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Preclinical Evidence for Plant-Derived Exosome-Like nanoprticles for Targeted Therapy in ulcerative colitis: a meta-analysis and systematic review

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 November 2025 and was last updated on 23 November 2025.

INTRODUCTION

Review question / Objective Research indicates that Plant-Derived Exosome-Like nanoprticles (PDELs) could provide targeted therapeutic benefits for ulcerative colitis (UC), although their exact pharmacological mechanisms are not yet fully clarified. This meta-analysis seeks to evaluate the pharmacological impact of PDELs in animal models of UC and explore their possible mechanisms of action.

Rationale Ulcerative colitis (UC) is a chronic inflammatory bowel disease that is difficult to cure and prone to relapse, significantly impacting patients' work and quality of life. Its incidence and global burden continue to rise. While traditional medications have achieved some success in alleviating and controlling the condition, they still face limitations such as inconsistent efficacy, considerable side effects, and high costs. Plant-derived exosome-like nanoparticles (PDELs), a novel type of natural product found in sources like green tea, ginger, and Andrographis paniculata, exhibit various biological effects including anti-inflammatory, immune-regulating, and gut microbiota-improving properties.

Condition being studied Recent studies have shown that PDELs can significantly alleviate ulcerative colitis. As therapeutic agents, PDELs have demonstrated efficacy in multiple animal disease models. Moreover, oral administration as a treatment strategy for UC offers advantages such as being non-invasive, safe, highly flexible, and promoting good patient compliance. Mechanistic research has revealed that PDELs can modulate inflammation-related pathways, suppress pro-inflammatory cytokines, encourage the colonization of beneficial bacteria, and enhance the integrity of the intestinal epithelial barrier by upregulating tight junction proteins like zonula occludens-1 (ZO-1).

Although PDELs has attracted increasing attention from researchers, current studies still have certain limitations and controversies, with most research remaining at the laboratory stage and urgently needing further clinical trial validation. Nevertheless, these findings hold significant potential for future development and clinical application. Therefore, this meta-analysis aims to evaluate the pharmacological effects and potential mechanisms of PDELs in animal models of ulcerative colitis, providing a reference for subsequent research.

METHODS

Search strategy We employed a comprehensive search strategy to ensure the inclusion of all relevant literature. The search terms included medical subject headings and free-text keywords such as "colitis" and "exosome." The search covered studies published up to September 15, 2025.

Participant or population The experimental animals were mice or rats; the disease models were ulcerative colitis (UC) induced by methods such as dextran sulfate sodium (DSS) or 2,4,6-trinitrobenzene sulfonic acid (TNBS); no other comorbidities were present, such as diabetes, immunodeficiency, or gene knockout.

Intervention The intervention group received only plant-derived exosome-like nanoparticles (PDELs) or vesicle treatments.

Comparator The model group did not receive any treatment.

Study designs to be included Literature type must be published full-text experimental studies.

Eligibility criteria
(1) Inclusion criteria
Selected studies must meet the following criteria: (1) experimental animals were mice or rats; (2) disease models were ulcerative colitis (UC) models induced by methods such as dextran sulfate sodium (DSS) or 2,4,6- trinitrobenzenesulfonic acid (TNBS); (3) No other comorbidities such as diabetes, immunodeficiency, or gene knockout; (4) The study must include independent intervention and model groups; (5) Intervention dosage, route, method, and administration schedule are unrestricted; (6) The intervention group receives only plant-derived exosome-like nanoparticles or exosome therapy, while the model group receives no treatment or only vehicle control; (7) Complete data must be provided, including specific values for outcome measures such as mouse body weight change rate, disease activity index, colon length, and other mandatory indicators, along with mean and standard deviation for optional indicators like TNF-α, IL-6, IL-1β, and gut microbiota for statistical analysis; (8) Study design must be randomized controlled trials; (9) Literature type must be published full-text experimental studies.
(2)Exclusion criteria
Exclude the following studies: (1) Clinical studies; (2) Non-plant-derived exosomes (e.g., animal/microbial-derived exosomes); (3) Reviews; (4) Case reports; (5) Studies not involving animal experiments; (6) Duplicate publications;(7) Studies failing to report primary outcome measures; (8) Non-randomized controlled studies; (9) Studies with significant data bias; (10) Studies where full text is unavailable.

