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Neurons, hormones, and herbs: The symphony of the brain-gut-genital axis

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Abstract

The brain-gut-genital (BGG) axis represents a complex, bidirectional communication network integrating the central and enteric nervous systems, endocrine signals, immune pathways, and microbiota. This axis governs key physiological domains including digestion, reproduction, emotion, and stress response. Central to its function is the vagus nerve, which facilitates real-time communication between the brain, gut, and reproductive organs. Disruptions in this axis caused by chronic stress, inflammation, dysbiosis, or hormonal imbalances can lead to multifaceted disorders such as irritable bowel syndrome (IBS), inflammatory bowel disease (IBD), sexual dysfunction, infertility, polycystic ovary syndrome (PCOS), menstrual irregularities, anxiety, depression, and neurodegeneration. Current pharmacological treatments often fail to address the integrated nature of BGG disorders and are associated with adverse effects. All the plants in this review offer a holistic and multi-targeted approach to restoring BGG homeostasis. These medicinal plants act through neuroendocrine modulation, anti-inflammatory effects, microbiota balance, and enhancement of vagal tone. This review explores the pathophysiology of BGG disorders and highlights the therapeutic potential of botanicals in re-establishing systemic equilibrium across the brain, gut, and reproductive systems.

1. Introduction

The brain-gut-genital (BGG) axis is a dynamic bidirectional communication network that integrates the central and enteric nervous systems, endocrine signals, immune pathways, and microbiota to regulate digestive, reproductive, and emotional functions (Carabotti *et al.*, 2015). The vagus nerve, the longest cranial nerve, plays a central role in this axis by transmitting afferent sensory inputs from the gut and reproductive organs to the brain and sending efferent motor outputs to regulate autonomic processes such as gastro-intestinal motility, secretion, sexual arousal, hormonal release, and immune modulation. It also connects with the hypothalamic-pituitary-adrenal (HPA) axis, influencing stress responses by regulating the release of CRF, ACTH, and cortisol. Gut microbes modulate vagal signaling by producing neuroactive compounds like short-chain fatty acids, GABA, tryptophan metabolites, and catecholamines, which affect brain and genital function *via* the vagus nerve (Bonaz *et al.*, 2018). Neurotransmitters such as serotonin, dopamine, GABA, norepinephrine, and acetylcholine are not only synthesized in the brain and gut but are also influenced by microbial composition and activity. For instance, approximately 90% of serotonin is produced in the gut, where it regulates motility and contributes to mood and sexual function, while microbes like *Lactobacillus* and *Bifidobacterium* enhance GABA synthesis, supporting vagal tone and emotional balance (Bravo *et al.*, 2003). Dopamine and oxytocin pathways, key to motivation, bonding, and reproductive behavior, are also modulated by microbial metabolites (Petersson *et al.*, 2024). The mucosal microenvironment, or mucomicrobiotic (MuMi) layer, facilitates cross-talk between host and microbiota, further influencing neuroendocrine and immune signaling within the BGG axis. However, when this integrated vagus neurotransmitter microbe network is disrupted due to chronic stress, infection, inflammation, diet, or antibiotic overuse it leads to loss of homeostasis, triggering a cascade of pathological conditions including irritable bowel syndrome, inflammatory bowel disease, sexual dysfunction, infertility, menstrual irregularities, polycystic ovary syndrome, anxiety, depression, chronic fatigue syndrome, and even neurodegenerative diseases (Ashonibare *et al.*, 2024).

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1.1 Irritable bowel syndrome (IBS)

IBS reflects dysfunction in the brain-gut-genital axis through impaired vagal signaling, altered enteric neurotransmission, and stress-induced HPA axis activation. Neurotransmitter imbalances especially serotonin and acetylcholine-disrupt gut motility and pain perception. Emotional stress, often linked to sexual or hormonal issues, worsens gut symptoms. Dysbiosis alters microbial metabolites like SCFAs, further disturbing BGG communication. IBS often coexists with anxiety, menstrual pain, and sexual dysfunction, highlighting BGG overlap. Botanicals like peppermint and ashwagandha aid both gut and neuroendocrine stability (Agnello *et al.,* 2020).

1.2 Inflammatory bowel disease (IBD)

In IBD, inflammation and immune dysregulation in the gut mucosa are amplified by impaired vagal anti-inflammatory pathways. The gut microbiota initiates systemic inflammation, influencing the HPA axis and neuroendocrine responses. Stress and hormonal fluctuations worsen flares, linking the condition to genital and neuropsychiatric symptoms. Poor gut barrier function allows cytokines and microbial toxins to reach the brain and reproductive tissues. Phytomedicines like turmeric and shatavari help modulate the immune-gut-brain interface (Giulia *et al.*, 2025).

1.3 Sexual dysfunction

Sexual dysfunction often results from disrupted BGG communication, where poor vagal tone and altered neurotransmitter signaling (dopamine, nitric oxide, and serotonin) impair genital blood flow and arousal. Gut dysbiosis can increase systemic inflammation, affecting hormone levels and sexual behavior. Chronic GI conditions and stress contribute to low libido and reproductive hormone suppression. The vagus nerve plays a direct role in mediating genital sensory input in both sexes. Adaptogens like Maca, Ginseng, and Ashwagandha restore BGG axis balance, improving function (He *et al.*, 2021).

1.4 Infertility

Infertility correlates strongly with BGG axis disruption, as vagal and HPA dysfunction suppress hypothalamic-pituitary-gonadal (HPG) signaling. Gut-derived inflammation and microbial toxins alter ovulation and spermatogenesis. Stress impairs GnRH, LH, and FSH secretion, disrupting cycles and sperm quality. Vagal imbalance worsens uterine receptivity and hormonal communication. Herbs like *Tribulus, Shatavari*, and fennel improve both gut integrity and reproductive hormone function (Qixiang *et al.*, 2023).

1.5 Menstrual irregularities

The menstrual cycle is tightly regulated by the BGG axis through HPG-HPA interplay, neurotransmitters, and microbiota. Gut microbes modulate estrogen recycling *via* the estrobolome. Chronic stress and vagal dysfunction affect GnRH pulsatility and ovulatory cycles. GI disorders like IBS often intensify menstrual symptoms. Dysbiosis and inflammation impair endometrial receptivity. Botanicals like chamomile, fennel, and ashwagandha help restore BGG-related hormonal balance (Ferin *et al.*, 1996).

