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ORIGINAL RESEARCH

Molecular dynamics simulations, molecular docking, and kinetics study of kaempferol interaction on Jack bean urease: Comparison of extended solvation model

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Abstract

Since the urease enzyme creates gastric cancer, peptic ulcer, hepatic coma, and urinary stones in millions of people worldwide, it is essential to find strong inhibitors to help patients. Natural products are well known for their beneficial effects on health and efforts are being made to isolate the ingredients, the so-called flavonoids. Flavonoids are now considered as an indispensable component in a variety of nutraceutical, pharmaceutical, and cosmetic applications. Kaempferol (KPF) is an antioxidant found in many fruits and vegetables. Many reports have explained the significant effects of dietary KPF in reducing the risk of chronic diseases such as cancer, ischemia, stroke, and Parkinson's. The current study aimed at investigating the inhibitory impact of KPF on Jack bean urease (JBU) using molecular dynamics (MD) simulations and molecular mechanics Poisson–Boltzmann surface area (MM-PBSA) calculations to confirm the results obtained from isothermal titration calorimetry (ITC), extended solvation model, and docking software. In addition, UV–VIS spectrophotometry was used to study the kinetics of urease inhibition. Calorimetric and spectrophotometric determinations of the kinetic parameters of this inhibition indicate the occurrence of a reversible and noncompetitive mode. Also, the docking and MD results indicated that the urease had well adapted to the kaempferol in the binding pocket, thereby forming a stable complex. Kaempferol displayed low binding energy during MMPBSA calculations. The inhibitory potential of kaempferol was confirmed by experimental and simulation data, but in vivo investigations are also recommended to validate our results.

KEYWORDS
Jack bean urease enzyme, kaempferol, MD simulations, MM-PBSA, molecular docking