



REVIEW ON SCHIFF BASES

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ABSTRACT

Schiff's base is versatile ligand which are synthesized from the condensation of primary amine with carbonyl group. These compounds are very important in medicinal and pharmaceutical field because of their wide spectrum of biological activities. Advantage of this efficient method is excellent yield of product in crystalline form, short reaction time, simplicity of work up procedure and no use of any type of hazardous solvent simply this reaction is environmentally proactive (non-polluted) and economically attractive method for this synthesis of Schiff base compound. All of these Schiff base compounds were characterizing of IR, H-NMR, and elemental analysis as (C, H, N, O) spectral analysis data. Above Schiff base compound show inherent new generation of series pharmaceutically important compound. This review compiles the various synthesis procedure and application and Schiff base metal their complex. They are widely used for industrial purpose and also exhibit a broad range of biological activities.

Keywords: Schiff's Base, Discover, Chemistry, Uses, Application

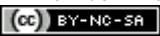
INTRODUCTION

A Schiff base named after Hugo Schiff base is a compound with a functional group that contain a carbon- nitrogen double bond with the nitrogen atom connected to an aryl or alkyl group. The general formula of the Schiff bases is $R^1R^2C=N-R^3$ Where, R^1 = aryl or alkyl group that makes the Schiff base a stable imine. Schiff bases from an important class of the most widely used organic compound and have a wide a variety of application in many fields including analytical, biological and

inorganic chemistry. Schiff bases have a gained importance in medicinal and pharmaceutical field due to broad spectrum of biological activities like anti- inflammatory, analgesic, antimicrobial, anticonvulsant, antitubercular, anticancer, antioxidant, anthelmintic, and so forth. The nitrogen atom of azomethine may be involved in the formation of a hydrogen bond with the active centre of cell constituents and interferes in normal cell process. Apart from biological activities, Schiff bases are also used as catalyst, intermediate in organic synthesis, dyes, pigments, polymer

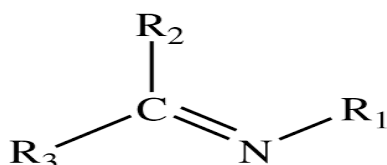
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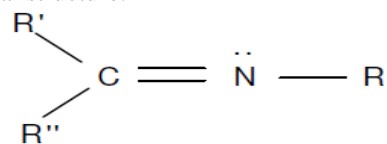
stabilizer, and corrosion intermediate in organic synthesis, dyes, pigments, polymer stabilizer, and corrosion inhibitors. Studies enlightened that metal complex show greater biological activity than free organic compound. Schiff base played an influencing role in development of inorganic biochemistry and optical materials Schiff base derivatives in various process promoted the researchers for designing of novel heterocyclic / aryl Schiff base for development of new environmental – friendly technology. Schiff's base compounds and their complexes have significant importance in chemistry. Every year number of reports is published on preparation of these compounds and their application in chemical reactions. Such type of ligands represents vast utilized classes of new series of compounds in metal coordination chemistry. The Schiff's base compounds and their complexes are widely applied in enantioselective cyclopropanation of styrene's. Asymmetric addition of cyanide to aldehydes. Schiff base compounds containing imines group (-RC=N-) are usually formed by the condensation of primary amine and Diamine with an active carbonyl compound in a methanol solvent. Some synthesis methods have not been entirely satisfactory owing to a number of drawbacks such as low yields and tedious workup procedures. According to the tremendous scope Schiff bases possess an inherent imidazopyridine, with a high class of compounds of medicinal importance and oblige. Over the past few decades, significant research has been directed towards the development of new technologies for environmentally benign processes (green chemistry). Schiff bases are crystalline or oily substances that are insoluble in water and soluble in organic solvents. They are weak bases, forming salts with acids in an anhydrous medium; in aqueous acid solutions, they undergo hydrolysis to yield an amine and aldehyde. The majority of Schiff bases are stable in alkaline solutions. Schiff bases are valuable intermediate products of organic synthesis, for example, in the preparation of secondary amines and various heterocyclic compounds.



