

The Effectiveness of Curcumin Nanoparticle-coated Titanium Surfaces in Osteogenesis: A Systematic Review

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Suresh, N ; Mauramo, M; Waltimo, T; Sorsa, T; Anil, S.

Corresponding author:

Sukumaran Anil

drsani@gmail.com

Author Affiliation:

Oral Health Institute, Hamad
Medical Corporation, Qatar
University, Doha, Qatar.

ADMINISTRATIVE INFORMATION**Support** - No financial support.**Review Stage at time of this submission** - Completed but not published.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202470105**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 26 July 2024 and was last updated on 26 July 2024.**INTRODUCTION**

Review question / Objective This systematic review critically appraises and synthesizes the evidence from in vitro studies investigating the effects of curcumin nanoparticles on titanium surface modification, with a specific focus on cell adhesion, proliferation, osteogenic differentiation, and mineralization. The review question based PICOS criteria is:

What is the effect of curcumin nanoparticles coated on titanium surfaces in enhancing osteogenesis in vitro, focusing on cell adhesion, proliferation, osteogenic differentiation, and mineralization?

Rationale The rationale for this systematic review on curcumin nanoparticle-coated titanium surfaces in osteogenesis addresses a critical need in biomaterials and orthopedic implantology. While titanium and its alloys are widely used in orthopedic and dental implants due to their biocompatibility and mechanical properties, enhancing their osteogenic potential remains

challenging. Curcumin, a natural compound with anti-inflammatory, antioxidant, and osteogenic effects, has shown promise in nanoparticle form for improving bioavailability and efficacy. Combining curcumin nanoparticles with titanium surfaces represents an innovative approach to enhancing implant performance. However, the current research on this application is scattered and has not been systematically evaluated. This review aims to synthesize available evidence, assess research quality, identify potential mechanisms of action, and highlight knowledge gaps. By providing a comprehensive understanding of the current state of research, this review will inform researchers and clinicians working on implant technologies. Ultimately, it has the potential to contribute to the development of more effective orthopedic and dental implants, potentially improving patient outcomes and reducing healthcare costs associated with implant failures or prolonged healing times. This systematic review provides compelling evidence from in vitro studies supporting the osteogenic potential of curcumin nanoparticle-coated titanium surfaces.

The findings suggest that curcumin nanoparticles may be promising for enhancing titanium implants' biocompatibility and osteogenic properties, with potential implications for improving dental and orthopaedic implant outcomes. However, further research, particularly in vivo studies and clinical trials, is essential to validate these findings and gain a more comprehensive understanding of the translational potential of this surface modification strategy.

Condition being studied Osteogenesis, the process of new bone formation, is crucial for the successful integration of orthopaedic and dental implants. It involves the differentiation of mesenchymal stem cells into osteoblasts, which then produce and mineralize the bone matrix. In implant dentistry and orthopedics, enhanced osteogenesis around the implant surface leads to better osseointegration, the direct structural and functional connection between living bone and the implant surface. This process is critical for implant stability and long-term success. However, the rate and quality of osteogenesis can vary depending on factors such as implant surface properties, local bone quality, and the patient's overall health. The study examines how curcumin nanoparticles, when applied as a coating on titanium surfaces, might influence this osteogenic process. Curcumin, known for its anti-inflammatory and antioxidant properties, may enhance osteoblast activity, reduce inflammation, and promote a more favourable environment for bone formation. By systematically reviewing the literature on this specific surface modification technique, the study aims to elucidate its effectiveness in promoting osteogenesis, which could have significant implications for improving implant outcomes in orthopaedic and dental applications.

METHODS

Search strategy A comprehensive electronic search was performed using PubMed, Cochrane Central Register of Controlled Trials, and Google Scholar databases up to March 2024, with no lower date limit. The search strategy included combinations of controlled terms (MeSH) and text words related to curcumin nanoparticles, titanium, surface modification, and osteogenesis.

Participant or population In-vitro studies analyzing osteogenicity after incorporating curcumin on titanium surfaces.

Intervention Curcumin-modified titanium discs.

