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## **SYNTHESIS, CHARACTERISATION OF PYRIDOXA ISONICOTINOYL HYDRAZONE COMPLEX AND ITS BIOLOGICAL ACTIVITY**

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### **Keywords:**

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### **ABSTRACT**

Pyridoxal isonicotinoyl hydrazone (PIH) has been synthesized. Complex of Pyridoxal isonicotinoyl hydrazone (PIH) with transition metals, Ni (II) has been synthesized in methanol medium. The formation of the complex are endothermic processes. The ligand was characterized by melting point, elemental analysis, absorption spectra and antimicrobial activity while the complex was characterized by melting point, absorption spectra. A simple and sensitive spectrophotometric method was developed for transition metal complex of pyridoxal isonicotinoyl hydrazone (PIH). The optimum condition for complete colour development have been established. The stability constant, dissociation constant & change in free energy of Ni(II) has been determined by Job's variation & mole ratio method indicate that the M:L is 2:1. Tolerance limit of diverse ions in the determination of Ni(II) with pyridoxal isonicotinoyl hydrazone (PIH) is investigated.

## INTRODUCTION

Hydrazones are important organic analytical reagent for the determination of metal ions in microgram quantities. They react with many metal ions forming coloured complexes and act as chelating agents. In general, the techniques of solvent extraction is widely used in the spectrophotometric determination of metal ions<sup>1-2</sup>. However organic solvents such as benzene and chloroform are often carcinogenic, toxic and cause environmental pollution. It is significant to develop a method which does not involve solvent extraction. The potential application of hydrazone derivatives for the spectrophotometric determination of metal ions has been reviewed<sup>3</sup>. The coordination chemistry of hydrazones is an intensive area of study and numerous transition metal complexes of these hydrazones as ligands have been investigated in view of their application in various fields<sup>4-6</sup>. Hydrazones are interesting ligands with multiple functional groups, which display variable coordination modes under different chemical environmental<sup>7</sup>. The chemical properties of hydrazones have been widely investigated due to their chelating capability<sup>8</sup>, pharmacological activity<sup>9-10</sup> and analytical applications<sup>11</sup>. The variety of hydrazone derivatives play various biological activities viz anticancer, anti-HIV<sup>12</sup>, anthelmintic<sup>13</sup>, antimycobacterial<sup>14</sup>, anti-inflammatory<sup>15-16</sup>, antidiabetic<sup>17</sup>, antimicrobial<sup>18-20</sup>, trypanocidal<sup>21</sup>, analgesic<sup>22</sup>, anti-tuberculosis<sup>23-27</sup>, antimalarial activities<sup>28</sup> antiparasitic activity<sup>29</sup>. Pyridoxal isonicotinoyl hydrazone (PIH) is an iron chelator with antioxidant activity, low toxicity and is useful in the experimental treatment of iron overload diseases. Pyridoxal isonicotinoyl hydrazone (PIH) prevents copper mediated in vitro free radical formation<sup>30</sup>.

