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An overview of biological aspects of Schiff base metal complexes

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Abstract

Schiff bases, having azomethine (RHC=N-R') group and their metal complexes are widely used for industrial purposes and also reveal a wide range of biological applications. This review describes the most promising biological activities of Schiff bases and their metal complexes of cerium. A general idea for synthetic methodologies used for the synthesis of Schiff bases and their metal complexes is also discussed.

Keywords: Schiff bases; metal complexes; Amine; Aldehydes or ketones; Nucleophilic; Biological Aspects.

Introduction

Inorganic elements play crucial role in biological and biological medical processes, and it is evident that many organic compounds used in medicine do not have a purely organic mode of action, some are activated or bio-transformed by metal ions metabolism [1]. Schiff bases are condensation products of primary amines with carbonyl compounds and they were first reported by Hugo Schiff in 1864. The common structural feature of these compounds is the azomethine group with a general formula RHC=N-R' where R and R' are alkyl, aryl, cyclo alkyl or heterocyclic groups which may be variously substituted. These compounds are also known as anils, imines or azomethines [2]. Several studies showed that the presence of a lone pair of electrons in sp^2hybridized orbital of nitrogen atom of the azomethine group is of considerable chemical and biological importance. Because of the relative easiness of preparation, synthetic flexibility, and the special property of C=N group, Schiff bases are generally excellent chelating agents, especially when a functional group like –OH or –SH is present close to the azomethine group so as to form a five or six membered ring with the metal ion [3] . Versatility of Schiff base ligands and biological, analytical and industrial applications of their complexes make further investigations in this area highly desirable.

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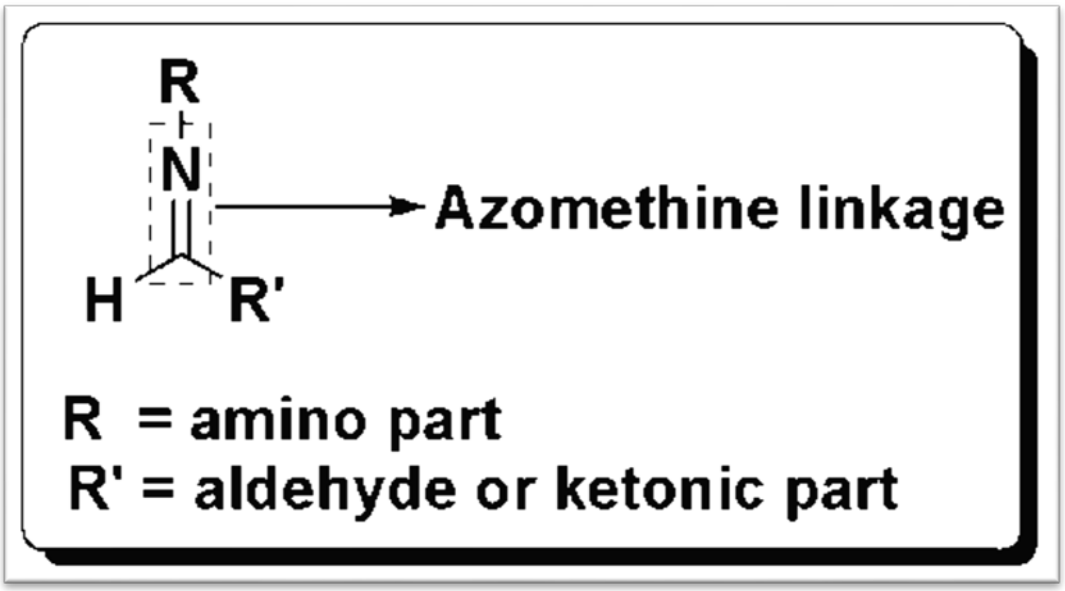

Figure1. *Structure of azomethine group*

The formation of Schiff bases is generally favored by making use of dehydrating agents. A great care should be taken for the purification of Schiff bases as they are degradable.

General synthesis of Schiff bases

The acid/base catalysis or heating is employed for the synthesis of Schiff bases as their reactions are mostly reversible. The Schiff bases are formed by the reaction of amines with carbonyl compounds but it does not follow simple nucleophilic addition, but give an unstable addition compound called carbinolamine [4]. The compound thus obtained is unstable and loses water molecule. The dehydration step during formation of Schiff base is actually the rate determining step and the reaction shown in scheme is catalyzed by acid. The removal of product or separation of water from the reaction mixture assists the formation of product [5]. The aqueous acids or bases may hydrolyze Schiff bases towards their respective aldehydes or ketones and amines as well.

In this regard, high concentration of acid is not needed due to basic character of amines. The formation of carbinolamine cannot occur and equilibrium is shifted towards left side because protonated amine does not act as nucleophile [6]. This is the reason that mildly acidic pH

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arequite good for the formation of Schiff bases. Moreover, bases can also catalyze dehydration of carbinolamines.

