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PYRIDOXAL ISONICOTINOYL

HYDRAZONE:

A PROMISING AGENT FOR CHELATION THERAPY OF IRON OVERLOAD

The chemistry of pyridoxal isonicotinoyl hydrazone (PIH) has been investigated with emphasis on the chemical characteristics pertinent to the assessment of its value as a biological iron chelator. In acidic environments, PIH is remarkably stable, with a decomposition of $\leq 3\%$ after 72 hr at pH 2, 37°C. The acid dissociation constants of the several ionisable groups present in PIH have been determined by potentiometric titration and the formation of the iron complexes studied by potentiometry and UV-Vis spectrophotometry. The systems are quite complex due to the number of dissociable protons in both the free and coordinated ligands, the high affinity of these compounds towards iron(III) and the formation of sparingly soluble species at pH 5.

At pH 7.4, $[\text{Fe}^{3+}] = 10^{-6} \text{ M}$ and a 1000-fold excess of ligand, PIH has a pM value of 27.7 which, when compared to 25.6 for transferrin, indicates that PIH is thermodynamically capable of removing iron from transferrin.

The distribution of the complex species as a function of pH shows that in each case a significant fraction is present as the electrically neutral Fe(L)(HL) at pH 7.4. A model of the coordina-

tion geometry of this species, supported by spectroscopic data, is proposed.

The affinity of PIH for iron(II) is significantly lower than for iron(III), as indicated by a formation constant of 7.0 for $[\text{Fe(II)(HL)}_2]$ compared to 12.47 for $[\text{Fe(III)(HL)}_2]$.

PIH therefore possesses many chemical features desirable in an effective iron chelating drug. Furthermore, this chelating agent has been reported to be effective in several cellular and animal bioassays and is currently a highly promising pharmacological agent for the treatment of iron overload.



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ASCORBATE OXIDASE, DIAMINE OXIDASE AND THEIR USE IN DIAGNOSIS OF COPPER DEFICIENCY IN PLANTS

Copper deficiency in soils and crops is a cause of concern in many agricultural industries. In general, copper deficiency leads to significant decreases in crop yield and plant fertility. However, it is often difficult to diagnose deficiency without complex laboratory procedures and at a sufficiently early stage in the plant's growth to allow remedial measures to be adopted, *e.g.* by including copper compounds in fertiliser. Analysis of the range of copper compounds present in plants,