

# Effects of Herbs on Hypothalamic-Pituitary-Gonadal (HPG) Axis and Hypothalamic-Pituitary-Adrenal (HPA) Axis

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## ABSTRACT

The hypothalamic pituitary gonadal axis (HPG), which plays a critical role in development of body systems including immune and reproductive systems all of which need to be in balance for optimum functioning of the body, mind, and spirit. Modern mechanisms of herbal remedy focus on adjusting immune dysfunction, regulating abnormal activity in the hypothalamic-pituitary-adrenal (HPA) axis and serving as an antioxidant. Some herbs nourish the HPA axis and promotes adrenal, thyroid and reproductive function.

(HPG) axis is activated, leading to increases in luteinizing hormone (LH), follicle stimulating hormone (FSH) and sex steroids (testosterone and estradiol) levels. The HPG axis, which regulates gonadal steroid production, is a multiple level hormonal system involving brain and pituitary with feed forward and feedback elements.

**Key words:** hypothalamic-pituitary-gonadal (HPG) axis, hypothalamic-pituitary-adrenal (HPA) axis, herbs

## BİTKİLERİN HİPOTALAMUS-HİPOFİZ-GONAD (HPG) AKSİSİNE VE HİPOTALAMUS-HİPOFİZ-ADRENAL AKSİSİNE (HPA) AKSİSİNE ETKİLERİ

### ÖZET

Hipotalamus-hipofiz-gonad aksisi, bağışıklık ve üreme dahil olmak üzere vücut sistemlerinin gelişiminde önemli bir rol oynar, ayrıca vücut, akıl ve hafıza fonksiyonlarının ayarlanmasını da etkiler. Bitkisel tedavinin modern uygulaması; bağışıklık sistemindeki bozuklukların giderilmesi, HPA-HPG aksislerindeki anormalliklerin düzeltilmesi ve tedaviye bir antioksidan olarak yardımcı olunması yönündedir. Bazı bitkiler, HPA aksisini besler ve adrenal, tiroid ve üreme organlarının fonksiyonlarını destekler.

Hipotalamus-hipofiz-gonad aksisi (HPG) aktive edildiğinde, luteinizan hormon (LH), folikül uyarıcı hormon (FSH) ve seks steroidlerinin (testosteron ve estradiol) artışına yol açar. Aynı zamanda gonadal steroid üretimini düzenleyen HPG aksisi, ileri bildirim ve geri bildirim yöntemi ile çalışan hipofiz ve beyinin de dahil olduğu çok yönlü hormonal bir sistemdir.

**Anahtar sözcükler:** hipotalamus-hipofiz-gonad (HPG) aksisi, hipotalamus-hipofiz-adrenal (HPA) aksisi, bitkiler

**T**he pituitary tells the adrenal glands to help for dealing with stress. The adrenal glands produce stress hormones that, among other things, tells the hypothalamus there is a stressful situation. Hypothalamus, Pituitary, Adrenal (HPA) Axis modulates body's response to stress and helps support hormonal balance during premenopause, menopause and postmenopause. The anti-fatigue, anti-stress, immuno-enhancing effect, enhanced neuro-cognitive, and anti-depressive effects associated with regular use may be associated with effects on the HPA axis, which plays a primary role in the reactions of the body to repeated stress and adaptation to stressors (1).

Herbs with identifiable hormone-like activities on the HPA axis are considered in Interactions, although detailed

studies and reports of interactions between pharmaceutical drugs and these agents are not available (2). Basically, there are 4 mechanisms by which drugs and medications impair male fertility: by exerting a gonadotoxic effect on the testicles, by altering the Hypothalamic Pituitary Gonadal (HPG) axis, by impairing ejaculation and erectile function, and by decreasing libido.

The Endocrine Society defines hypogonadism in men as a clinical syndrome that results from failure of the testes to produce adequate levels of testosterone and a normal number of sperm due to a disruption of the HPG axis. The follicle stimulating hormone (FSH) stimulates spermatogenesis by acting on the Sertoli cells, while the Luteinizing hormone (LH) stimulates the Leydig cells of the testes to secrete testosterone. Testosterone levels modulate the HPG axis, such that high testosterone levels inhibit the frequency and amplitude of the GnRH pulsatile release

from the hypothalamus (3). Several substances alter the delicately balanced HPG axis, causing either a decline in pituitary-secreted gonadotropins or an alteration in intratesticular testosterone concentrations (4).

## Mechanism of action

The HPA glands and their interactions are responsible for the secretion of hormones vital to the control of carefully orchestrated production, synthesis, and communication of these hormones. In response to stress, the hypothalamus secretes corticotropin-releasing hormone (CRH) that then stimulates the anterior lobe of the pituitary gland to secrete adrenocorticotrophic hormone (ACTH). ACTH then reaches the adrenal cortex and cortisol is synthesized and secreted into the bloodstream. This hormone, cortisol, is the major glucocorticoid that acts as both mediator and inhibitor of the stress response. (5).

Herbs with HPA axis activity: Oxytocic synergists: *Asclepias asperula* (Immortal), *Capsella bursa-pastoris* (Shepherd's Purse), *Cinchona* spp. (*Cinchona* bark), *Claviceps purpurea* (Ergot of Rye), *Cytisus scoparius* (Scotch Broom), *Gossypium* spp. (Cotton root Bark), *Leonurus cardiaca* (Motherwort), *Myristica fragrans* (Nutmeg), *Petroselinum crispum* (Parsely), *Senecio aureus* (Life Root), *Stachys betonica* (Wood Betony).