1.6 Polycystic ovary syndrome (PCOS)

PCOS represents endocrine and metabolic dysfunction linked to the BGG axis disruption. Dysbiosis promotes low-grade inflammation and insulin resistance, impairing ovulation. Vagal dysfunction and stress alter HPG axis function, increasing androgen excess and anovulation. GI symptoms and mood disorders often co-occur, supporting a BGG link. Estrogen-metabolising gut bacteria impact hormonal homeostasis. Adaptogens like fenugreek and shatavari target all three BGG systems: gut, brain, and ovary (Ferin *et al.*, 1996).

1.7 Anxiety

Anxiety is tightly associated with vagal tone and gut microbiota signaling to the brain and genital axis. Disrupted BGG signaling, especially from stress, leads to HPA overdrive and reduced GABA and serotonin in both gut and brain. Gut inflammation increases intestinal permeability, allowing neurotoxins to enter circulation. Hormonal imbalances from reproductive dysfunction can exacerbate anxiety. Phytomedicines like valerian, lavender, and bacopa improve vagal resilience and neurotransmitter stability (Martin *et al.*, 2016).

1.8 Depression

Depression involves neurotransmitter deficiencies (*e.g.,* serotonin, dopamine) and is exacerbated by gut inflammation and dysbiosis. Vagal impairment reduces anti-inflammatory control and blunts emotional regulation. Estrogen declines or irregular cycles can worsen mood. The BGG axis explains mood shifts during PMS, perimenopause, and chronic GI illness. Probiotics and herbal adaptogens like St. John's Wort and Schisandra show efficacy in restoring BGG function and mood (Martin *et al.*, 2016).

1.9 Chronic fatigue syndrome (CFS)

CFS stems from dysregulated immune-neuroendocrine pathways, with reduced vagal tone, gut dysbiosis, and mitochondrial stress at its core. Poor gut barrier integrity leads to systemic inflammation and neuroinflammation. Hormonal imbalances and neurotransmitter deficits cause fatigue, sleep disturbance, and sexual dysfunction. The BGG axis links these multisystem symptoms. Botanicals like rhodiola and maca restore energy, reduce inflammation, and rebalance the gut-brain loop (Sapra *et al.*, 2023).

1.10 Neurodegenerative diseases

Emerging evidence shows that gut dysbiosis and vagus nerve dysfunction contribute to diseases like Parkinson's and Alzheimer's. Misfolded proteins may travel from the gut to the brain *via* vagal pathways. Chronic gut inflammation and microbial imbalance impair brain function and accelerate neurodegeneration. Sex hormones modulate neuroplasticity, tying genital function into the disease process (Han *et al.*, 2022). Bacopa, turmeric, and ginkgo biloba support neuroprotection *via* gut-brain-genital axis modulation (Loh *et al.*, 2024).

Current treatments for BGG axis-related disorders primarily rely on pharmacological agents such as SSRIs, antispasmodics, hormonal therapies, anti-inflammatory drugs, and neuroactive compounds. While these drugs offer symptomatic relief in conditions like IBS, IBD, PCOS, anxiety, or sexual dysfunction, they often target isolated aspects of the disorder either the brain, gut, or reproductive system without addressing the integrated pathophysiology of the axis. Additionally, many of these medications cause side effects such as GI distress, weight gain, mood swings, hormonal disruption, or sexual dysfunction, and are unsuitable for long-term use. Although techniques like vagus nerve stimulation (VNS) and transcutaneous VNS (tVNS) are emerging as neuromodulatory treatments, their application remains limited due to cost, invasiveness, and variable outcomes (Abouelmagd *et al.*, 2024). Phytotherapeutic interventions using medicinal plants such as *W. somnifera*, *C. longa*, *R.rosea*, and *O. tenuiflorum* offer a holistic alternative by simultaneously acting on neurotransmitters, hormonal balance, inflammation, and gut microbiota. These plants modulate vagal tone, reduce cortisol, improve reproductive hormone regulation, and restore gut-brain signaling pathways. Their adaptogenic and anti-inflammatory properties provide integrative, low-toxicity options for managing complex BGG axis disorders like PCOS, depression, IBS, and neurodegeneration (Dharmalingam *et al.*, 2024).

2. Treatment

Current treatments for BGG axis-related disorders primarily rely on pharmacological agents such as SSRIs, antispasmodics, hormonal therapies, anti-inflammatory drugs, and neuroactive compounds. While these drugs offer symptomatic relief in conditions like IBS, IBD, PCOS, anxiety, or sexual dysfunction, they often target isolated aspects of the disorder either the brain, gut, or reproductive system, without addressing the integrated pathophysiology of the axis.

Additionally, many of these medications cause side effects such as GI distress, weight gain, mood swings, hormonal disruption, or sexual dysfunction, and are unsuitable for long-term use (Garcia *et al.*, 2022). Although, techniques like vagus nerve stimulation (VNS) and transcutaneous VNS (tVNS) are emerging as neuromodulatory treatments, their application remains limited due to cost, invasiveness, and variable outcomes. Phytotherapeutic interventions using medicinal plants offer a holistic alternative by simultaneously acting on neurotransmitters, hormonal balance, inflammation, and gut microbiota. These plants modulate vagal tone, reduce cortisol, improve reproductive hormone regulation, and restore gut-brain signaling pathways. Their adaptogenic and anti-inflammatory properties provide integrative, low-toxicity options for managing complex BGG axis disorders like PCOS, depression, IBS, and neurodegeneration (He *et al.*, 2021).

