in pregnancy that causes fetal abnormalities during pregnancy and after the birth. Unfortunately, the usual anti-fat drugs are associated with high morbidity in fetus and due to people's inclination towards taking herbs, it is required to identify side effects of medicinal herbs in pregnancy. The aim of this study was to present hypolipidemic herbs that would not any complications for mother and fetus.

METHODS: In this review article, the major electronic databases such as EBSCO, Central Register of Controlled Trials (CENTRAL), China Network Knowledge Infrastructure (CNKI), Cochrane, Google scholar, MEDLINE, SciVerse, Scopus, and Web of Science were searched using the key words “herbal” and “hyperlipidemia”, “herbal” and “pregnancy” matched by MeSH from their respective inceptions till September, 2016. Total of 1723 publications (145 review articles, 855 original research articles, and 723 abstracts) about the effect of herbals on hyperlipidemia and 682 publications (200 abstracts, 423 original research articles, and 59 review articles) about the effect of herbals in pregnancy were retrieved. At the end, a list of medicinal plants effective on hyperlipidemia alongside their effects on pregnancy was developed. Finally, the plants effective on hyperlipidemia and safe during pregnancy were determined and their dosage, complications, mechanism of action, and side effects were reported.

RESULTS: A total of 110 effective herbs on hyperlipidemia were identified and complications of 95 plants in pregnancy were studied. At last, among the 55 selected plants effective on hyperlipidemia and examined for pregnancy, we reported 12 herbs with their dosage and special considerations that can be used to treat hyperlipidemia during pregnancy.

CONCLUSION: Some medicinal plants can be used to treat hyperlipidemia during pregnancy without any significant side effects both on mother or fetus.

Keywords: Hyperlipidemias, Pregnancy Outcome, Fertility, Dyslipidemia, Herbals, Medicinal Plants, Oxidative Stress

Introduction

Exposure to elevated levels of cholesterol and oxidative stress due to products of cholesterol metabolism during fetal period has been shown to result in programmed death of fetal arterial cells with a predisposition to atherosclerosis later in life.1 Commonly, during reproductive years (about 2 decades), risk of cardiovascular diseases reduces. Besides, lipid and lipoproteins is not been measured routinely during pregnancy as gestational dyslipidemia is considered physiologic with little clinical significance.2 However, recent discoveries of fatty streaks in the aorta of 6-month-old fetuses and also evidences of aortic atherosclerosis in autopsy of deceased infants with normal levels of cholesterol born to mothers with
hypercholesterolemia, has highlighted the importance of correcting or preventing maternal dyslipidemia for the benefit of the mother and the child.\(^3\) Currently, no reference standards exist for lipid parameters during pregnancy, although it is well-known that pregnancy is a state of insulin resistance, which is reflected by lipoprotein lipid profiles. Pregnancy-related hypertriglyceridemia is rare, but it can be life threatening in some patients with genetic susceptibility. Complications can include acute pancreatitis, hyperviscosity syndrome, and potentially preeclampsia. Overweight and obese women are significantly more likely to exceed the pregnancy-related weight gain recommendations. Women with gestational diabetes and/or preeclampsia are also at increased risk for elevated triglyceride levels, development of chronic hypertension, recurrent gestational diabetes and/or overt diabetes, recurrent preeclampsia, and development of albuminuria later in life.\(^4\)

Two registered clinical trials are currently evaluating the effects of lipophilic statins to prevent preeclampsia in pregnancy. The true risk of congenital anomalies caused by statins in pregnancy has not been well confirmed in humans yet. However, because statins are category X, they should only be used in a research setting during pregnancy until more information is available. Fenofoibrate has been assigned to pregnancy category C by the Food and Drug Administration (FDA). Fenofoibrate should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. The side effects of statins and other antihyperlipidemic drugs in animal models of pregnancy showed delayed delivery, increased postimplantation loss, decreased litter size and pup birth weight, 40% pup survival rate, 4% neonate survival, no pup survival to weaning, and increased incidence of spina bifida, abortion, and fetal skeletal abnormalities (domed head, hunched shoulders, rounded body, abnormal chest, kyphosis, stunted fetuses, altered skeletal formation of ribs, sternabrae, vertebrae, and palate). Delayed delivery, decreased live births, and death of 17% of fetuses occurred at doses 18 times higher than the maximum human dosage. In addition, studies on animal reproductive system with doses 7 to 10 times higher than the recommended human dosage based on body surface area (BSA) have demonstrated to have embryocidal and teratogenic effects.\(^5,6\)

Lifestyle changes and glycemic control should be instituted if necessary. During pregnancy, a bile acid sequestrant can safely treat elevated cholesterol levels. Women must be educated about dietetic measures and body mass reduction even in preconception period. In addition, during pregnancy, mothers must be monitored and due to risk of pancreatitis in case of triglyceride above 11.5 mmol/l, other therapy options must be taken into account. In the last trimester of pregnancy, severe hypertriglyceridemia associated with pancreatitis can be treated with omega-3 fatty acids, parenteral nutrition, plasmapheresis, and other lipid-lowering agents.\(^7\)

The use of herbal medicines has been increasing in many developing and industrialized countries. More and more pregnant women are using herbal remedies to treat pregnancy-related problems due to cost-effectiveness of therapy and easy access to these products.\(^8\)

To date, over 200 plants have been recommended for treatment of hyperlipidemia. As with chemical drugs, medicinal plants can cause permanent damage to fetus. Therefore, despite people's willingness to use medicinal plants, certain precautions with these plants should be taken into account. In addition, couples are likely to use these plants on the verge of fertility to treat hyperlipidemia or other disorders.\(^9,10\)

Therefore, it is highly necessary for both physicians and patients to know which plants have optimal effects on hyperlipidemia during and before pregnancy without having side effects.\(^11\) The aim of this review article was to investigate the effect of plants on hyperlipidemia and plant-based side effects in pregnancy and fertility as well as to introduce the plants that are effective on hyperlipidemia during pregnancy.

### Materials and Methods

In this study, 2405 publications (204 review articles, 1278 original full text articles, and 923 abstracts) were retrieved. The major electronic databases including Web of Science, Scopus, PubMed, Google scholar, MEDLINE, EBSCO, China Network Knowledge Infrastructure (CNKI), and Cochrane Central Register of Controlled Trials (CENTRAL) were searched from their respective inceptions till September 2016. To identify herbs used to treat hyperlipidemia the following keywords were used and matched by the MeSH: “herbal in hyperlipidemia”, “botany in hyperlipidemia”, “herbal therapy in hypertriglyceridemia”, “systematic review of herbal in hypercholesterolemia”, “herbal medicine for hypercholesterolemia”, “herbal with anti-lipid effect”, “natural remedies for hyperlipidemia”, “herbal therapy for atherosclerosis and “hypo lipidemic diet”.

---

**Reference:**

1. **ARYA Atheroscler 2017; Volume 13; Issue 3**

---

**www.mui.ac.ir**

15 May
Total of 1723 publications (145 review articles, 855 original research articles, and 723 abstracts) were analyzed and their findings are registered in checklist 1.

We selected herbal drugs based on safety in pregnancy. All steps for searching and data extraction was based on the Cochrane protocol and checklist for systematic review (Figure 1).

In addition, to find evidence on the efficacy of herbals in pregnancy, fertility and infertility, 692 publications (200 abstracts, 423 original research articles, and 59 review articles) were analyzed. The headings that were used included “herbal in pregnancy”, “phytomedicine in pregnancy”, “side effects of herbal in pregnancy”, “herbals in pregnancy and lactation”, “herbal therapy in fertility”, “herbal therapy in infertility”, “herbal in infertility”, “phytomedicine in infertility”, “botany in pregnancy”, “medicinal plants in fertility”, “Chinese herbal in pregnancy”, “review of herbal in pregnancy”, and “Ayurvedic herbal in pregnancy”. The results of this investigation were registered in checklist 2. A plant was included in the analysis if its name appeared in at least two publications. Then, the plants effective on hyperlipidemia, fertility, and pregnancy were determined after the two checklists were integrated (Table 1). Finally, the plants effectiveness on hyperlipidemia and safety during pregnancy were determined and after analysis of 110 publications, their dosage, complications, mechanisms of action, and side effects were reported (Table 2).