Prolactin inhibitors: *Glycyrrhiza glabra* (Licorice root), *Paeonia lactiflora* (Peony), *Rehmannia glutinosa* (Chinese Foxglove), *Vitex agnus-castus* (Chasteberry), Chinese herbal formula: *Rehmannia Eight*, Chinese herbal formula: *Paeonia* and *Glycyrrhiza*. FSH/LH modifiers: *Cimicifuga racemosa* (Black Cohosh), *Tripterygium wilfordii* (Lei Gong Teng), *Vitex agnus-castus* (Chasteberry).

Progestagenics: *Alchemilla vulgaris* (Ladie's mantle), *Angelica sinensis* (Dong Quai), *Areca catechu* (Betel nut), *Ceanothus americanus* (Red Root), *Vitex agnus-castus* (Chasteberry) (6).

*Panax* roots are known to contain phytoestrogens, which are dietary estrogens. Dietary estrogens mildly imitate the action of natural estrogen and may also act as neutralize the effect of estrogens. Ginsenosides in ginseng can help in obtaining sustainable penile erection. The active compounds in ginseng are known as ginsenosides, and most of the top-quality ginseng supplements will be standardized for ginsenoside content. It is thought that the ginsenosides interact within the HPA axis to balance the body's secretion of ACTH and cortisol. ACTH has the ability to bind directly to brain cells and can affect a variety of stress-related processes in the body.

Phytoestrogens may be defined as plant constituents possessing the ability to mimic the biological effects of beta-estradiol in laboratory tests by their ability to bind to the nuclear estrogen receptor, activate transcriptional response and to promote growth of estrogen dependent MCF7 cells in culture (7).

Alcoholism and hepatic cirrhosis cause alterations in the HPG axis, resulting in testicular dysfunction (8). In addition, the oxidation of alcohol competes with testicular production of testosterone. These mechanisms lead to subsequent decrease in semen volume and sperm density. Another factor appears to be an elevation in serum estrogen caused by peripheral conversion of testosterone to estrogen through increased activity of the enzyme aromatase, which is present both in the liver and in peripheral fat cells (9).

Another group of researchers in China studied the effects of salidroside, an extract of *Rhodiola*, on the function and change of the HPG axis of rats in experimental navigation and intensive exercise (10). They found that negative psychological stress and intensive exercise can significantly suppress the function of the HPG axis, and therapy with the salidroside from *Rhodiola* protects the activity of this axis.

*Tribulus* may be the best resensitizer of the HPG axis of both men and women, reducing the requirement for hormone replacement therapy. As well as its receptor-sensitizing effects, it is likely that *Tribulus* can enhance the effectiveness of hormone replacement therapy, while reducing adverse effects and receptor downregulation.

Dopamine is one of the neurotransmitters, which has inhibitory effect on the HPG axis (11). This axis maintains the normal physiology of the female and male reproductive systems. Endocrine disorders in a woman's reproductive system can lead to menstrual problems, endometriosis, delayed puberty, polycystic ovary syndrome, and sexual problems as well as infertility and breast problems. Ingredients that can promote the sex glands and increase the level of estrogen include: *Epimedium*, ginseng, *polygala* root, fennel, honey, liquorice root, black soybean, *astragalus* root (12).

Most antipsychotics block dopamine in the CNS, leading to suppression of the HPG axis and decreased libido. Anabolic steroids are being used not only by body builders, but also by athletes in all age groups. Unfortunately, these agents may have devastating effects on fertility. Anabolic steroids suppress the HPG axis via feedback inhibition (13). Testosterone is also converted to estrogen in

peripheral fat cells by the enzyme aromatase, increasing the negative feedback on the HPG axis.

Neuroendocrine abnormalities have been observed in both disorders, including dysregulation of the HPA and HPG axes (14). Interaction between HPA and HPG axes in stress-induced amenorrhea suggests that there may be perturbation of these axes in Chronic fatigue syndrome (CFS). One important confound is co-morbid depressive illness, present in approximately 50% of CFS patients (15).

## Conclusion

Adaptogenic herbs help the liver detoxify and support the HPA axis, including the adrenal glands which are heavily taxed by stress. Used properly, they are safe, non-toxic and non-habit forming.

These herbs also facilitate optimal function of regulatory mechanisms such as the HPA Axis, that control hormones involved in the stress response. Herbs may assist in regulating the menstrual cycle by encouraging a normal, healthy balance of estrogen and progesterone in women, through support of the HPG axis. Herbs may assist in maintaining a healthy balance of LH and FSH in the body, as well as stimulating the secretion of progesterone in the luteal phase of a woman's cycle.

The hypothalamic-pituitary-gonadal axis is a critical part in the development and regulation of a number of the

body's systems, such as the reproductive and immune systems. Fluctuations in the hormones cause changes in the hormones produced by each gland and have various widespread and local effects on the body.

The endocrine response to stress is not limited to activation of the hypothalmo-hypophyseal-adrenocortical system, but involves the hypothalmo-hypophyseal-gonadal system and other neuroendocrine axes physical or emotional stress is a profound disruptive factor to reproductive function. In males, stress induces suppression of testosterone secretion, spermatogenesis and libido. Activation of the HPA axis by stressors is a presumable mechanism for the inhibition of male reproductive functions through a depression in the hypothalamic-pituitary-testicular axis. Chronic exposure to stress increase HPA activity and concomitantly reduces HPG axis activity (16).

These HPA axis abnormalities are similar to those seen in depression, suggesting that activation of the HPA axis may be linked to inhibition of the HPG axis (17).

Botanical researchers look at the effect of adaptogens on regulating the HPA axis and use them to regulate the neuroendocrine and immune systems. Adaptogenic herbs support the entire neuroendocrine system, in particular the adrenal function and the stress response, which result in a modulating and regulating effect on the use of cortisol. Stress-induced activation of HPA hormonal axis plays an important role in suppressing the HPG axis.

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