Naveen Shodh Sansar (An International Refereed / Peer Review Multidisciplinary Research Journal)
RNI No.- MPHIN/2013/60638, ISSN 2320-8767, E- ISSN 2394-3793, Scientific Journal Impact Factor (SJIF)- 8.054,
January to March 2025 E-Journal, Volume I, Issue XLIX, ISO 9001:2015 - E2024049304 (QMS)

Ayurvedic Management of Central Sensitization: Mechanistic Insights in Fibromyalgia Care

Dr. Rajesh Yadav*

***Asst. Prof. (Zoology) Ramabai Govt. Women P.G. College, Akbarpur, Ambedkar Nagar (U.P.) INDIA**

Abstract: Fibromyalgia is a chronic disorder of widespread pain, fatigue, sleep disturbance, cognitive dysfunction, and affective symptoms. Central sensitization is characterized by heightened responsiveness of central nociceptive pathways, impaired descending inhibition, and neuroinflammatory processes, is widely recognized as a core pathophysiological mechanism in fibromyalgia. Conventional pharmacologic and behavioral interventions provide partial relief, leaving many patients to pursue complementary approaches. Ayurveda, an individualized medical system emphasizing dosha balance, detoxification (Panchakarma), tissue nourishment (Rasayana), and lifestyle modulation, offers a multimodal framework that aligns with several mechanistic features of Central sensitization. This review synthesizes contemporary neuroscience and immunology of Central sensitization with classical and contemporary Ayurvedic theory to create a translational model linking Vata aggravation, Ama accumulation, and Majja (nervous tissue) depletion to neurochemical, neuroimmune, autonomic, and gut–brain axis dysfunction observed in fibromyalgia. Evidence from preclinical studies on key medhya (neuroprotective) herbs (Withaniasomnifera, Bacopamonnieri, Centellaasiatica), clinical pilot studies of Panchakarma protocols (including Snehana, Swedana, Basti, and Shirodhara), and emerging biomarker and neuroimaging data are reviewed. Proposed mechanistic pathways include modulation of NMDA/GABA balance, attenuation of microglial activation and pro-inflammatory cytokines, restoration of HPA and autonomic tone, and gut microbiome normalization. We identify key research gaps that need for randomized controlled trials, standardized intervention protocols, biomarker-driven endpoints, and mechanistic neuroimaging and propose a roadmap for integrative clinical trials that can validate Ayurvedic interventions within modern pain science. Integrative care grounded in rigorous research could expand therapeutic options for fibromyalgia patients with central sensitization.
Keywords: Fibromyalgia, Central Sensitization, Ayurveda, Panchakarma, Rasayana Therapy, Neuroinflammation, VataVyadhi.

Introduction - Fibromyalgia is a chronic pain disorder affecting approximately 2–4% of the global population and is characterized by widespread musculoskeletal pain, fatigue, sleep disturbance, cognitive impairment ("fibro fog"), and frequent comorbidity with mood and somatic disorders (Clauw, 2014; Häuser et al., 2015). Central sensitization, defined as enhanced responsiveness of central nervous system (CNS) nociceptive pathways, is widely considered the principal pathophysiological mechanism underlying fibromyalgia symptomatology (Woolf, 2011; Fitzcharles et al., 2023). Central sensitization encompasses maladaptive synaptic plasticity, increased excitatory neurotransmission, impaired descending inhibitory modulation, and neuroimmune activation, resulting in amplified pain perception and multisystem symptom expression (Clauw, 2014; Sluka&Clauw, 2016).

Despite advances in pharmacologic management, including serotonin–norepinephrine reuptake inhibitors, gabapentinoids, and low-dose tricyclic antidepressants, as well as non-pharmacologic interventions such as exercise and cognitive behavioral therapy, therapeutic outcomes remain suboptimal for many patients due to limited efficacy or adverse effects (Häuser et al., 2015). Consequently, there is growing interest in complementary and integrative strategies that address the multidimensional neurobiological, endocrine, immune, metabolic, and psychosocial contributors to Central sensitization. Ayurveda, a personalized and systems-oriented medical tradition, employs multimodal interventions—including Panchakarma procedures, Rasayana herbal formulations, dietary regulation, and mind–body practices—that may align with contemporary mechanistic models of nociplastic pain. This review synthesizes current evidence on Central sensitization in fibromyalgia with Ayurvedic constructs, particularly Vata predominance, Ama accumulation, and Majja depletion, and outlines translational hypotheses and research priorities

bridging traditional knowledge and modern pain science.

Central Sensitization in Fibromyalgia: mechanistic overview

1. Neurophysiology and synaptic plasticity: Central sensitization in fibromyalgia is characterized by maladaptive neurophysiological changes and activity-dependent synaptic plasticity within central nociceptive pathways (Clauw, 2014; Woolf, 2011). Persistent peripheral input enhances excitatory neurotransmission in the dorsal horn through increased glutamatergic signaling and sustained activation of N-methyl-D-aspartate (NMDA) receptors, leading to intracellular calcium influx and kinase-mediated transcriptional modifications that resemble long-term potentiation (LTP) phenomena (Latremoliere& Woolf, 2009; Häuser et al., 2015). Concurrently, diminished inhibitory modulation—particularly involving ã-aminobutyric acid (GABA), serotonin, and norepinephrine—compromises descending pain control systems, thereby amplifying central neuronal excitability (Clauw, 2014). Neuroimmune interactions further contribute to synaptic facilitation, as activated microglia release pro-inflammatory cytokines that modulate receptor sensitivity and ion channel conductance (Ji et al., 2018). Collectively, these neuroplastic alterations lower activation thresholds, expand receptive fields, and sustain aberrant pain processing, forming the neurobiological substrate of chronic widespread pain in fibromyalgia.

