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DEVELOPMENT OF A TRANSLATIONAL AI-DRIVEN INTEGRATIVE FRAMEWORK COMBINING INDIAN KNOWLEDGE SYSTEMS (AYURVEDA, ETHNOBOTANY, AND ETHNOPHARMACOLOGY) FOR PERSONALIZED MANAGEMENT OF AUTOIMMUNE DISEASES USING TRIPHALA AS A MULTI-TARGET THERAPEUTIC AGENT

Abhinaba Gupta*[1&2], Anushree Karmakar[3], Afsana Parveen[3], Ankana Musib[3], Jayita Mondal[4]

[1]Faculty, Teaching Assistant, Department of Medical Laboratory Technology, School of Allied Health Sciences, Swami Vivekananda University, Barrackpore, 700121.
[2]Ph.D. Research Scholar, Centre for Healthcare Science and Technology, Indian Institute of Engineering Science And Technology, Shibpur, 711103.
[3]Assistant Professor, Dept. of Medical Laboratory Technology, Paramedical College, Durgapur, 713212.
[4]M.Sc Physiology, Dept. of Physiology, Hooghly Mohsin College, Hooghly, 712101.

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***Corresponding Author: Abhinaba Gupta**
Faculty, Teaching Assistant, Department of Medical Laboratory Technology, School of Allied Health Sciences, Swami Vivekananda University, Barrackpore, 700121. **DOI:** https://doi.org/10.5281/zenodo.22159420

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ABSTRACT

Autoimmune diseases are chronic, multifactorial disorders driven by dysregulated immune responses and persistent inflammation, often requiring multi-target therapeutic strategies beyond conventional pharmacological approaches. For the individualized treatment of autoimmune, the research study suggests a translational AI-based integrated paradigm that integrates IKS, such as Ayurveda, ethnobotany, and ethnopharmacology, with contemporary computational and clinical sciences. The framework is centered on Triphala, a classical Ayurvedic polyherbal formulation composed of *Terminalia chebula* (Haritaki), *Terminalia bellirica* (Bibhitaki), and *Phyllanthus emblica* (Amalaki), known for its potent immunomodulatory, antioxidant, and anti-inflammatory properties. The Aim of the study is to highlights ability to enhance both cellular and humoral immunity, supported by evidence of increased lymphocyte proliferation, elevated antioxidant enzyme levels, and modulation of cytokine production. By regulating immunological homeostasis and lowering oxidative stress, the integrated approach shows that triphala functions as a multi-component, multi-target therapeutic system. This study shows how AI and IKS can be combined to create a comprehensive, precision medicine framework for autoimmune illnesses. The integrative approach demonstrates that Triphala acts as a multi-component, multi-target therapeutic system, modulating immune homeostasis and reducing oxidative stress. This study highlights the potential of combining AI with IKS to develop a holistic, precision medicine framework for autoimmune diseases. The findings support the translational applicability of Triphala as a scientifically validated, systems-level intervention capable of improving clinical outcomes and advancing next-generation integrative healthcare.

KEYWORDS: Triphala, Autoimmune diseases, immunomodulatory, pharmaceuticals.