2.1 Ashwagandha (*Withania somnifera* (L.) Dunal)

Ashwagandha (*W.somnifera*), a well-known adaptogenic herb in traditional Ayurvedic medicine, plays a crucial role in modulating the BGG axis through its multifaceted neuroendocrine, immunological, and gastrointestinal effects. Its active constituents, particularly withanolides, exert anxiolytic, anti-inflammatory, neuroprotective, and hormone-regulating actions that enhance vagal tone and parasympathetic activity. By attenuating overactivation of the hypothalamic-pituitary-adrenal (HPA) axis, Ashwagandha reduces circulating cortisol levels, thus mitigating stress-induced disturbances in gut motility, secretion, microbiota composition, and reproductive hormone balance. It also enhances central neurotransmitter activity especially GABA and serotonin which supports emotional regulation, improves sleep, and reduces anxiety and depressive symptoms, all of which contribute to improved gastrointestinal and reproductive function. In the reproductive domain, Ashwagandha improves sperm count, motility, and testosterone levels in males, and supports menstrual cycle regularity and fertility in females by modulating endocrine function and reducing oxidative stress. It may also positively influence the gut microbiota by promoting microbial diversity and reducing proinflammatory cytokine activity, thereby enhancing mucosal immunity and gut-brain signaling. These properties collectively restore homeostasis across the BGG axis and make Ashwagandha a valuable phytotherapeutic agent in the management of irritable bowel syndrome, polycystic ovary syndrome, infertility, sexual dysfunction, anxiety, depression, and chronic stress-related disorders (Speers *et al.*, 2021).

2.2 Rhodiola (*Rhodiola rosea* L.)

Rhodiola (*R. rosea*), a renowned adaptogenic herb used traditionally in Eurasian systems of medicine, exerts potent effects on the BGG axis through its root-derived phytochemicals, chiefly rosavin, salidroside, and tyrosol. These compounds exhibit a combination of neuroprotective, endocrine-modulating, anti-fatigue, and anti-inflammatory actions. According to Panossian *et al.* (2010), salidroside is primarily responsible for Rhodiola's modulation of the hypothalamic-pituitary-adrenal (HPA) axis by downregulating cortisol release and improving cellular resistance to stress. Rosavin, on the other hand, has been shown to enhance serotonin and dopamine signaling in the central nervous system, which improves mood, reduces anxiety, and indirectly supports gastrointestinal and reproductive stability. These mechanisms support the enhancement of vagal tone, reducing sympathetic overactivity and supporting gut-brain communication, emotional regulation, and hormonal balance. In the gastrointestinal tract, Rhodiola's bioactives suppress pro-inflammatory cytokines like TNF-α and IL-6, reduce oxidative stress, and help maintain gut barrier function, which is crucial for the integrity of the brain-gut axis (Panossian *et al.,* 2010). Rhodiola also shows regulatory effects on gut motility and may support microbial balance by creating an anti-inflammatory environment. In the genital system, tyrosol and rosavin have demonstrated the ability to stimulate dopaminergic pathways that enhance libido, support ovulation, and improve sexual function, particularly under stress-related hormonal imbalance (Labachyan *et al.*, 2018). In women, Rhodiola may support menstrual regularity and reduce symptoms of PMS and PCOS, while in men, it improves testosterone levels and semen parameters such as sperm motility and concentration. A daily dose of 200-400 mg of standardized extract has been clinically validated for safety and efficacy. Through these combined actions-supporting neurotransmitter modulation, reducing inflammation, stabilizing hormones, and enhancing vagal output *R. rosea* proves to be an effective botanical therapeutic for conditions like IBS, depression, infertility, chronic fatigue, sexual dysfunction, and stress-exacerbated reproductive disorders (Ivanova *et al.*, 2018).

2.3 Chamomile (*Matricaria chamomilla* L.)

Chamomile, a well-established medicinal herb in traditional European and Unani medicine, is widely used for its calming, anti-inflammatory, and digestive properties. Its pharmacological activity is attributed to various bioactive constituents, including apigenin, bisabolol, chamazulene, and flavonoids, which act on multiple targets within the brain-gut-genital axis. Among these, apigenin, a flavone, exhibits GABAergic activity by binding to benzodiazepine receptors, producing anxiolytic and mild sedative effects that help in modulating stress responses and reducing HPA axis hyperactivity. This downregulation of cortisol not only improves mood and sleep quality but also supports gastrointestinal and reproductive hormonal balance under chronic stress (Srivastava *et al.*, 2010). Bisabolol and chamazulene, found in chamomile essential oil, exhibit anti-inflammatory and antispasmodic properties, which soothe the gastrointestinal mucosa, regulate intestinal motility, and reduce visceral hypersensitivity often seen in conditions like IBS and dysmenorrhea. Chamomile also supports gut microbiota balance by promoting beneficial bacteria and reducing oxidative stress and mucosal inflammation, thereby reinforcing the gut-brain and gut-genital pathways. It has shown effectiveness in modulating uterine contractions, reducing menstrual cramps, and improving premenstrual syndrome through its smooth muscle-relaxant effects and influence on prostaglandin synthesis. In the genital system, apigenin contributes to hormonal modulation by influencing estrogen receptor activity, which may assist in regulating ovulation and menstrual cycles. Chamomile's sedative and mood-stabilizing actions also indirectly improve libido and reproductive function by enhancing parasympathetic tone and reducing stress-mediated dysfunction (Afiat *et al.*, 2022).

2.4 Lavender (*Lavandula angustifolia* Mill.)

Lavender (*L. angustifolia*), a well-known aromatic plant in Mediterranean and traditional medicine, possesses therapeutic effects on the brain-gut-genital axis due to its volatile oil components, primarily linalool and linalyl acetate, along with polyphenols and coumarins. These constituents exhibit anxiolytic, antidepressant, antispasmodic, and anti-inflammatory properties. Linalool modulates GABA-A receptors, producing sedative and anxiolytic effects, while linalyl acetate supports serotonin and parasympathetic activity, helping downregulate the HPA axis and reduce stress-related dysfunctions. Through vagal activation, lavender enhances gut-brain signaling and emotional regulation, leading to improved gastrointestinal motility, reduced visceral pain, and lowered inflammation. Lavender also positively affects gut microbiota by inhibiting pathogenic bacteria and promoting mucosal healing, thereby strengthening intestinal barrier function. In the genital system, lavender has been shown to alle*via*te dysmenorrhea, PMS symptoms, and sexual dysfunction through its muscle-relaxant effects, hormonal balancing capacity, and stress reduction. Clinical trials using lavender oil capsules (80 mg/day) or aromatherapy have demonstrated significant improvements in anxiety, sleep quality, IBS symptoms, and reproductive mood disorders. Thus, through its regulation of neurotransmitters, inflammation, and vagal tone, *L. angustifolia* offers integrative support in restoring homeostasis within the BGG axis (Batiha *et al.*, 2023).