Chemistry of Schiff bases

Schiff bases are condensation products of primary amines and carbonyl compounds and they were discovered by a German chemist, Nobel Prize winner, Hugo Schiff. Structurally, Schiff base (also known as imine or azomethine) is an analogue of a ketone or aldehyde in which the carbonyl group (C=O) has been replaced by an imine or

azomethine group (Figure-1). A Schiff base or Schiff's base is a type of chemical compounds containing a carbon-nitrogen double bond as functional group, where the nitrogen atom connected to aryl group or alkyl group (R) but not hydrogen. The Schiff base is synonymous with an azomethine. These compounds were named after Hugo Schiff on honour and have the following general structure:



Where R stands for a phenyl or alkyl group which makes the Schiff base a stable imine. This kind of ligands is able to coordinate metal ions through the imine nitrogen and another group, usually linked to the aldehyde. The chemists still prepare Schiff bases and nowadays active and well-designed Schiff base ligands are considered "privileged ligands". The bridged Schiff's bases have the following structure which contains many functional groups able to change according to the purpose required

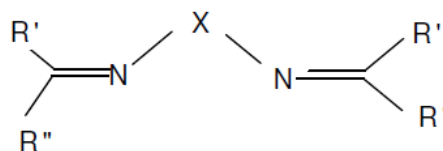


Fig 2: bridged Schiff's base

Where R' = H or alkyl group, R'' = phenyl or substituted phenyl, X = alkyl or aryl group. In fact, Schiff bases are able to stabilize many different metals in various oxidation states controlling the performance of metals in a large variety of useful catalytic transformations. Most commonly Schiff bases have NO or N₂O₂-donor groups but the oxygen atoms can be replaced by sulphur, nitrogen, or selenium atoms. It is usually formed by condensation of an aldehyde or ketone with a primary amine according to the following scheme:

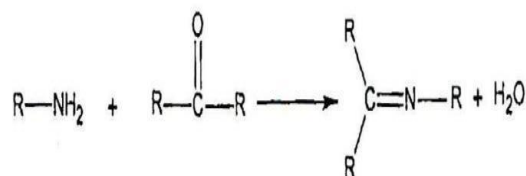


Fig 3: Formation of Schiff base by condensation reaction.

Where R, may be an alkyl or an aryl group. Schiff bases that contain aryl substituents are substantially more stable and more readily synthesized, while

those which contain alkyl substituents are relatively unstable. Schiff bases of aliphatic aldehydes are relatively unstable and readily polymerizable. While those of aromatic aldehydes having effective conjugation are more stable. The formation of a Schiff base from an aldehydes or ketones is a reversible reaction and generally takes place under acid or base catalysis, or upon heating.

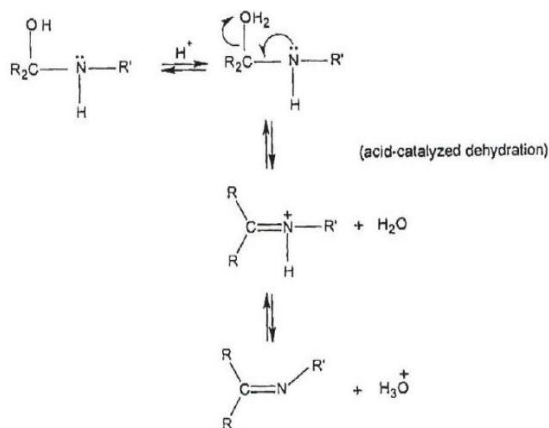


Fig 4: Reversible reaction of a Schiff base formed from an aldehydes or ketones

The formation is generally driven to the completion by separation of the product or removal of water, or both. Many Schiff bases can be hydrolysed back to their aldehydes or ketones and amines by aqueous acid or base. The mechanism of Schiff base formation is another variation on the theme of nucleophilic addition to the carbonyl group. In this case, the nucleophile is the amine. In the first part of the mechanism, the amine reacts with the aldehyde or ketone to give an unstable addition compound called carbinolamine. The carbinolamine loses water by either acid or base catalysed pathways. Since the carbinolamine is an alcohol, it undergoes acid catalysed dehydration

