
Chapter – 1

INTRODUCTION

Section i : A brief review of isonicotinoyl hydrazones and their analytical applications

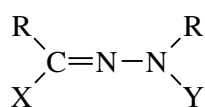
The role of metal ions in catalysis and living systems is of great interest. They are present in micro or even nanogram levels and still influence major activities of living beings. Mostly they act through the formation of coordination complexes. Werner's¹ theory of complex compounds stimulated a systematic study of the reactivity of organic reagents in inorganic analysis. Further, advancement in the development of reagents is followed by the Tschugaeff² discovery of the selective reaction between dimethylglyoxime with nickel (II) which led to a successful gravimetric determination of nickel by Brunk³⁻⁵.

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 or soluble complex compounds with metal ions. These metal complexes find wide use in analytical chemistry in general and in spectrophotometric analysis in particular.

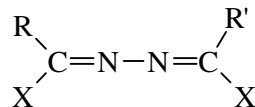
Hundreds of organic reagents are available for the spectrophotometric determination of almost all the elements in the periodic table. Among the numerous organic analytical reagents⁶⁻⁸ employed, the azomethines having O, N donor atoms have been extensively used to complex metal ions for their photometric determinations. However not much is reported on the use of isonicotinoyl hydrazones as complexing analytical agents.

Hydrazones are azomethines containing the characteristic grouping $>C=N-N<$. 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



(1)



(2)

Where

R and R' = H, Alk, Ar, RCO, Ht (heterocyclic group);

Y = H, Alk, Ar, Ht, RCO;

X and X' = H, Alk, Ar, Ht, Hal, OR", SR, CN, SO₂R, NO₂, NHN R" R"', N= NR",

COOR, 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 hydrazide and ketone or aldehyde dissolved in a suitable solvent. The compound usually crystallizes out on cooling.

Many of physiologically active hydrazones find application⁹ in the treatment of diseases such as tuberculosis, leprosy and mental disorder. Aroyl hydrazones (3) are also known to possess tuberculostatic activity^{10,11}. This is due to formation of stable chelates with transition metal ions present in the cell.



(3)

Thus many vital enzymatic reactions catalysed by these transition metals cannot take place¹²⁻¹⁴ in the presence of hydrazones. Hydrazones also act as herbicides, insecticides, nematocides, rodenticides and plant growth regulators. They show spasmolytic activity, hypotensive action and activity against leukaemia, sarcomas and other malignant neoplasms. Hydrazones of 3-N-methyl-N-(4-chlorophthalazinyl) and 3-N-methyl-N-(4-oxo-1-phthalazinyl) hydrazones possess anthelmintic activity¹⁵.

Isonicotinoyl hydrazones play an important role in medicinal chemistry. They are used as their complexes with metal ions for the treatment of number of diseases. As these organic compounds contain nitrogen as well as oxygen, they have the ability to form complexes easily with many metal ions, the heteroatoms, nitrogen as well as oxygen can form co-ordinate bonds with many metal ions and thus, form stable complexes. Number of reports are available on the medicinal importance of these compounds. A brief account of these reports is presented in the following paragraphs.

Chaitamber et al reported¹⁶ that Pyridoxal Isonicotinoyl hydrazone (PIH) is useful in the treatment of lymphoma and bladder cancer. According to them, transferrin, an iron transport protein, increases gallium uptake by cells, whereas pyridoxal isonicotinoyl hydrazone is an iron chelator transports iron into cells. $50\mu\text{g mL}^{-1}$ Ga-PIH inhibited cellular proliferation by 50 percent whereas similar concentration of PIH or gallium nitrate were not growth inhibitory. They reported that their studies suggest further evaluation of PIH as a potential antineoplastic agent.

Sterba et al¹⁷ carried out investigations relating to safety and tolerability of repeated administration of pyridoxal-2-chloro benzoyl hydrazone. The data from the study suggests that O-108 PCB remains a promising drug from the stand point of the possibility of its repeated administration and warrant further investigations.

Dimitrov¹⁸ et al carried out investigations to find out whether 3, 5-dichlorosalicylaldehyde isonicotinyl hydrazone (SH-7) an analogue of the anti tuberculosis

drug isoniazid (INH) could prevent isoniazid induced liver damage. Forty one healthy mice were treated with solution of INH and SH-7 in laboratory studies.

Cocco¹⁹ and coworkers studied the activities of six derivatives of a new class of isonicotinoylhydrazones. They investigated invitro against mycobacterium tuberculosis, isoniazid resistant mycobacterium tuberculosis ATCC 35822, rifampicin-resistant ATCC 35838, pyrazinamide resistant ATCC 35828, Streptomycin resistant ATCC 35820 and sixteen clinical isolates of mycobacterium tuberculosis. They reported that this compound for future development for the treatment of mycobacterium tuberculosis infections. They cited number of references²⁰⁻³⁰.

Seior and Eisele³¹ studied the relationship between structure, disintegration and anti tuberculotic invitro activity of over 200 derivatives of isonicotinoic acid hydrazide. Conclusive evidence reflects that many compounds do not with stand the *in vitro* conditions.

