

ADAPTOGENS IN ANXIETY RELIEF AND COGNITIVE ENHANCEMENT: A REVIEW OF MECHANISMS, CLINICAL EVIDENCE, AND FUTURE DIRECTIONS

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ABSTRACT

Adaptogens are natural substances, primarily derived from herbs that enhance the body's resilience to stress and promote homeostasis without significant side effects. Traditionally utilized in systems like Ayurveda and Traditional Chinese Medicine, adaptogens such as Ashwagandha, Rhodiola, Ginseng, and Bacopa monnieri have gained scientific interest for their potential mental health benefits. This review explores the historical use, mechanisms of action, clinical evidence, and regulatory considerations surrounding adaptogens, particularly in the context of anxiety and cognitive function. Key mechanisms include modulation of the hypothalamic-pituitary-adrenal (HPA) axis, antioxidant and neuroprotective effects, and regulation of neurotransmitters like serotonin, dopamine, and GABA. Clinical trials suggest these herbs can reduce anxiety, improve memory, and combat fatigue; however, limitations such as small sample sizes, lack of standardization, underreported adverse effects, and high placebo responses challenge the validity of findings. Regulatory discrepancies and insufficient long-term safety data further complicate clinical integration. Future research must address these gaps through large-scale, standardized, and rigorously designed trials. Adaptogens hold potential as complementary therapies for mental health but require cautious use and further validation before widespread adoption.

KEYWORDS: Adaptogens, anxiety, cognitive function, herbal medicine, stress relief, antioxidant.

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INTRODUCTION

Adaptogens are plant-derived compounds that assist the body in maintaining physiological balance during times of physical, psychological, or environmental stress. These substances are recognized for enhancing the body's resistance to stressors while restoring internal equilibrium, all with minimal adverse effects. Panossian and Wagner (2005) outlined three core characteristics of adaptogens: (1) enhancing non-specific resistance to stress, (2) exerting a normalizing effect on physiological functions regardless of the direction of change, and (3) being non-toxic and free from disruption to standard biological processes.

Traditional Roots in Herbal Medicine

The term "adaptogen" was first introduced by Soviet scientist Dr. Nikolai Lazarev in the 1940s to describe substances that enhance general resistance to stress. Later, Brekhmanin 1969 refined the concept, introducing criteria such as non-toxicity and normalization of physiological functions. In Ayurveda, Ashwagandha (*Withania somnifera*) has long been classified as a *Rasayana*, a rejuvenating herb used for improving memory, vitality, and stress resilience (Singh et al 2011.). Similarly, traditional Chinese medicine (TCM) has relied on herbs like ginseng (*Panax ginseng*) and *Schisandra*

chinensis for their effects on endurance, energy, and mental clarity (Panossian & Wagner, 2005; Jia et al., 2009).

Growing Research in Mental Health

Contemporary studies increasingly focus on the mental health benefits of adaptogens. Conditions such as anxiety, depression, cognitive dysfunction, and chronic fatigue have attracted attention due to the multi-targeted actions and favourable safety profiles of these compounds.

Mechanisms of Action Relevant to Mental Health

Adaptogens influence various biological systems, with primary effects observed in the following pathways:

HPA Axis Modulation

Adaptogens regulate the hypothalamic-pituitary-adrenal (HPA) axis, thereby modulating cortisol levels and attenuating the physiological stress response, which plays a central role in the body's stress response. By modulating cortisol secretion, adaptogens reduce excessive physiological responses to stress and help maintain homeostasis, thereby improving resilience to physical and psychological stressors. (Panossian & Wikman, 2010).

Antioxidant and Neuroprotective Properties

Adaptogens like medicinal plant example of *Ashwagandha*, *Rhodiola rosea*, *Bacopa monnieri*,

and *Panax ginseng* have significant antioxidant and neuroprotective effects, which are central to their activity in anxiety relief and cognitive enhancement.

