

The Impact of Certain Medicinal Plants on Fertility in Men and Women

Chahra Boudoukha, Halima Douibi, Ilhem Guerguit and Rachid Belhattab

Laboratory of Applied Microbiology, Department of Biochemistry, Faculty of Nature and Life Sciences, University Farhat Abbas Sétif1, Sétif 19000, Algeria

Abstract: *The aim of this study is to examine the impact of certain medicinal plants on fertility in men and women, as well as their influences on the concentrations of sex hormones (LH, FSH, estrogen...) in the production cycles of sperm and ovocytes. The studied plants was Salvia officinalis L, Origanum Majorana, Vitex agnus castus and Lepidium meyenii. The effect of these plants is variable, some of them mainly affect the production of hormones in the sexual cycle in the male like Lepidium meyenii, and others mainly affect the production of hormones in the sexual cycle in the female, such as Salvia officinalis L, Origanum majorana and Vitex agnus castus. In addition, studied plants exert other effects on various physiological functions. Therefore, these herbs could be used as an accompanying or alternative treatment for hormonal imbalances in men and women, responsible for several problems such as infertility. These plants, within the limits of the studied doses, may contribute to the improvement of the production of sex hormones in men and women, which guarantees the continuation of sexual cycles, and therefore fertility in both sexes*

Keywords: *Fertility, FSH, Infertility, Salvia officinalis, LH, Origanum majorana,, Vitex agnus castus.*

1. Introduction

The use of medicinal plants for the treatment of disease usually comes from the belief that they have very low toxicity due to their natural origin. According to the World Health Organization, around 80% of the world's population uses traditional medicine for health care. Among these plants are; Vitex Agnus- castus, Lepidium meyenii, Salvia officinalis L and Origanum Majorana, widely used in the treatment of fertility disorders or infertility

Infertility is one of the disorders affecting the reproductive system. It affects a wide range of married couples in society and currently remains treated in a traditional way in a few areas. Infertility is defined as a couple's inability to conceive after two years of unprotected sexual intercourse. It is estimated that one third of infertility cases come from the man, one third from the woman, and one third due to a lack of compatibility between the two partners.

The purpose of this study is to examine the effect of four medicinal plants (mentioned above) on female and male fertility. (Salvia officinalis, Origanum majorana, Vitex agnus castus, lepidium meyenii), and their effects on female and male hormones

1.1.1. Salvia officinalis

Salvia officinalis or sage is a perennial plant with a woody stem at the base, whitish below and greyish-green above, usually reaching a height of 30-70 cm (Pereira et al., 2018), forming quadrangular branches erect and hairy, with rather large, opposite oval-shaped, elongated leaves, greenish-gray due to cottony pubescence on the underside (Benkherara et al., 2011). The root of sage is brownish and fibrous. Light blue-violet flowers in

loose terminal spikes, arranged in 3 to 6 in spaced whorls (Hans, 2007), with a calyx and corolla divided into two lips (Cutillas et al., 2017), appear towards the May into early summer and remain open into early fall (Kintzios, 2000). The fruits are small achenes resting on open cupules, and they have a characteristic aromatic smell. (Fleurentin, 2008) Sage tolerates a wide variety of climates and soils, with a pH ranging from 5 to 9. The adult plant resists temperatures of -10°C, but it is preferable to mulch the young plant (Gilly, 2005), sage Persists in winter thanks to the coating of woolly hairs that protect them.

Sage contains phytoestrogens and Phytoestrogens are nonsteroidal molecules of plant origin, capable of binding to estrogen receptors thanks to their chemical structures and stereochemistry similar to endogenous natural estrogens (17-β estradiol in particular) (Chatenet C, 2008). They belong to the classes of isoflavonoids, coumestans, flavonoids, stilbenes, lignans or enterolignans (figure 1), and all of these substances are part of the vast group of polyphenols (Bruneton et al., 1999).