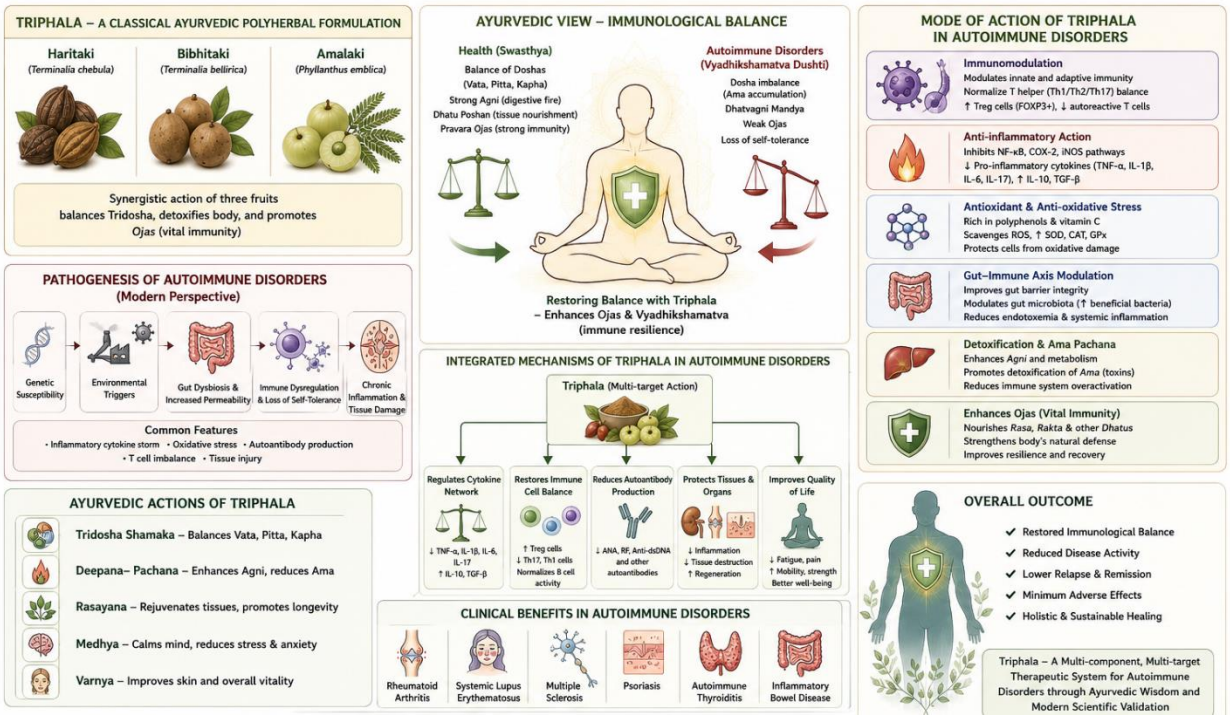

Fig:-Graphical Abstract Represents that From Tradition to Precision Medicine: An Integrative AI-Driven Mechanistic Map of Triphala in Autoimmune Disease Control.

1. INTRODUCTION

Ayurveda, the ancient system of traditional medicine originating in India over 5,000 years ago, is based on the principles of maintaining balance in the body's three doshas: Vata, Pitta, and Kapha (Parasuraman et al., 2014). It emphasizes a holistic approach to health, integrating diet, lifestyle, and herbal medicine to promote well-being and prevent diseases. One of the key therapeutic strategies in Ayurveda is the use of polyherbal formulations, which involve combining multiple medicinal plants to create synergistic effects.[1] Unlike single-herb remedies, polyherbal formulations are believed to enhance efficacy, reduce toxicity, and address multiple aspects of a disease . The combination of herbs allows for a balanced therapeutic action, where different constituents work together to enhance absorption, bioavailability, and overall efficacy. Autoimmune diseases (AIDs) represent one of the fastest-growing categories of chronic non-communicable disorders worldwide, affecting nearly 5–10% of the global population. These diseases arise when the immune system loses its ability to distinguish self from non-self, resulting in inappropriate immune activation against healthy tissues. Common autoimmune disorders include rheumatoid arthritis, systemic lupus erythematosus, multiple sclerosis, psoriasis, inflammatory bowel disease, Hashimoto's thyroiditis, Sjögren's syndrome, and type 1 diabetes mellitus. Although the clinical manifestations differ among these conditions, they share common pathogenic mechanisms involving chronic inflammation, oxidative stress, cytokine imbalance, immune dysregulation, genetic susceptibility, epigenetic modifications, and environmental triggers.[2]

Conventional therapeutic strategies primarily rely on corticosteroids, non-steroidal anti-inflammatory drugs, disease-modifying anti-rheumatic drugs (DMARDs), biologics, and targeted immunotherapies.[3] While these interventions effectively suppress inflammation and delay disease progression, they often fail to achieve complete remission and may be associated with severe adverse effects including opportunistic infections, hepatotoxicity, nephrotoxicity, metabolic complications, and immune suppression.[4] Furthermore, significant inter-individual variability in drug response

necessitates the development of personalized therapeutic strategies that address the underlying complexity of autoimmune disorders.[5]