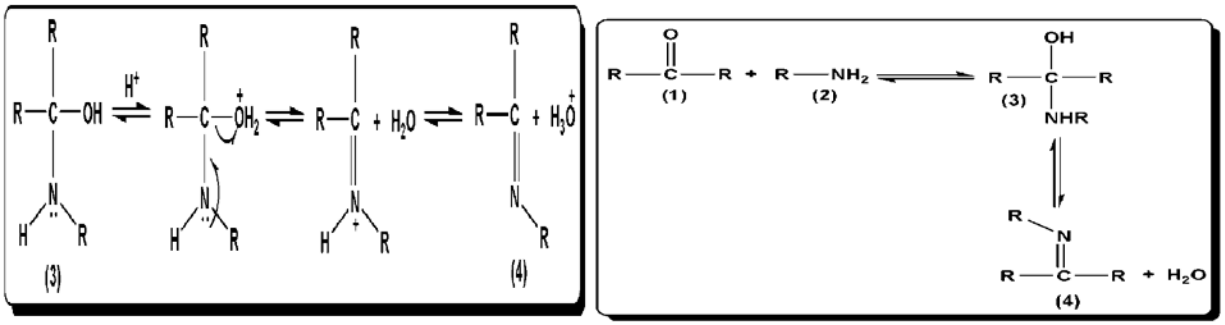

Figure 2. *Rate determining step in the synthesis of Schiff bases*

This reaction shows similar trends as E_2 elimination of alkyl halides but this reaction does not occur in a single step. It involves an ionic intermediate and completes in two steps. In real sense, the formation of Schiff bases is a combination of two type of reactions i.e., elimination after addition. Schiff bases can undergo hydrolysis on silica gel and due to this reason; purification of Schiff bases by chromatography is not recommended [7]. The general formula of azomethine group is the most common structural feature of Schiff bases.

Chelated Schiff bases

The chelating ability is enhanced when nitrogen atom is present in the vicinity of one or more donor groups. The azomethine group carrying ligands i.e., Schiff bases have achieved a considerable position and become ligands of interest in coordination chemistry due to the fact that formation of such compounds proceeds with greater ease.

(ONNO)-Tetradentatebis-Schiff ligands: The condensation of a diamine derivative with salisaldehyde leads to the formation of a Schiff base which possesses such a structural set up that two nitrogen atoms and two oxygen atoms are available for chelation [8]. Thes ligands are known as Salen ligands and are analogous to the porphyrin in structural aspects but can be easily prepared [10]. Since the tetradentate ligands obtained by condensation of salicyldehyde and ethylenediamine were originally termed as salen ligands but another term “salen-type” is now employed to discuss the class of (O, N, N, O) tetradentatebis-Schiff ligands in literature.

