

Phytochemicals as Modulators of Human Endocrine Function: Bridging Traditional Remedies and Hormonal Health

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ABSTRACT: The cases of endocrine disorders increasing across industrialized nations and societies have long been correlated to extended exposure to synthetic substances or chemicals. The majority of these chemicals can act as endocrine disruption and disrupt normal hormonal pathways. The prolonged exposure to socioeconomic conditions, urban environments, poor health lifestyles, and many other factors causes a large number of cases of metabolic and hormonal disorders commonly observed among the general population, including obesity, type II diabetes mellitus, cardiovascular disease, reproductive disorders, and thyroid dysfunction. The long-term use of synthetic pharmacotherapy results in increased adverse responses associated with the medications. The use of plant-derived, natural alternatives to synthetic medications has been receiving an increasing level of interest and attention. The objective of this chapter is to provide information regarding phytochemicals and their potential for modulation of human endocrine function, bridging traditional forms of herbal medicine with contemporary hormonal health care.

Keywords: Endocrine disruption, cardiovascular disease, reproductive disorders, phytochemicals

INTRODUCTION

In the current industrialized world, synthetic chemicals have been more heavily introduced into the ecosystem than before. Growing interactions between chemicals and people increase exposure and consequently health risks. In addition to documented pulmonary pathways, there is increasing evidence from many sources that chemical manufacturers of pharmaceutical drugs that have effects on hormones have the power to impact a number of biological circuits. (Seetharaman et al., 2024). Endocrine disorders can be caused by hormone imbalances and can be associated with health-related concerns, including obesity, diabetes, and cardiovascular diseases. A life stage, sex (gender), and eating habits may relate to limitations to this unhealthy risk. The majority of synthetic medications are often associated with unwanted adverse side effects, which prompts a desire for alternatives. Herbal and natural treatments - phytochemicals and polyherbal treatments - can effectively address health deficiencies and disorders related to these conditions and are often less toxic and just as effective without unwanted side effects, hence advantageous. (Bhandari et al., 2025).

Plants contain low-molecular-weight secondary metabolites, referred to as phytochemicals, which are naturally occurring and critical for cellular metabolism and health. Proteins, fats, carbohydrates, and dietary fibers are referred to as primary metabolites in plants that contribute to cell structure and energy metabolism. Unlike these primary metabolites, secondary metabolites contribute to plant protection against

fungi and insects. Under high doses the phytochemical, the phytochemical toxicity (i.e., death) may occur. (Rodríguez-Negrete et al., 2024). These phytochemicals are actually produced for plant self-protection. They come from a variety of foods, including fruits, vegetables, whole grains, nuts, and herbs. More than a thousand phytochemicals have been identified so far. Some key phytochemicals include carotenoids, polyphenols, isoprenoids, phytosterols, saponins, dietary fibers, and specific polysaccharides. These phytochemicals provide phytochemicals' significant antioxidant actions, but they also possess antibacterial, anti-diarrheal, anti-parasitic, anti-allergic, anti-spasmodic, and anti-viral actions. They also stimulate immunity, enhance gap junction communication, regulate gene transcription, and provide a defense against prostate and lung cancers. (Kumar et al., 2023).

PHYTOCHEMICALS AND ENDOCRINE FUNCTION

Phytochemicals

Phytochemicals are naturally occurring compounds produced by plants that are beneficial for health as nutrients and medicinal ingredients. They protect the plant from disease, damage, and hostile environments. When phytochemicals are consumed in quantities as part of a diet quantity they have been shown to protect human health. (Koche et al., 2016) Phytochemicals are bioactive compounds, which include carotenoids, polyphenols, isoprenoids, phytosterols, saponins, dietary fibers, and, in some cases, polysaccharides. They offer

antioxidant, antimicrobial, anthelmintic, antidiarrheal, antiallergic, antispasmodic, and antiviral properties. (Kumar et al., 2023).

Endocrine System

A delicate stroma of connective tissue surrounds the ductless islands of polygonal secretory epithelial cells that comprise endocrine organs. These cells synthesize, store, and release polypeptides, steroids, and derivatives of amino acids into a rich array of capillaries, where they act upon distant target cells after binding with a receptor. (La Perle, 2021). In this industrialized era, Prolonged exposure to chemicals, including endocrine-disrupting substances, may negatively impact the health of individuals via both direct and indirect mechanisms. Non-chemical agents, physical factors such as artificial light, radiation, temperature, and stress exposure, while having the capacity to alter endocrine functioning by affecting hormone action, have not been studied as thoroughly in terms of their impacts on the endocrine system. (Guarnotta et al., 2022).