Artificial Intelligence (AI) has emerged as a transformative technology in precision medicine. Machine learning, deep learning, natural language processing, and explainable AI facilitate the integration and interpretation of multidimensional biomedical datasets, including genomics, transcriptomics, proteomics, metabolomics, microbiomics, and clinical phenotypes. AI-based predictive models enable early diagnosis, patient stratification, biomarker discovery, treatment optimization, and disease prognosis. Nevertheless, most AI-driven healthcare frameworks are predominantly designed around synthetic pharmaceuticals, with limited integration of traditional medicinal systems.Indian Knowledge Systems (IKS), particularly Ayurveda, offer a holistic and individualized approach to health and disease. Ayurveda conceptualizes health as a dynamic equilibrium among the three biological principles (Vata, Pitta, and Kapha), balanced digestion (Agni), optimal tissue nourishment (Dhatu), proper waste elimination (Mala), and mental well-being. Personalized treatment in Ayurveda is based on an individual's constitutional type (Prakriti), disease stage, environmental influences, dietary habits, and lifestyle. This patient-centric philosophy closely aligns with the principles of modern precision medicine.[6]

Among the numerous Ayurvedic formulations, Triphala has attracted considerable scientific attention due to its broad pharmacological profile. Composed of *Terminalia chebula*, *Terminalia bellirica*, and *Phyllanthus emblica*, Triphala contains diverse bioactive compounds such as gallic acid, ellagic acid, chebulagic acid, chebulinic acid, emblicanin A and B, quercetin, rutin, and tannins.[7] These phytochemicals exhibit antioxidant, anti-inflammatory, immunomodulatory, antimicrobial, hepatoprotective, neuroprotective, and gut microbiome-modulating activities. Contemporary studies suggest that Triphala influences multiple signaling pathways implicated in autoimmune diseases, including NF-κB, JAK/STAT, MAPK, Nrf2/Keap1, PI3K/Akt, TLR signaling, and inflammasome activation.[8]

Ethnobotany and ethnopharmacology further strengthen the translational relevance of Triphala by documenting centuries of traditional use alongside modern pharmacological evidence. The convergence of these disciplines with AI, systems biology, and network pharmacology provides an unprecedented opportunity to develop a scientifically validated, multi-target therapeutic framework capable of addressing the multifactorial nature of autoimmune diseases.

This review proposes an AI-driven translational integrative framework that combines Ayurvedic principles, ethnobotanical knowledge, ethnopharmacological evidence, and computational intelligence to facilitate personalized Triphala-based interventions. By integrating traditional wisdom with contemporary biomedical science, the framework seeks to advance evidence-based precision medicine while promoting the global acceptance of Indian Knowledge Systems within mainstream healthcare.[9]

