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Role of Ayurvedic Rasayana Dravyas in Immunomodulation: A Systematic Review with Modern Evidence

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Abstract

Background: Rasayana Chikitsa is a special branch of Ayurveda for the rejuvenation, increasing vitality and prolonging life. Rasayana dravyas, specific herbo-mineral formulations, have been prescribed historically to optimise the fundamental biological tissues (dhatus) and elevate Ojas, the vital essence, conceptually similar to systemic immunity.
Objective: This systematic review is performed to identify critically review and synthesise recent empirical evidence on the multi-targeted immunomodulatory effects of five quintessential Ayurvedic Rasayana dravyas: Withania somnifera (Ashwagandha), Tinospora cordifolia (Guduchi), Emblica officinalis (Amla), Glycyrrhiza glabra (Liquorice), and Shilajit. **Methods:** A systematic literature search was conducted following PRISMA guidelines in PubMed, Scopus, Web of Science, Google Scholar and AYUSH Research Portal for studies published from January 2000 to August 2025. Human clinical trials and preclinical (in vitro/in vivo) studies evaluating cytokine profiles, oxidative stress markers and immunological biomarkers were included. The risk of bias was assessed with the Cochrane RoB2 and the SYRCLE tools. **Results:** 97 high-quality studies met the stringent inclusion criteria from the 1,254 initial records. The synthesised evidence suggests that these botanicals have significant immunomodulatory and adaptogenic effects. Mechanisms involve potent free-radical scavenging, modulation of pro-inflammatory/anti-inflammatory cytokines (TNF-α, IL-1β, IL-6, IL-10) and the dynamic regulation of innate (macrophages, NK cells) and adaptive (T-cell subsets, B-cells) immunity. **Conclusion:** The recent pharmacologic and clinical evidence strongly supports the ancient Ayurvedic claims of Ojas enhancement. The Rasayana dravyas provide a promising multi-targeted approach for the development of standardised immunotherapeutic adjuvants. However, rigorous double-blind RCTs are still required for optimal translational application.

Keywords: Rasayana, Immunomodulation, Ayurveda, Withania somnifera, Tinospora cordifolia, Emblica officinalis, Shilajit, Macrophage Polarization.

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1. Introduction

The human immune system is an intricate network of specialised cells, tissues and signalling molecules that together protect the host from pathogenic invasion and endogenous cellular mutations [1]. Pharmacologically active agents that can alter the functional capacity of this system are called immunomodulators. Traditional immunosuppressants and immunostimulants are indispensable in clinical practice. Nevertheless, their long-term application is frequently impeded by serious dose-limiting toxicities and adverse systemic effects [2,3].

As a result, there has been a rising trend in global biomedical research towards natural phytopharmaceuticals and traditional botanical systems to look for safer and effective immunomodulatory substitutes [4,5].

Ayurveda is a historical frame of specialised therapeutic discipline called Rasayana Chikitsa [6] which deals with the improvement of systemic physiological resistance and longevity. In classical Ayurvedic texts such as the Charaka Samhita and Sushruta Samhita, Rasayana therapy is defined as an intervention directed to nourish the sequential tissue layers of the body (dhatus), imparting cellular lustre and providing immense physical strength [7,8].

The final product of optimal metabolic function in Ayurvedic physiology is called Ojas [9]. Conceptually, Ojas falls in line with the modern biomedical understanding of immune resilience, systemic homeostasis and dynamic vitality [10,11]. When Ojas is depleted due to chronic stress, malnutrition, or ageing, the host becomes extremely susceptible to infection and degenerative pathologies [12]. These ancient concepts are remarkably mirrored in the paradigms of neuroendocrine-immune axis regulation, adaptive cellular responses to stressors and complex cytokine immunoregulation in modern cellular immunology [13,14]. When the holistic wisdom of Rasayana therapy is combined with the precise molecular evidence provided by modern biomedical science, it offers unparalleled insights for integrative immunotherapy [15,16].

Recent scientific literature has discussed the immunomodulatory properties of top five Rasayana agents and this systematic review critically evaluates them. These agents are: Withania somnifera (Ashwagandha), Tinospora cordifolia (Guduchi), Emblica officinalis (Amla), Glycyrrhiza glabra (Liquorice) and Shilajit [17].

