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Investigation of Dexamethasone Interactions with Blood Plasma Proteins by Isothermal Titration Calorimetry (ITC) and Differential Scanning Calorimetry (DSC)

Anelia Zasheva, **Silviya Abarova**, **Boris Tenchov**

Department Medical Physics and Biophysics, Medical University – Sofia

Indroduction. Characterization of the thermodynamics of drug binding with human blood serum (HBS) proteins is of essential importance for a better understanding of drug absorption, distribution and turnover in the circulation. Human serum albumin (HSA), the most prominent protein in plasma, plays a fundamental role in the transport of drugs. Dexamethasone (DM) is a medication, corticosteroid, used to treat various diseases and allergic states.

In this work, we used Isothermal Titration Calorimetry (ITC) and Nano Differential Scanning Calorimetry (DSC) to investigate the energetics of DM binding to HBS proteins.

ITC is a thermodynamic technique for directly measuring the heat change of the molecular interactions. The Nano DSC has the versatility and precision for characterizing molecular stability, and determining high affinity ligand binding..

The aim of this study is to characterize the mechanism of DM interaction with HBS proteins, in particular, with HSA.

Materials and Methods. The thermal effects of dexamethasone binding to HBS from healthy volunteers and to HSA (Sigma Aldrich) was examined by ITC (Nano ITC, TA Instruments). ITC measurements were conducted in 0.05 mM PBS (pH 7.4). The sample cell was filled with 10 μM HSA, and a HBS, respectively. The 250 μl injection syringe was loaded with 0.5 mM solution of DM. The DM solution was injected 25 times in 10 μl increments with 400 s intervals into the isothermal cell. The titration process was computer-controlled. The cell temperature was kept at 37°C.

After ITC measurement, the sample and reference were loaded into the cells of DSC. Scans were performed immediately with a temperature increase from 20°C to 110°C at a scanning rate of 1°C/min, under a pressure of 3 atm.

Results. The ITC measurements demonstrate high binding affinity of DM to HBP proteins and to HSA as evidenced by the exothermic thermal

effects. The differences, recorded by DSC, between the thermal denaturation of the proteins in HBS and HSA, as well as the thermograms of the drug-protein complexes suggest preferential binding of DM by albumin.

Conclusion. The present study helps to better understand the binding mechanism of dexamethasone with major BP proteins and suggests preferential binding of DM to albumin.