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Selenium and Autoimmune Thyroid Disease: Mechanistic Insights and Clinical Evidence — A Scoping Review

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ADMINISTRATIVE INFORMATION

Support - Universidad del cauca.

Review stage at the time of initial registration - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 November 2026 and was last updated on 18 November 2026.

INTRODUCTION

Review question / Objective In adults with autoimmune thyroid disease (AITD) — Hashimoto's thyroiditis (HT) and Graves–Basedow disease (GBD), including Graves' orbitopathy (GO) — what is the extent, nature, and consistency of the human evidence on selenium status and selenium supplementation and, secondarily, on myo-inositol (MI) alone or combined with selenium, in relation to clinically relevant disease features? Objectives: (i) to map the evidence published between 1996 and 2026 on selenium status or supplementation and AITD in adults, including HT, GBD, and GO; (ii) to map the evidence on MI, alone or with selenium; (iii) to appraise the methodological quality of primary studies and systematic reviews; and (iv) to identify consistencies, contradictions, and gaps to inform research and clinical practice.

Background Autoimmune thyroid disease (AITD), comprising Hashimoto's thyroiditis (HT) and Graves–Basedow disease (GBD), is the leading cause of acquired thyroid dysfunction. Selenium is essential for selenoprotein-mediated antioxidant defense and immune regulation in the thyroid.

Rationale AITD is the most common organ-specific autoimmune disorder and the leading cause of acquired thyroid dysfunction in iodine-replete populations. Selenium is incorporated as selenocysteine into 25 human selenoproteins (glutathione peroxidases, thioredoxin reductases, iodothyronine deiodinases, and selenoprotein S) that mediate antioxidant defense, thyroid hormone metabolism, and immune regulation; the thyroid has one of the highest selenium concentrations per gram of tissue. Selenium deficiency has therefore been hypothesized to favor thyroid autoimmunity, and supplementation to exert an antibody-lowering, immunomodulatory effect. However, clinical results are heterogeneous: several meta-analyses report lower thyroid peroxidase antibody (TPOAb) titers in HT, whereas others rate the certainty of clinically meaningful benefit as low,

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and the largest randomized controlled trials (RCTs) in HT and GBD found no improvement in quality of life (QoL), remission, or thyroid function. A guideline-endorsed benefit exists only for mild GO. In addition, the therapeutic window of selenium is narrow, with excess mortality reported at 300 µg/day. Small trials suggest that MI may enhance the effect of selenium in subclinical hypothyroidism due to HT. Existing reviews have generally addressed a single phenotype, intervention, or outcome; no synthesis has mapped the human evidence on selenium and MI across both poles of AITD while appraising its methodological quality. A scoping design was chosen because the aim is to map the breadth, nature, and consistency of evidence across heterogeneous designs rather than to estimate a single pooled effect.

METHODS

Strategy of data synthesis This review follows the methodological frameworks of Arksey and O'Malley, Levac et al., and the Joanna Briggs Institute (JBI), and is reported in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR). Records were identified by two routes: (1) an initial record set derived from bibliographic searches conducted by the authors on selenium, micronutrients, and thyroid autoimmunity; and (2) a structured search of PubMed/MEDLINE, Scopus, Web of Science (Core Collection), Embase, Google Scholar, and ClinicalTrials.gov covering 1 January 1996 to 31 October 2026, complemented by backward citation chasing of the largest trials. The core search string was: ("selenium" OR "selenomethionine" OR "selenium-enriched yeast" OR "myo-inositol") AND ("autoimmune thyroid disease" OR "Hashimoto*" OR "chronic autoimmune thyroiditis" OR "Graves*" OR "Basedow*" OR "thyroid autoimmunity" OR "thyroid peroxidase antibod*" OR "thyroglobulin antibod*" OR "TSH-receptor antibod*"), adapted to the syntax of each database (full strategies provided as Supplementary Methods S1 of the manuscript). The Population–Concept–Context (PCC) framework recommended for scoping reviews was used. The combined search yielded 139 records (96 from the initial bibliographic searches and 43 from the structured search and citation chasing) before deduplication and screening.

Eligibility criteria Adults (≥18 years) of either sex with, or evaluated for, autoimmune thyroid disease (HT, GBD, or GO). Studies conducted exclusively in children or adolescents, pregnant women, or animal/in vitro models were excluded from the primary evidence synthesis and used, if at all, only as mechanistic background.

Source of evidence screening and selection Randomized controlled trials, non-randomized interventional studies, cohort, case–control, and cross-sectional studies, genome-wide association studies (GWAS), and systematic reviews/meta-analyses (SR/MA) were eligible for data charting. Narrative reviews were retained for comparative discussion. Conference abstracts were eligible only in the absence of a full-text publication.

Data management After removal of duplicates, full texts were assessed against the PCC eligibility criteria; co-publications of the same dataset were counted once, and the selection process is summarized in a PRISMA-ScR flow diagram. A standardized data-charting form captured, for each source: citation, country/setting, design, sample size and population, AITD phenotype, exposure (form, dose, duration), comparator, outcomes, and principal quantitative findings. Charting was performed by the corresponding authors, and every extracted value was cross-checked line by line against the source text in a second verification pass. Charted sources were organized by phenotype (HT/AITD in general, GBD/GO) and by exposure (selenium alone versus MI alone or combined with selenium).

Reporting results / Analysis of the evidence Given the heterogeneity of populations, interventions, and outcome definitions, no quantitative pooling was undertaken, consistent with scoping-review methodology. Findings were synthesized narratively and tabulated by phenotype (HT/hypothyroid-phase versus GBD/hyperthyroid-phase AITD, including GO) and by exposure (selenium alone versus MI alone or combined with selenium). When several meta-analyses reported pooled estimates for the same outcome, these were presented side by side without re-pooling because their primary studies overlapped. Results are complemented by evidence maps (publication year and study design by clinical focus) and a comparison with previous systematic reviews and meta-analyses.

Presentation of the results Given the heterogeneity of populations, interventions, and outcome definitions, no quantitative pooling was undertaken, consistent with scoping-review methodology. Findings were synthesized narratively and tabulated by phenotype (HT/hypothyroid-phase versus GBD/hyperthyroid-phase AITD, including GO) and by exposure

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Language restriction English.

Country(ies) involved Colombia.

Other relevant information None

Keywords selenium; autoimmune thyroid disease; Hashimoto's thyroiditis; Graves–Basedow disease; Graves' orbitopathy; myo-inositol; scoping review.

Dissemination plans Publication in a peer-reviewed journal.

Contributions of each author

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