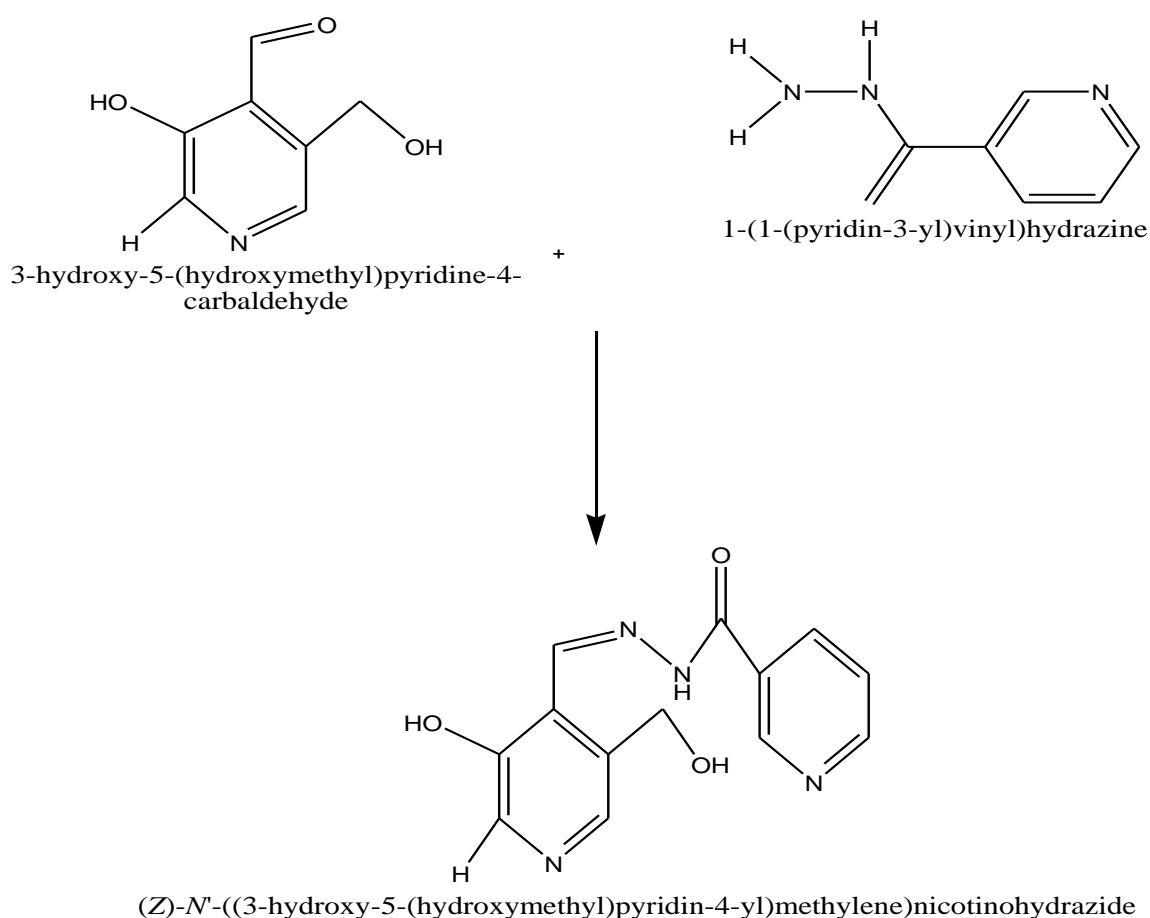
Nickel is very important metal for both industrially and biologically. It is one among the essential trace elements along with cobalt, copper, zinc and manganese in the human diet<sup>31</sup>. Experiments on synthetic nutrition that nickel and cobalt play a direct role in nutritional phenomenon<sup>32</sup>. Nickel bound to ribonucleic acid has special affinity for bone and skin and plays an important role in pigmentation<sup>33</sup>. It has been reported that normal human plasma contains 0.12-0.085 g ml<sup>-1</sup> of nickel(II). Nickel is one of the important alloying element for steel and cast iron. A nickel metal enzyme is an essential micronutrient<sup>34-36</sup> for plants arose from ureases. Literature survey indicated that several spectrophotometric methods<sup>37-47</sup> were reported for the determination of nickel(II) by using various chromogenic reagent. Hydrazones are important class of analytical photometric reagents, the potential of which were reviewed<sup>48</sup>.

## MATERIALS AND METHODS

All chemical and solvents used were of analytical grade . An Elico pH meter LI-610 is used for the pH measurements. An Elico UV-visible spectrophotometer model UV-SL-164 equipped with 1 cm quartz cell used for spectrophotometric measurements taken on the instrument. Elemental analysis and antimicrobial activity was done in Laboratory approved by Central Government for AGMARK.

### SYNTHESIS AND CHARACTERISATION OF PYRIDOXAL ISONICOTINOYL HYDRAZONE (PIH)

#### Synthesis of Pyridoxal Isonicotinoyl Hydrazone (PIH)



The crude product is crystallized in methanol. The recrystallized product has melting point is 176 °C and molecular weight by formula is 284 .00.

**Characterization of Pyridoxal isonicotinoyl hydrazone (PIH)****Absorption Spectra of Pyridoxal isonicotinoyl hydrazone (PIH)**

Absorption Spectra of pyridoxal isonicotinoyl hydrazone (PIH) was recorded against a blank solution containing buffer (pH 4). Absorption spectra was recorded in the wave length range 220 nm to 500 nm. It shows an absorption maximum at 300 nm wavelength the molar absorptivity of PIH is  $0.87321 \times 10^3 \text{ L.mol}^{-1}.\text{cm}^{-1}$ . **Fig 1.**

**Elemental Analysis of pyridoxal isonicotinoyl hydrazone (PIH)**

The elemental analysis of PIH was done in Laboratory approved by Central Government for AGMARK. It shows the result of elemental analysis in **Table 1.**

**Effect of Reagent concentration**

Effect of Reagent concentration was studied by taking varying amount of reagent and fixed amount of transition metal.

