Abstract No.3

Comparative Studies on PSH, Drug Binding Characteristics and Conformational Stability of Native and Modified Forms of Bovine Serum Albumin

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Interaction of drugs with proteins, especially Serum albumin (SA), has a great significance in pharmacology. SA can affect the biological activity and toxicity of drug. The binding parameters are helpful in the study of pharmacokinetics and the design of therapeutic dosages. Determination of the impact of various factors such as chemical modifications which may occur in vivo is also important when drug binds with albumin to a significant degree. In this study, the effect of some modifications on protein stability, surface hydrophobicity and interaction with furosemi dewas investigated by intrinsic and extrinsic fluorescence techniques at physiological conditions. Bovine serum albumin (BSA) has been chemically modified with Citraconic anhydride and Sodium hypochlorite under nondenaturing conditions. The Job's plot indicated that drug binds to the native and modified BSAs with 1:1 stoichiometry. Binding constants underwent 11% increase and 73% decrease upon citraconylation and oxidation, respectively. Additionally, stability of oxidized and citraconylated BSA showed 50% decrease and 30% increase, respectively. Thermodynamic analyses of the binding process suggested that the major forces involved in the interaction of furosemide to native and oxidized BSA are hydrophobic, whereas drug mainly binds to citraconylated form v iahydrogen bonds and van der waals interactions. Changes in the protein surface hydrophobicity (PSH), were also investigated. We will discuss the importance of PSH and stability in citraconylated/oxidized BSA and their effects on the furosemide binding characteristics.

Keywords: Bovine Serum Albumin, Furosemide, Binding Site, Fluorescence Quenching, Protein Surface Hydrophobicity, Conformational Stability.

Abstract No.4

Comparative Studies on Drug Binding Characteristics and Protein Surface Hydrophobicity of Native and Modified forms of Bovine Serum Albumin: Possible Relevance to Change in Protein Structure Upon Glycation

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The interaction between serum albumin (SA) and drugs has provided an interesting ground for understanding of drug effects, especially in drug distribution and drug–drug interaction on SA, in the case of multi-drug therapy. Determination of the impact of various factors on drug–protein interaction is especially important upon significant binding of drug to albumin. In the present study, the interaction of two drugs (furosemide and indomethacin) with native and modified albumins were investigated by using various spectroscopic methods. Fluorescence data indicated that 1:1 binding of drugs to bovine serum albumin (BSA) is associated with quenching of albumin intrinsic fluorescence. The Job's plot also confirmed that drug binds to BSA via mentioned stoichiometry. Analysis of the quenching and thermodynamic parameters indicated that intermolecular interactions between drug and albumin may change upon protein modification. The theoretical analyses also suggested some conformational changes of interacting side chains in subdomain IIA binding site (at the vicinity of W237), which were in good agreement with experimental data. Decrease of protein surface hydrophobicity (PSH) was also observed upon both albumin modification and drug binding.

Keywords: Protein Hydrophobicity, Bovine Serum Albumin, Binding Site, Glycation.
