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INPLASY

Potential Application Value of Berberine for Periodontal Dis-ease: A Systematic Review and Meta-Analysis Based on Animal Models

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - 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 21 September 2026 and was last updated on 21 September 2026.

INTRODUCTION

Review question / Objective The review question was defined using the PICOS framework. The population included animals with experimentally induced periodontal disease; the intervention was administration of berberine; the comparators were no berberine treatment or vehicle-only controls. The primary outcome was reduction in alveolar bone loss, while secondary outcomes comprised levels of inflammatory cytokines (TNF-α, IL-1β, IL-6, IL-17A), bone metabolism markers, gingival index (GI), and the general condition of animals. Only preclinical animal studies assessing berberine in periodontal disease models of any species were eligible, with no restrictions placed on publication date or language.

Rationale Although individual animal experiments have suggested that berberine may alleviate periodontal inflammation and inhibit alveolar bone loss, inconsistencies exist among published studies regarding dosage, administration routes and observed outcomes. No systematic review and meta-analysis has synthesized the pre-clinical evidence of berberine for periodontal disease in animal models. Therefore, this meta-analysis was performed to pool available animal data and provide comprehensive pre-clinical evidence for further research and potential clinical translation.

Condition being studied Periodontal disease comprises a group of chronic inflammatory conditions affecting the gingiva, periodontal ligament, and alveolar bone, which collectively maintain tooth stability. The pathological progression of the disease can result in persistent gingival inflammation, periodontal pocket formation, progressive alveolar bone destruction, and ultimately irreversible tooth loss. Epidemiological data indicate that severe

periodontitis ranks as the sixth most prevalent disease globally, with an overall estimated prevalence of 11.2% and roughly 743 million individuals affected worldwide. Considerable socioeconomic burdens are attributable to periodontitis: in 2018, its related costs were estimated at approximately €154 billion in the United States and €159 billion in Europe, placing a heavy burden on public healthcare systems. Beyond oral-local damage, accumulating evidence demonstrates that periodontal disease is closely linked to multiple systemic disorders, which may further impair general physical condition and patients' quality of life. Current conventional therapeutic strategies cannot completely halt alveolar bone resorption, driving the search for adjuvant natural-derived therapeutic agents such as berberine.

METHODS

Participant or population Animals with induced periodontal disease.

Intervention Berberine administration.

Comparator Comparative interventions included vehicle control, normal saline, blank model control (periodontitis model without drug administration), or conventional periodontal drugs. Animal studies without any comparative intervention group were excluded.

Study designs to be included Only preclinical studies with berberine administration in animal models (all species) of periodontal disease were analyzed.

Eligibility criteria The inclusion criteria were as follows: (1) the study subjects were animal models of experimentally induced periodontal disease, without restrictions on animal species, age, or sex; (2) the study investigated the effects of berberine intervention on periodontal disease-related lesions; (3) the study design involved qualified preclinical in vivo animal experiments; and (4) the publication language was limited to English or Chinese.
Studies were excluded if they met any of the following criteria: (1) duplicate pub-lications; (2) reviews, meta-analyses, case reports, conference abstracts, or other non-original studies; (3) studies for which the full text was unavailable; (4) studies lacking valid and extractable experimental data; (5) in vitro cell-based studies, clinical trials, or studies with inappropriate experimental designs.

Information sources Electronic databases.

Main outcome(s) Alveolar bone loss reduction.

Additional outcome(s) Levels of inflammatory cytokines (TNF-α, IL-1β, IL-6, IL-17A), bone metabolism markers, gingival index (GI), and general condition of animals.

Data management Zotero.

Quality assessment / Risk of bias analysis The risk of bias in the included animal studies was assessed using the Systematic Review Centre for Laboratory Animal Experimentation (SYRCLE) risk-of-bias tool.

Strategy of data synthesis All statistical analyses were performed using RevMan software (version 5.4; Cochrane Collaboration) and Stata software (version 15.1). Continuous outcomes were expressed as standardized mean differences (SMDs), and pooled effects were visualized using forest plots. Considering the potential variations in intervention protocols, dosages, and other experimental characteristics among the included studies, a random-effects model was applied for all meta-analyses. Statistical heterogeneity was assessed using the I^2 statistic. A p-value < 0.05 was considered statistically significant.

Subgroup analysis No subgroup analysis was planned for this meta-analysis.

Sensitivity analysis Sensitivity analyses were conducted using a leave-one-out approach to evaluate the robustness of the pooled estimates. Publication bias was assessed by funnel plots when more than 10 studies were available for a specific outcome.

Language restriction No language restrictions were imposed during the electronic search. However, only studies published in English and Chinese were included because of the lack of translation resources for other languages.

Country(ies) involved This study was carried out in China. Participating authors are affiliated with institutions located in mainland China and Hong Kong, China.

Keywords berberine; periodontal disease; animal model; systematic review; meta-analysis.

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