2. Descending modulation and neurochemical milieu: Alterations in descending pain modulatory systems and the broader neurochemical environment are central to the pathophysiology of fibromyalgia and central sensitization (Clauw, 2014; Häuser et al., 2015). Under physiological conditions, descending inhibitory pathways originating in the periaqueductal gray and rostroventromedial medulla regulate spinal nociceptive transmission through serotonergic and noradrenergic projections. In fibromyalgia, dysfunction of these monoaminergic systems results in reduced inhibitory tone and impaired endogenous analgesia, thereby facilitating pain amplification (Arnold et al., 2019). Neurochemical studies have demonstrated altered levels of serotonin, norepinephrine, dopamine, glutamate, and substance P in patients, reflecting an imbalance between excitatory and inhibitory signaling (Sluka&Clauw, 2016). Moreover, dysregulation of the hypothalamic–pituitary–adrenal (HPA) axis and altered cortisol secretion patterns contribute to stress sensitivity and persistence of central sensitization (Martínez-Lavin, 2021). Emerging neuroimaging and cerebrospinal fluid analyses further support aberrant connectivity and neurotransmitter metabolism within pain-processing networks (Fitzcharles et al., 2023). Collectively, impaired descending inhibition combined with neurochemical disequilibrium sustains hyperexcitability of central nociceptive circuits in fibromyalgia.

3. Neuroinflammation and glial activation: Neuroinflammation and glial cell activation are increasingly recognized as central contributors to the pathophysiology of fibromyalgia and persistent nociplastic pain states (Fitzcharles et al., 2023; Häuser et al., 2015). Activated microglia and astrocytes within the spinal cord and supraspinal regions release pro-inflammatory cytokines, chemokines, and neuromodulators, including interleukin-1â, interleukin-6, tumor necrosis factor-á, and brain-derived neurotrophic factor, which enhance synaptic transmission and neuronal excitability (Ji et al., 2018). This glial-neuron crosstalk promotes central sensitization by facilitating N-methyl-D-aspartate receptor activity, altering ion channel conductance, and reducing inhibitory signaling. Neuroimaging studies using positron emission tomography have provided preliminary evidence of increased glial activation markers in patients with fibromyalgia, supporting a neuroimmune component to symptom generation (Albrecht et al., 2019). Additionally, peripheral immune dysregulation and altered cytokine profiles may contribute to sustained central neuroinflammatorysignaling (Fitzcharles et al., 2023). Collectively, glial-mediated neuroinflammation represents a mechanistic bridge between immune activation and maladaptive synaptic plasticity underlying chronic widespread pain.

4. Systems interactions: HPA axis, autonomic imbalance, and gut–brain axis: Neuroinflammation and glial cell activation are increasingly recognized as central contributors to the pathophysiology of fibromyalgia and persistent nociplastic pain states (Fitzcharles et al., 2023; Häuser et al., 2015). Activated microglia and astrocytes within the spinal cord and supraspinal regions release pro-inflammatory cytokines, chemokines, and neuromodulators, including interleukin-1â, interleukin-6, tumor necrosis factor-á, and brain-derived neurotrophic factor, which enhance synaptic transmission and neuronal excitability (Ji et al., 2018). This glial-neuron crosstalk promotes central sensitization by facilitating N-methyl-D-aspartate receptor activity, altering ion channel conductance, and reducing inhibitory signaling. Neuroimaging studies using positron emission tomography have provided preliminary evidence of increased glial activation markers in patients with fibromyalgia, supporting a neuroimmune component to symptom generation (Albrecht et al., 2019). Additionally, peripheral immune dysregulation and altered cytokine profiles may contribute to sustained central neuroinflammatorysignaling (Fitzcharles et al., 2023). Collectively, glial-mediated neuroinflammation represents a mechanistic bridge between immune activation and maladaptive synaptic plasticity underlying chronic widespread pain.

Ayurvedic conceptualization of fibromyalgia and central sensitization: Within the Ayurvedicnosological framework, fibromyalgia can be interpreted as a Vata-predominant disorder falling under the broader category of *VataVyadhi*, particularly conditions resembling

Mamsagatavata (involvement of muscle tissue) and *Majjagatavata* (involvement of nervous tissue) (Sharma & Dash, 2018). The hallmark clinical features of fibromyalgia—migratory pain, stiffness, fatigue, sleep disturbance, and cognitive dysfunction—correspond to classical descriptions of aggravated Vata, whose qualities (*ruksha*, *laghu*, *chala*) signify dryness, lightness, and instability. From a mechanistic perspective, Vataaggravation may parallel heightened neuronal excitability and dysregulated signal transmission observed in central sensitization (Clauw, 2014).

