

Research Paper :

Complexes of diphenyl amine mercapto carboxylic acid : A new anti-inflammatory agent

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ABSTRACT

Diphenyl amine-2-mercapto-2'-carboxylic acid and its Cu(II), Ni(II), Co(II) and Zn(II) complexes have been synthesized and characterized by their elemental analyses, molecular weight determination, molar conductance, infrared and electronic spectra and magnetic measurements. In acute anti-inflammatory test Cu(II) complex was found to be more potent than Ibuprofen in normal and adrenalectomized rats but less effective in subacute and chronic anti-inflammatory tests. It inhibited PGE₂ like substance (25%) and Castor oil induced diarrhoea (30%) but did not protect the mice against arachidonic acid induced mortality. However, it had very low degree of gastric irritation but without analgesic effect.

Key words : Metal complex, NSAID'S, Prostaglandins, Anti inflammatory agent

Inflammation is a multi mediated response of tissue and cells to an injury or injurious agents involving physiological, morphological and biochemical changes. As inflammation, specially chronic inflammatory diseases, affect the quality of patient's life. Extensive search for a new drug effective to treat inflammation and other orthopathies have got added impetus. Unfortunately, most of the anti-inflammatory (AI) drugs, available today, reveal a high incidence of gastric irritation, apart from the effects on kidney, liver, bone marrow and skin. Therefore, there is a need for a non steroid anti-inflammatory drug (NSAID) effective in rheumatoid arthritis, osteoarthritis, gout and related diseases with reduced side effects as compared to the existing clinically effective drugs.

Classical pharmacological studies have measured the ability of a chemical compound to reduce the symptoms of inflammation. It will be beneficial to eliminate the symptoms either by suppressing normal or correcting an impaired inflammatory response. However, the suppression may lead to more serious consequences e.g. by corticoids and therefore, an agent which corrects the impaired response without serious toxicity, should have potential for therapeutic usefulness. The metal complexes meet these later criteria and have been shown to be effective in treatment of connective tissue diseases. It has been suggested that in human the rheumatoid arthritis may be the result of a deficiency or lack of superoxide dismutase enzyme¹, which mostly contain Copper, required for dismutase activity².

Inspired by the clinical success of gold salts, copper

and zinc chelates of known AI compounds, they have been extensively investigated for use as potential AI agents. It has been established that copper chelates of known AI drugs show more AI activity than the parent compound³ and exhibit intrinsically low ulcerogenicity⁴, whereas, zinc has been used in rheumatoid arthritis⁵ and is beneficial in ulcer healing⁶. Nickel protects aspirin induced mucosal damage⁷ and cobalt complexes have been reported to exhibit AI activity from this laboratory⁸⁻¹⁰.

Keeping above facts in view and in search for an ideal AI agent devoid of common side effects, the Diphenyl amine-2-mercapto-2'-carboxylic acid (DPMC) and its complexes involving copper, nickel, cobalt and zinc as metal ions have been synthesized and evaluated for its anti-inflammatory activity. The compound and chelates were subjected to primary screening against carrageenan induced rat paw oedema test. It has been found that copper chelate of DPMC is most active among all the compounds. Therefore, it has been further investigated and the results are reported here.

MATERIALS AND METHODS

All the chemicals used were of AR grade either, BDH or E.Merck.

Synthesis of Diphenyl amine-2-mercapto-2'-carboxylic acid :

Diphenyl amine-2-mercapto-2'-carboxylic acid (Fig. 1) was synthesized by condensing a equimolar amount of O-chlorobenzoic acid and Thiophenol in the presence of