**Results**

A total of 110 plants have been reported to be effective on hyperlipidemia and 95 plants were reported to be effective on fertility and pregnancy. Overall, 12 and 55 plants have been reported to be effective on lipid and safe during pregnancy, respectively. The potential side effects, dosage, and special considerations regarding these plants are shown in table 2. Moreover, 21 plants could be used in normal diet during pregnancy but were not recommended as medicinal plants.

**Discussion**

Hyperlipidemia can affect maternal and fetal health. Many side effects of chemical drugs on mother and fetus have led to prevention of their use during pregnancy. In this study, we found that the effective medicinal plants on hyperlipidemia contributed greatly to reducing oxidative stress via their antioxidant properties in addition to directly exerting hypolipidemic effects.

Reactive oxygen species cause damage to the structure of different cells and tissues including heart and vessels. Napoli et al. demonstrated that low levels of superoxide dismutase (SOD) in pregnant rabbits that had hyperlipidemia for over six months led to formation of fatty streaks in the aortic arch in their fetus.
### Table 1. Study of hypolipidemic plants and their effects on fertility and pregnancy

| Scientific name       | Common name | Family      | Part of use | Pre pregnancy effects                                                                 | Strong scientific evidence | Good scientific evidence | Fair scientific evidence | Weak scientific evidence | End result or explain certain points |
|-----------------------|-------------|-------------|-------------|----------------------------------------------------------------------------------------|-----------------------------|--------------------------|--------------------------|---------------------------|----------------------------------|
| *Achillea millefolium* | Yarrow      | Asteraceae  | Leaf        | May interfere with spermatogenesis                                                        | -                           | -                        | -                        | Abortifacient, emmenagogue         | Reduces fetal weight, increases placental weight, neurotoxic component, Potential harmful. Prohibited in pregnancy, even with nutritional values |
| *Allium cepa*         | Onion       | Liliaceae   | Leaf, bulb  | -                                                                                      | -                           | -                        | -                        | -                         | Lower risk of spontaneous preterm delivery In clinical and animal studies, at doses lower than 1 g, no complications were seen This plant was used to lower preeclampsia and hyperlipidemia during pregnancy Lower risk of spontaneous preterm delivery |
| *Allium sativum*      | Garlic      | Liliaceae   | Leaf, bulb  | Minimal risk – third trimester, crosses into the amniotic fluid                        | Minimal risk – third trimester, crosses into the amniotic fluid | -                        | -                        | Potential abortifacient, emmenagogue, uterine stimulant | |
| *Aloe vera*           | Cap aloe    | Liliaceae   | Leaf        | Antifertility effect in male                                                            | -                           | Potentially nephrotoxic, potential hepatic dysfunction | Potentially genotoxic, mutagenic, carcinogenic | Potential abortifacient, emmenagogue, uterine stimulant, abortifacient, and emmenagogue | Prohibited in pregnancy, even with nutritional values |
| *Anethum graveolens*  | Dill        | Apiaceae    | Leaf, seed  | Induces infertility without any effect on oocyte structure, decreases sexual potency and spermatogenesis in males | Uterine muscles of rat contracted in the presence of dill | -                        | -                        | -                         | Induction of labor |
| *Apium graveolens*    | Celery      | Umbellifera | Leaf        | -                                                                                      | -                           | -                        | -                        | -                         | -                                |
Table 1. Study of hypolipidemic plants and their effects on fertility and pregnancy (continue)

| Scientific name | Common name | Family | Part of use | Pre pregnancy effects | Strong scientific evidence | Good scientific evidence | Fair scientific evidence | Weak scientific evidence | End result or explain certain points |
|-----------------|-------------|--------|-------------|------------------------|---------------------------|------------------------|-----------------------|-----------------------|-------------------------------------|
| Artemisia vulgaris | Mugwort | Compositae | Leaf | - | Emmenagogue and abortifacient effects | - | - | - | Prohibited in pregnancy, even with nutritional values |
| Arctium loppa | Burdock | Compositae | Root | - | Oxytocic and uterine stimulant action | - | - | - | Prohibited in pregnancy, even with nutritional values |
| Avena sativa | Oats | Germinaceae | Fruit | - | - | - | - | - | No data available |
| Berberis vulgaria | Barberry | Berberidaceae | Root and fruit | - | - | - | May cause newborn jaundice (kernicterus) | Uterine stimulant | - |
| Boswellia carterii | Indian tree | Burceraeae | Resin | An aphrodisiac and a fertility promoting agent, increases sperm motility and sperm density | - | - | - | - | There is lack of evidence on safe use of boswellia during pregnancy and lactation |
| Calendula officinalis | Marigold | Compositae | Flower | Spermicide, anti-embryonic | - | - | Uterotonic effect | Emmenagogue, potential abortifacient, estrogenic | Topical-unknown |
| Chicorium intybus | Chicory | Compositae | Root | - | Reduces body weight, weight gain, body length and serum free fatty acids, uterine contractions | - | - | - | Prohibited in pregnancy, even with nutritional values |
| Citrus limon | Lemon | Rutaceae | Fruit | Anti-fertility effect in men | - | - | - | - | Lemon inhalation can be effective in reducing nausea and vomiting of pregnancy |
### Table 1. Study of hypolipidemic plants and their effects on fertility and pregnancy (continue)

| Scientific name | Common name | Family | Part of use | Pre pregnancy effects | Strong scientific evidence | Good scientific evidence | Fair scientific evidence | Weak scientific evidence | End result or explain certain points |
|-----------------|-------------|--------|-------------|-----------------------|----------------------------|--------------------------|--------------------------|---------------------------|---------------------------------------|
| Cinnamomum verum | Cinnamon | Lauraceae | Bark | Significant increase in reproductive organ weights, sperm motility, sperm count | - | - | - | - | - |
| Citrus paradisi | Grapefruit | Rutaceae | Fruit | - | Safe | - | - | - | - |
| Coffea Arabica | Arabica coffee | Rubiaceae | Seed | - | Spontaneous abortion, increased risk of stillbirth, low birth weight infants | - | Teratogenic compounds, impairs trace mineral absorption in fetus | - | Harmful to the fetus (crosses the placenta) |
| Commiphora mukul | Guggul | Burseraceae | Gum | - | - | - | - | - | Potential abortifacient, Emmenagogue, uterine stimulant |
| Cornus mas | Cranberry | Cornaceae | Fruit | - | - | - | - | - | Prohibited in pregnancy, even with nutritional values |
|                  |            |         |             |                       |                            |                          |                          |                          | Herbal compendium reported that cranberry is of minimal risk when consumed safe in food quantities |
|                  |            |         |             |                       |                            |                          |                          |                          | It is used to treat uterine tract infections during pregnancy |
**Table 1. Study of hypolipidemic plants and their effects on fertility and pregnancy (continue)**

| Scientific name | Common name | Family | Part of use | Pre pregnancy effects | Strong scientific evidence | Good scientific evidence | Fair scientific evidence | Weak scientific evidence | End result or explain certain points |
|-----------------|-------------|--------|-------------|-----------------------|---------------------------|-------------------------|------------------------|--------------------------|-------------------------------------|
| Crataegus microphylla C. Koch<sup>68,69</sup> | Howthorn | Rosaceae | Leaf, fruit | - | - | - | - | Uterine activity | - |
| Dioscorea nipponica<sup>70</sup> | Wild yam | Dioscoreaceae | Rhizome | - | Contractile agonist for the uterus, abortion | - | - | - | - |
| Eleutherococcus<sup>71-74</sup> | Ginseng | Araliaceae | Rhizome | - | - | - | - | - | Panax ginseng should be consumed with caution during pregnancy, especially during the first trimester |
| Equisetum arvense<sup>74</sup> | Horsetail | Equisetaceae | - | - | - | - | - | May cause autism | There are few studies about this plant and it is better not to be used in pregnancy |
| Eucalyptus globulus<sup>75,76</sup> | Eucalyptus | Myrtaceae | Leaf | Decreases fertility in male | - | - | - | - | There has been no adverse outcome in mice injected on days 6 and 15 of gestation |
| | | | | | | | | | There has been no evidence of adverse reproductive effects of eucalyptus oil in humans |
| | | | | | | | | | Topically, it is safe |
| | | | | | | | | | Fresh or dried fig fruit is likely safe in amounts found in food, but there is not enough information to know if it is safe in the larger amounts that are used as medicine |
| | | | | | | | | | Lower risk of spontaneous preterm delivery |

| Ficus carica<sup>77</sup> | Fig | Moraceae | Leaf and fruit | - | - | - | - | - | - |
## Medicinal herbs and lipid-lowering in pregnancy

