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Investigation of the interaction of caffeine with three selected drug molecules: A molecular modeling approach

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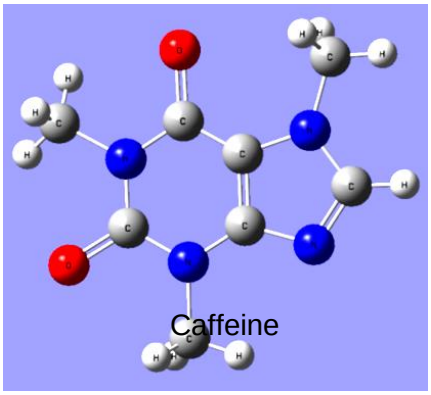
Caffeine is the most widely consumed psychoactive stimulant drug as a majority of the world's population consumes coffee and tea on a daily basis. It is an intensely bitter, odorless white crystalline xanthine alkaloid of plant origin. Caffeine possesses beneficial pharmacological actions as well as withdrawal effects on human health due to excessive ingestion.



Existing literature describes the affinity of caffeine to self-aggregate in aqueous environment and to form complexes with aromatic drug molecules. Upon complexation, the therapeutic efficacy of the drug molecules tends to reduce significantly.

Self- and hetero- interaction between caffeine and three drug molecules that are currently prescribed for cancer, diabetic and Alzheimer's diseases (Cytarabine, Dapagliflozin and Rivastigmine) were investigated using molecular dynamics (MD) techniques. GROMACS software package on a LINUX operating system was employed to perform the MD simulations and analysis of the MD trajectories. The MD simulations were carried out for 40 ns in each molecular system containing two or four molecules (however with the same concentration) under isothermal-isobaric condition maintaining the temperature and pressure at 300 K and 1 bar, respectively. The analysis of data incorporating techniques such as center-of-mass distances variation, correlation of interaction energies, studying the free energy of complex formation, diffusion coefficient and surface accessibility leads to the determination of caffeine-drug complexation ability. Significant interactions of caffeine with cytarabine, dapagliflozin and rivastigmine were not observed in the current study. Therefore, it may be concluded that under low caffeine concentrations, caffeine consumption has no impact on the activity of the above three drugs.

Keywords: Caffeine-drug interactions, molecular dynamics.

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