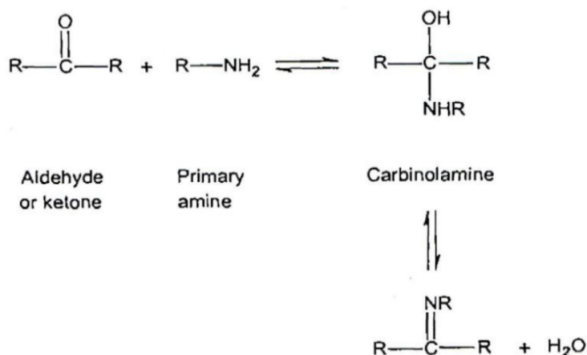


Fig 5: Mechanism of formation Schiff base

Typically the dehydration of the carbinolamine is the rate-determining step of Schiff base formation and that is why the reaction is catalysed by acids.

Yet the acid concentration cannot be too high because amines are basic compounds. If the amine is protonated and becomes non-nucleophilic, equilibrium is pulled to the left and carbinolamine formation cannot occur. Therefore, many Schiff bases synthesis are best carried out at mildly acidic pH. The dehydration of carbinolamines is also catalysed by base. This reaction is somewhat analogous to the E2 elimination of alkyl halides except that it is not a concerted reaction. It proceeds in two steps through an anionic intermediate. The Schiff base formation is really a sequence of two types of reactions, i.e. addition followed by elimination.

Experimental:

Melting points were determined in open capillary tube and are uncorrected. The purity of the compound was checked on silica-gel coated aluminium plate. IR spectra were recorded in KBR on a Perkin elmer Spectrum RX-1 FTIR Spectrophotometer. 1H -NMR and ^{13}C -NMR spectra were measured on jeol JNM-ECX 400P at 400 MHz. Microwave irradiation were carried out in microwave synthesizer. (CEM- Discover). All chemical used were of analytical grade.

Conventional Method:

Schiff bases are prepared by condensation of aldehyde (0.004 mol) with various aromatic amines (2a-e) (0.004 mol) in water (10ml) and the mixture was stirred at ambient temperature. The progress of reaction was monitored by TLC. On completion of reaction the product was separated as yellow – coloured amorphous product which was filtered dried and recrystallization from methanol.

Microwave method:

A mixture of aldehyde (0.004 Mol) and substituted aromatic amines (2a-e) (0.004 mol) in water (1 ml) were added in microwave irradiation at 200 W for about 30 sec-2 min. Progress of the reaction was monitored by TLC. After the complete reaction, solid product was obtained in reaction mixture which was filtered and recrystallized with methanol. Recrystallization provide the title compound as solid crystals.

Characterization

The Schiff base ligands and their complexes are characterized on the basis of following

- UV- Visible
- IR Spectroscopy
- 1H and ^{13}C NMR
- EPR
- Mass Spectrometry
- TGA/ DTA

UV-Visible: It is mainly applied for the detection of functional groups (chromospheres) the extent of

conjugation detection of polynuclear compounds etc. The radiation in the wavelength range 200-400 nm correspond to ultra-violet region while radiation in the wavelength range 400-800 nm correspond to visible region. The absorption of radiation in the UV-Visible region cause the excitation of π electron in a conjugation or a non-conjugation system. Thus UV-Visible spectrum is quite useful for detection of conjugation, Carbonyl group etc.

IR SPECTRA:

A strong intensity band (sharp) 1618-1622 cm^{-1} ($\nu(\text{C}=\text{N})$). A medium intensity band 440-460 cm^{-1} ($\nu(\text{M}-\text{N})$). A weak absorption band 2906-2942 cm^{-1} ($\nu(-\text{CH}_3)$). A Broad Absorption band 3330 cm^{-1} ($\nu(-\text{OH})$). The formation of Schiff base complexes and bonding mode are inferred from position of characteristic bands in IR spectra and resonance signals in ^1H and ^{13}C -NMR Spectra.