### Table 1. Study of hypolipidemic plants and their effects on fertility and pregnancy (continue)

| Scientific name                  | Common name | Family       | Part of use | Pre pregnancy effects | Strong scientific evidence | Good scientific evidence | Weak scientific evidence | End result or explain certain points |
|----------------------------------|-------------|--------------|-------------|------------------------|----------------------------|--------------------------|---------------------------|---------------------------------------|
| **Ginco biloba**<sup>76-80</sup> | Ginkgo      | Ginkgoaceae  | Leaf        | -                      | Malformation s including round shaped eye and orbits, syndactyly, malformed pinnae, nostrils, lips and jaws. | Unsafe when adulterated with colchicine, antiplatelet, emmenagogue, hormonal changes | Ginkgo leaf has antiplatelet activity, which may be of concern during labor as ginkgo use could prolong bleeding time | Emmenagogue, hormonal changes | Prohibited in pregnancy, even with nutritional values |
| **Glycine soja**<sup>81,82</sup> | Soy         | Leguminosae  | Seed        | -                      | -                          | -                        | -                         | -                                     | Prohibited in pregnancy, even with nutritional values |
| **Glycyrrhiza glabra**<sup>83,84</sup> | Licorice    | Leguminosae  | Root        | -                      | -                          | Likely to be born before 38 weeks of gestation, risk of pre-term pregnancy (before 37 weeks), does not affect birth weight, does not affect maternal blood pressure | Potential abortifacient, emmenagogue, uterine stimulant, causes high prolactin and estrogen levels, risk of pre-term pregnancy (before 37 weeks), does not affect birth weight | -                                     |
| **Hibiscus sabdariffa**<sup>85,86</sup> | Hibiscus    | Malvaceae    | Flower      | -                      | -                          | -                        | -                         | Decrease both pregnancy weight gain and postpartum weight loss, decrease maternal fluid and food intake with increased plasma sodium and corticosterone concentration | There is some evidence that hibiscus might start menstruation, and this could cause a miscarriage. Aromatic ketones may present some hazard |
Table 1. Study of hypolipidemic plants and their effects on fertility and pregnancy (continue)

| Scientific name | Common name       | Family       | Part of use | Pre pregnancy effects | Strong scientific evidence | Good scientific evidence | Fair scientific evidence | Weak scientific evidence | End result or explain certain points |
|-----------------|-------------------|--------------|-------------|------------------------|----------------------------|--------------------------|--------------------------|--------------------------|-------------------------------------|
| Lavandula stoechas | Lavender          | Labiatae     | Leaf        | -                      | -                          | -                        | -                        | -                        | Emmenagogue effects
| Malus orientalis | Apple             | Rosaceae     | Fruit       | -                      | -                          | -                        | -                        | -                      | Safe in pregnancy
| Medicago sativa  | Alfalfa           | Leguminaceae | Leaf        | Antifertility in man   | Estrogenic activity        | -                        | -                        | -                        | Emmenagogue, antigonadotrophic activity
| Nigella sativa   | Black cumin       | Ranunculaceae| Seed        | Nigella sativa oil L, (Ranunculaceae) and Cinnamon zeylanicum J. Presl (Lauraceae) were found to enhance fertility | -                          | -                        | -                        | -                      | Minimal risk in food
| Oenothera biennii | Evening primrose  | Onagraceae   | Seed        | Teratogenic and induces labor15 | May induce labor but effectiveness is unclean, increased risk of pregnancy complication (evidence level 1b), prolonged rupture of membranes, oxytocin augmentation, arrest of descent, vacuum extraction | -                        | -                        | -                        | Oral administration of evening primrose oil from the 37th gestational week until birth does not shorten gestation or decrease the overall length of labor Further, the use of orally administered evening primrose oil may be associated with an increase in the incidence of prolonged rupture of membranes, oxytocin augmentation, arrest of descent, and vacuum extraction |
Table 1. Study of hypolipidemic plants and their effects on fertility and pregnancy (continue)

| Scientific name       | Common name | Family      | Part of use | Pre pregnancy effects | Strong scientific evidence | Good scientific evidence | Fair scientific evidence | Weak scientific evidence | End result or explain certain points |
|-----------------------|-------------|-------------|-------------|-----------------------|---------------------------|--------------------------|-------------------------|-------------------------|-------------------------------------|
| Ocimum basilicom      | Basil       | Labiatae    | Leaf        | -                     | -                         | -                        | -                       | Fair scientific             | Emmenagogue, abortifacient, mutagenic |
| Peganum harmala       | Harmala     | Zygophyllaceae | Seed       | -                     | -                         | -                        | -                       | -                       | Prohibited in pregnancy, even with nutritional values |
| Persea Americana      | Avocado     | Lauraceae   | Seed, fruit | -                     | -                         | -                        | -                       | -                       | There is not enough reliable information about the safety of taking avocado as medicine if you are pregnant or breast-feeding, stay on the safe side and stick to food amounts |
| Petroselinum crispus  | Parsley     | Umbelliferae | Leaf        | -                     | Abortifacient             | -                        | -                       | -                       | Emmenagogue, estrogenic, uterine stimulant constituent |
| Plantago psyllium     | Plantain    | Plantaginaceae | Leaf, seed | -                     | -                         | -                        | -                       | -                       | Psyllium powder could significantly decrease the number of surgeries resulting from anorectal complications, hemorrhoid diseases, anal fissure and constipation It is in concordance of several other studies which emphasized the effect of fiber in diet on preventing constipation in the course of pregnancy If used in low amounts in diet, it causes no problem Sweet cherry is safe for pregnant and breast-feeding women in food amounts, but larger medicinal amounts should be avoided until more is known |
| Purtolaca oleracea    | Purslane    | Purtulaceae  | Leaf        | Antifertility effect in male rat | -                         | Abortifacient             | -                       | -                       | -                                   |
| Pronus avium          | Cherry      | Rosaceae    | Fruit, cherry tails | -                     | -                         | -                        | -                       | -                       | -                                   |
| Scientific name | Common name | Family | Part of use | Pre pregnancy effects | Strong scientific evidence | Good scientific evidence | Fair scientific evidence | Weak scientific evidence | End result or explain certain points |
|----------------|-------------|--------|-------------|-----------------------|-----------------------------|---------------------------|--------------------------|-------------------------|-------------------------------------|
| Punica granatum | Pomegranate | Punicaceae | Fruit, leaf | -                     | -                           | -                         | -                        | -                       | Use cautiously in pregnant and breastfeeding women, due to a lack of safety data |
| Rhus coriaria L. | Sumac | Anacardiaceae | Fruit | -                     | -                           | -                         | -                        | -                       | Cautionary herb during pregnancy |
| Solanum lycopersicum | Tomato | Solanaceae | Fruit | -                     | -                           | -                         | -                        | -                       | Safe in pregnancy |
| Tea sinensis | Tea, green tea | Theaceae | Leaf | -                     | Spontaneous abortion, increased risk of stillbirth, low birth weight infants | -                         | -                        | -                       | Three cups or more of tea per day was associated with an increased risk of spina bifida |
| Tarraxacum officinale | Dandelion | Compositae | Root, leaf | -                     | -                           | -                         | -                        | -                       | Minimal risk in food amounts No negative effects on humans have been reported during pregnancy or lactation, in children, or in combination with pharmaceutical drugs |
Table 1. Study of hypolipidemic plants and their effects on fertility and pregnancy (continue)