Additionally, Ayurveda attributes chronic pain states to the accumulation of *Ama*, a toxic metabolic by-product resulting from impaired *Agni* (digestive/metabolic function). Ama is described as obstructing bodily channels (*srotorodha*), potentially analogous to systemic inflammation and neuroimmune activation implicated in persistent nociplastic pain (Fitzcharles et al., 2023). Progressive Vata aggravation may also lead to *Majjadhatukshaya* (depletion of nervous tissue), conceptually aligning with neurotransmitter imbalance and impaired descending inhibition. Thus, Ayurvedic pathophysiology provides a multidimensional explanatory model integrating neural, metabolic, and systemic dysfunction in fibromyalgia.

1. Vata aggravation and neural hyperexcitability: In Ayurvedic pathophysiology, Vatadosha governs movement, neural conduction, sensory perception, and autonomic regulation. Aggravation of Vata (*Vataprakopa*) is characterized by qualities such as mobility (*chala*), dryness (*ruksha*), lightness (*laghu*), and instability, which collectively reflect dysregulated and excessive physiological activity (Sharma & Dash, 2018). Clinically, fibromyalgia presents with migratory pain, paresthesia, sleep disturbance, anxiety, and variable symptom intensity—features consistent with Vata predominance. From a neurobiological perspective, these manifestations parallel the concept of neural hyperexcitability underlying central sensitization (Clauw, 2014).

Central sensitization involves enhanced synaptic transmission, lowered nociceptive thresholds, and amplification of sensory input due to persistent excitatory signaling within spinal and supraspinal pathways (Woolf, 2011). The dynamic and fluctuating nature of fibromyalgia pain may therefore be interpreted as the clinical correlate of aggravated Vata influencing *Majjadhatu* (nervous tissue). Furthermore, Vata imbalance is associated with autonomic instability, which aligns with documented sympathetic predominance and reduced heart rate variability in fibromyalgia (Sluka&Clauw, 2016). Thus, Vata aggravation offers a conceptual framework analogous to maladaptive neuronal excitability and impaired inhibitory modulation in central sensitization.

2. Ama and neuroimmune activation: In Ayurvedic doctrine, *Ama* denotes incompletely metabolized or improperly processed biological substrates that accumulate due to impaired *Agni* (digestive and metabolic function) and obstruct physiological channels (*srotas*) (Sharma & Dash, 2018). Clinically, Ama is associated with heaviness, fatigue, inflammatory symptoms, and chronic pain states. From a contemporary biomedical perspective, this construct may be interpreted through the lens of systemic low-grade inflammation, altered gut permeability, and immune activation, all of which are implicated in fibromyalgia and central sensitization (Fitzcharles et al., 2023). Emerging evidence indicates that dysregulated immune responses and elevated pro-inflammatory cytokines can promote microglial activation and neuroinflammatorysignaling within pain-processing regions (Ji et al., 2018). Additionally, gut microbiome alterations observed in fibromyalgia may facilitate metabolite-driven immune modulation and nociceptive amplification (Minerbi et al., 2019). Thus, the Ayurvedic concept of Ama provides a plausible translational framework linking metabolic dysfunction and immune activation to persistent neuroinflammation and maladaptive synaptic plasticity in fibromyalgia..

3. Majjadhatu depletion and neurotransmitter imbalance: In Ayurvedic physiology, *Majjadhatu* represents the nervous tissue and marrow components responsible for cognitive integrity, sensory processing, and neuromuscular coordination (Sharma & Dash, 2018). Depletion of Majja (*Majjakshaya*) is described as manifesting through symptoms such as generalized weakness, cognitive impairment, sensory disturbances, and chronic pain—features that overlap substantially with fibromyalgia. From a neurobiological standpoint, these manifestations may correspond to alterations in central neurotransmitter systems implicated in nociplastic pain. Studies in fibromyalgia have demonstrated reduced serotonergic and noradrenergic activity, altered dopaminergic signaling, and increased excitatory neurotransmitters such as glutamate, contributing to impaired descending inhibition and persistent pain amplification (Clauw, 2014; Sluka&Clauw, 2016).

Furthermore, dysregulation of brain-derived neurotrophic factor (BDNF) and other neurotrophic mediators may influence synaptic plasticity and central sensitization processes (Fitzcharles et al., 2023). Conceptually, Majja depletion can be interpreted as diminished neurochemical resilience and impaired neural homeostasis. Thus, restoration of Majja through Rasayana and medhya interventions aligns with therapeutic strategies aimed at rebalancing neurotransmitter systems and enhancing central inhibitory control in fibromyalgia.

Ayurvedic interventions and putative mechanisms relevant to central sensitization: Ayurvedic interventions for fibromyalgia target aggravated *Vata*, accumulated *Ama*, and *Majjadhatu* imbalance. Panchakarma therapies such as *Snehana* and *Basti* may modulate autonomic tone and gut–brain axis signaling, reducing stress-driven nociceptive

amplification. Medhya and Rasayana herbs exhibit antioxidant, anti-inflammatory, and neuroprotective effects, potentially restoring neurotransmitter balance and synaptic stability. Dietary regulation and mind–body practices further attenuate hypothalamic–pituitary–adrenal axis dysregulation, collectively addressing neuroimmune and neuroplastic mechanisms underlying central sensitization thus, ayurvedic care is multimodal. Below we review major categories and their plausible mechanisms in relation to central sensitization and fibromyalgia.