**Validity of Beer's Law and Composition of Complex**

For the study of Beer's law the solutions were prepared which containing different amounts of Ni (II), same amount of ligand pH 4. The composition of the Ni (II)-metal complex is found to be 1:2. It was determined by studying Job's method. The ratio of metal ion to ligand molecule in the coloured complex was found to be 1:2 composition of complex.

**Antimicrobial Activity of Pyridoxal isonicotinoyl hydrazone (PIH)**

The elemental analysis of PIH was done in Laboratory approved by Central Government for AGMARK. It shows the result of elemental analysis in **Table 2.**

**Physico-chemical Characteristic Pyridoxal isonicotinoyl hydrazone (PIH)**

Physico-chemical and Analytical characteristic of transition metal complex of ligand was studied and given in **Table 4** and Tolerance limit of diverse ions in the determination of ligand shown in **Table No. 5**

**RESULT AND DISCUSSION****Table No. 1. Elemental Analysis of PIH**

Sr.No.	Chemical Analysis	Percentage Found	Percentage Expected
1)	Carbon	54.92 %	55.55 %
2)	Hydrogen	04.22 %	05.38 %
3)	Oxygen	16.90 %	18.02 %
4)	Nitrogen	23.94 %	22.39 %

**Table No. 2. Antimicrobial Activity of PIH**

Sr.No.	Antimicrobial	Activity
1)	<i>Klebsiella Pneumoniae</i>	Nil
2)	<i>Vibriae Cholerease</i>	Nil
3)	<i>Bacillus Megaterium</i>	Nil
4)	<i>Salmonalla typhi</i>	Nil
5)	<i>Shigella Flexneri</i>	Nil

**Table 3. Experimental Result & Physical data of PIH & Ni (II) - Complex**

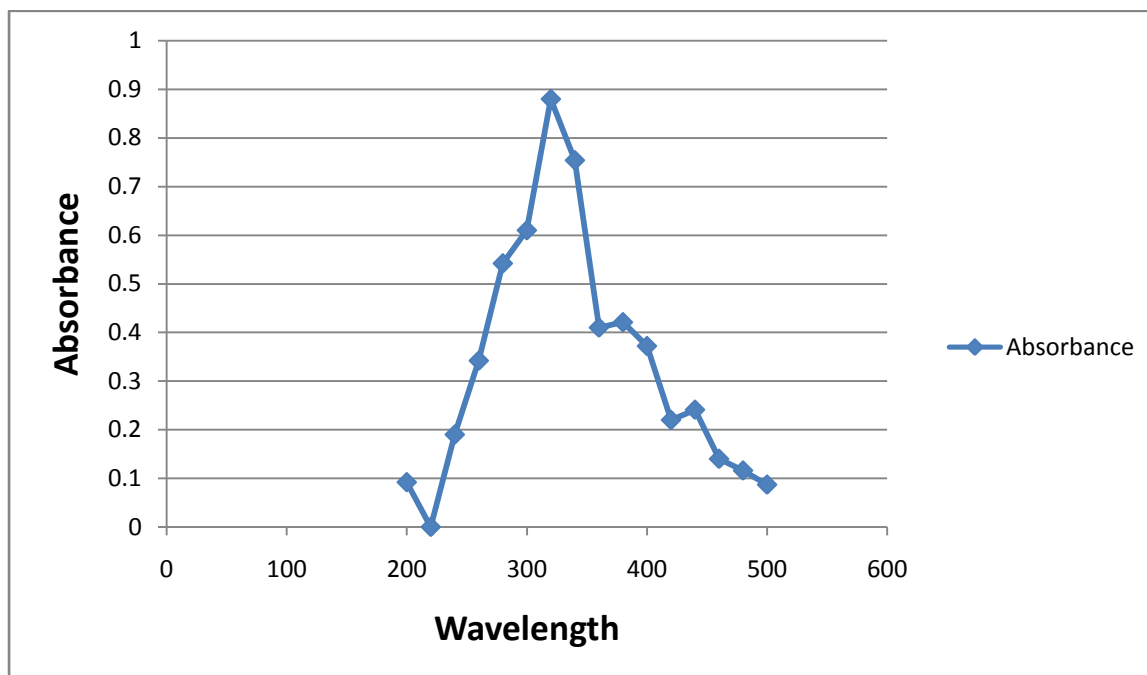
Code No	Compound M.P. ( °C )	Colour	Molecular weight by formula gm/mole	Yield
Ligand	176 <sup>0</sup> C	Greenish	284.00	85 %
Ni (II)-Ligand	137 <sup>0</sup> C	Greenish yellow	299.845	71%