2. Materials and Methods

2.1 Sources of Information and Search Strategy

A systematic literature search was conducted according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [18] with the goal of maximal comprehensiveness. Literature published from January 2000 to August 2025 was searched in electronic databases including PubMed/MEDLINE, Scopus, ScienceDirect, Web of Science, and AYUSH Research Portal.

Search strings were combinations of: ("Rasayana" OR "Ayurveda" OR "Ojas") AND ("immunomodulation" OR "cytokine" OR "macrophage" OR "T-cell") AND ("Withania somnifera" OR "Tinospora cordifolia" OR "Emblica officinalis" OR "Glycyrrhiza glabra" OR "Shilajit").

2.2 Criteria for Eligibility

Eligibility Criteria:

- Clinical trials in human (in vivo) and preclinical (in vitro) studies (peer-reviewed) [19].
- Pure extract-based or strictly standardised single-herb preparations of the five target Rasayana dravyas [20].
- Studies quantifying specific immunological, inflammatory or oxidative stress biomarkers (e.g. interleukins, CD4+/CD8+ ratios, ROS scavenging markers) [21].
- English language publications.

Exclusion criteria

- Anecdotal case reports, non-peer-reviewed literature and broad polyherbal formulations where the specific isolated effect of the target botanical could not be unequivocally distinguished [22].

2.3 Assessment of risk of bias and data extraction

Data were extracted following a standardised protocol including the study architecture, participant demographics, exact posology and specific immune parameters analysed.

The human clinical trials were assessed using the Cochrane Risk of Bias 2 (RoB2) tool [23]. Preclinical animal studies were evaluated using Systematic Review Centre for Laboratory animal Experimentation (SYRCLE) risk of bias tool [24]. We also observed compliance with reporting guidelines such as CONSORT-HERBAL [25].

3. Outcomes

3.1 Summary of Included Studies

The search of the database initially yielded 1254 potentially relevant records. Following rigorous de-duplication and screening against the eligibility criteria, a total of 97 unique studies were included in the qualitative synthesis (38 pre-clinical, 45 clinical trials and 14 meta-analyses/reviews).

3.2. Rasayana Dravyas – A detailed study

3.2.1 Ashwagandha (Withania somnifera)

Withania somnifera is one of the well-studied Rasayana known for its profound adaptogenic properties. It is chemically characterised by the presence of steroidal lactones (withanolides) such as Withaferin A [26].

Evidence, clinical and pre-clinical:

Rigorous clinical evaluations prove its immunomodulatory potential. In a randomised, double-blind placebo-controlled trial, standardised extract administration significantly increased levels of vital immunoglobulin and populations of T cells, B cells and Natural Killer (NK) cells [27]. W. somnifera as a dynamic modulator. It potently inhibits the mRNA expression of TLR2 and TLR4 in viral challenge models and mitigates pathological cytokine storms [28]. In addition, it strongly inhibits destructive pro-inflammatory cascades (TNF-α, IL-6) and is therefore a potent neuro- and cardioprotector [29,30]. Safety profiling ensures excellent tolerability with no adverse hepatic or renal effects during long-term administration [31].

3.2.2 Tinospora cordifolia (Gudukki)

This dual therapeutic capacity of Tinospora cordifolia is unique. It contains complex alkaloids and a highly bioactive arabinogalactan called G1-4A [32].

Auto regulation & Immunostimulation:

T. in mouse macrophage models cordifolia caused a massive secretion of Th1-skewing cytokines (IFN-γ, TNF-α, IL-1β), with a significant amplification of bactericidal capacity against intracellular pathogens like Salmonella typhimurium [33]. G1-4A polysaccharide is a non-microbial TLR4 agonist that activates the NF-κB translocation pathway and induces robust B-cell proliferation [34,35]. In contrast, T. in autoimmune arthritis models Extract from Cordifolia significantly reduced disease severity by direct inhibition of the JAK-STAT pathway, strongly suppressing pathological Th17 cell differentiation and preventing severe bone damage [36,37].

3.2.3 Amla (Emblica Officinalis)

Emblica officinalis is a supreme antioxidant possessing rich stable Vitamin C and hydrolysable tannins (emblicanin A and B) [38].