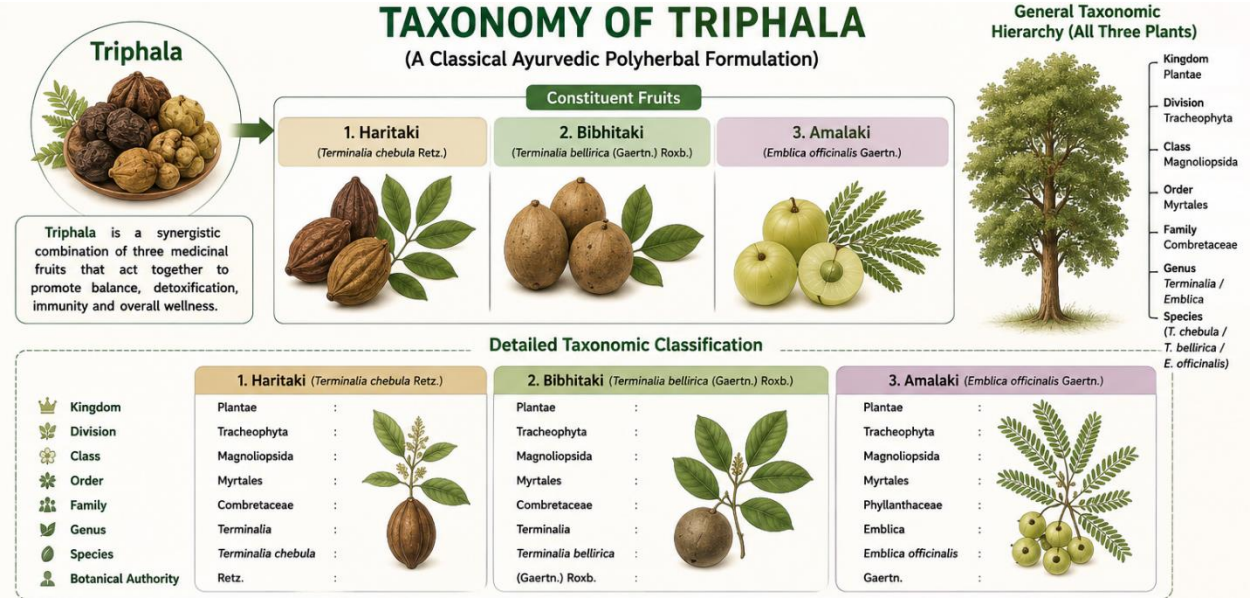

Fig. 2: An ayurvedic perspective on immunological balance for the role of triphala in managing autoimmune disorders.[8,9]

2. AIM &OBJECTIVES

The primary aim of this chapter is to develop a comprehensive translational Artificial Intelligence (AI)-driven integrative framework that combines Ayurveda, ethnobotany, and ethnopharmacology to enable personalized, evidence-based management of autoimmune diseases using Triphala as a multi-target therapeutic intervention. The framework seeks to bridge traditional Indian Knowledge Systems with contemporary computational biology, systems pharmacology, precision medicine, and clinical decision-support technologies to improve therapeutic efficacy, safety, and patient-centered care.

1. To establish the scientific rationale for integrating Indian Knowledge Systems with Artificial Intelligence.

The aims of the article to demonstrate how Ayurvedic principles can complement AI-driven precision medicine by incorporating constitutional profiling (Prakriti), disease phenotype, lifestyle factors, and molecular biomarkers into personalized therapeutic models.

2. To evaluate the ethnobotanical significance of Triphala.

The objective is to document the historical, cultural, and geographical utilization of the constituent plants of Triphala across diverse traditional healthcare systems and evaluate their relevance in autoimmune disease management.

3. To analyze the ethnopharmacological mechanisms of Triphala.

This objective focuses on reviewing the phytochemical composition, pharmacological activities, molecular targets, and immunomodulatory mechanisms responsible for the therapeutic effects of Triphala.

4. To integrate systems biology and network pharmacology approaches.

The framework aims to identify complex interactions between phytochemicals, genes, proteins, signaling pathways, immune cells, and disease networks responsible for autoimmune pathogenesis.

5. To incorporate Artificial Intelligence and machine learning methodologies.

Advanced computational models including supervised learning, deep learning, explainable AI, and predictive analytics will be incorporated to optimize diagnosis, patient stratification, biomarker identification, treatment response prediction, and personalized dosage recommendations(10).

3. MATERIALS AND METHODS

The proposed translational framework integrates Indian Knowledge Systems with artificial intelligence, systems biology, network pharmacology, and precision medicine to investigate the therapeutic potential of Triphala for personalized management of autoimmune diseases. The methodology comprises multiple sequential stages that combine traditional medical knowledge with modern computational and experimental approaches.

