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Metal Complexes Driven from Schiff Bases and Semicarbazones for Biomedical and Allied Applications: A Review

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Abstracts

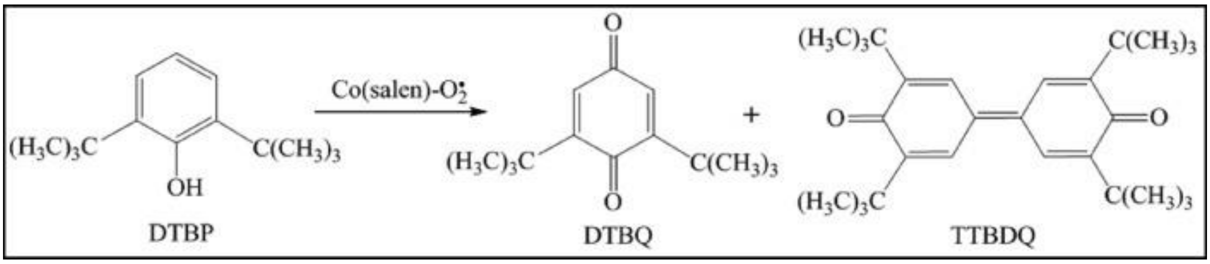
Schiff bases are versatile organic compounds which are widely used and synthesized by condensation reaction of different amino compound with aldehydes or ketones known as imine. Schiff base ligands are considered as privileged ligands as they are simply synthesized by condensation. They show broad range of application in medicine, pharmacy, coordination chemistry, biological activities, industries, food packages, dyes, and polymer and also used as an O2 detector. Semicarbazone is an imine derivative which is derived from condensation of semicarbazide and suitable aldehyde and ketone. Imine ligand–containing transition metal complexes such as copper, zinc, and cadmium have shown to be excellent precursors for synthesis of metal or metal chalcogenide nanoparticles. In recent years, the researchers have attracted enormous attention toward Schiff bases, semicarbazones, thiosemicarbazones, and their metal complexes owing to numerous applications in pharmacology such as antiviral, antifungal, antimicrobial, antimalarial, antituberculosis, anticancer, anti-HIV, catalytic application in oxidation of organic compounds, and nanotechnology. In this review, we summarize the synthesis, structural, biological, and catalytic application of Schiff bases as well as their metal complexes.
Keywords : Schiff Base, Semicarbazone, Metal Complexes, Biological/Biomedical Activities.

Introduction:
Schiff base is known in the name of Hugo Schiff who first reported the reversible acid-catalyzed condensation reaction between primary amine with carbonyl compounds . They are also known as imines with general structure R─CH=N─R′, where R and R′ is linear or cyclic alkyl and/or aryl group which may be differently substituted . Schiff bases are an important class of ligands for co-ordination chemistry, and they coordinate to metal ions *via* azomethine nitrogen . Schiff base ligands have been extensively studied in the field of coordination chemistry mainly because of their facile syntheses, easy availability, and electronic properties. In recent times, Schiff base coordination chemistry has attracted much attention because of their significance in organic synthesis, analytical chemistry, refining of metals, metallurgy, electroplating, and photography . Schiff bases have wide applications in dye industry, catalysis, fungicidal, and agrochemical . Several Schiff bases are reported to possess remarkable antibacterial, antifungal, and anticancer activities. In such class of compounds, the C=N moiety is important for biological activity. Abdel-Rahman et al. have reported number of transition metal complexes by using variety of Schiff base ligands and have studied their different biological activities such as antimicrobial, anticancer, antifungal, etc. For example, a number of Fe (II) complexes have designed and synthesized by using variety of Schiff bases ligands derived from 5-bromosalicylaldehyde (bs) and various α-amino acids such as L-alanine (ala), L-phenylalanine (phala), L-aspartic acid (aspa), L-histidine (his), and L-arginine (arg). These complexes were screened for their antibacterial and antifungal activity against *Escherichia coli, P*seudomonas*aeruginosa,* and *Bacillus cereus* and different antifungal cultures such as *Penicillium purpurogenium, Aspergillus flavus,* and *Trichothecium rosium*. It is found that Fe (II) complexes exhibited strong antibacterial and