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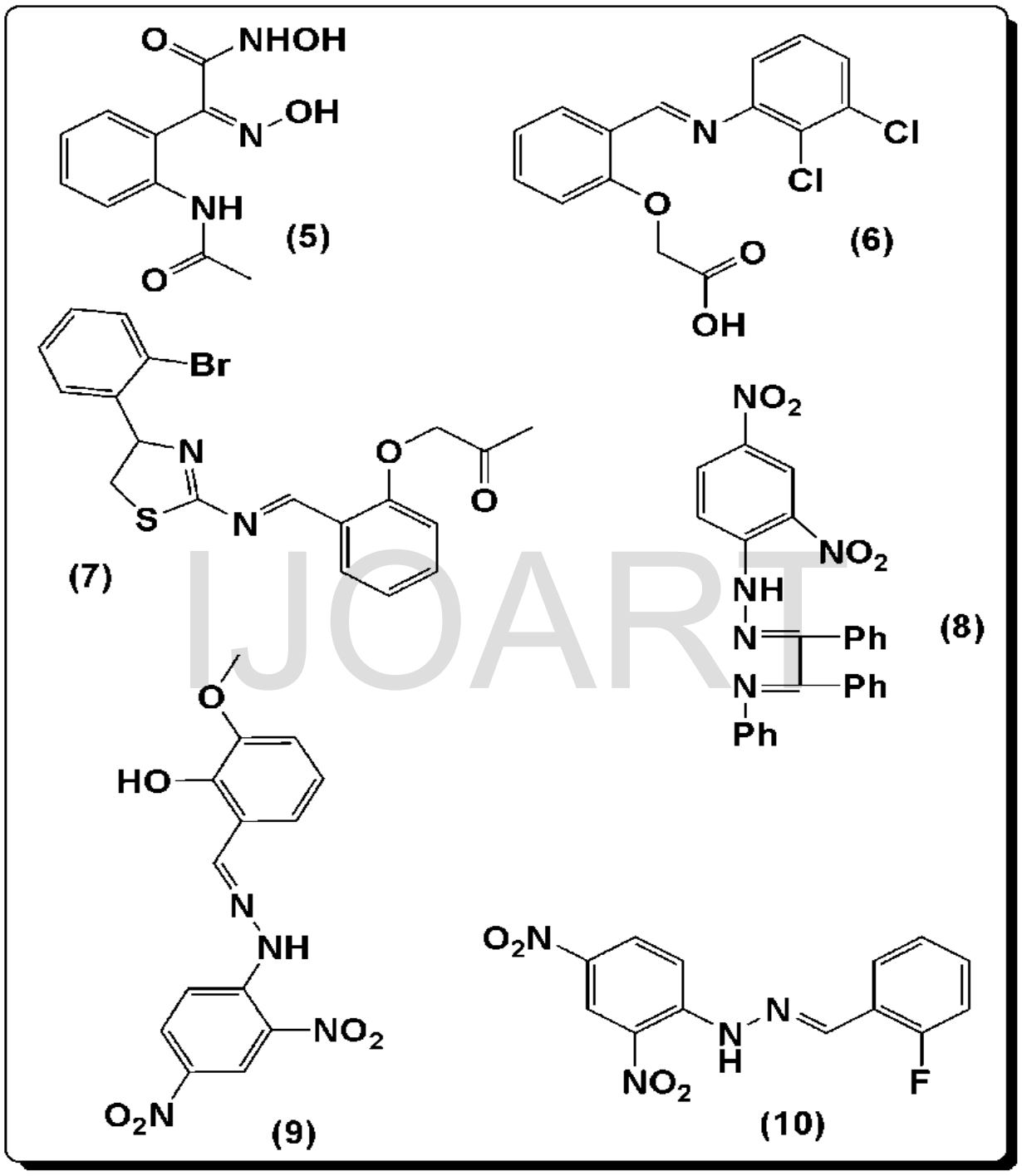
Moreover, the synthetic design of Schiff bases may involve stereogenic centers and other elements of chirality.



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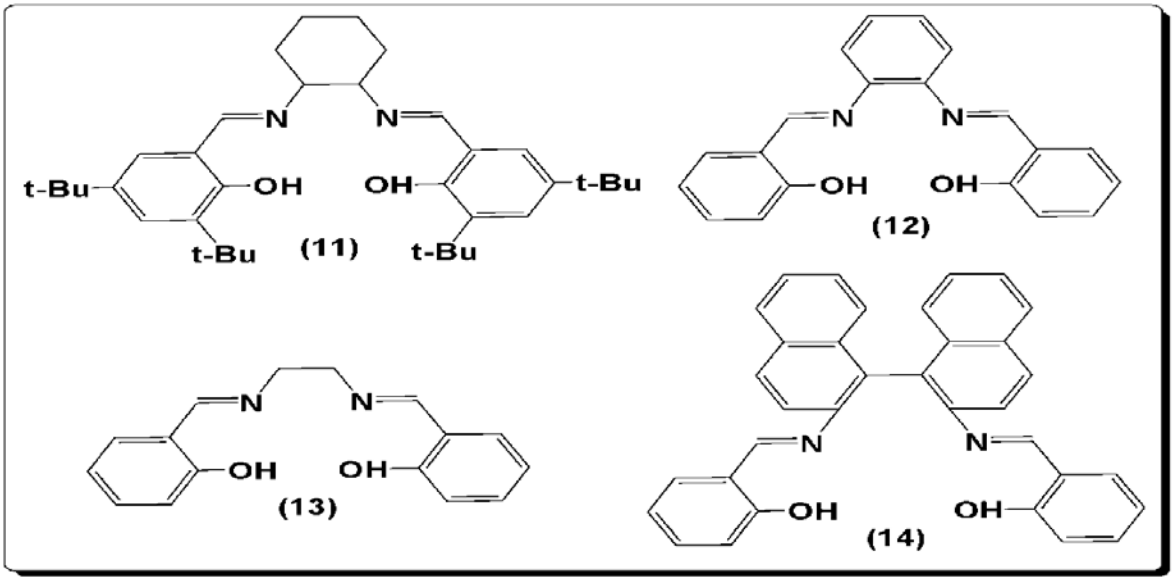

Structure of Schiff base macrocycles

Furthermore, the well known self condensation reaction of appropriate formyl- or keto- and primary amine precursors leads to the formation of Schiff base macrocycles and has a wide range of utilization in supramolecular and coordination chemistry [2,3]. The excellent capability of Schiff bases to stabilize the metal ions in various oxidation states has enhanced their uses in metal complexes [11].