2.5 Turmeric (*Curcuma longa* L.)

Turmeric (*C. longa*), a rhizomatous plant from the Zingiberaceae family, has long been valued in Ayurvedic and Chinese medicine for its potent anti-inflammatory and neuroprotective properties. The key bioactive compound curcumin, along with demethoxycurcumin and bisdemethoxycurcumin, modulates several systems involved in the BGG axis. Curcumin suppresses the HPA axis, inhibits NF-κB signaling, and reduces pro-inflammatory cytokines like IL-6 and TNF-α, thus mitigating chronic inflammation associated with stress, gastrointestinal disorders, and hormonal dysregulation. It also improves serotonin and dopamine levels, offering antidepressant and anxiolytic effects beneficial for gut and reproductive health. In the gut, curcumin enhances microbiota diversity, supports mucosal healing, and reduces intestinal permeability, making it effective for managing IBS, ulcerative colitis, and gut-brain inflammation. In the genital system, curcumin regulates ovarian function, lowers oxidative stress, and improves symptoms of PCOS, infertility, and menstrual irregularities by modulating estrogen metabolism and inflammatory pathways. In males, it improves testosterone levels, sperm quality, and reduces testicular inflammation under stress. Clinical doses typically range from 500-1000 mg/day of standardized extract. With its multi-targeted activity on neurotransmitters, gut microbes, immune cells, and reproductive hormones, *C. longa* offers a powerful phytotherapeutic approach to restoring BGG axis balance and treating complex systemic disorders (Enayati *et al.*, 2023).

2.6 Peppermint (*Mentha piperita* L.)

Peppermint (*M. piperita*), a hybrid mint species widely used in herbal medicine, exerts therapeutic effects on the BGG axis primarily due to its essential oils especially menthol and menthone. Menthol acts as a calcium channel blocker and has antispasmodic, analgesic, and anti-inflammatory properties that relax smooth muscles of the gastrointestinal tract and uterus. Peppermint enhances vagal tone and modulates the enteric nervous system (ENS), reducing visceral hypersensitivity and improving motility in patients with IBS, abdominal pain, and bloating. It also interacts with TRPM8 receptors and modulates serotonergic and opioid pathways, supporting both gut and emotional regulation. Peppermint's antimicrobial effects help maintain a healthy gut microbiota and reduce dysbiosis, supporting gut-brain communication. In the genital system, peppermint oil has been shown to reduce dysmenorrhea, menstrual cramps, and uterine muscle spasms due to its myorelaxant and anti-inflammatory properties. Topical and oral preparations have also been reported to improve mental alertness, reduce anxiety, and enhance sexual function by modulating neurotransmitters such as serotonin and dopamine. Standardized doses of 180-225 mg/day of enteric-coated capsules are commonly used in clinical practice. Through modulation of neurotransmission, smooth muscle tone, and microbiota balance, *M. piperita* offers integrative benefits for BGG axis-related conditions, including IBS, menstrual disorders, anxiety, and sexual dysfunction (Kazemi *et al.*, 2025).

2.7 Lemon balm (*Melissa officinalis* L.)

Lemon balm (*M. officinalis*), a lemon-scented perennial herb from the mint family, is known for its mild sedative, anxiolytic, and spasmolytic effects on the BGG axis. The main active constituents include rosmarinic acid, caffeic acid, citral, and flavonoids, which exert GABA-transaminase inhibition, leading to increased GABA availability and calming effects. These neurochemical actions modulate the HPA axis, reduce cortisol levels, and promote vagal activation, thereby improving stress resilience, gut function, and reproductive hormonal stability. Lemon balm enhances emotional well-being, reduces nervous tension, and improves sleep quality, all of which are linked to better gut and reproductive health. In the gastrointestinal tract, Lemon balm reduces motility-related discomfort, alle*via*tes bloating, gas, and abdominal cramps, and supports gut microbiome balance by reducing inflammation and oxidative stress. In the genital system, it has shown benefits in reducing premenstrual syndrome, dysmenorrhea, and menopausal symptoms, largely by influencing estrogenic pathways and uterine muscle relaxation. It may also improve sexual desire and function by reducing stress-induced libido suppression. Effective forms include infusions, standardized extracts (300-600 mg/day), or essential oil aromatherapy. Through its gentle, broad-spectrum regulation of neurotransmitters, endocrine balance, and microbial ecology, *M. officinalis* represents a holistic and well-tolerated phytomedicine for treating BGG axis-related conditions such as anxiety, IBS, PMS, and insomnia (Mathews *et al.*, 2009).

2.8 Holy basil (*Ocimum tenuiflorum* L.)

Holy basil (*O. tenuiflorum*), also known as Tulsi, is a revered adaptogenic herb in Ayurvedic medicine, known for its capacity to modulate stress, inflammation, and hormonal balance across the BGG axis. Its key phytoconstituents include eugenol, ursolic acid, rosmarinic acid, and apigenin, which contribute to antioxidant, cortisol-lowering, and neuroprotective effects. Holy Basil supports vagal tone by reducing sympathetic overactivity and restoring parasympathetic balance, thereby improving gut motility, mucosal integrity, and reproductive hormone regulation. Eugenol specifically shows anti-inflammatory and anxiolytic activity through modulation of GABAergic and serotonergic pathways, while apigenin promotes relaxation by enhancing GABA transmission. In the gastrointestinal tract, *O. tenuiflorum* reduces gastric ulcers, IBS symptoms, and gut inflammation, while also modulating the gut microbiome by promoting beneficial bacteria. In the reproductive system, Holy Basil improves sperm quality, ovarian function, and menstrual regulation through anti-inflammatory and hormonal actions, while also boosting libido under stress. Clinical and preclinical studies confirm its role in managing PCOS, infertility, and stress-induced sexual dysfunction. A standardized dose of 300-600 mg/day has shown efficacy in supporting emotional and physical resilience. Through its integrative neuroendocrine-immune activity, *O. tenuiflorum* enhances BGG axis function and offers therapeutic value for disorders like anxiety, IBS, PMS, and reproductive dysfunctions (Lopresti *et al.*, 2022).