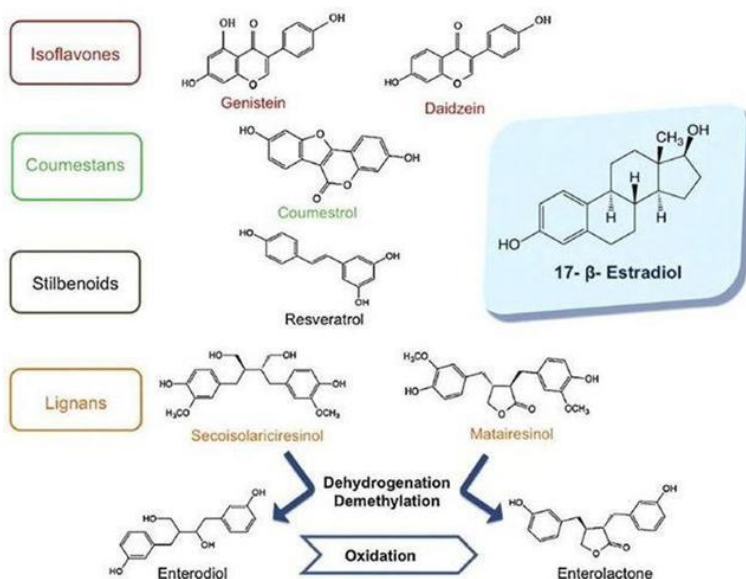


Fig. 1: Structure of the main phytoestrogens (Moreira et al., 2014)

1.1.2. Influence of phytoestrogens on the menstrual cycle and hormonal balance in premenopausal women

Phytoestrogens have potential estrogenic activity due to their binding affinity for estrogen receptor alpha (ER α) or beta (ER β). They can also alter circulating levels of sex steroid hormones by interacting with synthetic or peripheral converting enzymes (Makela et al., 1995). They can also disrupt the balance of circulating hormones by binding to the sex steroid transport protein, “sex hormone binding globulin” (SHBG) or by influencing its level of concentration through an effect on its hepatic synthesis (Mousavi et al. , 1993).

Studies suggest that an intake of isoflavones (phyto-estrogen) could modify cycle length and decrease ovarian secretion of estradiol. Two studies report this link following the direct intake of genistein (Watanabe 2000, Kumar 2002). None of these studies reported an estrogenic effect of isoflavones on endometrial proliferation before menopause (Kurzer, 2002 and 2003) but none mentioned having researched it.

1.1.3. Influence of phytoestrogens on hormones in men

Data in humans on the effect of phytoestrogens are limited and the small number of available studies does not allow a final conclusion to be drawn to an effect of isoflavones on testicular function and androgen metabolism in men. If these effects exist, they seem discreet with a tendency towards the increase of SHBG which influences the metabolism and the biological activity of testosterone and estradiol. The influence of nutritional factors and in particular the inhibitory effect of insulin on the expression of the SHBG gene in the liver could explain the effect of isoflavone consumption on the level of SHBG (Crave, 1995).

1.1.4. Toxicity

Like all aromatic plants, sage *officinalis* is not without its dangers. Its essence is poisonous and can cause epileptic seizures and heart attacks. It is not recommended for pregnant or breastfeeding women (Hans et al., 2007)

1.1.5. Origanum majorona.L

Majorana hortensis (*Origanum Majorana* L) or marjoram is an evergreen herbaceous plant. It is an annual plant 20 to 40 cm high. Its erect stems bear small, opposite, rounded, greyish-green leaves. The white flowers, grouped in spikes terminating the stems and surrounded by characteristic rounded bracts. For this reason, it is often referred to as shell marjoram. When crushed, the plant gives off an aromatic odor (Bimala et al., 2016).

1.1.6. Hormonal effects of Origanum majorona. L

In a study carried out on a group of wistar albino rats to study the effect of the aqueous extract of marjoram (*Origanum majorana*. L) on ovulatory induction (Messaid. Moussaou, 2019), the results obtained illustrated in (figure 2) show that the concentration of LH and FSH shows a very highly significant increase ($p < 0.001$) in the 2nd batch 0.28 and the 3rd batch 0.3 respectively compared to the control, from there, the aqueous extract of marjoram improves the female hormonal profile. Reported that quantitative or qualitative changes in food intake, relayed by changes in hormonal signals and by significant variations in metabolic fluxes, modulate the activity of the hypothalamic-pituitary-ovarian axis. *Origanum majorona* L can treat polycystic ovary syndrome by modulating the female hormones LH /FSH.

