Title: "Topical Wound - Care Formulation of Carbopol Hydrogel Loaded with Ellagitannin mediated Selenium Nanoparticles for management of Multidrug resistant wound infections"

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Abstract:

The increased frequency of chronic and infected cutaneous wounds, compounded by the global development of antibiotic resistance, has escalated the hunt for sustainable, multifunctional wound-care materials. Fruit-processing by-products such as pomegranate (*Punica granatum* L.) peel, rich in ellagitannins, gallotannins and flavonoids, offer an affordable and renewable feedstock for the green manufacture of therapeutically active nanomaterials. In the present investigation, selenium nanoparticles (PgpSeNPs) were phytofabricated by reducing sodium selenite with an aqueous Punica granatum peel (Pgp) extract acting simultaneously as a reducing and capping agent. The optimised nanoparticles were later integrated into Carbopolbased hydrogels at varied concentrations (PgpSeNHG) to improve topical application and residence time on the wound bed.

The nanoparticles and nanohydrogels were comprehensively characterised using UV–Visible spectroscopy, Fourier-transform infrared (FTIR) spectroscopy, dynamic light scattering (DLS) and zeta potential analysis, field-emission scanning electron microscopy with energydispersive spectroscopy (FESEM-EDS), thermogravimetric analysis (TGA), differential scanning calorimetry (DSC), X-ray diffraction (XRD), and oscillatory rheometry. Antimicrobial activity was tested by disc-diffusion and broth microdilution (MIC) assays against therapeutically relevant bacterial and fungal pathogens. Biocompatibility was examined using the MTT assay on L929 fibroblast cells, while the wound-healing capacity of the nanohydrogels was investigated in Wistar rats employing excision and incision wound models, with a commercially available wound-healing gel employed as the reference standard. The plant-mediated selenium nanoparticles displayed higher antibacterial activity compared with the crude plant extract and precursor solution, and the nanohydrogel formulations preserved their antimicrobial efficacy while displaying improved biocompatibility for topical application.

Furthermore, *in vivo* investigations demonstrated quicker wound healing, greater collagen deposition, improved tissue regeneration, and favourable histopathological characteristics, including fibroblast proliferation, neovascularisation, and re-epithelialization. Overall, the findings demonstrate that the Punica granatum peel-derived selenium nanoparticle nanohydrogel is a promising biocompatible, antimicrobial, and pro-regenerative topical formulation with significant translational potential as a sustainable and cost-effective alternative for wound management.