

INPLASY

Polyphenol-Mediated Modulation of Oxidative Stress Pathways in Type 1 Diabetes

INPLASY202640104

doi: 10.37766/inplasy2026.4.0104

Received: 28 April 2026

Published: 29 April 2026

Mittal, R; Ho, A; Adivikolanu, H; Patel, D; Wang, S; Hirani, K.

Corresponding author:

Rahul Mittal

r.mittal11@med.miami.edu

Author Affiliation:

University of Miami.

ADMINISTRATIVE INFORMATION

Support - Not Applicable.

Review Stage at time of this submission - Formal screening of search results against eligibility criteria.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202640104

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 29 April 2026 and was last updated on 29 April 2026.

INTRODUCTION

Review question / Objective This systematic review aims to evaluate the effects of dietary polyphenols on glycemic control and oxidative stress in type 1 diabetes. It will assess whether polyphenol interventions improve outcomes such as blood glucose, insulin, and antioxidant markers in preclinical animal models of type 1 diabetes, and explore their potential as adjunctive therapies through antioxidant and anti-inflammatory mechanisms.

Condition being studied Type 1 Diabetes.

METHODS

Participant or population This review will include in vivo animal models of type 1 diabetes. Eligible models include chemically induced models (e.g., streptozotocin- or alloxan-induced) and autoimmune models (e.g., non-obese diabetic mice).

Intervention The intervention of interest is the administration of dietary polyphenols, including isolated compounds (e.g., flavonoids, stilbenes, curcuminoids) or polyphenol-rich extracts, as the primary treatment. Interventions may be delivered through oral, dietary, or parenteral routes at any dose or duration. Studies evaluating polyphenols alone or in combination with standard treatments (e.g., insulin) will be included, provided the polyphenol component is clearly defined.

Comparator Comparators will include untreated, vehicle-treated, or placebo control groups. Studies comparing polyphenol interventions to standard care or baseline conditions will also be eligible, provided an appropriate control condition is present.

Study designs to be included This review will include controlled in vivo animal studies. Ex vivo analyses conducted on tissues derived from in vivo-treated animals will also be considered where applicable.

Eligibility criteria Studies will be included if they involve in vivo animal models of type 1 diabetes mellitus, evaluate a clearly defined dietary polyphenol or polyphenol-rich intervention, include an appropriate comparator group, and report at least one outcome related to glycemic control or oxidative stress. Eligible study designs include controlled in vivo animal experiments and ex vivo analyses derived from in vivo-treated animals. Studies must be published in English within the predefined time frame. Studies will be excluded if they are in vitro-only, lack a comparator group, do not involve a confirmed T1D model, or are non-original research articles (e.g., reviews, editorials, commentaries, case reports, or case series). Studies will be included if they involve animal models or human participants with confirmed type 1 diabetes mellitus and evaluate a clearly defined dietary polyphenol or polyphenol-rich intervention. Eligible studies must include an appropriate comparator group (e.g., placebo, vehicle, untreated, or standard care) and report at least one outcome related to glycemic control or oxidative stress. Included study designs comprise controlled in vivo animal studies, randomized controlled trials, and prospective cohort studies. Ex vivo analyses using tissues from in vivo-treated subjects will also be considered. Studies must be published in English and fall within the predefined time frame. Studies will be excluded if they focus exclusively on type 2 diabetes, gestational diabetes, or prediabetes without extractable type 1 diabetes data; lack a comparator group; are in vitro-only; or are non-original research articles (e.g., reviews, editorials, commentaries, case reports, or case series). Pediatric-only populations and studies without confirmed T1D diagnosis or model will also be excluded.

Information sources A systematic search will be conducted in the following electronic databases: PubMed/MEDLINE, Scopus, and Embase. Reference lists of included studies will also be screened to identify additional relevant articles.

Main outcome(s) The primary outcomes are measures of glycemic control and oxidative stress. Glycemic outcomes include blood glucose levels (fasting or random), insulin, and related indices. Oxidative stress outcomes include markers of lipid peroxidation, antioxidant enzyme activity, and overall antioxidant capacity.

Quality assessment / Risk of bias analysis Risk of bias in included studies will be assessed using SYRCLE's Risk of Bias tool for animal studies. Assessments will be performed independently by two reviewers, with disagreements resolved

through discussion or consultation with a third reviewer.

Strategy of data synthesis A narrative synthesis will be conducted due to expected heterogeneity in animal models, polyphenol classes, dosing regimens, and outcome measures. Studies will be grouped by polyphenol class (e.g., flavonoids, stilbenes, curcuminoids, and polyphenol-rich extracts) and summarized descriptively. Findings will be synthesized according to key outcome domains, including glycemic control and oxidative stress markers. Where appropriate, results will be further stratified by animal model, intervention characteristics (compound, dose, duration, and route of administration), and study design features.

Subgroup analysis Not Applicable.

Sensitivity analysis Not Applicable.

Country(ies) involved United States.

Keywords Type 1 diabetes;; polyphenols; flavonoids; resveratrol; quercetin; curcumin; oxidative stress; antioxidants; glycemic control; blood glucose; insulin; preclinical studies; animal.

Contributions of each author

Author 1 - Rahul Mittal.

Email: r.mittal11@med.miami.edu

Author 2 - Alan Ho.

Author 3 - Harini Adivikolanu.

Author 4 - Dilan Patel.

Author 5 - Serena Wang.

Author 6 - Khemraj Hirani.