Chapter 1

INTRODUCTION
Section-1

A BRIEF REVIEW OF ISONICOTINOYLHYDRAZONES AND THEIR ANALYTICAL APPLICATIONS:

The growth of interest in coordination chemistry has been greatly stimulated by the developments in metal ion catalysis and the role of metals in biochemistry. Coordination compounds are not only a great theoretical importance but also find vast practical applications in living systems and in chemical industry. The advancement of the theory of complex compounds by Werner\(^1\) stimulated the systematic study of the reactivity of organic reagents in inorganic analysis. Further advancement in the development of reagents is followed by the Tschugaeff\(^2\) discovery of the selective reaction between dimethylglyoxime with nickel(II), which led to a successful gravimetric estimation of nickel by Brunk\(^3\)\(^\text{-}^5\).

Analytical chemistry involving metal complexes is based mainly on the synthesis of selective and sensitive reagents. In this context, organic reagents occupy a special place in the field of complexation of metal ions. These reagents, due to their chelating nature and complexing ability, are capable of forming stable, highly coloured, insoluble and soluble complex compounds with metal ions. These metal complexes find wide use in analytical chemistry in general and in spectrophotometric analysis in particular.

Hundreds of organic reagents are available for the spectrophotometric determination of almost all the elements in the periodic table. Among the numerous organic analytical reagents\(^6\)\(^\text{-}^8\) employed, the azomethines having O,N donor atoms have been extensively used to complex metal ions for their photometric determinations. However not much is reported on the utility of isonicotinoylhydrazones as complexing analytical agents.

Hydrazones are azomethines containing the characteristic grouping \(> \text{C} = \text{N} \cdot \text{N} <\). They are differentiated from other members of this class (imines, oximes etc) by the presence of two interlinked nitrogen atoms. The hydrazone grouping occurs in organic compounds of the types:

\[
\text{X} \quad \text{C} = \text{N} \cdot \text{N} \quad \text{Y} \]

\[\text{[1]}\]

\[
\text{X} \quad \text{C} = \text{N} \cdot \text{N} = \text{C} \quad \text{X} \]

\[\text{[2]}\]
Where \( R \) and \( R_1 = H, \text{Alk, Ar, RCO, Ht (Heterocyclic group)}; \ Y = H, \text{Alk, Ar, Ht, RCO}; \ X \) and \( X_1 = H, \text{Alk, Ar, Ht, Hal OR}, \text{SR, CN, SO}_2R, \text{NO}_2, \text{NHNR}^{''}, \text{N}=\text{NR}^{''}, \text{COOR}^{''}, \text{CONR}^{''}R^{''} \). The general name 'hydrazone' is used for all the compounds having the structure (1). Compounds of type (2) are termed 'azines'.

Hydrazones are usually named after the carbonyl compounds from which they are obtained. Hydrazones in general, are prepared by refluxing the stoichiometric amounts of the appropriate hydrazine and ketone or aldehyde dissolved in a suitable solvent. The compound usually crystallizes out on cooling.

Many of physiologically active hydrazones find application in the treatment of diseases such as tuberculosis, leprosy and mental disorder. Aroyl hydrazones (3) are also known to possess tuberculostatic activity. This is due to formation of stable chelates with transition metal ions present in the cell.

\[ R - \text{CH} = \text{N-NH-CO-R'} \]

(3)

Thus many vital enzymatic reactions catalysed by these transition metals can not take place in the presence of hydrazones. Hydrazones also act as herbicides, insecticides, nematocides, rodenticides and plant growth regulators, hypotensive action and activity against leukaemia, sarcomas and other malignant neoplasms. Hydrazones of 3-N-Methyl-N-(4-chloro-phthalazinyl) and 3-N-Methyl-N-(4-oxo-1-phthalazinyl) hydrazones possess anthelmintic activity.

Isonicotinic acidhydrazide (INH) is an important antitubercular agent and has potential sites for formation of complexes with metal ions. A survey of the literature reveals that only a few isonicotinoylhydrazones of benzaldehyde and its derivatives are prepared and relatively less work is done with regard to their metal complexes. It is also observed that isonicotinic acidhydrazones and their metal complexes possess higher activity and lower resistivity to tuberculosis bacteria. Isonicotinoylhydrazones are also potential analytical reagents for the determination of several metal ions by different physico-chemical techniques, of which the spectrophotometric determination occupy a special place.

Singh et al. reviewed critically the applications of hydrazones as analytical reagents. However as the author is interested in the use of isonicotinoylhydrazones derived from carbonyl...
compounds, a brief review of the past work reported on the isonicotinoylhydrazones derived from carbonyl compounds is presented.

