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REVIEW ARTICLE

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EFFECTS AND MECHANISMS OF MEDICINAL PLANTS ON OXYTOCIN: A SYSTEMATIC REVIEW

Farinaz Farahbod [1], Saeid Heidari-Soureshjani [2*]

[1] Isfahan University of Medical Sciences, Isfahan, Iran;
[2] Medical Plants Research Center, Basic Health Sciences Institute, Shahrekord University of Medical Sciences, Shahrekord, Iran.

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Correspondence to Author:
Saeid Heidari-Soureshjani
Circuit of Research and Technology, Sahrekord University of Medical Sciences, Iran, Tel: +989131833509, Fax: +98383351031

E-mail:
heidari_62@yahoo.com

ABSTRACT

Oxytocin (OT) plays different roles in the body and contributes mainly to humans' love behaviors, sexual function and childbirth. Given the various and determinative roles of OT, this review article is to report the effects of medicinal plants on OT and their action mechanisms. Articles indexed in the databases *Institute for Scientific Information* and *PubMed* were retrieved by the relevant search terms using the *EndNote* software. Then, the articles regarding the effects of medicinal plants and the related products in intensifying, modulating and neutralizing the adverse effects of OT, published between 2007 and 2017, were included in final analysis. Certain plants and their derivatives such as *Psidium guajava* Linn., *Ficus capensis*, *Ficus deltoidea*, *Dracaena arborea*, *Artemisia monosperma*, *Scutellariae Radix*, *Citrus aurantium*, genistein, daidzein, moxibustion, Danggui-Shaoyao-San, Shao-Fu-Zhu-Yu decoction, and Xiang-fu-si-wu decoction are effective to decrease dysmenorrhea and early miscarriage and to increase lactation. Herbs can induce their tocolytic effects by inhibiting OT-induced uterine contractions via influencing its levels in the body including the neuraxis, and therefore relieve dysmenhorea and increase lactation. Therefore, they can be used as alternatives to produce effective drugs on OT-dependent disorders. However as with chemical drugs, certain cautions should be taken into account in consuming such medications during pregnancy to minimize fetal and maternal side effects.

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INTRODUCTION

Oxytocin (OT) is a neurohypophysial peptide that is secreted from the posterior pituitary and enters into the blood flow. This hormone is synthesized in the peripheral tissues such as heart, testicles, uterus, placenta, and corpus luteum (1). OT plays different roles in the body and contributes mainly to humans' love and erotic behaviors and childbirth, and therefore serves important purposes in women's bodies. Besides that, OT plays a role in sexual activity, genital erection, ejaculation, uterine contraction at delivery, lactation, maternal behavior, stress (2), ethical behaviors (3, 4), parenting behaviors (5), aggressive behaviors and other mental states (6). Regarding the various functions of OT in the body, identifying its agonists and receptor antagonists in the body can contribute to the development of pharmacology and the treatment of certain disorders and diseases (7).

Despite the availability of different treatments for different aspects of health, chemical and herbal treatments remain significant in treating different disorders and diseases (8, 9). Meanwhile, medicinal plants are increasingly being used due to comparatively lower cost and fewer side effects. These plants have potential to serve as effective therapies for different diseases including psychological and physiological (10-17). Regarding the physiological significance of OT, this review article is to report the effects of medicinal plants on OT and their action mechanism in intensifying, modulating, and neutralizing the adverse effects of OT.

In this systematic review, the key words such as *"*oxytocin*"* in combination with *"medicinal plant"*, "*herb*"* and "*phyto*"* were searched via *Endnote* software. Relevant papers from *institute for scientific information (ISI)* and *PubMed* databases were retrieved. Then, the plants and the plant-based products that were effective on oxytocin were selected. The papers included in this review were published between 2007-2017. The articles whose full texts were not accessible, studies with non-positive effects, non-English language studies, and were not related to the purpose of this study were excluded after the authors' agreement was achieved. Figure 1 is the flowchart to illustrate how the articles were selected for final analysis.

