Effects and mechanisms of medicinal plants on stress hormone (cortisol): A systematic review

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Abstract

Stress is a psychological and physiological state that leads to release of cortisol from the adrenal gland, and is associated with several complications if left untreated. This review was conducted to investigate the effects and action mechanisms of medicinal plants and their derivatives on cortisol. To conduct this systematic review, the key words of interest were used to retrieve relevant articles from databases the Information Sciences Institute and PubMed. Then, the plants and the plant-based products that were effective in corticotropin-releasing hormone, adrenocorticotropic hormone, and cortisol and therefore control stress, were selected. According to the inclusion and exclusion criteria, the results of 19 articles were analyzed. The plants and their derivatives help regulate the key mediators and cytokines effective in stress response via targeting the hypothalamic-pituitary-adrenal (HPA) axis. In addition, they can induce anti-stress properties via changing and modulating oxidative and nitrosative stress biomarkers. Regulation of certain stress hormones receptors and corticotropin releasing factor is another mechanism of the plants and their derivatives in reducing stress. The plants and their derivatives have exhibited their therapeutic effects on mild stress and they are also effective in treating more severe disorders such as chronic stress through affecting the HPA. They can be considered an independent or supplementary treatment alongside chemotherapies to decrease cortisol levels and to induce calmness.

Key words: Medicinal plant; Cortisol; Stress; Hypothalamo-pituitary-adrenal.

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Introduction

Stress refers to a state in which the balance between the living organism and the environment is disrupted. This bothering condition can be due to heavy workload, educational pressure (examinations), trauma-induced physical and psychological stress, surgery, and other hard conditions of life (1). Stress can be influenced by certain factors such as age, gender, suffering from psychiatric disorders such as depression and anxiety (2) and external factors such as genetic characteristics (3). Inducing stressful conditions is dependent on biological changes in the body. Meanwhile, the hormonal balance of the body is disrupted. Certain hormones such as catecholamines, vasopressin, gonadotropins, thyroid hormones, prolactin, growth hormone, and insulin fluctuate in response to stressful conditions (1).

Activating the pituitary-adrenal axis is the most important neuroendocrine response to stress that leads to release of certain glucocorticosteroids such as cortisol from the cortical part of the adrenal gland that is essential for homeostasis and survival during stress (4). Imbalance of cortisol levels leads to different diseases such as cardiovascular diseases (5), gastrointestinal diseases, inflammation, immunodeficiency, and psychiatric disorders (6,7). Different treatments are available for stress. Currently, despite the availability of several psychotherapies (8-13) and chemotherapies for chronic psychiatric disorders, treating stress remains relatively difficult (14).

Medicinal plants can represent effective treatments for different diseases including psychiatric disorders and have become increasingly popular due to being less expensive and causing fewer side effects (15-25). Moreover, phytotherapies have demonstrated positive effects in treating stress (26). With regards to the significant role of the endocrine system in stress induction and the several health-related complications due to stress in humans, this review was conducted to investigate the effects and action mechanisms of medicinal plants and their derivatives on cortisol.

Materials and methods

To conduct this systematic review, the key words of interest and Endnote software were used. The key words corticotropin-releasing hormone, adrenocorticotropic hormone, or cortisol in combination with herb, medicinal plant, and phyto were used to retrieve relevant articles from databases of the Information Sciences Institute and PubMed. Then, the plants and the plant-based products that were effective in corticotropin-releasing hormone, adrenocorticotropic hormone, and cortisol and therefore control stress, were selected. The articles included in this review were published between 2007 and 2017. The articles whose full texts were not accessible 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.

