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BIOMARKERS OF CHITTODWEGA WITH REFERENCE TO ANXIETY: EMERGING EVIDENCE AND THE SCOPE OF AYURVEDIC THERAPEUTICS

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ABSTRACT

Chittodwega is an important Ayurvedic concept characterized by psychological and somatic manifestations that closely resemble the clinical presentation of anxiety. While anxiety is traditionally assessed using clinical evaluation and psychometric scales, increasing evidence suggests that it is also associated with measurable alterations in neuroendocrine, autonomic, inflammatory, oxidative, and neuroplasticity-related pathways. Biomarkers such as cortisol, brain-derived neurotrophic factor (BDNF), inflammatory mediators, oxidative stress markers, and heart rate variability offer objective insights into these biological changes. This review examines the emerging evidence on biomarkers relevant to anxiety and explores their potential significance in understanding the biological dimensions of *Chittodwega*. It also discusses the possible relationship between Ayurvedic concepts, including *Manas*, *Dosha*, *Manovaha Srotas*, *Rajas*, and *Vata*, and contemporary physiological mechanisms involved in anxiety. Furthermore, the review evaluates the scientific evidence supporting Ayurvedic therapeutic approaches such as *Medhya Rasayana*, *Rasayana*, *Yoga*, *Satvavajaya Chikitsa*, and selected herbal interventions, with particular emphasis on their potential to modulate anxiety-related biological pathways. By integrating classical Ayurvedic knowledge with modern biomarker research, this review proposes a translational framework for the objective assessment of *Chittodwega* and identifies future directions for evidence-based Ayurvedic clinical research.

KEYWORDS: *Chittodwega*, Anxiety, Biomarkers, Cortisols.

INTRODUCTION

Anxiety disorders are among the most prevalent mental health conditions worldwide and are a major cause of psychological distress, functional impairment, and reduced quality of life. According to the World Health Organization, approximately 359 million people were living with anxiety disorders in 2021, with a global prevalence of about 4.4%.[1] Women are affected more frequently than men, and many individuals still do not receive adequate treatment. Clinically, anxiety is characterized by excessive fear and worry accompanied by restlessness, irritability, impaired concentration, sleep disturbances, muscle tension, and autonomic symptoms.

In Ayurveda, psychological disorders are described under *Manovikara*, and *Chittodwega* represents a state of mental agitation, apprehension, worry, fear, and associated somatic manifestations. Contemporary Ayurvedic literature correlates *Chittodwega* with anxiety disorders, particularly generalized anxiety disorder, while recognizing that this correlation is conceptual rather than diagnostically equivalent. The involvement of *Manas*, *Rajas*, *Vata*, *Prana Vayu*, *Sadhaka Pitta*, and *Manovaha Srotas* provides the Ayurvedic basis for understanding its pathophysiology.

The clinical presentation of anxiety shows considerable overlap with *Chittodwega*, including excessive worry (*Chinta*), fear (*Bhaya*), restlessness, disturbed sleep,

palpitations, sweating, fatigue, tremors, and gastrointestinal discomfort. These similarities provide a meaningful framework for integrating Ayurvedic and contemporary perspectives.

Currently, anxiety is assessed through clinical evaluation, structured diagnostic interviews, and validated psychometric instruments such as the Hamilton Anxiety Rating Scale (HAM-A), Generalized Anxiety Disorder-7 (GAD-7), Beck Anxiety Inventory (BAI), State-Trait Anxiety Inventory (STAI), Hospital Anxiety and Depression Scale (HADS-A), and Zung Self-Rating Anxiety Scale. Although these tools effectively measure symptom severity, they primarily rely on subjective reporting and may vary across individuals and clinical settings.

Consequently, growing attention has shifted toward biomarkers—objective biological indicators of physiological or pathological processes. Emerging evidence suggests that alterations in cortisol, brain-derived neurotrophic factor (BDNF), inflammatory mediators, oxidative stress markers, and heart rate variability reflect important neuroendocrine, autonomic, inflammatory, and neuroplastic changes associated with anxiety.

The present review examines the emerging evidence on these biomarkers and explores their relevance in understanding the biological dimensions of *Chittodwega*. It further discusses the potential of Ayurvedic therapeutics, including *Medhya Rasayana*, *Rasayana*, *Satvavajaya Chikitsa*, *Yoga*, and selected herbal interventions, as possible modulators of these biological pathways, while highlighting the need for future integrative biomarker-based Ayurvedic research.

