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A Review on Metal Complexes Derived from Schiff Base of Cuminaldehyde

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Abstract
Schiff bases and their metal complexes cover up a larger area in the field of coordination chemistry. Schiff bases are considered as one of the important ligands which is generally synthesized from the condensation of amines and carbonyl compounds. Imine or azomethine linkages (>C=N) in the Schiff bases are responsible for the pharmacological activities. Today natural products act as a prominent source for the synthesis of novel drugs. Cuminaldehyde (4-isopropylbenzaldehyde) is one of the major constituents presents in an essential oil of spices like cumin which are commonly used. The constituents present in cumin show prominent medicinal properties such as antioxidant, antidiabetic, antimicrobial and anticarcinogen. The biological properties of the active constituents present in essential oils have been enhanced when they are converted into Schiff base metal complexes. These complexes show remarkable activities on various strains of microorganisms and hence pave the way for the synthesis of effective drug to emerging diseases.

Keywords
Schiff bases, metal complexes, cuminaldehdye, biological properties, drug.

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INTRODUCTION:

Schiff base ligands have significant importance in inorganic chemistry and show enormous applications in many fields. As a very good chelating agent Schiff bases can form complexes readily with most of the metal ions.[1] Schiff bases named after Hugo Schiff [2] are obtained when any primary amines react with a carbonyl compounds either an aldehyde or a ketone under specific conditions. During the formation of the reaction >C=O group is replaced by the >C=N group and form Schiff base. These compounds are typically known as azomethine or imine. Azomethine group (-C=N-) play a significant role in medical and pharmaceutics as an antibacterial, antifungal, antioxidant, anticancer, neurological disorders and diuretic agents.[3,4,5] Over the past few years, researchers has been successfully reporting the Schiff bases as well as its coordinated metal complexes possessing very good biological activities. Reports on the Schiff base metal complexes with remarkable activities paved the way for many researchers to pursue their work in coordination chemistry.

Natural products have been a continuing source of novel drugs leads to formation of effective pharmaceutical agents for the emerging diseases.[6] Naturally occurring carbonyl compounds such as

cuminaldehyde can also be used to prepare Schiff bases.

Cuminaldehyde [4-(propan-2-yl) benzaldehyde] is an aromatic monoterpenoid [7] mostly found in plants like *Cuminum cyminum.* It is one of the major constituents present in an essential oil of spices like cumin which are commonly used.[8] The constituents present in cumin show prominent medicinal properties such as anti-platelet, antioxidant, antidiabetic, antimicrobial and anticarcinogen effects.[9,10] One of the special property of cuminaldehyde was useful in ameliorating symptoms of diabetes and Parkinson's.[11] The general structure of cuminaldehyde is shown in the Fig 1.

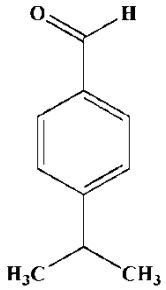

Figure 1. Structure of cuminaldehdye

Cuminaldehyde has been found to contribute to the antidiabetic effects and also had glucose dependent insulin tropic effect in diabetic rats.[12] Cuminaldehyde protected pancreatic β cells against cytotoxicity induced by streptozotocin. It was effective in reducing elevated blood glucose levels, enhancing insulin secretion and exerting antioxidant protective effects on insulin secreting cells.[13]

Cuminaldehyde itself stimulate different biological activities such as antibacterial, antifungal and antioxidant. [14,15] This review summarizes the synthesis, structure and biological activities of Schiff bases derived from cuminaldehyde.

DISCUSSIONS:

Schiff base metal complexes of cuminaldehyde

A series of Co (II), Ni(II), Cu(II), Zn(II) and Ru(II) metal complexes synthesised using the Schiff base ligand prepared by condensation of cuminaldehyde and glycylglycine. The complexes were characterised based on analytical and spectral studies. The geometrical structures of the complexes were found to be octahedral. The nano rod structure of the Co (II) complex was proved by the SEM micrograph.[16]

Crystal structure of cuminaldehyde Schiff bases:

The Schiff base 2-hydroxy-2'-(4-isopropylbenzylbenzylidene) benzohydrazide was synthesized by the reaction of 2-hydroxybenzoyl-hydrazine with 4-isopropylbenzaldehyde. The structure was non-planar, and the crystal structure shows intermolecular O-H...O and intramolecular N-H...O hydrogen bonds.[17]

Monoclinic crystal structure of 1,5-bis(4-isopropylbenzylidene) thiocarbonohydrazide, was reported by Yan-Hua Han and et al. The reported compound was obtained by condensation of 4-iso-propylbenzaldehyde with thiocarbohydrazide. The existence of intermolecular N-H···S hydrogen bonds link the molecules into centrosymmetric dimmers.[18]

Franco Bisceglie et al., have reported the crystal structures of the Schiff base cuminaldehyde thiosemicarbazone (Htcum) and its nickel (II) complex $[Ni(tcum)_2]$. The crystal data of Htcum showed that the two-sulfur atom and the hydrazine nitrogen are in trans position with respect to the bond between carbon and hydrazinic nitrogen atom. The molecular conformation comprises of the strong intramolecular hydrogen bond. In the complex the Schiff base behave as a bidentate ligand through the sulphur and imine nitrogen atoms.[19]