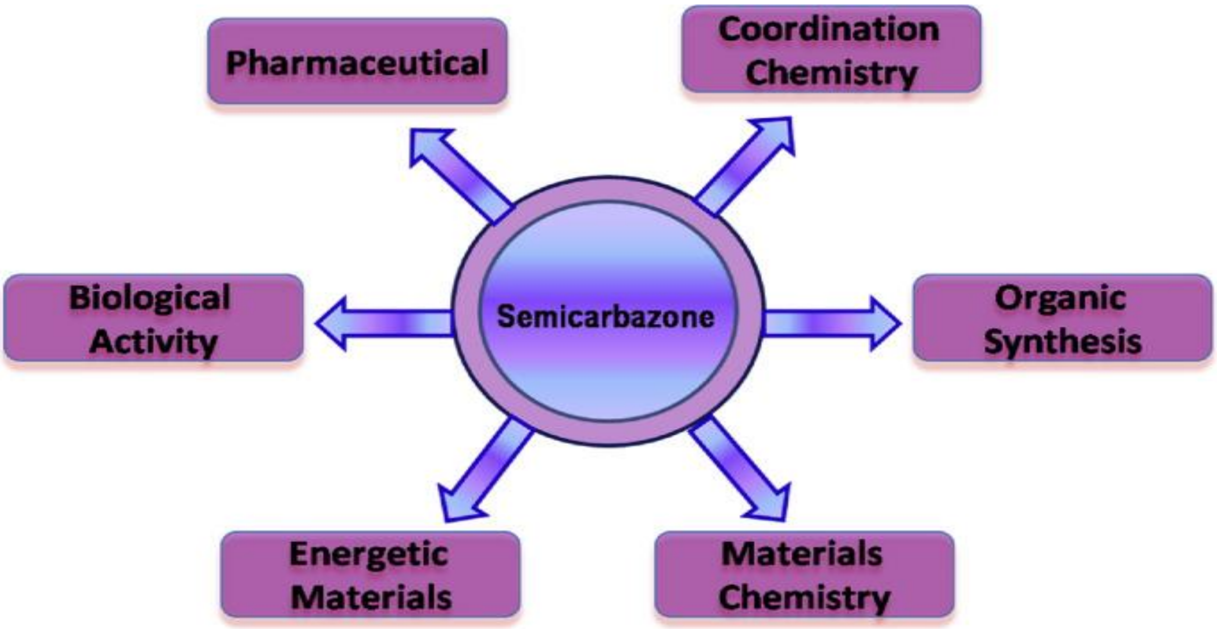
antifungal activity compared with the amino acids Schiff base ligands. Also, this complexes were tested for their interaction with calf thymus (CT) DNA by utilizing viscosity, UV-visible spectroscopy, and agarose gel electrophoresis measurements at pH = 7.2. The results revealed that the studied complexes showed different DNA binding constants that depend on the Schiff base ligands, and they strongly bind to CT DNA through intercalative mode.

Some Cu (II), Co (II), and Ni (II) complexes have been reported by using Schiff base ligand derived from 2-amino-3-hydroxypyridine and 3-methoxysalicylaldehyde and were investigated for their *in vitro* antimicrobial activities against the numerous bacteria and fungi. Also, these complexes were tested for DNA binding, and it was found that these compounds could bind to DNA through intercalative mode. However, the cytotoxicity of these metal Schiff base complexes on different cell line such as human colon carcinoma cells, (HCT-116 cell line), as well as breast carcinoma cells, (MCF-7 cell line), illustrated effective cytotoxicity effect against the growth of carcinoma cells as compared with the clinically used vinblastine standard . Among most popular ones, the salen/salophen-based metal coordination complexes have found immense applications in sensors, catalysis, biology, and material science. Many researchers have investigated a large number of Schiff base ligands as chelating compounds, e.g. metal chelates of copper, cobalt, etc. for a variety of interesting catalytic application. Co (II) salen complex of N,N-bis(3,5-di-tert-butyl-salicylidene-1,2-cyclohexane diaminato) was used as catalyst in oxidation of 2,6-di-tert-butylphenol (DTBP) and 3,5-di-tert-butylphenol (35-DTBP) in super-critical carbon dioxide ($scCO_2$).

The oxidation of DTBP resulted into 2,6-di-*tert*-butyl-4,4′-benzoquinone(DTBQ) along with the side product of radical coupling, i.e. 3,5,3′,5′-tetra-*tert*-butyl-4,4′-diphenoquinone (TTBDQ). The conversion and selectivity of catalyst were examined as a function of pressure, temperature, and concentration of catalyst.

