Gold Levels in Rat Blood after Topical Application

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Gold drugs have been used for many years in the treatment of rheumatoid arthritis [1]. Generally they are administered intramuscularly by injection, although recently an oral drug has been developed [2]. A third method of drug administration that apparently has not been tested is that of topical application. This method has the obvious advantage that the drug can be applied directly to the affected area.

The first problem, however, is to establish the type of gold complex that is likely to permeate the skin and give measurable gold levels in blood. Some gold(III) compounds are known to react with skin, giving purple stains of colloidal gold. Thus, gold(I) complexes seem a more likely proposition. This note describes the results obtained for two gold(I) complexes currently used as drugs, namely, sodium gold(I) thiomalate (Myocrysin) and triethylphosphine gold(I) 2,3,4,5-tetra-*o*-acetyl-1-thio-β-D-glucopyranoside (auranofin).

Experimental

Hairless Lewis-strain rats were used in three trials, in groups of five. The first trial was run over five days – on each of the first four days, 20 mg quantities of each drug dissolved in 0.2 ml ethanol, was applied over an area 2 × 2 cm on the dorsal region of each rat and allowed to dry. On day five, all animals were sacrificed and blood removed. This was then separated into serum and whole blood for gold analysis. The second trial was similar but, to alleviate surface removal of gold, the test areas were occluded with cellophane-backed plaster. The third trial compared two groups of test animals. In the first, auranofin was given as above for three days and the animals sacrificed after twenty-one days. In the second group, the animals were given twenty daily applications of auranofin and sacrificed on the twenty-first day.

In the second trial, skin samples from the dorsal region where thoroughly washed with water to remove surface drug and then analysed for gold. Kidney samples in these animals were also analysed for gold.

Gold levels in all cases were measured using atomic absorption spectrometry [3].

Results

These are given in the Table below.

Table. Gold Levels (ppm ±SD)

	First Trial			
	Skin	Whole Blood		
Auranofin	2.61 ± 0.24	5.42 ± 0.26		
Myocrysin	0.56 ± 0.03	0.73 ± 0.14		
	Second Trial			
	Serum	Whole Blood	Skin	Kidney
Auranofin	3.07 ± 0 78	5.77 ± 1 36	3.99 ± 2 26	3 95 ± 1.66
Myocrysin	0.82 ± 0.36	1.28 ± 0.33	4 23 ± 2.93	1.68 ± 0.53
	Third Trial			
	Serum	Whole Blood		
Auranofin (20 days)	4.33 ± 2.27	10.80 ± 2.15		
(3 days)	0.18 ± 0 06	0.16 ± 0.07		

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Discussion

These results show that significant levels of gold can be absorbed fairly rapidly through topical application. Auranofin was more effective in permating the skin than was Myocrysin – these results being comparable with oral administration, where auranofin was again more successful [4]. The effect of occlusion was to increase the amount of gold absorbed slightly. Prolonged treatment showed, as expected, an enhanced level of gold, particularly in whole blood. After a gap of eighteen days after treatment, measurable quantities of gold were still detected in whole blood and serum.

The skin samples, removed from the dorsal area where the gold drugs were applied, gave gold levels that were similar to those found in guinea pigs undergoing oral treatment [5], suggesting that topical application of gold compounds need not necessarily lead to very high local skin concentrations of gold.

Gold levels in blood at any time represent a kinetic equilibrium between absorption and secretion. Since, with the different gold drugs, both absorption and secretion rates could be different, it was felt that measurement of kidney gold levels could give another indication of relative gold absorption. Quite a high level was formed, suggesting, as was expected [6], that gold was accumulating in the kidneys. The levels for the two drugs roughly paralleled the gold levels found in blood.

Thus, it seems that gold drugs can be administered topically to produce significant blood gold levels. Further work will be required to elucidate the mechanisms of this absorption but, as a first approximation, it appears that gold complexes which are absorbed orally may also be suitable candidates for topical studies.

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