

# Medicinal plants effect on prolactin: A systematic review

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## Abstract

Prolactin has many roles in the human body and in other mammals. Increased prolactin can cause many diseases, including infertility, sexual dysfunction, and mental illness. Therefore, in this study, we sought to identify and investigate the action mechanisms of medicinal plants and their derivatives in increasing, modulating and neutralizing the harmful effects of prolactin (PRL). In this systematic review, articles indexed in the Institute for Scientific Information (ISI) and PubMed databases were retrieved using relevant search terms by using the Endnote software. Of the 432 retrieved articles, finally 37 articles were included in analysis. Plants and herbal compounds such as *Withania somnifera*, *Fructus Hordei Germinatus*, resveratrol and kolaviron, are effective in reducing PRL and improving hyperprolactinemia (hyperPRL). But, some plants such as *Cnidioscolus aconitifolius*, *Meenakshi Cissampelos pareira* Linn., *Mimosa pudica*, *Cyperus rotundus* Linn., *Urtica dioica*, soybean and compounds such as silymarin and puerarin are effective in increasing PRL and lactation. Certain plants and their derivatives increase PRL levels due to phytoestrogenic properties and isoflavones by influencing dopamine receptors and other mechanisms that need to be further investigated. On the other hand, by inhibiting dopamine-2 receptors, these compounds can be effective in modulating or reducing PRL and treating diseases such as hyperPRL.

**Key words:** Medicinal plant; Prolactin; Phytotherapy

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## Introduction

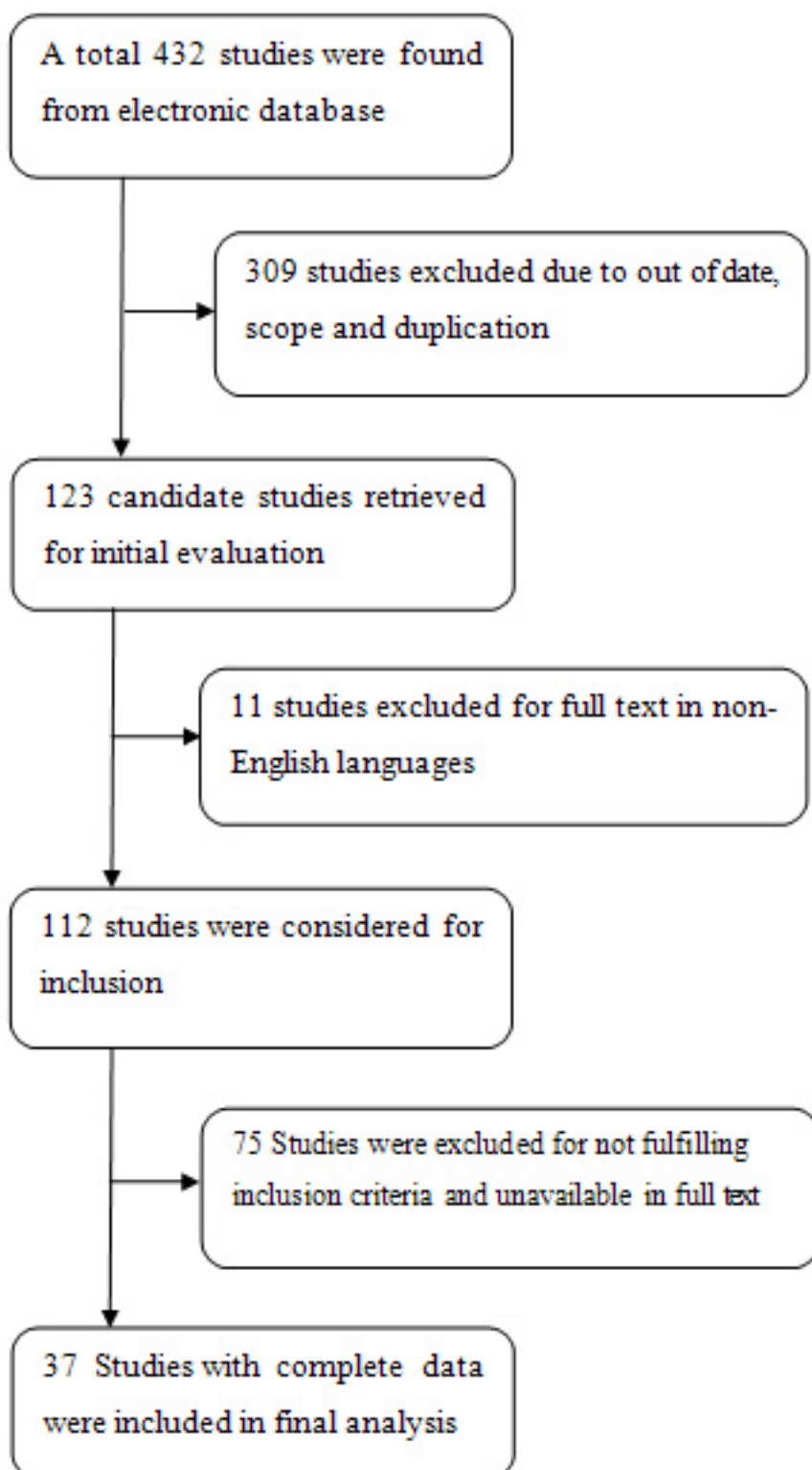
Prolactin (PRL) is a hormonal protein that is widely distributed in animals and is secreted from the anterior pituitary (1). The balance of this hormone in the body is very important, because its increase or decrease in the body causes many complications. Increased PRL secretion, known as hyperPRL, is associated with ovulatory disorder and subsequently secondary amenorrhea or oligomenorrhea (2) and also is considered a male infertility factor (3). It is associated with other disorders such as hypothyroidism (4, 5), osteopenia (6), depression, hostility, and anxiety (7). On the other hand, PRL deficiency in lactating women may disrupt the growth of infants, necessitating therapeutic measures (8, 9). In addition, the presence of PRL disrupts the process of breast cancer chemotherapy and thus its production should be reduced in the body [10].