NMR:

Nuclear magnetic resonance (NMR), include changes in the magnetic properties of certain atomic nuclei, notably that of hydrogen (hydrogen atoms in different environments can be detected, counted and analyzed for structure determination. In the nuclear magnetic resonance (NMR), Radiation of longest wavelength range Radio waves are useful which lie in the frequency range about 60-300 MHz.

EPR:

Electron paramagnetic resonance (EPR) spectroscopy investigates those system which are organic or inorganic free radicals and ions of transition metals which contain unpaired d or f electron.

MASS:-

Mass spectrometry is the most accurate method for determining molecular mass of the compound and its elemental composition and deduction of molecular structure from fragments. Mass spectrum of a substance is plotted between m/z values of ions versus relative abundance.

THERMAL STUDIES:

The thermal stabilities of Schiff metal complexes are investigated using (TGA/DTA) under N_2 atmosphere at a heating rate of $20^\circ\text{C min}^{-1}$ in the temperature range 25-800 $^\circ\text{C}$. The thermal analysis results are in agreement with the elemental analysis findings. Elemental analysis confirms the stoichiometry of ligand and their complexes.

USE:

Schiff bases are also used as catalysts, intermediates in organic synthesis, dyes, pigments, polymer stabilizers, and corrosion inhibitors.

Studies enlighten that metal complexes show greater biological activity than free organic compounds Schiff bases are some of the most widely used organic compounds. They are used as pigments and dyes, catalysts, intermediates in organic synthesis, and as polymer stabilizers.

Applications of Schiff's bases chelates in quantitative analysis:

Jungreis and Thabet¹⁴ have reported several applications for Schiff bases in qualitative and quantitative classical analyses. All these applications did not cover a wide area in analytical chemistry. Advances in analytical techniques and the development and application of new analytical reagents are as important in trace analyses as the development of analytical instruments. A number of Schiff's base chelating agents used for the detection of metal ions can also be applied for their quantitative determination. The procedures in most cases remain similar. The main step in the above applications is the complex formation which depends mainly on pH, temperature, cation size, and the structure of the ligand. Optimization of these factors to enhance the stability of the complex leads to high selectivity of the developed analytical method.

A. Photometric methods

Developments in photometric methods have been extensive, particularly for the determination of trace amount of metals. A number of these procedures are based on colour formation resulting from the reaction between Schiff's base and the metal ion. For example, o-[N-(o-formimidoyl)hydroxyphenyl]phenol, known as Manganon, forms with manganese(II) at pH 9.1 to 11.6 a brown complex, the absorbance of which is measured at 428 nm. 2,2'-(2,6-Pyridinediyl) BIS (Methyldiylidene Nitrile) Phenol has been used by Abdelnaby and Anter for spectrophotometric determination of Uranium (VI). The red colour developed is measured at 500 nm and the molar absorptivity is $1.19 \times 10^4 \text{ L mol}^{-1} \text{ cm}^{-1}$. It was found that a 100-fold excess of Barium, Strontium, Calcium, Lead, Cadmium, Chloride, Nitrate, Sulphate, and Phosphate did not interfere. The interference of some elements such as Fe(III), Cr(III), Hg(II), V(V), and Ti(V) could be eliminated by applying the ion exchange technique using the resin Dowex 1x 8 in the chloride form. N,N'-Bis(salicylidene)ethylenediamine forms with iron(III) a complex, which is red-violet at a pH less than 5 and yellow at a pH higher than 6, with maximum wavelength 495 and 470 nm respectively. G. Tantar et al. have prepared Salen-type Schiff's base, 1-ethyl-salicylidene-bis-ethylenediamine by condensing ethyl-o-hydroxyphenyl ketone with ethylene diamine. These Schiff's bases present a

