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The Impact of Rasayana Therapy on Cell-Mediated Immunity in Functional Gastrointestinal Disorders

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Abstract

Gastrointestinal disorders (FGIDs) affecting up to 40% of individuals, characterized by chronic digestive symptoms without clear structural causes. *Rasayana* therapy from Ayurvedic medicine is explored as a novel strategy for enhancing cell-mediated immunity and managing FGIDs. The literature search focused on Rasayana therapy's impact on gastrointestinal health and disease prevention, integrating clinical trials and experimental studies. Rasayana formulations like *Chyawanprash* and *Ashwagandha* demonstrate significant immunomodulatory effects, activating immune cells and balancing cytokines to support immune homeostasis in the gastrointestinal tract. These formulations also possess antioxidant properties crucial for gut health and immune function. Clinical studies provide strong evidence of Rasayana therapy's efficacy in improving immune responses and managing FGIDs.

This review highlights *Rasayana* therapy's potential as an adjunctive or complementary treatment for FGIDs, emphasizing its ability to target immune dysregulation and improve patient outcomes. Further research is recommended to elucidate *Rasayana* therapy's mechanisms and optimize therapeutic strategies for FGIDs.

ISSN PRINT 2319 1775 Online 2320 7876

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Keyword: Functional gastrointestinal disorders, Rasayana, Cell-mediated immunity.

सारांश

पाचन तंत्रिका विकार (FGIDs) जो लंबे समय तक पेटीय लक्षणों के साथ 40% लोगों को प्रभावित करते हैं और जिनका कोई स्पष्ट संरचनात्मक कारण नहीं होता। अयुर्वेदिक चिकित्सा से रसायन चिकित्सा को एक नया रणनीति के रूप में खोजा गया है जो सेल-माध्यमिक प्रतिरक्षण को बढ़ावा देने और FGIDs का प्रबंधन करने के लिए उत्कृष्ट है। पुस्तक संदर्भ में रसायन चिकित्सा के प्रभाव का अध्ययन रसायन चिकित्सा का प्रभाव जो जीआई स्वास्थ्य और रोग निवारण पर होता है, केंद्रित किया गया है, क्लिनिकल ट्रायल्स और प्रयोगशालात्मक अध्ययनों को समाहित किया गया है। रसायन योजनाएं जैसे कि च्यावनप्राश और अश्वगंधा में महत्वपूर्ण प्रतिरक्षण प्रभावों का परीक्षण करते हुए, इम्यून सेलों को सक्रिय करने और साइटोकाइंस का संतुलन करके पेटीय तंत्रिका में इम्यून संतुलन को समर्थन करने के लिए उत्कृष्ट हैं। ये योजनाएं पेटीय स्वास्थ्य के लिए महत्वपूर्ण एंटीऑक्सीडेंट गुणों को पोसेस करती हैं और इम्यून कार्य को समर्थन करती हैं। क्लिनिकल अध्ययनों में रसायन चिकित्सा के प्रभाव के प्रमाण मिलते हैं और FGIDs का प्रबंधन करने के लिए रसायन चिकित्सा की अनुप्रयुक्तता को जोर देते हैं। आगे के अनुसंधान में रसायन चिकित्सा के तंत्रों को स्पष्ट करने के लिए और FGIDs के लिए उत्तम चिकित्सा योजनाएं बनाने की सलाह दी गई है ।

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INTRODUCTION

Gastrointestinal symptoms affect up to 40% of the population, with many diagnosed with functional gastrointestinal disorders (FGIDs) like irritable bowel syndrome, functional dyspepsia, or functional constipation when no organic cause is identified. [1] FGIDs involve chronic, fluctuating gastrointestinal symptoms without clear structural or biochemical explanations. The complex pathophysiology includes gut-brain axis dysregulation, microbial dysbiosis, altered mucosal immunity, visceral hypersensitivity, and abnormal motility.[2]

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11 ,Iss 13, 2022

Emerging evidence suggests that dysregulation of the mucosal immune system plays a key role in the pathogenesis of FGIDs.[3]Alterations in gut-associated lymphoid tissue (GALT) function, including changes in T cell populations and cytokine profiles, have been observed in FGID patients[4] Enhancing cell-mediated immunity, particularly T cell function, may be a promising therapeutic approach for managing FGIDs and preventing disease progression.[5] Modulating the GALT and restoring immune homeostasis could help alleviate gastrointestinal symptoms and improve patient outcomes.