METHODOLOGY

The search included combinations of keywords: *Chittodwega*, anxiety, anxiety disorders, biomarkers, cortisol, BDNF, inflammatory markers, oxidative stress, heart rate variability, Ayurveda, *Medhya Rasayana* and *Satvavajaya Chikitsa* Articles published up to 2025, including systematic reviews, clinical trials, observational studies, and experimental studies, were considered.

Studies focusing on anxiety biomarkers and Ayurvedic therapeutic interventions were included, while articles lacking scientific relevance or sufficient methodological details were excluded. The retrieved evidence was critically analysed and organized.

Chittodwega and anxiety: A conceptual Correlation

In Ayurveda, *Chittodwega* is described as a state of mental agitation (*Udwega*) arising from the disturbance of Manas, predominantly influenced by *Rajas* and aggravated *Vata*, particularly *Prana Vayu*, along with the involvement of Sadhaka *Pitta* and *Manovaha Srotas*. It is characterized by excessive worry (*Chinta*), fear (*Bhaya*), emotional instability, disturbed sleep, restlessness, and associated somatic manifestations.[2] Although *Chittodwega* is not mentioned as a distinct nosological entity in classical texts, its symptom complex closely resembles the clinical features observed in anxiety disorders.

From the contemporary perspective, anxiety is a multifactorial disorder involving dysregulation of emotional processing, autonomic nervous system activity, neuroendocrine responses, and cognitive functioning. Patients commonly experience persistent apprehension, excessive worry, irritability, difficulty concentrating, sleep disturbances, palpitations, sweating, tremors, and gastrointestinal discomfort. These manifestations demonstrate considerable phenomenological overlap with the Ayurvedic description of *Chittodwega*, making it a meaningful conceptual correlate rather than a direct diagnostic equivalent.

The Ayurvedic understanding emphasizes the interaction between *Manas* and *Sharira*, where psychological disturbances influence physiological functions through *Dosha* imbalance. Similarly, modern research recognizes that chronic anxiety affects the hypothalamic–pituitary–adrenal axis, autonomic regulation, inflammatory pathways, and oxidative stress. This convergence suggests that *Chittodwega* and anxiety may share common functional dimensions despite originating from different medical paradigms.

Emerging Biomarkers in Anxiety: Biological Correlates of *Chittodwega*

1. Neuroendocrine biomarkers

Neuroendocrine biomarkers reflect the activity of the hypothalamic–pituitary–adrenal (HPA) axis, the body's principal stress-response system. Chronic psychological stress and anxiety are associated with dysregulation of this axis, making its hormones important objective indicators in anxiety research.

Corticotropin-Releasing Hormone (CRH)

CRH is released from the hypothalamus in response to stress and initiates the HPA-axis cascade. Increased CRH activity has been linked with heightened fear, anxiety, and autonomic arousal, suggesting its role as an early neuroendocrine marker of stress-related disorders.

Adrenocorticotropic Hormone (ACTH)

ACTH is secreted by the anterior pituitary following CRH stimulation and regulates adrenal cortisol production. Altered ACTH secretion reflects HPA-axis dysregulation and has been reported in individuals experiencing chronic stress and anxiety.

Cortisol

Cortisol is the most extensively investigated neuroendocrine biomarker of anxiety. Elevated or irregular serum, salivary, hair, or urinary cortisol levels

have been associated with excessive worry, sleep disturbances, emotional dysregulation and chronic stress. Although not a standalone diagnostic marker, cortisol remains the most reliable objective indicator of HPA-axis activity in anxiety research.

Dehydroepiandrosterone (DHEA/DHEA-S)
DHEA is an adrenal steroid with neuroprotective and anti-glucocorticoid properties. Recent studies suggest that reduced DHEA-S levels and an increased cortisol/DHEA ratio are associated with greater anxiety severity, indicating that both hormones together may better reflect stress resilience than cortisol alone.

2. Inflammatory biomarkers
Among inflammatory mediators, Interleukin-6 (IL-6), Tumour Necrosis Factor-α (TNF-α), and C-reactive Protein (CRP) are the most consistently investigated biomarkers. Clinical studies have demonstrated elevated circulating levels of IL-6 and TNF-α in patients with anxiety, while higher CRP concentrations have been associated with greater anxiety symptom severity, indicating persistent activation of inflammatory pathways.