| Scientific name | Common name | Family      | Part of use | Pre pregnancy effects | Strong scientific evidence | Good scientific evidence | Fair scientific evidence | Weak scientific evidence | End result or explain certain points |
|-----------------|-------------|-------------|-------------|-----------------------|---------------------------|--------------------------|--------------------------|--------------------------|-------------------------------------|
| Terminalia chebula | Haritaki    | Combretaceae | Fruit       | -                     | -                         | -                        | -                        | -                        | There is some evidence that Terminalia arjuna is possibly unsafe during pregnancy. The safety of the other two species during pregnancy is unknown. It is best to avoid using any terminalia species. Topically, it is safe. |
| Thymus vulgaris | Thyme       | Labiatae    | Leaf        | Decreases fertility in male | -                         | -                        | -                        | -                        | Emmenagogue, abortifacient Emmenagogue. |
| Trigonella foenum-graecum | Fenugreek | Leguminosae | Seed        | -                     | -                         | -                        | -                        | -                        | Minimal risk in food. Use of nettle should be avoided during pregnancy or lactation. |
| Urtica dioica | Nettle      | Urticaceae  | Root, leaf  | Increasing fertility in women and men, increase the quality of spermatozoa and inhibits nicotine-induced adverse effects on sperm parameters. | Induce uterine stimulation | -                        | -                        | -                        | Use of vitex agnus cactus (VAC) should be avoided during pregnancy or lactation. |
| Vitex doniana | Black plum  | Lamiaceae   | Fruit       | Due to treatment of hyperprolactinemia, premenstrual syndrome, abnormal menstrual cycle, amenorrhea, mastodynia, this herb can induce fertility in woman | Uterine muscle contractions and also potentiated the contractile effects of prostaglandins, ergometrine and oxytocin | -                        | -                        | -                        | Use of vitex agnus cactus (VAC) should be avoided during pregnancy or lactation. |
### Table 1. Study of hypolipidemic plants and their effects on fertility and pregnancy (continue)

| Scientific name         | Common name | Family         | Part of use | Pre pregnancy effects                                      | Strong scientific evidence | Good scientific evidence | Fair scientific evidence | Weak scientific evidence | End result or explain certain points                                                                                                                                 |
|-------------------------|-------------|----------------|-------------|------------------------------------------------------------|-----------------------------|--------------------------|--------------------------|--------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| *Vitis vinifera*¹²⁹, ¹³⁰ | Grape       | Vitaceae       | Fruit, leaf, seed | -                                                          | -                           | -                        | -                        | -                        | Topically, it is safe. The grape seed extract was non-mutagenic in mice. There are no adverse outcomes in mice. Prohibited in pregnancy, even with nutritional values. |
| *Withania somnifera* (L.) *Dunal*¹³¹, ¹³² | Winter cherry | Solanaceae     | Fruit       | Increasing sperm motility and treatment of libido, sexual performance, sexual vigor, and penile erectile dysfunction | Abortion                    | -                        | -                        | -                        |                                         |
| *Zingiber officinalis*¹³³, ¹⁴¹ | Ginger      | Zingiberaceae  | Root        | Minimal risk (up to 1000 mg of dried ginger per day), unlikely cause of spontaneous abortion | Does not increase rates of major malformations | Non-mutagenic, non-teratogenic Mutagenic constituents Anti-mutagenic constituents Potential embryotoxicity | -                        | Non-teratogenic. Ginger could be considered a harmless and possibly effective alternative option for women suffering from nausea and vomiting of pregnancy (NVP) |
| *Zizyphus vulgaris*¹⁴², ¹⁴³ | Jujuba      | Rhamnaceae     | Fruit       | Antifertility/contraception, antisteroidogenic activity and hence fertility in adult female mice It was found to arrest the normal estrus cycle of adult female mice at diestrus stage and reduced the wet weight of ovaries significantly Hematological profiles, biochemical estimations of whole blood and serum remained unaltered in extract-treated mice | Consumer safety in pregnancy has not been established | -                        | -                        | -                        |                                         |
### Table 2. Hypolipidemic herbs that seem safe in pregnancy

| Common name | Dosage | Side effects | Special notification |
|-------------|--------|--------------|----------------------|
| Onion**     | 50 g of fresh onions or 5 g of dried drug | No health hazards or side effects are known in conjunction with the proper administration of designated therapeutic dosages. The intake of large quantities can lead to stomach complaints. | Popular; pressed juice and onion syrup, made of 500 g onions, 500 g water, 100 g honey and 350 g sugar. |
| Garlic**    | 300 mg dry powder or 2 g fresh garlic | Abdominal discomfort, nausea, vomiting, diarrhea and a feeling of fullness have occurred with garlic therapy. | Fresh garlic is not recommended in pregnancy. |
| Lemon**     | 1 g dry powder infuse | No health hazards or side effects are known in conjunction with the proper administration of designated therapeutic dosages. | Avoid the use of commercial liquid products because additional ingredients or fake lemon. |
| Cranberry** | 10 ripe fruit twice a day after meal, 10 ml cranberry juice twice daily after meal | Mild stomach upset and diarrhea. | It is better to be soaked in water. |
| Fig**       | 5 fruit twice daily | No health hazards or side effects are known in conjunction with the proper administration of designated therapeutic dosages. | Apple seeds are highly toxic, avoid taking it. |
| Apple**     | 3 fruit/day | No health hazards or side effects are known in conjunction with the proper administration of designated therapeutic dosages. | The dose should be taken 30 min to one hour after taking other medications. |
| Psyllium**  | 1 g in 100 ml water twice daily | Allergic reactions ranging from sneezing to chest congestion and wheezing were reported in three nurses after psyllium use. | Storage: pomegranate should be sealed in containers and protected from moisture. |
| Cherry**    | 2-5 g dry powder, 10-15 fresh fruit | No health hazards or side effects are known in conjunction with the proper administration of designated therapeutic dosages. | Storage: pomegranate should be sealed in containers and protected from moisture. |
| Pomegranate | 10 ml of juice twice a day or 20 g pomegranate seeds twice a day or 1 tablet/day (90 mg ellagic acid) | No health hazards or side effects are known in conjunction with the proper administration of designated therapeutic dosages. | - |
| Tomato**    | Three tomatoes a day, or 1 g dry powder three times/day | No health hazards or side effects are known in conjunction with the proper administration of designated therapeutic dosages. | - |
| Grape**     | 10 g fresh fruit, 1 g dry powder | No health hazards or side effects are known in conjunction with the proper administration of designated therapeutic dosages. | - |
| Ginger      | 1 g dry powder/day | Increases appetite | Not recommended more than 1 g/day. |
Besides, Rumbold et al.\textsuperscript{159} and Mistry et al.\textsuperscript{160} investigated the role of antioxidants in reducing oxidation of fatty acids and decrease in fatty streaks in fetal heart. Clinical trials have demonstrated that oxidative stress due to hyperlipidemia during pregnancy causes circulatory disorders in fetus, delayed fetal development, and increased eclampsia.

Moreover, Jenkins et al. reported that there was significant association between decrease in SOD and increase in miscarriage in pregnant women with hyperlipidemia.\textsuperscript{101} According to the evidence, the antioxidant properties of the plants are due to polyphenols, flavonoids, flavonols, gallic acid, and anthocyanins that cause decrease in malondialdehyde (MDA) and increase in SOD, catalase, and glutathione peroxidase (GPX).\textsuperscript{102}

Some of the potent antioxidants that not only improve hyperlipidemia in pregnant women but also play a role in protecting the cardiovascular system of the fetus and the mother are as follows: allyl propyl disulphide, sterol, saponin, and quercetin in onion, allicin, allyl di- and trisulphide, alliin, ajones, vinylthiins in garlic, cyanidin, malvidin,peonidin, pelargonidin, petunidin and bioflavonoids in cranberry, bioflavonoids, polyphenols and triterpenoids, quercetin, catechin, phloridzin and pelargonidin, petunidin and bioflavonoids in pomegranate, vitamins A, B, and E and lycopene in tomato, flavonoids, flavonols, gallic acid, and echinocystic acid, unicic acid, coumaroylquinic acid) in cherry, punicalagins, ellagic acid, phytoestrogens, and anthocyanins in pomegranate, vitamins A, B, and E and lycopene in tomato, anthocyanin, vitamins A and E, polyphenols, oligostibenes, and ampelopsins in red grapes and zebrubone in ginger.\textsuperscript{103}

## Conclusion

There are effective plants that can play a fundamental role in cardiovascular health in mother and fetus by reducing hyperlipidemia.