Panchakarma: Snehana, Swedana, Basti, and Shirodhara

1. Snehana and Swedana (therapeutic oleation and fomentation): *Snehana* (therapeutic oleation) and *Swedana* (sudation/fomentation) constitute foundational preparatory procedures within Panchakarma, primarily indicated for pacifying aggravated *Vatadosha* in chronic pain disorders (Sharma & Dash, 2018). Snehana, typically administered through medicated oil massage (*Abhyanga*), is described as alleviating dryness (*rukshata*), stiffness, and neuromuscular instability—features consistent with Vata predominance. Swedana involves controlled application of heat or steam to promote channel clearance (*srotoshodhana*) and facilitate toxin mobilization.

From a biomedical perspective, these interventions may exert analgesic and neuromodulatory effects through multiple mechanisms. Manual oil massage has been associated with enhanced parasympathetic activity, reduced sympathetic tone, and improved heart rate variability, thereby modulating autonomic imbalance implicated in fibromyalgia (Field, 2016). Thermal therapies may increase local blood flow, reduce muscle spindle hyperactivity, and attenuate peripheral nociceptive input, indirectly lowering central sensitization (Clauw, 2014). Furthermore, relaxation responses induced by these therapies may attenuate hypothalamic–pituitary–adrenal axis activation and decrease stress-related amplification of pain (Fitzcharles et al., 2023). Collectively, Snehana and Swedana represent integrative modalities targeting neurophysiological, autonomic, and inflammatory components of chronic nociplastic pain.

2. Basti (medicated enemas): *Basti* (medicated enema therapy) is regarded in Ayurveda as the principal intervention for disorders arising from aggravated *Vatadosha*, particularly those involving neuromuscular and systemic dysregulation (Sharma & Dash, 2018). Classical texts describe Basti as exerting systemic effects beyond the gastrointestinal tract, influencing *Vata* at its primary seat in the colon and thereby restoring physiological homeostasis. In the context of fibromyalgia, which demonstrates features consistent with Vata predominance and central sensitization, Basti may have translational relevance.

From a biomedical standpoint, the colon represents a critical interface within the gut–brain axis. Rectal administration of medicated oils or herbal decoctions may influence enteric nervous system signaling, vagal afferent pathways, and immune modulation (Fitzcharles et al., 2023). Alterations in gut microbiota composition and intestinal permeability—documented in fibromyalgia—suggest that therapies targeting gastrointestinal homeostasis could indirectly attenuate systemic inflammation and neuroinflammatorysignaling (Minerbi et al., 2019). Additionally, lipid-based formulations may facilitate absorption of bioactive phytochemicals with potential anti-inflammatory or neuromodulatory properties. Although high-quality randomized trials remain limited, Basti represents a biologically plausible modality for modulating gut–brain interactions implicated in chronic nociplastic pain.

3. Shirodhara: *Shirodhara* is a classical Ayurvedic therapy involving the continuous, rhythmic pouring of warm medicated oil or decoction over the forehead, traditionally indicated for disorders of the mind (*manovahasrotas*), sleep disturbances, and aggravated *Vata* (Sharma & Dash, 2018). In the context of fibromyalgia, which frequently presents with insomnia, cognitive dysfunction, anxiety, and stress sensitivity, Shirodhara may have mechanistic relevance to central sensitization.

From a neurophysiological perspective, Shirodhara is hypothesized to induce a relaxation response mediated through modulation of the hypothalamic–pituitary–adrenal (HPA) axis and autonomic nervous system activity. Preliminary clinical observations suggest reductions in stress markers, improvements in sleep quality, and enhanced parasympathetic tone following therapy (Rao et al., 2017). Given that autonomic imbalance and stress dysregulation contribute to impaired descending pain inhibition in fibromyalgia, such modulation may indirectly attenuate central nociplastic amplification (Fitzcharles et al., 2023). Additionally, sensory stimulation of the frontal scalp region may influence limbic and cortical networks involved in emotional regulation and pain perception. Although rigorous randomized trials remain limited, Shirodhara represents a plausible adjunctive intervention targeting stress-related neurobiological mechanisms in fibromyalgia.

Medhya and Rasayana herbs: neuroprotective, anti-inflammatory, adaptogenic actions: *Medhya* and *Rasayana* herbs, such as *Withaniasomnifera*, *Bacopamonnieri*, and *Centellaasiatica*, are traditionally indicated for cognitive enhancement and neural rejuvenation. Pharmacologically, they exhibit antioxidant, anti-inflammatory, adaptogenic, and neuroprotective properties, potentially modulating neurotransmitter balance, reducing neuroinflammation, and enhancing synaptic resilience in central sensitization disorders such as fibromyalgia. Above herbs with preclinical and some clinical data relevant to fibromyalgia and central sensitization described below:

1. Withaniasomnifera (Ashwagandha): *Withaniasomnifera* (Ashwagandha) is a prominent

AyurvedicRasayana herb traditionally indicated for Vata disorders, fatigue, and neurocognitive dysfunction (Sharma & Dash, 2018). Contemporary research demonstrates its adaptogenic, anti-inflammatory, and neuroprotective properties, which are mechanistically relevant to fibromyalgia and central sensitization. Experimental studies indicate that Ashwagandha modulates hypothalamic–pituitary–adrenal (HPA) axis activity, reduces cortisol levels, and attenuates oxidative stress and pro-inflammatory cytokines (Lopresti et al., 2019). Preclinical models further suggest its potential to reduce hyperalgesia and improve mitochondrial function, thereby influencing nociceptive processing (Singh et al., 2023). Clinical trials in stress-related conditions report improvements in sleep quality, anxiety, and overall well-being, factors closely linked to pain modulation (Salve et al., 2019). Collectively, Ashwagandha represents a biologically plausible adjunct in managing nociplastic pain syndromes.

