2026 Volume: 02 Issue: 09 www.ijrpa.com ISSN 2456-9995 Review Article

International Journal Research Publication Analysis

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EXPLORING THE IMMUNOMODULATORY POTENTIAL OF HOMOEOPATHIC MEDICINE: A REVIEW

Divya N.*[1], Dikxitha M.[1], Sibin R. A.[2]

[1]Interns BHMS Sarada Krishna homoeopathic medical college (affiliated to Tamilnadu Dr,MGR Medical university, chennai), Tamilnadu -629161.

[2]Assistant professor, Department of organon of medicine, Sarada krishna Homeopathic medical college, (affiliated to Dr.MGR medical university, Chennai), Tamilnadu- 629161.

Article Received: 25 July 2026
Article Revised: 14 August 2026
Published on: 03 September 2026

***Corresponding Author: Divya N.**
Interns BHMS Sarada Krishna homoeopathic medical college (affiliated to Tamilnadu Dr,MGR Medical university, chennai), Tamilnadu -629161.

DOI: https://doi-doi.org/101555/ijrpa.8988

ABSTRACT

Background: Immunomodulation maintains immune homeostasis by regulating innate and adaptive responses; dysregulation of immunomodulation contributes to autoimmune and inflammatory diseases. Homoeopathic medicines may influence cytokines, immune cells, inflammation and gene expression.

Objective: To review the evidence on immunomodulatory effects of homoeopathic medicines from experimental, preclinical and clinical studies.

Methods: We conducted a PRISMA 2020-based review of peer-reviewed in vitro, animal and clinical studies that assessed outcomes including cytokines, immune cells, inflammatory markers, antibodies and gene expression.

Results: Evidence suggests possible regulation of cytokines, restoration of Th1/Th2 balance, activation of immune cells and reduction of inflammation and oxidative stress. Animal and in vitro studies showed increased immunity and alterations in inflammatory mediators. Clinical data demonstrated symptomatic and biomarker improvement.

Conclusion: Experimental findings suggest immunomodulatory potential, but robust clinical trials are needed.

KEYWORDS: Homoeopathy; Immunomodulation; Immune system; Cytokines; Autoimmune diseases.

INTRODUCTION

The immune system maintains body defense by distinguishing self from non-self through innate and adaptive immune responses. Innate immunity provides immediate protection, while adaptive immunity involves antigen-specific T and B lymphocyte responses with immune memory. Cytokines and other mediators regulate immune communication and maintain immune balance; disruption of these mechanisms can contribute to immunological disorders [1,2].

Immunomodulation refers to the regulation of immune responses through stimulation or suppression of immune activity by therapeutic agents. Autoimmune diseases result from immune dysregulation leading to attacks against self-tissues and include conditions such as rheumatoid arthritis, Hashimoto's thyroiditis, and systemic lupus erythematosus [3,4].

Recent experimental studies have explored the immunomodulatory potential of homoeopathic medicines, including *Rhus toxicodendron*, *Mercurius solubilis*, *Echinacea*, *Aconitum*, *Lachesis*, *Apis*, and combination preparations such as Canova®, suggesting possible effects on cytokine regulation, immune cell activity, and inflammatory pathways. These findings provide a basis for investigating homoeopathic medicines as potential modulators of immune responses [2].

Understanding immune regulation and identifying therapeutic approaches that can restore immune balance may provide new perspectives in the management of immune-related disorders. Therefore, the immunomodulatory potential of homoeopathic medicines remains an area of ongoing experimental and clinical investigation.

RESEARCH QUESTION

What is the current evidence regarding the immunomodulatory effects of homoeopathic medicines in experimental, preclinical, and clinical studies?

AIM AND OBJECTIVE

AIM

To critically review the available scientific evidence on the immunomodulatory potential of homeopathic medicines and evaluate their possible role in regulating immune responses across autoimmune disorders.

OJECTIVES

- To summarize the current understanding of immunomodulation and its relevance in health and disease.

- To review the published experimental, preclinical, and clinical studies evaluating the immunomodulatory effects of homeopathic medicines.
- To identify the proposed mechanisms through which homeopathic medicines may influence the immune system.
- To assess the quality, strengths, and limitations of the existing evidence.
- To identify research gaps and suggest future directions for high-quality studies on the immunomodulatory potential of homeopathic medicines.

