

## Exploring the Therapeutic Potential of Phytochemicals in Autoimmune Diseases: A Systematic Literature Review

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### ADMINISTRATIVE INFORMATION

**Support** - Nil.

**Review Stage at time of this submission** - Preliminary searches.

**Conflicts of interest** - None declared.

**INPLASY registration number:** INPLASY202460031

**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 09 June 2024 and was last updated on 31 July 2024.

### INTRODUCTION

**Review question / Objective** Following the PICO framework for this Research.

1. Population (P): Individuals diagnosed with any autoimmune disease (e.g., rheumatoid arthritis, multiple sclerosis, lupus, etc.).

2. Intervention (I): Administration of phytochemicals (e.g., curcumin, resveratrol, quercetin, etc.), either alone or in combination with conventional treatments.

3. Comparison (C): Placebo, no treatment, or conventional treatments alone.

4. Outcomes (O): Primary outcomes include disease activity scores, inflammatory markers, and quality of life. Secondary outcomes include adverse effects and patient-reported outcomes.

Study Types: Randomized controlled trials (RCTs), Clinical trials (CTs), cohort studies, case-control studies, and observational studies.

#### Research question

1. What are the effects of phytochemicals on improving the quality of life in individuals with autoimmune diseases?

2. What is the safety profile of phytochemicals used in the management of autoimmune diseases?

#### Objectives:

- To evaluate the efficacy of phytochemicals in the treatment of autoimmune diseases.

- To compare the effectiveness of phytochemicals with conventional treatments in managing symptoms and disease progression in autoimmune diseases.

• To assess the safety profile of phytochemicals used in autoimmune disease management.

**Rationale** Autoimmune diseases involve an abnormal immune response against self-antigens, resulting in chronic inflammation and tissue damage. Conventional treatments often rely on immunosuppressive drugs, which can have significant side effects. Phytochemicals, which are bioactive compounds found in plants, have shown promise in modulating immune responses and reducing inflammation, suggesting their potential as alternative or adjunctive therapies for autoimmune diseases. This systematic review aims to synthesize current evidence on the therapeutic potential of phytochemicals in autoimmune diseases.

**Condition being studied** Autoimmune disease conditions in humans and animal models.

## METHODS

**Search strategy** A comprehensive search strategy will be developed for each database, using a combination of Medical Subject Headings (MeSH) terms and keywords related to autoimmune diseases and phytochemicals along with Boolean operators. An example of search strategy for PubMed is provided:

("Autoimmune Diseases" OR "autoimmune disease" OR "rheumatoid arthritis" OR "multiple sclerosis" OR "lupus" OR "autoimmune" AND ("Phytochemicals" OR "phytochemical\*" OR "curcumin" OR "resveratrol" OR "quercetin" OR "plant extract\*" AND ("therapeutic use" OR "therapeutic potential" OR "treatment" OR "therapy" OR "efficacy"))).

**Participant or population** Patient, Participant, or population Individuals diagnosed with any autoimmune disease (e.g., rheumatoid arthritis, multiple sclerosis, lupus, etc.).

**Intervention** Administration of phytochemicals (e.g., curcumin, resveratrol, quercetin, etc.), either alone or in combination with conventional treatments.

**Comparator** Placebo, no treatment, or conventional treatments alone.

**Study designs to be included** Randomized controlled trials (RCTs), Clinical trials (CTs), cohort

studies, case-control studies, and observational studies.

**Eligibility criteria** Inclusion criteria:

- The review only considers Randomized controlled trials (RCTs), Clinical trials (CTs), cohort studies, case-control studies, and observational studies.
- Studies published between 2013 to 2023 are only included.
- Only fully open-access studies are included.
- Studies that have a detailed and scientific methodology for the therapeutic potential of phytochemicals

Exclusion criteria:

- Studies published in languages other than English are not considered.
- Studies that don't have a clear definition of the AID studied.
- Conference presentations are excluded.

**Information sources** PubMed, Web of Science, and the Cochrane Central Register of Controlled Trials (CENTRAL). Other Sources: Reference lists of included studies and grey literature sources (e.g., clinical trial registries).

**Main outcome(s)** Conventional treatments often rely on immunosuppressive drugs, which can have significant side effects. Phytochemicals, which are bioactive compounds found in plants have shown promise in modulating immune responses and reducing inflammation, suggesting their potential as alternative or adjunctive therapies for autoimmune diseases. This review will provide a systematic qualitative summary of all available literature and published studies per the protocol.

Main outcomes:

- Finding the therapeutic potential of different phytochemicals against auto-immune diseases.
- List the phytochemical compounds and their mechanisms of action.

**Quality assessment / Risk of bias analysis** The risk of bias will be assessed using the Cochrane Risk of Bias tool for RCTs and the Newcastle-Ottawa Scale for observational studies, and SYRCLE's risk of bias tool for animal studies. Two reviewers will independently assess the risk of bias, and disagreements will be resolved by consensus.

**Strategy of data synthesis** A narrative synthesis will be conducted for all included studies. If feasible, meta-analyses will be performed using a random-effects model. Heterogeneity will be assessed using the  $I^2$  statistic. Subgroup analyses

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will be conducted based on the type of autoimmune disease and type of phytochemical.

**Subgroup analysis 1.** Subgroup Analysis Plan

A. Type of Autoimmune Disease:

Rheumatoid arthritis

Multiple sclerosis

Lupus

Other autoimmune diseases (e.g., psoriasis, inflammatory bowel disease, Sjogren's syndrome, etc.)

B. Type of Phytochemical:

Curcumin

Resveratrol

Quercetin

Other phytochemicals (e.g., flavonoids, polyphenols, plant extracts, etc.)

C. Form of Phytochemical Administration:

Oral supplements

Topical applications

Intravenous administration

Dietary sources.

**Sensitivity analysis** Not applicable.

**Language restriction** Review is limited to works that have been published in English or that are fully available in English.

**Country(ies) involved** India.

**Keywords** Phytochemicals; autoimmune diseases; quality of life; safety profile; bioactive compounds; immunomodulation; inflammation.

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