good capacity of complexing Mn(II) ions, resulting brown complexes. The Schiff base forms a brown complex with Mn(II) cation, with maximum absorbance at 460 nm. The complex showed a maximum stability at pH 6.0. Spectrophotometric determination of Mn(II) using this Schiff base as reagent were successfully applied to pharmaceutical products containing Mn(II) cation N,N'-bis(3-methylsalicylidene)-ortho-phenylene diamine (MSOPD), has been synthesized and used in the spectrophotometric determination of nickel. At pH 8, MSOPD can react with nickel ion at room temperature to form a 1:1 complex. The apparent molar absorptivity is $9.5 \times 10^4 \text{ l mol}^{-1} \text{ cm}^{-1}$ at 430 nm. With a detection limit of $1.36 \times 10^{-8} \text{ M}$. Nickel in some natural food samples has been determined N-bis(pyridinyl methylene) ethylenediamine was studied by Leyva and Palma. The optimum experimental conditions for the spectrophotometric determination of copper were established. Beer's law is obeyed between 1 and 10 ppm of copper. The precision of the procedure, expressed in terms of relative standard deviation, was 0.31%.

A.G. Asuero has reviewed Schiff's bases derived from diacetyl as analytical reagent, more than 50 reagents and their related cation, method used, and medium have been reported. Number of spectrophotometric determinations have been carried out, for biacetyl bis(4-phenyl-3-thiosemicarbazone) (BBPT). It has been used as a reagent for the extractive spectrophotometric determination of cadmium and bismuth. Analytical applications of biacetyl bis(4-phenyl-3-thiosemicarbazone) and bipyridyl glyoxal bis(4-phenyl-3-thiosemicarbazone) has been reported.²⁰ Trace levels of palladium(II) has been determined by Asuero et al. The method relies upon the extraction of palladium(II)-biacetylmonoxime 2-pyridylhydrazone (BMPH) from aqueous acidic solution into chloroform to form a purple-reddish complex. The molar absorptivity of the Pd-BMPH complex is about $7500 \text{ L mol}^{-1} \text{ cm}^{-1}$ at 560 nm in the chloroform extract.²¹

B. Fluorometry

Fluorometric methods often provide excellent means for the detection and determination of inorganic ions. The reagents employed to produce fluorescence are often highly selective and very sensitive. In most cases a chelate is formed with the metal. There is often a dependence of fluorescence on the pH Nabil Ramadan Bader similar to that of acid-base fluorescence indicators. The analytical importance of such indicators lies in the fact that they make possible acid-base titrations in coloured solutions when the use of conventional indicators would preclude. Holzbecher reported that Schiff's bases obtained from salicylaldehyde and aniline

fluoresce in the alkaline medium and therefore, can be used for titration of acids with bases also proposed O-[N-(O-hydroxyphenyl) formimidoyl] phenol, for quantitative determination of aluminium. Sabry studied the fluorescence properties of Schiff bases derived from 2-acetylbutyrolactone and spectrofluorimetric determination of primary amine-containing compounds. 2-Acetylbutyrolactone (ABL) has been characterized for use as a fluorogenic reagent for the spectrofluorimetric determination of primary amines. The reagent forms strongly fluorescent Schiff bases upon the reaction with primary amines in acid-catalysed aqueous solutions or in dimethylformamide (DMF).²⁴ Determination of trace cadmium with GBHA has been developed by Dong Gai. The cadmium ion can form a stable chelate with GBHA, having a ratio of 1:3 in the 12.0 -13.0 pH range with maximum excitation and emission wavelengths are 227.4 nm and 320.0 nm for the cadmium chelate, respectively, and fluorescence intensity from 20 to 150 min. Linear function of concentration in the range 1.0-10.0 ng mL⁻¹ of cadmium and the detection limit is 0.65 ng mL⁻¹ of cadmium.²⁵

C. Schiff's bases as potentiometric sensors

Since the 1930s, potentiometric membrane sensors have found great practical applicability in different fields. The response mechanism of these sensors is based on the measurement of a potential under a zero current regime or a under a low electrical current flow. Potentiometric membrane sensors, which have been designed based on molecular recognition, contain a molecule that selectively recognizes another target species through various molecular interactions. As it is widely known, potentiometric electrodes possess as advantages the direct, simple, rapid, inexpensive and selective detection of ionic activities. Anjali et al. have prepared potentiometric sensors for Dy(III) based on a Bis-pyrrolidine Schiff's bases, the electrode has been also used in the potentiometric determination of Fluoride ions in mouthwash by the titration against Dy(III). They also prepared a novel Bromide ion sensor based on Iron(III)-salen, this sensor has high Bromide selectivity over a wide variety of organic and inorganic anions, specially iodide, chloride and hydroxide ions. A large number of different Schiff base ligands have been used as cation carriers in potentiometric sensors as they have shown excellent selectivity, sensitivity, and stability for specific metal ions.