Richardson et al³² made systematic study on pyridoxal isonicotinoyl hydrazone and its analogues. They are orally effective Fe (III) chelators which show potential as drugs to treat iron overload disease. They discussed the relationship of the partition co-efficient of their iron chelators and their Fe (II) complexes.

In vitro and *In vivo* activities of acylated derivatives of isoniazid against mycobacterium tuberculosis were carried out by Hearn and Cynamon³³. It represents a major metabolic pathway for INH in human beings. The authors conclude that such close structural component of metabolites of INH may serves significant leads in antituberculosis discovery and explanation of the mode of action of INH. Hearn and Cynamon³⁴ prepared mycobacterium tuberculosis. They observed that acetylation greatly reduces the therapeutic activity of the drug, resulting in understanding decreased bio-availability and acquired INH resistance. Chemical modification of INH with a functional group that blocks acetylation, increasing the bio-availability of

drug and maintaining strong antibacterial action. They quoted several references to prove their observations.

Blaha and Coworkers³⁵ studied biliary iron excretion in rats following treatment with analogues of pyridoxal isonicotinoylhydrazone(PIH) over four analogues of PIH were used and some of them proved to be very potent in mobilizing Fe invitro from Fe-I study.

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

Isonicotinoyl hydrazones of carbonyl compounds act as good analytical reagents, but they have not been fully exploited. Hence, in the present investigation a detailed study of these reagents has been made with a view to find out their potentialities in inorganic analysis. Hydrazones are usually named after the carbonyl compounds from which they are obtained. Isonicotinoylhydrazones are the condensation products of isonicotinicacidhydrazide and the carbonyl compounds. These isonicotinoylhydrazones are prepared by refluxing a mixture of isonicotinic-acid hydrazide and the desired carbonyl compound for 2-3 hrs in slightly alkaline medium. The compound usually crystallizes out on cooling.

Brief review of hydrazones employed in spectrophotometric determination of metal ions were presented in Table 1.i.1.

Table 1.i.1
A Brief Review of Hydrazones employed in spectrophotometric determination
of Metal ions

Reagent	Metal ion	λ_{\max} (nm)	pH / medium	Beer's law (ppm)	$\epsilon \times 10^4$ L mol ⁻¹ cm ⁻¹	Aqueous / Extraction	Remarks/Applications
3,5 dimethoxy4-hydroxy benzaldehyde isonicotinoyl hydrazone	Ni(II)	470	8.5-9.5	0.2-2.94	1.22	Aqueous	Applied to synthetic mixtures, edible oils, Alloy samples
	Au(III)	500	4.0	0.197-1.97	1.14	Aqueous	-
	Cu(II)	440	9.0	0.317-3.17	3.37	Aqueous	-
	Pb(II)	430	9.0	0.414-10.360	1.82	Aqueous	-
Di-2-pyridyl ketone benzoyl hydrazone	Pd(II)	455	-	0.0-10.0	0.94	Extraction	Au, Pt, Ag, Hg, Cu interfere seriously
	Fe(II)	379	4.7-6.0	0.0-30.00	1.59	Extraction	-
	Ni(II)	-	-	-	-	-	-
2,4 dihydroxy benzaldehyde isonicotinoyl hydrazone	Pd(II)	392	3-4	0.852-8.42	1.62	Aqueous	Applied to hydrogenation catalysts, alloy steel samples
	Ni(II)	-	-	-	-	-	Numerous cations & anions interfere
	Ti(IV)	430	1-7	0.09-2.15	1.35	Aqueous	-

Continued table 1.i.1

Reagent	Metal ion	λ_{\max} (nm)	pH / medium	Beer's law (ppm)	$\epsilon \times 10^4$ L mol ⁻¹ cm ⁻¹	Aqueous / Extraction	Remarks/ Applications	R
	Zn(II)	390	6-8	0.10-1.50	3.55	Aqueous	Applied to the determination of zinc in Zn based alloys	4
	Th (IV)	391	2-8	0.3-7.00	2.20	Aqueous	-	4
Cinamaldehyde Isonicotinoyl hydrazone	Ru(III)	402	3.0	0.202- 4.04	1.25	Aqueous	Applied to the determination of Ruthenium in Zn-Mg alloy	4
2-hydroxy 5-methyl acetophenone isonicotinoyl hydrazone	Mo(VI)	385	-	0.4-10	-	Extraction	-	4
	Mo(VI)	410	-	3-16	-	Extraction	Ni(II), Mn(II), Cu(II), Ca(II), Al(III), Fe(III) and Cr(III) interfered seriously	5
	Cu(II)	440	3.4	0.5-4.0	1.93	Extraction	-	5
2-hydroxy-1-naphthaldehyde isonicotinoyl hydrazone	U(VI)	430	-	0.2-3.3	9.61	Extraction	-	5
	Th(IV)	-	-	-	-	-	Most of the common cations and anions do not interfere	5