## Acknowledgments

This article has been derived from the PhD thesis of the first author and financially supported by the Research Deputy of Shahrekord University of Medical Sciences, Shahrekord, Iran.

## Conflict of Interests

Authors have no conflict of interests.

## References

1. Dukic A, Zivancevic-Simonovic S, Varjacic M, Dukic S. Hyperlipidemia and pregnancy. Med Pregl 2009; 62(Suppl 3): 80-4.
2. Laelago T, Yohannes T, Lemango F. Prevalence of herbal medicine use and associated factors among pregnant women attending antenatal care at public health facilities in Hossana Town, Southern Ethiopia: Facility based cross sectional study. Arch Public Health 2016; 74; 7.
3. Potter JM, Nestel PJ. The hyperlipidemia of pregnancy in normal and complicated pregnancies. Am J Obstet Gynecol 1979; 133(2): 165-70.
4. Maymunah AO, Kehinde O, Abidoye G, Oluwatosin A. Hypercholesterolaemia in pregnancy as a predictor of adverse pregnancy outcome. Afr Health Sci 2014; 14(4): 967-73.
5. Kusters DM, Hassani LH, van de Post JA, Wiegman A, Wijburg FA, Kastelein JJ, et al. Statin use during pregnancy: A systematic review and meta-analysis. Expert Rev Cardiovasc Ther 2012; 10(3): 363-78.
6. Godfrey LM, Erramouss J, Cleveland KW. Teratogenic risk of statins in pregnancy. Ann Pharmacother 2012; 46(10): 1419-24.
7. Ali-Shtayeh MS, Jamous RM, Jamous RM. Plants used during pregnancy, childbirth, postpartum and infant healthcare in Palestine. Complement Ther Clin Pract 2015; 21(2): 84-93.
8. John LJ, Shantakumari N. Herbal medicines use during pregnancy: A review from the Middle East. Oman Med J 2015; 30(4): 229-36.
9. Rouhi-Boroujeni H, Rouhi-Boroujeni H, Gharipour M, Mohammadizadeh F, Ahmadi S, Rafieian-Kopaei M. Systematic review on safety and drug interaction of herbal therapy in hyperlipidemia: A guide for internist. Acta Biomed 2015; 86(2): 130-6.
10. Rouhi-Boroujeni H, Rouhi-Boroujeni H, Heidarian E, Mohammadizadeh F, Rafieian-Kopaei M. Herbs with anti-lipid effects and their interactions with statins as a chemical anti- hyperlipidemia group drugs: A systematic review. ARYA Atheroscler 2015; 11(4): 244-51.
11. Napoli C, Witztum JL, Calara F, de Nigris F, Palinski W. Maternal hypercholesterolemia enhances atherogenesis in normocholesterolemic rabbits, which is inhibited by antioxidant or lipid-lowering intervention during pregnancy: an experimental model of atherogenic mechanisms in human fetuses. Circ Res 2000; 87(10): 946-52.
12. Montanari T, de Carvalho JE, Dolder H. Antispermatogenic effect of Achillea millefolium L. in mice. Contraception 1998; 58(5): 309-13.
13. Millet Y, Jouglard J, Steinmetz MD, Tognetti P, Joanny P, Arditti J. Toxicity of some essential plant oils. Clinical and experimental study. Clin Toxicol 1981; 18(12): 1485-98.
14. Bonkovsky HL, Cable EE, Cable JW, Donohue SE, White EC, Greene YJ, et al. Phytoremediative properties of the terpenes camphor, pinene, and thujone (with a note on historic implications for
absinthe and the illness of Vincent van Gogh). Biochem Pharmacol 1992; 43(11): 2359-68.
15. Ige SF, Akhigbe RE. Common onion (Allium cepa) extract reverses cadmium-induced organ toxicity and dyslipidaemia via redox alteration in rats. Pathophysiology 2013; 20(4): 269-74.
16. McGuffin M, Hobbs C, Upton R, Goldberg A. Botanical safety handbook. Boca Raton, FL: CRC Press; 1997.
17. Bercaw J, Maheshwari B, Sangi-Hagheypkar H. The use during pregnancy of prescription, over-the-counter, and alternative medications among Hispanic women. Birth 2010; 37(3): 211-8.
18. El-Sayyad HI, Abou-El-Naga AM, Gadalila AA, Bakr IH. Protective effects of Allium sativum against defects of hypercholesterolemia on pregnant rats and their offspring. Int J Clin Exp Med 2010; 3(2): 152-63.
19. Ziaei S, Hantoshzadeh S, Rezasoltani P, Lamyian M. The effect of garlic tablet on plasma lipids and platelet aggregation in nulliparous pregnancies at high risk of preeclampsia. Eur J Obstet Gynecol Reprod Biol 2001; 99(2): 201-6.
20. Mennella JA, Johnson A, Beauchamp GK. Garlic ingestion by pregnant women alters the odor of amniotic fluid. Chem Senses 1995; 20(2): 207-9.
21. Oyewopo A, Oremosu A, Akang E, Noronha C, Oyewopo A, Oremosu A, Akang E, Noronha C, Oyewopo A, Oremosu A, Akang E, Noronha C. Antifertility effect of ethanolic extract of Aloe Vera (Aloe barbadensis) aqueous leaf extract on testicular weight, sperm count and motility of adult male Sprague-Dawley rats. Journal of American Science 2011;7(4): 31-4.
22. Seetharam YN, Sujeeth H, Jyothishwaran G, Barad A, Sharanabasappa G, Umareddy B, et al. Antifertility effect of ethanolic extract of Amalakiyadi churna in male albino mice. Asian J Androl 2003; 5(3): 247-50.
23. Suzuki I, Saito H, Inoue S, Migita S, Takahashi T. Purification and characterization of two lectins from Aloe arborescens Mill. J Biochem 1979; 85(1): 163-71.
24. Nath D, Sethi N, Singh RK, Jain AK. Commonly used Indian abortifacient plants with special reference to their teratologic effects in rats. J Ethnopharmacol 1992; 36(2): 147-54.
25. Farnsworth NR, Bingel AS, Cordell GA, Crane FA, Fong HH. Potential value of plants as sources of new antifertility agents I. J Pharm Sci 1975; 64(4): 535-98.
26. Malhezeman M, Mojaba M, Elham H, Farnaz G, Ramin M. Anti-fertility effects of different fractions of Anethum graveolens L. extracts on female rats. Afr J Tradit Complement Altern Med 2012; 9(3): 336-41.
27. Monsefi M, Ghasemi M, Bahaoddini A. The effects of Anethum graveolens L. on female reproductive system. Phytother Res 2006; 20(10): 865-8.
28. Monsefi M, Ghasemi M, Bahaoddini A. The effects of anethum graveolens L. on female reproductive system of rats. DARU J Pharm Sci 2006; 14(3): 131-5.
29. Monsefi M, Ghasemi A, Alaee S, Aliabadi E. Effects of Anethum graveolens L. (dill) on oocyte and fertility of adult female rats. J Reprod Infertil 2015; 16(1): 10-7.
30. Akbari M, Javadnoori M, Sirahpoosh A, Afshari P, Haghhighi MH, Lake E. Comparison the effect of anethum graveolens and oxytocin on induction of labor in term pregnancy: A randomized clinical trial. Jundishapur J Nat Pharm Prod 2016; 11(1): e27876.
31. Wilkinson JM. What do we know about herbal morning sickness treatments? A literature survey. Midwifery 2000; 16(3): 224-8.
32. Tigno XT, Gumila E. In vivo microvascular actions of Artemisia vulgaris L. in a model of ischemia-reperfusion injury in the rat intestinal mesentery. Clin Hemorheol Microcirc 2000; 23(2-4): 159-65.
33. Tigno XT, de Guzman F, Flora AM. Phytochemical analysis and hemodynamic actions of Artemisia vulgaris L. Clin Hemorheol Microcirc 2000; 23(2-4): 167-75.
34. Singh R, De S, Belkheir A. Avena sativa (Oat), a potential neutraceutical and therapeutic agent: An overview. Crit Rev Food Sci Nutr 2013; 53(2): 126-44.
35. Gasparis S, Nadolska-Orczyk A. Oat (Avena sativa L.). Methods Mol Biol 2015; 1223: 143-53.
36. Criquet M, Roure R, Dayan L, Nollent V, Bertin C. Safety and efficacy of personal care products containing colloidal oatmeal. Clin Cosmet Investig Dermatol 2012; 5: 183-93.
37. Chan E. Displacement of bilirubin from albumin by berberine. Biol Neonate 1993; 63(4): 201-8.
38. Khalid Nasier M, Nayef Bataineh H, Mohydeen Bataineh Z, Daradka HM. Effect of frankincense (Boswellia thurifera) on reproductive system in adult male rat. J Health Sci 2007; 53(4): 365-70.
39. Kulkarni RR, Patki PS, Jog VP, Gandage SG, Patwardhan B. Treatment of osteoarthritis with a herbonimerial formulation: A double-blind, placebo-controlled, cross-over study. J Ethnopharmacol 1991; 33(1-2): 91-5.
40. Jellin JF, Gregory P, Batz F. Natural Medicines Comprehensive Database. Stockton, CA: Therapeutic Research Faculty; 2000. p. 1521.
41. Shipochliev T. Uterotonic action of extracts from a group of medicinal plants. Vet Med Nauki 1981; 18(4): 94-8.
42. Mennitti LV, Oyama LM, de Oliveira JL, Hachul AC, Santamarina AB, de Santana AA, et al. Oligofructose supplementation during pregnancy and lactation impairs offspring development and...
alters the intestinal properties of 21-d-old pups. Lipids Health Dis 2014; 13: 26.

