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Note

Chromatographic properties of two gold compounds used in the therapy of polyarthritis

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Gold compounds are used in chemotherapy mainly in the treatment of arthritis, although other chemotherapeutic effects have also been noted. The products available range from water-soluble gold(I) complexes to oil-soluble complexes to colloidal gold(I) sulphide.

The mechanism of the action of gold compounds is believed to be a tanning effect of inflamed collagen in arthritic joints, leading to a considerable decrease in the volume of the collagen and a consequent reduction in the inflammation. For this to happen, one might suppose that the gold compound must somehow reach the inflamed collagen region and if possible be concentrated there rather than be diffused through the whole body.

Chromatographic methods have been employed in recent years in the study of structure–activity relationships in series of drugs and much useful information has been obtained. We felt that a chromatographic study of therapeutic gold complexes may also throw some light on the therapeutic action and we report here our preliminary findings with two commercial gold preparations.

EXPERIMENTAL AND RESULTS

Gold compounds studied

The two preparations studied were Aurosulfo (Lab. G. Manzoni, Milan, Italy), a 2% injectable aqueous solution of colloidal gold sulphide, which is a brown rather stable solution and Sanocrysin (Ferrosan, Denmark), 100-mg ampoules of sodium aurothiosulphate to be dissolved in water or sodium chloride for injection; the solution in water decomposes slightly within a few days, producing a faint brown precipitate.

Techniques used

Thin-layer and paper chromatography were carried out in closed jars by the usual ascending method and electrophoretic experiments were performed in a Camag high-voltage apparatus. Gel filtration was carried out in the Pharmacia thin-layer gel filtration apparatus.

The colloidal Aurosulfo is dark brown and did not require a reagent for detection. The aurothiosulphate Sanocrysin is difficult to detect with specific reagents

owing to the high stability of the complex; however, a dark brown spot was formed when the chromatogram was held over iodine fumes and this spot was stable for several days, indicating that some decomposition of the complex had taken place.

Chromatography on various supports

On filter paper (Whatman No. 3MM). On development with isotonic saline, Aurosulfo produces a long trail from the origin, the main portion, however, travelling with the liquid front. Sanocrysin is found only at the liquid front.

On a Polyamid 6 MN thin layer. On this support, which in some ways is similar to a protein surface, Aurosulfo is completely retained from isotonic saline at the point of origin, whereas Sanocrysin moves with the liquid front.

DEAE-cellulose. On Polygram Cel 300 DEAE thin layers, Aurosulfo moves in 0.9% sodium chloride solution essentially with the liquid front, with a trail to the origin. Sanocrysin moves as a compact spot with $R_F = 0.19$.

Carboxymethyl-cellulose. On Polygram Cel 300 CM in 0.9% sodium chloride solution Aurosulfo is strongly adsorbed at the origin, with a forward comet to about $R_F = 0.5$, whereas Sanocrysin moves with the liquid front.

Salting-out properties. From saturated (8 *N*) ammonium sulphate solution Aurosulfo is strongly adsorbed at the origin on Whatman No. 3MM filter paper whereas Sanocrysin moves as a compact spot at $R_F = 0.5$. Thus both are "salted out", but to very different extents. On Polyamid 6 MN layers, saturated ammonium sulphate solution does not move, *i.e.*, it is unable to wet the layer. However, half-saturated ammonium sulphate solution does move and in this solvent Aurosulfo remains at the origin whereas Sanocrysin is found as an elongated spot in the region of $R_F = 0.5$. Thus there is pronounced salting-out on polyamide also.

Paper electrophoresis. In 0.9% sodium chloride solution with a voltage of 1500 V for 30 min on Whatman No. 1 paper, Aurosulfo remains as a compact spot at the origin and thus seems to have no or a very low charge. Sanocrysin moves as a compact spot for 10.2 cm. Chromate run side-by-side for comparison moves 11.5 cm. Hence the electrophoretic mobility of Sanocrysin is about that of an average divalent anion.

Gel filtration. On a thin layer of Sephadex G-75 (fractionation range 5000–40,000) with 0.9% sodium chloride solution as eluent, Aurosulfo is completely excluded as a compact spot moving with the speed of dextran blue, and unlike the result on cellulose paper, does not produce a comet. Sanocrysin moves with the same speed as as a small ion $[Co(NH_3)_6^{3+}]$ and thus penetrates the gel completely.

Behaviour in some organic solvents. On paper chromatograms developed with a mixture of isotonic saline and acetone (1:1), Aurosulfo remains at the origin whereas Sanocrysin moves with $R_F = 0.8$. In mixtures of ethanol and isotonic saline Aurosulfo is retained strongly from 50% ethanol while both compounds are retained from 90% ethanol.

DISCUSSION

We chose some chromatographic systems that have some bearing on the possible transport mechanism of substances in biological systems. Thus cellulose paper chromatography will give an indication of how a substance may behave on a

neutral polysaccharide surface, polyamide chromatography will give an indication of how a neutral polypeptide will react with it, carboxymethyl- and DEAE-celluloses will show similar behaviour to acidic or basic soluble or insoluble macromolecules, and finally the gel filtration behaviour will be indicative of roughly how a substance may diffuse in a swollen polymer such as a collagen (not considering possible reactive groups).

The only conclusion that we can draw is that the two products have radically different properties in almost all systems and thus presumably different transport properties in biological systems. This raises the question of how they can possibly carry out the same or even similar functions as therapeutic agents.

This study is part of a collaboration between our laboratory and the Institute of Physiology of the Czechoslovak Academy of Sciences, and it is planned to survey other gold compounds used in therapy and their behaviour in actual biological substances.