METHODOLOGY

STUDY DESIGN

❖ Review and Analysis

❖ Conducted in accordance with the PRISMA 2020 Statement guidelines.

ELIGIBILITY CRITERIA

Inclusion Criteria

➢ Original research studies evaluating the immunomodulatory effects of homoeopathic medicines - In vitro, animal, and human clinical studies.

➢ Randomized controlled trials, non-randomized clinical studies, cohort studies, case-control studies, and experimental studies.

➢ Studies published in peer-reviewed journals.

➢ Studies reporting immune-related outcomes, such as cytokine levels, immune cell activity, inflammatory markers, antibody responses, or other immunological parameters.

Exclusion Criteria

➢ Studies not evaluating immunomodulatory effects.

➢ Studies lacking sufficient methodological details or outcome data.

Review of experimental studies

IN VIVO STUDY

1) Homeopathic remedies with antineoplastic properties have immunomodulatory effects in experimental animals

This study investigated the immunomodulatory effects of *Thuja occidentalis*, *Carcinosinum*, and *Ruta graveolens* at different potencies in BALB/c mice. The treatments enhanced white blood cell count, bone marrow activity, antibody production, and B- and T-lymphocyte proliferation, with notable effects from *Thuja* and *Ruta*. No toxicity was observed. The study

suggests potential immune-modulating effects of these preparations in mice, but further human studies are required[5].

2) Modulatory action of Bryonia alba on the immune system in cyclophosphamide induced immunosuppression in BALB/c mice.

This study evaluated the immunomodulatory effects of *Bryonia alba* (6C, 30C, and 200C potencies) in cyclophosphamide-induced immunosuppressed BALB/c mice. Treatment with *Bryonia alba* improved hematological parameters (RBC, WBC, and Hb), increased thymus and phagocytic indices, enhanced cytokine levels (IL-2, IL-4, TNF-α, and IFN-γ), and preserved spleen structure. The study suggests that *Bryonia alba* may reduce chemotherapy-induced immune suppression and exhibit immunostimulatory effects in mice[6].

3) A review on immunomodulatory response of homoeopathic medicines through cytokine induction as evidenced in in vivo and in vitro studies.

This review examined the immunomodulatory effects of homoeopathic medicines through cytokine regulation in in vivo and in vitro studies. The findings showed significant modulation of cytokine synthesis in most studies, although research methods varied and the mechanisms involved remain unclear. Further well-designed studies are needed to understand cytokine-mediated effects of homoeopathic medicines[7].

4) Investigation of immunomodulatory effects of Ferrum phosphoricum in normal and immunosuppressed mouse models.

Ferrum phosphoricum 200C demonstrated significant immunomodulatory activity in both normal and cyclophosphamide-induced immunosuppressed mouse models. Treatment enhanced humoral immunity by increasing primary and secondary antibody titers and improved immune function by elevating the spleen index, phagocytic index, and cytokine levels in immunocompromised mice. These findings suggest that Ferrum phosphoricum has the potential to strengthen immune responses and reverse immunosuppression. The study highlights the possible role of homeopathic preparations as immunomodulatory agents and supports further research to explore their mechanisms and therapeutic applications[8].

5) Impact of high-dilution homeopathic remedies on autoimmune disorders.

This review examines the potential role of high-dilution homeopathic remedies in autoimmune disorders, summarizing evidence from in vitro and animal studies that suggests anti-inflammatory, immunomodulatory, and gene-regulatory effects. The findings indicate that these remedies may influence cytokine expression, immune cell activity, and genes involved in immune homeostasis, potentially reducing inflammation and immune dysregulation. Although proposed mechanisms such as solvent structural changes and

nanoscale signaling remain speculative, the review highlights the need for well-designed clinical trials and mechanistic studies to confirm the efficacy, safety, and therapeutic value of high-dilution homeopathic remedies in autoimmune disease management[9].