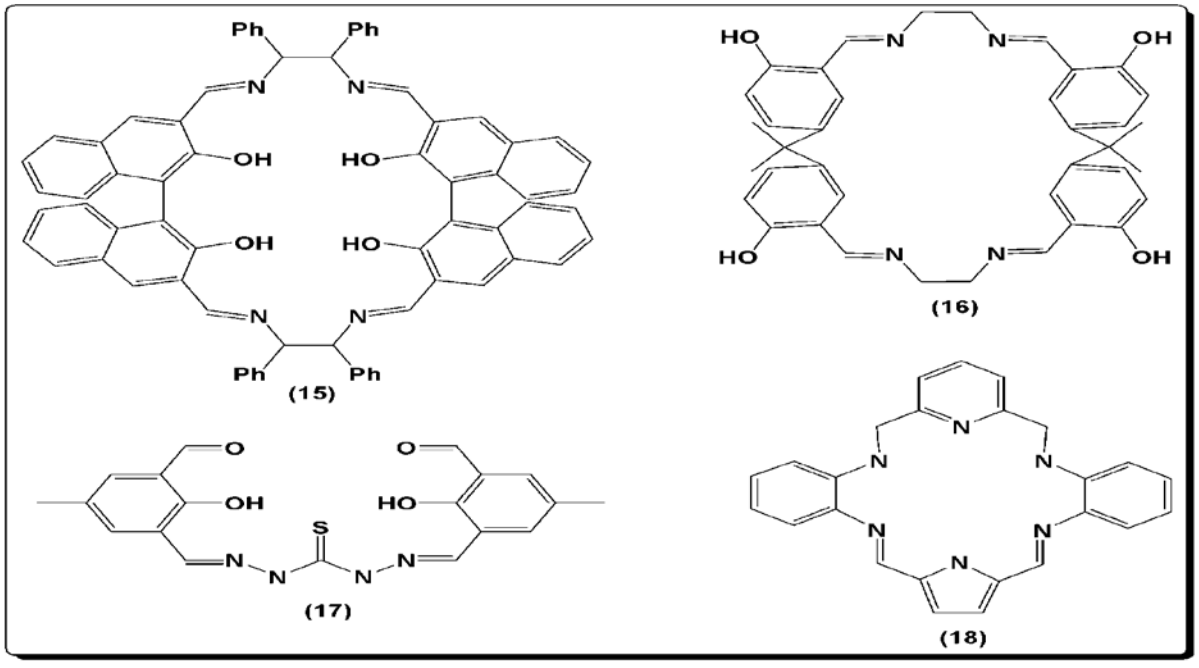

Figure 3. ***Molecular structure of O,N,N,O tetra dentate Schiff base ligands***

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An interesting application of Schiff bases is their use as an effective corrosion inhibitor, which is based on their ability to spontaneously form a monolayer on the surface to be protected [12] . Many commercial inhibitors include aldehydes or amines, but presumably due to the C=N bond the Schiff bases function more efficientlyin many cases [13]. The principal interaction between the inhibitor and the metal surface is chemisorptions [14]. The inhibitor molecule should have centers capable of forming bonds with the metal surface by electron transfer. In such cases the metal acts as an electrophile and the inhibitor acts as a Lewis base [15]. Nucleophilic centers, such as oxygen and nitrogen atoms, of the protective compound have free electron pairs which are readily available for sharing [16]. Together with the atoms of the benzene rings they create multiple absorption sites for the inhibitor thus enabling stable monolayer formation. Imines also have biological importance [17]. An imine linkage between the aldehyde derived from vitamin-A and the protein opsin in the retina of the eye plays an important role in the chemistry of vision [18]. Vitamins are also called coenzymes, meaning that they are to the functioning of many enzymes, which are large proteins that catalyze chemical changes in cell [19]. An example of a biologically important aldehyde is *pyridoxalphosphate*, which is the active form of the vitamin B6. Vitamin B6 serves as a coenzyme by forming an imine with an amino acid grouping an enzyme [20]. The coenzyme, bound to the enzyme, is involved in transamination reaction, the transfer of the amino group from one amino acid to another, which is important in the metabolism and the biosynthesis of amino acids. In the last step, enzyme-catalyzed hydrolysis cleaves the imine to pyridoxal and the modified amino acid.