- **Oxidative stress reduction:** Adaptogens increases endogenous antioxidant enzymes (superoxide dismutase, catalase, glutathione peroxidase), thereby decrease lipid peroxidation and DNA damage in neurons. Many adaptogens resulted neuroprotective benefits by reducing oxidative stress and neuroinflammation, preserving neuronal function, and supporting brain health (Ishaque et al., 2022).
- **Neuroinflammation control:** A Withanolides and ginsenosides responsible for suppression NF-κB signaling and lower pro-inflammatory cytokines (IL-6, TNF-α), mitigating neuroinflammation (Bansal & Paul, 2021).
- **Mitochondrial protection:** A Rhodiola and Ginseng produces stabilization off mitochondrial membranes, improve ATP synthesis, and prevent energy deficits in brain cells (Panossian & Wikman, 2010).
- **Neurogenesis support:** Bacopa monnieri responsible for upregulation brain-derived neurotrophic factor (BDNF) and CREB, promoting synaptic plasticity and cognitive resilience (Stough et al., 2008)

NEUROTRANSMITTER BALANCE:

Adaptogens have been shown to modulate neurotransmitters such as serotonin, dopamine, and gamma-aminobutyric acid (GABA), contributing to improved mood and cognitive performance (Bansal & Paul, 2021). Neurotransmitter balance mean to maintaining appropriate levels and activity of chemical messengers in the nervous system thereby brain cells can easily communicate properly. These neurotransmitters responsible for regulation mood, sleep, memory, movement, appetite, and many other body functions. Neurotransmitter balance responsible for crucial role in maintaining normal neuronal communication, emotional stability, cognitive function, and behavioral responses (Purves et al., 2018). Neurotransmitters like dopamine, serotonin, gamma-aminobutyric acid (GABA), glutamate, norepinephrine, and acetylcholine these are responsible for regulation various physiological and psychological processes including mood, memory, learning, sleep, and motor coordination (Rang et al., 2020; Katzung & Vanderah, 2021). A right equilibrium between excitatory neurotransmitters such as glutamate and inhibitory neurotransmitters like GABA is need for homeostasis of central nervous system (Stahl, 2021). Disturbances in neurotransmitter balance have been resulted in several neurological and psychiatric disorders such as Parkinson's disease, Alzheimer's disease, Schizophrenia, anxiety, depression, and cognitive impairment (Katzung &

Vanderah, 2021). Sleep deprivation has been responsible for alteration of neurotransmitter levels by rising glutamatergic activity and reducing serotonergic and GABAergic transmission, which may contribute to anxiety-like behavior, memory deficits, and neuronal dysfunction (McCoy & Strecker, 2011; Machado et al., 2004). Therefore, maintaining neurotransmitter balance is considered need for preserving mental health and proper neurological functioning.

Prominent Adaptogens for Mental Health

Table.1: Prominent Adaptogens for Mental Health

S . No	Adaptogen	Botanical Name	Primary Mental Health Benefits	Mechanism of Action	Key Clinical Findings	Reference
1	Ashwagandha	Withania somnifera	Reduces anxiety, stress, and insomnia	Modulates HPA axis, lowers cortisol, enhances GABAergic signaling	Reduced stress scores and cortisol levels	Chandrasekhar et al., 2012
2	Rhodiola rosea	Rhodiola rosea	Reduces mental fatigue and enhances stress tolerance	Influences monoamine neurotransmitters and energy metabolism	Improved cognition and reduced fatigue	Darbinyan et al., 2000
3	Bacopa monnieri	Bacopa monnieri	Improves memory and reduces anxiety	Enhances cholinergic transmission and antioxidant protection	Improved memory retention and anxiety reduction	Calabrese et al., 2008
4	Panax ginseng	Panax ginseng	Enhances cognition and	Modulates neurotransmission	Improved memory and	Reay et al., 2005

