tumors of 0.17 cm^3 ($P < 0.001$) and the PCPH-Cu treated group was free from detectable tumors. Treatment was ceased at this point. Tumors in PCPH-Cu and SBH-Cu treated mice remained quiescent for an additional three weeks after which their growth resumed. However, 5 of 15 tumor-bearing mice (from three separate experiments) treated with PCPH-Cu have remained free of the tumor for four months post-treatment. Administration of free PCPH and SBH did not significantly reduce tumor growth. Treatment of non-tumor bearing mice with similar dosages of SBH-Cu and PCPH-Cu produced a thickening of the skin at the area of injection. No other effects have been observed in these mice in the subsequent four months.

In acute toxicity studies, the dosage of inhibitor that killed 50% of normal mice within 24 hours was 1.9 g/kg for SBH, 60 mg/kg for SBH-Cu, 1.0 g/kg for PCPH and 18 mg/kg for PCPH-Cu. Thus, chelation to copper potentiated both the antitumor and acute toxicity of these chelators.

These results demonstrate that two hydrazone-copper complexes, PCPH-Cu and SBH-Cu are potent mitotic inhibitors. The antineoplastic activity of these two hydrazone-copper analogs of GHL-Cu may reside either in their general cytotoxicity or might possibly be due to an interference with the mechanisms which concentrate the copper ions required for tumor angiogenesis.

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V27

Difference in the Metabolic Patterns of Cr^{III} and Cr^{VI} Ions in the Rat

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Different aspects of the biochemistry of chromium in laboratory animals have been investigated using ^{51}Cr radiotracer methods. ^{51}Cr-labelled chromium compounds such as cationic trivalent $^{51}Cr^{3+}$ and anionic hexavalent $^{51}Cr^{6-}$ were prepared and administered *I.V.* to rats in doses ranging from 0.1 to 100 μg/rat. The results show remarkably different metabolic patterns in the two chemical species. They refer (1) to the distribution in the blood. More than 95% of the ^{51}Cr in the blood of rats administered with the trivalent form was present in the plasma while the corresponding value in the case of the hexavalent species was of about 25%. Gel permeation chromatography on sephadex G-150 and ion exchange chromatography in DEAE show that the ^{51}Cr plasma of rats treated with $^{51}Cr^{3+}$ is associated with β-globulin transferrin. Dialysis experiments indicate the strong nature of the binding of chromium to transferrin. They also refer (2) to the biliary excretion patterns. The biliary excretion of ^{51}Cr has been studied in bile duct-cannulated rats 120 min after the intravenous administration of 0.1 μg Cr/rat to 100 μg Cr/rat as trivalent or hexavalent chromium. The biliary levels of ^{51}Cr-derived radioactivity reached their peak 30 min after injection of both Cr^{III} and Cr^{VI} and decreased slowly thereafter. The 2 hour biliary concentrations of Cr in the animals treated with Cr^{VI} were up to 60 times higher than those found in the rats given the same amount of the trivalent Cr form. 2.6 per cent of the dose was recovered in the bile of rats injected with Cr^{VI} within 2 hours while the 2 hours cumulative excretion of ^{51}Cr in the bile of Cr^{III}-treated animals was approximately 50 times lower.

In the first 120 min period after treatment of the bile-fistula rats the urinary excretion of ^{51}Cr ranged from 7 to 15% of the administered dose without any obvious relation to the chemical form and the dosage level. Chromium had no effect on the rate of biliary flow. The plasma levels of ^{51}Cr-radioactivity of the animals treated with Cr^{VI} were significantly lower than those detected after injection of the same doses of Cr in the trivalent form. No valency-related differences were found with respect to the liver concentrations of ^{51}Cr labelled chromium. These findings indicate that the distinctive pattern of Cr biliary excretion observed in the rat after treatment with Cr^{III} and Cr^{VI} are independent of the plasma-to-bile and liver-to-bile concentration gradients of this chemical species.

In this study, evidence has also been obtained for a direct excretion of Cr across the intestinal wall as indicated by the presence of appreciable levels of ^{51}Cr activity in feces in the gastrointestinal segments of rats with ligated bile duct after intravenous injection of 100 μg of ^{51}Cr-labelled chromium.

Average values of 4% and 1.5% of the injected Cr dose were measured in the gut (stomach and intestine plus contents) 24 hrs after the injection of Cr^{VI} and Cr^{III}, respectively. This finding provided further support for the concept that the trivalent and hexavalent forms of Cr exhibit different behaviour in their elimination patterns by the digestive tract.