Therapeutic Effects of Medicinal Herbs on Reproductive System Disorders: A Review

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Abstract
Reproductive systems in humans not only serve the birth and survival of generations, but also regulate many of the psychological and behavioral characteristics of humans. Regarding the side effects of chemical drugs used in the treatment of reproductive system disorders; this study was conducted to investigate the effect of medicinal plants on the performance of this system. In this review, an extensive literature search was conducted using relevant articles published between 2000 and 2018, and indexed in Google Scholar, PubMed, Elsevier, Scientific Information Database, and Islamic world science citation center (ISC) were studied. The search terms used to retrieve the articles were as follows: Herbal medicinal extract, Names of medicinal plants, Reproductive System. The use of medical plants has been commonplace in ancient civilizations, and hence since ancient times plants have long been an important source of medicine. Research on herbal medicine in recent years has shown that plants such as, Ginseng, Ginger and Aloe Vera have formerly been used to treat reproductive system disorders. In the present study, the effects of 30 plant types on the treatment of reproductive system have been investigated. According to the results of this study, many medicinal plants have beneficial effects due to flavonoid and antioxidant compounds in the treatment of reproductive system disorders, as some also have a negative effect on the system, so the use of medicinal plants in this regard should be made under the supervision of a specialist physician.

Key words: Medicinal Plants, Reproductive System, Disorder

Introduction
Reproduction is an essential characteristic of living organisms, especially mammals. Reproductive systems in mammals and, especially in humans, not only serve the birth and survival of generations, but also regulate many of the psychological and behavioral characteristics of humans. It also has a tremendous effect and, in principle, a relatively large number of human physical and mental illnesses are rooted in the bad functioning of this system. Regarding the prevalence of reproductive disorders, especially infertility in human societies around the world, including Iran, and also due to the high cost of treatment and the side effects of most chemical drugs used in the treatment of these patients, on the one hand, and many couples' desire to have children with male or female gender, today, there are many studies in the world about the effect of medicinal herbs on the treatment of reproductive system disorders and even on the sex determination of children and the prevention of unintentional fetal abortions (1). Medicinal plants are an important source for the treatment of many diseases. But before using these plants in pregnant women, their potential risk for pregnancy should be checked (2) and this study was also carried out to investigate the effect of medicinal plants on reproductive system disorders.
The effect of herbal drugs on the sex hormones

In a study it was shown that walnut oil had stimulating effects on the male reproductive system and could increase plasma testosterone levels by influencing the pituitary - testicular axis (3). In one study, we showed that leaf extract of parsley leaves an increase in the hormones of the pituitary-gonad axis (FSH, LH and testosterone) due to the presence of antioxidant compounds (4). It has been shown that Hops extract, probably by stimulating the secretion of hormones and with steroidal, flavonoids compounds, caused to increase the sexual hormones and the ovarian follicles (5). It has been shown that the palm pollen aqueous extract increases the amount of sexual hormones and secondary and antral follicle numbers in adult female mice (6). All types of pepper are widely used in traditional medicine (7). Secretion of pituitary-gonad axis hormones may be affected by the pepper. Oral intakes of red and black peppers powder have increasing impact on FSH and testosterone hormones. Therefore, these peppers may have androgenic properties (7). Cinnamon with the scientific name *cinnamomum verum* belongs to the Lauraceae family, which has anti-hypertensive agents (8). This plant has many therapeutic effects one of them is the increasing of sexual desire. The findings of this research indicated the positive effects of cinnamon extract on male reproductive system and hormonal changes in pituitary-gonad axis because sperm count and secretion of FSH hormone (9). The effective concentration of hydroalcoholic leaf extract of *Salvia officinalis* has excitatory effects on male reproductive system leading to increase in serum testosterone level and spermatogenesis (10). It has been shown that the Aloe Vera sap may have favorable effects on estrogen synthesis due to its phytoestrogen components such as beta sitosterol, and can increase the estrogen level (11). According to the findings of a study, phoenix dactylifera increases estrogen and progesterone, but has no effect on the gonadotropins (12).