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			reduces fatigue	and glucose metabolism	calmness	
5	Holy Basil	Ocimum sanctum	Reduces stress and depressive symptoms	Regulates cortisol and provides antioxidant effects	Improved sleep and mood	Jamshidi & Cohen, 2017
6	Schisandra	Schisandra chinensis	Enhances stress resistance	Modulates nitric oxide and cortisol pathways	Improved concentration and reduced fatigue	Panosian & Wikman, 2010
7	Eleuthero (Siberian Ginseng)	Eleutherococcus	Improves endurance and stress adaptation	Regulates stress hormones and oxygen utilization	Improved work capacity	Panosian et al., 1999
8	Licorice Root	Glycyrrhiza glabra	Supports adrenal function	Inhibits cortisol breakdown	Traditionally used for adrenal exhaustion	Asl & Hossain, 2008
9	Gotu kola	Centella asiatica	Enhances cognition and reduces anxiety	Improves neuronal growth and cerebral circulation	Improved memory and attention	Orhan, 2012
10	Macaca	Lepidium meyenii	Enhances mood and energy	Improves endocrine balance and mitochondria	Improved psychological well-being	Gonzales, 2012

				neuroendrial activity		
11	Turmeric	Curcuma longa	Neuroprotective and mood enhancing	Reduces neuroinflammation and oxidative stress	Anti-depressant and cognitive supportive effects	Hewlings & Kalmann, 2017
12	Ginkgo biloba	Ginkgo biloba	Enhances memory and concentration	Improves cerebral blood flow	Improved cognitive performance	Smith & Luo, 2004
13	Saffron	Crocus sativus	Reduces anxiety and depression	Modulates serotonin and dopamine	Demonstrated antidepressant effects	Lopresti & Drummond, 2014
14	Cordyceps	Cordyceps sinensis	Reduces fatigue	Enhances ATP production	Improved energy metabolism	Pateron, 2008
15	Shatavari	Asparagus racemosus	Supports emotional balance	Antioxidant and neuroprotective effects	Improved mental well-being	Alok et al., 2013
16	Lion's mane mushroom	Hericium erinaceus	Supports cognition	Stimulates nerve growth factor synthesis	Improved cognition and reduced anxiety	Nagano et al., 2010
17	Lavender	Lavandula angustifolia	Reduces anxiety and improves sleep	Modulates GABAergic signaling	Demonstrated calming effects	Kouivand et al., 2013
18	Chamomile	Matri	Reduces	Binds	Reduces	Amst

8	momile	caria chamomilla	ces generalized anxiety	benzodiazepine receptors	ced anxiety symptoms	erdam et al., 2009
19	Valearian	Valeriana officinalis	Improves sleep and reduces anxiety	Enhances GABA neurotransmission	Improved sleep latency	Bent et al., 2006
20	Passiflora	Passiflora incarnata	Promotes relaxation	Modulates GABA receptors	Anxiolytic effects	Akhozandeh et al., 2001
21	Lemon balm	Melissa officinalis	Improves mood and cognition	Enhances GABA signaling	Reduced stress and improved calmness	Kennedy et al., 2004
22	Mucuna pruriens	Mucuna pruriens	Enhances mood and cognition	Supports dopaminergic neurotransmission	Improved stress tolerance	Manyam et al., 2004
23	Green tea	Cameliasinesis	Reduces stress and enhances attention	L-theanine modulates neurotransmitters	Improved relaxation and attention	Juneja et al., 1999
24	Rosemary	Rosmarinus officinalis	Enhances memory and alertness	Improves cholinergic activity	Improved memory performance	Moss et al., 2003
25	Peppermint	Mentha piperita	Improves attention and reduces fatigue	Enhances cerebral blood flow	Improved alertness	Kennedy et al., 2018
26	Skullcap	Scutellaria lateriflora	Reduces anxiety	Provides calming	Reduced anxiety	Brock et al.,

		lora	y	g GABAergic effects	ty and improved mood	2014
27	Jatamansi	Nardostachyos jatamansi	Neuroprotective and anti-anxiety	Modulates monoamine neurotransmitters	Improved memory and stress symptoms	Ahmad et al., 2006
28	Guduchi	Tinospora cordifolia	Enhances stress resistance	Immunomodulatory and antioxidant activity	Improved mental clarity	Sharma et al., 2012

A bibliometric analysis demonstrated a substantial increase in scientific publications related to adaptogens and mental health, particularly after 2015, reflecting growing global interest in their therapeutic potential for stress-related disorders and cognitive dysfunction (Zhou et al. 2021)

Importance of Evidence-Based Evaluation

The integration of adaptogens into clinical practice necessitates rigorous evidence to validate safety and efficacy. Evidence-based evaluation (EBE) combines high-quality research with clinical expertise and patient preferences to guide therapeutic decisions.

