GOLD(I) WEAK BINDING SITES: HISTIDINE RESIDUES OF SERUM ALBUMIN

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Et_3PAuCl , an analogue of the antiarthritic drug auranofin [$\text{Et}_3\text{PAuSATg}$ = triethylphosphine-(2,3,4,6-tetra-O-acetyl-1-thio- β -D-glucopyranosato-S)gold(I)] binds to weak binding sites of serum albumin *in vitro*. Up to 17 equivalents of Et_3PAu^+ react with bovine serum albumin (BSA). These weak binding sites are characterized by ^{31}P NMR shifts of 23-29 ppm and may be the seventeen histidine residues.

In order to investigate these sites, a ^1H NMR study was performed. With a spin echo pulse sequence ($\tau=30\text{ms}$), most of the C2H resonances (7.5-8.5 ppm) of the histidine imidazole rings of BSA were resolved. Their assignments as the C2H of the histidines were confirmed by a ^1H NMR pH titration. Upon titrating BSA with Et_3PAuCl , shifting and broadening of these C2H resonances occurred. Et_3PAu^+ bound preferentially to the more hydrophobic histidine residues characterized by shorter T_2 relaxation times. All the resonances were eventually undetectable. The same phenomena (broadening and shifting of the C2H resonance) were observed in model studies in which L-histidine and N-acetyl-L-histidine were titrated with Et_3PAuCl .