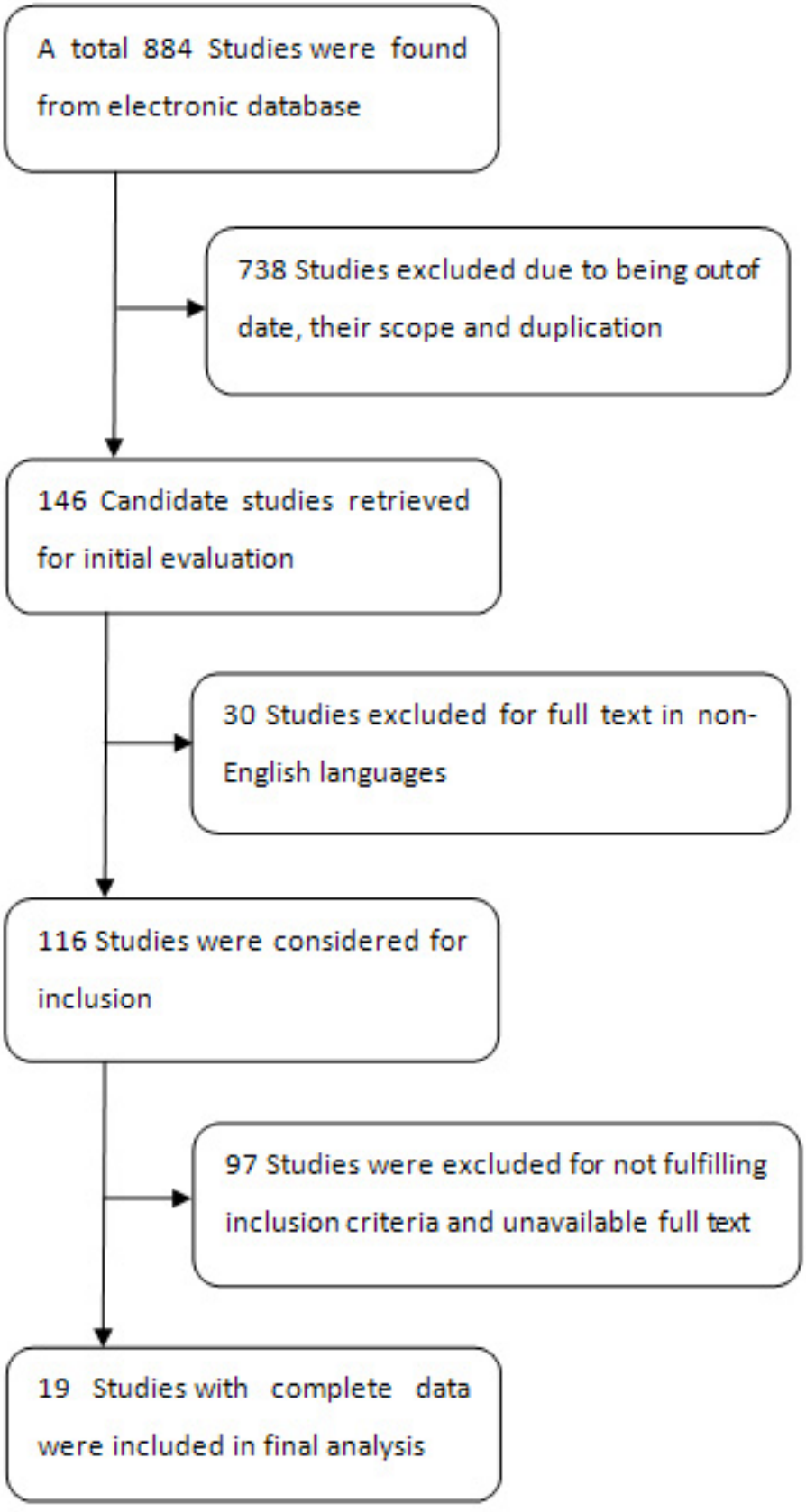
The plants regulate cortisol levels mainly through affecting the HPA axis. Several studies have been conducted on the plants (Table 1 - page 114) and the plant-based compounds (Table 2 - page 115) that are effective in modulating hormone.

Besides that, certain plants, as formulated or combined with other plants, have been approved and used in traditional medicine and experimental research. For example, Si Ni Tang is a Chinese herbal combination consisting of Glycyrrhiza uralensis, Zingiber officinale, and Aconitum carmichaeli. A study on a rat model of chronic unpredictable stress showed that Si Ni Tang modulated increase in corticosterone and therefore helped relieve stress (41). Another study demonstrated that Si Ni powder extract modulated serum levels of corticosterone and ACTH. In addition, this extract causes increase in mRNA expression of hippocampal glucocorticoid receptors (42). The use of combination of Magnolia officinalis and Phellodendron amurense for four weeks caused decrease in salivary cortisol levels in patients with stress (43). A study reported that Zhi-Zi-Hou-Po, consisting of Gardenia jasminoides Ellis fruit, Citrus aurantium L. fruit and Magnolia officinalis Rehd. et Wils. bark, caused normalization of ACTH and CORT levels in a rat model of unpredictable chronic mild stress (44).