Kamni et al., have reported the yellow coloured crystals of (4Z)-2-Phenyl-1-{(E)-[4-(propan-2-yl)benzylidene]-amino}-4-[(thiophen-2-yl)methylidene]-1Himidazol-5(4H)-one obtained by refluxing a mixture of 3-hydrazinyl-3-oxo-1-(thiophen-2-yl)prop-1-en-2-yl]benzamide (with 4-(propan-2-yl)benzaldehyde. The crystal system exhibits monoclinic with the space group P21/c and showing pi-pi interactions between thiophene and imidazole ring.[20]

Biological activity:

An assay of the nucleolytic cleavage activities of binuclear copper(II) complexes derived from the Schiff base of cuminaldehyde and substituted thiosemicarbazides $NH_2NHC(S)NHR$,(where, R = H, Me, Et and Ph) on pUC18 plasmid DNA using gel electrophoresis in the presence and absence of H_2O_2 was performed.[21] The results revealed that the ligands showed increased nuclease activity when administered as copper complexes. The copper (II) complexes acted as an efficient chemical nuclease with hydrogen peroxide activation. The data emphasised that the complex exhibit both oxidative and hydrolytic chemistry in DNA cleavage.

A series of Co (II), Ni(II), Cu(II) and Zn(II) complexes with the Schiff base of L-histidine and cuminaldehyde were synthesized and studied for CT-DNA cleavage and screened for antimicrobial activity against *E. coli, S. aureus, A. flavus C. albicans* and *P. aeruguinosa*. The results revealed that these complexes show enhanced activity than the free ligand.[22]

A series of transition metal complexes of Co(II), Ni(II), Cu(II) and Zn(II) obtained from Schiff base of 4-aminoantipyrene and cuminaldehyde were synthesised and screened for *in vitro* antimicrobial studies using bacterial strains like *Escherichia coli, Staphylococcus aureus, Klebsiella pneumonia, Proteus vulgaris* and fungal strains like *Candida albican, Aspergillus niger*, employing agar-well diffusion method. The results revealed that both the Schiff base as well as its complexes possessed significant antimicrobial activity.[23]

Trivalent cobalt[27] and divalent nickel[24] complexes of hydrazinecarbothioamides derived from 4-(propan-2-yl) benzaldehyde and substituted thiosemicarbazides $NH_2NHC(S)NHR$, where R = H, Me, Et and Ph were, assayed on pUC18 plasmid DNA using gel electrophoresis in the presence and absence of H_2O_2. The ligands showed increased nuclease activity when administered as cobalt (II) complexes. All the complexes behave as efficient chemical nucleases with hydrogen peroxide activation. The study indicated that the complexes exhibit both oxidative and hydrolytic DNA cleavage.

Nine odorant Schiff bases were prepared by condensation of anthranilic acid with corresponding naturally occurring carbonyl compounds *viz.* anisaldehyde, benzaldehyde, cinnamaldehyde, citral, citronellal, cuminaldehyde, veratraldehyde, acetophenone and α-ionone *via* conventional and microwave irradiation methods. The compounds were screened for antimicrobial activities. Results revealed that the compounds showed moderate to good antimicrobial activity against bacteria (*Staphylococcus aureus* and *Escherichia coli*) and fungi (*Aspergillus niger* and *Penicillium chrysogenum*).[25]

Three mononuclear copper (II), nickel(II) and cobalt(II) complexes derived from the Schiff base of 2-(4-isopropylbenzylidene) – N - phenyl hydrazine carbothioamide were screened for their DNA interaction and antibacterial studies. All the complexes bound to DNA molecule in an intercalative mode and exhibited an average activity against the gram-positive bacterial strains such as *Staphylococcus aureus, Bacillus subtilis* and gram negative bacterial strains such as *Pseudomonas aeruginosa* and *Escherichia coli.* Docking studies revealed their binding affinity with VEGF-C protein.[26].

Coordination behaviours as well as the DNA interaction of Schiff bases derived from cuminaldehyde and aromatic amines *viz.* 2-aminophenol and 4-aminoantipyrene towards the facial tricarbonylrhenium(I) core was reported. The results indicated that the metal compounds showed affinities towards CT-DNA.[28]

Thiosemicarbazone cuminaldehyde and its Ni (II) and Cu(II) metal complexes were tested *in vitro* for their antileukemic activity on U937 human cell line. The ligand inhibited cell proliferation with an IC_{50} value of 3.2µM. The copper (II) complex inhibit topoisomerase IIa activity.[20]

CONCLUSIONS:

Cuminaldehyde is an active component of *Cuminum cyminum*. Schiff bases and the metal complexes derived from cuminaldehyde have been shown to exhibit biological properties including antibacterial, antifungal and nuclease activities. But still much attention has not been paid in the synthesis of Schiff bases derived from cuminaldehyde. Only a few such compounds and its metal complexes has been synthesized and characterized. Hence there is a need to synthesize novel complexes obtained from Schiff bases of cuminaldehyde and to explore the biological activities.

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