Medicinal herbs and polycystic ovary treatment

The cause of polycystic ovary syndrome (PCOS) has not yet been definitely determined; however, it is mainly characterized by hyperandrogenism, infertility, lack of ovulation (13), increased level of LH (14), increased insulin resistance, decreased sex hormone-binding globulin (SHBG) (15) and hirsutism (16). PCOS is a common endocrine disorder in women of reproductive age. Its cause is unknown and it remains the most enigmatic of reproductive disorders (17). PCOS is one of the most important gynecological disorders among reproductive-age women. In patients with PCOS, the secretion rate and metabolism of androgens and estrogens are disrupted (18). In Korea, herbal remedies are widely used to treat PCOS, as Korean herbal remedies reduce weight, arrange menstrual cycles and improve serum levels of sex hormones in women with PCOS (19). The results of two studies showed that in animals with polycystic ovarian dysfunction, the number of atretic follicles, estrogen hormones and testosterone increased and other follicles and FSH decreased, and ginger and ginseng extract as well as metformin chemical can reduce follicles atretic and other follicles and FSH, and decrease testosterone and estrogen in these animals (20, 21). According to evidence, herbal extracts containing phytoestrogens cause decrease in hyperandrogenism, insulin resistance, and ovary weight as well as increase in ovulation. Therefore, these plants can be partly effective in this syndrome via affecting the serum levels of different hormones and ovarian weight and morphology, representing an opportunity to investigate and discovery new bioactive products (18). The hydro-alcoholic extract of *Aloe vera L*, decreased estrogen levels and increased the concentration of progesterone hormone in rat, respectively. So it appears that
the use of *Aloe vera* L. would be effective in the treatment of infertility disorders and PCOS (22). The effects of letrozole abuse have the potential to reduce the reproductive capacity of the female and the use of appropriate doses of licorice extract as an antioxidant could reduce somewhat adverse effects of hyperandrogenism resulted of polycystic ovary syndrome on the fertility of female mice (23). The results of a study showed that in animals with polycystic ovarian Palm pollen extract can improve tissue symptoms and adjust the levels of sex hormones in PCOS (24).

**The effect of medicinal plants on the ratio of sex**
The determination of the child's gender has always been the dreams of mankind. Over the centuries, many efforts have been made and various theories and assumptions have been presented. The theory that is currently popular is the theory of the effect of changing the ratio of ions to gender change. These findings, while confirming the existing Islamic-Iranian medicine, suggest that the effect of chicory consumption on the sex of the infant implies that the administration of aqueous extract of chicory leaf may possibly be altered blood ion ratios and, consequently, electrolyte alteration of the internal environment and uterine secretion affect the acceptability of Y or X-shaped eggs, altering the sex ratio of newborns (25). The results of the study showed that consumption of celery in male decreases the number of offspring and increase the male genesis because it does not affect childbirth. It may be safely useful in pregnancy controlling (26). Various plants are used in Iranian traditional medicine to increase fertility and to affect fetus gender. Fennel increases fertility rate and neonates number in rats, but chicory and dill do not have such effects. None of the plants affect the neonates' gender in rats (27). Tarragon is a plant of Asteraceae family that has both medical and edible uses. The results in a study showed that tarragon extract by having Ca$^{2+}$, Mg$^{2+}$ and increasing serum ions mentioned and possibly by changing vagina environment pH caused to increase the gynogenesis percentage, so it is recommended that supplementary research on tarragon effects on infants’ sex in human samples also be considered (28). Findings of another study showed that probably pollen extract minerals such as potassium and sodium have effect on the increase of male infants than the female ones, which needs more biochemical investigations in the future (29). In one study, it was shown that the extract of celery leaves contains substances that are effective on the delivery rate, sex ratio, and the number of newborns in the female rats. It may affect the ionic changes in the rats, by modifying the activity of follicle-stimulating and testosterone hormones, and/or changing the rate of fertilizing ability of sperms containing Y chromosome. This phenomenon may also be due to lowering serum fats, acidity levels, and accordingly reducing the acidity of the uterus secretions (30). The results showed that the consumption of celery leaf in females can increase the number of infants, and is associated with weight loss. These changes could be associated with compounds such as phytosterols and flavonoids such as beta cystosterol and quercetin (31).