3. Oxidative stress biomarkers
Oxidative stress results from an imbalance between reactive oxygen species and antioxidant defence mechanisms. Malondialdehyde (MDA), a marker of lipid peroxidation, is frequently reported to be elevated in anxiety-related disorders. Conversely, antioxidant enzymes such as Superoxide Dismutase (SOD) and Glutathione Peroxidase (GPx) are often reduced, reflecting impaired antioxidant capacity. These alterations suggest that oxidative damage may play a significant role in the pathophysiology of anxiety.

Together, inflammatory and oxidative stress biomarkers provide objective evidence of the biological processes underlying anxiety and represent promising targets for evaluating the effects of Ayurvedic therapeutic interventions.

4. Heart Rate Variability (HRV)
It is the most widely studied autonomic biomarker in anxiety. It reflects the balance between sympathetic and parasympathetic nervous system activity. Individuals with anxiety typically exhibit reduced HRV, indicating impaired vagal tone and autonomic dysregulation. HRV is a non-invasive, objective marker that has been extensively used to assess stress regulation and therapeutic response.

Brain-Derived Neurotrophic Factor(BDNF)
BDNF is a neurotrophin essential for neuronal survival, synaptic plasticity, and cognitive function. Clinical studies have reported reduced serum BDNF levels in patients with anxiety disorders, suggesting impaired neuroplasticity. Restoration of BDNF has been associated with improved emotional regulation and resilience following therapeutic interventions.

Together, HRV and BDNF provide complementary insights into the autonomic and neuroplastic mechanisms underlying anxiety and represent promising objective biomarkers for future integrative research in *Chittodwega*.

Ayurvedic Therapeutics and Their Potential for Biomarker Modulation in *Chittodwega*
Ayurvedic therapeutic approaches may influence several biological pathways involved in anxiety, including the HPA axis, autonomic regulation, inflammation, oxidative stress, and neuroplasticity. Among these, *Yoga* and *pranayama* have comparatively stronger clinical evidence, with studies reporting improvements in anxiety along with changes in cortisol, BDNF, inflammatory markers, and autonomic function.

Medhya Rasayana
Medhya Rasayana includes classical drugs—*Mandukaparni* (Centella asiatica), *Yashtimadhu* (Glycyrrhiza glabra), *Guduchi* (Tinospora cordifolia) and *Shankhapushpi* (Convolvulus pluricaulis). Other drugs commonly discussed for *Medhya* activity include *Brahmi* (Bacopa monnieri), *Jatamansi* (Nardostachys jatamansi), *Vacha* (Acorus calamus), and *Jyotishmati* (Celastrus paniculatus). Research on these drugs has demonstrated varying degrees of anxiolytic, anti stress, neuroprotective, antioxidant, and cognitive-enhancing effects, particularly in experimental studies. *Mandukaparni* and *Shankhapushpi* have shown anxiolytic and antioxidant effects, while *Brahmi* has demonstrated neuroprotective and stress-modulating properties. Yashtimadhu and *Guduchi* have also shown antioxidant and neuroprotective effects, with experimental evidence suggesting potential relevance to stress and anxiety-related pathways. A clinical trial of an Ayurvedic formulation containing several *Medhya* drugs, including *Brahmi*, *Shankhapushpi*, *Vacha* and *Jatamansi*, also reported improvement in generalized anxiety disorder.

Available experimental and clinical research on *Medhya Rasayana* drugs suggests potential anxiolytic, anti stress, antioxidant, anti-inflammatory, neuroprotective, and neuroplasticity-related effects, although the strength of evidence and biomarkers investigated vary considerably among individual drugs.

Table no 1: Research Evidence on *Medhya Rasayana* Drugs Relevant to Anxiety and Biomarker Modulation.

