A bioconjugate of Hecate lytic peptide with gallic acid targeting different stages of Hepatitis C virus life cycle in genotype 2a and 3

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HCV infection is a global health problem, affecting approximately 185 million individuals globally. HCV research and treatment has entered a new era with the advent of direct-acting antiviral agents (DAAs). Despite that advances, the search for new compounds against HCV is still important aiming alternative therapies, cost reduction, treatment resistance, etc. The use of peptide with antiviral activity is a growing research area and has shown satisfactory results against much type of viruses. The aim of this study was to evaluate the antiviral activity of Hecate and the bioconjugate Gallic acid-Hecate in different stages of HCV life cycle, the toxicity in normal cells and the action mechanism. The peptides Hecate (FALALKALKKALKKLKKALKKAL) and his new conjugate (Gallic Acid-Hecate) were synthesized by solid phase peptide synthesis. Purification and characterization were performed by HPLC and mass spectrometry, respectively. An evaluation of toxicity in keratinocytes and liver cells by MTT methodology and replicative activity by luciferase assay suggest that GA-Hecate is more active than Hecate peptide in HCV (2a and 3) replication and less toxic in normal cells. Data obtained by BODIPY and biophysics assays with membrane mimetics (mainly cholesterol and phosphatidylcholine) showed that the conjugate can interact with lipids droplets (LDs) avoiding the replication of the virus inside of the cell. The CD measurements showed that GA-Hecate presented lower incidence of α-helical structures in the LDs mimetic, suggesting that the N-terminus modification of Hecate plays an important role in the antiviral activity of the peptide. Furthermore, GA-Hecate was capable to inhibit the virus entry and release, acting on the virus envelope. In summary, antiviral peptides may offer hope for the design more specific, potent and less expensive therapeutics to help prevent HCV infections.
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