Comparator Uncoated or hydroxyapatite-coated titanium discs.

Study designs to be included Experimental study design as it includes on in vitro studies only.

Eligibility criteria The PICOS (Population, Intervention, Comparison, Outcome, Study design) criteria were employed to define the eligibility criteria for this systematic review:

- Population: In vitro studies analyzing osteogenicity after incorporating curcumin on titanium surfaces.
- Intervention: Curcumin-modified titanium discs.
- Comparison: Uncoated or hydroxyapatite-coated titanium discs.
- Outcome: Cell adhesion, proliferation, osteogenic differentiation, and mineralisation.
- Study design: Original research articles published in English.

Inclusion criteria: Original research articles published in English that investigated the effects of curcumin nanoparticles on titanium surface modification in an in vitro setting.

Exclusion criteria: Review articles, case reports, conference abstracts, editorials, in vivo or clinical studies, and studies that did not involve curcumin nanoparticles or titanium surface modification.

Information sources A comprehensive electronic search was performed using PubMed, Cochrane Central Register of Controlled Trials, and Google Scholar databases up to March 2024, with no lower date limit. The search strategy included combinations of controlled terms (MeSH) and text words related to curcumin nanoparticles, titanium, surface modification, and osteogenesis.

Main outcome(s) The main outcome of the study Cell adhesion, proliferation, osteogenic differentiation, and mineralization.

Quality assessment / Risk of bias analysis The quality assessment of the included studies was performed using the SciRAP (Science in Risk Assessment and Policy) method (Roth et al., 2021). This method was chosen for its comprehensive evaluation of relevance, reporting quality, and methodological quality in toxicological and ecotoxicological studies.

Strategy of data synthesis For our systematic review on the effectiveness of curcumin nanoparticle-coated titanium surfaces in osteogenesis, a comprehensive data synthesis strategy with a qualitative approach will be employed. Two reviewers extracted data independently using a pre-designed Microsoft

Excel spreadsheet. Extracted data included titanium disc characteristics, curcumin concentration, incorporation method, cell type, osteogenicity assessment tests, key findings, and outcomes.

Author 3 - Tuomas Waltimo.
Email: tuomas.waltimo@gmail.com
Author 4 - Timo Sorsa.
Email: timo.sorsa@helsinki.fi
Author 5 - Sukumaran Anil.
Email: drsanil@gmail.com

Subgroup analysis Subgroup analyses will not be conducted in this study. Given the specific focus of the research question and the anticipated heterogeneity in study designs and outcome measures, it has been determined that subgroup analyses would not provide meaningful or reliable insights. Instead, focus on a comprehensive narrative synthesis of the included studies, presenting the findings in a clear and structured manner that highlights the overall trends and patterns in the effectiveness of curcumin nanoparticle-coated titanium surfaces in osteogenesis. This approach will allow to provide a holistic overview of the current state of research without potentially overinterpreting limited data through subgroup comparisons.

Sensitivity analysis Sensitivity analyses will not be conducted in this review. Given the nature of the research question on curcumin nanoparticle-coated titanium surfaces in osteogenesis and the expected variability in study designs and outcome measures, it was determined that sensitivity analyses would not provide additional meaningful insights. The focus will be on presenting a comprehensive narrative synthesis of the included studies, carefully considering the quality and characteristics of each study in our interpretation. This approach will allow for a more nuanced understanding of the current evidence without potentially introducing bias through selective analyses. By refraining from sensitivity analyses, the aim is to present a clear and straightforward assessment of the available literature, acknowledging the limitations and heterogeneity inherent in this emerging field of research.

Language restriction Studies in English language will be included in the study.

Country(ies) involved Qatar, Finland, India.

Keywords Curcumin nanoparticles; Titanium; Surface modification; Osteogenesis; Cell adhesion; Cell proliferation; Osteogenic differentiation; Mineralization.

Contributions of each author

Author 1 - Nandita Suresh.
Email: nandita.suresh@helsinki.fi
Author 2 - Matti Mauramo.
Email: matti.mauramo@helsinki.fi