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Continued table 1.i.1

Reagent	Metal ion	λ_{\max} (nm)	pH / medium	Beer's law (ppm)	$\epsilon \times 10^4$ L mol ⁻¹ cm ⁻¹	Aqueous / Extraction	Remarks/ Applications	R
3,4 dihydroxy benzaldehyde isonicotinoyl hydrazone	V(V)	360	5.5	0.5-5.3	1.29	Aqueous	Low sensitivity	5
2,3 dihydroxy benzaldehyde isonicotinoyl hydrazone	Fe(II)	-	-	-	-	Aqueous	Cu and Fe determined in alloys, ores	5
2-hydroxy 3-methoxy benzaldehyde isonicotinoyl hydrazone	U(VI)	374	4.0	1.19-11.19	1.05	Aqueous	Heating is necessary	5
2,3,4 Tri hydroxyl acetophenone phenyl hydrazone	Th(VI)	370	3.5	-	32.4	-	In presence of 70% DMF	5
Diacetylmonoxime-p-hydroxy bezoylhydrazone	Sn (II)	430	-	0.25-2.76	3.2	-	-	5
Di-2-pyridylketone benzylhydrazone	Fe(II)	-	-	-	-	-	Applied to the determination of Fe in Vinyl Foods	5
	Fe(III)	-	-	-	-	-	-	6
	Co(II)	-	-	-	-	-	-	6

Continued table 1.i.1

Reagent	Metal ion	λ_{\max} (nm)	pH / medium	Beer's law (ppm)	$\epsilon \times 10^4$ L mol ⁻¹ cm ⁻¹	Aqueous / Extraction	Remarks/ Applications	R
	Ni(II)	-	-	-	-	-	-	6
Diacetyl monoxime Isonicotinoyl hydrazone	Th(VI)	352	4.0-6.0	1.16-13.92	2.265	Aqueous	Applied to the determination in synthetic alloy samples	6
	Al(III)	355	8-9	0.828-8.0	2.64	Aqueous	Cd (II),Bi (III), thiourea, halogens do not interfere	6
	Ni(II)	365	7-8	0.188-1.886	2.08	Aqueous	-	6
	Hg(II)	351	5.5	1.003-12.03	2.23	Aqueous	-	6
	U(VI)	364	3.25	1.19-14.28	1.63	Aqueous	Applied to Rocks & synthetic samples	6
	Au(III)	361	4.5	-	1.50	Aqueous	Applied to synthetic alloy samples	6
2-amino acetophenone isonicotinoyl hydrazone	Au(III)	440	3.0-6.0	0.40-5.00	3.50	Aqueous	Excess of reagent is required	6

Continued table 1.i.1

Reagent	Metal ion	λ_{\max} (nm)	pH / medium	Beer's law (ppm)	$\epsilon \times 10^4$ L mol ⁻¹ cm ⁻¹	Aqueous / Extraction	Remarks/ Applications	Re
	Pd(II)	494	4.0	0.3-0.5	3.00	Aqueous	Au & Pb interfere seriously	70
2-hydroxy 1-naphthaldehyde p-hydroxy benzoic hydrazone	Ln (III)	415	-	0.227- 8.334	2.38	Aqueous	-	71
	Fe(II)	405	-	0.118- 3.534	5.6	Aqueous	Applied to determination of Fe in ferrities and blood	72
	Co(II)	425	-	0.055- 1.373	2.3	Aqueous	Pd, Au & V interfere seriously	73
4-hydroxy 3,5 dimethoxy benzaldehyde 4 hydroxy benzoyl hydrazone	Fe(III)	380	5.0	0.279- 2.79	1.71	C-TAB (5%)	-	74
	Pd(II)	373	3.0-4.0	0.106- 1.064	6.0	Triton-X- 100	In presence of 70% DMF	75
	Cu(II)	383	8.0-9.0	0.063- 0.635	3.41	Triton-X- 100	-	76

Continued table 1.i.1

Reagent	Metal ion	λ_{\max} (nm)	pH / medium	Beer's law (ppm)	$\epsilon \times 10^4$ L mol ⁻¹ cm ⁻¹	Aqueous / Extraction	Remarks/ Applications
	Mo(VI)	387	5.5	0.191-0.863	4.56	TritonX-100	-
	Ni(II)	408	8.0-9.0	0.058-0.586	3.22	TritonX-100	Applied to alloys and synthetic samples
	Cd(II)	400	9.0	0.112-1.124	4.81	TritonX-100	Heating at 50-60 ⁰ C
3-methoxy salicylaldehyde 4-hydroxy benzoyl hydrazone	Ni(II)	425	1-6	-	1.27	Aqueous	-
	Cu(II)	390	1-6	-	1.17	Aqueous	Applied for the determination of Zn and Cu in milk samples
Diacetyl monoxime 4-hydroxy benzoylhydrazone	Sn (II)	430	-	0.25-2.76	3.20	-	-
Bis (D-glucose)oxalyldihydrazone	Cu(II)	608		-	1.55	-	-
Biacetyl mono(2-pyridyl) hydrazone	Co(II)	505	6.0	-	2.30	-	-

