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 tisPsue 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).

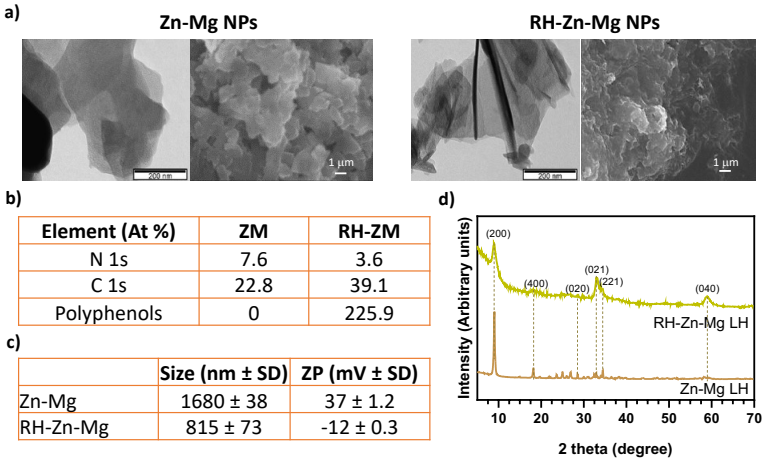
Antioxidant activity was evaluated via free radical scavenging assays.

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.



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

	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).

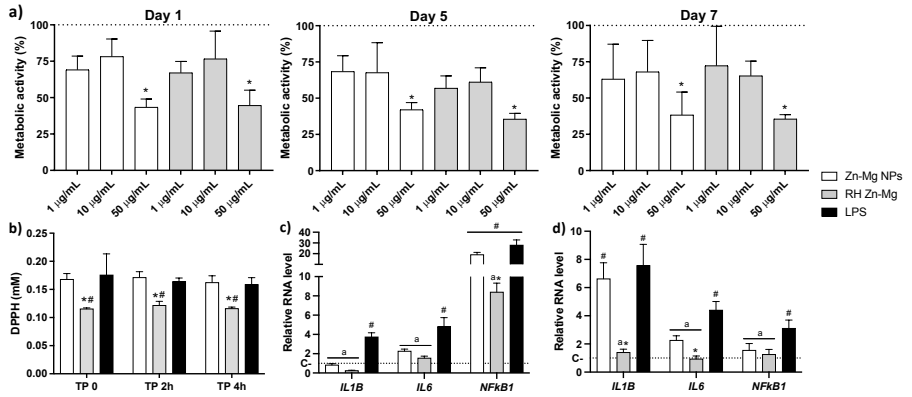


Fig. 2. Biological characterization of NPs. a) Metabolic activity, normalized by the control (100%). (*) Statistically different from control. b) ROS scavenging activity. (*) Statistically different from control; (#) Significantly different from Zn-Mg NPs group. Anti-inflammatory activity of NPs in c)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

Conclusion

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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