Interaction of anticancer drug clofarabine with human serum albumin and human -1 acid glycoprotein. Spectroscopic and molecular docking approach

Mohammad Rehan Ajmal , Saima Nusrat , Parvez Alam , Nida Zaidi , Mohsin Vahid Khan , Masihuz Zaman , Yasser E. Shahein , Mohamed H. Mahmoud , Gamal Badr , Rizwan Hasan Khan

Abstract:

The binding interaction between clofarabine, an important anticancer drug and two important carrier proteins found abundantly in human plasma, Human Serum Albumin (HSA) and -1 acid glycoprotein (AAG) was investi gated by spectroscopic and molecular modeling methods. The results obtained from fluorescence quenching ex periments demonstrated that the fluorescence intensity of HSA and AAG is quenched by clofarabine and the static mode of fluorescence quenching is operative. UV vis spectroscopy deciphered the formation of ground state com plex between anticancer drug and the two studied proteins. Clofarabine was found to bind at 298 K with both AAG and HSA with the binding constant of 8.128 × 10 and 4.120 × 10 for AAG and HSA, respectively. There is stronger interaction of clofarabine with AAG as compared to HSA. The Gibbs free energy change was found to be negative for the interaction of clofarabine with AAG and HSA indicating that the binding process is sponta neous. Binding of clofarabine with HSA and AAG induced ordered structures in both proteins and lead to molec ular compaction. Clofarabine binds to HSA near to drug site II. Hydrogen bonding and hydrophobic interactions were the main bonding forces between HSA-clofarabine and AAG-clofarabine as revealed by docking results. This study suggests the importance of binding of anticancer drug to AAG spatially in the diseases like cancers where the plasma concentration of AAG increases many folds. Design of drug dosage can be adjusted accordingly to achieve optimal treatment outcome.

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