**Herbs and contraceptive properties**
*Ruta graveolens* (RG) has been used for sexual impotence in men and abortion in women. The aqueous extract of RG diminishes the reproductive system activity and might be useful as a substance for birth control process (32). Nowadays using herbal products as an alternative or supplement to contraceptive synthetic drugs is common. There are reports of anti-estrogenic effects of nettle resulting in sterility in mammals. Hydro-alcoholic extract of nettle root has a positive effect on LH hormone (33). The regulation of fertility control using compounds of medicinal plants is mentioned in many of the old medical-related sources. The results of a research showed that alcoholic extract of *Achillea*
millefolium flowers in higher doses could decrease fertility in male rats (34). *Falcaria vulgaris* has different properties and it used as dietary and medicinal herb in the west of Iran. *Falcaria vulgaris* extract showed antifertility effect in female rat (35). One study showed that purpella (*Portulaca oleracea*) extract with anti-estrogenic and anti-aromatase compounds reduced serum levels of estradiol, so its long-term consumption could cause hormonal disorders and reduced fertility in female animals (36). Lavendula officinalis has sedative properties of aqueous extract. It is effective on diabetes and depression and has antimicrobial properties and manages. Consumption of lavender on a high dose has a damaging effect on the ovary and its use can be dangerous and maybe in the future it may be used as an oral contraceptive pill (37).

**Aborted herbal remedies**

*Heracleum persicum* is an Iranian herbal medicine used traditionally to treat many diseases. The results of one study showed that *Heracleum persicum* has a teratogenic effect and abortion. Therefore, during pregnancy, the crop should be taken with caution (38). In one study, it has been shown that Origanum Vulgare extract did not have any positive effect on fetal development; and high dosages led to an increased incidence rate of abortion and fetal malformations in the fetuses of women who received it (39). According to the traditional beliefs Henna causes abortion. Hydro-alcoholic extract of Henna has teratogenic properties, so it should be consumed with caution during pregnancy (40). Using saffron is one of the common habits in eastern parts of Iran which has been used with tea, Saffron is also used for ending unwanted pregnancy; and it can impress site effect on embryo (41). Several studies have shown that many pregnant women use medicinal plants without knowing that some of them have abortifacient and teratogenic effects during pregnancy. The use of *Stachys lavidulifolia* during pregnancy may cause abortion and therefore it should be considered as contraindication or use with caution (42).

Given that infertility and abortion in women are one of the most important issues in the medical world. The results of a study showed that chamomile extract decreased LH and FSH, thereby decreasing ovarian follicles, sexual hormones and aborted fetuses (43).

**Herbs and fertility**

Treating herbs and using herbal medicines is now one of the most popular ways to treat infertility. In the meantime, ginseng belonging to the genus *Panax* of the family Araliaceae has been among top ten common plants in people's food basket. The use of ginseng extract increases the number of primary, secondary, graafian follicles and reduces the number of atritic follicles and also increases the thickness of the perimeter and endometrial layer of the uterus. We can say that using red ginseng water extract is effective on oogenesis and uterus tissue (44). Therefore, it increases the fertility of women and also protects the wall of the uterus in preventing abortion. Infertility is one of the major issues in medical science that is often caused by the lack of sex cells and various chemical and herbal medicines are used to treatment it. It was shown in a study that parsley leaf caused an increase in weight and sexual dynastic cells by 5alpha-reductase and aromatase inhibition, reinforcing antioxidant defense and reducing oxidative stresses (45). And so it can be effective in treating infertility caused by a lack of sex cells. *Glycyrrhiza glabra* is a perennial plant with some major food and medicinal compounds that has received attention by food and pharmaceutical industries. The results of a study showed that following the consumption of sweet pepper extract, there is a positive effect on the number of follicles, oocyte maturation, the number of double-cell embryos and four cells and beneficial effects of licorice extract due to its phytoestrogenic properties on oocyte maturation and infertility (46). It seems that *Artemisia absinthium*
hydroalcoholic extract in high doses has damaging effects on the process of oogenesis, which may be due to α and β thujon, alkaloid and saponin constituents in this plant (47). The hydroalcoholic extract of Nasturtium Officinalis with antioxidant properties have efficacy on ovarian follicle to improve oogenesis following toxicity by doxorubicin in rats (48). Ginger with the scientific name Zinger officinale from Zingibracea family is one of the medicinal plants that has been widely used in traditional medicine (49).

