**Objectives:** *Candida* infections are increasingly common and linked to serious health issues. Treatment options for candidiasis are limited by antifungal resistance, drug interactions, side effects, and toxicity. Cinnamaldehyde (CIN), a potent natural antifungal phytocompound, faces clinical challenges due to poor solubility, bioavailability, and toxicity, but remains a promising candidate for novel anti-Candidal therapies.

In the present study, we synthesized and characterized cinnamaldehyde-loaded gelatin nanoparticles (GNPs) and evaluated their *in-vitro* anti-candidal efficacy against *Candida albicans* (ATCC 3017). Furthermore, we investigated the anti-Candidal activity of CIN-loaded GNPs against vaginal candidiasis in Swiss albino mice.

**Materials and Methods:** Gelatin nanoparticles were synthesized and subsequently lyophilized. The synthesized GNPs were characterized using UV-Visible spectroscopy, Fourier-transform infrared (FT-IR) spectroscopy, Raman spectroscopy and scanning electron microscopy (SEM) to confirm their structural and morphological properties. CIN was then loaded onto the surface of the synthesized GNPs. Anti-candidal activity of CIN loaded GNPs against *Candida albicans* (ATCC 3017) through the disc diffusion method (CLSI guidelines) was conducted. Further*, in-vitro* hemocompatibility and cytotoxicity of CIN loaded GNPs were evaluated. Furthermore, the *in-vivo* efficacy of CIN-loaded GNPs was assessed in a mouse model of vaginal candidiasis. Vaginal candidiasis was induced in Swiss albino mice under pseudo-estrus conditions. After confirming persistent infection following *C. albicans* challenge, CIN loaded GNPs was administered orally. Treatment efficacy was assessed by CFU counts in vaginal smears, fungal load (blood, ovaries, and vaginal tissues), PAS staining of vaginal sections, and evaluation of hematological parameters to determine systemic impact.

**Results:** After lyophilization, a powdered form of GNPs was obtained. UV-Vis and FT-IR spectra indicating preserved gelatin structure. SEM images showed irregular, lumpy particles with varied sizes. Raman spectra confirmed protein backbone and amide vibrations, validating successful GNP synthesis and gelatin modification. Overall, the results confirmed effective nanoparticle formation. CIN-loaded GNPs exhibited strong antifungal activity against *Candida albicans*, with significant zones of inhibition. Hemolysis assays revealed a concentration-dependent increase in RBC lysis with compared to CIN. Cytotoxicity studies showed reduced WBC and splenocyte viability at higher concentrations, while lower concentrations demonstrated improved cell viability, indicating a dose-dependent safety profile of the CIN-loaded GNPs.

CIN-loaded GNPs effectively treated vaginal candidiasis in mice, eliminating *C. albicans* from vaginal lavages and reducing fungal loads in vaginal and ovarian tissues. Treated groups showed normalized WBC counts and restored tissue building. CIN-loaded GNPs restored vaginal histology to normal, unlike fluconazole (control) and CIN groups, which showed mild epithelial thickening. These findings highlight CIN-loaded GNPs as a promising and safe antifungal therapy. The hematological parameters (RBC count, WBC count, and hemoglobin percentage) showed significant improvement in treatment groups compared to infected controls.

**Conclusion:**

CIN-loaded GNPs showed better efficacy against vaginal candidiasis by overcoming limitations of native cinnamaldehyde. With no observed tissue pathology, GNPs showed promise for safer, targeted antifungal therapy. Moreover, it paves the way for translating CIN-loaded GNPs from experimental research to clinical application or from “bench to bedside”.Top of FormBottom of Form