Endocrine-Disrupting Chemicals

In the medical profession, the antioxidant and anti-inflammatory properties of polyphenols are very significant for improving human health, especially for the treatment of cancer.

Effects on the Reproductive System

In females, having a protective effect against the toxicity induced by endocrine-disrupting chemicals. For example, in pregnant rats, ginseng extract successfully alleviated the offspring reproductive toxicity effects of BPA and phthalates (such as DEHP) through regulating mRNA transcripts of steroidogenic enzymes (either directly or via the Akt/PTEN pathway), bringing altered steroid hormones back towards baseline conditions. In Males, it has a protective role of different polyphenols against the toxicity induced by EDCs on the male reproductive system. For example, *Eruca sativa* aqueous extract (ESAE) was able to protect human spermatozoa from the toxicity of Bisphenol A BPA, and it has been shown that ESAE at low doses after exposure, particularly affects motility and membrane potential recovery.

Effects on the Gastrointestinal System

The administration of quercetin against the exposure to BPA in mice exhibited prevention of liver enlargement, reduction in plasma creatinine, and attenuation of ALT, AST, and ALP activity. Phenolic compounds may confer hepatoprotection from BPA via their anti-inflammatory and antioxidant properties.

Effects on the Urinary System

The triazine insecticide ATR is cytotoxic to mouse TCMK-1 kidney cells due to oxidative stress, causing DNA damage and cellular proptosis. CUR significantly reduced ATR-induced TCMK-1 cell cycle arrest and cell proptosis by decreasing oxidative stress.

Effects on the Endocrine System

The impact of BPA on metabolic syndrome in male albino Wistar rats and the protective benefits of RES and grape seed extract. BPA negatively affected blood pressure, the lipid profile, and hepatic expression of ABCG5 and ABCG8. Furthermore, chronic exposure to BPA increased leptin levels, adiponectin levels, and body fat index, while simultaneously decreasing the blood levels of paraoxonase-1 (PON1). It disrupted insulin signaling by raising fasting blood sugar and serum insulin levels while lowering the hepatic phosphorylated-Akt/Akt and phosphorylated-phosphatidylinositol-3 kinase (PI3K)/PI3K ratios. In this regard, the preventative benefits of RES and grape seed extract may be related to their properties of enhancing insulin signaling and hepatic ABCG8 expression, as well as their antioxidant capabilities (Leti Maggio et al., 2024).

Endocrine-Disrupting Activities of Flavones

A significant family of micronutrients in human diets is flavonoids, which are polyphenolic compounds that occur in herbs. While cell culture assays have demonstrated evidence of various actions, the in vivo activities of flavonoids remain largely undiscovered, despite their anti-inflammatory, antioxidant, and anti-proliferative properties. The research discovered that most active flavones have antagonist activity on androgen and progesterone receptors, acting as estrogen receptor agonists in an active state. The synthesis of a novel flavone composition opens up potential applications for topical use, while also revealing the potential for endocrine disruption (Al-Khayri et al., 2022).

The Role of Phytochemicals in Endocrine Modulation

Endocrine disorders associated with hormone imbalances can lead to health complications such as obesity, diabetes, and cardiovascular diseases, among other things. Life stage, gender, and diet can influence the risk of endocrine disorders. Synthetic medications often have adverse side effects, which makes the need for alternative treatments strong. Herbal and natural remedies, including phytochemicals and poly-herbal remedies, have been shown as reasonable options to manage endocrine disorders because they are usually lower in toxicity and/or have fewer side effects. (Bhandari et al., 2025)

Traditional Remedies and Phytochemicals

Medicinal plants are often utilized to treat a number of diseases. According to the World Health Organization, approximately 80% of the global population continues to use herbal and other traditional remedies for their basic health care needs (Abdu et al., 2015). Western medicine practitioners frequently rely on strong, repeatable support, particularly related to the pharmacological activity of herbal treatments, to accept their clinical efficacy and tolerability. A herbal remedy usually has multiple biochemical and physiological effects on the various systems of the body due to the diversity of active components included in herbal remedies. In contrast, often a single conventional drug has a dominant pharmacological mode of action associated with its therapeutic effect. (Bhikha and Glynn, 2018). The advantages of some plants have been

recognized in the past; there are many plants that, based on this study, still require substantial research. To assess their biological activities, reviewing their uses and conducting pharmacognostic and pharmacological studies is necessary (Ahmad et al., 2009).