Catalysts

Co(II), Fe(III) and Ru(III) complexes of Schiff bases derived from hydroxybenzaldehyde are used in oxidation of cyclohexane into cyclohexanol and cyclohexanone in presence of hydrogen peroxide. The most efficient catalysts are the Fe(III) complexes which is unusual because, in general, the cobalt(II) complexes have high activity for alkane oxidation reactions [21]. Chromium-salen complexes are wellknown catalysts both in heterogeneous and homogeneous. Binucleating complexes of Fe, Co, Ni, Zn with Schiff bases neytralbis(iminopyridyl)benzene and monoanionicbis(iminopyridyl)phenolate acts as catalysts in the oligomerisation of ethylene. New manganese(II) and manganese(III) complexes of substituted N,N'- bis(salicylidine)-1,2-diimino-

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2-methylene appear to be efficient models for peroxidase activity [22]. New Copper(II) complexes of indoxylthiosemicarbazone(ITSC) show one pair of well defined reduction peaks at different potential in the forward scan, which represent the reduction of Cu^{++} to Cu^{+} by one electron process and subsequent oxidation of Cu^{+}. The quasireversible nature of the Cu^{++}/Cu^{+} is due to inherent reducing tendency ofthiosemicarbazone ligands. Ruthenium and cobalt complexes with Schiff basesA wide variety of cobalt(II) complexes are known to bind dioxygen more or less reversibly and are therefore frequently studied as model compounds for natural oxygen carrier and for their use in O_2 storage, as well as in organic syntheses due to their catalytic properties under mild conditions [23].

Biological Systems and Metallo Elements

Introduction and general chemical principles

The variety and extent of metal ions involvement has been recently appreciated but it has a very long history in toxicology, medicine and pharmacology. For instance, Cr, V, Mn, Cu, Ni, Co, Fe, Zn and Mo among the transition metals are very essential to life. The rare earth metals also involve in the biological activity [24]. Some other elements like Ag, Ir, Pt, Au, Os, Pd, Ti and others have some therapeutic value because of their use in therapy.

The physiological activity may or may not be associated directly with the determination of complex ions and their concentration and this fact raises another problem. Yet, chemistry of metal ions is affected by the solvent or absorption of metal ion on surface [25]. The action of platinum believed to be on DNA and drugs are usually administered in milligram quantities. Platinum interacts with DNA and remaining excess amount makes complexes with other cellular and extracellular fractions. The problems faced with the least knowledge of inorganic chemistry but the introduction of more powerful tools [26]. Physical techniques and better understanding of inorganic chemistry reflects that more issues can be addressed with significant chances of success. Therefore, it is primarily important to concentrate basic principles developed for transition metal ions for considering individual metal systems. Following properties make the metal ions suitable for above mentioned reactions:

- Oxygen and sulphur donor ligands can be utilized for complexation by employing metal ions as Lewis acids.

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- They have capability to react with variable oxidation states and unfilled d-orbitals are also available in them

Therefore, the properties of a complex are not only the function of ligand alone but also a direct result of nature of nature of complex metals is due to such reasons. The bonding characteristics of complexes and alteration in size of the metal ion are related to thermodynamic aspects. The stability constants for the complexes formed from various metal ions and one ligand have a particular sequence.

Biological Aspects

1. Urease Inhibitory Activity

The urease enzyme (EC 3.5.1.5) is present in bacteria, yeast, higher plants and exceptional in *Helicobacter pylori* and is basically a protein. Urease is also produced by various pathogens in gastrointestinal and urinary tract. The enzyme possesses nickel metal and is involved in the formation of carbamate and ammonia by hydrolysis of urea. The carbamate further decomposes to carbonic acid and ammonia, which causes an increase in pH [27].

2. The Breakdown of Urea to Ammonia and Carbamate.

Urease inhibitors the new drug targets and antiulcer agent to treat urinary and some hepatic diseases can be obtained by urease inhibitors. Hp induced pathologies are a major cause. The first line of treatment for prevention from infections caused by urease producing bacterium like *Helicobacter pylori* (Hp) therefore, include strategies based on urease inhibition which are being considered now. The colonies of gram-negative bacterium are developed in gastric mucosa of ~50 % of all humans. The bacterial persistence is by Hp which contributes to the treatment failure occupies and protected intra-cellular environment [28]. The infections by various organisms may be developed by broad spectrum of diseases, which include gastric cancer, gastritis and peptic ulceration. Hp survival is one of the major factors for urease in the stomach which is also involved in the formation of infectious stones and adds to the pathogenesis of hepatic encephalopathy, urolithiasis, urinary catheter encrustation and hepatic coma. The important class of urease inhibitor is hydroxamic acid and some of its derivatives. The binding of metal ions to the active site of enzyme is involved in the mechanism of inhibition and they serve as good metal chelators [29]. AHA causes rapid and complete inhibition of urease inhibitor and

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acetohydroxamic acid (AHA) is the best studied hydroxamate which is the best inhibitor at 25 °C with *Ki* value of 5 μM [30].