6) **Apoptosis mediated leishmanicidal activity of Azadirachta indica bioactive fractions is accompanied by Th1 immunostimulatory potential and therapeutic cure in vivo.**

This experimental study investigated the antileishmanial and immunomodulatory effects of bioactive fractions from Azadirachta indica in vitro and in vivo. The extracts demonstrated apoptosis-mediated leishmanicidal activity against Leishmania donovani, reduced parasite burden in infected BALB/c mice, and enhanced Th1-mediated immune responses. The bioactive fractions also showed minimal toxicity to host cells and no significant adverse effects on liver or kidney function. These findings suggest that Azadirachta indica possesses promising antileishmanial and immunostimulatory properties, supporting its potential as a safe therapeutic agent against visceral leishmaniasis[10].

7) The immunomodulatory effects of a commercial antiviral homeopathic compound in C57BL/6 mice, pre and post vaccine challenge

This experimental study evaluated the immunomodulatory effects of the homeopathic antiviral preparation Engystol® in C57BL/6 mice before and after H5N1 vaccine challenge. While Engystol® alone did not significantly alter immune responses, treatment following antigenic challenge modulated immune function by reducing CD4+/CD8+ T-cell ratios, altering cytokine and chemokine profiles, and increasing H5N1-specific IgG antibody titers at the higher dose. These findings suggest that Engystol® may enhance immune responses during antigenic stimulation and has potential immunomodulatory activity following vaccination[11].

IN VITRO STUDY

Cell line studies

This review summarizes experimental in vitro and in vivo studies investigating the effects of homeopathic medicines against bacterial, fungal, and protozoan infections. The evidence suggests that selected homeopathic preparations may modulate host immune responses, reduce pathogen-related damage, and enhance resistance to infections in experimental models. The review concludes that although the findings are promising, further well-designed studies are needed to confirm the mechanisms and clinical relevance of these immunomodulatory effects[12].

2) **Effects of ultra-high dilutions of sodium butyrate on viability and gene expression in HEK 293 cells**

This in vitro study evaluated the effects of ultra-high dilutions (30C and 200C) of sodium butyrate on gene expression in HEK 293 cells. Exposure to the remedies for 48 hours altered the expression of genes associated with the senescence-associated secretory phenotype (SASP), indicating modulation of the cellular transcriptome. These findings support previous experimental evidence suggesting that ultra-high dilution homeopathic preparations may influence gene expression, although further studies are required to clarify the underlying mechanisms and biological significance[13].

3) Homeopathic potencies of Arnica montana L. change gene expression in a Tamm-Horsfall protein-1 cell line in vitro model

This in vitro study investigated the effects of homeopathic potencies of Arnica montana on gene expression in IL-4-treated THP-1 monocyte/macrophage cells. The findings indicated that Arnica montana dilutions altered the expression of genes associated with inflammation, apoptosis, and cellular function. The study also suggested that the ethanol present in the homeopathic dilutions may contribute to these gene expression changes, particularly at potencies ranging from 5C to 15C. These results support further investigation into the mechanisms underlying the biological activity of homeopathic preparations in cell models[14].

REVIEW OF CLINICAL STUDIES

1) Exploring The Efficacy of Homeopathic Treatment in Immunologic Disorders: A Case Series Analysis

This retrospective case series evaluated the potential role of individualized homeopathic treatment in five patients with autoimmune and immunologic disorders, including rheumatoid arthritis, dermatitis, Graves' disease, and mixed connective tissue disease. Clinical outcomes were assessed using symptom improvement and laboratory markers such as rheumatoid factor (RF), antinuclear antibody (ANA), and thyroid antibodies over treatment periods ranging from 24 to 60 months. The authors reported improvements in symptoms, quality of life, and several immune-related biomarkers in the treated patients. However, the study acknowledges important limitations, including its small sample size, lack of a control group, retrospective design, and the possible influence of concurrent treatments. The authors conclude that while the findings suggest homeopathy may have potential as a complementary approach for autoimmune disease management, larger randomized controlled trials are required to establish its safety and effectiveness[15].