Ginger as a medicinal herb is used as a food flavoring and therapy of many diseases including infertility and male sexual disabilities. The oral consumption of ginger extract in prenatal and infant periods dose-dependently increase the level of testosterone and the number of spermatogenic cells (Leydig cells, spermatogonia, sertoli, spermatocytes and spermatids) (50). Another study results showed that aqueous extracts of palm pollen dose-dependently caused significant increasing the levels of estrogen, progesterone and testosterone and increasing the numbers of spermatocytes and spermatid cells. The presence of compounds such as cadmium, zinc, steroids, flavonoids, saponins, lipids, and by substances that inhibiting the enzyme 5- alpha reductase could increase testosterone and sexual dynastic cells (51). Therefore, it can be useful in the treatment of oligo-sperm infertility. In another study, it has been shown that Hops extract, possibly by having phytoestrogen compounds and by stimulating LH secretion, increases estrogen and testosterone levels, and spermatogonia, spermatocytes and spermatid cells number. Therefore, further investigation on hops can utilize to help infertile men (52).

The effect of medicinal herbs on menstrual pain, dysmenorrhea and menorrhagia

Pain and heavy menstrual bleeding has a negative impact on quality of life. It seems that the extract of Capsella bursa pastoris can be effective in reducing the amount and duration of bleeding in women of reproductive age with heavy menstrual bleeding (53). Primary dysmenorrhea is seen in over 90% of adult women in cycles with ovulation, and is the common cause of absenteeism from school and workplaces. Several chemical drugs are used today to treat primary dysmenorrhea, but each has its own side effects. The use of medicinal herbs in traditional medicine has a special place in the treatment of this disorder. The use of medicinal herbs in traditional medicine has a special place in the treatment of this disorder, and one of the herbs used in traditional medicine as a suppressor, anesthetist, antispasmodic, anti-inflammatory and analgesic drugs, and can improve the severity of primary dysmenorrhea, it is a cinnamon plant (54). Primary dysmenorrhea is one of the common problems in women, especially in young women. Although dysmenorrhea is not life threatening, it can have adverse effect on quality of life and cause disability or ineffectiveness. With regard to the young society suffering from it, various treatments are offered for dysmenorrhea one of which is medicinal plants. Generally, it was shown that Melissa officinalis and Salvia officinalis signifi-cantly reduced pain severity and pain duration in the girls with primary dysmenorrhea. These medicinal plants can be used as a therapy method and raise the life quality of suffering women (55).

Considering the importance and prevalence of dysmenorrhea and its effects on the life of half the world population (women), research on its treatment is necessary. The results of a study showed that the use of Stachys Ivanulifolia on traditional method is effective in curing primary dysmenorrhea and it has no side effects resulting. In addition, it is effective on pattern of pain and increases tolerance (56). The primary dysmenorrhea is one of the most common problems that women complain about and at least 50% of them experience it during the productivity period. Mefenamic acid and Anethum graveolens are effective in
dysmenorrhea. Although this effect was more obvious in mefenamic acid group as *Anethum graveolens* is an herbal combination, which has less side effects and people's interest in herbal treatments is considerable, so it is recommended to use it for treatment of primary dysmenorrhea (57). Dysmenorrhea is one of the most common gynecological problems in women which can be treated with chemical drugs, herbal medicines, acupuncture, acupressure, and massage therapy. Decreased dysmenorrheal pain was higher in the group of *Achillea Millefolium* and Mefenamic-acid capsule compared to the group of Mefenamic-acid capsules that may be is due to the effect of AM on dysmenorrheal pain (58). The results of a study showed that the use of *Valeriana officinalis* is a plant of which have positive effects on primary dysmenorrhea (50). Traditional Persian medicine has proposed many different medicinal plants for treatment of oligomenorrhea and amenorrhea. Although just few plants have been proven to be effective for treatment of menstrual irregularities, the results and the classification in present study can be used as an outline for future studies and treatment (59). It seems that the extract of *Capsella bursa pastoris* can be effective in reducing the amount and duration of bleeding in women of reproductive age with heavy menstrual bleeding (60). The results of study showed that decoction of herbal plants Anthemis, Salvia and Zataria could decrease the intensity of menstrual bleeding (61). Results of a study showed that valerian has positive effect on treatment of primary dysmenorrheal. More clinical trials are needed to establish the efficacy of Valeriana officinalis in primary dysmenorrhea (62).

**Conclusion**
According to the results of various studies, the use of medicinal plants is useful in the treatment of many reproductive system disorders, but given the adverse effects of some of these herbal medicines, the use of this treatment should be made under the physician's supervision.

**Ethical issues**
Not applicable.

**Authors’ contributions**
Only one author contributed to the writing and revision of this paper.

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