2. Bacopamonnieri (Brahmi): *Bacopamonnieri* (Brahmi) is classified in Ayurveda as a *MedhyaRasayana*, traditionally prescribed to enhance cognition, memory, and mental clarity, particularly in conditions associated with aggravated *Vata* and *Majjadhatu* imbalance (Sharma & Dash, 2018). Contemporary pharmacological studies demonstrate that standardized Bacopa extracts exert neuroprotective, antioxidant, and anti-inflammatory effects, modulating cholinergic transmission and synaptic plasticity (Aguiar&Borowski, 2013). Preclinical evidence suggests that Bacopa enhances dendritic branching and supports long-term potentiation, thereby influencing learning and neuronal resilience (Peth-Nui et al., 2012). Clinical trials in healthy adults and elderly populations report improvements in attention, processing speed, and working memory (Kongkeaw et al., 2014). Given that fibromyalgia is frequently associated with cognitive dysfunction (“fibro fog”) and altered central processing, Bacopa’s multimodal neurochemical actions may offer adjunctive benefits in modulating central sensitization and cognitive impairment.

3. Centellaasiatica, Convolvulus pluricaulis and other medhya plants: *Centellaasiatica* (Mandukaparni) and *Convolvulus pluricaulis* (Shankhapushpi) are classified as *MedhyaRasayana* herbs in Ayurveda, traditionally indicated for cognitive enhancement, stress modulation, and disorders involving *Majjadhatu* and aggravated *Vata* (Sharma & Dash, 2018). Contemporary pharmacological studies demonstrate that *Centellaasiatica* possesses neuroprotective, antioxidant, and anti-inflammatory properties, with evidence suggesting enhancement of brain-derived neurotrophic factor (BDNF) expression and synaptic plasticity (Gray et al., 2018). Clinical trials indicate improvements in cognitive performance and anxiety symptoms (Farooqui et al., 2022). *Convolvulus pluricaulis* has shown anxiolytic, anti-stress, and memory-enhancing effects in preclinical models, potentially through modulation of cholinergic and GABAergic systems (Nahata et al., 2010). Given that fibromyalgia is associated with cognitive dysfunction, stress sensitivity, and central sensitization, these medhya plants may exert adjunctive benefits by attenuating oxidative stress, modulating neuroinflammation, and supporting synaptic resilience.

4. Diet, Agni, Ama, and microbiome modulation: In Ayurveda, optimal health depends upon balanced *Agni* (digestive and metabolic fire), which governs nutrient assimilation and prevents the formation of *Ama*, a pathological metabolic residue implicated in systemic dysfunction (Sharma & Dash, 2018). Impaired Agni leads to Ama accumulation, described as obstructing physiological channels (*srotas*) and contributing to chronic inflammatory states. Translationally, this concept parallels contemporary findings linking altered gut microbiota composition, increased intestinal permeability, and low-grade systemic inflammation to fibromyalgia and central sensitization (Minerbi et al., 2019; Fitzcharles et al., 2023). Dysbiosis-associated metabolites may influence neuroimmunesignaling through vagal, endocrine, and cytokine-mediated pathways, thereby modulating nociceptive processing. Ayurvedic dietary prescriptions (*Pathya*) emphasize easily digestible, anti-inflammatory foods and individualized regimens aimed at restoring Agni and reducing Ama burden. Such approaches may favorably influence microbiome diversity, metabolic homeostasis, and immune regulation. Consequently, dietary modulation represents a plausible mechanistic bridge between Ayurvedic metabolic theory and gut–brain axis–mediated pain amplification in fibromyalgia.

5. Mind-body practices (Yoga, Pranayama, Meditation): Mind–body interventions, including yoga, pranayama, and meditation, are integral components of Ayurvedic lifestyle therapy and are increasingly supported by contemporary pain research. In fibromyalgia, these practices have demonstrated beneficial effects on pain intensity, fatigue, sleep quality, and psychological distress (Cramer et al., 2013; Häuser et al., 2010). Mechanistically, yoga-based interventions enhance parasympathetic tone, improve heart rate variability, and reduce sympathetic overactivation, thereby addressing autonomic imbalance associated with central sensitization (Sluka&Clauw, 2016).

Controlled breathing techniques (pranayama) modulate vagal afferent signaling and hypothalamic–pituitary–adrenal (HPA) axis activity, contributing to improved stress resilience and pain regulation. Meditation practices have been shown to alter functional connectivity in cortical and limbic pain-processing networks, enhancing top-down inhibitory control and reducing affective pain components (Zeidan et al., 2012). Collectively, these interventions may attenuate nociplastic amplification by restoring autonomic equilibrium, reducing neuroinflammatory stress responses, and strengthening descending pain modulation systems in fibromyalgia.

Clinical evidence: what exists and where are

limitations?