2) Homoeopathic intervention in dual autoimmune disorders: A case report on management of vitiligo and hashimoto thyroiditis

This case report describes the homeopathic management of a **57-year-old woman** diagnosed with two coexisting autoimmune disorders: **vitiligo** and **Hashimoto's thyroiditis**. Individualized homeopathic medicines were prescribed based on the patient's constitutional symptoms and clinical evolution. Progress was assessed through clinical examination, serial photographs, and laboratory investigations, including **serum TSH** and **anti-thyroid peroxidase (anti-TPO)** antibody levels. During follow-up, the patient showed improvement in skin depigmentation, thyroid-related symptoms, and laboratory parameters. The authors conclude that individualized homeopathic treatment may have potential in the management of coexisting autoimmune disorders; however, they emphasize that larger, well-designed clinical studies are required to confirm these findings[16].

3) Role of homoeopathic treatment for symptom management and improving quality of life in severe psoriatic disease: A case report

This case report describes the role of individualized homoeopathic treatment in managing symptoms and improving quality of life in a patient with severe psoriatic disease (psoriatic arthritis). A 21-year-old male with a history of psoriasis, joint pain, swelling, and stiffness was treated with individualized homoeopathic medicine Phosphorus and followed for one year. Treatment outcomes were assessed using clinical improvement, the Psoriasis Area and Severity Index (PASI), Psoriatic Arthritis Impact of Disease-12 (PsAID12) questionnaire, and the Modified Naranjo Criteria for Homoeopathy. The report noted improvement in skin lesions, joint symptoms, mobility, and quality-of-life scores after treatment. The authors concluded that individualized homoeopathy showed a positive outcome in this case, while recommending further well-designed studies with larger sample sizes to confirm effectiveness[17]

OBSERVATION

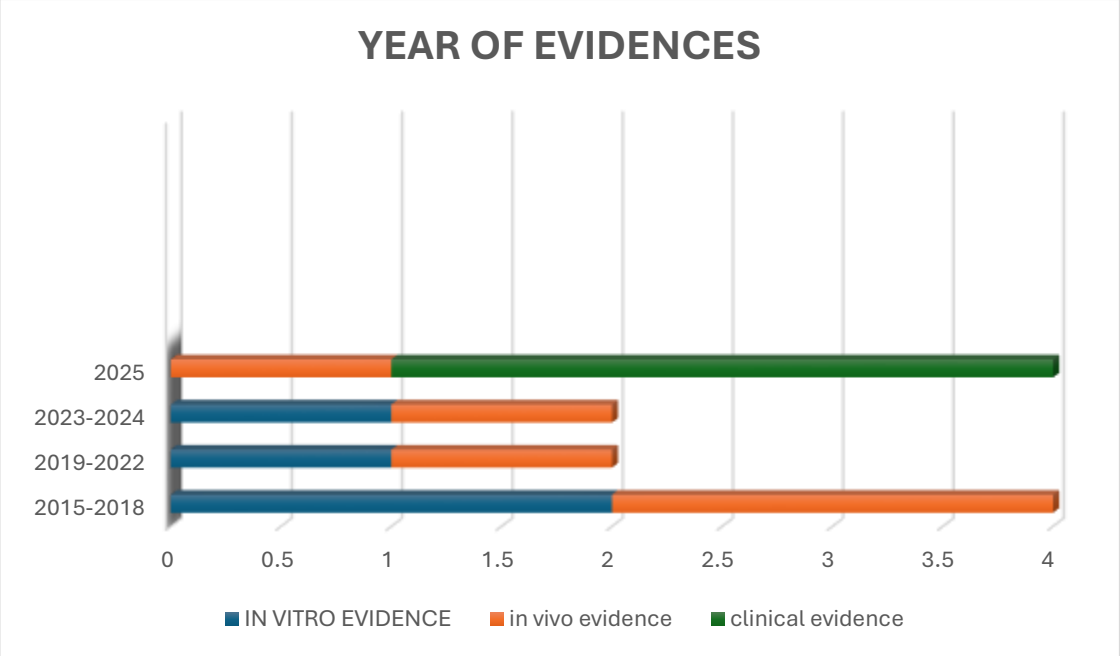
IN VITRO EVIDENCE

S.NO	Study	Model	Main Findings
1.	Olsen, 2017	HEK-293 cell line	Reported changes in gene expression after exposure to ultra-high dilution sodium butyrate
2.	Chirumbolo & Bjørklund, 2017	THP-1 cell model	Observed gene expression changes with Arnica montana potencies; methodological limitations were discussed
3.	Dalpati et al., 2023	Human blood cells	Reported modulation of inflammatory functions and adhesion receptor expression
4.	Bonamin, 2019	Cellular experimental models	Reviewed biological responses in infection-related experimental systems