***Medhya Rasayana* drug**	**Research evidence relevant to anxiety/stress**	**Biomarkers / biological parameters studied**	**Major findings**
Mandukaparni (Centella asiatica)	Clinical study in 33 patients with generalized anxiety disorder[3]	Psychological anxiety and stress measures	Significant reduction in anxiety, stress and depression scores; improvement in cognition was also reported
Brahmi (*Bacopa monnieri)*	Randomized controlled research in adults assessing stress, sleep and wellbeing[4]	Salivary cortisol, DHEA-S, sIgA, α-amylase, CRP	Bacopa showed effects on stress-related biological measures, including reductions in salivary sIgA and α-amylase; further biomarker studies are required
Guduchi (*Tinospora cordifolia****)***	*Experimental study using a sleep-deprivation-induced anxiety model*[5]	Cortisol, IL-6, TNF-α, IL-1β, MCP-1 and neuroinflammatory changes	Extract reduced anxiety-like behaviour, cortisol and pro-inflammatory cytokines, supporting possible HPA-axis and anti-inflammatory effects
Shankhapushpi (*Convolvulus pluricaulis****)***	Experimental research investigating stress-related behavioural and molecular changes[6]	Oxidative stress and antioxidant-related pathways, including SOD1 and GABAergic pathways	Demonstrated antioxidant and anxiolytic-related effects and modulation of molecular pathways associated with oxidative resilience.
Jatamansi **(***Nardostachys jatamansi***)**	Experimental anxiety model in mice with induced oxidative stress[7]	Cortisol, lipid peroxidation, protein carbonyls, GPx, GR, GST, SOD, CAT, GABA and monoamines	Reduced anxiety-like behaviour and oxidative stress markers while improving antioxidant status and GABA/monoamine levels.
Yashtimadhu **(***Glycyrrhiza glabra***)**	Experimental research on stress/anxiety-related mechanisms[8]	Neuroinflammatory and oxidative-stress-related pathways	Preclinical evidence suggests neuroprotective, antioxidant and anti-inflammatory activity relevant to anxiety-related pathways; direct human biomarker evidence remains limited

Similarly, *Satvavajaya Chikitsa* and *Rasayana* may contribute to stress regulation and psychological resilience, but biomarker-based clinical studies are still scarce. Therefore, current evidence suggests a potential role of Ayurvedic therapeutics in biomarker modulation rather than establishing definitive effects.

Future clinical studies should integrate Ayurvedic assessment of *Chittodwega*, validated anxiety scales, and objective biomarkers before and after treatment. Such an approach could help establish measurable biological correlates of therapeutic response and strengthen the scientific evaluation of Ayurvedic interventions.

DISCUSSION

The assessment of anxiety and *Chittodwega* is predominantly based on clinical symptoms and psychometric scales. Although these approaches are useful for diagnosis and monitoring treatment response, they are largely dependent on subjective reporting. Biomarkers may therefore serve as complementary objective tools, providing measurable information about the physiological processes associated with anxiety. Alterations in cortisol and other HPA-axis markers may reflect stress-response dysregulation, while inflammatory and oxidative stress markers may indicate associated systemic biological changes. Similarly, reduced HRV may reflect autonomic imbalance, whereas BDNF may provide insights into neuroplasticity. However, these biomarkers should presently be considered supportive rather than diagnostic markers, as no single biomarker has sufficient specificity to independently diagnose anxiety or *Chittodwega*.

From an Ayurvedic perspective, the interaction of *Manas*, Rajas, *Vata*, *Prana Vayu*, *Sadhaka Pitta*, and *Manovaha Srotas* may provide a conceptual framework for understanding these biological changes. Ayurvedic therapeutics may act through multiple pathways rather than a single molecular target. *Yoga*, *Pranayama*, meditation, and *Satvavajaya Chikitsa* may help regulate stress responses and autonomic function, potentially influencing cortisol and HRV. *Medhya Rasayana* and selected herbal drugs may exert antioxidant, anti-inflammatory, neuroprotective, and neuroplasticity-related effects, thereby potentially influencing oxidative stress markers, inflammatory mediators, and BDNF.

Thus, biomarker assessment may provide a valuable bridge between Ayurvedic clinical assessment and contemporary biological science. A combined approach using *Chittodwega* assessment, validated anxiety scales,

and biomarkers before and after Ayurvedic intervention could objectively evaluate therapeutic response. Nevertheless, further well-designed clinical studies are required to establish which biomarkers are most relevant and whether their changes correlate consistently with improvement in *Chittodwega* and anxiety symptoms.

CONCLUSION

Chittodwega shares several clinical features with anxiety, providing a useful framework for integrative understanding. Biomarkers such as cortisol, inflammatory and oxidative stress markers, HRV, and BDNF may complement conventional clinical and psychological assessment by providing objective information about underlying biological changes. Ayurvedic therapeutics, including *Yoga*, *Pranayama*, *Medhya Rasayana*, *Satvavajaya Chikitsa*, and selected herbal interventions, may potentially modulate these pathways through their stress-regulating, antioxidant, anti-inflammatory, autonomic, and neuroprotective effects. However, direct evidence in *Chittodwega* remains limited. Future studies combining Ayurvedic assessment, validated anxiety scales, and biomarkers may help establish objective therapeutic outcomes and strengthen the scientific evidence for Ayurvedic management.

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