1. Trials, pilot studies, and case series: The clinical evidence base for Ayurvedic interventions in fibromyalgia remains emerging and is largely composed of pilot studies, feasibility trials, and case series. A nonrandomized controlled pilot trial evaluating an add-on complex Ayurvedic treatment (KAFA trial) reported improvements in pain intensity, functional disability, and quality of life compared with conventional care alone; however, methodological limitations, including small sample size and lack of blinding, restrict generalizability (Michalsen et al., 2013). Observational studies conducted in integrative settings have similarly documented reductions in symptom burden following multimodal Panchakarma-based protocols incorporating Snehana, Swedana, Basti, dietary modification, and herbal Rasayana therapy (Rasmussen et al., 2012). Individual case reports describe clinically meaningful improvements in pain, stiffness, and sleep following personalized Ayurvedic regimens, though these designs inherently lack control groups and standardized outcome measures. Overall, while preliminary findings suggest potential benefit and feasibility, high-quality randomized controlled trials with standardized interventions and validated outcome measures are necessary to establish efficacy and mechanistic validity in fibromyalgia management.

2. Preclinical support and translational plausibility: Preclinical investigations provide important mechanistic insights supporting the translational plausibility of Ayurvedic interventions in fibromyalgia and central sensitization. Experimental models of chronic widespread pain demonstrate that neuroinflammation, oxidative stress, mitochondrial dysfunction, and altered monoaminergic signaling contribute to persistent nociceptive amplification (Sluka&Clauw, 2016). Several AyurvedicRasayana and *medhya* herbs, including *Withaniasomnifera* and *Bacopamonnieri*, have shown anti-inflammatory, antioxidant, and neuroprotective effects in animal studies, with evidence of reduced hyperalgesia and modulation of stress-responsive pathways (Lopresti et al., 2019; Singh et al., 2023). Additionally, phytochemicals from *Centellaasiatica* have demonstrated enhancement of synaptic plasticity and brain-derived neurotrophic factor expression, potentially counteracting maladaptive central sensitization (Gray et al., 2018). These findings suggest that multimodal Ayurvedic therapies may influence molecular targets implicated in nociplastic pain, including cytokine signaling, NMDA receptor activity, and hypothalamic–pituitary–adrenal axis regulation. Although direct fibromyalgia-specific models remain limited, existing preclinical data provide a biologically plausible foundation for further translational and clinical research.

3. Safety and quality control: Safety and quality assurance are critical considerations in the clinical translation of Ayurvedic therapies for fibromyalgia. Although many herbal formulations are traditionally regarded as safe when administered under qualified supervision, variability in manufacturing practices, contamination with heavy metals, and herb–drug interactions remain documented concerns (Ernst, 2002; Saper et al., 2008). Standardization of botanical extracts, authentication of raw materials, and adherence to Good Manufacturing Practices (GMP) are essential to ensure reproducibility and safety. Additionally, pharmacovigilance systems should be implemented to monitor adverse events and interactions, particularly in patients receiving concomitant pharmacologic therapies for chronic pain or mood disorders. From a regulatory perspective, harmonization of traditional formulations with contemporary quality standards—including quantification of active phytoconstituents and toxicological screening—can enhance credibility and clinical acceptance. Rigorous quality control measures, combined with practitioner oversight and individualized dosing, are fundamental to integrating Ayurvedic modalities safely within multidisciplinary fibromyalgia care.

Integrative mechanistic model: mapping Ayurveda to central sensitization: An integrative mechanistic model mapping Ayurvedic principles onto central sensitization offers a systems-level framework for understanding fibromyalgia. Within this paradigm, aggravated *Vatadosha*—characterized by mobility, instability, and heightened sensitivity—can be conceptually aligned with neuronal hyperexcitability, enhanced synaptic transmission, and impaired descending inhibitory control that define nociplastic pain (Clauw, 2014). The Ayurvedic construct of *Ama*, arising from impaired *Agni* (metabolic dysfunction), parallels contemporary evidence of low-grade systemic inflammation, gut dysbiosis, and neuroimmune activation contributing to persistent pain amplification (Fitzcharles et al., 2023). Additionally, *Majjadhatukshaya* (depletion of nervous tissue) may correspond to neurotransmitter imbalance, altered brain-derived neurotrophic factor signaling, and diminished neuroplastic resilience.

Therapeutically, Panchakarma procedures such as *Snehana* and *Basti* may influence autonomic regulation and gut–brain axis signaling, potentially attenuating stress-induced central sensitization. Rasayana and *medhya* botanicals exert antioxidant, anti-inflammatory, and neuroprotective actions, supporting synaptic stability and stress adaptation. Mind–body practices further enhance parasympathetic tone and hypothalamic–pituitary–adrenal axis regulation. Collectively, this integrative model conceptualizes fibromyalgia as a multidimensional disorder requiring coordinated modulation of neural, immune, metabolic, and psychosocial networks.

This model supports multimodal interventions combining detoxification (to remove systemic drivers of neuroinflammation), tissue nourishment (to restore neural health), and mind-body practices (to re-establish descending inhibition and autonomic balance).