Continued table 1.i.1

Reagent	Metal ion	λ_{\max} (nm)	pH / medium	Beer's law (ppm)	$\epsilon \times 10^4$ L mol ⁻¹ cm ⁻¹	Aqueous / Extraction	Remarks/ Applications
Salicylaldehyde aceto acetic acid hydrazone	Mo(VI)	470	-	0.097-0.968	1.60	Aqueous	Applied to Synthetic mixtures & alloy samples
	V(V)	560	-	0.243-2.438	2.20	Aqueous	-
	Fe(III)	525	-	0.054-0.270	-	Aqueous	-
	Ni(II)	395	-	0.112-0.56	-	Aqueous	Applied to synthetic samples
Pyridine -2-Aldehyde-2-Pyridylhydrazone	Ce (III)	205	-	-	2.56	Ethanol	Heating is necessary
	Th (IV)	200	-	-	3.60	Ethanol	Most of the cations and anions do not interfere
Pyridine -2- Carbaldehyde 2-hydroxybenzoyl hydrazone	Fe(II)	620	-	-	0.364	Extraction	-
Di-2-pyridylketone-2-furan carbothiohydrazone	Re(VIII)	546	-	0.70-14.0	1.64	MIBK	-

Continued table 1.i.1

Reagent	Metal ion	λ_{\max} (nm)	pH / medium	Beer's law (ppm)	$\epsilon \times 10^4$ L mol ⁻¹ cm ⁻¹	Aqueous / Extraction	Remarks/ Applications	Re
Isonitroso p-Isopropyl Acetophenone Phenyl hydrazone	Mo(VI)	470	-	-	1.0-3.2	Aqueous	-	93
	Se(IV)	513	4.0-6.0	0.24-10.0	9.32	Triton X-144	-	94
	Pb(II)	390	6.0	0.25-15.0	5.70	Triton X-100	-	95
Cinamaldehyde 4-hydroxy benzoyl hydrazone	Cd(II)	383	8.0-9.0	0.112-0.505	5.60	Micellar medium	Applied to the determination of Cd in biological materials, alloy samples	96
	Ni(II)	400	9.0-12.0	0.117-528	2.17	Micellar medium	-	97
	Pd(II)	375	1.0-6.0	0.212-0.957	7.50	Micellar medium	-	98
	Mo(VI)	404	3.0-4.0	0.047-0.479	6.82	Micellar medium	Applied to Foodstuffs, Pharmaceutical samples and in alloys	99
	Cu(II)	375	8.0-9.0	0.27-0.571	2.77	Micellar medium	-	100

Continued table 1.i.1

Reagent	Metal ion	λ_{\max} (nm)	pH / medium	Beer's law (ppm)	$\epsilon \times 10^4$ L mol ⁻¹ cm ⁻¹	Aqueous / Extraction	Remarks/ Applications	Ref
1,2-Cyclohexanedione-2-oxime-1-guanylhydrazone	Cu(II)	-	-	-	0.52	-	-	101
2,2'- Dipyridyl-2-benzothiazolyl hydrazone	Fe(II)	427	4.5-8.4	-	3.41	-	-	102
2-Hydroxybenzaldehyde-5-nitropyridyl hydrazone	Co(II)	470	6.5	-	-	Chloroform	-	103
Thiazole-2-carbaldehyde-2-quinolyl hydrazone	Pd(II)	625	acidic	0-4.2	1.93	Benzene	-	104
Benzyl-2-pyridyl ketone-2-quinolyl hydrazone	Hg(II)	475	basic	-	5.01	-	In presence of EDTA	105
2-Benzimidazolyl-3-sulphophenyl methanone-5-nitro-2- pyridyl hydrazone	Co(II)	517	2.7-9.4	0.02-1.00	6.65	-	-	106
Benzil isonicotinoyl hydrazone	Co(II)	-	-	-	-	-	-	107
3-Methoxy, 4-hydroxy Benzaldehyde 4-bromophenyl hydrazone	Cu(II)	462	2.0-4.0	-	2.05	-	-	108

Continued table 1.i.1

Reagent	Metal ion	λ_{\max} (nm)	pH / medium	Beer's law (ppm)	$\epsilon \times 10^4$ L mol ⁻¹ cm ⁻¹	Aqueous / Extraction	Remarks/ Applications	R
Benzothiazole -2-aldehyde-2-quinoyl hydrazone	Cu(II)	523	-	0.35-2.91	7.5	-		10
	Pd(II)	-	-	-	-	-	-	11
P-dimethyl amino benzaldehyde isonicotinoyl hydrazone	Hg(II)	-	-	-	-	-	-	11
2,4 Dimethoxy benzaldehyde isonicotinoyl hydrazone	Os(VIII)	393	5.0	0.951-11.412	1.48	-	50% DMF is present	11
	Hg(II)	390	7.0-9.0	-	2.80		-	11
	Ni(II)	410	9.0	0.1467-1.760	5.92		-	11
2-hydroxy benzaldehyde isonicotinoyl hydrazone	Zn(II)	-	-	-	-	-	-	11
	Mn(II)	-	-	-	-	-	-	11