D. Schiff's bases as solvent extraction reagents

Solvent extraction separation is based on the differences in the solubility of elements and their compounds in two immiscible liquid phases. Usually, the initial phase is an aqueous solution and the second phase is an organic solvent immiscible

with water. Extraction is usually fast and simple process; it demands only very simple equipments. Stripping (re-extraction, back-extraction or scrubbing) involves bringing the element from the organic extract back to the aqueous phase. A solvent extraction using salophen was studied by Kim et al. and applied for trace determination of Ni(II), Co(II) and Cu(II) in water samples. The salophen is another type of salen derivative. Unlike the ethylenediamine of salen, salophen included a phenyldiamine as a backbone.⁴⁶ In another study the salophen has been used in solvent extraction for trace determination of Fe(II) and Fe(III) in water samples. Gyo In et al. used salen (Net₂)₂ as a chelating agent for determination of Cu(II), Mn(II) and Zn(II) in water samples by FAAS. Macrocyclic Schiff bases containing either thiophene or phenol subunits were synthesized and the effect of ligand atoms on the liquid-liquid extraction of bivalent transition metal ions was studied. The phenol groups in the macrocycle led to a large increase in the extraction of transition metal ions. The least stable manganese (II) complex was extracted quantitatively into nitrobenzene as an ion pair with tetraphenylborate ion at pH. Copper(II) was selectively extracted from weakly acidic media, permitting its separation from manganese(II), cobalt(II), nickel(II) and zinc(II). The extractability of metal Schiff base has been compared with that of the corresponding acyclic Schiff base.⁴⁸ Mutual separation of zinc(II), copper(II) and manganese(II) can be achieved by a proper selection of pH using Acyclic and macrocyclic Schiff bases containing bisphenol A subunits compared with a macrocyclic Schiff base, the corresponding acyclic counterpart was found to have a reasonable reactivity toward metal ions and better solubility in organic solvents. In another application, a quantitative extraction of iron(III) and gallium(III) was achieved with macrocyclic Schiff base containing bisphenol A subunits. The phenol groups in the Schiff base moiety led to a large increase in the percent extraction of trivalent metal ions. The substitution of methoxy groups for phenolic OH ligands resulted in a marked decrease in the extractability of metal ions, and no iron(III) was extracted. The corresponding acyclic Schiff base was found to have a reasonable reactivity toward metal ions and a better solubility in organic solvents. The iron(III) and gallium(III) complexes with macrocyclic and acyclic Schiff bases were quantitatively extracted into nitrobenzene without the presence of bulky counter anions. A single extraction gave a good separation of iron(III) from iron(II) in the mole ratios 4:1 to 1:3. The red iron(III) complexes can be used for the extraction-spectrophotometric determination of iron(III). The apparent molar absorptivity at 518 nm is $5.43 \times 10^3 \text{ l mol}^{-1} \text{ cm}^{-1}$