Information sources To gather detailed data on preclinical animal studies using PDELs for treating ulcerative colitis (UC), we conducted a literature search across five databases: PubMed, Web of Science, Embase, Cochrane Library, and ScienceDirect.

Main outcome(s) In this study, the primary outcome measures for ulcerative colitis (UC) included the rate of body weight change in mice, Disease Activity Index (DAI) scores, and colon length. Compared to the UC model group, intervention with plant-derived exosome-like nanoparticles (PDELs) resulted in reduced diarrhea, which corresponded with alleviated weight loss, decreased DAI scores, and increased colon length, indicating a therapeutic effect of PDELs. Standardized mean differences (SMD) and 95% confidence intervals (CI) were calculated to assess the impact of PDELs on UC, with all outcomes being continuous variables. A p-value of 0.05 was set as the threshold for statistical significance when comparing the PDELs intervention group to the model group. Heterogeneity was evaluated using the I^2 statistic; an I^2 value of 50% or less indicated low heterogeneity, prompting the use of a fixed-effects model for meta-analysis. If I^2 exceeded 50%, indicating significant heterogeneity, a random-effects model was employed.

Additional outcome(s) Nothing.

Data management The following data were independently extracted by two authors: (1) First author and publication year; (2) Animal species, sex, and sample size; (3) Animal ulcerative colitis (UC) modeling method; (4) Intervention measures, including intervention cycle and dosage; (5)

Outcome measures, including body weight change (BWC), colon length (CL), disease activity index (DAI), IL-10, IL-1β, IL-6, TNF-α, spleen weight, tight junction protein ZO-1, occludin, myeloperoxidase (MPO), Chao-1 index, and Shannon index. When multiple dose levels were involved in the treatment group, the dose group with the best efficacy was selected for meta-analysis. GraphPad Prism 10 software was used to quantify the chart data.

Quality assessment / Risk of bias analysis Two authors independently conducted quality assessments using the Cochrane Risk of Bias Tool. Any disagreements were resolved through discussion or by consulting a third reviewer. The quality evaluation covered the following aspects: random sequence generation (selection bias); allocation concealment (selection bias); blinding of participants and personnel (performance bias); blinding of outcome assessment (detection bias); incomplete outcome data (attrition bias); selective reporting (reporting bias); and other potential biases.
Funnel plots and Egger's test were used to detect potential publication bias in the primary outcome measures.

Strategy of data synthesis Standardized mean differences (SMDs) and 95% confidence intervals (CIs) were calculated to assess the effect of PDELs on UC, with all outcomes being continuous measures. A P-value of 0.05 was set as the significance threshold for comparing PDELs interventions with the model group. The I2 statistic was used to assess heterogeneity. An I^2 statistic ≤50% indicated mild heterogeneity, thus a fixed-effect model was employed for the meta-analysis. If I^2> 50%, a random-effects model was used due to significant heterogeneity. Heterogeneity was assessed using the I^2 index. and if I2> 75%, we conducted subgroup analyses to identify sources of heterogeneity. Additionally, sensitivity analyses were performed by systematically excluding one study at a time from the meta-analysis results. Publication bias was assessed using funnel plots and Egger's test. The aforementioned analyses were conducted using Review Manager 5.4 and CMA software.

Subgroup analysis For studies with significant publication bias, we conducted subgroup analyses based on factors such as animal species, treatment dosage, treatment duration, and modeling methods.

Sensitivity analysis After sequentially removing each individual study, the overall effect size's direction (positive), significance (P<0.001), and magnitude (large effect size) remained essentially unchanged; this indicates that no single study had a decisive impact on the overall conclusion, and the results were minimally affected by publication bias or outliers from individual studies, confirming the reliability of the findings.

Language restriction No language restrictions.

Country(ies) involved China.

Other relevant information Nothing

Keywords Plant-Derived Exosome-Like nanoprticles (PDELs), targeted therapy, ulcerative colitis, systematic review, meta analysis.

Dissemination plans Although PDEL has attracted increasing attention from researchers, current studies still have certain limitations and controversies, with most research remaining at the laboratory stage and urgently needing further clinical trial validation. Nevertheless, these findings hold significant potential for future development and clinical application. Therefore, this meta-analysis aims to evaluate the pharmacological effects and potential mechanisms of PDEL in animal models of ulcerative colitis, providing a reference for subsequent research.

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