3. Lipoxygenases Inhibitory Activity

The hydroperoxidation of lipids is catalyzed by a class of iron-containing dioxygenases known as lipoxygenases possessing structure of cis-1, 4-pentadiene. They are very much wide spread in animals and plants. The metabolism of leukotrienes and prostaglandins is carried out by a number of lipoxygenasesisozymes in animals. The formation of hydroperoxides is catalyzed by hydroperoxides as the biosynthesis of several inflammatory mediators in first step, which leads to leukotriene synthesis. The large non-haeme iron-containing enzymes like lipoxygenases use molecular oxygen for the diooxygenation of arachidonic acid for the formation of hydroperoxides due to significance of such compounds, in a number of diseases, the extensive study has been conducted on lipoxygenase [31]. The broad range of cardiac, inflammatory diseases and human cancers involve the implication of such enzymes. These enzymes are actually peroxidases. The conversion of procarcinogen into carcinogens is catalyzed by these catalysts. The precursors of hormones, such as lipoxins and leukotriensleukotriens, are produced by human lipoxygenases (HLO) which have implications in critical signaling in a number of cancers and inflammatory diseases [32].

4. **Alpha-Glucosidase Inhibitory Activity**

The easily absorbing sugars are obtained upon break down of complex carbohydrates by alpha-glucosidase. Inhibition of leukotriene biosynthesis has been extensively studied as a potential for the development of inhibition of leukotriene biosynthesis has been extensively studied as a potential for the development of blood sugar levels in diabetic people [33]. The drugs which are used to block alpha-glucosidase (alpha-glucosidase inhibitors) are also beneficial for people suffering from diabetes.

5. **Chymotrypsin Inhibitory Activity**

The proteolysis of chymotrypsinogen is carried out by trypsin which is also involved in the activation of chymotrypsin. The chymotrypsin is produced in acinar cells of the pancreas. The enzyme inhibitors are the substances which intercede natural substrates of enzymes especially in their conversion. The enzyme inhibition study of reported compounds is involved in the investigation of the choice of drugs in the pharmaceutical research area. The hyperactivity of enzymes is debilitated due to physiological abnormalities and enzyme inhibitors are the urgent

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need in such circumstances [34]. The decimation of cellular proteins and peptides along with replication of viruses is brought about the proteases in the enzyme mundane. The targets of anti-HCV and anti-HIV drugs are the proteases of HCV (NS_3 protease) and HIV which are involved in the replication of viruses. The declared inhibitors in genetically engineered plants are also targets of plant pathogens.

6. **Antioxidant Activity**

The free radicals and reactive oxygen species (ROS) are involved in complete damage of our tissues and such type of damage can be avoided by employing antioxidants. The amount of ROS which is removed is detoxified by mitochondria and at the same time, ROS is generated at mitochondrial site [35]. The capacity of removal of ROS from mitochondria could be very much different from that of generated ROS. The difference in ROS removal and generation leads to the emission of ROS outside mitochondria. The rate of emission of ROS and the production of ROS by extra mitochondrial resources determines the steady state ROS concentration.

7. **DNA Cleavage Activity**

The importance of certain compounds in medical diagnosis and genomic research is based on the ability of such compounds to bind and cleave double stranded DNA under physiological conditions. The hydrolytic and oxidative cleavage pathways are involved in DNA cleavage reactions [36]. The formation of fragments may be considered to take place through enzymatic processes which occurs due to hydrolysis of phosphodiester. The nucleobase oxidation and/or degradation of sugar by abstraction of sugar hydrogen atoms take place during oxidative process. The oxidative cleavage of DNA is brought about by various methodologies and the methodology which involves irradiation with visible light of long wavelength, has achieved significant importance for their major use in photodynamic therapy (PDT) of cancer [37].

The binding ability of DNA is the main source for making comparison in cleavage efficiency of the complexes to that of the control. The open circular DNA is obtained from supercoiled DNA by complexes. The account of DNA cleavage by hydroxyl radicals abstraction of a hydrogen atom from sugar units and proposed general mechanisms that predicts the release of specific residues which arise from transformation of sugars, which also depends on the position of hydrogen atom removal. The hydroxyl radical mediated cleavage reactions and cleavage of peroxy derivatives is inhibited by free radical scavangers.

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8. **Brine Shrimp Activity**

The shrimp lava are often destroyed by employing bioactive compounds and new bioactive synthetic products can be preliminary monitored by *in vivo* lethality test of the shrimp larvae. The *in vivo* animal experiment on large scale can be carried out by making use of this is rapid, inexpensive, in-house general bioassay.

9. **Anti-Bacterial Activity**

The microorganisms adsorb metal ions on their cell walls and as a result respiration processes of cells are disturbed and protein synthesis is blocked which is the requirement for further growth of organisms. The growth inhibition effects of metal ions are considerable. The only passage of lipid soluble material is favored by the lipid membrane that surrounds the cell in accordance with the overtone's concept of cell permeability, as the antifungal activity is controlled by lipophillicity factor. The overlap of ligand orbitals and the behavior of metal ions to share charge with the donor groups is reduced upon chelation. Besides this, the delocalization of π electrons over the whole ring is due to chelation and liphophilicity of complexes is enhanced. The proliferation of microorganisms is further restricted because the penetration of complexes in lipid membranes is facilitated by increased lipophilicity [38]. The impermeability of microbial cells and differences in ribosomes of cells are the major reason for variations in the effectiveness of different compounds against a variety of organisms. In most of the cases, ligands are less effective antifungal agents than their metal complexes.