Phytochemicals are secondary metabolites produced by plants largely as defense mechanisms against parasites, herbivores, and environmental factors. They are also exploited for their various biomedical activities in different traditional healing practices. Phytochemicals can be classified into numerous main classes based on their molecular structures and their various roles, including alkaloids, flavonoids, terpenoids, polyphenols, saponins, and glycosides. Each class likely possesses different pharmacological properties that make them fit candidates for therapeutic purposes and drug discovery (Ogbuagu et al., 2022).

Herbal Drinks

Herbal drinks are created from parts of plants, such as the leaves, stems, roots, fruits, buds, and flowers, and they have been enjoyed for centuries. There are, however, few studies that have examined their efficacy. Herbal drinks have physicochemical, phytochemical and pharmacological properties. The properties of herbal drinks depend on the herbs and processing used to create the beverages. Herbal drinks have the potential to be commercialized for the health benefits they contain. In Africa, over 90% of individuals use herbal remedies for physical health. In many countries, including China, India, Brazil, Turkey, and more, herbal tea is an acceptable herbal beverage (Shaik et al., 2023). Herbal teas made from flowers are just one of the many ingredients used in traditional medicine and pharmacy in Greece and the Eastern Mediterranean countries. Many ayurvedic herb combinations are brewed to make herbal drinks, including turmeric, ginger, tulsi, mint, coriander, *Terminalia arjuna*, *Decalepis hamiltonii* root, *Piper longum*, *Tinospora cordifolia*, and others, depending on the desired outcome (Shaik et al., 2023).

Saussurea costus

Phytochemical assessment of *S. costus* has shown that it has a significant number of bioactive compounds and phytochemicals, e.g., sesquiterpenes, flavonoids, and essential oils that lead to its beneficial properties. Pharmacological studies have provided evidence for *S. Costus*' anti-inflammatory, anti-oxidant, anti-cancer, hepatoprotective, and immunomodulating activities, while ethnobotanical studies have shown relevance toward asthma, gastrointestinal issues, and skin issues (Kumari et al., 2024).

Dietary Supplements

The natural medications may serve as beneficial adjuncts for improving overall health and well-being in individuals with metabolic syndromes. The citrus flavonoid naringenin may also have the capacity to improve kidney damage in hyperuricemia through decreasing uric acid, inflammation, apoptotic processes, and DNA damage, and by promoting antioxidant activity (Halagali et al., 2025).

MECHANISM OF ACTION OF PHYTOCHEMICALS AS ENDOCRINE MODULATING AGENTS

Receptor Binding Mechanisms

Phytochemicals bind to nuclear receptors and specific non-nuclear hormone receptors. These binding events can produce agonist, partial agonist, or antagonist effects depending upon receptor subtype and tissue context. Phytoestrogens can differentially bind to estrogen receptor alpha and beta, resulting in SERM-like, tissue-selective effects. Other steroid receptor and xenobiotic sensors (PPARs, RXR, PXR) can also be directly targeted by plant-based ligands (D'Arrigo et al., 2021).

Estrogen receptors: There are many isoflavones, lignans and stilbenes that bind to estrogen receptors with a higher degree of affinities for ER β compared to ER α , producing agonist or antagonist responses based on receptor subtype and cellular environments (Solís et al., 2017).

Other steroid receptors: such as androgen and progesterone receptors, can be modulated by phytoosteroids and related plant compounds to alter receptor activation or antagonism, results that influence reproductive tissues. The consequences of phytoestrogenization of the father and the effects of phytoestrogens during puberty for male offspring.

Nuclear metabolic receptors: PPAR α/γ and RXR have been activated by terpenoids and similar phytochemicals, resulting in transcriptional changes in lipid metabolism and glucose metabolism. The effect of phytoestrogens and PAHs on endometriosis and the involvement of gut microbiota, inflammation, and molecular targets (Enayati et al., 2022).

Phytochemicals and Hormonal Health

Phytochemicals have numerous effects on the endocrine system, and depending on their safety and effectiveness, they may have a significant clinical impact on conditions including osteoporosis, cardiovascular disease, and type 2 diabetes. Animal and human studies indicate that polyphenol phytochemicals prevent the initiation, development, and progression of cancer, both in vitro and in vivo. In vitro studies have also shown that genistein, resveratrol, and quercetin inhibit the growth of thyroid cancer cell lines and not normal cultured cells. Some phytochemicals with anti-inflammatory and antioxidative stress activity may also facilitate the development of chronic complications of type 2 diabetes. Researchers have speculated that black tea may be a functional food for individuals with borderline type 2 diabetes (Solís et al., 2017).