Rasayana therapy, a concept from Ayurvedic medicine, may offer a novel approach to boosting cell-mediated immunity and managing FGIDs. *Rasayana* herbs and formulations are believed to have potent immunomodulatory properties, making them a rational target for investigation in the context of FGIDs. [6],[7]

MATERIALS & METHODS

For this review article, the literature search strategy involved comprehensive searches on PubMed, Scopus, and Web of Science using keywords pertaining to *Rasayana* therapy and immunomodulation in functional gastrointestinal disorders. We focused on including studies that assessed *Rasayana* therapy's impact on cell-mediated immunity in gastrointestinal health and disease prevention, encompassing both clinical trials and experimental studies. Non-English publications and studies not directly related to our topic were excluded from consideration. The selection process involved initial screening of titles and abstracts to identify relevant studies, followed by full-text review against our inclusion and exclusion criteria. Two reviewers independently conducted this process, resolving any discrepancies through discussion or consultation with a third reviewer. Data extraction encompassed study characteristics, participant demographics, *Rasayana* formulations used, immunomodulatory outcomes, and key findings related to cell-mediated immunity in gastrointestinal disorders. We utilized qualitative synthesis and thematic analysis to summarize the immunomodulatory mechanisms of *Rasayana* therapy, ensuring a comprehensive and systematic approach to data extraction and analysis.

ENHANCING CELL-MEDIATED IMMUNITY AND GUT HEALTH THROUGH RASAYANA THERAPY

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Research paper UGC CARE Listed (Group -I) Journal Volume 11 ,Iss 13, 2022

Rasayana therapy operates at a cellular level, boosting immune cell activity and genetic communication within our bodies. It acts like a skilled coach, enhancing immune cells' performance in maintaining gut health and responding effectively to challenges. Specific formulations like *Ashwagandha* play a significant role in activating immune cells such as macrophages, natural killer (NK) cells, and T lymphocytes. They also balance pro-inflammatory and anti-inflammatory cytokines, promoting immune homeostasis within the gastrointestinal tract and supporting overall gut health [8]. Rasayana therapy strengthens antioxidant defenses, scavenging free radicals and reducing oxidative stress, crucial for maintaining a healthy gut microbiota composition and optimal immune responses. *Rasayana* herbs like *Ashwagandha, Guduchi* and *Shatavari* possess adaptogenic properties, aiding in stress adaptation and indirectly supporting immune function and resilience in gastrointestinal disorders. [9] Scientific validation underscores Ashwagandha's specific immunomodulatory mechanisms, validating its role in immune homeostasis and disease prevention within the gastrointestinal system. This comprehensive approach offers a promising avenue for enhancing cell-mediated immunity and preventing gastrointestinal disorders, making *Rasayana* therapy a valuable component of integrative healthcare strategies.

Rasayana therapy exerts its immunomodulatory effects through several key mechanisms. These include the activation of cellular immune responses, modulation of cytokine balance, antioxidant defence and gut health support, and stress adaptation for improved immune function and resilience. Specific Rasayana herbs like *Ashwagandha* (*Withania Somnifera s*) have been studied extensively for their ability to stimulate immune cell activity, regulate cytokine production, and enhance immune surveillance. Experimental studies have provided mechanistic insights into these actions, demonstrating the impact of Rasayana formulations on immune cell signalling pathways, antioxidant activities, and stress adaptation mechanisms.

Activation of Cellular Immune Responses

Rasayana formulations like *Chyawanprash* and *Ashwagandha* (*Withania Somnifera*) are known for their ability to activate cellular immune responses. These formulations contain bioactive compounds that stimulate the activity of immune cells such as macrophages, natural killer (NK) cells, and T lymphocytes, thereby fortifying the body's defence against gastrointestinal pathogens and immune dysregulation[10].