Today, in spite of numerous therapies to promote different dimensions of health, chemical treatments and phytotherapy are still important with respect to the treatment of different disorders and diseases (11-15). Dopamine is a major inhibitor of PRL secretion by influencing D2 receptors in membrane cells of lactotrophs (16). Therefore, dopamine agonists can be used to treat hyperprolactinemia (2). But chemical treatments for PRL-related disorders are associated with several complications. Hence, finding several therapeutic strategies can help reduce these complications especially in lactating women (17, 18). In addition, medicinal plants are used for the treatment of psychological and physiological diseases due to their comparatively fewer side effects and lower cost (19-27). Therefore, in view of the importance of PRL in human health, we conducted this review to identify and investigate the action mechanisms of medicinal plants and their derivatives in increasing, modulating and neutralizing the adverse effects of PRL.

## Materials and methods

The search terms of interest, medicinal plant, herb and phyto, and the EndNote software were used to retrieve the relevant articles indexed in the Institute for Scientific Information (ISI) and PubMed. Then, the plants and the plant-based products that were effective on prolactin were selected by two colleagues. The manuscripts included in this review were published between 2007 and 2017 and reported the studies with clinical trial or experimental design. The articles published in non-English languages and not related to the purpose of this study were excluded after the authors agreed on it. Figure 1) is the flowchart that illustrates how the articles were selected for final analysis.

