Immunomodulatory Hydroxide Layered Nanoparticles for Local Periodontal Therapy

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Introduction

Periodontal and peri-implant diseases (PDPIs) are chronic inflammatory conditions driven by biofilms and an exacerbated host immune response, leading to tissue destruction and **implant failure** (1).
Conventional therapies fail to control inflammation, highlighting the need for local immunomodulatory strategies. Current standard therapies focus on mechanical debridement and antibacterial regimens, with limited emphasis on immunomodulation.

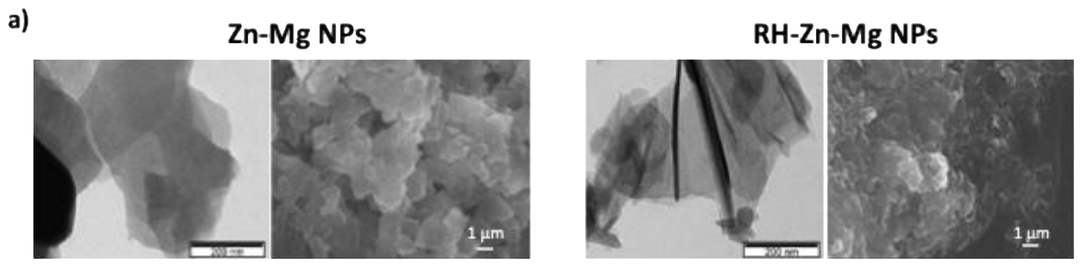
Objective: To develop **zinc-magnesium layered hydroxide nanoparticles** loaded with **rosehip**, an anti-inflammatory and antioxidant phytochemical (2).

Methods

Layered zinc-magnesium hydroxide nanoparticles (Zn-Mg NPs) were synthesized and doped with rosehip (RH) extract.
NPs were characterized for **crystalline** structure, **ionic composition**, **surface charge**, and **morphology.**
Cytocompatibility was assessed using human gingival fibroblasts (HGFs).
Antioxidant activity was evaluated via free radical scavenging assays.
Anti-inflammatory effects were analyzed by quantitative PCR of *IL1B, IL6*, and *NFkB1* in HGF monocultures and a 3D organotypic oral mucosal model.

Results

Zn-Mg NPs displayed a **nanolayered** zinc hydroxide structure with a plate-like morphology (**Fig. 1a**). The presence of RH phytochemicals was confirmed by the detection of polyphenols (**Fig. 1b**), further resulting in decreased particle size, surface charge (**Fig. 1c**), and lower crystallinity (**Fig. 1d**). Both NPs were cytocompatible at 1 and 10 µg/mL, and cytotoxic at 50 µg/mL (**Fig. 2a**). Only RH NPs displayed ROS scavenging capabilities (**Fig. 2b**).
NPs' anti-inflammatory activity (**Fig. 2c and 2d**), the expression of *IL1, IL6,* and *NFkB1* genes was significantly downregulated by both NPs, but RH-Zn-Mg NPs displayed a **superior efficacy in downregulating** all assessed pro-inflammatory genes in the 3D mucosal model, achieving values comparable to those of LPS-untreated cultures.



b)

Element (At %)	ZM	RH-ZM
N 1s	7.6	3.6
C 1s	22.8	39.1
Polyphenols	0	225.9

c)

	Size (nm ± SD)	ZP (mV ± SD)
Zn-Mg	1680 ± 38	37 ± 1.2
RH-Zn-Mg	815 ± 73	-12 ± 0.3

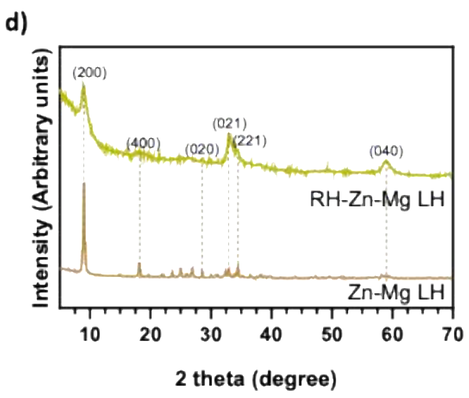


Fig. 1. Physicochemical characterization of Zn-Mg NPs: a) morphology (TEM), b) chemical composition (XPS), c) size and surface charge (DLS), d) crystallinity (XRD).