2.9 Ginseng (*Panax ginseng* C.A. Mey.)

Ginseng (*P. ginseng*), a cornerstone of traditional East Asian medicine, exhibits broad-spectrum activity on the BGG axis *via* its principal active compounds, ginsenosides (*e.g.,* Rb1, Rg1, Rg3), known for their adaptogenic, neuroendocrine, and immune-regulatory properties. Ginsenosides enhance cholinergic and dopaminergic signaling, reduce HPA axis overactivation, and improve vagal tone, thereby modulating mood, gastrointestinal motility, and reproductive hormonal equilibrium. These compounds also exhibit antioxidant activity, reduce neuroinflammation, and improve cognitive function, especially under chronic stress or fatigue. Ginseng supports gut health by protecting against inflammatory bowel disease, enhancing microbiota diversity, and improving gut barrier integrity. In the genital system, it enhances spermatogenesis, testosterone synthesis, ovarian function, and sexual performance through endocrine regulation and nitric oxide-mediated vasodilation. Clinical use includes 200-400 mg/day of standardized extract, often in managing stress-related infertility, erectile dysfunction, menstrual disorders, and IBS. With its comprehensive influence on neurotransmitter function, gut integrity, hormone balance, and stress adaptation, *P. ginseng* is a highly effective botanical for restoring BGG axis homeostasis (Jin *et al.*, 2019).

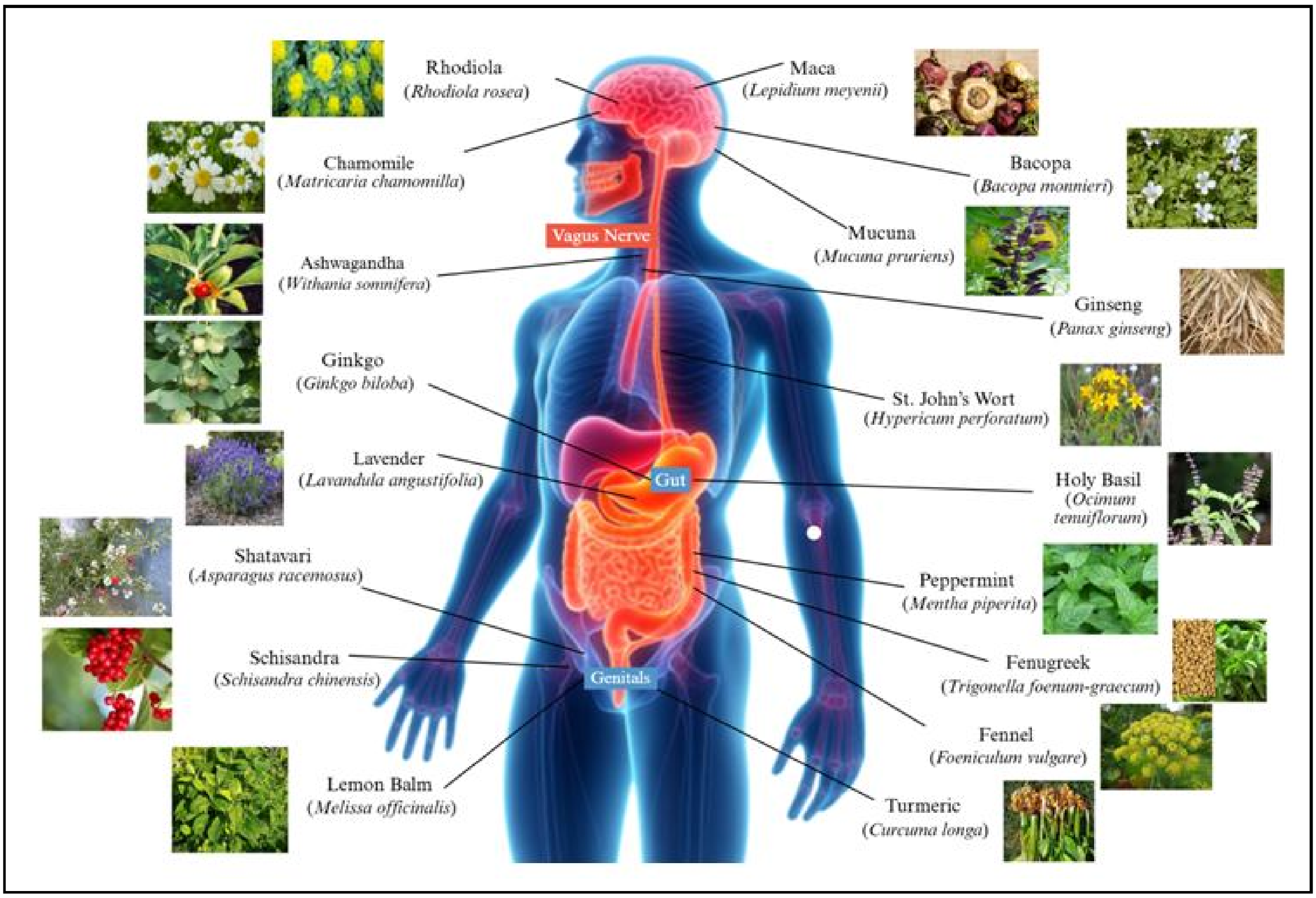

Figure 1: Representation of various medicinal plants used in the treatment of BGG axis-related disorders.

2.10 St. John's Wort (*Hypericum perforatum* L.)

St. John's Wort (*H. perforatum*) is a clinically validated herbal antidepressant that significantly affects the BGG axis through its modulation of neurotransmitter systems. Its major active compounds hypericin, hyperforin, and flavonoids exert serotonin, dopamine, and norepinephrine reuptake inhibition, making it particularly useful in the treatment of mood and stress-related gastrointestinal and reproductive disorders. Hyperforin enhances vagal activity by stabilizing emotional tone and reducing HPA axis hyperactivity, which indirectly benefits gut motility and reproductive hormone regulation. In the gut, St. John's Wort improves symptoms of functional dyspepsia and IBS by reducing stress-mediated dysregulation of the enteric nervous system. In the genital system, its mood-lifting properties aid in managing low libido, anorgasmia, and sexual dysfunction, particularly when stress or SSRIs are involved. However, caution is advised due to its interaction with cytochrome P450 enzymes, which may affect oral contraceptive efficacy or hormone therapy. Usual doses range from 300-900 mg/day of standardized extract. With its potent neuromodulatory and stress-adaptive properties, *H. perforatum* offers an evidence-based herbal approach to treating depression, anxiety, PMS, IBS, and reproductive dysfunctions within the BGG axis (Bravo *et al.,* 2003).

