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Gene expression of inflammatory markers in gingival tissue of rats with induced periodontitis: a scoping review protocol

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ADMINISTRATIVE INFORMATION

Support - No support.

Review Stage at time of this submission - Piloting of the study selection process.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202690079

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

INTRODUCTION

Review question / Objective What is the effect of the experimental induction of periodontal disease on the gingival expression levels of the inflammatory markers IL-1β, TNF-α, MMP-8, and IFN-γ in rats, compared to healthy controls, in experimental studies with a parallel design?

Rationale The condition under study is experimentally induced periodontal disease in rats. This animal model involves inducing periodontitis through standardized procedures—such as the use of ligatures or lipopolysaccharides—to evaluate the effect on the gingival expression of inflammatory markers. This condition is compared against healthy rats without periodontitis, which serve as a control group. The primary objective is to determine whether the presence of experimental periodontal disease alters the expression levels of IL-1β, TNF-α, MMP-8, and IFN-γ in gingival tissue, within the context of controlled experimental studies using a parallel-group design.everal studies have employed PCR/qPCR to assess the expression of inflammatory mediators like IL-1β, IL-6, TNF-α, and IL-17 in gingival tissue, using experimental periodontitis in rats as a model for studying the periodontal inflammatory response. The variety of molecules involved in the periodontal response is highlighted by the investigation of other potentially significant mediators, such as PTX3, IL-22, CXCL5, and CCL20, in addition to these traditional inflammatory markers. In order to identify new or understudied markers and ascertain which ones show a consistent response in comparison to healthy controls, this review attempts to systematically synthesize the evidence regarding changes in the gene expression of inflammatory markers in the gingival tissue of rats with experimental periodontal disease.

Condition being studied The condition under study is experimentally induced periodontal disease in rats. This animal model involves

inducing periodontitis through standardized procedures—such as the use of ligatures or lipopolysaccharides—to evaluate the effect on the gingival expression of inflammatory markers. This condition is compared against healthy rats without periodontitis, which serve as a control group. The primary objective is to determine whether the presence of experimental periodontal disease alters the expression levels of IL-1β, TNF-α, MMP-8, and IFN-γ in gingival tissue, within the context of controlled experimental studies using a parallel-group design.

METHODS

Search strategy The search strategy aims to locate both published and unpublished (grey literature) studies and will follow the JBI three-step approach for scoping reviews. An initial limited search of PubMed and Scopus was first conducted to identify keywords and index terms used in relevant titles and abstracts, which informed the development of the comprehensive search strategy described below.

The refined search strategy, adapted to the specific syntax of each source, will be applied across PubMed, Scopus, Web of Science, and Dimensions, SciELO, bioRxiv, and LILACS will additionally be searched to capture regionally indexed literature not covered by the databases above. Reference management and de-duplication will be performed as described in the Study/ Source of evidence selection section.

Citation searching will subsequently be performed on all studies meeting the inclusion criteria after full-text screening. Backward and forward citation chaining will be conducted using AI ResearchRabbit and Connected Papers tools, using the included studies as seed articles, in addition to manual screening of their reference lists. Grey literature and preprints will be searched in bioRxiv to identify relevant unpublished studies not yet indexed in the databases above.

Only studies published in English, Spanish, or Portuguese will be considered, with no restriction on publication date. The complete and final search strategies applied to each database/source will be reported in Appendix 1, including the number of records retrieved per source and the date on which each search was conducted. The search will be re-run prior to publication to identify any additional eligible studies. The complete search process will be developed and conducted by an experienced systematic search specialist.

Participant or population The participants in this review are rats (*Rattus norvegicus*) of any strain, sex, or age used in *in vivo* experimental studies. Animals with experimentally induced periodontal disease and healthy animals serving as controls will be included, provided the studies employ parallel designs. The condition of interest is experimental periodontitis, and the outcome evaluated is the expression of inflammatory markers quantified directly in gingival tissue using qPCR, RT-PCR, or RT-qPCR. Studies involving other species, *in vitro* studies, research lacking a healthy control group, studies measuring only systemic markers or markers in tissues other than gingival tissue, and studies that do not report gene expression data obtained via PCR or do not allow for comparison between the groups of interest will be excluded. Reviews and meta-analyses will also be excluded.

Intervention None.

Comparator None.

Study designs to be included The study design to be included in this systematic review comprises controlled experimental studies using a parallel-group design. Research comparing a group of rats with experimentally induced periodontal disease against a control group of healthy rats (without periodontitis) will be selected. Studies must employ clearly described induction methods—such as ligatures, lipopolysaccharides, or other standardized procedures—and assess the gingival expression of inflammatory markers using quantitative PCR, RT-PCR, or RT-qPCR techniques. Studies with parallel groups, in which animals are assigned t.

