Dipyrone Interacts Better With Serum Albumina at 37^0C than 45^0C.

Yamakami, L.C., Alencar, C.F.O., Moreira, D.C.A., Schneedorf, J.M.

Lab. Bioquímica, Dept. Ciências Exatas, Universidade Federal de Alfenas, Alfenas-MG

Dypirone (Metamizole) is a well-known painkiller drug used in developing countries, although little information concerning its binding properties with serum albumin are depicted. Dypirone was incubated with bovine serum albumin (BSA) in 50mM phosphate buffer pH 7.45 containing 150mM NaCl, with varying both protein and ligand concentrations. The interaction was followed during 60min by UV-difference spectra at 10, 22, 25, 37, 45 and 65^0C in a ultrathermostated cell. A red-shift was found with protein concentration. Binding isotherms at 279nm showed a non-asymptotic character with ligand concentration but a sigmoidal trend with protein increase, presenting n = 3 non-interacting binding sites and an apparent association constant of 183.9±5.8 μM for the complex. BSA-dipyrone complexes showed a higher absorbance differences with increasing ionic strength, although there was no mean differences found in the 0.8-5.0% NaCL range. Van´t Hoff analysis presented a bimodal view with the reciprocal of temperature. In this sense, at low dypirone concentration, thermodynamic quantities for the bound ligand were ΔH^0=-1.9 kJ·mol, ΔS^0=75.4 J/mol· K^{-1}, whereas at high ligand concentration it were presented ΔH^0=4.1 kJ·mol, ΔS^0=95.0 J/mol· K^{-1}. These data suggested an enthalpic-driven mechanism for the complex formation with electrostatic contribution, following by an entropy-driven mechanism at higher temperatures. Interestingly, the break point for the binding mode was found at 37^0C, decreasing the binding strength beyond this value.

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