REACTIVE ALDEHYDES INDUCE STRUCTURAL CHANGE AND DISFUNCTION OF HUMAN SERUM ALBUMIN

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Purpose: We previously reported that in vitro glycation of human serum albumin (HSA) with D-glucose alters its biological structure and ligand binding property. Furthermore, it is known that reactive aldehydes generated from several pathways such as glycolysis, inflammation and glycation play an important role in the protein modification. However, little is known about the effect of these aldehydes on the structure and function of proteins. The aim of this study was to investigate the effect of several aldehydes on HSA in terms of the physicochemical properties and function.

Methods: We prepared aldehyde-modified HSA (AM-HSA) by incubating HSA with several reactive aldehydes such as glyoxal, methylglyoxal, glycolaldehyde, glyceraldehyde, glucosone, and 3-deoxyglucosone, and then assessed the effect of these aldehydes on the structure and function of HSA.

Results and Discussion: Although the molecular weight and the net negative charge of AM-HSA were increased by modification with all aldehydes, especially the increase in the negative charge of AM-HSA prepared by glycolaldehyde and glyceraldehyde was significantly higher than the others. To evaluate the influence of aldehydes modification on the function of HSA, we examined the binding of warfarin to AM-HSA. The binding of warfarin to HSA was significantly decreased (about 80%) by modification with methylglyoxal, whereas glyceraldehyde showed relatively weak effect (about 30%).

Conclusions: The property of HSA modification is dependent on the variety of aldehydes, and methylglyoxal may play a role in the functional deterioration of HSA.

PHARMACOKINETIC STUDY OF ENCLOSED HEMOGLOBIN AND OUTER LIPID COMPONENT AFTER THE ADMINISTRATION OF HEMOGLOBIN VESICLES AS AN ARTIFICIAL OXYGEN CARRIER

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Purpose: Hemoglobin-vesicle (HbV) is an artificial oxygen carrier that encapsulates a concentrated Hb solution in lipid vesicles and has considerable promise for use in clinical setting. Despite the large body of pharmacological evidence for HbV, little is known concerning its pharmacokinetic properties, especially the fate of HbV components, such as internal Hb and lipid membrane. Therefore, in this study, the pharmacokinetic properties of HbV components were investigated in mice and rats.

Methods: The internal Hb and liposomal cholesterol were radiolabeled with iodine-125 (125I-HbV) and tritium-3 (3H-HbV), respectively. The ddY mice and SD rats received a single injection of 125I-HbV or 3H-HbV at a dose of 1400 mg Hb/kg containing 5% rHSA.

Results and Discussion: The time courses for the plasma concentration curves of 125I-HbV and 3H-HbV suggest that HbV maintain an intact structure in the blood circulation. 125I-HbV and 3H-HbV were distributed mainly to the liver and spleen. Internal Hb disappeared from both the liver and spleen 5 days after injection, and the liposomal cholesterol disappeared at approximately 14 days. Internal Hb was excreted into the urine and cholesterol into feces via biliary excretion. Based on the present findings, we propose the pharmacokinetic properties of HbV and its components, and these provide further support for the effectiveness and safety of the HbV for use as an oxygen carrier.