Continued table 1.i.1

Reagent	Metal ion	λ_{\max} (nm)	pH / medium	Beer's law (ppm)	$\epsilon \times 10^4$ L mol ⁻¹ cm ⁻¹	Aqueous / Extraction	Remarks/ Applications	Re
p-Methyl isonitroso acetophenone phenyl hydrazone	Pd(II)	470	0-5.0	0.1-10	1.30	Extraction	-	11
	Pt(IV)	465	5.0-7.2	0.1-12	1.07	Extraction	Applied to dental alloy	11
Di-2-pyridylmethanone-1-phthalazinyl- hydrazone	Ni(II)	500	4.3-10.7	0.1-1.0	5.40	Benzene	-	11
Salicylaldehyde carbo Hydrazone	Zn(II)	445	5.4	-	-	-	-	12
Salicylaldehyde guanyl hydrazone	Mn(II)	505	-	0.8-8.0	-	-	-	12
2,4- Dihydroxy acetophenone benzoyl hydrazone	Mo(VI)	440	3-6	0.5-8.0	-	-	-	12
	V(V)	410	3-6	0.22-4.9	-	-	-	12
3,4- Dihydroxy benzaldehyde guanyl hydrazone	Mo(VI)	550	5.0	0.3-9	0.88	-	-	12

Continued table 1.i.1

Reagent	Metal ion	λ_{\max} (nm)	pH / medium	Beer's law (ppm)	$\epsilon \times 10^4$ L mol ⁻¹ cm ⁻¹	Aqueous / Extraction	Remarks/ Applications
2-Hydroxy-1-Naphthalene carboxaldehyde phenyl hydrazone	Co(II)	410	9.2	0.1-1.0	0.97	-	-
Pyridoxal salicylal hydrazone	Ti(IV)	440	0.9-2.5	0.55	Ti(IV)	-	-
2,6-Diacetylpyridine bis (furoryl hydrazone)	U(VI)	400	3.0	0.72-10.80	1.5	Extraction	-
2,6-Di acetyl pyridine bis (benzoyl hydrazone)	U(VI)	420	-	-	-	Dichloro methane	-
Isoniazid-p-diethylamino salicylaldehyde hydrazone	Fe(III)	-	-	-	-	-	-
Pyridine-2-acetaldehyde salicylhylyl hydrazone	Pd(II)	425	2-4.5	-	1.3	chloroform	Instability constant is 1.5×10^{-4}
Pyridine-2-carboxal dehyde-2-hydroxybenzoyl hydrazone	U(VI)	375	3.5-4.6	1.0-5.6	4.74	MIBK	-
2-Pyridyl ketone benzoyl hydrazone	Fe(III)	-	-	-	-	-	-

Continued table 1.i.1

Reagent	Metal ion	λ_{\max} (nm)	pH / medium	Beer's law (ppm)	$\epsilon \times 10^4$ L mol ⁻¹ cm ⁻¹	Aqueous / Extraction	Remarks/ Applications	Ref
Thiazole-2-carbaldehyde-2-quinonyl hydrazone	Pd(II)	625	acidic	0-4.2	1.93	Benzene	-	133
2-hydroxy,3-methoxy benzaldehyde p-hydroxy benzoic hydrazone	La(III)	390	7.5-9.0	0.14 – 9.72	1.93	Aqueous	Determination in standard samples	134
5-Nitro-2-Pyridine carbaldehyde-5-nitro-2-Pyridylhydrazone	Ni(II)	561	5.5-10	-	1.35	benzene	-	135
Orthohydroxypropio phenone isonicotinoyl hydrazone	U(VI)	380	3.0	0.47-17	1.15	- -	-	136
Naphthyl ketone isonicotinoyl hydrazone	Ti(IV)	-	-	-	-	-	-	137
Benzil – α -Monoxime isonicotinoyl hydrazone	Cu(II)	346	-	0.5-5.08	1.20	-	-	138
2-hydroxy benzophenone benzoic acid hydrazone	Ni(II)	410	-	0.31-2.20	1.50	-	-	139
Pyridine-2-aldehyde-2-pyridylhydrazone(PAPH)	Fe(II)	405	basic	-	-	Extraction	-	140
	Pd(II)	560	Acidic	-	10-100	Extraction	-	141

Continued table 1.i.1

Reagent	Metal ion	λ_{\max} (nm)	pH / medium	Beer's law (ppm)	$\epsilon \times 10^4$ L mol ⁻¹ cm ⁻¹	Aqueous / Extraction	Remarks/ Applications	Re
Pyridine -2- aldehyde-2-quinoyl hydrazone	Pd(II)	594	1.5-2.3	0.2-2.9	1.20	Extraction	-	14
	Co(II)	519	8.0	0.1-1.0	3.0	Extraction	-	14
	Ni(II)	492	-	-	5.10	Extraction	Applied to alloys and synthetic samples	14
Quinolline -2- aldehyde -2 quinoyl hydrazone	Cu(II)	536	-	-	4.70	Extraction	-	14
Quinolline -2- aldehyde -2 pyridyl hydrazone	Zn(II)	512	9.0 borate	-	5.10	-	-	14
	Cd(II)	517	9.0 borate	-	4.10	-	-	14
Benzoyl salicylalhydrazone	Cu(II)	-	4.9-9.0	-	-	-	-	14
	Pd(II)	395	1.2-2.3	-	7.18	-	-	14

