Synthesis, characterisation and antioxidant properties of ferulate-based protic ionic liquids: experimental and modelling approaches

ABSTRACT

Active pharmaceutical ingredients (APIs) in the form of crystalline solid are commonly produced in drug manufacturing industries. However, crystalline solid APIs have a low solubility and the ability to cause polymorphism transformation. In order to overcome these problems, a modification of APIs in the form of protic ionic liquids (PILs) has been proposed. In the present study, a series of five ferulate-based PILs were successfully synthesised and characterised by appropriate spectral analysis. The antioxidant activity of synthesised PILs was determined through the 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging assays. The spectroscopy analysis confirmed the formation of PILs supported by the Density Function Theory (DFT) calculation. The synthesised ferulate-based PILs exhibited low EC_{50} ranging from 12.93 ± 0.05 to 17.40 ± 0.04 μM indicating a strong antioxidant activity compared to parent acid (EC_{50} of 21.40 ± 0.05 μM). Prediction of antioxidant activity of the PILs and their ionic interactions at the molecular level were studied by applying DFT calculation at B3-LYP/6-311G*** level and COSMO-RS. Based on the optimised geometry, the ion-pair of PILs formed a strong directional intermolecular hydrogen bond between the –NH group of the cation with the –COOH group of the anion with interaction energy of −111 to −120 kcal mol−1. Predicted antioxidant activity indicated that the PILs's cation has a weak interaction with an anion as observed from the σ-potential analysis.

Keyword: DFT calculation; COSMO-RS;Protic ionic liquids; Antioxidant; DPPH radical scavenging