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CHROMIUM (III) COMPLEXES AND THEIR RELATIONSHIP  
TO THE GLUCOSE TOLERANCE FACTOR

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ABSTRACT

To forms of the dinicotinate complex  $\text{Cr}(\text{nic})_2(\text{H}_2\text{O})_3\text{OH}$  were formed which were yellow and blue, respectively. For the yellow form the nicotinic acid ligands were coordinated via the pyridine ring nitrogen atom but this complex was biologically inactive, while for the blue form nicotinic acid was coordinated via the carboxylate group and this compound was biologically active. Only Cr(III) formed a stable carboxylate coordinated dinicotinate complex. No stable complexes were formed with Fe(III) and Mn(III) due to significant colation, even at acidic pH's, and the complexes of nicotinic acid with Cr(II), Mn(II), Co(II) and Ni(II) were all pyridine nitrogen atom coordinated and biologically inactive.

Several chromium (III) complexes with amino acids possessed biological activity also, and these included the  $\alpha$ -carboxylate coordinated species  $\text{Cr}(\text{gly})_n(\text{H}_2\text{O})_{6-n}^{3+}$  and  $\text{Cr}(\text{glu})_n(\text{H}_2\text{O})_{6-n}^{3+}$ , the bidentate coordinated  $\text{Cr}(\text{gln})_2(\text{H}_2\text{O})_2^+$  complex, and the  $\text{NH}_4\text{OH}$ - eluted complexes obtained when  $\text{Cr}(\text{gly})_2(\text{H}_2\text{O})_2^+$  and  $\text{Cr}(\text{glu})_2(\text{H}_2\text{O})_2^+$ , but not  $\text{Cr}(\text{cys})_2(\text{H}_2\text{O})_2^+$ , were eluted from a DOWEX 50W-X12 cation-exchange column (loss of the  $\alpha$ -amino coordination was postulated to have occurred).

The biologically active mixed ligand complex postulated as  $\text{Cr}_2(\text{nic})_4(\text{gly})_2(\text{OH})_2$  was prepared and found to be stable at neutral pH as a result of coordination of the glycine ligands.

The activity of the chromium (III) complexes in the yeast fermentation assay suggested that similar effects would be found in mammalian systems. The yeast assay system was found to be a simple, quick and reproducible method of determining biological activity.

All of the active chromium (III) complexes prepared were found to be similar, in structure, to the diguanide compound

1,4-diguanidinobutane which is known to lower blood sugar levels in mammals. This similarity in structure suggested a similar function might be possessed by the complexes reported in this thesis.

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