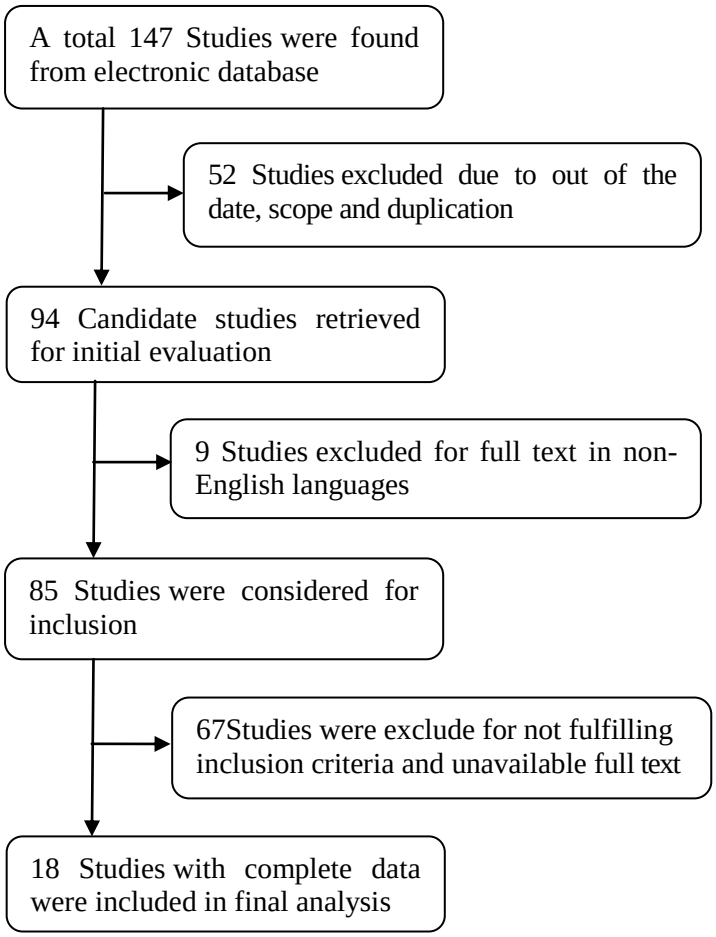

Figure 1. Flowchart of the process of analyzing the articles

Plants and herbal combinations can be effective to decrease dysmenhorea and early miscarriage through various mechanisms (Table 1).

Table 1. Medicinal plants and phytochemicals effective on oxytocin.

Plants/Phytocompound names	Type of administration/ Origin	Main effects and mechanisms	Ref.
Psidium guajava Linn.	Extract	Exerting spasmolytic effect to treat dysmenorrhoea	(18)
Ficus capensis	Extract	Reducing OT level and can be treatment for remedy against threatened abortion	(19)
Ficus deltoidea	Extract	Inducing uterine contraction mediated by multiple uterotonin receptors (muscarinic, oxytocin and prostaglandin F2 alpha)	(20)
Dracaena arborea	Extract	Inhibiting bulbospongiosus muscles activity by blocking oxytocinergic and dopaminergic receptors	(21)
Artemisia monosperma	Extract	Increasing serum oxytocin hormone level and inducing abortion	(22)
Citrus aurantium	Extract	Reducing oxytocin and barium chloride-induced uterine contractions and relieving dysmenorrhea	(21)
Scutellariae Radix	Root of Scutellaria baicalensis	Inhibiting oxytocin (IC50 12.34 microM) and exerting tocolytic effect.	(23)
Genistein and daidzein	Soy bean	Elevating plasma oxytocin and influencing the endocrine status of pigs; modulating the hypothalamic OXT neurons	(24, 25)

Certain compounds such as galactogogues (26) and moxibustion (27) have been reported to contribute to increasing OT and lactation. However, some other studies did not report any documented results regarding the effects of medicinal plants in increasing OT (28-30). In addition, controlling OT levels has been reported to be effective in treating diseases such as dysmenorrhea. In addition, Danggui-Shaoyao-San is a Chinese herbal combination that reduces inflammatory reactions by suppressing OT-evoked prostaglandins F2 alpha (PGF2-alpha) production and other mechanisms, and therefore helps to treat dysmenhorea (31). Shao-Fu-Zhu-Yu decoction (32-34) and Xiang-fu-si-wu decoction (35) are two Chinese herbal combinations that are are effective to reduce OT-induced complications such as dysmenhorea by inhibiting signaling pathways and expression of inflammatory cytokines, and modulating OT levels (33).

The treatments for modulating OT levels in the body, serve their purpose mainly by targeting OT receptors (2). Certain treatments for dysmenhorea, relieve the associated pains by decreasing (OT-induced) contraction of uterine smooth muscle via blocking calcium (Ca2+) channels and lowering the levels of Ca (2+), PGF2-alpha, and nitric oxide (35-37). Therefore, certain plants relieve dysmenhorea by analgesic and anti-inflammatory effects and affecting on nerve growth factor (NGF) and bradykinin, and protein and mRNA levels of NGF and bradykinin B1 receptor, and exerting anti-contractile properties rather than influencing OT levels (35-52).

However, available evidence suggests that the response to oxytocin is related to several factors including genetic factors and the presence of OT receptor genes (53), which highlights the need for more extensive studies. Medicinal plants are attracting attention due to exerting several effects mediated by antioxidant and anti-inflammatory effects on the different functions of the body's physiological system, and therefore their effects are being studied to find new therapeutic agents (54-63). However, the side effects of these drugs are often disregarded. The effects of the consumption of phytoestrogens on hormone-sensitive organs such as the brain and the genitalia during pregnancy and lactation, leads to many abnormalities in the endocrine system and genital cancers in adulthood (64,65).

On the other hand, the regulation of OT actions, which is performed by certain phytoestrogens, on uterine contractions is essential for maintaining pregnancy and preventing early miscarriage or abortion (66). The

oxytocic activities of certain plants, which are due to their compounds or high dosages, leads to severe spontaneous contractile frequency of the uterus and abortion (67,68). Certain phytoesterogens lead to ovarian dysfunction by affecting the OT synthesis in the ovary and the corpus luteum (69). Although most studies have been conducted *in vitro* and with laboratory animals, medicinal plants should be consumed in pregnancy and lactation with special cautions.

CONCLUSION

Herbs and their derivatives can induce their tocolytic effects through inhibiting OT-induced uterine contractions by influencing its levels in the body including the neuraxis, and relieve dysmenhorea and increase lactation. Therefore, they can be used with chemical drugs to treat OT-associated disorders. However as with chemical drugs, certain cautions should be taken into account in consuming these remedies during pregnancy to minimize fetal and maternal side effects.

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Conflicts of interest

There are no competing interests.

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