Continued table 1.i.1

Reagent	Metal ion	λ_{\max} (nm)	pH / medium	Beer's law (ppm)	$\epsilon \times 10^4$ L mol ⁻¹ cm ⁻¹	Aqueous / Extraction	Remarks/ Applications	Ref
o-Hydroxy benzaldehyde isonicotinoyl hydrazone	In(III)	380	-	-	3.30	-	-	150
	Tl (I)	-	5.0	0.3-2.5	-	-	-	151
Resacetophenone oxime salicylic acid hydrazone	V(V)	545	-	-	1.40	-	-	152
2,4-dihydroxy benzophenone benzoyl hydrazone	Ce (IV)	400	8.0-10.5	0.3-7.0	6.0	-	-	153
Anthranilic acid resocylaldehyde hydrazone	V(V)	410	4.5	-	1.35	-	-	154
2-Furaldehyde-2-pyridyl hydrazone	Pd(II)	430	8.0-8.5	0.5-2.5	-	-	-	155
Salicylaldehyde isonicotinoyl hydrazone	Mo(VI)	430	0.65	0.4-12.0	-	-	-	156
5-Chloro salicylaldehyde guanyl hydrazone	Pd(II)	400	7.5-9.0	0-6.0	0.7129	-	-	157

Continued table 1.i.1

Reagent	Metal ion	λ_{\max} (nm)	pH / medium	Beer's law (ppm)	$\epsilon \times 10^4$ L mol ⁻¹ cm ⁻¹	Aqueous / Extraction	Remarks/ Applications	Ref
2-Hydroxy acetophenone Benzoyl hydrazone	V(IV)	465	Acetic acid	0-1.5	1.05	-	-	158
Pyridoxal nicotinoyl hydrazone	Ti(IV)	410	2.1-2.3	-	0.69	-	-	159
5-Methyl furfural-2-benzthiozolyl hydrazone	Cu(II)	415	-	0-12	5.80	Extraction	-	160
1-Napthaldehyde2-benzothiozolyl hydrazone	Cu(II)	422	6.8-9.7	-	4.80	-	-	161
Furfural-2-benzthiozolyl hydrazones	Cu(II)	415	5.6-9.6	-	4.40	-	-	162
Benzyl-bis-2-pyridyl hydrazone	Cu(II)	-	-	-	-	-	-	163
Benzil mono-(2-pyridyl) hydrazone	Co(II)	535	Etanolic	-	2.70	-	-	164
Bis(ethylacetoacetate)oxaly l hydrazone	Cu(II)	585	9.0	-	1.39	-	-	165

Continued table 1.i.1

Reagent	Metal ion	λ_{\max} (nm)	pH / medium	Beer's law (ppm)	$\epsilon \times 10^4$ L mol ⁻¹ cm ⁻¹	Aqueous / Extraction	Remarks/ Applications	Re
Bicyclohexanone oxalyldihydrazone	Cu(II)	600	7.0-9.0	-	1.60	-	-	16
o-hydroxy acetophenone hydrazone	Ni(II)	425	10-10.5	0-11.6	7.25	-	-	16
2,2'-pyridyl mono-2-pyridyl hydrazone	Fe(II)	621	-	-	1.30	-	-	16
2,2'-pyridyl Dipyridyl-2-Pyrimidyl hydrazone	Co(II)	460	2.5-11.5	-	2.95	-	-	16
Pyridoin phenyl hydrazone	Cu(II)	-	-	0.25-2.55	2.05	-	-	17
2-Aceto thiophene guanyldihydrazone	Pd(II)	375	AcOH	0-3.5	8.93	-	-	17
2-hydroxy naphthaldehyde benzoic hydrazone	Fe(III)	410	5.0	-	2.24	-	-	17
Isonitroso acetylacetone benzoyl hydrazone	Ni(II)	400	10.0	0.09-3.0	-	1.1309	-	17
2-Methylisonicotinic salicylal hydrazone	Ti(IV)	425	1.0-2.5	-	-	-	-	17

Continued table 1.i.1

Reagent	Metal ion	λ_{\max} (nm)	pH / medium	Beer's law (ppm)	$\epsilon \times 10^4$ L mol ⁻¹ cm ⁻¹	Aqueous / Extraction	Remarks/ Applications	Ref
3,5-Dichloro-salicylaldehyde -2-benzothiozoyl hydrazine	Mn(II)	460	3.0-4.8	0-60	-	-	-	175
6-Methyl picolonaldehyde-hydrazone	Cu(I)	425	-	1-7	0.70	-	-	176
	Pd(II)	-	-	-	-	-	-	177
Salicylaldehyde hydrazone	Pd(II)	425	3.5-5.0	0-21	0.53	-	-	178
Gossypol isonicotinoyl hydrazone	UO ₂ (II)	440	3.0	3-12	-	-	-	179

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Section ii : Analytical aspects of derivative spectrophotometry

Derivative spectrophotometry has enjoyed extensive activity during the last fifteen years. Its dynamic development is due to the incorporation of electronic differentiates in most of the commercial spectrophotometers. These, together with associated software, are able to compute derivatives up to nth order of the spectrum. Today, this technique has become a standard in spectrophotometric laboratories. It has proved to be very useful, providing both qualitative and quantitative information derived from mathematical processing of UV and Visible spectra. Since the principles of the derivative spectrophotometry are formulated, several reviews are published dealing both with theoretical aspects¹⁸⁰⁻¹⁸⁴ and practical¹⁸⁵⁻¹⁹⁰ problems.