The study begins with knowledge acquisition from classical Ayurvedic texts, ethnobotanical records, ethnopharmacological literature, peer-reviewed scientific publications, and publicly available biomedical databases. Information regarding the traditional indications, phytochemical composition, pharmacological activities, molecular targets, and clinical evidence related to Triphala is systematically compiled. Standardized terminology is adopted to harmonize Ayurvedic concepts with biomedical nomenclature, facilitating computational analysis.[11]

The phytochemical profiling stage focuses on identifying the principal bioactive constituents of *Terminalia chebula*, *Terminalia bellirica*, and *Phyllanthus emblica*. Experimentally reported compounds are screened for physicochemical properties, oral bioavailability, drug-likeness, pharmacokinetic characteristics, and toxicity using established in silico prediction platforms. Candidate phytochemicals satisfying predefined pharmacological criteria are selected for subsequent computational analyses.Network pharmacology is employed to construct a comprehensive interaction network linking Triphala phytochemicals with protein targets implicated in autoimmune diseases. Disease-associated genes are obtained from publicly available genomic and disease databases, while protein–protein interaction networks are generated to identify central hub genes involved in immune regulation. Functional enrichment analyses using Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways are performed to determine the principal biological processes and signaling pathways affected by Triphala. Particular emphasis is placed on inflammatory pathways such as NF-κB, JAK/STAT, MAPK, PI3K/Akt, Nrf2/Keap1, TLR signaling, and inflammasome activation.[12]

Molecular docking studies are subsequently conducted to evaluate the binding affinity between selected phytochemicals and key inflammatory proteins, including TNF-α, IL-6, IL-1β, COX-2, JAK1, JAK3, STAT3, and NF-κB p65. High-affinity ligand–protein complexes are further validated through molecular dynamics simulations to assess structural stability and interaction persistence under physiological conditions.

Artificial Intelligence constitutes the central analytical component of the framework. Multi-omics datasets comprising genomic variants, transcriptomic profiles, proteomic signatures, metabolomic biomarkers, gut microbiome composition, inflammatory cytokine levels, demographic variables, lifestyle characteristics, and Ayurvedic constitutional (Prakriti) information are integrated into machine learning pipelines. Algorithms such as Random Forest, Support Vector Machine, Extreme Gradient Boosting (XGBoost), Artificial Neural Networks, and Deep Neural Networks are trained using supervised learning approaches to predict disease severity, therapeutic response, and individualized Triphala treatment strategies. Explainable AI techniques, including SHAP (Shapley Additive

Explanations) and Local Interpretable Model-Agnostic Explanations (LIME), are incorporated to improve model transparency and facilitate clinician interpretation.[13,14]

Model performance is evaluated using internal and external validation cohorts. Predictive accuracy, sensitivity, specificity, precision, recall, F1-score, receiver operating characteristic (ROC) curves, and area under the curve (AUC) are calculated to assess classification performance. Clinical translation is proposed through prospective observational studies and randomized controlled trials evaluating improvements in inflammatory biomarkers, disease activity indices, patient-reported outcomes, quality of life, and safety profiles following personalized Triphala-based interventions. This integrated methodology establishes a robust translational pipeline capable of bridging traditional Ayurvedic knowledge with evidence-based computational medicine, thereby supporting the development of personalized, scientifically validated therapeutic strategies for autoimmune diseases.

Critical Analysis of the Literature

The current literature demonstrates a rapidly growing convergence between artificial intelligence, precision medicine, systems biology, and traditional medicinal knowledge. Triphala, one of the most extensively studied Ayurvedic formulations, has consistently shown antioxidant, immunomodulatory, anti-inflammatory, antimicrobial, and microbiome-regulating activities, making it a promising candidate for the management of autoimmune diseases. Multiple experimental studies have demonstrated that Triphala modulates key inflammatory signaling pathways including NF-κB, MAPK, PI3K/Akt, Nrf2, JAK/STAT, and Toll-like receptor pathways, all of which are critically involved in autoimmune pathogenesis.[15,16]

Network pharmacology has significantly transformed the understanding of herbal medicines by demonstrating that complex phytochemical mixtures exert therapeutic effects through simultaneous regulation of multiple molecular targets. This paradigm is particularly relevant for Triphala because its diverse bioactive compounds—including gallic acid, chebulagic acid, ellagic acid, emblicanin A and B, rutin, and quercetin—interact with interconnected inflammatory and oxidative stress pathways. Unlike conventional single-target pharmaceuticals, this multi-target mechanism may offer broader therapeutic benefits for heterogeneous autoimmune disorders.[17]

Artificial intelligence has emerged as a powerful tool for integrating multidimensional biomedical data, including genomic, proteomic, metabolomic, microbiome, imaging, and electronic health record information. Machine learning algorithms have demonstrated remarkable success in disease prediction, patient stratification, biomarker discovery, and individualized treatment optimization. However, most existing AI platforms focus predominantly on synthetic pharmaceuticals, while the incorporation of traditional medicinal knowledge, particularly Ayurveda and ethnopharmacology, remains limited.