Qualitative Meta-analysis

The in vitro studies demonstrated three major outcomes:

1. Gene expression modulation
   - Two studies reported alterations in cellular gene activity.
2. Inflammatory regulation
   - Studies involving human blood cells showed possible changes in inflammatory responses.
3. Cellular immune function
   - Experimental models demonstrated biological responses after homoeopathic exposure.

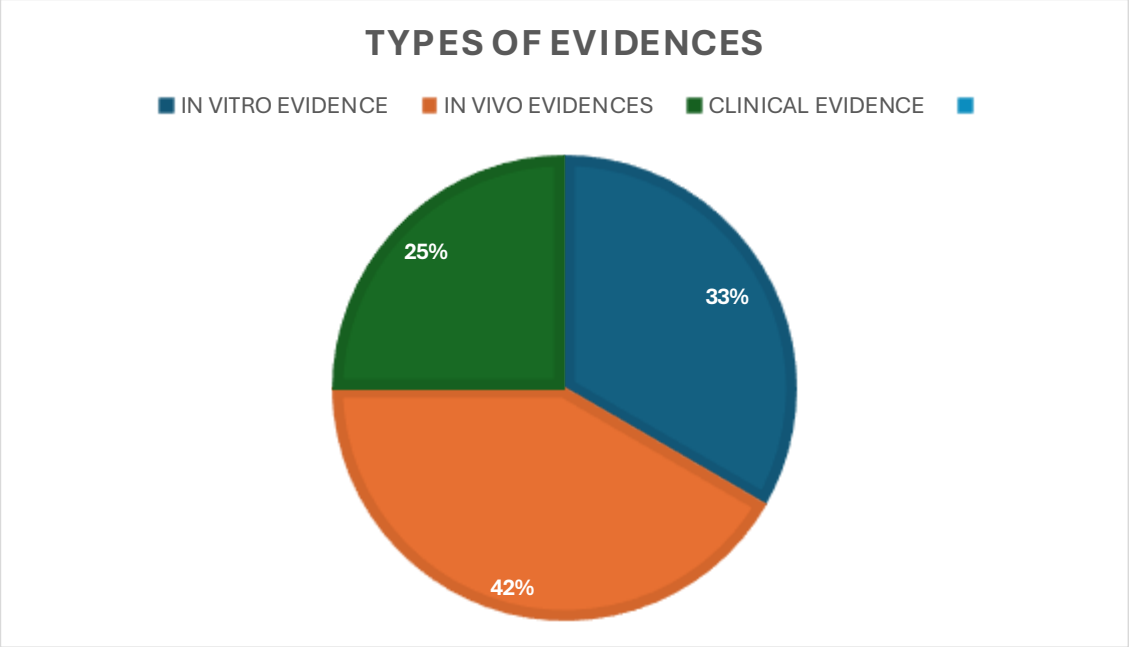


In Vivo Animal Evidence

S.NO	Study	Animal model	Findings
1.	Remya & Kuttan, 2015	Experimental animals	Reported immunomodulatory effects associated with homoeopathic remedies
2.	Mayer et al., 2016	C57BL/6 mice	Evaluated immune response modulation after vaccination challenge
3.	Saka et al., 2024	Cyclophosphamide-induced immunosuppressed BALB/c mice	Reported restoration of immune function with Bryonia alba
4.	Sharma et al., 2025	Normal and immunosuppressed mice	Investigated Ferrum phosphoricum-induced immune modulation
5.	Joshi et al., 2022	Leishmania donovani infected mice	Reported reversal of immunosuppression with Th1 immune response activation

CLINICAL EVIDENCE META-SYNTHESIS

S.NO	Study	Condition	Design	Findings
1.	Nee, 2025	Immunological disorders	Case series	Reported improvement in clinical symptoms
2.	Saklani, 2025	Vitiligo and Hashimoto thyroiditis	Case report	Reported improvement in autoimmune manifestations
3.	Das & Pal, 2025	Severe psoriasis	Case report	Reported symptom improvement and better quality of life