Research agenda and trial recommendations: To rigorously evaluate Ayurvedic interventions for fibromyalgia characterized by central sensitization, a structured and methodologically robust research framework is required. Priority should be given to adequately powered, multicenter randomized controlled trials (RCTs) employing standardized and reproducible Ayurvedic protocols. Comparative designs may assess integrated Panchakarma, Rasayana, and lifestyle-based interventions against active controls such as patient education and supervised exercise, with appropriate allocation concealment and blinding where feasible. Stratification based on validated central sensitization markers, including Central Sensitization Inventory (CSI) scores and relevant comorbidities, would enhance subgroup analyses.

Mechanistic evaluation should incorporate biomarker-driven endpoints, including pro-inflammatory cytokines, brain-derived neurotrophic factor (BDNF), diurnal cortisol patterns, autonomic indices (e.g., heart rate variability), and, where feasible, cerebrospinal fluid levels of substance P or glutamate. Neuroimaging modalities such as resting-state and pain-evoked functional MRI, alongside quantitative sensory testing, may elucidate central nervous system modulation. Longitudinal microbiome and metabolomic analyses could assess gut–brain axis effects of Basti and dietary interventions. Additionally, adherence to Good Manufacturing Practices (GMP) for herbal products and systematic pharmacovigilance are essential. Implementation research examining feasibility, cost-effectiveness, and integration within conventional multidisciplinary care is also warranted.

Practical clinical considerations: Incorporating Ayurvedic interventions into fibromyalgia management requires a cautious, patient-centered, and integrative approach until definitive RCT data are available. Therapies should be individualized based on constitutional assessment (*Prakriti*) and current imbalance (*Vikriti*), particularly evaluating features of Vata predominance. Ayurvedic modalities are best utilized as adjuncts rather than replacements for evidence-based conventional treatments, especially in patients with moderate to severe symptom burden. Collaboration between rheumatologists, pain specialists, and qualified Ayurvedic practitioners can optimize safety and therapeutic coherence. Standardized, quality-controlled herbal preparations should be prioritized to minimize risks of contamination or herb–drug interactions. Gradual introduction of mind–body practices, dietary adjustments, and gentle Panchakarma procedures may improve adherence and tolerability. Monitoring clinical outcomes using validated measures—such as pain intensity scales, sleep indices, and functional assessments—can enhance objectivity. Ultimately, an integrative care model emphasizing multimodal modulation of stress, autonomic balance, inflammation, and neural sensitization may offer practical benefits for patients with chronic nociplastic pain rather than single-modality approaches.

Limitations of the current review: This review has several limitations. First, the clinical evidence supporting Ayurvedic interventions in fibromyalgia is limited by small sample sizes, heterogeneous study designs, and a predominance of pilot trials and case reports, restricting the strength of conclusions. Second, variability in herbal formulations, individualized treatment protocols, and differences in practitioner expertise reduce reproducibility across studies. Third, direct mechanistic studies linking Ayurvedic therapies to validated biomarkers of central sensitization remain scarce. Finally, conceptual mapping between Ayurvedic constructs and biomedical mechanisms is interpretative and requires empirical validation through rigorously designed translational and randomized controlled trials.

Conclusion: Fibromyalgia represents a complex nociplastic pain disorder characterized by central sensitization, neuroimmune dysregulation, autonomic imbalance, and psychosocial vulnerability. Despite advances in pharmacological and behavioral therapies, a substantial proportion of patients continue to experience persistent symptoms, highlighting the need for multidimensional and integrative treatment strategies. Ayurveda offers a systems-based framework that conceptually aligns with contemporary understandings of central sensitization. The constructs of Vata aggravation, Ama accumulation, and Majjadhatu depletion provide a traditional explanatory model that parallels neural hyperexcitability, neuroinflammation, metabolic dysfunction, and impaired descending inhibition.

Multimodal Ayurvedic interventions including Panchakarma procedures, Rasayana and medhya botanicals, dietary modulation, and mind–body practices—demonstrate biological plausibility through potential effects on autonomic regulation, hypothalamic–pituitary–adrenal axis modulation, oxidative stress reduction, and gut–brain axis signaling. While preliminary clinical and preclinical evidence is encouraging, methodological rigor remains essential to validate efficacy and mechanistic pathways. Future biomarker-driven randomized controlled trials and translational research will be critical for integrating Ayurvedic approaches into evidence-based multidisciplinary care. A scientifically grounded integrative model may ultimately expand therapeutic options and improve quality of life for individuals living with fibromyalgia.

References :-

1. Aguiar, S., & Borowski, T. (2013). Neuro-pharmacological review of the nootropic herb *Bacopamonnieri*. *Rejuvenation Research, 16*(4), 313–326.
2. Albrecht, D. S., MacKie, P. J., Kareken, D. A., et al. (2019). Brain glial activation in fibromyalgia—A multi-site positron emission tomography investigation. *Brain, Behavior, and Immunity, 75*, 72–83.
3. Arnold, L. M., Clauw, D. J., &McCarberg, B. H. (2019).