Eligibility criteria In vivo experimental studies conducted on rats of any strain, sex, or age will be included, provided they evaluate the induction of experimental periodontitis and compare the results with animals subjected to induction or healthy controls using parallel experimental designs. The outcome of interest is the expression of inflammatory markers quantified directly in gingival tissue via qPCR: Quantitative Polymerase Chain Reaction, RT-PCR: Reverse Transcription Polymerase Chain Reaction, or RT-qPCR: Reverse Transcription Quantitative Polymerase Chain Reaction.
Studies involving other species, in vitro studies, studies lacking a healthy control group, studies evaluating exclusively systemic inflammatory markers or markers in tissues other than gingival tissue, and studies that do not report gene expression results obtained via PCR or do not

allow for a comparison between the groups of interest will be excluded. Reviews and meta-analyses will be excluded.

Information sources The literature search will be conducted in PubMed, Web of Science, SCOPUS, Dimensions, bioRxiv, LILACS, and Scielo. The search will take place in September 2026; no publication date restrictions will be applied, and only studies published in English will be included. The search strategy will combine terms related to rats, experimental periodontal disease, gingival tissue, and gene expression of inflammatory markers via qPCR, RT-PCR, or RT-qPCR; specific strategies will be adapted for each database. Records will be imported into Rayyan for duplicate removal and independent screening of titles/abstracts and full texts by three reviewers, with discrepancies resolved by consensus or a fourth reviewer. Data will be extracted independently using a standardized form covering animal characteristics, the induction model, the control group, the evaluation timeframe, inflammatory markers, and the PCR method. Risk of bias will be assessed using SYRCLE. Results will be presented through a narrative synthesis andtables.

Main outcome(s) The key findings will enable the identification and characterization of available evidence regarding the gene expression of inflammatory markers in the gingival tissue of rats with experimental periodontitis, compared to healthy or non-induced controls. This characterization will encompass the experimental models used, induction methods, markers studied, and PCR techniques employed. Furthermore, inflammatory marker expression profiles will be identified by comparing the various experimental induction models and time points of evaluation. Finally, knowledge gaps, understudied areas, and opportunities for future preclinical research will be highlighted.

Additional outcome(s) None.

Data management Extracted data will be summarized in tables and presented narratively, organized by inflammatory marker. Markers will be classified as traditional (IL-1β, IL-6, TNF-α, IL-17) or emerging/understudied (PTX3, IL-22, CXCL5, CCL20). For each marker, the direction of gene expression change relative to the control (increased, decreased, or unchanged) will be tabulated, and the proportion of concordant and discordant findings will be calculated. Discordant results will be cross-referenced with the risk-of-bias assessment to distinguish between methodological limitations and biological variability associated with the induction method, sampling time, or PCR protocol.

Findings will also be presented as an evidence matrix or bubble plot relating each marker to the number of studies, direction of change, and induction model, in order to visually identify evidence clusters and gaps. Where the number and diversity of studies permit, a Sankey diagram will be used to visualize the flow between induction method, marker, and direction of change. Markers reported in few studies (≤2) or showing unexplained discordance will be flagged as evidence gaps. No meta-analysis will be performed, given the exploratory nature of this review.

Quality assessment / Risk of bias analysis As this is a scoping review, no GRADE certainty assessment will be conducted, and risk of bias will not be used as a criterion for study inclusion or exclusion. Prior to full assessment, a pilot calibration exercise will be conducted on 3–5 included studies, led by a reviewer experienced in risk-of-bias assessment [JRGB], to standardize the application of the SYRCLE Risk of Bias tool for animal intervention studies among reviewers. Following calibration, risk of bias will be assessed for all included studies using this tool, independently by two reviewers [AJIV, JAIV, MSG], with disagreements resolved through discussion or consultation with a third reviewer [JRGB]. Results will be reported narratively and in tabular form. Risk of bias findings will be considered alongside gene expression outcomes when synthesizing the consistency of results across studies for each inflammatory marker.

Strategy of data synthesis Data will be extracted from papers included in the scoping review by three independent reviewers [AJIV, JAIV, MSG] using a structured data extraction form, developed by the reviewers within the Rayyan platform. Extracted data will include study characteristics (authors, year of publication, country, and study design), population details (rat strain, sex, and periodontitis induction method), concept-related details (target gene/marker, PCR method used, and direction of gene expression change relative to control), context (housing/laboratory conditions and time point of tissue sampling), and key findings relevant to the review question. Any disagreement will be resolved through discussion or, if necessary, consultation with a senior researcher to reach consensus [EOMS]. The draft data extraction form will be modified and revised as necessary during the extraction process, and any modifications will be detailed in the scoping

review. Where appropriate, study authors will be contacted to request missing or additional data.

Subgroup analysis No subgroup analysis will be conducted.

Sensitivity analysis No sensitivity analysis will be conducted.

Language restriction The language restrictions for this systematic review are as follows: Only studies published in English ,Spanish or Portuguese will be included.

Country(ies) involved The study is being conducted in Mexico, at the Autonomous University of the State of Hidalgo (UAEH).

Other relevant information None

Keywords Gene expression; inflammatory marker; Periodontitis; Rat; Real time PCR; Reverse Transcriptase Polymerase Chain Reaction; quantitative PCR.

Dissemination plans Publication.

Contributions of each author

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