E. Schiff's bases as solid phase extraction sorbents

The solid phase typically consists of small, porous particles of silica with a bonded organic phase or of an organic polymer, such as crosslinked polystyrene. The extraction can take place in a batch mode in which the solid extractant is intimately mixed with liquid sample solution. In chemical analysis it is more common to pack the solid extractant into a small tube and pass the liquid sample through the tube. The nature and properties of the sorbent are of prime importance for effective retention of metallic species. Careful choice of the sorbent is thus crucial to the development of SPE methodology. Two approaches are used for loading the surface with specific organic compounds, chemical immobilization and physical adsorption. In the first case, a chemical bond is formed between the solid support surface groups and those of the organic compound (functionalized sorbent). In the second approach, the organic compound is directly adsorbed on the functional groups of the solid support surface (impregnated or loaded sorbent), either by passing the reagent solution through a column packed with the adsorbent, or by soaking the adsorbent in the reagent solution. Ganjali et al. separated and pre-concentrated ultra-trace amounts of Cu(II) by solid phase extraction on octadecyl-bonded silica membrane disk modified with (Bis- (2-hydroxyacetophenone) - 2,2-dimethyl-1,3- propanediimine) SBTD followed by elution and ICP-AES detection in environmental and biological samples, the concentration factor was 500. Shemirani et al. proposed a method for the preconcentration of Cd(II), Cu(II), Zn(II), and Ni(II) using a minicolumn filled with silica gel modified with (N,N'-bis(salicylene) phenylene-1,3-diamine Schiff' base. The proposed method was applied to the analysis of the metal ions in natural water samples and to a standard reference aluminium alloy material. Thallium ions have been separated and concentrated selectively and quantitatively during passage of aqueous real samples through an octadecyl bonded silica membrane disk modified by 4-(4-Chlorophenylazo)-2-[(4-hydroxy-phenylamino)-methyl]-phenol. The retained Thallium ions are then stripped from the disk quantitatively with a minimal amount of thiosulfate solution as eluent and measured by FAAS with an enrichment factors of about 130 and higher and limit of detection of 11.2 ng/L. The use of niobium(V) oxide, chemically adsorbed on silica gel surface (Nb₂O₅-SiO₂), as an adsorbent in a pre-concentration system of copper (II) and cadmium (II) by flow system with FAAS was proposed by Budziak et al. The enrichment factor when using a sample volume of 10.2ml and 2 min of preconcentration was 17.5 and 20.3 for copper (II) and cadmium (II), respectively. Good accuracy was obtained by the analysis of water reference materials and environmental samples. Mashhadizadeh et al. have

developed a selective method for extraction of Cu(II) by sorption on octadecyl silica membrane disk modified with bis-(3-methoxy salicylaldehyde)-1,6-diaminohexane and determination with atomic absorption spectrometry. The retained copper eluted with a minimum volume. The maximum capacity of the disk was found to be 150 µg of copper ion on the disk. In another work they have used octadecyl silica membrane disk modified by a recently synthesized Schiff base (Bis-(4-nitro phenyl azo) salicylidine-1,3-diamino propane) for flame atomic absorption spectrometric determination of µg amounts of Fe (III) ions in aqueous samples. The time taken for the separation and analysis of iron in 500 ml sample is 30 min at the most. Iron (III) has been determined by Sham spur et al. by flame atomic absorption spectroscopy (FAAS) after preconcentration on modified analcime zeolite with 5-((4-nitrophenylazo)-N-(2,4-dimethoxyphenyl)) salicylaldimine. The recoveries were > 99%, and the developed method was applied to the determination of trace Fe(III) ions in drinking water and river water samples.⁵⁸ Dadfarina et al. have determined silver, zinc and copper employing FI-FAAS and a microcolumn of immobilized salen, 2,2'-[3-aza-1,5-pentanedyle bis (nitrilomethylidyne)]-bis-phenol, on surfactant coated alumina. The practical concentration factors of 125, 210 and 166 for Ag, Zn and Cu, respectively and the detection limits of 0.3, 0.8 and 0.47 µg/L for Cu, Ag and Zn, respectively. The data obtained by their method agreed well with the results of independent analysis of GFAAS. Jadid et al. applied the modified activated carbon with 5 - ((4 - heptyloxyphenyl) azo) -N - (4-butylloxyphenyl)-salicylaldimine (HPBS) as a new sorbent for preconcentration of Cu(II) ions. The detection limit was 2.26µg/L. The procedure has been applied for the determination of copper in water samples. Ahmadi et al.⁶¹, have used octadecyl silica membrane disks modified by N,N'-disalicylidene-1,2-phenylenediamine (salophen) for extraction and determination of Zn by FAAS. The limit of detection was 14ng/L. Their method has been applied to the determination of zinc in natural water samples, the results has been checked by spiking experiments and comparing the results with data obtained by GFAAS. Bader has used four different structures of slanes for coating silica gel, C18 silica gel, and aminopropyl silica gel in order to extract Zn, Cd, and Cu from aqueous solutions before AAS measurements. A preconcentration factor of 100 was obtained, considering the relation between final small volume and initial large volume of sample. The limit of detections of SPE-FAAS have been calculated. The improved LODs are 0.007, 0.3, and 0.102 ng/ml for Zn, Cd, and Cu respectively. The improved LODs are much lower than the LODs of FAAS and approaching the

