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Thermo-Responsive Mucoadhesive Nanocarrier Systems for Localized Periodontitis Therapy: Development, Characterization, and Biopharmaceutical Evaluation

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Background: Periodontitis is a chronic inflammatory disease characterized by microbial infection–driven tissue destruction, where effective local drug delivery remains challenging due to limited retention and rapid clearance from periodontal pockets. Nanostructured lipid carriers (NLCs) and *in situ* gelling systems offer a promising strategy to enhance localized, sustained therapy.

Methods: In this study, apigenin (AP) and clove essential oil (CEO) were co-incorporated into NLCs, which were subsequently embedded in thermoresponsive polymer *in situ* gels at varying polymer concentrations. The formulations were comprehensively characterized for particle size, morphology, thermal behavior (DSC), chemical distribution (Raman mapping), rheological and gelling properties, mucoadhesion, and *in vitro* drug release kinetics.

Results: TEM and DSC analyses confirmed the successful formation of spherical, well-dispersed NLCs present in an amorphous state. Incorporation of NLCs significantly enhanced gel strength, reduced gelation time, and slightly increased gelation temperature compared to blank polymeric gels. Mucoadhesive testing demonstrated a concentration-dependent increase in adhesive force and work of adhesion, with NLC-loaded gels exhibiting up to a two-fold improvement over corresponding blank formulations. *In vitro* release studies revealed sustained AP release from NLCs and NLC-loaded gels over 48 hrs, following predominantly Korsmeyer–Peppas kinetics, indicative of diffusion-controlled transport mechanisms. **Conclusions:** The developed AP and CEO loaded NLC-based *in situ* smart gels exhibit favorable physicochemical properties, strong mucoadhesion, and prolonged drug release, highlighting their potential as an effective localized delivery system for periodontal therapy.

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