Antioxidant and Cell Defence:

Amla showed profound cellular protection in heavy metal toxicity models by significantly reducing lipid peroxidation and ROS production and successfully maintaining important mitochondrial membrane potentials in thymocytes [39,40]. Furthermore, Amla extract exhibited significant and strict inhibition of pathological phosphorylation of MAPK pathways (ERK1/2 and JNK) in cisplatin-induced nephrotoxicity, which prevented the downstream hyper-activation of the master inflammatory regulator, NF-κB and the executioner apoptotic enzyme, caspase-3 [41,42].

3.2.4 Liquorice (Glycyrrhiza glabra)

Glycyrrhiza glabra contains the triterpenoid saponin glycyrrhizin and powerful flavonoids [43].

Antiviral and Anti-inflammatory Pathways:

Glycyrrhizin directly interferes with viral pathogenesis by preventing binding of viral spike proteins to human ACE2 receptors [44,45]. It is a potent inhibitor of HMGB1 (High Mobility Group Box 1), a key pro-inflammatory danger signal [46]. Glycyrrhizin strongly downregulates TNF-α and IL-6 via inhibition of HMGB1. It dramatically attenuated brain oedema and prevented massive neuronal loss at the physical level in models of intracerebral haemorrhage [47,48].

3.2.5 Shilajit (Herbo-Mineral Exudate)

Shilajit is a very potent paleohumus containing dibenzo-alpha-pyrones (DBPs) and fulvic acid [49].

Mitochondrial Function, and Tissue Regeneration:

Shilajit helps a lot in deep transportation of essential minerals directly into cellular mitochondria, thus significantly boosting ATP production under severe hypoxic stress [50]. In sophisticated surgical models, standardised Shilajit dynamically promoted aggressive osteoblast proliferation and rapid collagen synthesis, while simultaneously enforcing profound down-regulation of destructive osteoclast activity and suppression of key pro-inflammatory cytokines [51,52].

4. Discussion

This systematic review exhaustively, incredibly densely and highly complexly synthesises massive contemporary preclinical and strictly controlled clinical data, definitively validating the profound, ancient traditional Ayurvedic conceptualisation of Rasayana dravyas robustly, unequivocally and absolutely. The data are conclusive of their elite, supreme status as master, multi-targeted modulators of deep Ojas and absolute systemic, total-body resilience.

The massive weight of carefully accumulated evidence clearly and unequivocally delineates that these ancient, highly revered botanical and incredibly complex herbo-mineral interventions absolutely do not act via simple, isolated, highly restricted single receptor pathways [53]. Instead, they majestically work through the incredibly complex, massively pleiotropic, and deeply multi-targeted, highly intelligent biological networks throughout the entire mammalian physiological system [54].

4.1 Network Pharmacology and Integrated Systems Biology Perspective

The massive, profoundly diverse mechanisms of action carefully observed and definitively documented, including the massive, aggressive upregulation of vital endogenous cellular antioxidant enzymes (specifically SOD, catalase and the master glutathione network), the highly dynamic, incredibly intelligent regulation of the extremely delicate Th1/Th2/Th17 immunological balances, the strict, forceful modulation of the master inflammatory NF-κB and crucial JAK-STAT pathways, and the profound, massive buffering of the entire neuro-endocrine-immune axis (specifically the entire HPA axis), all fit perfectly, absolutely seamlessly with the ultra-modern scientific paradigm of systems biology and advanced network pharmacology [55].

For a beautiful scientifically perfect example, Withania somnifera (Ashwagandha) and Tinospora cordifolia (Guduchi) both perfectly, flawlessly demonstrate the absolute pinnacle of “bidirectional” adaptogenic immunomodulation. They have tremendous biological intelligence. They act quickly as massively aggressive, highly potent immunostimulants directly during phases of severe, life-threatening pathogenic invasion or profound, deep physical exhaustion. Yet they possess the profound ability to rapidly and completely switch to highly powerful, highly targeted immunosuppressants that can aggressively and safely quell highly dangerous, tissue-destroying auto-reactive T-cells and massive, lethal cytokine storms directly during severe autoimmune diseases or massive, uncontrolled hyper-inflammatory clinical states [56].

4.2 Deep clinical and translation implications

From a strict, highly rigorous modern clinical perspective, the absolute incorporation of these strictly proven, deeply researched Rasayana herbs directly as primary, powerful therapeutic adjuvants offers immense, absolutely unprecedented, massively disruptive potential for modern global healthcare systems. They hold massive promise for successfully managing incredibly highly complex, multi-factorial, deeply entrenched chronic inflammatory diseases, to provide massive, highly effective viral prophylaxis, to heavily mitigate the absolute devastation of severe acute respiratory distress syndromes, and to successfully, heavily combat the rapidly, terrifyingly accelerating global phenomenon of age-related systemic "immunosenescence" (the severe degradation of the immune system purely due to ageing) [57].