Studies have shown that certain compounds in the plants lead to relief of stress through increasing resistance to mental exhaustion and increasing attention. However, several mechanisms can be considered in this regard such that they help regulate the key mediators that are effective on stress response consisting of molecular chaperons stress-activated c-Jun N-terminal protein kinase 1 (JNK1), (e.g., HSP70), Forkhead box O (FOXO) transcription factor DAF-16, cortisol, and nitric oxide (45) through targeting the HPA axis (27, 36, 45, 46). In addition, the plants decrease the expression of CRF and regulate the activities of certain receptors of stress hormones such as GRs (36, 37). On the other hand, some medicinal plants such as Hypericum perforatum, Melissa officinalis, Valeriana officinalis, and Passiflora incarnata can induce anti-stress properties through changing and modulating oxidative and nitrosative stress biomarkers (47). Also other studies have shown that medicinal plants and their extracted compounds can be effective via their antioxidant activities (48-54).

However, studies have not consistently confirmed usefulness of plant-based compounds to relieve stress. For example, a study reported that medicinal plants do not cause any change in ACTH or corticosterone (55). In addition, certain issues should be taken into account in using medicinal plants such as effective dose and associated drug-induced side effects, and interaction with chemical drugs. It is therefore recommended to use medicinal plants and their derivatives under physicians' supervision.

Figure 1. Flowchart of the process of analyzing the articles



Findings

The plants regulate cortisol levels mainly through affecting the HPA axis. Several studies have been conducted on the plants (Table 1) and the plant-based compounds (Table 2) that are effective in modulating hormone.

Table1: Medicinal plants effective on cortisol

Plants	Type of use	Main effects and mechanisms	References
Valeriana jatamansi Jones	Extract	Reducing blood levels of 3-endorphin and corticosterone and regulating HPA	**(27)**
Shuyusan (a Chinese herb)	Decoction	Reducing corticotropin-releasing factor (CRH), adrenocorticotropic hormone (ACTH), corticosterone (CORT) and decreasing activity levels of glucocorticoid	**(28)**
Laminaria japonica	Sulfated polysaccharide	Reducing plasma cortisol	(29)
Andrographis paniculata	Extract	Reducing plasma cortisol levels, and suppressing expressions of the cytokines TNF-alpha, IL-10 and IL-1beta in blood and brain	(30)
Hippophae rhamnoides L.	Oil	Suppressing cortisol, ACTH, IL-1beta, and TNF-alpha levels	(31, 32)
Sceletium tortuosum	Extract	Inhibiting forskolin-associated increases in cortisol levels and basal cortisol levels	(33)
Camellia sinensis L.	Extract	Reducing in serum cortisol	(34)

Table 2: Phytochemicals effective on cortisol

Phytocompound names	Origin	Main effects and mechanisms	References
YZ-50	Polygala tenuifolia Willd	Neutralization of the harmful effect in HPA and brain-derived neurotrophic factor (BDNF) system in the hippocampus	(35)
Icariin	Epimedium brevicornum	Reducing the expression of the corticotropin releasing factor (CRF) and modulating the glucocorticoid receptor (GR) and 5-hydroxytryptamine 1A receptor (5-HTR1A) in the hippocampus and frontal cortex	(36)
XBXT-2	Xiaobuxin-Tang	Reducing corticotropin-releasing factor (CRH), adrenocorticotropic hormone (ACTH), corticosterone (CORT)	(37)
Gastrodin	Tall gastrodia tuber	Reducing anxiety-like behavior, levels of IL-6 and IL-1 beta, and the expression of iNOS and the p38 MAPK phosphorylation	(38)
Tribulus terrestris saponins	Tribulus terrestris fruit	Reducing serum concentrations of CRH and cortisol	(39)
Andrographolide	*Andrographis paniculata*	Reducing plasma cortisol levels, and suppressing expressions of the cytokines TNF-alpha, IL-10 and IL-1beta in blood and brain	(30)
Cipadesin	*Xylocarpus granatum*	Inhibiting increase in serum levels of CORT and ACTH	(40)

Conclusion

Of the 19 articles included in this review, only one study was conducted on humans as a clinical trial. Therefore, because studies on humans are more vigorous to determine the mechanism process of medicinal plants, further studies should be conducted on human subjects under controlled conditions to investigate this issue. However, it is obvious that the plants and their derivatives have exhibited their therapeutic effects on mild stress and they are also effective in treating more severe disorders such as chronic stress through affecting the HPA. They can therefore be considered as supplementary treatment alongside chemical drugs to decrease cortisol levels and to induce peace.

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