Derivative spectrophotometry enables the detection of the presence of small amounts of impurities in samples, a more accurate determination of a minor component in the presence of bulk components, and its combination with spectrophotometric multicomponent analysis. With the development of microcomputer technology, derivative spectra are developed almost instantly. Therefore, the analytical use of derivative spectrophotometry has become very popular.

The differentiation of absorption spectra has many advantages for spectrophotometry in the UV and visible regions. It is the key for the potential enhancement of resolution of overlapping bands. It facilitates the detection of poorly resolved absorption peaks arising from admixtures or impurities in solution or for structural reasons and it enables the exact determination of λ_{\max} of the particular analyte species and increases sensitivity of the spectrophotometric procedures. In addition, it is an excellent background elimination technique. The influence of Rayleigh scattering constant, background absorbance, non-selective absorption of the matrix or accompanying components are removed and the resolution of signal-to-noise ratios improve¹⁹¹⁻¹⁹⁸.

The main characteristic of derivative spectrophotometry is the enhancement of the resolution of overlapping spectral bands. The differentiations discriminate against broad bands emphasizing sharper features to an extent that increases parallel to derivative order, because for bands (Gaussian or Lorentzian) the amplitude D of the n^{th} derivative is related to the n^{th} power of the inverse of the band width, W , of the normal spectrum¹⁹⁹.

$${}^n D \alpha \frac{1}{W^n}$$

Thus, for two bands (X and Y) are of same intensity, but of different width, the derivative amplitude of the sharper band (X) is greater than that of the broader one (Y) by a factor that increases with increase in derivative order²⁰⁰.

$$\frac{{}^n D(X)}{{}^n D(Y)} \propto \left(\frac{W_y}{W_x} \right)^n$$

For this reason, the uses of derivative spectra can increase the detection sensitivity of minor spectral features.

The first, second etc. derivative absorption spectrum of an analyte is defined as the first, second etc. derivative of the absorbance as a function of wavelength. The first or the second derivative is easily accessible instrumentally. The higher derivatives are calculated on the basis of computer generated functions. The first derivative spectrum is useful for the determination of the component more accurately in presence of matrix component. It is also useful for the multi component analysis or identification of derivatives with high spectral similarity. The resolution of overlapping bands is considerably improved since bandwidth of a Gaussian peak decreases to 51, 41 or 34% of the original bandwidth for the 2nd, 4th or 6th order derivatives respectively. Even order derivatives having a central peak of alternating sign narrower but coincident with the original peak may have greater analytical use than the odd functions^{181, 201}. Thus the first, second etc. order derivatives can eliminate unwanted effects such as various scattering, instrumental effects, differences by replacing cells or base line shifts caused by continual background, which all allow a more accurate quantitative evaluation of data.

Quantitative evaluation of derivative plots

Assuming that the Beer-Lambert's law is obeyed for the zero order spectrum, various amplitudes of the derivative curves are proportional to the analyte concentration in a similar way as is the absorbance of the primary absorption peak. The Beer's law for first and second derivative methods can be written as follows respectively.

$$\left(\frac{dA}{d\lambda} = -0.434 \frac{l}{l} \frac{dI}{d\lambda} = \frac{d\varepsilon}{d\lambda} Cl \right) \quad \dots 1.2.1$$

$$\frac{d^2A}{d\lambda^2} = 2.303C^2l^2 \left(\frac{d\varepsilon}{d\lambda} \right)^2 - 0.434 \frac{l}{l} \frac{d^2A}{d\lambda^2} = \frac{d^2\varepsilon}{d\lambda^2} Cl \quad \dots 1.2.2$$

Assuming $\frac{dl_o}{d\lambda} = 0$ the amplitude which is least affected by variation in the matrix and gives the best calibration statistics¹⁹⁴ is selected for quantitative measurements. The procedures used for quantitative evaluation are (p) peak-peak, (t) peak- tangent or (z) peak-base line methods which were shown in Fig. 1.ii.1. In principle both the peak to valley amplitude, D_s , D_L and the base line to valley distance. D_B , are proportional to the analyte concentration. In fact, the situation is more complicated for higher derivatives. But the proportionality of the derived signal to the analyte concentration is often maintained^{181,202}.