Endocrine Disorders and Management from Traditional Remedies

Diabetes mellitus: a common chronic disease that affects people's metabolic systems impaired glucose metabolism, insulin resistance, and β -cell dysfunction, and which can be predicted at early stages through artificial intelligence models and data analysis models. A novel deep gated network model

for explainable diabetes mellitus prediction at early stages based on trustworthy data.

Gymnema Sylvester: *Gymnema sylvestre* is a source of gymnemic acids, saponins, and flavonoids, which boost glucose uptake in peripheral tissues, regulate insulin production, regenerate pancreatic β -cells, and resist intestinal glucose absorption. Therapeutic Role of *Gymnema sylvestre* and *Momordica charantia* in Diabetes Management: A Detailed Review of Their Mechanisms in Insulin Resistance, Glucose Metabolism Regulation, and Clinical Efficacy in Type 2 Diabetes Mellitus (Bhatt and Sharma, 2025).

Berberine: AMPK activation by berberine plays a central role in cellular energy homeostasis, modulating key processes such as gluconeogenesis, lipogenesis, oxidative stress, and inflammation, which contribute to its therapeutic efficacy in metabolic dysfunction and DM-related complications. Targeting AMPK signaling: The therapeutic potential of berberine in diabetes and its complications (Shrivastava et al., 2023).

Fenugreek: *Fenugreek* significantly improved the lipid profiles of people with diabetes. It increased high-density lipoprotein cholesterol (HDL-C) and reduced both triglycerides and the total cholesterol to low-density lipoprotein cholesterol (LDL-C) ratio.

Hyperthyroidism

In hyperthyroidism, stimulation of the thyrotropin receptor results in mesenchymal tissue proliferation and pretibial myxedema, and some other cutaneous findings include onycholysis and hyperhidrosis. Due to excess carotene, hypothyroid patients have brittle hair, cold, dry skin, and a yellowish tint to their skin (Cohen et al., 2023).

Ashwagandha: Supplementing with ashwagandha methanolic extracts improves thyroid function via decreased oxidative stress and improved thyroid hormones.

Guggul: Guggul is a major source of guggulsterones, which metabolize lipids by working on the bile acid receptor and also support the hypolipidemic effects.

Cushing Syndrome

Cushing syndrome is characterized by a prolonged elevation of plasma cortisol levels that cannot be attributed to physiological causes. It is estimated that the incidence of Cushing syndrome caused by endogenous excess of cortisol is between two and eight per million persons per year, even if exogenous steroid use is a more common etiology (Nieman et al., 2025). Cushing syndrome is associated with hyperglycemia, protein breakdown, immunosuppression, hypertension, weight gain, inactivity of the neurocognitive domain, and psychiatric disorders. In pediatric Cushing's syndrome, truncal obesity and growth delay are nearly always observed; skin atrophy and striae abdomen are due to disruptions in collagen synthesis and hypercortisolism's catabolic effect (Scaroni et al., 2017). Ashwagandha increases

circulating cortisol levels and improves insulin sensitivity in the body.

Polycystic Ovary Syndrome

Patients with polycystic ovary syndrome (PCOS) frequently present with hirsutism, acne vulgaris, and androgenetic alopecia, common findings among women with hyperandrogenism (Guzel et al., 2012).

Fenugreek: Fenugreek decreased ovarian volume and cysts, increased luteinizing hormone/follicle-stimulating hormone (LH/FSH) concentrations, and restored regular menstrual cycles in patients with polycystic ovarian syndrome.

CONCLUSION

Phytochemicals are a promising bridge across conventional medicine and current endocrine science, providing biologically active substances capable of influencing hormonal production, release, and receptor signaling. Experimental, clinical, and ethnopharmacological research have shown that flavonoids, alkaloids, terpenoids, and polyphenols can affect important endocrine axes such as the thyroid, adrenal, pancreatic, and reproductive systems. These natural compounds may help prevent and manage endocrine problems by restoring hormonal balance, lowering oxidative stress, and reducing inflammation. However, the heterogeneity in plant composition, dose, and bioavailability emphasizes the importance of consistent formulations and rigorous clinical validation. Integrating phytochemical-based therapies into modern endocrinology may result in safer, more cost-effective, and culturally acceptable techniques for enhancing hormonal health and overall well-being.

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