Table I. Effect of 5-azacytidine on lymphoid leukaemia in AK inbred mice

Dose of 5-azacytidine and no. of doses i.p.	No. of leukaemic deaths after 20 days	% 20-day survivors
100 mg/kg 1 ×	1[a]/8	75[b]
10 mg/kg 5 ×, alternate day schedule	0/8	100
5 mg/kg 7 ×, daily	1[a]/8	87.5

Eight control mice died after 6.6 ± 0.5 days of leukaemia. Therapy initiated always 24 h after inoculation of leukaemic cells (10^7). – [a] 18th day after inoculation. [b] 1 mouse died on the tenth day of intestinal haemorrhage, lymphoid hypoplasia and bone-marrow depression without macroscopical or cytological signs of leukaemia.

Table II. Effect of various cancerostatic substances on lymphoid leukaemia in AK inbred mice

Substance tested	Dose and no. of doses i.p.	% response[a]
4-Amino-pteroyl-glutamic acid	0.250 mg/kg 4 ×, alternate day schedule	30.5
5-Bis-(2-chloroethyl)-aminomethyluracil	0.250 mg/kg 9 ×, daily	16
6-Azauridine	500 mg/kg 6 ×, daily	36.6
6-Mercaptopurine riboside	10 mg/kg 7 ×, daily	11

[a] Response is given in % increase in survival time. Therapy initiated always 24 h after inoculation of leukaemic cells (10^7).

possesses cancerostatic activity. Another cancerostatic of the same type, 6-azauridine, inhibits the growth of *E. coli* B by 50% at 1300 μg per ml. The inhibitory effects of 5-AzCR on *E. coli* can be reversed by uracil, uridine and cytidine; this clearly indicates that 5-AzCR is interfering with the biosynthesis of the pyrimidine components of the nucleic acids or with their incorporation into biopolymers.

5-AzCR is somewhat toxic to mammals. In mice of inbred strain AK, the acute toxicity (LD_{50}) is about 150 mg/kg. Depression of the bone marrow and the hypoplastic involution of the lymphatic system are the main toxic manifestations.

In agreement with these effects, the new antimetabolite is a potent inhibitor of the lymphoid leukaemia of the inbred AK mice (Table I). It is remarkable that even a single dose (100 mg/kg), though provoking some toxic effects, increases the survival time very considerably. The leukaemia of AK mice is relatively resistant to chemotherapy, especially as compared with lymphoid leukaemia L1210. For comparison, the effects of various well-known cancerostatic agents on AK leukaemia, as determined in our laboratory, are listed in Table II.

An extensive investigation of the new cancerostatic substance, including clinical trials, is under way.

Zusammenfassung. Die hohe bakteriostatische und cancerostatische Wirkung eines neuen Antimetaboliten, 5-Azacytidin, wird beschrieben.

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Reaction of Gold with Collagen *in vivo*

Gold in the form of thio-complexes is successfully used in the treatment of rheumatoid arthritis, one of the so-called collagen diseases. Although this method of treatment is comparatively old, the mode of action of gold complexes has not been definitely elucidated. As it can be assumed that reaction of gold compounds with collagen is similar to that of other heavy metals, we have tried to prove experimentally the binding of gold into the collagen structure.

For this purpose collagen fibres from tail tendon of rats (RTT) of Wistar strain (*Rattus norvegicus* var. *alba*), treated with gold sodium thiosulfate ('Sanocrysin' – Dansk Chemoterapeutisk Selskab, Denmark), 2 mg/100 g of body weight per week, were subjected to electron microscope observations and to measurements of temperature of shrinkage[1], swelling[2], and contraction-relaxation[3].

We have found that, in the electromicrograph of RTT collagen from a rat treated for 18 weeks with Sanocrysin, three dark bands can be detected, two of them appearing comparatively dark. These two bands, 60 and 100 Å units wide, are 60 Å units apart. The third band in the middle of the light band is 30 Å units wide (Figure 1). As far as we are informed from the literature, this is the first case of electron microscope demonstration of the binding of gold with collagen under conditions *in vivo*.

Other methods used in our experiments were to prove the binding of gold with collagen in the earlier stages of the treatment. With the use of all methods mentioned above, distinct changes in the measured quantities were observed even after first injections of gold (Figures 2–4). From the results obtained, it can be assumed that interaction of collagen with gold is principally similar to

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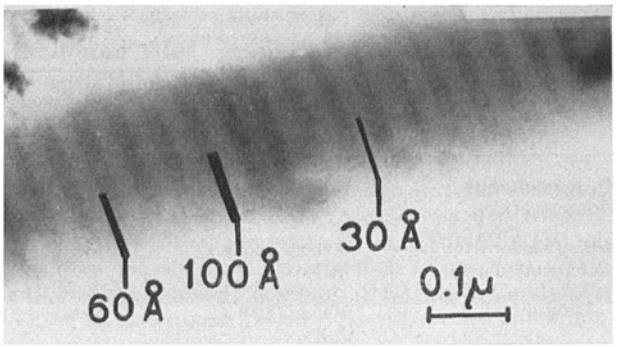

Fig. 1. Electron micrograph of rat tail tendon collagen (RTTC) from the experimental animal treated with gold sodium thiosulfate (Sanocrysin) *in vivo*.

