BIOLOGICAL IMPORTANCE OF SCHIFF BASES

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Abstract : Schiff base ligands are able to coordinate metals through imine nitrogen and another group, usually linked to the aldehyde/ketone. A large number of Schiff bases and their complexes have been investigated for their interesting and important properties, such as their ability to reversibly bind oxygen, their catalytic activity in the hydrogenation of olefins, their photochromic properties and their complexing ability towards some toxic metals.

Key Words : Schiff base ligands, aldehyde/ketone.

Introduction : Complexes of Schiff bases have shown promising applications in biological activity and biological modelling applications. It is well known that Schiff base derivatives possess antifungal and antibacterial activity. In particular, amino acid Schiff bases are active against a wide range of organisms since they play an important role in living organisms, such as the carboxylation, transamination and C-C bond cleavage. Furthermore, Schiff bases are known to have slight antitumour activities; a large number of these compounds have been synthesized in order to find compounds with greater antitumour activities. Schiff bases are important in enzyme catalysis, as they maintain the oxidation state of the carbonyl group. They also form a covalent bond with the substrate, so that the substrate cannot diffuse away in the middle of the reaction and they act as electron sinks.Many Schiff bases are known to be medicinally important and are used to design medicinal compounds.Schiff bases appear to be important intermediates in a number of enzymatic reactions involving interaction of the amino group of an enzyme, with a carbonyl group of the substrate.

Schiff bases have been reported in literature possessing, antibacterial, antifungal, antimicrobial, anticonvulsant and antitumour activities. Also certain polymeric Schiff bases have also been found to possess antitumour activity. The Schiff bases have the highest degree of hydrolysis at pH and the solubility in water is also highest at this pH. The antitumour activity of the Schiff bases towards ascetic tumours increases considerably with the slight increase in water

solubility.Another important role of Schiff base structure is in transamination. Transamination reactions are catalyzed by a class of enzymes called transaminases or aminotransferases. Transaminases are found in mitochondria and cytosal of eukaryotic cells. All the transaminases appear to have the same prosthetic group, i.e pyridoxal phosphate, which is covalently attached to them via, an imine or Schiff base. Schiff base formation is also involved in the chemistry of vision, where the reaction occurs between the aldehyde function of 11-cis-retinal and amino group of the protein (opsin).

METALLO-ELEMENTS IN BIOLOGICAL SYSTEMS

The study of the biological role of metal ions has a long history in medicine, in pharmacology and in toxicology, but is only recently that the extent and variety of metal ion involvement has been appreciated. The metalloelements, which are present in trace and ultra-trace quantities play vital roles at the molecular level in a living system. For example, among the transition metals, the elements V, Cr, Mn, Fe, Co, Ni, Cu, Zn and Mo have been shown to be essential to life and the elements Au, Ag, Pt, Pd, Ir, Os, Ti and others have either been used in therapy or claimed to be of therapeutic values. The transition metal ions are responsible for the proper functioning of different enzymes. Metal ions play essential roles in about one third of enzymes. These ions can modify electron flow in a substrate or enzyme, thus effectively controlling an enzyme-catalyzed reaction. They can serve to bind and orient substrate with respect to functional groups in the active site, and they can provide a site for redox activity if the metal has several valence states. Without the appropriate metal ion, a biochemical reaction catalyzed by a particular metalloenzyme would proceed very slowly. If their concentration exceeds certain level, the toxic effects are evident. It has been found that the biological activity of the transition metals is mainly due to the formation of complexes with different bioligands. The mode of biological action of the complexes are governed by the thermodynamic and kinetic properties of the complexes. The toxicity of heavy metal ions is partly due to their binding with the nucleic acids. In addition to this, in designing efficient anticancer drugs, the knowledge of binding of metal ions is helpful.

Metal ion distribution can be effected by alterations in the in vivo concentration of naturally occurring low molecular weight ligands or of complexing sites of proteins. In case of diabetes, chromium metabolism plays an important role. A number of diseases and their remedies are dependent of the metabolism of inorganic constituents.

'Hard' metal ions are small, and are either not easily oxidized or reduced, or have a relatively high positive charge, eg.,Na+, K+, Mg2+. On the other hand, 'Soft' metal ions are large with a low positive charge, e.g., Cu+, Au+, Hg+, Cd2+, Pt2+. Divalent first-row transition- metal ions lie intermediate between those extremes. In general, 'hard' metal ions favour complexing with oxygen and nitrogen donors and 'Soft' metal ions with sulphur and phosphorus donors. This concept is difficult to apply absolutely, but it is useful in a relative sense. The transition metal ions are good lewis acids forming wide ranges of complexes with nitrogen, oxygen and sulphur donor ligands.

In recent years, considerable interest has been developed in copper complexes with Schiff base ligands as structural models for active site of copper proteins. Copper is a bioelement and an active site in several metalloenzymes and proteins. Copper ions are found in the active sites of a large number of metalloproteins such as haemocyanin,

tyrosinase, cytochrome C oxidase, and ascorbate oxidase. Copper can exist under normal conditions in four oxidation states 0, 1, 2, 3. These copper proteins are involved in various biological processes such as biological electron-transfer reaction, oxygen atom insertion into substrates, dioxygen reduction to hydrogen peroxide or water and hydrolytic reactions. The blue copper proteins have received considerable interest because of their unusual spectral and structural properties. Among all the transition metal complexes, copper (II) Schiff base complexes are well known for their preparational accessibilities, exhibiting the flexibility of the coordination geometry around the metal center. Azide copper (II) complexes are also of great interest for bioinorganic chemists to explore the structure and role of active sites in copper proteins such as metazido haemocyanins and tryosinases. Copper Schiff-base complexes act as key intermediates in some pyridoxal dependent enzyme processes and possibly in the cross linking of collagen by lysyl oxidase. In medicine, ligands specifically designed to complex and to remove copper in Wilson's disease, a condition involving the accumulation of excess copper, have been synthesized and the discovery that copper aspirinate is a more effective and less ulcerogenic anti-inflammatory agent has led to the reinvestigation and extension of the chemistry of complexes of this type. Nickel is an essential component in atleast four types of enzymes: urease, carbon monoxide dehydrogenase(CODH), hydrogenase and methyl-S-coenzyme M reductase.

Morrow and Kolasa reported the cleavage of plasmid DNA by square planar nickel-salen in presence of oxidizing agents. Urease catalyzes the hydrolysis of urea to ammonium and carbamate (H2NCO2 -) ions; it appears to contain a redox-inactive Ni2 unit in which the nickel atom is octahedrally coordinated and probably act as lewis acid for substrate binding.

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