Ensuring Efficacy and Safety

The clinical integration of adaptogens essential for rigorous evaluation to ensure both efficacy and safety. Unlike conventional pharmaceuticals, herbal drugs often face challenges such as variability in active compounds, inconsistent regulation, and underreporting of adverse effects.

1 Efficacy Considerations

- **Evidence-based evaluation:** Adaptogens must be examined through randomized controlled trials (RCTs) comparable to those used for SSRIs and benzodiazepines (Bandelow et al., 2017).
- **Biomarkers:** Cortisol levels, BDNF expression, and neuroimaging should complement subjective scales like GAD-7 and MoCA.
- **Standardized formulations:** Extracts must be chemically consistent to permit reproducibility across studies.

2 Safety Considerations

- **Herb-drug interactions:** St. John's Wort may be responsible for serotonin syndrome with SSRIs; Ginkgo biloba increases bleeding risk along with anticoagulants (Izzo & Ernst, 2009).

- **Population-specific risks:** Limited data exist for elderly, pregnant women, and chronically ill patients are include for safety point.
- **Long-term safety:** Few studies extend beyond 12 weeks, leaving gaps in chronic use data should in

3Pharmacovigilance: Pharmacovigilance refers to identification of previously unrecognized adverse drug reactions (ADRs), monitor increases in known adverse effects, assess risk factors, and improve patient safety. It contains continuous monitoring of medicines throughout their lifecycle, including post-marketing surveillance, spontaneous reporting systems, signal detection, risk management, and regulatory decision-making. Weak monitoring systems often underreport adverse effects, especially in non-regulated settings (Ernst, 2007).

WORLD HEALTH ORGANIZATION FOR SAFETY ISSUES IN HERBAL MEDICINE:

The **World Health Organization (WHO)** reported “*Safety Issues in the Preparation of Herbal Medicines*” (Geneva: WHO Press, 2004) highlights critical concerns in the global use of herbal medicines, including adaptogens.

- **Quality control:** Emphasizes the essential for standardized extraction and manufacturing processes to ensure consistency in active compounds.
- **Contamination risks:** There are Warns against microbial contamination, heavy metals, pesticides, and adulteration in herbal preparations.
- **Pharmacovigilance:** There are the stronger monitoring systems must to detect and report adverse effects of herbal medicines for pharmacovigilance.
- **Regulatory harmonization:** There are wide variation in safety and quality standards across countries, urging international harmonization.
- **Special populations:** There are insufficient safety data for vulnerable groups such as pregnant women, children, and the elderly.

Clinical tools such as SSRIs have well-documented efficacy through numerous randomized controlled trials (Bandelow et al., 2017). Herbal agents like *Bacopa monnieri* also show promise but require comparable rigor in evaluation (Calabrese et al., 2008).

Diagnostic and Monitoring Tools

Assessment of anxiety and cognitive dysfunction need of reliable and validated diagnostic tools for accurate screening and monitoring of disease progression.

- **Generalized Anxiety Disorder-7 (GAD-7):** The GAD-7 defines as a validated seven-item self-report questionnaire widely used for

screening generalized anxiety disorder and assessing symptom severity. It demonstrates high diagnostic accuracy, along with a sensitivity of 89% and specificity of 82% for identifying generalized anxiety disorder (Spitzer et al., 2006).

- **Montreal Cognitive Assessment (MoCA):** The Montreal Cognitive Assessment is referes as a brief cognitive screening tool designed to evaluate multiple cognitive domains, including memory, attention, language, visuospatial abilities, and executive functions. It is demonstrate highly sensitive for the early detection of mild cognitive impairment and is widely used in both clinical and research settings (Nasreddine et al., 2005).