In 1975 Kouimtzis et al. published a paper describing the extraction and spectrophotometric determination of gallium and indium at pH 6-6.5. Belal and Chaaban determined Fe(II) and Fe(III) colorimetrically in the presence of each other and other metal ions and applied to various pharmaceuticals by using 2-hydroxy-1-napthaldehyde isonicotinoylhydrazone. Mo(VI) in Steels is also determined. The complexes formed by vanadium (V) in acidic 50% aqueous ethanol medium with acetone isonicotinoylhydrazone and with 4-hydroxy benzaldehyde isonicotinoylhydrazone have been examined and used for the spectrophotometric determination of vanadium.

The 2-hydroxy isomer has been used for the determination of Al(III) and Zn(II), Co(II), Ni(II) and Mn(II). Naphthylmethylketone isonicotinicacidhydrazone is employed for the spectrophotometric determination of Ti(IV). Uno and Taniguchi studied the fluorescent activity of isonicotinicacidhydrazones of a number of carbonyl compounds (2-hydroxy-1-napthaldehyde, salicylaldehyde, 2-hydroxy-m-tolualdehyde, 3-hydroxy-p-tolualdehyde, 4-hydroxy-m-tolualdehyde, 3-chloro-2-hydroxybenzaldehyde, 5-chloro-2-hydroxybenzaldehyde and 2-hydroxyacetophenone).

Vasilikiotis used P-dimethylamino-benzaldehyde isonicotinoylhydrazone as spot test reagent, which forms an intense orange-yellow precipitate with mercury (I or II) in slightly acidic, neutral or slightly alkaline medium.

Manganese(II) forms four and six coordinated hydrazone complexes with isonicotinoylhydrazones of salicylaldehyde and its 5-methyl, 5-chloro, 5,6-benzo derivatives and 2-OH acetophenone and its 5-methyl, 5-chloro derivatives. The aldehyde derivative reacts in the keto form while the keto derivative reacts in the enol form. Both types of ligands are tridentate.

Isonicotinic acidhydrazide (INH) and its acetone derivatives are used for the spectrophotometric determination of V(V) from vanadium-iron alloy and iron-ores. Fe(III) is masked with NaF. Synthesis and structural studies of some first row transition metal complexes with acetone isonicotinoyl hydrazones are carried out by Aggarwal and Rao.

Teotia et al. synthesized and characterised the dimeric, five and six coordinated complexes of oxovanadium(IV) with bi, tri and tetradendate ligands of picolinic acid hydrazone (PH), orthohydroxyacetophene picolinoyl hydrazone (APH), Isonicotonic acidhydrazide and orthohydroxyacetophenone isonicotinoylhydrazone.
Kinetics of acid catalysed hydrolysis of 2,4-dihydroxy- acetophenone isonicotinoylhydrazone is examined by Murali Mohan et al. and found that the reagent hydrolysed rapidly at pH < 4.

Diacetyl bis (isonicotinyl hydrazone) is used for the spectrophotometric determination of Bi(III) and also for the spectrofluorometric studies of Zr(IV) complexes.

Aluminium(III) is determined spectrophotometrically by using 2,4-dihydroxyacetophenone isonicotinoylhydrazone (RPINH). The same reagent is used for the spectrophotometric determination of Ni(II), Mo(VI) and V(V).

Kinetics of acid hydrolysis of RPINH in presence of Zn is carried out photometrically by Rao et al. They also carried out the kinetic photometric determination of Hg(II) and Ag(I) through their catalysis of the reaction between hexacyanoferrate(II) and isonicotinoylhydrazide or RPINH or phenylhydrazine chloride. RPINH is used for the colorimetric studies of Mn(II), Co(II), Ni(II) and Ti(IV).

Singh et al. used pyridine-2-carboxaldehyde thioisonicotinoylhydrazone for synthetic, structural and antibacterial studies of Co(II), Ni(II), Cu(II) and Zn(II) complexes. Salicylaldehyde isonicotinoylhydrazone (SAIH) is employed as a special analytical reagent for the selective extraction spectrophotometric determination of Mo(VI) in presence of several cations by Kavlentis. He also carried out the spectrophotometric determination of antimony(III) by using isonicotinoylhydrazone of 4-dimethylaminobenzaldehyde (4-DBIH) and 2-hydroxy-napthaldehyde (2-HNIH).

Thorium (IV) and Uranium(VI) are determined in presence of each other with 2-hydroxy-1-napthaldehyde isonicotinoylhydrazone spectrophotometrically. The formation of ternary complex of Fe(III) with isoniazid-2-hydroxybenzaldehyde hydrazone (INSH) in a cetyltrimethyl-ammoniumbromide (CTAB) micellar medium is exploited to develop simple, sensitive spectrophotometric method for the determination of Fe(III) by Issopoulos and Economou. The colour reaction between uranium(VI) and 2-hydroxy-1- napthaldehyde isonicotinoylhydrazone in HClO4-acetate buffers is used to develop a sensitive spectrophotometric method for the determination of uranium(VI). A sensitive spectrophotometric method for the determination of Fe(II) in anti-anaemic pharmaceutical formation using the formation of ternary complex of Fe(III) with isoniazid-p-diethylamino salicylaldehyde hydrazone in triton X-100 micellar medium is reported. Richardson et al. reported the potentiality of iron chelators of the pyridoxalisonicotinoylhydrazone class as effective antiproliferative agents.
IMPORTANCE OF THE PRESENT INVESTIGATIONS:

The precise determination of metal ions at micro gram level in the area of analytical chemistry has given added impetus to the analytical chemist to discover simple, speedy and accurate methods. Moreover, the choice of selecting a suitable method from the innumerable methods presented in the literature has also become difficult. Thus inspite of the availability of new methods and modern techniques for the determination of metal ions, the demand for newer methods of analysis is increasing in view of the problems constantly faced by the analytical chemist.

Though strong claims are made for the specificity and sensitivity of atomic absorption and plasma atomic emission analysis, atomic fluorescence emission, some of the interferences to which these methods are subject to use poorly understood and continue to cause problems. Further these techniques are not within the reach of many laboratories. Besides the cost involved they are not amenable to easy operation.

In this context spectrophotometry, a widely employed analytical technique, is more popular because of the common availability of instrumentation and simplicity of procedures as well as speed, precision and accuracy resulting in extensive literature being published. The advent of a new-generation of spectrophotometers equipped with diode array detectors and extensive use of microprocessors in data acquisition and handling have brought about dynamic progress in the simultaneous analysis based on multiwavelength and derivative measurements.

Spectrophotometric analysis of metal ions at microgram level involves synthesis of selective and sensitive reagents. Among the numerous organic-photometric reagents used, hydrazones occupy a special place due to their good chelating properties with the metal ions to form stable as well as characterised complexes.

Of the hydrazone derivatives, isonicotinoyl hydrazones are potential analytical reagents due to their capacity of these molecules to form insoluble complexes and their ability to produce characteristic absorption spectra when reacted with transition metal ions. Thus they serve as better separating reagents, even at sub microgram level.

Though large number of spectrophotometric methods are available for the determination of almost all the metal ions in the periodic table at microgram levels, these methods suffer either from lack of specificity or selectivity. Further, it is also difficult to develop a highly selective spectrophotometric procedure for a given metal ion making use of a given organic reagent in view of the matrix differences. This necessitates the development of more or less complicated procedures.
to overcome this detrimental influence. Therefore, in order to achieve greater degree of selectivity, the emphasis is being devoted to develop derivative spectrophotometric and direct spectrophotometric procedures for the simultaneous determination of two or more metal ions when present in admixture. The simultaneous spectrophotometric procedures and derivative spectrophotometric procedures for the determination of metal ions in admixture are sparcely reported in the literature.

In addition, derivative spectrophotometry is an excellent background elimination technique which enables the exact determination of $\lambda_{\text{max}}$ of the particular analyte species and facilitates the detection of poorly resolved absorption peaks and also increases the sensitivity and enhances the selectivity of the spectrophotometric procedures. Further, this enables the simultaneous determination of two species with or without the need to solve simultaneous equations. But only few data have been reported on the determination of mixtures of metal ions.
Section-3

OBJECTIVES:

Analytical methods play a vital role in checking the composition of the raw materials and finished products in controlling various processes in the metallurgical processes and in the analysis of environmental pollutants. The analytical chemistry of some rare elements like molybdenum, vanadium etc are important in biochemical processes. The metal ions such as titanium, iron, tungsten, molybdenum, tantalum and neobium of high purity are widely employed in electronic industries.

The determination of trace amounts of copper, iron, nickel and manganese which are present as micronutrients in plants is highly important.

Isonicotinoyl hydrazones constitute an important class of analytical reagents. The sensitivity of a reagent is enhanced with the increase in conjugation. Further the presence of a phenolic group ortho to the chromophoric group, enhances the sensitivity of the spectrophotometric determination.

Detailed survey of the past work (cf section 1) shows that very few isonicotinoyl hydrazones are employed as analytical reagents for the spectrophotometric determination of transition elements. Further derivative spectrophotometric procedures and simultaneous procedures by direct spectrophotometry and derivative spectrophotometry for the determination of metal ions in admixture are sparcely reported in the literature. In view of these the author has

a. under taken the synthesis of 2,4-dihydroxy-benzaldehyde isonicotinoyl hydrazone to study its potentiality as a new spectrophotometric reagent.

b. developed sensitive direct spectrophotometric and first derivative spectrophotometric methods for titanium, molybdenum, vanadium, iron, nickel and copper in various real samples.

c. developed spectrophotometric procedures for the simultaneous determination of two metal ions present in admixture without the need for prior separation or masking.

d. developed first derivative spectrophotometric methods for the simultaneous determination of two metal ions, mainly without the need for the use of simultaneous equations.
REFERENCES :

2. Tschugaeff, L., Ber., 38, 2520 (1905).