LODs of GFAAS. The microcolumn of salen I (N,N'-bis (salicylidene) ethylenediamine) immobilized on surfactant-coated alumina has been used by Dadfarina et. al., for on-line preconcentration of copper and lead with a flow injection-flame atomic absorption spectrometry (FI-AAS). A good relative standard deviation of 4.5 and 3.8% at 30µg l⁻¹ (n = 7), high enrichment factors of 100 and 75, and detection limits of 0.3, 2.6µg l⁻¹ (3S) for Cu(II) and Pb(II) were obtained, respectively. The method developed provides an alternative procedure to techniques such as GFAAS, ICP-AES for determination of copper and lead at µg l⁻¹ level. The elution step in solid phase extraction is mostly done in acidic medium, which cause decomposition of Schiff's base, in this case reloading of the ligand on the column is needed in case of physically modified sorbents. The chemically modified sorbents shows stability toward acidic elution solutions, making them more convenient for multi-use, and therefore for flow injection analysis system.

F. High-Performance Liquid Chromatography

In the last few years the rapid development of high-performance (pressure) liquid chromatography (HPLC) has also extended the possibilities for chromatographic methods in inorganic analysis. In particular liquid chromatographic methods in columns are of great importance for those inorganic compounds which are not suitable for the usual gas chromatographic methods because of low volatility or low thermal stability.⁶⁴ Chromatographic methods are very suitable for the separation and determination of extractable metal chelates. Different types of ligands or groups of compounds are suitable for HPLC such Schiff base chelates, hydrazones, dithizonates, and metal dithiocarbonates. For these groups of substances principally The separation of neutral copper and nickel chelates of two representative Schiff base ligands, N,N'-ethylene is (acetylacetone mine) and N,N'-ethylenebis(salicylaldimine) is reported on a column of 10 micrometer diameter silica. Both pairs of chelates are well resolved with good peak shape and efficiencies when the mobile phase is 4 : 1 methylene chloride-acetonitrile. An HPLC method for the determination of scandium(III) was developed, with diacetyl-N,N-bis(4-hydroxybenzoylhydrazone) (DBHB) as a pre-column chelating agent. Tetradentate DBHB formed a 1 : 1 chelate with Sc(III) ion. The Sc(III)-DBHB chelate was separated on a C18-silica gel column with a mobile phase of acetonitrile-water (30+70m/m) containing tetramethylammonium bromide and hexane ethylenediamine buffer. Kanbayashi. et al. have developed a method for highly selective determination of trace amounts of Co²⁺, Cu²⁺, Ni²⁺ and V⁵⁺ ions by reversed phase high-performance liquid chromatography

(HPLC) and spectrophotometric detection has been accomplished without the addition of a chromogenic reagent to the eluent. Six tetradentate Schiff-base ligands, all N,N'-o-phenylenebis(salicylaldehyde) (PBS) derivatives, were synthesized and made to react with the metal ions.

Conclusion

Schiff base ligands are formed by the condensation reaction between aldehyde/ ketones and aliphatic amine. Their complexes are prepared by the interaction of ligand with metal salts. The stoichiometry and the nature of bonding was ascertained on the basis of elemental analysis and

conductivity data. Schiff bases are one of the most important chemical classes of compounds having a common integral feature of a variety of medicinal agents. This review reflects the contribution of Schiff bases to the design and development of novel lead having potential biological activities with fewer side effects. This bioactive core has maintained the interest of researchers in gaining the most suggestive and conclusive access in the field of various Schiff bases of medicinal importance from last decades. The present paper is an attempt to review all the biological activities reported for Schiff bases in the current literature with an update of recent research findings. Schiff base ligands and their complexes have numerous applications in the field of pharmacy.

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