TYPES OF EVIDENCES
IN VITRO EVIDENCE
IN VIVO EVIDENCES
CLINICAL EVIDENCE
25%
33%
42%

RESULTS


Identification and Literature search
Studies identified on immunomodulatory effects of homoeopathic medicines
Screening
Eligibility
Included Studies
In vivo studies – 5
In vitro studies – 4
Clinical studies – 3
Excluded
Studies not evaluating immunomodulation
Qualitative Evidence Synthesis
Assessment of:
* Cytokine modulation
* Immune cell activity
* Gene expression
* Inflammatory pathways
* Clinical outcomes

Mechanisms Involved in the Immunomodulatory Action of Homoeopathic Medicines

Mechanism	Immunological Pathway/Target	Proposed Action of Homoeopathic Medicines	Supporting References
Cytokine modulation	IL-1, IL-4, IL-6, IL-10, TNF-α, IFN-γ and other cytokine networks	May influence cytokine balance and regulate excessive or insufficient immune responses	Gupta & Mathur (2018); Mathur & Kapoor (2020)
Regulation of Th1/Th2 immune balance	$CD4^+$ T-helper cell differentiation and cytokine polarization	May promote immune equilibrium by influencing Th1-mediated inflammatory responses and Th2 regulatory pathways	Joshi et al. (2022); Mathur & Kapoor (2020)
Modulation of inflammatory pathways	NF-κB signaling, inflammatory mediators, adhesion molecules	May reduce or regulate inflammatory mediator expression and immune cell activation	Dalpati et al. (2023); Bonamin (2019)
Immune cell activation and regulation	Macrophages, lymphocytes, dendritic cells, natural killer (NK) cells	May alter immune cell activity, proliferation, and functional responses	Remya & Kuttan (2015); Mayer et al. (2016)
Restoration of immune homeostasis	Balance between immune stimulation and immune suppression	May help regulate abnormal immune responses rather than producing only immune activation or suppression	Gupta & Mathur (2018); Saroj et al. (2012)
Modulation of oxidative stress pathways	Reactive oxygen species (ROS), antioxidant defense mechanisms	May influence oxidative stress-related pathways involved in inflammation and immune dysfunction	Remya & Kuttan (2015); Saka et al. (2024)
Gene expression regulation	Cellular transcriptional pathways and gene activity	May induce changes in expression of immune-related genes and cellular signaling molecules	Olsen (2017); Chirumbolo & Bjørklund (2017)
Regulation of immune receptor expression	Adhesion molecules and immune cell surface receptors	May influence immune cell communication and migration through modulation of receptor expression	Dalpati et al. (2023)
Recovery from immunosuppression	Bone marrow activity, leukocyte recovery, immune response restoration	May enhance immune function in experimentally immunosuppressed models	Saka et al. (2024); Sharma et al. (2025)
Enhancement of cellular immune response	Cell-mediated immunity, particularly Th1 response	May restore protective cellular immunity during immune suppression or infection models	Joshi et al. (2022)
Regulation of	Programmed cell	May influence apoptosis-	Chouhan et al.

apoptosis pathways	death and immune cell turnove	related mechanisms associated with immune regulation	(2015)
Modulation of inflammatory cell migration	Leukocyte adhesion and migration pathways	May affect immune cell trafficking and inflammatory site recruitment	Dalpati et al. (2023)

DISCUSSION

The current evidence indicates that homoeopathic medicines may influence immune-related biological processes through modulation of inflammatory pathways, cytokine responses, immune cell activity, and gene expression. Experimental studies provide preliminary evidence supporting biological activity; however, clinical evidence remains limited.

CONCLUSION

According to PRISMA-based evidence synthesis, homoeopathic medicines demonstrate potential immunomodulatory effects in laboratory and animal models, including regulation of inflammatory responses and immune cell functions. Clinical reports suggest possible benefits in autoimmune and immune-related conditions; however, current evidence is insufficient for definitive therapeutic recommendations. High-quality controlled studies with measurable immunological endpoints are required.

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