2.11 Ginkgo (*Ginkgo biloba* L.)

Ginkgo (*G. biloba*), one of the oldest medicinal trees, influences the BGG axis primarily through ginkgolides, bilobalide, and flavonoids, which exhibit neuroprotective, vasodilatory, and antioxidant effects. *Ginkgo* enhances cerebral blood flow, improves memory, and modulates neurotransmitters such as acetylcholine and dopamine, making it effective for cognitive and emotional regulation. It also reduces stress-induced HPA axis activity and supports vagal tone, indirectly benefiting gastrointestinal and reproductive health. In the gastrointestinal system, *Ginkgo* improves microcirculation, reduces mucosal inflammation, and enhances gut-brain signaling, offering relief in functional GI disorders. In the genital system, it enhances nitric oxide-mediated blood flow, thereby improving erectile function in men and clitoral sensitivity in women. *Ginkgo* also helps alleviate SSRI-induced sexual dysfunction, anxiety, and menopausal symptoms. A clinical dose of 120-240 mg/day of standardized extract is typically recommended. With its multi-targeted action on brain function, gut motility, and sexual health, *G. biloba* is a valuable neurovascular botanical for maintaining BGG axis balance, particularly in ageing populations (Diamond and Bailey, 2013).

2.12 Schisandra (*Schisandra chinensis* (Turcz.) Baill.)

Schisandra (*S. chinensis*), a traditional adaptogenic herb in Chinese medicine, is known for its ability to enhance physical endurance, cognitive function, and sexual health by regulating the BGG axis. Its primary bioactive constituents, schisandrins (A, B, and C) and gomisins, exhibit potent antioxidant, anti-inflammatory, and neuroprotective effects. Schisandra modulates dopaminergic and serotonergic pathways, supports mitochondrial function, and improves vagal tone, thus optimizing communication between the central nervous system, enteric system, and reproductive organs (Li *et al.*, 2023). By stabilizing the hypothalamic-pituitary-adrenal (HPA) axis it helps mitigate the negative impact of chronic stress on gut and reproductive functions. In the gut, Schisandra has shown efficacy in treating gastric ulcers, IBS, and stress-induced dysbiosis by enhancing mucosal defenses and improving intestinal barrier integrity. In the reproductive system, it enhances libido, semen quality, and ovarian function by modulating gonadal hormone levels and reducing oxidative stress in reproductive tissues. Traditional use includes addressing fatigue-related sexual dysfunction and menopausal symptoms. Clinical doses of 500-1500 mg/day of standardized extract are commonly employed. Through its multitargeted action on neuroendocrine, gut, and reproductive pathways, *S.chinensis* supports BGG axis resilience and helps treat disorders like fatigue, infertility, mood instability, and digestive dysfunctions (Xia *et al.*, 2016).

2.13 Bacopa (*Bacopa monnieri* L.)

Bacopa (*B. monnieri*), also known as *Brahmi*, is a nootropic and nervine tonic traditionally used in Ayurvedic medicine to enhance memory, cognition, and emotional balance. It acts on the BGG axis *via* bacosides A and B, which are known to enhance synaptic plasticity, serotonin regulation, and cholinergic transmission. *Bacopa* reduces cortisol and normalizes HPA axis activity, thereby enhancing vagal tone, reducing neuroinflammation, and improving mood and gut function. It also exhibits GABAergic modulation, supporting relaxation and resilience under stress. In the gastrointestinal tract, *Bacopa* reduces gut inflammation, supports gut-brain signaling, and promotes microbiota diversity. Preclinical studies show improved intestinal barrier function and reduced visceral hypersensitivity, relevant for conditions like IBS and functional dyspepsia. In the genital system, *Bacopa* has been reported to enhance libido, sperm count, and ovarian protection *via* antioxidant mechanisms and stress reduction. Its adaptogenic properties help address stress-induced reproductive issues and sexual dysfunctions. Clinical doses of 300-600 mg/day of standardized extract are generally used. With its broad impact on cognitive function, gut-brain interaction, and hormonal regulation, *B. monnieri* is a valuable botanical for integrative BGG axis health (Gosciniak *et al.*, 2016).

2.14 *Mucuna* (*Mucuna pruriens* (L.) DC.)

M. pruriens, commonly known as velvet bean, is a powerful medicinal legume used in traditional Ayurvedic and African medicine for neurological and reproductive disorders. Its primary bioactive, L-DOPA, serves as a direct precursor to dopamine, making it highly effective in restoring dopaminergic tone and improving neuroendocrine regulation. By enhancing central dopamine levels, it improves mood, motivation, gut motility, and sexual function all regulated through the BGG axis. *Mucuna* also modulates serotonin and noradrenaline, supports vagal tone, and exhibits potent antioxidant and anti-inflammatory effects. In the gut, *Mucuna* reduces gastrointestinal inflammation and enhances peristalsis by increasing enteric dopamine levels, which in turn supports the enteric nervous system (ENS) and gut-brain communication. In the reproductive system, it enhances spermatogenesis, testosterone levels, and libido, especially in men with infertility or sexual dysfunction. Clinical doses of 5-15 g/day of seed powder or 250-500 mg/day of extract are used. With its targeted action on dopaminergic pathways, gonadal hormones, and gut motility, *M. pruriens* provides a robust botanical intervention for conditions like Parkinson's, IBS, infertility, and stress-related sexual dysfunctions (Katzenschlager *et al.*, 2004).

