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REVIEW PAPER

## A Systematic Review of Iranian Medicinal Plants Effective on Female Infertility

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**Abstract:** Infertility is one of the common and rising problems of women. To treat female infertility, medicinal plants may be used in addition to chemical drugs and assisted reproductive technology. To conduct this review, the terms *Fertility* and *Pregnancy* in combination with *Medicinal plants*, *Herb*, and *Phyto* were used to search for and retrieve relevant publications indexed in international databases ISI and PubMed and domestic databases Iran Medex and ISC. The articles that fulfilled the inclusion criteria were analyzed. In this systematic review article, the medicinal plants that were found to be effective on female infertility indices were reported. These plants, according to this review article, are *Nigella sativa*, *Panax ginseng*, *Phoenix dactylifera* L., salep, *Glycyrrhiza glabra*, *Apium graveolens* L., and *Foeniculum vulgare* Mill. The medicinal plants used by Iranian people have been reported to exert optimal effects on female fertility in animal studies through antioxidant properties, increasing folliculogenesis, hormonal compounds, and other effective compounds on hormonal system as well as enhancing sex cells viability.

**Keywords:** *Infertility, Female, Medicinal plants, Iran.*

### Introduction

The prevalence of infertility is on rise in different countries including Iran (1, 2). Female infertility is due to several reasons such as obesity (3), infection (4), diabetes (5), and hypothyroidism (6) and may be associated with certain factors including physical inactivity, the number of abortions, and lifestyle (7). Treatment cycles of infertility such as in vitro fertilization and use of chemical drugs cause certain complications and high levels of psychological and emotional stress for the patients in addition to imposing stupendous costs (8, 9). For several reasons, treatments for infertility may be unsuccessful and associated problems of the patients can be considerably intensified (2). Besides that, infertile women in Iran experience certain

social problems such as stigma and social exclusion that affect their quality of life adversely (10). Therefore, attempts are continuously made to enhance and develop alternative therapies for infertility.

Plant-based treatments for infertility can increase fertility in infertile women even by 100% regarding effective factors on infertility (3, 4). Medicinal plants and nature-based compounds have recently been commonly used to treat different diseases because of fewer side effects (11-22). However, use of complementary therapies and medicinal plants to treat infertility is still controversial (5). Medicinal plants have been found to be potential appropriate alternative therapies for infertility (6). This

systematic review was conducted to assess the medicinal plants effective on female infertility indices. This review article can help provide new pharmaceutical compounds for researchers and pharmacists to produce effective herbal drugs on female infertility.

To conduct this review, the terms *Fertility* and *Pregnancy* in combination with *Medicinal plants*, *Herb*, and *Phyto* were used to search for and retrieve relevant publications indexed in international databases ISI and PubMed and domestic databases Iran Medex and ISC. Then, the abstracts and data drawn from other resources were examined and only those studies that were conducted mainly to investigate the effects of the plants and their derivatives on female infertility in Iran and on medicinal plants native to Iran were included in analysis.

## Results

*Nigella sativa*, ginseng, *Aloe vera*, *Phoenix dactylifera* L., salep, *Glycyrrhiza glabra*, *Apium graveolens* L., *Foeniculum vulgare* Mill., *Allium sativum*, *Vitex agnus-castus* L., and *Portulaca oleracea* have been reported to be used to increase female infertility in Iran according to traditional medicine (23); however, only *N. sativa*, ginseng, *P. dactylifera*, salep, *G. glabra*, *A. graveolens*, and *F. vulgare* were studied in experimental works with animals.

### *N. Sativa*

*N. sativa* is an annual flowering plant that produces black seeds and is from family Ranunculaceae (24). Hydroalcoholic *N. sativa* seed extract causes increase in folliculogenesis and corpus luteum, which can be due to the optimal outcome in female fertility (25).

### *Panax Ginseng*

A study demonstrated that treatment with vitamin E and ginseng caused increase in the number of laboratory pregnant mice and babies born due to inducing antioxidant property in sex cells (26).

### Date Palm Pollen (*P. Dactylifera* L.)

A study demonstrated that 400 mg/kg *P. dactylifera* pollen extract caused increase in the levels of sex hormones and the number of secondary and antral follicles in adult

female BALB/c mice (27). This extract increases female fertility in BALB/c mice through stimulating folliculogenesis (28).

### Salep

A study indicated that aqueous salep root extract caused significant modulation of serum FSH and increase in serum estrogen in female rats (29).