43. Kulkarni TR, Kothekar MA, Mateenuddin M. Study of anti-fertility effect of lemon seeds (Citrus limonum) in female albino mice. Indian J Physiol Pharmacol 2005; 49(3): 305-12.

44. Nwoha PU. The immobilization of all spermatozoa in vitro by bitter lemon drink and the effect of alkaline pH. Contraception 1992; 46(6): 537-42.

45. Yavari KP, Safajou F, Shahnazi M, Nazemiyeh H. The effect of lemon inhalation aromatherapy on nausea and vomiting of pregnancy: A double-blinded, randomized, controlled clinical trial. Iran Red Crescent Med J 2014; 16(3): e14360.

46. Kuhn MA, Winston D. Winston & Kuhn’s herbal therapy and supplements: A scientific and traditional approach. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2012.

47. Shah AH, Al-Shareef AH, Ageel AM, Qureshi S. Toxicity studies in mice of common spices, Cinnamomum zeylanicum bark and Piper longum fruits. Plant Foods Hum Nutr 1998; 52(3): 231-9.

48. Akour A, Kasabri V, Afifi PU, Bulatova N. The use of medicinal herbs in gynecological and pregnancy-related disorders by Jordanian women: A review of folkloric practice vs. evidence-based pharmacology. Pharm Biol 2016; 54(9): 1901-18.

49. Lindhout D, Omtzigt JG. Pregnancy and the risk of teratogenicity. Epilepsia 1992; 33(Suppl 4): S41-S48.

50. Cameron EL. Pregnancy and olfaction: a review. Front Psychol 2014; 5: 67.

51. Lepik K. Safety of herbal medications in pregnancy. Can Pharm J 1997; 130(3): 29-33.

52. Dugoua JJ, Seeley D, Perri D, Cooley K, Forelli T, Mills E, et al. From type 2 diabetes to antioxidant activity: A systematic review of the safety and efficacy of common and cassia cinnamon bark. Can J Physiol Pharmacol 2007; 85(9): 837-47.

53. Zaidi SF, Aziz M, Muhammad JS, Kadowaki M. Review: Diverse pharmacological properties of Cinnamomum cassia: A review. Pak J Pharm Sci 2015; 28(4): 1433-8.

54. Hajhoseini L. Importance of optimal fiber consumption during pregnancy. International Journal of Women’s Health and Reproduction Sciences 2013; 1(3): 76-9.

55. Arguelles N, Alvarez-Gonzalez I, Chamorro G, Madrigal-Bujaidar E. Protective effect of grapefruit juice on the teratogenic and genotoxic damage induced by cadmium in mice. J Med Food 2012; 15(10): 887-93.

56. Rasch V. Cigarette, alcohol, and caffeine consumption: Risk factors for spontaneous abortion. Acta Obstet Gynecol Scand 2003; 82(2): 182-8.

57. Wisborg K, Kesmodel U, Bech BH, Hedegaard M, Henriksen TB. Maternal consumption of coffee during pregnancy and stillbirth and infant death in first year of life: prospective study. BMJ 2003; 326(7386): 420.
72. Chan LY, Chiu PY, Lau TK. Embryotoxicity study of ginsenoside Rc and Rein in vitro rat whole embryo culture. Reprod Toxicol 2004; 19(1): 131-4.
73. Choi J, Kim TH, Choi TY, Lee MS. Ginseng for health care: A systematic review of randomized controlled trials in Korean literature. PLoS One 2013; 8(4): e59978.
74. Alsaad AM, Fox C, Koren G. Toxicology and teratology of the active ingredients of professional therapy MuscleCare products during pregnancy and lactation: A systematic review. BMC Complement Altern Med 2015; 15: 40.
75. Dreisinger N, Zane D, Etwaru K. A poisoning of topical importance. Pediatr Emerg Care 2006; 22(12): 827-9.
76. Darben T, Cominos B, Lee CT. Topical eucalyptus oil poisoning. Australas J Dermatol 1998; 39(4): 265-7.
77. Duke JA. Handbook of medicinal herbs. Boca Raton, FL: CRC Press; 2002.
78. Zehra U, Tahir M, Lone KP. Ginkgo biloba induced malformations in mice. J Coll Physicians Surg Pak 2010; 20(2): 117-21.
79. Dugoua JJ, Mills E, Perri D, Koren G. Safety and efficacy of ginkgo (Ginkgo biloba) during pregnancy and lactation. Can J Clin Pharmacol 2006; 13(3): e277-e284.
80. Leung AY. Encyclopedia of common natural ingredients used in food, drugs, and cosmetics. New York, NY: Wiley; 1980.
81. Natarajan SS, Xu C, Bae H, Caperna TJ, Garrett WM. Characterization of storage proteins in wild (Glycine soja) and cultivated (Glycine max) soybean seeds using proteomic analysis. J Agric Food Chem 2006; 54(8): 3114-20.
82. Benaiges A, Marcet P, Armengol R, Betes C, Girones E. Study of the refirming effect of a plant complex. Int J Cosmet Sci 1998; 20(4): 223-33.
83. Strandberg TE, Jarvenpaa AL, Vanhanen H, McKeigue PM. Birth outcome in relation to licorice consumption during pregnancy. Am J Epidemiol 2001; 153(11): 1085-8.
84. Rees WD, Rhodes J, Wright JE, Stamford LF, Bennett A. Effect of deglycyrhizinated liquorice on gastric mucosal damage by aspirin. Scand J Gastroenterol 1979; 14(5): 605-7.
85. Iyare EE, Iyare FE. Maternal consumption of aqueous extract of hibiscus sabdariffa during pregnancy attenuates pregnancy weight gain and postpartum weight loss. Afr J Biomed Res 2007; 10(3): 257-61.
86. Iyare EE, Adegoke OA. Maternal consumption of an aqueous extract of Hibiscus sabdariffa during lactation accelerates postnatal weight and delays onset of puberty in female offspring. Niger J Physiol Sci 2008; 23(1-2): 89-94.
87. Henley DV, Lipson N, Korach KS, Bloch CA. Prepubertal gynecomastia linked to lavender and tea tree oils. N Engl J Med 2007; 356(5): 479-85.
88. Basch E, Foppa I, Liebowitz R, Nelson J, Smith M, Sollars D, et al. Lavender (Lavandula angustifolia Miller). J Herb Pharmacother 2004; 4(2): 63-78.
89. Ernst E. Herbal medicinal products during pregnancy: Are they safe? BJOG 2002; 109(3): 227-35.
90. Farnsworth NR, Bingel AS, Cordell GA, Crane FA, Fong HS. Potential value of plants as sources of new antifertility agents II. J Pharm Sci 1975; 64(5): 717-54.
91. Casanova M, You L, Gaido KW, Archibeque-Engle S, Janssen DB, Heck HA. Developmental effects of dietary phytoestrogens in Sprague-Dawley rats and interactions of genistein and daidzein with rat estrogen receptors alpha and beta in vitro. Toxicol Sci 1999; 51(2): 236-44.
92. Aqel M, Shaheen R. Effects of the volatile oil of Nigella sativa seeds on the uterine smooth muscle of rat and guinea pig. J Ethnopharmacol 1996; 52(1): 23-6.
93. Salarinia R, Rakhshandeh H, Oliaei D, Gul GS, Ghorbani A. Safety evaluation of Phytovagex, a pessary formulation of Nigella sativa, on pregnant rats. Avicenna J PhytoMed 2016; 6(1): 117-23.
94. Kenny FS, Pinder SE, Ellis IO, Gee JM, Nicholson RI, Bryce RP, et al. Gamma linolenic acid with tamoxifen as primary therapy in breast cancer. Int J Cancer 2000; 85(5): 643-8.
95. Dove D, Johnson P. Oral evening primrose oil: Its effect on length of pregnancy and selected intrapartum outcomes in low-risk nulliparous women. J Midwifery Nurs 2016; 44(3): 229-35.
96. McFarlin BL, Gibson MH, O’Rear J, Harman P. A national survey of herbal preparation use by nurse-midwives for labor stimulation. Review of the literature and recommendations for practice. J Nurse Midwifery 1999; 44(3): 205-16.
97. Brinker FJ. Herb contraindications and drug interactions: With appendices addressing specific conditions and medicines. Sandy, OR: Eclectic Medical Publications; 1998.
98. Berdai MA, Labib S, Harandou M. Peganum harmala L. Intoxication in a pregnant woman. Case Rep Emerg Med 2014; 2014: 783236.
99. Blotman F, Maheu E, Wulwik A, Caspard H, Lopez A. Efficacy and safety of avocado/soybean unsaponifiables in the treatment of symptomatic osteoarthritis of the knee and hip. A prospective, multicenter, three-month, randomized, double-blind, placebo-controlled trial. Rev Rhum Engl Ed 1997; 64(12): 825-34.
100. Rezazad M, Farokhi F. Protective effect of Petroserinum crispum extract in abortion using...
prostaglandin-induced renal dysfunction in female rats. Avicenna J Phytomed 2014; 4(5): 312-9.