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11 ,Iss 13, 2022

Tinospora cordifolia's immunomodulatory potential through the isolation and characterization of seven active compounds, including known immunomodulators like cordifolioside A and syringin, alongside novel compounds such as 11-hydroxymustakone and N-methyl-2-pyrrolidone. These compounds significantly enhance phagocytic activity and nitric oxide/reactive oxygen species generation, suggesting a synergistic effect on cell-mediated immunity. Incorporating Tinospora cordifolia or its active compounds into Rasayana therapy could offer therapeutic benefits for enhancing immune function in functional gastrointestinal disorders [11].

Modulation of Cytokine Balance

One of the key mechanisms of Rasayana therapy is its role in modulating the balance of cytokines involved in immune regulation. By regulating pro-inflammatory and anti-inflammatory cytokines, *Rasayanas* promote immune homeostasis within the gastrointestinal tract, mitigating inflammation and supporting immune cell function. [12]

Antioxidant Defence and Gut Health

Rasayana formulations are rich in antioxidants that play a vital role in maintaining gut health and supporting immune function. These antioxidants scavenge free radicals, reduce oxidative stress, and promote a healthy gut microbiota composition, which is crucial for optimal immune responses in gastrointestinal disorders. [13]

Stress Adaptation and Immune Function

Chronic stress is known to affect immune function, particularly in the gastrointestinal system. Rasayana herbs such as *Ashwagandha* and *Shatavari* (*Asparagus racemosus*) possess adaptogenic properties that help the body adapt to stressors, thereby indirectly supporting immune function and resilience in gastrointestinal disorders. [14]

Immunomodulatory Actions of Specific Rasayana Herbs

Ashwagandha (*Withania Somnifera*) exhibits its immunomodulatory effects through scientifically validated mechanisms. Studies have shown that *Ashwagandha* stimulates the activity of immune cells such as macrophages, natural killer (NK) cells, and T lymphocytes, enhancing their phagocytic activity, cytokine production, and antigen-presenting capabilities [15][16]. This leads to a stronger immune response against pathogens and promotes immune surveillance. Additionally, bioactive compounds like withanolides and alkaloids in

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Research paper UGC CARE Listed (Group -I) Journal Volume 11 ,Iss 13, 2022

Ashwagandha regulate immune cell signalling pathways, particularly those involved in inflammation and immune regulation. [17][18] These compounds modulate the balance of pro-inflammatory and anti-inflammatory cytokines, promoting immune homeostasis and reducing excessive inflammation. Furthermore, Ashwagandha's adaptogenic properties have been demonstrated in studies to help the body cope with stress-induced immunosuppression, maintaining optimal immune function [19][20].

Many Clinical studies provide substantial evidence supporting the efficacy of *Rasayana* therapy in enhancing cell-mediated immunity and managing functional gastrointestinal disorders. For instance, a randomized controlled trial by Tharakan et al. (2021) demonstrated significant improvements in immune parameters such as T cell activity and cytokine levels following *Rasayana* treatment.[21] Similarly, Tubaki et al. (2022) conducted a retrospective cohort study showing reduced inflammation and enhanced gut immune function in patients receiving *Rasayana* formulations, which is in line with the broader impact of traditional therapies on immune health observed in their study on liver cirrhosis with ascites.[22] These clinical findings underscore the therapeutic potential of *Rasayana* therapy in improving immune responses and gastrointestinal health Experimental studies offer mechanistic insights into *Rasayana* therapy's immunomodulatory effects. For example, Trivedi et al. (2016) demonstrated the impact of biofield energy treated herbomineral formulations on modulating pro-inflammatory cytokines using mouse dendritic and splenocyte cells, showcasing innovative approaches in immune modulation. [23] Similarly, Trivedi et al. (2017) characterized the immunomodulatory properties of a novel *Withania Somnifera* based formulation supplemented with minerals in rats, providing insights into biomarkers and properties enhancing immune function. [24] Additionally, Chahar et al. (2012) observed in vivo antioxidant and immunomodulatory activities of mesuol from Mesua ferrea L. seed oil, contributing to the understanding of natural compounds' immunomodulatory potential. [25]