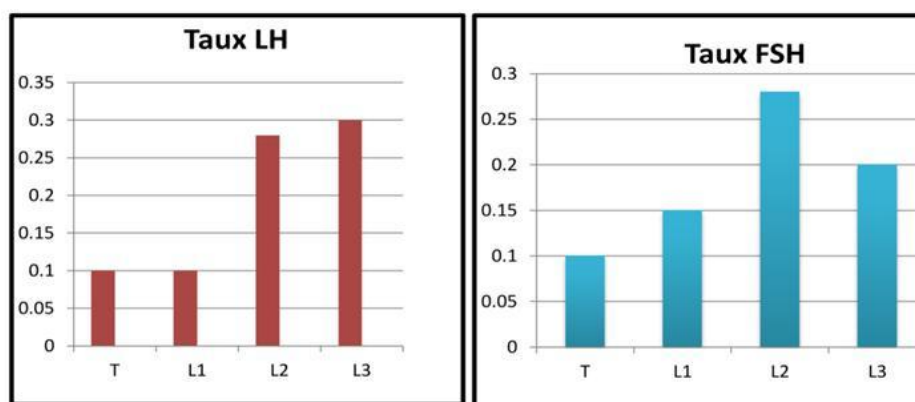


Fig 2: Variation in LH and FSH levels in the control (T) group and the experimental (L1, L2, L3) groups over 15 days. (Messaid. Moussaou, 2019)

1.1.7. Toxicity

In the light of the results obtained during the study of the effect of the aqueous extract of marjoram on some biochemical parameters on albino wistar rats such as the concentration of triglycerides and cholesterol, the concentration of transaminases (liver enzymes), Tissue concentrations of Malondialdehyde (MDA) and reduced glutathione (GSH) or it was positive on this biochemical parameters and from there, the toxic effect of marjoram is limited (Messaid. Moussaou, 2019).

1.1.8. Vitex Agnus Castus

Vitex agnus-castus is a deciduous shrub, about 1–6 m tall, with an aromatic smell. The leaves are opposite, The flower is perfect, symmetrical campanulate, tomentose white, tube 6-7 mm long, limb 2-lipped, upper lip 2-lobed, lower lip 3-lobed; stamens 4, exerted, 2 long, 2 short, inserted near top of corolla tube, alternating with corolla lobes; superior ovary, style exerted and stigma bifid. Fruits are drupe, globose to subglobose, 2–4 mm in diameter, reddish (Zahid et al., 2016)

1.1.9. Hormonal effects

The methanolic fruit extract showed significant effects of estrogen receptor α and estrogen receptor β for the expression of progesterone receptors and presentin-2 mRNA, it is an estrogen enhancing gene. The main component linoleic acid is responsible for these activities. The same result was obtained in a ligand binding assay which was conducted to investigate the effect of flavonoids isolated from 68% ethanol extract of *V. agnus-castus* fruits, including apigenin, vitexin and penduletin upon binding to the ER α or ER β isoforms. Apigenin has been found to be the most active ER β -selective phytoestrogen in the plant. The results indicated that the phytoestrogens of this plant are ER β selective. The estrogenic activity of ethanolic fruit extract was studied by vaginal smear and uterine weight methods in normal and ovariectomized female rats. A marked increase in uterine weight, plasma progesterone, total estrogen levels, and a decrease in prolactin and plasma hormones were observed in ovarian mice compared to the control group.