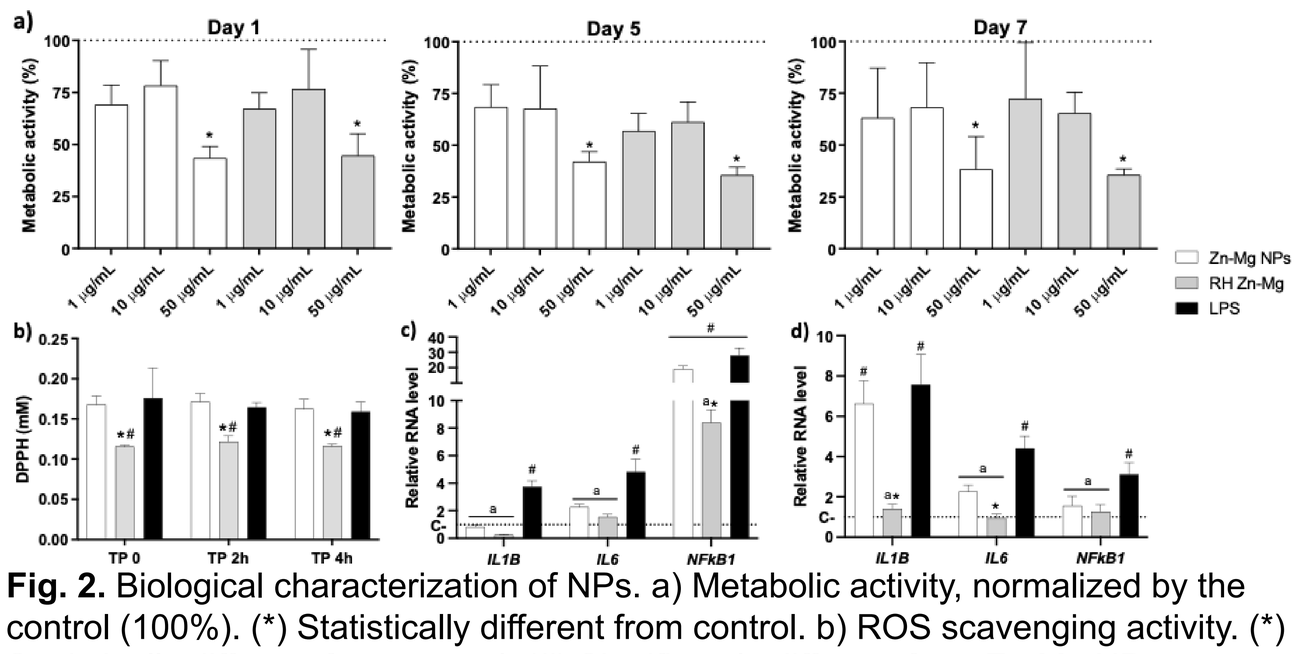


Fig. 2. Biological characterization of NPs. a) Metabolic activity, normalized by the control (100%). (*) Statistically different from control. b) ROS scavenging activity. (*) Statistically different from control; (#) Significantly different from Zn-Mg NPs group. Anti-inflammatory activity of NPs in c) HGF cultures and d) in 3D organotypic mucosal model. (#) different from negative control; (*)Different from Zn-Mg NPs; (a) Different from LPS. $p<0.05$.

Conclusions

Rosehip-doped layered Zn-Mg hydroxide NPs exhibit favorable physicochemical properties, cytocompatibility, and enhanced immunomodulatory activity, supporting their potential as local controlled release systems for the treatment of periodontal and peri-implant diseases.

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