101. Greenhalf JO, Leonard HS. Laxatives in the treatment of constipation in pregnant and breast-feeding mothers. Practitioner 1973; 210(256): 259-63.

102. Ghahramani L, Hosseini SV, Rahimikazerouni S, Bananzadeh AM, Jahromi B, Samsam A. The effect of oral psyllium herbal laxative powder in prevention of hemorrhoids and anal fissure during pregnancy, a randomized double blind clinical trial. Ann Colorectal Res 2013; 1(1): 23-7.

103. McRorie JW, Daggy BP, Morel JG, Diersing PS, Miner PB, Robinson M. Psyllium is superior to docusate sodium for treatment of chronic constipation. Aliment Pharmacol Ther 1998; 12(5): 491-7.

104. Cheskin LJ, Kamal N, Crowell MD, Schuster MM, Whitehead WE. Mechanisms of constipation in older persons and effects of fiber compared with placebo. J Am Geriatr Soc 1995; 43(6): 666-9.

105. Londonkar R, Nayaka H. Evaluation of anti implantation and abortifacient properties ofportulaca oleracea L. In albino rats. Int J Pharma Bio Sci 2011; 2(4): 501-3.

106. Hooman N, Mojaf B, Nickavar A, Pouryousefi-Kermani P. Diuretic effect of powdered Cerasus avium (cherry) tails on healthy volunteers. Pak J Pharm Sci 2009; 22(4): 381-3.

107. West T, Atzeva M, Holtzman DM. Pomegranate polyphenols and resveratrol protect the neonatal brain against hypoxic-ischemic injury. Dev Neurosci 2007; 29(4-5): 363-72.

108. Shidfar F, Rahideh ST, Rajab A, Khandozi N, Hosseini S, Shidfar S, et al. The effect of sumac (Rhus coriaria L.) Powder on Serum Glycemic Status, ApoB, ApoA-I and total antioxidant capacity in type 2 diabetic patients. Iran J Pharm Res 2014; 13(4): 1249-55.

109. Chaube S, Swinyard CA. Teratological and toxicological studies of alkalioidal and phenolic compounds from Solanum tuberosum L. Toxicol Appl Pharmacol 1976; 36(2): 227-37.

110. Klebanoff MA, Levine RJ, DerSimonian R, Clemens JD, Wilkins DG. Maternal serum paraxanthine, a caffeine metabolite, and the risk of spontaneous abortion. N Engl J Med 1999; 341(22): 1639-44.

111. Sindos M, Pisan N, Michala S. Consumption of coffee during pregnancy: Authors should adjust for history of drug abuse. BMJ 2003; 326(7401): 1268.

112. Balat O, Balat A, Ugur MG, Pence S. The effect of smoking and caffeine on the fetus and placenta in pregnancy. Clin Exp Obstet Gynecol 2003; 30(1): 57-9.

113. Bracken MB, Triche EW, Belanger K, Hellenbrand K, Leaderer BP. Association of maternal caffeine consumption with decrements in fetal growth. Am J Epidemiol 2003; 157(5): 456-66.

114. Yazd MM, Tinker SC, Mitchell AA, Demner LA, Werler MM. Maternal tea consumption during early pregnancy and the risk of spina bifida. Birth Defects Res A Clin Mol Teratol 2012; 94(10): 756-61.

115. Yarnell E, Abascal K. Dandelion (Taraxacum officinale and T mongolicum). Integrative Medicine 2009; 8(2): 35-8.

116. Sharma PV. Classical Uses of Medicinal Plants. Varanasi, India: Chaukhambha Visvabharati; 1996.

117. Youdim KA, Deans SG. Effect of thyme oil and thymol dietary supplementation on the antioxidant status and fatty acid composition of the ageing rat brain. Br J Nutr 2000; 83(1): 87-93.

118. Blumenthal M. Herbal medicine: Expanded commission e monographs. Newton, MA: Integrative Medicine Communications; 2000.

119. Heinonen OP, Stone D, Shapiro S. Birth defects and drugs in pregnancy. Littleton, MA: Publishing Sciences Group; 1977.

120. Korman SH, Cohen E, Preminger A. Pseudomaple syrup urine disease due to maternal prenatal ingestion of fenugeek. J Paediatr Child Health 2001; 37(4): 403-4.

121. Abdo MS, al-Kafawi AA. Experimental studies on the effect of Trigonella foenum-graecum. Planta Med 1969; 17(1): 14-8.

122. Edrime T, Arica SG, Gucuk S, Yildizhan R, Kolusari A, Adali E, et al. Use of complementary and alternative medicines by a sample of Turkish women for infertility enhancement: A descriptive study. BMC Complement Altern Med 2010; 10: 11.

123. Jalili C, Salahshoor MR, Naseri A. Protective effect of Urtica dioica L against nicotine-induced damage on sperm parameters, testosterone and testis tissue in mice. Iran J Reprod Med 2014; 12(6): 401-8.

124. Bercovich E, Saccomanni M. Analysis of the results obtained with a new phytotherapeutic association for LUTS versus control. [corrected]. Urologia 2010; 77(3): 180-6.

125. Azarnia M, Ejtemaee-Mehr S, Shakoor A. Effects of vitex agnus castus on mice fetus development. Acta Med Iran 2007; 45(4): 263-70.