CLINICAL RESEARCH ON ADAPTOGENS:

Recent clinical research has aim of an evaluating the efficacy of adaptogenic herbs in stress management, fatigue reduction, cognitive enhancement, immune modulation, and overall well-being. Several clinical trials support the efficacy of adaptogens in mental health

Table 2. Clinical Research on Adaptogens in Mental Health and Stress Management

Adap togen	Clin ical Dose / Dur atio n	Maj or Clin ical Effe cts	Key Findi ngs from Clinic al Studie s	Mecha nism / Thera peutic Releva nce	Refere nce
Ashw agan dha (With ania somni fera)	300–600 mg/d ay for 60 days	Anti - stres s, anxi olyti c, corti sol redu ctio n, impr oved slee p	A rando mized double -blind placeb o- contro lled trial demon strated signifi cant reduc tions in stress assess ment scores and serum cortiso l levels in partici	Regulat es HPA axis, reduces cortisol secretio n, enhanc es GABA ergic signali ng, antioxi dant neuropr otectio n	(Chan drasek har et al., 2012)

			patients receiving Ashwagandha extract compared with placebo							
Rhodiola rosea	200–400 mg/day during stress exposure	Reduces mental fatigue, improves attention, emotional stability, and endurance	Students under examination stress showed improved mental performance, reduced fatigue, and better concentration after Rhodiola supplementation	Modulates monoamine neurotransmitters (dopamine, serotonin), improves mitochondrial energy metabolism, adaptive stress resistance	(Spasov et al., 2000)					
Bacopa monnieri	300 mg/day for 12 weeks	Enhances memory retention, information processing, cognitive speed, and learning	Healthy adults receiving Bacopa supplement demonstrated significant improvement in memory performance	Enhances cholinergic transmission, antioxidant neuroprotection, increases cerebral blood flow and synaptic communication	(Raghav et al., 2006)					
Valerian root (Valeriana officinalis)	Variable standardized extract doses	Improves sleep quality and relaxation	Meta-analysis of 16 randomized placebo-controlled trials involving 1,093 participants showed valerian may improve sleep quality with relative risk of 1.8 (95% CI: 1.2–2.9)	Modulates GABA receptors and promotes sedative-hypnotic effects useful in stress-associated insomnia	(Bent et al., 2006)					
Holy basil (Ocimum sanctum)	300–1200 mg/day	Reduces stress, improves emotional well-being, metabolic support	Clinical and experimental studies demonstrated reduced psychological stress, improved mood, better glucose	Cortisol regulation, antioxidant and anti-inflammatory activity, metabolic stabilization	(Cohen, 2014)					

			metabolism, and improved resilience against physical and emotional stressors		
Rhodiola rosea	200–600 mg/day	Reduces burnout symptoms and fatigue, improves physical endurance	Clinical trials reported enhanced attention, improved mental performance, and reduced burnout symptoms under stressful conditions	Adaptogenic modulation of stress hormones and neurotransmitter balance	(Hung et al., 2011)
Panax ginseng	200–400 mg/day	Improves cognition, immunity, fatigue resistance, and quality of life	Clinical studies demonstrated enhancement of memory, attention, mental performance, and physical	Ginsenosides improve neurotransmission, neuroprotection, immune modulation, and energy metabolism	(Reay et al., 2010)

			endurance		
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Table 3. Mechanistic Insights of Adaptogens in Neuropsychological Health

Mechanism	Physiological Action	Adaptogens Involved	Mental Health Relevance	Reference
HPA Axis Regulation	Stabilizes cortisol rhythms and regulates stress hormone secretion	Ashwagandha, Rhodiola rosea	Reduces chronic stress, anxiety, and stress-induced hormonal imbalance	(Panosian & Wikman, 2010)
Neurotransmitter Modulation	Enhances GABA activity and balances serotonin and dopamine levels	Ashwagandha, Bacopa, Valerian	Improves mood, reduces anxiety, promotes relaxation and emotional stability	(Choudhary et al., 2017)
Neuroprotection	Antioxidant and anti-inflammatory effects protect neurons from oxidative damage	Bacopa monnieri, Panax ginseng, Holy basil	Prevents cognitive decline and neurodegeneration	(Sarris et al., 2011)
Neurogenesis and Brain Plasticity	Upregulates BDNF and CREB signaling pathways to support	Bacopa monnieri, Panax ginseng	Enhances memory, learning capacity, and cognitive flexibility	(Stough et al., 2008)

	synaptic plasticity			
Immune Modulation	Enhances immune surveillance and reduces inflammatory mediators	Panax ginseng, Holy basil	Supports resilience against stress-related immune dysfunction	(Reay et al., 2010)
Mitochondrial Energy Enhancement	Improves ATP synthesis and cellular energy metabolism	Rhodiola rosea	Reduces fatigue and improves mental endurance	(Hung et al., 2011)