The concept of Prakriti**,** which forms the foundation of Ayurvedic personalized medicine, closely resembles modern precision medicine approaches. Nevertheless, there is currently no comprehensive AI framework capable of integrating constitutional profiling, molecular biomarkers, gut microbiome composition, lifestyle factors, environmental exposures, and phytochemical network pharmacology into a unified decision-support system.[18]

Recent advances in explainable artificial intelligence, systems pharmacology, Alpha Fold-based protein prediction, and multi-omics technologies provide unprecedented opportunities to overcome these limitations. Despite these

developments, substantial research gaps remain in clinical validation, standardization of Ayurvedic formulations, regulatory harmonization, and multicenter translational studies.

Overall, the literature strongly supports the development of an AI-driven integrative framework that combines Ayurveda, ethnobotany, ethnopharmacology, network pharmacology, and precision medicine. Such a framework has the potential to facilitate personalized Triphala-based interventions for autoimmune diseases while advancing the global scientific acceptance of Indian Knowledge Systems.[19]

4. Autoimmune Diseases and Their Molecular Basis

Autoimmune diseases are a heterogeneous group of disorders in which the immune system loses effective tolerance to self-antigens, resulting in persistent immune activation and tissue injury. Diseases such as rheumatoid arthritis, systemic lupus erythematosus, multiple sclerosis, inflammatory bowel disease, autoimmune thyroid disorders and psoriasis differ in their target organs, but share interconnected mechanisms involving genetic susceptibility, environmental triggers, innate immune activation, adaptive immune dysregulation, cytokine imbalance, epigenetic alterations and disturbances of immune–metabolic homeostasis. Autoimmunity can therefore be conceptualized as a systems-level failure of mechanisms responsible for maintaining self–non-self discrimination and immune tolerance.[20]

At the molecular level, autoimmune pathology involves abnormal antigen presentation, activation of autoreactive T and B lymphocytes, defective regulatory T-cell activity, production of pathogenic autoantibodies and dysregulation of inflammatory pathways. Important signaling networks include NF-κB, JAK/STAT, MAPK, PI3K/AKT, NLRP3 inflammasome and interferon-associated pathways. Cytokines including TNF-α, IL-1β, IL-6, IL-17, IL-21 and type-I interferons may amplify inflammatory responses, whereas regulatory mediators such as IL-10 and TGF-β participate in immune suppression and tissue repair. Importantly, these pathways do not operate independently; their interactions generate disease-specific molecular networks.

Genetic susceptibility is particularly important in autoimmune disease. Variants affecting human leukocyte antigen molecules, cytokine signaling, antigen processing, lymphocyte activation and immune checkpoints can alter disease susceptibility. However, genetic variation alone cannot explain disease onset. Epigenetic mechanisms—including DNA methylation, histone modifications, chromatin remodeling and non-coding RNAs—provide a dynamic interface between environmental exposure and immune phenotype. Environmental pollutants, diet, infections, stress, smoking and altered intestinal microbial communities may influence these mechanisms.[21]

5. Ayurveda and Indian Knowledge Systems

Ayurveda represents a traditional Indian medical knowledge system based on an individualized interpretation of health, disease, diet, lifestyle, pharmacological substances and therapeutic interventions. Its conceptual framework differs from contemporary biomedical terminology, and direct one-to-one translation between Ayurvedic concepts and molecular biology should therefore be avoided. Instead, an integrative research approach should investigate whether traditional phenotypic classifications and therapeutic principles can be systematically correlated with measurable biological variables.