The lanthanide complexes of the newly reported Schiff base were tested for antibacterial activity against bacteria *E.Coli* and *B.Subtilis* in which both ligand and metal complexes are active against the two microorganisms namely *E.Coli* and *B.Subtilis.* All metal complexes namely $[LaL_2(NO_3)_3]$, $[CeL_2(NO_3)_3]$, $[PrL_2(NO_3)_3]$, $[NdL_2(NO_3)_3]$, $[SmL_2(NO_3)_3]$, $[GdL_2(NO_3)_3]$, $[TbL_2(NO_3)_3]$, $[DyL_2(NO_3)_3]$ and $[ErL_2(NO_3)_3]$ are all highly active against the two bacteria. *E.coli* was found to show high activity towards complexes of praseodymium and erbium, moderately active towards lanthanum and samarium. *B.subtilis* was found to be highly active against cerium, praseodymium and erbium complexes and moderately active with lanthanum complex. The ligand was active towards both *E.coli* and *B.subtilius* [39].

The cerium(III) complexes are less active towards Bacillus subtilis and Escherichia coli in comparison to the free ligand, while The free ligand and the metal complexes showed higher and moderate antifungal activities. The binary cerium(III) complex showed no effect towards

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Alternaria alternata and less activity towards Syncephlastrum racemosum while the cerium(III) and The comparison of the biological activities of the synthesized compounds and some known antibiotics.

The formation of the polymeric Ce(IV) Schiff base complex is four salen units are coordinated with one Ce(IV) ion. For steric reasons, it is likely that two salen units in neighboring positions at the polymerbackbone always take part in the complex formation. The model Ce(IV) do not indicate a reversible redox behavior in any of the investigated coordination polymer films.

Effect of azomethine (-C=N-) group

The mechanism of working of such compounds may be on the basis of hydrogen bond formation by the azomethine group (-C=N-) at the active centers of cellular entities, which cause the interferences in normal cellular phenomenon.

- *Staphylococcus intermedius*is a coagulase-positive, a Gram-positive zoonotic organism, found in dogs, horses, mink, foxes, and pigeons as a common flora and invasive diseases are caused. It is responsible for invasive infections or some canine-inflicted wound infections in humans.
- *Bacillus subtilis*is commonly found in soil and vegetation and is a gram-positive organism which is responsible for causing ropiness.
- *Staphylococcus aureus*is found in skin, soft tissue, bone joint, endovascular and wound infections and is a facultative anaerobic, gram-positive, coagulase-positive catalase-positive potential pathogen. A range of illnesses from minor skin infections like scalded skin syndrome and cellulitis folliculitis to life-threatening diseases as toxic shock syndrome, pneumonia and sepsis. A more active strain of *S. aureus*is Methicillin-resistant *S. aureus*, which is now resistant to most of the antibiotics.
- *Escherichia coli* is a facultative anaerobic, gram-negative, and non-sporulating bacterium. Some serotypes among its strains can cause food poisoning in human and bacterial infections including cholecystitis, bacteremia, cholangitis, pneumonia, urinary tract infection (UTI), vomiting and bloody diarrhea but most of them are harmless.
- *Salmonella typhi*affects the 17 million people and is the reason behind 60 thousands deaths annually in the world. It is a Gram-negative, facultative anaerobic pathogen and results in enteric fever and typhoid.

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References

[1] Afanas'ev B, Dorozhko A I, Brodskii A V, Kostyuk V A, Potapovitch A I, *Biochemical Pharmacology*, **38**. 1763-1739 (1989).

[2] Cohen B, *Biochimicaet BiophysicaActa*, **391**, 193 (1975).

[3] Price C, Elsegood M R J, Clegg W, Houlton A, *Journal of the Chemical Society, Chemical Communications*, 2285 (1995).

[4] Stehlik C, *Arthritis and Rheumatism*, **60**, 3524 (2009).

[5] Clements N M, Willemsen S A, Myers, Dong Y, *Critical Reviews in Clinical Laboratory Sciences*, **41**, 265 (2004).

[6] Schiff H . *Justus LiebigsAnnalen Der Chemie*, **131**, 118-119 (1864).

[7] Zollner H, *Handbook of Enzyme Inhibitors*, VCH, Weinheim (1989).

[8] Costamagna J, Vargas J, Latorre R, Alvarado A,Mena G, *Coordination Chemistry Reviews*, **119**, 67-88 (1992).