HERB-DRUG INTERACTIONS:

Herb–drug interactions refer to pharmacokinetic or pharmacodynamic interactions that occur when herbal medicines are used concurrently with conventional drugs, potentially altering drug efficacy or increasing the risk of adverse effects (Izzo and Ernst, 2009). The growing global use of herbal medicines alongside prescription medications has raised significant concerns regarding their safety, effectiveness, and interaction potential (World Health Organization, 2004). Pharmacokinetic interactions commonly involve changes in drug absorption, distribution, metabolism, and excretion. Many herbal products can influence cytochrome P450 (CYP450) enzymes and drug transporters such as P-glycoprotein, thereby altering plasma drug concentrations (Williamson, 2003). For instance, St. John's Wort (*Hypericum perforatum*) is a well-known inducer of CYP3A4 and P-glycoprotein, which significantly reduces plasma concentrations of drugs such as Cyclosporine, oral contraceptives, anticoagulants, and antiretroviral agents, potentially leading to therapeutic failure (Markowitz et al., 2003).

Table 4. Herbal drug reaction

Herb	Drug Interactions	Effect	Reference
Valerian	Benzodiazepines, barbiturates	Enhanced CNS depression	Fugh-Berman (2000)

Kava	CNS depressants	Risk of sedation, liver toxicity	Fugh-Berman (2000)
St. John's Wort	SSRIs, benzodiazepines	Serotonin syndrome, altered Metabolism	Izzo & Ernst (2009)
Ginkgo biloba	Anticoagulants	Increased bleeding risk	Izzo & Ernst (2009)
Passion flower	Benzodiazepines	Additive sedative effect	General herbal texts NCCIH

LONG-TERM USE AND REGULATION:

The long-term use of herbal medicines has taken considerable attention due to the increasing global reliance on traditional and complementary therapies for chronic disease management and general wellness. Although many herbal products are perceived as safe due to their natural origin, prolonged use may lead to adverse effects, toxicity, drug interactions, and variability in therapeutic outcomes if not properly monitored (World Health Organization, 2004). Several herbal products may accumulate toxic metabolites or result in organ toxicity with chronic consumption. For example, prolonged use of Licorice (*Glycyrrhiza glabra*) may produce hypertension, hypokalemia, and fluid retention due to excessive mineralocorticoid activity (Asl and Hosseinzadeh, 2008). Similarly, long-term consumption of Kava (*Piper methysticum*) has been associated with hepatotoxicity concerns (Teschke et al., 2011). Standardization and quality control remain major challenges in herbal medicine regulation due to variations in plant species, cultivation conditions, harvesting methods, and processing techniques that can significantly alter the concentration of active constituents (Ekor, 2014). Contamination with heavy metals, pesticides, microbial toxins, and adulteration with synthetic drugs has also been found in some herbal formulations, posing serious public health risks (World Health Organization, 2004).

Regulatory frameworks for herbal medicines vary across countries. In India, herbal products are regulated under the Government body, Ministry of AYUSH and the Central Drugs Standard Control Organization, whereas in the United States, herbal supplements are regulated by the Government body, the U.S. Food and Drug Administration under the Dietary Supplement Health and Education Act (DSHEA) of 1994. In Europe, herbal medicinal products are regulated by the Government body, the European Medicines Agency through traditional herbal drug product directives (Barnes et al., 2007). Pharmacovigilance

systems play a required role in monitoring the long-term safety of herbal medicines by detecting adverse reactions, evaluating risks, and ensuring public safety. Strengthening regulatory policies, promoting evidence-based clinical studies, and improving quality assurance measures are recent need for the safe long-term use of herbal therapies