Indian Knowledge Systems provide an extensive historical record of medicinal plants, formulations, food–medicine relationships, preparation techniques and disease-management principles. Contemporary research can use this

knowledge as a hypothesis-generating resource rather than treating historical use as proof of clinical efficacy. The Ministry of Ayush maintains research and standardized terminology resources intended to support evidence-based research and documentation of traditional medical systems.

A major scientific challenge is the translation of traditional concepts into reproducible experimental variables. For example, individualized Ayurvedic assessment could potentially be studied alongside anthropometric measurements, metabolic biomarkers, inflammatory markers, microbiome profiles, dietary patterns and patient-reported outcomes. Such studies could determine whether traditional phenotypic classifications contain reproducible biological information or whether their clinical utility is independent of conventional molecular categories.[22]

6. Triphala as a Multi-Target Therapeutic Agent

The multi-component nature of Triphala makes it a potential candidate for investigation within a multi-target pharmacological framework. Conventional drug development often focuses on identifying a highly selective molecular target, whereas complex chronic diseases such as autoimmune disorders involve interacting inflammatory, metabolic, oxidative and immune-regulatory networks. A multi-target strategy may therefore be scientifically attractive, although its therapeutic efficacy must be established experimentally and clinically.

Potential mechanisms requiring investigation include modulation of inflammatory signaling, oxidative-stress pathways, immune-cell activation, cytokine production, apoptosis, cellular metabolism and intestinal microbial ecology. Network pharmacology provides an appropriate computational approach because it can represent relationships among phytochemicals, proteins, pathways and disease phenotypes. Previous Triphala research has specifically demonstrated the use of pharmacological networks to explore interactions between Triphala bioactives and molecular targets.[23]

7. Mechanistic Systems Biology of Triphala: Integrating Gut Barrier Restoration,Immune Modulation, and Anti-Inflammatory Signaling

Triphala enhances gut barrier integrity, reduces intestinal permeability (“leaky gut”), and promotes beneficial microbiota such as *Lactobacillus* and *Bifidobacterium*. This leads to increased production of short-chain fatty acids (SCFAs), which are key immunoregulatory metabolites. Consequently, immune balance is restored through upregulation of regulatory T cells (Treg) and suppression of pro-inflammatory Th17 and Th1 responses, establishing immune tolerance. A novel AI-integrated, multi-disciplinary framework for the management of autoimmune diseases using Triphala as a central therapeutic agent. It begins by highlighting autoimmune diseases as complex, chronic conditions characterized by immune dysregulation, persistent inflammation, and the need for multi-target interventions. The core of the framework is Triphala, a classical Ayurvedic formulation composed of Terminalia chebula, Terminalia bellirica, and Phyllanthus emblica, which together exhibit synergistic immunomodulatory, antioxidant, anti-inflammatory, and adaptogenic properties.[24,25]

From a mechanistic perspective, the image illustrates that Triphala operates through multi-target biological pathways, including regulation of T-cell responses (Th1/Th2/Th17 balance), reduction of oxidative stress via enhanced antioxidant enzymes (SOD, CAT, GPx), suppression of pro-inflammatory mediators (NF-κB, TNF-α, IL-6), and modulation of the gut–immune axis. These mechanisms collectively contribute to restoring immune homeostasis and preventing tissue damage. Importantly, the framework integrates Indian Knowledge Systems (IKS)—including

Ayurveda, ethnobotany, and ethnopharmacology with modern scientific validation, thereby ensuring both traditional relevance and evidence-based applicability.[26]

A key innovative aspect of this model is the incorporation of multi-omics and artificial intelligence. Genomics, transcriptomics, proteomics, metabolomics, and microbiomics data are combined with AI tools such as machine learning, deep learning, and network pharmacology to enable biomarker discovery, pathway mapping, and predictive modeling. This allows for precision medicine approaches**,** including patient stratification, personalized formulation design, and optimized dosing strategies.[27]

The translational pipeline further emphasizes clinical applicability through biomarker validation, individualized treatment protocols, and continuous therapeutic monitoring. The expected outcomes include restoration of immune balance, reduction in inflammatory burden, protection of target organs, improved quality of life, and long-term remission.The novelty of this framework lies in its holistic integration of traditional medicine with cutting-edge computational biology**,** proposing Triphala as a multi-component, multi-target therapeutic system. This integrative paradigm advances beyond reductionist drug discovery by embracing systems biology and personalized healthcare, offering a scalable and sustainable strategy for managing autoimmune diseases.

