THE EXCHANGE RATE OF THE THIOL LIGAND OF $iPr_3PAuSATg$ WITH THE CYS-34 RESIDUE OF BOVINE SERUM ALBUMIN

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Auranofin [$Et_3PAuSATg$ =triethylphosphine-(2,3,4,6-tetra-O-acetyl-1-thio- β -D-glucopyranosato-S)-gold(I)] is an antiarthritic drug. Its metabolism includes two ligand displacements at gold(I). A reversible displacement of the thiol ligand of the drug by the Cys-34 residue of serum albumin is observed as a first step in the *in vitro* reactions of the drug and albumin. This reversible feature may facilitate gold(I) transfer from site to site *in vivo*. To investigate the rate of this thiol ligand exchange, a ^{31}P NMR saturation transfer study was performed. In order to minimize the side reaction in which phosphine is displaced and oxidized, $iPr_3PAuSATg$ [iPr_3 =tri(iso)propyl] was used instead of auranofin:

The results show that the forward ($k_f = 0.12 \times 10^{-3} \text{ M}^{-1} \text{ s}^{-1}$) and reverse ($k_r = 0.39 \times 10^{-4} \text{ M}^{-1} \text{ s}^{-1}$) rates occur at a similar order of magnitude. As expected, since the protein thiol, Cys-34, has a higher affinity than the tetraacetyl thioglucose for gold(I), the forward reaction is more rapid than the reverse reaction. The equilibrium constant for the reaction calculated from the rate constants, $K_{eq} = 3.1$, is smaller than expected for the nearly complete transfer of gold(I) from the thioglucose to the Cys-34. The equilibrium constant of the reversible reaction was also measured by a liquid chromatography method, which gave $K_{eq} = 3.0$. This value is consistent with that derived from the kinetic constants. An explanation for this unexpectedly small equilibrium constant is that the gold binding to albumin is driven by further reactions of the displaced acetyl thioglucose.