Novel formulated nanocomposite containing Indolicidin and Graphene Oxide against *Candida albicans*: in vitro and in vivo study

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Objectives: Candidiasis is one of the most important opportunistic fungal infections in immunocompromised patients. The emergence of multidrug-resistant *Candida* species necessitates the development of novel antifungal agents. Seeking to the discovery of natural antifungal agents, this study aimed to synthesize a novel formulated nanocomposite containing Indolicidin (IN), antimicrobial peptide, and Graphene Oxide (GO), kind of nanomaterial, against *Candida* growth using in vitro and in vivo experiments for the first time.

Methods: The IN peptide was conjugated with the GO. The formulated nanocomposite (GO-IN) was characterized using Scanning electron microscopy, equipped with an energy dispersive X-ray accessory, X-ray power diffraction, and Fourier transform infrared method analysis. The in vitro antifungal activity of fluconazole (FLU), GO, IN, and GO-IN was determined against *Candida albicans* (*C. albicans*) Compared to control groups. Cell cytotoxicity assay against intestinal epithelial cells (IEP) and hemolytic activities of GO-IN were performed. Moreover, in vivo experiments of nanocomposite efficacy were assessed in BALB/c mice infected with disseminated candidiasis.

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Results: Our results showed that nanocomposite had the highest inhibitory effect against *C. albicans* (MIC 3.12 µg/mL) compared with Flu (MIC 4 µg/mL), IN (MIC 12.5 µg/mL), and GO (MIC 6.25 µg/mL). The formulated nanocomposite had a low cytotoxic effect at the tested concentration ($p < 0.05$). The hemolytic activity of nanocomposite considered as 2.73%. For in vivo experiments, infected mice were successfully treated with GO-IN once a day within 7 days. GO-IN treated group eliminated the *Candida* infection in the spleen and liver of BALB/c mice ($P = 0.001$) similar to fluconazole. Although there was no significant difference in histological manifestations between Flu and GO-IN groups, these manifestations were greater in GO-IN group than Flu group.

Conclusion: Altogether, our finding suggests that synergistic combination of GO and IN provide a new option, representing a potential therapeutic efficiency against disseminated candidiasis in an animal model as well as might be used as adjunct therapy in the management of candidiasis.

However, further investigation is needed to evaluate the efficacy of the nanocomposite.

Keywords: Indolicidin; Graphene Oxide; Nanocomposite; disseminated candidiasis; BALB/c