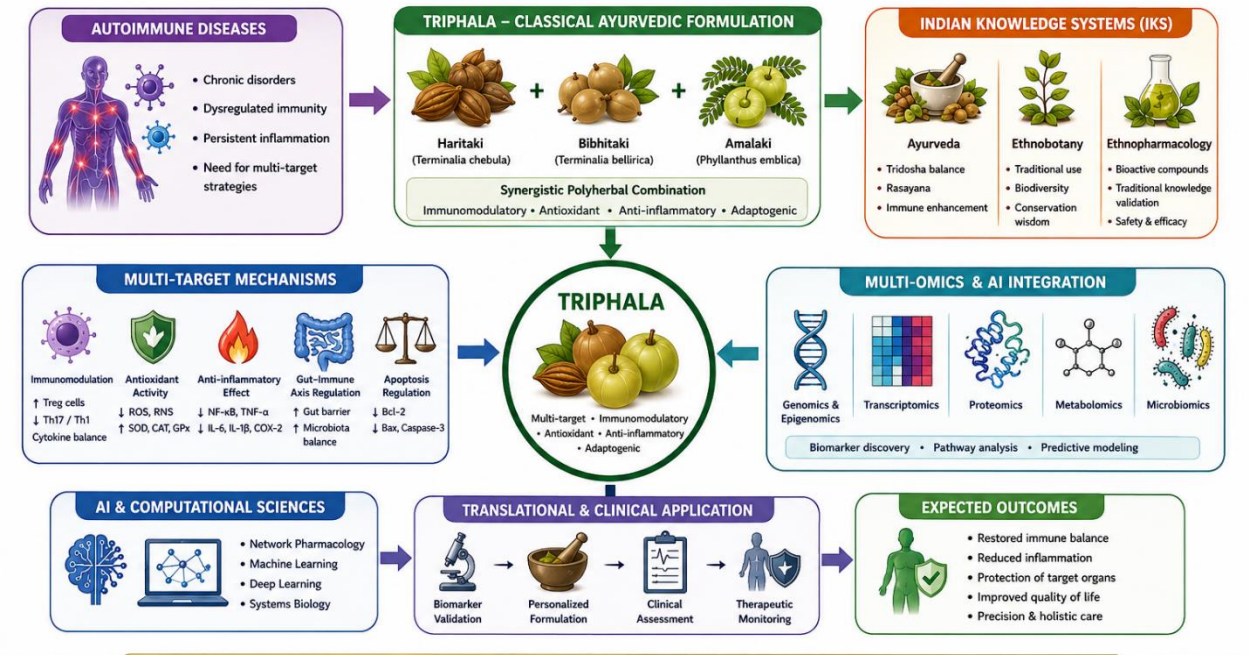

Fig. 3: Triphala as a Systems-Level Therapeutic: Linking Gut Microbiome, Molecular Pathways, and Immune Homeostasis in Autoimmunity.[27,28]

8. CONCLUSION

The current review paper comprehensively examines the traditional and modern scientific evidence supporting the therapeutic potential of Triphala Churna and its constituent fruits: Amalaki (Emblica officinalis), Bibhitaki (Terminalia bellirica), and Haritaki (Terminalia chebula). While Triphala Churna itself exhibits a wide range of pharmacological activities, individual ingredients contribute unique bioactive compounds.[29] Amalaki is rich in vitamin C and antioxidants, Bibhitaki possesses anti-inflammatory properties, and Haritaki demonstrates laxative and anti-diabetic effects. These synergistic interactions among the ingredients likely contribute to the multifaceted health benefits

observed with Triphala Churna. Further research is warranted to elucidate the precise mechanisms of action and optimize formulations for specific clinical applications.[30]

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