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Synthesis and evaluation of analgesic, anti-inflammatory and anti-bacterial activity of beta and meso 5,10,15,20-tetraphenylporphyrins Schiff bases and their metal complexes

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Abstract

Series of novel ß and meso 5,10,15,20-tetraphenylporphyrins Schiff bases were synthesized via Schiff base condensation reaction, the ß-linked 5,10,15,20-tetraphenylporphyrins Schiff bases were synthesized starting from ß-formyl 5,10,15,20-tetraphenylporphyrin and aminolkanes in moderate yields while meso-linked 5,10,15,20-tetraphenylporphyrins Schiff bases were synthesized via refluxing 5-(4-aminophenyl)-10,15,20-triphenylporphyrin and different aromatic benzaldehyde . The two newly synthesized seies of porphyrin Schiff bases were compared and characterized based on their chemical properties, stability and spectral data.

The properties of these new ß-linked 5,10,15,20-tetraphenylporphyrin Schiff bases and meso linked 5,10,15,20-tetraphenylporphyrin were investigated and were observed with different stability. The rotational stability of these ß-linked and meso-linked 5,10,15,20-tetraphenylporphyrin Schiff bases deduced by 1HNMR, was calculated and all newly synthesized compounds were further characterized by UV-VIS spectroscopy and high resolution mass spectroscopy. They were further tested for their potential analgesic and anti-inflammatory activities in acetic acid induced writhing test in mice and carrageenan induced paw edema in rats. The compounds were also evaluated for antibacterial activity in disc diffusion method. Compounds 1a 1b 1c 1d showed significant analgesic and anti-inflammatory activity at 10 and 30 mg/kg (b.w), comparable to the standard reference drugs. Furthermore, all the tested compounds possessed significant anti-bacterial activity against both gram positive and gram negative bacteria. The analgesic, anti-inflammatory and anti-bacterial activities of the tested compounds were found comparable to reference drugs. These compounds can serve as precursors for the development of clinically useful analgesics, anti-inflammatory and anti-bacterial agents

A series of certain novel Schiff bases as fenamate isosteres (VI:a-k) were synthesized to locate analgesic, anti-inflammatory agent with minimal ulcerogenic potential. The structures of the newly synthesized compounds were elucidated based on their elemental analysis as well as IR, and NMR and mass spectroscopic data. All the compounds were evaluated for their anti-inflammatory activity by carrageenan induced paw oedema method. The compounds possessing good anti-inflammatory activity were further tested for analgesic, ulcerogenic, lipid peroxidation potentials and liver toxicity. Compounds (VI-c), (VI-f), (VI-h) and (VI-i) showed the best anti-inflammatory and significant analgesic activities at doses comparable to that of the standard drug Indomethacin. However, compounds (VI-c) and (VI-f) could be considered the most potent anti-inflammatory and analgesic molecules with maximum reduction in gastro-intestinal ulceration with no hepatocyte necrosis or liver degeneration.

A new series of Mn (II), Co (II), Ni (II), Cu (II), and Zn (II) complexes of the Schiff base ligand, 4-chloro-2-{(E)-[(4-fluorophenyl)imino]methyl}phenol (C13H9ClFNO), was synthesized in a methanolic medium. The Schiff base was derived from the condensation reaction of 5-chlorosalicylaldehyde and 4-fluoroaniline at room temperature. Elemental analysis, FT-IR, UV-Vis, and NMR spectral data, molar conductance measurements, and melting points were used to characterize the Schiff base and the metal complexes. From the elemental analysis data, the metal complexes formed had the general formulae [M(L)2(H2O)2], where L = Schiff base ligand (C13H9ClFNO) and M = Mn, Co, Ni, Cu, and Zn. On the basis of FT-IR, electronic spectra, and NMR data, “O” and “N” donor atoms of the Schiff base ligand participated in coordination with the metal (II) ions, and thus, a six coordinated octahedral geometry for all these complexes was proposed. Molar conductance studies on the complexes indicated they were nonelectrolytic in nature. The Schiff base ligand and its metal (II) complexes were tested in vitro to evaluate their bactericidal activity against Gram-negative bacteria (Escherichia coli and Pseudomonas aeruginosa) and Gram-positive bacteria (Bacillus subtilis and Staphylococcus typhi) using the disc diffusion method. The antibacterial evaluation results revealed that the metal (II) complexes exhibited higher antibacterial activity than the free Schiff base ligand.

The chemistry of metal complexes with Schiff base ligands containing oxygen and nitrogen as donor atoms has continued to attract the attention of researchers. These ligands are known to coordinate to metal atom in different ways under different reaction conditions. The ligands are derived from the condensation reaction of aldehydes and primary amines.
One of the major areas of research on the Schiff base metal complexes is their biological activity with the main aim being the discovery of safe and effective therapeutic agents for the treatment of bacterial infections and cancers. A number of Schiff base metal complexes have a diverse spectrum of

biological and pharmaceutical activities. For instance, transition metal complexes of Schiff base ligands bearing “O” and “N” donor atoms are very important because of their biological properties such as antibacterial, antifungal, anti-inflammatory, analgesic, anticonvulsant, antitubercular, antioxidant, and anthelmintic. The Schiff base transition metal complexes have also been used as biological models to understand the structure of biomolecules and biological processes.

Mn (II), Co (II), Ni (II), Cu (II), and Zn (II) complexes of the Schiff base, 4-chloro-2-{(E)-[(4-fluorophenyl)imino]methyl}phenol, which to the best of our knowledge has neither been synthesized nor antibacterial activities carried out, was studied in our laboratories. The antibacterial activity of the new Mn (II), Co (II), Ni (II), Cu (II), and Zn (II) complexes of the Schiff base ligand, 4-chloro-2-{(E)-[(4-fluorophenyl)imino]methyl}phenol ($C_{13}H_9ClFNO$) has been investigated and is now reported in this article. The antibacterial evaluation results revealed that the metal complexes, with a proposed six coordinated octahedral geometry, exhibited higher antibacterial activity than the free Schiff base ligand against Gram-negative bacteria (E. coli and P. aeruginosa) and Gram-positive bacteria.