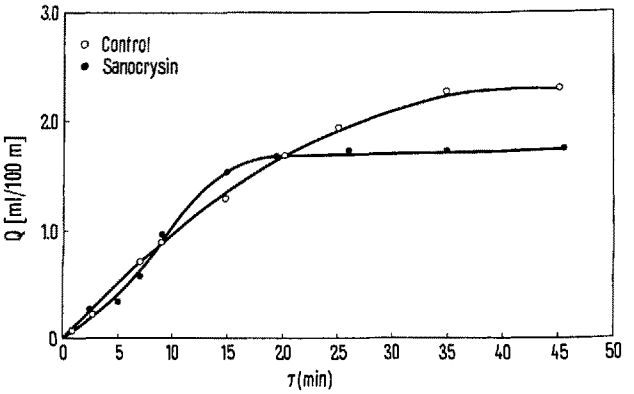

Fig. 4. Swelling of RTTC after 4 weeks of treatment.

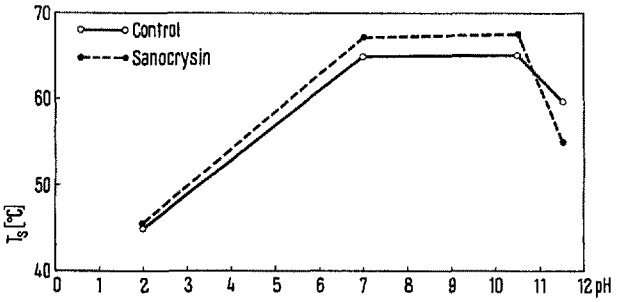

Fig. 2. Temperature of shrinkage of RTTC after 4 weeks of treatment with gold sodium thiosulfate.

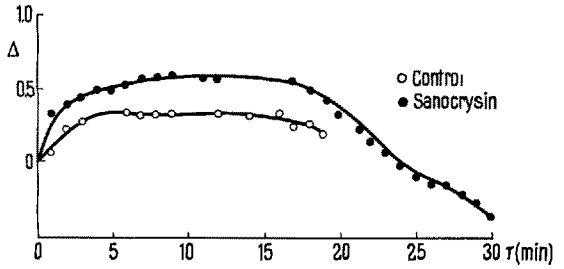

Fig. 3. Contraction-relaxation of the same specimen.

tanning of collagen with some heavy metals (Zr, Cr) *in vitro*.

From the biological point of view, most interesting seems to be the fact that gold reacts with collagen *in vivo* when compounds of gold are administered to the experimental animal. The application of gold results in an increase of the number of cross linkages leading to higher structural stability or, according to the biological terminology, to a specific type of the ageing of collagenous structures. It may be assumed that an increased structural stability and decreased swelling ability favourably influence the course of some inflammatory processes of connective tissue.

Zusammenfassung. Männliche Ratten wurden wöchentlich mit Natriumaurothiosulfat «Sanocrysin» 2 mg/100 g Körpergewicht i.m. behandelt. Es wird eine elektronenmikroskopische «Anfärbung» und erhöhte hydrothermale Stabilität des Rattenschwanzkollagens beschrieben, was zur Erklärung der Wirkungsweise der Goldbehandlung bei Polyarthritis beitragen könnte.

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Sur l'identification des résidus C-terminaux d'une protéine après hydrazinolyse

En voulant aborder l'étude des résidus C-terminaux de l'hirudine[1] au moyen d'une hydrazinolyse[2], nous nous sommes aperçus que les méthodes existantes ne permettaient pas d'identifier certains résidus susceptibles de se trouver en position C-terminale. Si, en effet, le traitement par des aldéhydes[2-4] permet de séparer les hydrazides des acides aminés C-terminaux libérés par hydrazinolyse, les résidus de glutamine et d'asparagine qui se trouvent en position C-terminale échappent à ce procédé. Il se produit, à partir de ces deux derniers acides aminés, des hydrazides qui réagissent également avec les groupes carbonyles.

La dinitrophénylation du mélange réactionnel, obtenu après une hydrazinolyse[5], ne résout pas plus ce problème. Cette méthode permet certes de récupérer les dérivés correspondant aux résidus C-terminaux d'asparagine et de glutamine, mais ils sont accompagnés le plus souvent

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