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Review article

Reports on in vivo and in vitro contribution of medicinal plants to improve the female reproductive function

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ABSTRACT

Medicinal plants are known as a prolific source of secondary metabolites which have important function both in vivo and in vitro during the ovarian folliculogenesis and steroidogenesis in many animal species. Some secondary metabolites can act as antioxidants generally through their ability to scavenge reactive oxygen species (ROS) or can regulate ovarian hormonal production. In general, these properties are responsible for the medicinal functions to treat woman infertility disorder. Some plants are constituted of biological actives substances which have been used to treat reproductive dysfunction. However, until recently, little was known about the implication of plants and/or their secondary metabolites on in vitro folliculogenesis and steroidogenesis. With the development of the technology, there is an increase implication of those substances in assisted reproductive technology (ART). The present review highlights some medicinal plants used in the treatment of woman disorders related to infertility. In addition, it provides an in vivo and in vitro overview of herbs and their active compounds with claims for improvement of ovarian activity thus showing their implication in female reproductive health care.

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Relatos sobre a contribuição in vivo e in vitro de plantas medicinais na melhora da função reprodutiva feminina

RESUMO

Palavras-chave: Fitoterapia Antioxidantes Sabe-se que as plantas medicinais são uma fonte abundante de metabólitos secundários que têm função importante tanto in vivo quanto in vitro durante a foliculogênese e a esteroidogênese ovarianas em muitas espécies animais. Alguns metabólitos secundários

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Mulheres infertilidade Folículos ovarianos

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podem atuar como antioxidantes, geralmente através de sua capacidade de eliminar espécies reativas de oxigênio (ROS) ou podem regular a produção hormonal ovariana. Em geral, essas propriedades são responsáveis pelas funções medicinais usadas para tratar distúrbios da infertilidade feminina. Algumas plantas contêm substâncias biológicas ativas que têm sido utilizadas para tratar a disfunção reprodutiva. No entanto, até recentemente, pouco se sabia sobre o efeito das plantas e/ou seus metabólitos secundários na foliculogênese e na esteroidogênese in vitro. Com o desenvolvimento da tecnologia, há uma implicação crescente dessas substâncias na tecnologia de reprodução assistida (TRA). A presente revisão destaca algumas plantas medicinais utilizadas no tratamento de distúrbios femininos relacionados à infertilidade. Além disso, fornece uma visão in vivo e in vitro de ervas e seus compostos ativos com alegações de melhora da atividade ovariana, mostrando assim seu envolvimento nos cuidados de saúde reprodutiva feminina.

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Introduction

Infertility is a disease of the reproductive system which affects both men and women with almost equal frequency. It is a global phenomenon affecting an average of 10% of human reproductive age population. 1 Many conditions can be associated to this problem, including intrinsic (anatomic, genetic, hormonal and immunological disorders) and extrinsic factors such as sexually transmitted infections (STIs), infections after parturition or surgery, tuberculosis of the pelvis, and obesity.^{2,3}

There are a range of medical treatment options for infertility, such as the use of commercial treatments to stimulate "superovulation" which correspond to the development and release of more than one egg per ovulatory cycle. In addition, ART is commonly applied to solve infertility problems, including procedures to bring about conception without sexual intercourse. Among the available techniques, in vitro maturation (IVM), in vitro fertilization (IVF), intracytoplasmic sperm injection (ICSI) and intrauterine insemination (IUI)⁴ are frequently applied. As an alternative, medicinal plants can also be used to solve part of the reproductive problems. Due to their chemical composition, many plants have showed beneficial properties in the folliculogenesis and steroidogenesis through their antioxidant properties and regulation of some enzyme of the steroidogenesis.5-8

For a better understanding of the medicinal properties of crude plant extract or secondary metabolites on the regulation of reproductive function (folliculogenesis and steroidogenesis), many in vivo studies have been performed. 5,6,8,9 Several studies showed that the plant secondary metabolites act either directly on ovarian cells to eliminate the ROS or through action on several enzymes such as catalase, glutathione, superoxide dismutase and glutathione peroxidase. 10-12 On the other hand, plants (infusion, decoction, beverages, crude extracts) showed their implication during the steroidogenesis through their capacity to mimic the biologic effects of endogenous hormones. These plant medicine derivatives can act by binding to their nuclear receptor or regulating the activities of key enzymes of their metabolisms.^{6,13}

The present review is an attempt to consummate the available scientific information on various medicinal plants, which have been evaluated for their effect on female reproduction. Among all the female reproductive organs, only the ovary is discussed on this review since it is the site of the folliculogenesis and steroidogenesis.¹⁴ The review also includes known evidences collected for the involvement of plant extracts in vivo and in vitro. A number of plants and/or secondary metabolites have been discussed in detail and a few others were only tabulated; a major criterion for this arrangement was the ethnopharmacological relevance of the plant.

Mammalian ovary, folliculogenesis and ovarian follicles

The mammalian ovary is the female gonad which contains germ cells responsible for the perpetuation of the species. Furthermore, it is also the reproductive gland controlling many aspects of female development and physiology. 15 That is why it is important for the reproductive biologists to understand not only the normal functioning of the ovary but also the pathophysiology and genetics of diseases such as infertility.

The ovary consists of many types of differentiated cells, which work together, promoting an ideal environment to perform the endocrine and exocrine functions. Those functions are performed by different factors such as autocrine, paracrine, juxtacrine and endocrine are essential for ovarian folliculogenesis. 16 Folliculogenesis is the result of a complex and closely integrated series of events which start generally soon after conception. This process can be defined as the formation, growth and maturation of follicle, starting with the formation of the oocyte surrounding by the granulosa cells which formed the primordial follicles.¹⁷

Besides the granulosa cells, the thecal cells are recruited to the oocyte and are directly or indirectly necessary for the oocyte development, physiology and survival. The dynamic of the ovarian folliculogenesis is classified in different stages known as: (a) formation of the primordial follicles; (b) recruitment into the growing pool to form a primary, secondary, and tertiary follicles; (c) lastly ovulation and subsequent formation of a corpus luteum. 18 In most species, the mammalian ovary shows extensive variation mainly in relation to the interstitial tissue of the organ, the so-called interstitial gland, and

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