1.1.10. Effects on fertility disorders

Vitex agnus-castus is a plant commonly known as the "chaste tree". It was traditionally used in ancient Greek to treat female fertility dysfunctions such as dysmenorrhea, infertility, menopausal complications, cyclical mastalgia, and premenstrual syndrome. This plant affects the hypothalamic-pituitary axis which leads to the release of LH, the decrease of FSH and the increase of progesterone, which ultimately causes an increase in the estrogen/progesterone ratio (Niazi et al., 2019)

1.1.11. Toxicity

Adverse effects of *V. agnus-castus* have been shown to be mild and reversible. The most common include: Nausea, mild gastrointestinal disturbances, fatigue, menstrual disturbances, dry mouth, acne, pruritus and erythematous rash (Rani and Sharma, 2013). In view of the documented pharmacological actions and the absence of toxicity data, the use of *V. agnus-castus* in pregnancy should be avoided. *V. agnus-castus* has been reported to stimulate milk secretion without altering the composition of breast milk. Nevertheless, *V. agnus-castus* should be avoided during oviposition until more information is available (Zahid et al., 2016)

2. Conclusion

Based on the information obtained, we concluded that the effects of these plants and their extracts are different depending on both the plant and the sex (male or female). The aqueous extract of *Origanum majorana* controls follicular development by modulating the female hormones LH /FSH. *Vitex agnus-castus* affects the hypothalamic-pituitary axis which leads to the release of LH, the decrease in FSH and the increase in progesterone, which ultimately causes an increase in the estrogen to progesterone ratio and for this females showed longer cycle lengths and follicular phases. The aqueous extract and the ethanolic extract of *Lepidium meyenii* mainly improved spermatogenesis in men.

3. References

- [1] Benkherara S., Bordjiba O., Djahra A. B. Etude de l'activité antibactérienne des huiles essentielles de la Saugé officinale: *Salvia officinalis* L. sur quelques entérobactérie pathogènes. *Revue des Sciences et de la Technologie*:23, 72-80, 2011.
- [2] Cutillas A. B., Carrasco A., Martinez-Gutierrez R., Tomas V., Tudela J. *Salvia officinalis* L. essential oils from Spain: determination of composition, antioxidant capacity, antienzymatic, and antimicrobial bioactivities. *Chemistry et biodiversity*, 14(8), e1700102: 2017.
<https://doi.org/10.1002/cbdv.201700102>
- [3] Hans W.K. 100 plantes aromatiques et médicinales. Terre édition, 2007.
- [4] Kintzios S.E. Sage the Genus *Salvia*; Harwood Academic Publisher: Amsterdam, *The Netherlands*, ISBN 0203303660, 2000.
- [5] Fleurentin J. Plantes médicinales : Traditions et thérapeutique. Ed. OUEST –France: 92-93, 2008.
- [6] Gilles Figueredo. Étude chimique et statistique de la composition d'huiles essentielles d'origans (Lamiaceae) cultivés issus de graines d'origine méditerranéenne, thèse Doctorat, Université Blaise Pascal - Clermont-Ferrand II. Français ,2007.
- [7] Zahid H., Rizwani G. H., Ishaq S. Phytopharmacological review on *Vitex agnus-castus*: a potential medicinal plant. *Chinese Herbal Medicines*, 8(1): 24-29, 2016.
[https://doi.org/10.1016/S1674-6384\(16\)60004-7](https://doi.org/10.1016/S1674-6384(16)60004-7)
- [8] Rani A., Sharma A. *The genus Vitex: A review. Pharmacognosy Reviews*, 7(14): 188, 2013.
- [9] Niazi A., Rahimi V. B., Hatami H., ShiraziniaR., Esmailzadeh-dizaji R., Askari N., Askari V. R. Effective Medicinal Plants in the Treatment of the Cyclic Mastalgia (Breast Pain): A Review. *Journal of pharmacopuncture*: 22(3): 131, 2019.
<https://doi.org/10.3831/KPI.2019.22.017>
- [10] Niazi A., Rahimi V. B., Hatami H., ShiraziniaR., Esmailzadeh-dizaji R., Askari N., Askari V. R. Effective Medicinal Plants in the Treatment of the Cyclic Mastalgia (Breast Pain): A Review. *Journal of pharmacopuncture*: 22(3): 131, 2019.
<https://doi.org/10.3831/KPI.2019.22.017>
- [11] Messaid S., Moussaoui C. L'effet d'*Origanum majorana*. L sur l'induction ovulatoire chez les rattes albinos wistar. Mémoire master uni Hamma Lakhdar -El OUED: 74-77, 2019.