**Figure 1. Process of selecting articles for final analysis**



**Table 1: Medicinal plants effective on PRL**

Plants	Kind of use	Main effects and mechanisms	References
<i>Cnidoscopus aconitifolius</i>	Leaves extract	Increasing serum prolactin concentration	(28)
<i>Meenakshi Cissampelas pareira Linn.</i>	Methanolic leaf extract	Altered gonadotropin release (LH, FSH and PRL) and estradiol secretion and cause infertility	(29)
<i>Mimosa podia</i>	Root extract	Increasing level of PRL secretion and altered gonadotropin release	(30)
<i>Lithuania somniferous</i>	Root extract	Reducing levels of PRL and increasing the chance of male fertility	(31)
<i>Fructus Hordei Germinatus</i>	Total alkaloids and aqueous extract	Regulating serum PRL levels to normal in the rats with hyperprolactinemia and reducing the secretion of PRL in hyper PRL rats	(32-35)
<i>Cyperus rotundus Linn</i>	Aqueous extract	Stimulating synthesis of PRL significantly and consequently effective in increasing the lactation	(36)
<i>Urtica dioica</i>	Hydroalcoholic extract	Increasing in serum prolactin and alveolar diameter	(37)
Soybean	Hulls	As a phytoestrogen can increase level of PRL	(38)

**Table 2: Phytochemicals effective on PRL**

Phytocompound names	Origin	Main effects and mechanisms	References
Genistein	Soy bean	Estrogenic effect of genistein can increase serum prolactin and gene expression and prolactin release	(39, 40)
Daidzein and Equol	Soy bean	Exerts estrogenic like effects on the lactotropes in ovariectomized rats and increases level of serum prolactin and regulate PRL and prolactin receptors (PRLR) and regulating gene mRNA levels in the hypothalamus-pituitary-gonadal axis	(41-43)
Silymarin	Milk thistle (Silybum marianum fruits)	Increasing circulating prolactin through involving, at least in part, dopamine D(2) receptors	(44)
Rutin	Supplement	Promoting pituitary PRL and up-regulated the gene expression of PRLR	(45)
Resveratrol	Supplement	Decreasing prolactin level via impact on estrogen receptors and suppression of GH3 cell growth and through the inhibition of PRL synthesis	(46)
Kolaviron	<i>Garcinia kola</i>	Ameliorating the PRL in benign prostatic hyperplastic rats	(47)
Puerarin	<i>Pueraria lobata</i>	Increasing levels of PRL and effect on somatotropes and pituitary estrogen-responsive mRNA expressions	(48)

Several plants and herbal formulations were found to contribute to increasing, modulating and neutralizing the harmful effects of PRL in the body (Tables 1 and 2).

## Discussion

Several herbal formulations are used to counteract variations in PRL level in the body. For example, Lirukang Granule is a herbal formulation used in traditional Chinese medicine that regulates PRL levels in patients with hyperplasia of mammary gland (49). Ushiroyama et al. conducted a study on Xiong-gui-tiao-xue-yin with women

in the postpartum period. The results of Ushiroyama et al. indicated that this herbal formulation increased PRL and subsequently increased the breast milk in the mothers treated with it (50). The combination of two herbs called ayahuasca vine (*Banisteriopsis caapi*) and a shrub called chacruna (*Psychotria viridis*) is a herbal formulation called Ayahuasca, which is used in some regions as tea. This formulation increased the levels of PRL by influencing neuroendocrine stimuli (51). The studies of Wang et al. and Yuan et al. on Peony-Glycyrrhiza Decoction, which is a dopamine agonist, with animal models indicated that this combination could lead to a decrease in PRL production in

MMQ cells via modulation of dopaminergic (52-54). Two compounds of this combination, paeoniflorin and liquiritin, are also effective in treating hyperprolactinemia (55). Li et al. examined the use of a Chinese herbal formulation called Lirukang Granule with psychotherapy in patients with cyclomastopathy and menoxenia. They found that treatment with this formulation reduced PRL levels (56). A study on a Chinese formulation called Huiru Yizeng Yiha showed that this formulation reduced PRL levels, increased estradiol levels and led to hormone modulation in hyperPRL (57). In a study on the effect of a herbal mixture called formula malt decoction (FMD) on hyperPRL, this Chinese herbal mixture was found to exert a potent anti-hyperplastic activity by suppressing PRL synthesis and influencing dopamine D2 receptor (58).

## Conclusion

Certain plants and their derivatives can increase PRL levels due to phytoestrogenic properties and isoflavones by influencing dopamine receptors and other mechanisms that should be further examined. Besides that, by inhibiting dopamine-2 receptors, these combinations can be effective in modulating or reducing PRL and to treat diseases such as hyperPRL.

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