FGIDs encompass a range of chronic conditions affecting the gastrointestinal tract, characterized by symptoms such as abdominal pain, bloating, and altered bowel habits. The aetiology of FGIDs is multifactorial, involving complex interactions between genetic, environmental, and psychosocial factors. Recent research has highlighted the role of immune dysregulation in the pathogenesis of FGIDs, specifically implicating alterations in the mucosal immune system and gut-associated lymphoid tissue (GALT) function. The immunomodulatory effects of Rasayana therapy, rooted in Ayurvedic medicine, offer a promising avenue for addressing immune dysregulation in FGIDs. Rasayana herbs and formulations are known for

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Research paper UGC CARE Listed (Group -I) Journal Volume 11 ,Iss 13, 2022

their ability to modulate immune responses, enhance cell-mediated immunity, and promote immune homeostasis. By targeting key components of the immune system, Rasayana therapy may exert beneficial effects in alleviating gastrointestinal symptoms and improving overall gut health. The therapeutic potential of Rasayana therapy in managing FGIDs extends beyond symptom management to disease prevention and long-term therapeutic strategies. Enhancing cell-mediated immunity, particularly the function of T cells and immune cell activity within the gastrointestinal mucosa, presents a targeted approach to addressing the underlying immune dysregulation associated with FGIDs. This not only provides symptomatic relief but also addresses the root cause of immune-mediated gastrointestinal disorders.

Thus, *Rasayana* therapy's immunomodulatory effects may complement existing therapeutic strategies, including lifestyle modifications, dietary interventions, and pharmacological treatments. Integrating Rasayana therapy into comprehensive treatment plans for FGIDs could optimize patient outcomes and reduce the reliance on symptomatic management alone.

Limitations of Current Evidence

Despite the promising evidence supporting the immunomodulatory effects of *Rasayana* therapy in FGIDs, several limitations exist within the current body of literature. These limitations include the heterogeneity of *Rasayana* formulations used across studies, variations in study designs, and the relatively small sample sizes in some clinical trials. Additionally, most studies focus on short-term outcomes, necessitating long-term follow-up studies to evaluate the sustained benefits of Rasayana therapy in FGID management. Standardization of Rasayana formulations, rigorous study designs incorporating placebo controls and blinding, and multicentre trials involving diverse patient populations are essential steps to overcome these limitations and strengthen the evidence base for Rasayana therapy in FGIDs.

Future Research Directions

Future research in *Rasayana* therapy and FGIDs should prioritize several key areas to advance our understanding and clinical application of this therapeutic approach. Firstly, investigating the mechanisms of action underlying *Rasayana* therapy's immunomodulatory effects within the gastrointestinal tract, including its impact on immune cell signalling

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11 ,Iss 13, 2022

pathways, cytokine profiles, and gut microbiota interactions, is crucial. Furthermore, long-term prospective studies assessing the efficacy of *Rasayana* therapy in preventing disease progression, reducing symptom severity, and improving quality of life in FGID patients are warranted. Comparative studies evaluating the effectiveness of different *Rasayana* formulations, dosage regimens, and administration routes can provide valuable insights into optimizing therapeutic strategies.

DISCUSSION

The review of *Rasayana* therapy's impact on FGIDs reveals promising avenues for immune modulation and disease management. Key findings from clinical and experimental studies indicate that Rasayana formulations effectively enhance cell-mediated immunity by activating immune cells and modulating cytokine balance. These formulations also exhibit antioxidant properties that contribute to gut health, support immune function, and protect against gastrointestinal pathogens. Furthermore, Rasayana herbs with adaptogenic qualities aid in stress adaptation, indirectly bolstering immune resilience in FGIDs, where chronic stress can impact immune responses negatively.

CONCLUSION

Clinical practice recommendations stemming from this evidence emphasize the incorporation of Rasayana therapy as adjunctive or complementary treatment for FGIDs. Tailoring Rasayana formulations based on individual immune profiles and disease severity can optimize therapeutic outcomes. Long-term management strategies should focus on integrating Rasayana therapy with lifestyle modifications and dietary interventions to promote sustained immune health and address the chronic nature of FGIDs. Overall, the scientific validation of Rasayana herbs' immunomodulatory mechanisms and their efficacy in clinical settings underscore their potential in comprehensive patient care for FGIDs, signalling a hopeful direction for future research and therapeutic interventions.

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ISSN PRINT 2319 1775 Online 2320 7876

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ISSN PRINT 2319 1775 Online 2320 7876

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