

ABSTRACT

Wound infections have become a serious threat at the global level due to biofilm forming bacterial pathogens. There is a need for the development of alternative strategies to prevent complications of drug resistance. Natural compounds have been a prime choice for microbial treatment but have a poor pharmacokinetic profile. To circumvent these challenges, a suitable drug delivery system is of paramount importance, utilizing the host-guest complexation to protect the drug from premature degradation and deactivation. Hence, the current study was designed to explore the host-guest inclusion complexes for the prevention and treatment of wound infections. Isatin, an alkaloid isolated from the *Couroupita guianensis* Aubl. flower, was selected as the drug molecule owing to its traditional use in treating various infections. Likewise, pillar[5]arenes (P[5]A) and bis-ethanolamine functionalized pillar[4]arene[1]quinine (BEA) were selected as supramolecular hosts to capture isatin into their electron-rich cavities to reinforce the controlled release and targeted activity. The pharmacokinetic profiles of the selected hosts revealed their potential druggable nature. The synthesized P[5]A and BEA were characterized by proton NMR and UV-visible spectroscopy which revealed that P[5]A exhibited a superior capacity to encapsulate isatin in comparison with BEA. Job's plot analysis validated the 1:1 binding stoichiometry between P[5]A and isatin, highlighting the specificity and stability of the formed complexes. Further, the synthesized P[5]A-isatin inclusion complexes showed enhanced antibacterial properties and exhibited strong membrane-damaging potential. P[5]A-isatin inclusion complexes have proved their antibiofilm potential against *Staphylococcus aureus* and *Pseudomonas aeruginosa*. The isatin was found to be released from the P[5]A-isatin inclusion complexes in a controlled manner as validated by various mathematical models. The formulated P[5]A-isatin inclusion complexes based ointment showed significant wound healing effects *in vitro* with 90% wound closure within 48 hours and was found to be non-toxic. Conclusively, the synthesized pillar[5]arene-isatin inclusion complexes have proved to be unique for combating wound infections and promoting the wound healing processes in an effective manner.

Keywords: Biofilms, Controlled drug release, Isatin, Pillar[5]arene, Wound healing.