2.15 Fenugreek (*Trigonella foenum-graecum* L.)

Fenugreek (*T. foenum-graecum*) is a leguminous plant with wide-ranging therapeutic effects on metabolic, gastrointestinal, and reproductive systems. Its bioactive constituents trigonelline, 4-hydroxyisoleucine, diosgenin, and saponinsmodulate androgen and estrogen activity, enhance dopaminergic tone, and stabilize blood glucose and lipids (Singh *et al.*, 2020). By improving HPA axis balance, reducing inflammation, and enhancing vagal tone, Fenugreek influences emotional stability, gut health, and reproductive function. It has anxiolytic effects by indirectly modulating GABA and serotonin, making it beneficial for mood disorders and metabolic stress. In the gut, Fenugreek's high fiber and mucilage content soothes mucosa, regulates bowel motility, and improves gut microbiota composition. It has shown benefits in managing gastritis, IBS, and hyperacidity. In the genital system, Fenugreek enhances libido, testosterone levels, and sperm quality in males, while promoting lactation and hormonal regulation in females. Clinical use ranges from 500-1000 mg/day of seed extract or 5-10 g/day of powdered seeds. With its ability to modulate metabolic, neuroendocrine, and reproductive functions, *T. foenum-graecum* is a multipurpose phytotherapeutic agent for BGG axis-related conditions such as sexual dysfunction, PCOS, diabetes, and IBS (Singh *et al.*, 2022).

2.16 Maca (*Lepidium meyenii* Walp.)

Maca (*L. meyenii*), a Peruvian root traditionally used as a fertility and vitality enhancer, exerts regulatory effects across the BGG axis.

Its primary active compounds macaenes, macamides, glucosinolates, and sterols modulate hypothalamic-pituitary-gonadal (HPG) axis function, influence dopamine and serotonin, and act as adaptogens. Maca enhances vagal tone, balances sex hormones, and reduces anxiety and depression symptoms through modulation of neuroendocrine signals. In the gut, Maca improves intestinal tone, supports gut microbiota, and reduces stress-induced dysbiosis, aiding conditions like functional bowel disorders. In the reproductive system, Maca has been shown to enhance spermatogenesis, libido, ovarian follicle maturation, and alle*via*te menopausal symptoms without directly altering hormone levels, suggesting a regulatory rather than hormonal replacement mechanism. Typical therapeutic doses include 1.5-3 g/day of dried root or 500-1000 mg/day of extract. Through its hormone-balancing, mood-stabilizing, and gut-modulating properties, *L.meyenii* offers holistic support for BGG axis-related conditions such as infertility, low libido, IBS, and menopausal transition (Ullao *et al.*, 2001).

2.17 Fennel (*Foeniculum vulgare* Mill.)

F. vulgare, commonly known as fennel, is a culinary and medicinal herb known for its carminative, estrogenic, and antispasmodic effects, acting across the BGG axis. Its primary bioactive constituents include anethole, fenchone, and estragole, which exert antioxidant, antimicrobial, and phytoestrogenic actions. Fennel enhances vagal tone, regulates neuroendocrine signaling, and modulates gut-brain communication, thereby alleviating mood and gastrointestinal disturbances associated with hormonal imbalances. In the gastrointestinal system, fennel reduces flatulence, colic, and spastic colon symptoms, and improves motility by relaxing intestinal smooth muscle. In the reproductive system, its phytoestrogenic activity supports menstrual regulation, reduces dysmenorrhea, and improves lactation, while also relieving menopausal symptoms like hot flashes and anxiety. Doses of 250-500 mg/day of seed extract are commonly used in clinical settings. With its combined gut-calming, mood-balancing, and hormonal support effects, *F. vulgare* is beneficial in BGG axis-linked conditions like IBS, PMS, infertility, and menopause (Mahboubi, 2019).

2.18 Shatavari (*Asparagus racemosus* Willd.)

A. racemosus, known as shatavari in Ayurvedic medicine, is a revered female reproductive tonic and adaptogen with extensive effects on the BGG axis. The key phytoconstituents shatavarins (I-IV), steroidal saponins, and flavonoids modulate estrogenic activity, enhance antioxidant defense, and regulate HPA axis stress response. Shatavari supports vagal balance and calms the enteric nervous system by influencing GABAergic and serotonergic transmission. In the gut, it soothes mucosal linings, reduces acidity, and supports gut flora balance, offering protection in IBS and ulcerative conditions. In the reproductive axis, shatavari promotes ovarian function, supports fertility, improves libido, and is effective in lactation enhancement and managing menstrual irregularities. It is often used in 300-600 mg/day of root extract. As a hormonal regulator and gut-protective adaptogen, *A. racemosus* effectively treats BGG disorders including PCOS, dysmenorrhea, infertility, and anxiety-related gastrointestinal distress (Torres *et al.*, 2013).

2.19 Valerian (*Valeriana officinalis* L.)

V. officinalis, commonly used as a sedative herb, plays a key role in modulating the BGG axis through its effect on neurotransmitters and gut motility. The herb contains valerenic acid, valepotriates, and iridoids, which enhance GABAergic activity, reduce cortisol levels, and improve vagal tone, thereby promoting relaxation, sleep, and emotional stability. Its actions on the central nervous system extend to the enteric nervous system, improving gut-brain signaling. In the gastrointestinal tract, valerian reduces visceral hypersensitivity, helps manage IBS, and alleviates spasmodic abdominal pain, especially stress-induced. In the genital system, its calming effects reduce stress-induced sexual dysfunction and menstrual pain, and it supports sleep and hormonal balance, indirectly enhancing fertility. Typical dosages include 300-600 mg/day of root extract. Valerian's influence on GABA and its calming effect across brain, gut, and reproductive systems makes it valuable for treating insomnia, IBS, dysmenorrhea, and anxiety (Kennedy *et al.,* 2007).

2.20 Tribulus (*Tribulus terrestris* L.)

T. terrestris, a traditional tonic for male vitality and libido, influences the BGG axis through its steroidal saponins, especially protodioscin, which enhance androgen receptor activity, increase nitric oxide, and modulate dopamine levels. It indirectly strengthens vagal tone by reducing stress and enhancing testosterone-driven neuromodulation, impacting both central and peripheral reproductive circuits. In the gut, it exhibits mild laxative effects and supports gut motility, but its major impact is in the genital system, where it improves spermatogenesis, libido, and erectile function by increasing LH and testosterone levels and enhancing vascular perfusion. In women, it improves ovulation and sexual arousal, especially under hormonal imbalance or stress. A typical dose ranges between 250-750 mg/day of extract. *T. terrestris* is clinically used in addressing sexual dysfunction, infertility, low libido, and stress-related hormonal dysregulation within the BGG axis (Martino *et al.*, 2010).