Improving the recognition and diagnosis of fibromyalgia. *Mayo Clinic Proceedings, 94*(3), 493–505.
4. Clauw, D. J. (2014). Fibromyalgia: A clinical review. *JAMA, 311*(15), 1547–1555.
5. Cramer, H., Lauche, R., Haller, H., et al. (2013). A systematic review and meta-analysis of yoga for fibromyalgia. *Rheumatology, 52*(3), 1–10.
6. Ernst, E. (2002). Toxic heavy metals and undeclared drugs in Asian herbal medicines. *Trends in Pharmacological Sciences, 23*(3), 136–139.
7. Farooqui, T., Farooqui, A. A., & Madan, A. (2022). *Centellaasiatica* and its neuroprotective effects: A systematic review. *Phytotherapy Research, 36*(4), 1525–1542.
8. Field, T. (2016). Massage therapy research review. *Complementary Therapies in Clinical Practice, 24*, 19–31.
9. Fitzcharles, M. A., Cohen, S. P., Clauw, D. J., et al. (2023). Nociplastic pain and central sensitization: An update. *The Lancet Rheumatology, 5*(2), e102–e112.
10. Gray, N. E., Alcazar Magana, A., Lak, P., et al. (2018). *Centellaasiatica* phytochemicals enhance neuronal plasticity and BDNF expression. *Scientific Reports, 8*, 10468.
11. Häuser, W., Ablin, J., Fitzcharles, M. A., et al. (2015). Fibromyalgia. *Nature Reviews Disease Primers, 1*, 15022.
12. Häuser, W., Bernardy, K., Arnold, B., Offenbächer, M., &Schiltenwolf, M. (2010). Efficacy of multicomponent treatment in fibromyalgia: A meta-analysis of randomized controlled trials. *Arthritis Care & Research, 62*(10), 1367–1376.
13. Ji, R. R., Donnelly, C. R., &Nedergaard, M. (2018). Astrocytes in chronic pain and itch. *Nature Reviews Neuroscience, 20*(11), 667–685.
14. Kongkeaw, C., Dilokthornsakul, P., Thanarangsarit, P., et al. (2014). Meta-analysis of randomized controlled trials on cognitive effects of *Bacopamonnieri*. *Journal of Ethnopharmacology, 151*(1), 528–535.
15. Latremoliere, A., & Woolf, C. J. (2009). Central sensitization: A generator of pain hypersensitivity. *Journal of Pain, 10*(9), 895–926.
16. Lopresti, A. L., Smith, S. J., Malvi, H., &Kodgule, R. (2019). An investigation into the stress-relieving and pharmacological actions of an ashwagandha extract: A randomized, double-blind, placebo-controlled study. *Medicine, 98*(37), e17186.
17. Martínez-Lavín, M. (2021). Fibromyalgia and stress: The hypothalamic- pituitary - adrenal axis revisited. Current Rheumatology Reports, 23(5), 34.
18. Michalsen, A., Jeitler, M., Brunnhuber, S., et al. (2013). Additive complex Ayurvedic treatment in patients with fibromyalgia syndrome compared to conventional standard care alone: A nonrandomized controlled clinical pilot study (KAFA trial). *Evidence-Based Complementary and Alternative Medicine, 2013*, 751403.
19. Minerbi, A., Gonzalez, E., Brereton, N. J. B., et al. (2019). Altered microbiome composition in individuals with fibromyalgia. *Pain, 160*(11), 2589–2602.
20. Nahata, A., Patil, U. K., & Dixit, V. K. (2010). Anxiolytic activity of *Convolvulus pluricaulis* in rodents. *Pharmacology Biochemistry and Behavior, 95*(1), 100–106.
21. Peth-Nui, T., Wattanathorn, J., Muchimapura, S., et al. (2012). Effects of 12-week Bacopamonnieri supplementation on attention and cognitive processing. *Evidence-Based Complementary and Alternative Medicine, 2012*, 606424.
22. Rao, R. M., Nagendra, H. R., Raghuram, N., Vinay, C., Chandrashekara, S., &Gopinath, K. S. (2017). Influence of Shirodhara on stress and sleep parameters: A pilot study. *Journal of Ayurveda and Integrative Medicine, 8*(3), 160–164.
23. Rasmussen, L. B., et al. (2012). Treatment of fibromyalgia at the Maharishi Ayurveda Health Centre: A pilot study. *Clinical Rheumatology, 31*(4), 673–679.
24. Salve, J., Pate, S., Debnath, K., &Langade, D. (2019). Adaptogenic and anxiolytic effects of ashwagandha root extract in healthy adults: A randomized, double-blind, placebo-controlled clinical study. *Cureus, 11*(12), e6466.
25. Saper, R. B., Phillips, R. S., Sehgal, A., et al. (2008). Lead, mercury, and arsenic in U.S.- and Indian-manufactured Ayurvedic medicines sold via the Internet. *JAMA, 300*(8), 915–923.
26. Sharma, P. V., & Dash, B. (2018). *Charaka Samhita* (English translation). ChaukhambhaOrientalia.
27. Singh, N., Bhalla, M., de Jager, P., &Gilca, M. (2023). An overview on ashwagandha: A Rasayana (rejuvenator) of Ayurveda. *Journal of Ethnopharmacology, 308*, 116276.
28. Sluka, K. A., &Clauw, D. J. (2016). Neurobiology of fibromyalgia and chronic widespread pain. *Neuroscience, 338*, 114–129.
29. Woolf, C. J. (2011). Central sensitization: Implications for the diagnosis and treatment of pain. *Pain, 152*(3 Suppl), S2–S15.
30. Zeidan, F., Grant, J. A., Brown, C. A., McHaffie, J. G., & Coghill, R. C. (2012). Mindfulness meditation-related pain relief: Evidence for unique brain mechanisms. *Journal of Neuroscience, 32*(11), 3819–3828.

****