126. Rani A, Sharma A. The genus Vitex: A review. Pharmacogn Rev 2013; 7(14): 188-98.

127. Ladeji O, Udoh FV, Okoye ZS. Activity of aqueous extract of the bark of Vitex doniana on uterine muscle response to drugs. Phytother Res 2005; 19(9): 804-6.

128. Daniele C, Thompson Coon J, Pittler MH, Ernst E. Vitex agnus castus: A systematic review of adverse events. Drug Saf 2005; 28(4): 319-32.

129. Takahashi T, Yokoo Y, Inoue T, Ishii A. Toxicological studies on procyandin B-2 for external application as a hair growing agent. Food Chem Toxicol 1999; 37(5): 545-52.
130. Erexson GL. Lack of in vivo clastogenic activity of grape seed and grape skin extracts in a mouse micronucleus assay. Food Chem Toxicol 2003; 41(3): 347-50.

131. Ahmad MK, Mahdi AA, Shukla KK, Islam N, Rajender S, Madhukar D, et al. Withania somnifera improves semen quality by regulating reproductive hormone levels and oxidative stress in seminal plasma of infertile males. Fertil Steril 2010; 94(3): 989-96.

132. Malviya N, Jain S, Gupta VB, Vyas S. Recent studies on aphrodisiac herbs for the management of male sexual dysfunction—a review. Acta Pol Pharm 2011; 68(1): 3-8.

133. Fischer-Rasmussen W, Kjaer SK, Dahl C, Asping U. Ginger treatment of hyperemesis gravidarum. Eur J Obstet Gynecol Reprod Biol 1991; 38(1): 19-24.

134. Keating A, Chez RA. Ginger syrup as an antiemetic in early pregnancy. Altern Ther Health Med 2002; 8(5): 89-91.

135. Portnoi G, Chng LA, Karimi-Tabesh L, Koren G, Tan MP, Einarson A. Prospective comparative study of the safety and effectiveness of ginger for the treatment of nausea and vomiting in pregnancy. Am J Obstet Gynecol 2003; 189(5): 1374-7.

136. Weidner MS, Sigwart K. Investigation of the teratogenic potential of a zingiber officinale extract in the rat. Reprod Toxicol 2001; 15(1): 75-80.

137. Nakamura H, Yamamoto T. Mutagen and anti-mutagen in ginger, Zingiber officinale. Mutat Res 1982; 103(2): 119-26.

138. Nakamura H, Yamamoto T. The active part of the [6]-gingerol molecule in mutagenesis. Mutat Res 1983; 122(2): 87-94.

139. Wilkinson JM. Effect of ginger tea on the fetal development of Sprague-Dawley rats. Reprod Toxicol 2000; 14(6): 507-12.

140. Jewell D, Young G. Interventions for nausea and vomiting in early pregnancy. Cochrane Database Syst Rev 2003; (4): CD000145.

141. Viljoen E, Visser J, Koen N, Musekiwa A. A systematic review and meta-analysis of the effect and safety of ginger in the treatment of pregnancy-associated nausea and vomiting. Nutr J 2014; 13: 20.

142. Gupta RB, Sharma S, Sharma J, Goyal R. Study on the physicochemical characters of fruits of some wild and cultivated forms/spp.” Ziziphus spp. Haryana J Horticul Sci 2004; 33(3/4): 167-69.

143. Gupta M, Mazumder UK, Vamsi ML, Sivakumar T, Kandar CC. Anti-steroidogenic activity of the two Indian medicinal plants in mice. J Ethnopharmacol 2004; 90(1): 21-5.

144. Wiesbaden Wagner H, Wiesenauer M. Phytotherapie: Phytopharmae und pflanzliche Homöopathika. Jena, Germany: Gustav Fischer Verlag; 1995.

145. Isaacsohn JL, Moser M, Stein EA, Dudley K, Davey JA, Liskov E, et al. Garlic powder and plasma lipids and lipoproteins: A multicenter, randomized, placebo-controlled trial. Arch Intern Med 1998; 158(11): 1189-94.

146. Holzgarter H, Schmidt U, Kuhn U. Comparison of the efficacy and tolerance of a garlic preparation vs. bezafibrate. Arzneimittelforschung 1992; 42(12): 1473-7.

147. Fleming T. PDR for Herbal Medicine. 1st ed. Montvale, NJ: Medical Economics Co; 1998.

148. Calomme M, Pieters L, Vlieittenck A, Vanden Bergh D. Inhibition of bacterial mutagenesis by Citrus flavonoids. Planta Med 1996; 62(3): 222-6.

149. Stapleton AE. Cranberry-containing products are associated with a protective effect against urinary tract infections. Evid Based Med 2013; 18(3): 110-1.

150. Oh HG, Lee HY, Seo MY, Kang YR, Kim JH, Park JW, et al. Effects of Ficus carica paste on constipation induced by a high-protein feed and movement restriction in beagles. Lab Anim Res 2011; 27(4): 275-81.

151. Ravn-Hansen G, Dragsted LO, Buch-Andersen T, Jensen EN, Jensen RI, Nemeth-Balogh M, et al. Intake of whole apples or clear apple juice has contrasting effects on plasma lipids in healthy volunteers. Eur J Nutr 2013; 52(8): 1875-89.

152. Anderson JW, Allgood LD, Turner J, Oeltgen PR, Daggy BP. Effects of psyllium on glucose and serum lipid responses in men with type 2 diabetes and hypercholesterolemia. Am J Clin Nutr 1999; 70(4): 466-73.

153. Zhang Y, Neogi T, Chen C, Chaisson C, Hunter DJ, Choi HK. Cherry consumption and decreased risk of recurrent gout attacks. Arthritis Rheum 2012; 64(12): 4004-11.

154. Blaschek W, Hänsel R, Keller K, Reichling J.,.rembrt L, Hänsel R, Keller K, Reichling J., Blaschek W, Hänsel R, Keller K, Reichling J., Rimpler H, Schneider G. Hagers Handbuch der Pharmazeutischen Praxis. Berlin, Germany: Springer-Verlag Berlin Heidelberg; 1990.

155. Kalume DE, Sousa MV, Morhy L. Purification, characterization, sequence determination, and mass spectrometric analysis of a trypsin inhibitor from seeds of the Brazilian tree Dipteryx alata (Leguminosae). J Protein Chem 1995; 14(8): 685-93.

156. Henriet JP. Veno-lymphatic insufficiency. 4,729 patients undergoing hormonal and propranolol oligomer therapy. Phlebologie 1993; 46(2): 313-25.

157. Tebib K, Rouanet JM, Besancon P. Effect of grape seed tannins on the activity of some rat intestinal enzyme activities. Enzyme Protein 1994; 48(1): 51-60.

158. Muller JL, Clauson KA. Pharmaceutical considerations of common herbal medicine. Am J Managed Care 1997; 3(11): 1753-70.

159. Rumbold A, Duley L, Crowther CA, Haslam RR. Antioxidants for preventing pre-eclampsia. Cochrane Database Syst Rev 2008; (1): CD004227.

160. Mistry HD, Williams PJ. The importance of
antioxidant micronutrients in pregnancy. Oxid Med Cell Longev 2011; 2011.

161. Jenkins C, Wilson R, Roberts J, Miller H, McKillop JH, Walker JJ. Antioxidants: Their role in pregnancy and miscarriage. Antioxid Redox Signal 2000; 2(3): 623-8.

162. Park H. Effects of antioxidants and oxidative stress on pregnancy and infant growth: Korean perspectives. In: Preedy VR, Editor. Handbook of growth and growth monitoring in health and disease. Berlin, Germany: Springer Science & Business Medi; 2011. p. 1585-98.

163. Rouhi-Boroujeni H, Heidarian E, Rouhi-Boroujeni H, Deris F, Rafieian-Kopaei M. Medicinal plants with multiple effects on cardiovascular diseases: A systematic review. Curr Pharm Des 2017; 23(7): 999-1015.

How to cite this article: Rouhi-Boroujeni H, Heidarian E, Rouhi-Boroujeni H, Khoddami M, Gharipour M, Rafieian-Kopaei M. Use of lipid-lowering medicinal herbs during pregnancy: A systematic review on safety and dosage. ARYA Atheroscler 2017; 13(3): 135-55.