### *G. Glabra*

*G. glabra* is from family Leguminosae. Aqueous *G. glabra* extract was reported to be effective on the levels of sex hormones and cause increase in the in vitro maturity of the oocytes and in vitro fertility in laboratory mice with polycystic ovary syndrome (30).

### *F. Vulgare*

A study on the effects of *Cichorium intybus*, *F. vulgare*, and *A. graveolens* on fertility and infant gender in rats demonstrated that *F. vulgare* caused increase in fertility and the number of the infants (31). Another study demonstrated that alcoholic *F. vulgare* seed extract caused stimulation of folliculogenesis in mouse ovaries, which is due to its estrogenic property (32). Study of serum levels of estrogen, progesterone, and prolactin in female mice demonstrated that *F. vulgare* was effective in increasing the serum levels of these hormones and could be used as a drug for infertility (33).

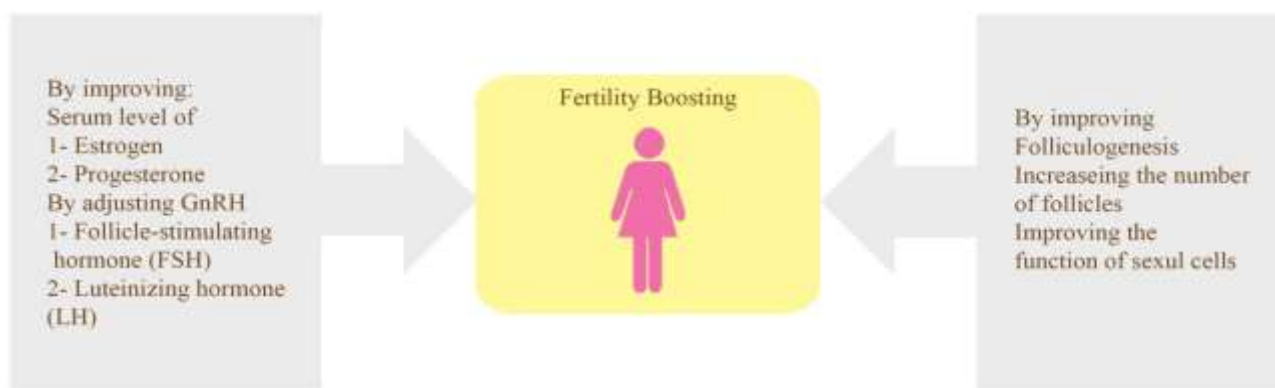
### *A. Graveolens*

*A. graveolens* caused increase in the number of babies in female mice due to several flavonoids such as quercetin and cytoesterol, phytoesterol, and antioxidants that are usually produced from protein. Therefore, hydroalcoholic *A. graveolens* leaf extract is effective in increasing fertility indices in female mice but causes reduction in weight of their infants (34).

This study was conducted to investigate the plants and plant-based compounds that are effective on female infertility. In the previous studies, oxidative stress has been reported to be a reducing agent of fertility. The studied plants have been found to increase fertility due to antioxidant properties (35, 36). Also natural antioxidants can be effective in prevention of various diseases (37-48). However, an important

point which should be seriously considered is that gynecological oxidative stress is an important mediator of conception, but higher than threshold levels of oxidative stress cause toxic effects and challenge conception. This issue, however, is dependent on the stage of preconception and anatomic location (49, 50).

Therefore, ovulation, administered dose, nutritional factors, and other confounders are issues that have been less frequently investigated (51-53), which challenge the available findings. According to reviewed studies in laboratory female animals, some plants exert their effects due in different mechanisms (Figure 1).



**Figure 1: Several mechanisms herbal medicine to increase fertility**

However, certain plants that have phytoestrogenic properties and therefore cause hormonal changes in females are likely to prevent fertility in males. For example, hydroalcoholic *F. vulgare* extract has been demonstrated to reduce male fertility (54, 55).

Besides that, some plants increase fertility in both genders. *P. dactylifera* pollen, *Panax ginseng*, extract, and *A. graveolens* extract are certain plant-based compounds that enhance fertility indices in both females (26, 27, 34) and males (26, 56-59). In addition, the teratogenic properties of the compounds of the plants that are used to increase female infertility should be taken

into account. As a result, such plants should be used in the light of necessary precautions and under supervision of specialists.

## Conclusion

Several plants are used to treat infertility in Iran a small number of which have already been investigated in experimental studies. These plants cause promotion of fertility indices through inducing antioxidant property in the tissues and reproductive organs of females as well as activating gonads due to phytochemicals and pseudohormonal compounds. In addition, they stimulate folliculogenesis and increase healthy sex cells.

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