Abstract: Gold compounds have been in use for treatment of rheumatoid arthritis for about 70 years but several questions relating to efficacy and toxicity still remain unanswered. The gold drugs include several injectable and the only oral compound auranofin \[5,(1\text{-thio-ß-D-glucopyranose-2,3,4,6-tetraacetato-S)-(triethylphosphine) gold(I)}\]. These are different chemical entities shown to have different in vivo chemistry and pharmacokinetics. Drug–protein interactions provide highly useful information for interpretation of pharmacokinetic parameters. Reactions of metal-based drugs with proteins are even more important with reference to their mode of action and toxicity. Interaction of aurothiomalate (an injectable drug) in vivo with plasma/serum proteins suggests that most of the gold is bound to albumin and a small fraction to immunoglobulins and low-molecular-weight substances. In humans the distribution after administration of auranofin was: 81.8% to albumin, 4.8% to α1-globulin, 6.9% to α2-globulin, and 6.5% to β and γ globulins at blood gold level of 1.5 μg mL$^{-1}$. The gold in erythrocyte membrane was initially very high and decreased rapidly afterwards with aurothiomalate, and auranofin produced constant high levels up to 36 weeks. A study with sodium aurothiomalate, gold keratinate, and triethylphosphine gold showed different distribution patterns. The aurothiomalate gold was 94% bound to albumin and only 6% to globulin, whereas in case of phosphine gold the corresponding figures were 70% and 30%, respectively. The affinity of keratinate gold to globulin was found to be high (20%). It appears that the affinity of gold to globulins changes with the nature of the drugs. These results provide understanding about different behaviour of sodium aurothiomalate and auranofin. These results can be used to design more effective and less toxic gold drugs.

Chrysotherapy, Sodium aurothiomalate, Auranofin, Gold drugs, Drug-protein interaction

Presentation: Poster