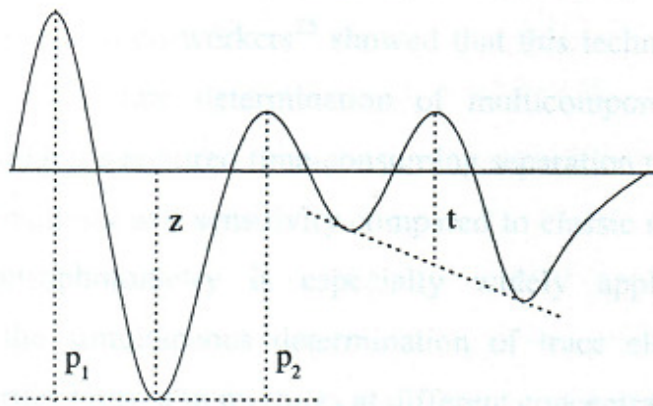


Fig. 1.ii.1: Graphical measures for amplitudes in derivative spectrophotometry:

(P) peak-peak; (t) peak-tangent; (z) peak-baseline method

The derivative techniques have been used in pharmaceutical²⁰³, environmental analysis²⁰⁴ and in the finger print analysis of proteins²⁰⁵, but only few data have been reported on the determination of metal ions.

In the present thesis, an attempt has been made by the author to develop new derivative spectrophotometric methods of the determination of Mn (II), Ni (II), Mo (VI) and Fe (III) by using 2-AAINH. The results of the present investigations are reported in this thesis.

Section iii: Importance of the present investigations

The precise determination of metal ions of microgram 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 chemists.

Although 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 subjected to are poorly understood and continue to cause problems²⁰⁶. Further these techniques are not within the reach of many laboratories. Besides the cost involved they are not amenable to easy operation.

Atomic absorption, atomic fluorescence emission and X-ray fluorescence techniques were employed for the purpose in the past decade. the disadvantages with these techniques that they are not within the reach of many laboratories. Also some of the interferences to which these methods are subject to are poorly understood and continue to cause problems. They are not amenable to easy operation besides the cost involved.

In this context spectrophotometers, 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 every year. The advent of a new generation of spectrophotometers

equipped with diode array detectors and extensive use of micro processors in data acquisition and handling have brought about dynamic progress in the simultaneous analysis based on multi-wavelength and derivative measurements. When reacted with transition metal ions. Thus they serve as better separating reagent, 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. Spectrophotometric and derivative spectrophotometric procedures for the simultaneous determination of metal ions are sparsely reported.

Analytical chemistry seeks ever improved means of measuring the chemical composition of natural and artificial materials, separation, identification and determination of the relative amounts of the components in simple or complex system(s) are the techniques of this science involved. An important role is played in nearly all aspects of chemistry, like agriculture, chemical, environmental forensic, manufacturing, metallurgical and pharmaceutical by analytical chemistry. To improve the reliability of existing techniques and to meet the demands for better chemical

measurements which arise constantly in one society, analytical chemists keep working.

Spectrophotometric analysis of metal ions at microgram level involves synthesis of selective and sensitive reagent. 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 characteristic complexes.

Of the hydrazone derivatives, isonicotinoylhydrazones are potential analytical reagents due to the ability of these molecules to form insoluble complexes and their ability to produce characteristic absorption spectra in the literature. In addition, derivative spectrophotometer is an excellent background elimination technique which enables the exact determination of λ_{\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 without the need to solve simultaneous equations. But the data on the determination of mixtures of metal ions are few.

Section iv : Objectives of the present investigations

Analytical methods play a vital role in checking the composition of the raw materials and finished products in controlling various processes in industry, in the metallurgical products, in identifying new sources for rare elements and in the analyses of environmental pollutants. The analytical chemistry of certain metal ions like manganese (II), nickel (II), molybdenum (VI), and iron (III) are important in biological and industrial process. The metal ions such as nickel, iron are widely employed in electronic industries. The determination of trace amounts of manganese and iron which are present as micro nutrients and macro nutrients in plants is highly important.

Isonicotinoyl hydrazones constitute an important class of analytical reagents. The sensitivity of the reagent is enhanced with the increase in conjugation. Further, the presence of auxochromic group such as NH₂ ortho to the chromophoric group, enhances the sensitivity of the spectrophotometric determination. Further hydrazones which react with only a few metal ions are scarce.

Detailed survey of the past work (cf. Section i) shows that very few isonicotinoyl hydrazones are employed as analytical reagents for the spectrophotometric determination of metal ions. Further few derivative spectrophotometric procedures for the determination of metal ions individually or simultaneously are reported in the literature. In view of the above observations, the author has

- i. Undertaken the synthesis of 2-amino acetophenone isonicotinoyl hydrazone to exploit its potentiality as a new selective spectrophotometric reagent.

- ii. Developed sensitive direct spectrophotometric and first and second derivative spectrophotometric methods for the determination of manganese (II), nickel(II), molybdenum (VI), and iron (III) in various real samples.
- iii. Developed spectrophotometric procedures for the simultaneous determination of two metal ions present in admixture without the need for prior separation or masking
- iv. Developed first and second derivative spectrophotometric methods for the simultaneous determination of two metal ions without the need to solve simultaneous equations.

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