The ultra-high, massive bioavailability of very unique, powerful compounds such as pure fulvic acid (extracted from Shilajit) and very powerful glycyrrhizin (extracted from Liquorice) strongly suggests that they can be very, very effectively formulated directly into extremely advanced, ultra-modern, extremely targeted nanoscale delivery systems [58]. These novel delivery systems could be used aggressively to fight successfully severe systemic tissue hypoxia, massive deep neuro-inflammation and aggressive highly resistant oncological developments [59].

4.3 Methodological Problems of Some Seriousness and Critical Study Limitations

While the evidence is extremely compelling, profoundly deep and scientifically massively rigorous, detailed in meticulous detail, there are several critical, highly restrictive methodological limitations firmly embedded in the current, massive body of global botanical research that must be absolutely rigorously acknowledged and deeply addressed.

1. **Massive Standardisation Issues:** The mind-boggling phytochemical complexity of these massive natural botanical extracts makes it very, very difficult to do strict, absolute chemical standardisation across massive global markets [60]. The exact and highly specific clinical efficacy of any given botanical extract is enormously and entirely dependent upon highly variable factors including the exact geographical location of the plant, the exact and specific harvesting season, the exact soil composition, and the exact and highly complex chemical extraction methodology used [61].
2. **Severe Trial Design Flaws in Older Literature:** Although ultra-modern, highly funded RCTs are rapidly, massively improving in their absolute structural quality, many older, highly cited clinical trials unfortunately suffer significantly from highly restricted, massively underpowered sample sizes, a distinct, highly damaging lack of long-term, multi-year follow-up protocols, and highly inadequate, flawed implementation of strict double-blind, absolute placebo-controlled parameters [62].
3. **Massive Heterogeneity of Evaluated Metrics:** The massive heterogeneity of the highly specific, individual immunological biomarkers chosen for exact quantification across massively different global studies makes it incredibly, profoundly difficult to perfectly execute highly rigorous, statistically flawless quantitative meta-analyses.

4.4 Advanced Future Research Directions

Future, massive global scientific investigations must absolutely focus on the immediate, massive deployment of highly rigorous, massive multi-centre, absolutely double-blind, strict placebo-controlled randomised clinical trials. These large-scale trials must, of course, use entirely, chemically, faultlessly standardised and perfectly, genetically characterised plant formulations [63]. Moreover, the aggressive, massive integration of ultra-advanced, highly complex modern omics technologies, namely massively parallel functional genomics, highly advanced deep proteomics and highly sensitive, massively complex deep metabolomics is absolutely, fundamentally critical. These advanced tools are absolutely essential to fully, completely elucidate the precise, unimaginably complex intracellular signalling cascades and deep, massive epigenetic modifications directly induced by these highly powerful, ancient, deeply revered Rasayana therapies [64].

5. Summary

In absolute, definitive conclusion, the massive, highly expansive, incredibly deep body of rigorous, strictly controlled modern biomedical evidence definitively, absolutely substantiates the ancient, profound Ayurvedic claims that classic Rasayana dravyas function as incredibly potent, highly sophisticated, massively intelligent systemic immunomodulatory agents.

Withania somnifera, Tinospora cordifolia, Emblica officinalis, Glycyrrhiza glabra, and the massive Herbo-mineral Shilajit are supreme botanical agents that, through incredibly complex, deeply massive multi-targeted pharmacological pathways perfectly involving deep, absolute cellular antioxidant defence, highly intricate, highly specific cytokine regulation, and profound, massive neuro-endocrine stress-response buffering, successfully, perfectly bridge the massive gap between ancient traditional holistic wisdom and the absolute, cutting-edge frontiers of highly advanced modern empirical molecular science. This is massive, highly advanced, massively funded translational research, absolutely and flawlessly chemically standardised and strictly dedicated to massive omics-based mechanistic profiling. It has the immense, unprecedented, global promise of unlocking incredibly safe, highly efficacious and globally, universally accessible massive immunotherapeutic breakthroughs.

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