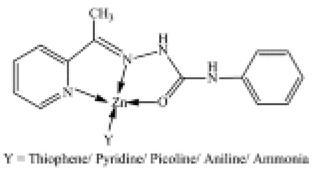
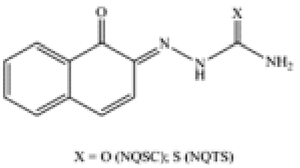
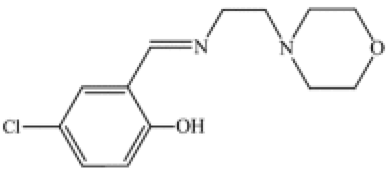
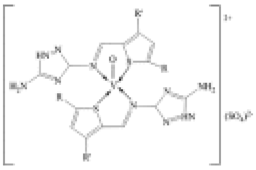
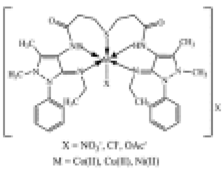


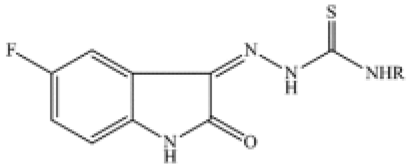
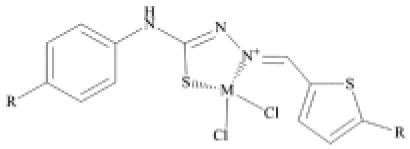
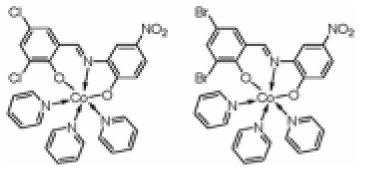
Similarly, Semicarbazone is an imine derivative, usually obtained by condensation of semicarbazide with suitable aldehyde or ketone. Semicarbazones have potentially wide range of biological applications, such as anticancer, antioxidant, antifungal, anticonvulsant, antiinflammatory, analgesic, and antibacterial agents . Semicarbazone and its metal complexes play the significant role in an industrial, pharmaceutical, and agricultural chemistry. They are also used as polymers, dyes, and as catalysts in different biological systems, like Schiff base ligands. It is observed that the metal complex can be more active than the free ligand. Transition metal complexes of semicarbazone have been widely studied because of their coordinating ability and analytical application .



1) Table

Various semicarbazones, Schiff bases, and their biological applications

Structure	Biological application	Reference
	**Antimicrobial activity** against *Staphylococcus aureus, Bacillus anthracis, Aspergillus niger,* and *Candida albicans*	*Int. J. Scientific Technology Res.*,**3** (2014) 73–77.
	**Anticancer activity** against MCF-7 breast cancer cell lines	*J. Inorg. Biochem.*, **99** (2005) 1526–1531.
	**Antibacterial activity** against Gram +ve bacterial (*Bacillus subtilis* and *S. aureus*) and Gram –ve bacterial (*E. coli* and *P. fluorescence*)	*J. Coord. Chem.*, **62** (2009) 3471–3477.
	**Antibacterial activity** against Gram –ve bacterial strains (*E. coli*, *S. flexneri*, *P. aeruginosa*) and Gram +ve bacterial (*S. aureus* and *B. subtilis*)	*J. Enz. Inhib. Med. Chem.*, **27** (2) (2012) 187–193.
	**Antifungal activity** against *Alternaria brassicae, Aspergillus niger,* and *Fusarium oxysporum*	*Molecules*,**14** (2009) 174–190.

Structure	Biological application	Reference
	**Antiviral activity**, Inhibits the replication of vesicular stomatitis virus and shows cytotoxicity in Vero clone CCL-81 cell lines	*Monatsh Chem.,***144** (2013) 1725
	**Antiviral activity** against DNA and RNA viruses e.g. human cytomegalovirus strains AD-169, **cytostatic activity** against human cervix carcinoma (HeLa) cells	*Eur. J. Med. Chem.*, **46**(11) (2011) 5616–5624.
	**Antitumor activity** were tested for human cancer cell line (A-431, HT-144, and SK-MEL-30)	*Brazilian J. Med. Bio. Res.,***50**(7) (2017) 6390.