[9] Barton J K , Kumar C V, Turro N J , *Journal of the American Chemical Society*, **108(20)**, 6391 (1986).

[10] McCord J, Fridovich M, *Journal of Biological Chemistry*, **244**, 6049-6055 (1969).

[11] Patick K, Potts K E, *Clinical Microbiology Reviews*, **11**, 614 (1998).

[12] Ingold K V, *Inhibition of Antioxidation-Advances Chemistry Series*, 1st edition and revision (1968).

[13] Calderon L A, Teles R C L, Leite J R S A, Bloch C J, Astolfi-Filho S. S. M, *Protein* and *Peptide Letters*, **8**, 485 (2001).

[14] Allen L A H, Schlesinger L S, Kang B. *Journal of Experimental Medicine*, **191**, 115-127 (2000).

[15] Hedstrom L, Szilagyi L, Rutter W, *Science*, **255**, 1249 (1992).

[16] Andersen L P, Blom J, Nielsen H, *APMIS*, **101,** 61-72 (1993).

ISSN 2278-7763

[17] Calin M A, Parasca S V, *Journal of Optoelectronics and Advanced Materials*, **8(3)**, 1173 (2006).

[18] Aviram M, Hardak E, Vaya J, Mahmood S, Milo S, Hoffman A, Billicke S, Draganov D, Rosenblat M, *Circulation*, **101**, 2510-2517 (2000).

[19] Kojima M, Taguchi H, Tsuchimoto M , Nakajima K, *Coordination Chemistry Reviews*, **237**, 183-196 (2003).

[20] Borisova N E, Reshetova M D, Ustynyuk Y A, *Chemical Reviews*, **107**, 46-79 (2007).

[21] Vigato P A, Tamburini S, *Coordination Chemistry Reviews*, **248**, 1717-2128 (2004).

[22] Cozzi PG, *Chemical Society Reviews*, **33**, 410-421 (2004).

[23] Granger R M, Davies R, Wilson K A, Kennedy E, Vogler B, Nguyen Y, Mowles E, Blackwood R, Ciric A, White P S , *Journal of Undergraduate Chemistry Research*, **2**, 48 (2005).

[24] Rauh R Diakov A, Tzschoppe A, Korbmacher J, Azad A.K, Cuppens H Cassiman H, Dötsch, H, Korbmacher C, *The Journal of Physiology*, **588**, 1211 (2010).

[25] Stein R, Strimpler A, *Biochemistry*, **26**, 2611 (1987).

[26] Masoud S A, Jhonson L, White F, *Plant Molecular Biology*, **21**, 655 (1993).

[27] Cohen S, Vaidya V, Schultz R, *Proceedings of the National Academy of Sciences USA*, **66**, 249 (1970).

[28] Grey S, Nurse G, Visser L, *Biochemical and Biophysical Research Communications*, **52**, 687 (1973).

[29] Syamal, Maurya M R, *Coordination Chemistry Reviews*, **95**, 183-238 (1989).

[30] Hilder V.A, Gatehouse A, Sheerman E, Barker R, Boulter D, *Nature*, **330**, 160 (1987).

[31] Marcos V, Latzin P, Hector A, Sonanini F, Hoffmann, M, Lacher B. Koller, P. Bufler, T, Nicolai D, *Respiratory Research*, **11**, 32 (2010).

[32] Andreyev Y, Kushnareva Y E, Starkov A, *Biochemistry*, **70**(2), 246-264 (2005).

[33] Amtul Z, Atta-ur-Rahman R, Siddiqui A, Choudhary M, *Current Medicinal Chemistry*, **9**, 1323 (2002).

[34] Qin D, Han F, Yao Y, Zhang Y, Shen Q, *Dalton Transaction*, 28,5535-41(2009).

[35] Qiu J, Lu M, Yao Y, Zhang Y, Wang Y, Shen Q, *Dalton Transaction*, 42(28):10179-89(2013).

ISSN 2278-7763

[36] Abd El-Wahab, Z H, Mashaly, M M, Salman A A, El-Shetary, B A, and Faheim, A A, *Spectrochim. Acta, Part A,* **60,** 2861 (2004).

[37] Prasad, R. N., Agrawal, M, Sharma, M., *Jounal of Serbian Chemical Society,* **67**, 229 (2002).

[38] Li, Y. T., Yan, C.W, Zeng, X. C., *Polish Journal of Chemistry,* **74**, 631 (2000).

[39] Jayabalakrishnan, C, Natarajan K, *Transition Metal Chemistry,* **27,** 75 (2002).

[40] Sondhi, S. M, Sharma, V. K, Singhal, N, Verma, R.P, Shukla, R, Raghubir, R, Dubey, M. P, *Phosphorus, Sulfur, Silicon and Related. Elements,* 156, **21** (2000).