Table 1: Medicinal plants with their therapeutic applications and effective doses in the management of BGG axis-related disorders

S.No.	Plant name	Part used	Chemical constituents	Mechanism of action	Dose	References
1	*Ashwagandha (W. somnifera)*	Root	Withanolides, Withanine, Saponins	Reduces cortisol, supports HPA axis, boosts sperm and GI motility	300-600 mg/day extract	Speers *et al.*, 2021.
2	*Rhodiola (R. rosea)*	Root	Rosavin, Salidroside, Tyrosol	Adaptogen; regulates ANS, anti-inflammatory, modulates hormones	200-400 mg/day extract	Ivanova *et al.*, 2018.
3	*Chamomile (M. chamomilla)*	Flowers	Apigenin, Chamazulene, Bisabolol	Calms CNS, digestive relaxant, menstrual regulator	1.5-2 g dried flower tea	Afiat *et al.*, 2022.

4	*Lavender (L. angustifolia)*	Flowers/oil	Linalool, Linalyl acetate	Enhances vagal tone, reduces anxiety, improves genital blood flow	80-160 mg/day oil capsule	Batiha *et al.*, 2023.
5	*Turmeric (C. longa)*	Rhizome	Curcumin	Reduces neuroinflammation, supports gut flora, antioxidant	500-1000 mg/day extract	Enayati *et al.*, 2023.
6	*Peppermint (M. piperita)*	Leaves/oil	Menthol, Menthone	Relieves IBS, improves gut motility, urinary antiseptic	0.2-0.4 ml oil 3x/day	Kazemi *et al.*, 2025.
7	*Lemon Balm (M. officinalis)*	Leaves	Rosmarinic acid, Flavonoids	Improves vagal tone, reduces anxiety, supports menstruation	300-600 mg/day extract	Mathews *et al.*, 2009.
8	*Holy Basil (O. tenuiflorum)*	Leaves	Eugenol, Ursolic acid, Rosmarinic acid	Adaptogen, reduces cortisol, improves libido, gut health	300-500 mg/day extract	Lopresti *et al.*, 2022
9	*Ginseng (P. ginseng)*	Root	Ginsenosides, Panaxans	Boosts cognition, modulates microbiota, improves ED	200 -400 day mg/ extract	Jin Y *et al.*, 2019.
10	*St. John's Wort (H. perforatum)*	Aerial parts	Hypericin, Hyperforin	Elevates serotonin, neuropro-tective, enhances testosterone	300 mg 2-3x/day extract	Bravo *et al.,* 2003.
11	*Ginkgo (G. biloba)*	Leaves	Ginkgolides, Bilobalide	Improves brain/genital circulation, antioxidant	120-240 mg/day extract	Diamond and Bailey, 2013.
12	*Schisandra (S. chinensis)*	Fruit	Schisandrins, Schisandrol A	Adaptogen, spermatorrhoea, improves premature ejaculation	500-1000 mg/day extract	Xia *et al.*, 2016.
13	*Bacopa (B. monnieri)*	Whole plant	Bacosides A and B	mproves memory, neurotrans-Imitter balance, anxiolytic	300-600 mg/day extract	Gosciniak *et al.*, 2016.
14	*Mucuna (M. pruriens)*	Seeds	L-DOPA	Enhances dopamine, libido, fertility	5-15 g/day seed powder	Katzenschlager *et al.*, 2004.
15	*Fenugreek (T. foenum -graecum)*	Seeds	Saponins, Diosgenin	Enhances testosterone, libido, digestion	500-600 mg/day extract	Singh *et al.*, 2020.
16	Maca *(L. meyenii)*	Root	Macamides, Macaenes	Balances hormones, libido and fertility enhancer	1.5-3 g/ day root powder	Ullao *et al.*, 2001
17	Fennel *(F. vulgare)*	Seeds	Anethole, Fenchone	Carminative, menstruation support, libido	1-2 g/ day seed or tea	Mahboubi, 2019
18	Shatavari *(A. racemosus)*	Root	Shatavarins (saponins)	Female tonic balances estrogen, improves gut health	250-500 mg/day extract	Torres *et al.*, 2013.
19	Valerian *(V. offi-cinalis)*	Root	Valerenic acid, Isovaleric acid	Sedative, sleep enhancer, improves vagal tone	300-600 mg/day extract	Kennedy *et al.,* 2007.
20	*Tribulus (T. ter-restris)*	Fruit	Protodioscin, Saponins	Boosts testosterone, libido, improves sperm count	250-500 mg/day extract	Martino-Andrade *et al.*, 2010.

3. Conclusion

The brain-gut-genital (BGG) axis is an intricate biological interface that plays a central role in the maintenance of digestive, reproductive, and emotional well-being. Dysfunction in this axis can lead to a wide spectrum of interrelated disorders that are often difficult to manage with conventional pharmacotherapy alone. While synthetic drugs offer symptomatic relief, they frequently overlook the underlying interconnected pathophysiology and may cause systemic side effects. In contrast, phytomedicines present a promising, integrative approach that targets multiple pathways simultaneously modulating neurotransmitter levels, regulating hormonal balance, reducing inflammation, and restoring microbiota diversity. Adaptogenic and neuroprotective herbs such as ashwagandha, turmeric, maca, and shatavari have demonstrated efficacy in clinical and preclinical settings for conditions like IBS, PCOS, anxiety, and infertility. Future research should focus on well-designed clinical trials, standardization of herbal extracts, and mechanistic studies to validate and optimize these natural interventions. By addressing the holistic needs of the BGG axis, phytotherapeutics can serve as a safe and effective strategy for promoting systemic health and resilience.

Availability of data and material

All data are provided within the manuscript.

Authorship contribution statement

Ayesha Fatima contributed to writing the original draft, reviewing and editing the manuscript, software handling, project administration, and methodology. **Dandotikar Neha and Esha Thakur** contributed to writing the original draft, reviewing and editing the manuscript, software handling, project administration, and methodology. **Fathima Tabassum** contributed to writing the original draft, reviewing and editing the manuscript, software handling, project administration, and methodology. **Khushita Singh** contributed to writing the original draft, reviewing and editing the manuscript, software handling, project administration, and methodology. **Fatima Umaira Saeed** contributed to conceptualization, data curation, investigation, methodology, supervision, validation, and visualization of the study.

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All authors gave their full consent for publication and submission to this journal.

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