A variety of structural and coordination aspects of semicarbazones and thiosemicarbazone metal complexes of different group element have been discussed by Casas et al. . Large number of thiosemicabazones is used for the detection and determination of different cations and anions. Spectrophotometry or extractive spectrophotometry are often employed for the quantitative determination of ions; in addition to these, some other techniques are also used such as gravimetry, titrimetry, and fluorimetry by Suvarapu et al. . Asuero et al. and Singh et al. described application of thiosemicarbazone in inorganic analysis where they showed that biacetyl bis(4-phenyl-3-thiosemicarbazone) (BBPT) as well as bipyridyl glyoxal bis(4-phenyl-3-thiosemicarbazone) (BGPT) can be employed in the spectrophotometric determination of copper, zinc, mercury, and palladium. Such studies explained that the complexing properties of BBPT and BGPT are much better than those exhibited by biacetyl monothiosemicarbazone (BMTS) and picolinealdehyde-4-phenyl-3-thiosemicarbazone (PPTS). Also, BBPT is recommended as a reagent for the extractive spectrophotometric determination of cadmium and bismuth. In addition to their interesting coordination chemistry, semicarbazone and thiosemicabazones have attracted enormous attention because of their potentially useful biological activities . There are several reports existing on biological activity of thiosemicabazones and their transition metal complexes . The mechanism of biological activity of thiosemicarbazones are because of their ability to inhibit the biosynthesis of DNA, probably by blocking the enzyme ribonucleotide diphosphate reductase; binding to the nitrogen bases of DNA, by hindering base replication; and by creating the lesions in DNA strands by oxidative rupture. Zn (II) complexes of 2-acetylpyridine-4-phenyl semicarbazone have also been reported for their antimicrobial activity against various bacteria and fungi . The synthesis of metal complexes of 1-vinyl-pyrrole-2-carbaldehyde semicarbazone and thiosemicarbazone and their importance in pharmaceutical as well as in medicinal field have been reported by Milkhaleva et al. . *ortho*-Naphthoquinone thiosemicarbazone (NQTS) as well as naphthoquinone semicarbazone (NQSC) and their different Ni (II) complexes were investigated for their *in vitro* anticancer activity in MCF-7 human breast cancer cells. It is observed that nickel complex with NQTS and NQSC is more active in the inhibitory action of MCF-7 cell proliferation than the free ligands. This exposed the remarkable anticancer properties of these compounds. Chandra and Tyagi have reported the synthesis, electron paramagnetic resonance (EPR), and electronic spectral studies of Mn (II) and Cr (III) complexes of vanillin thiosemicarbazone and semicarbazone, and they observed octahedral geometry for these complexes. Several novel semicarbazones and their Zn (II) and Cd (II) complexes were reported by Jadhav et al. for their use as precursor for the synthesis of nanostructured metal selenides with particle diameter typically below 5–10 nm. Such precursors gave new dimension to their utility and possibly allowed their entry in the field of nanotechnology.

Conclusion:

Schiff bases have been reported for a long time and their applications have been mainly limited to chemistry of pharmaceutical importance (biological importance) and catalysis. In recent years, the scope of such compounds has broadened, and their new synthetic methodology has been evolved that are based on normal chemical reactions as well as by solid state reaction. There are also some reports on use of other source of energy during their synthesis. Recent literature also highlights the modern day application that has extended to materials chemistry as well as into nanotechnology. Schiff bases and semicarbazones offer a variety in their coordination of vast majority of transition metals and therefore offer great potential as precursors for new generation nanomaterials of respective metal or their compound semiconductors. Imine ligands such as Schiff base, semicarbazones, and their derivatives have therefore been widely explored for catalytic, pharmacological, industrial, etc. applications. Schiff base ligands are considered as interesting ligand because of the ease of preparation with versatility and variable denticity. Nowadays, Schiff base and their metal complexes are fascinating research topic that continuously provides us with new information about newly synthesized compounds. In this review, the biological, catalytic activity along with some miscellaneous applications of imine ligands and its metal complexes have been summarized taking the scope into materials chemistry directly or indirectly.

References:

1. Schiff H. *Ann. Suppl.* 1864;3:343.
2. Carey F.A. fifth ed. MacGraw-Hill; New York: 2003. Organic Chemistry; p. 724.
3. Kajal A., Bala S., Kamboj S., Sharma N., Saini V. *J. Catal.* 2013;2013:1–14.
4. vigato P.A., Tamburini S. *Coord. Chem. Rev.* 2004;248:1717.

5. Pfeiffer P., Bucholz E., Bouer O. *J. Prakt. Chem.* 1931;129:163.
6. Pfeiffer P., Brieith E., Lubbe E., Tsumaki T., Leibigs J. *Ann. Chem.* 1933;84:503.
7. Pfeiffer P., Pfitzinger H. *J. Prakt. Chem.* 1936;145:243.
8. Gaur S. *Asian J. Chem.* 2003;15(1):250.
9. Gemi M.J., Biles C., Keiser B.J., Poppe S.M., Swaney S.M., Tarapley W.G., Romeso D.L., Yage Y. *J. Med. Chem.* 2000;43:1034.
10. Bhattacharjee R., Datta C., Das G., Chakrabarty R., Mondal P. *Polyhedron.* 2012;33(1):417–424.
11. Ding F., Jia Y., Wang J., Huaxue Yingyong. *Chem. Abstr.* 2004;21:835–837. 142 (2005) 189480.
12. Srivastava V., Srivastava S.K., Mishra A.P. *J. Indian Chem. Soc.* 1995;72:47–48. P. Mishra, P. N. Gupta, A. K. Shakya, J. Indian Chem. Soc., 68 (1991) 539-541.
13. Mishra P., Gupta P.N., Shakya A.K. *J. Indian Chem. Soc.* 1991;68:539–541.
14. Singh A.K., Pandey O.P., Sengupta S.K. *Spectrochim. Acta A Mol. Biomol. Spectrosc.* 2012;85(1):1–6.