Table 5. Long-Term Effects and Regulatory Status

RESEARCH GAPS AND CHALLENGES:

Research on adaptogens faces several important

term clinical trials	are short-term or involve small sample sizes.	Ernst (2009);
Inadequate safety data for vulnerable populations	Few studies in elderly, pregnant, or chronically ill individuals.	Fugh-Berman (2000); Teschke (2010)

Herb	Long-Term Effects	Regulatory Status
Valerian	Potential dependency and drowsiness	FDA: Supplement; AYUSH: Approved in some texts
Kava	Risk of hepatotoxicity and skin issues	FDA: Warning issued; banned in some countries
St. John's Wort	Photosensitivity, GI discomfort	FDA: Supplement; EMA: Herbal medicinal product
Ginkgo biloba	Seizures, GI upset, bleeding risk	FDA: Supplement; AYUSH: Used in proprietary meds
Ashwagandha	Mild, reversible liver enzyme elevation	FDA: Supplement; AYUSH: Pharmacopoeia-listed
Bacopa monnieri	Improves cognition, occasional GI issues	FDA: Supplement; AYUSH: Classical Ayurvedic herb
Schisandra chinensis	May enhance working capacity and reduce fatigue; mild GI symptoms possible with long-term use	FDA: Supplement EMA: Herbal product AYUSH: Referenced in traditional texts(Szolomicki S et al. (1998))

challenges that impact the interpretation of their efficacy and safety. Firstly, poor pharmacovigilance systems lead to underreporting of adverse effects, particularly in non-regulated settings where monitoring may be lax (Ernst, 2007; WHO, 2004). Secondly, the lack of regulatory harmonization across countries means that safety and quality standards vary widely, complicating the assessment and comparison of adaptogen products (WHO, 2004; EMA, 2016). Finally, many clinical trials on anxiety relief and cognitive enhancement depend heavily on subjective outcome measures, which are susceptible to a high placebo effect. This phenomenon can inflate perceived benefits, as noted in studies employing self-reported scale.

Table 6. Research Gaps and Challenges

Challenge	Description	Reference
Lack of large, long-	Most studies	Izzo &

Poor pharmacovigilance systems	Adverse effects underreported, especially in non-regulated settings.	Ernst (2007); WHO (2004)
lack of regulatory harmonization	Different countries have varying safety and quality requirements.	WHO (2004); EMA (2016)
High placebo effect in anxiety/cognition studies	Many studies rely on subjective scales with strong	Lakhan & Vieira (2010); Bent et

	placebo responses.	al. (2006)
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CURRENT LIMITATIONS:

Regulatory inconsistencies across different countries also pose challenges for commercialization as well as clinical integration of adaptogens. Unlike conventional pharmaceuticals, large no of herbal adaptogens are marketed as dietary supplements without rigorous clinical testing requirements (Ekor, 2014). Along with, herb–drug interactions remain an important concern, especially in patients using conventional medications simultaneously. Additionally Limited pharmacovigilance data and underreporting of adverse effects further complicate safety assessment (World Health Organization, 2004) remain an important concern. So that , future research System should have to focus on large-scale randomized controlled trials, standardized herbal formulations, detailed mechanistic investigations, and stronger pharmacovigilance systems to establish the safety and therapeutic reliability of adaptogens .

Table 7. Current limitation

Limitation	Description
Lack of long-term, large-scale trials	Most studies are short duration and include small sample sizes
Variability in active compound levels	Standardization of herbal extracts remains inconsistent
Limited data in special populations	Few studies include the elderly, pregnant individuals, or chronically ill
Inadequate adverse event reporting	Weak pharmacovigilance systems hinder safety assessment
Regulatory inconsistencies	Safety and quality standards vary across countries
Placebo effects	Many outcomes rely on subjective measures vulnerable to bias

DISCUSSION:

Established evidence suggests that adaptogens may provide advantageous effects for stress-related conditions, particularly anxiety and cognitive decline. Clinical findings support their activity in reducing cortisol, improving mood, and enhancing memory. However, methodological flaws—such as small sizes of sample, absent of extract

standardization, and subjective outcome reliance—reduce the strength of the evidence. The placebo effect is also one of a significant confounder in many trials, again emphasizing an essential for objective biomarkers and neurocognitive testing. However, despite these encouraging findings, several limitations remain. The lack of standardized herbal formulations, variations in phytochemical composition, limited large-scale clinical trials, and insufficient long-term safety data restrict their widespread clinical use. Herb–drug interactions and inconsistent regulatory frameworks further complicate their safe application (World Health Organization, 2004; Ekor, 2014). Future research system should have focus on conducting well-designed randomized controlled trials, identifying, bioactive compounds, establishing standardized dosing guidelines, and strengthening pharmacovigilance data systems. Greater collaboration between traditional medicine practitioners, researchers, and regulatory agencies will be requiring to integrate adaptogens into evidence-based healthcare practices in society. Overall, adaptogens represent a promising area of phytopharmacological research, Additionally further scientific validation is an essential before their full therapeutic potential can be realized.

FUTURE DIRECTIONS:

For the better determination of the clinical utility of adaptogens, future research should point on overcoming existing limitations in efficacy evaluation, safety assessment, and standardization. Large-scale randomized controlled trials with adequate sample sizes and longer study durations are requiring to establish stronger clinical evidence regarding the effectiveness of adaptogens in managing and medication on anxiety and improving cognitive function. Standardization of herbal formulations, extraction techniques, dosage regimens, and phytochemical composition is essential to ensure consistency and reproducibility across research studies. Future investigations should also focus to involvement of objective biomarkers such as cortisol levels, inflammatory markers, oxidative stress parameters, and neurotransmitter profiling along with validated neurocognitive assessment tools to accurately evaluate therapeutic outcomes. Long-term safety studies are necessary to identify potential adverse effects, toxicity, and herb–drug interactions associated with chronic adaptogen use. Additionally, future clinical research should include vulnerable populations such as elderly individuals, patients with psychiatric disorders, and individuals with chronic medical conditions to enhance the generalizability of findings. furthermore, harmonization of international regulatory frameworks for herbal supplements is requires to ensure product quality, safety monitoring, and broader entry of adaptogens in

evidence-based healthcare and research systems. Continued interdisciplinary research also one of tool to establish adaptogens as effective complementary therapies for stress-related disorders and cognitive dysfunction.

CONCLUSION:

Adaptogens represent a promising adjunctive therapeutic approach for the management and treatment of anxiety and cognitive dysfunction due to their ability to modulate stress-response pathways, regulate neurotransmitter balance, and produce neuroprotective effects (Panossian and Wikman, 2010). Herbal adaptogens such as Ashwagandha, Rhodiola rosea, Panax ginseng, and Holy basil have reported potential benefits in reducing stress, improving cognitive performance, and increasing overall resilience to stress-related disorders (Chandrasekhar et al., 2012; Hung et al., 2011). Despite these promising findings, limitations in current research designs, including small sample sizes, short study durations, lack of standardized formulations, inadequate safety monitoring, and inconsistent regulatory frameworks, restrict their widespread clinical application and use (Ekor, 2014; World Health Organization, 2004). Potential herb–drug interactions and insufficient long-term toxicity data further emphasize the need for cautious use, preferably alongside evidence-based conventional therapies. Further well-designed randomized controlled trials, mechanistic studies, and stronger pharmacovigilance systems are requiring to establish the long-term efficacy, safety, and therapeutic reliability of adaptogens in clinical practice and application. With continued scientific validation, adaptogens may emerge as valuable components of integrative approaches for managing and medication for anxiety and cognitive impairments. Adaptogens represent a promising adjunctive approach for the management of neurogenic disorder like alzimer. Through modulation of stress response pathways and neuroprotective mechanisms, they offer therapeutic potential. However, due to limitations in current research design, safety monitoring, and regulatory consistency, adaptogens should be used cautiously and preferably alongside evidence-based conventional treatments. Further high-quality research is essential to validate their long-term efficacy and safety.

CONFLICT OF INTREST:

The author declares that there is no any conflict of interest.

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