Molecular Insights into Dapagliflozin–Albumin Binding: Evidence from Dsc, Itc, and Fluorescence Spectroscopy

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Abstract

Dapagliflozin (Forxiga), a selective sodium–glucose co-transporter 2 (SGLT2) inhibitor, is widely prescribed for type 2 diabetes and increasingly for heart failure and chronic kidney disease. Its pharmacokinetics are strongly influenced by plasma protein binding, particularly to human serum albumin (HSA), the predominant carrier protein. However, detailed molecular insights into this interaction remain scarce. This study investigated the binding characteristics of dapagliflozin with HSA, focusing on affinity, thermodynamics, and conformational effects. Purified HSA was incubated with dapagliflozin. Differential Scanning Calorimetry (DSC) assessed thermal stability changes. Isothermal Titration Calorimetry (ITC) determined binding affinity, enthalpy, and stoichiometry. Fluorescence spectroscopy evaluated intrinsic tryptophan quenching to monitor conformational changes. DSC revealed increased HSA thermal stability upon drug binding. ITC indicated a defined 1:1 binding stoichiometry with moderate affinity, governed predominantly by enthalpic contributions. Fluorescence quenching confirmed close contact between dapagliflozin and HSA, with detectable conformational alterations. These complementary biophysical approaches demonstrate that dapagliflozin binds specifically and moderately to HSA, stabilizing its structure while inducing subtle conformational changes. The findings provide mechanistic insights into dapagliflozin's pharmacokinetic behavior in circulation and reinforce its clinical relevance.

Keywords

Dapagliflozin, Human serum albumin, SGLT2 inhibitor, DSC, ITC, Fluorescence spectroscopy.

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