

Targeting Acanthamoeba proteins interaction with flavonoids of Propolis extract by in vitro and in silico studies for promising therapeutic effects

ABSTRACT

Background: Propolis is a natural resinous mixture produced by bees. It provides beneficial effects on human health in the treatment/management of many diseases. The present study was performed to demonstrate the anti-Acanthamoeba activity of ethanolic extracts of Propolis samples from Iran. The interactions of the compounds and essential proteins of Acanthamoeba were also visualized through docking simulation. Methods: The minimal inhibitory concentrations (MICs) of Propolis extract against Acanthamoeba trophozoites and cysts was determined in vitro. In addition, two-fold dilutions of each of agents were tested for encystment, excystment and adhesion inhibitions. Three major compounds of Propolis extract such as chrysin, tectochrysin and pinocembrin have been selected in molecular docking approach to predict the compounds that might be responsible for encystment, excystment and adhesion inhibitions of *A. castellanii*. Furthermore, to confirm the docking results, molecular dynamics (MD) simulations were also carried out for the most promising two ligand-pocket complexes from docking studies. Results: The minimal inhibitory concentrations (MICs) 62.5 and 125 µg/mL of the most active Propolis extract were assessed in trophozoites stage of *Acanthamoeba castellanii* ATCC30010 and ATCC50739, respectively. At concentrations lower than their MICs values (1/16 MIC), Propolis extract revealed inhibition of encystation. However, at 1/2 MIC, it showed a potential inhibition of excystation and anti-adhesion. The molecular docking and dynamic simulation revealed the potential capability of Pinocembrin to form hydrogen bonds with *A. castellanii* Sir2 family protein (AcSir2), an encystation protein of high relevance for this process in Acanthamoeba. Conclusions: The results provided a candidate for the development of therapeutic drugs against Acanthamoeba infection. In vivo experiments and clinical trials are necessary to support this claim.