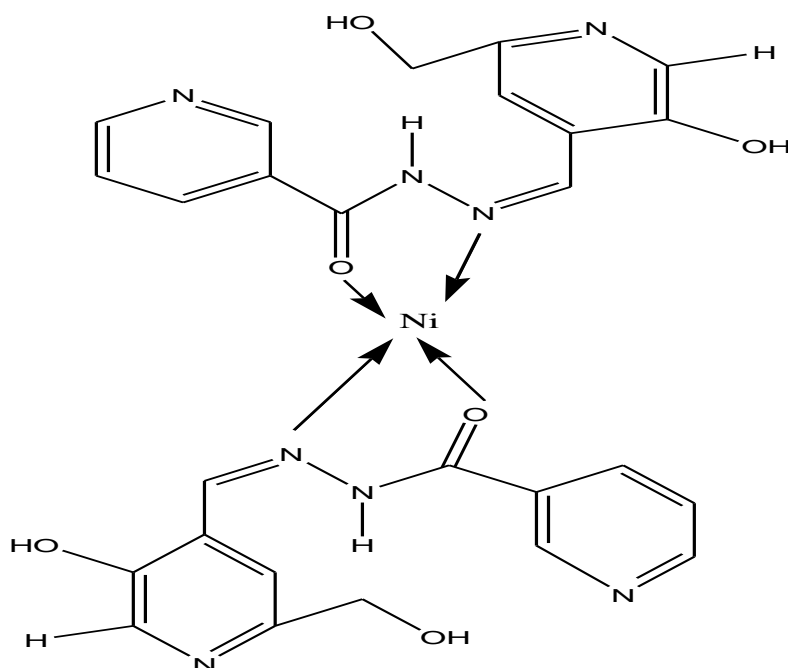
**Table . 4. Physico-Chemical and Analytical Characteristic of Ni (II) Complex of PIH**

Sr.No.	Characteristics	Result
		<b>Ni (II)-ligand</b>
1)	Absorption Spectra	300 nm
2)	Molar absorptivity	$0.87321 \times 10^3 \text{ Lit. mol}^{-1} \cdot \text{cm}^{-1}$
3)	pH range ( optimum )	4.0
4)	Reagent required for maximum complexation	0.227 ml
5)	pKa	$6.004 \times 10^8$
6)	Beer's law validity range ( ppm)	7 ppm
7)	Composition of complex ( M : L )	1:2
8)	Stability Constant	$3.925031 \times 10^7$
9)	Dissociation Constant	$4.352416 \times 10^{-8}$
10)	Change in free energy	-37.67 KJ/mole
11)	Sandell's Sensitivity ( $\mu\text{g}/\text{cm}^2$ )	$0.002954 \mu\text{g}/\text{cm}^2$

**Table No.5 Tolerance limit of diverse ions of Ni (II) Metal complex of PIH**

Sr. No.	Metal ion	Salt	Interference
1)	Mg (II)	MgSO <sub>4</sub>	121
2)	Ca(II)	CaCl <sub>2</sub> .2H <sub>2</sub> O	46
3)	Cd (II)	CdCl <sub>2</sub>	53
4)	Mn (II)	MnCl <sub>2</sub>	39
5)	Co (II)	CoSO <sub>4</sub>	52
6)	Ce (IV)	Ce (SO <sub>4</sub> ) <sub>2</sub>	Interferes
7)	Ba (II)	BaCl <sub>2</sub>	25
8)	Cr (III)	K <sub>2</sub> Cr <sub>2</sub> O <sub>7</sub>	32
9)	Hg (II)	HgCl <sub>2</sub>	54
10)	Ti (V)	K-titanyl oxalate	72
11)	Ni (II)	NiCl <sub>2</sub>	34
12)	Sn (II)	SnCl <sub>2</sub>	27
13)	Na (I)	NaCl	67
14)	Pb (II)	PbSO <sub>4</sub>	15
15)	V (v)	V <sub>2</sub> O <sub>5</sub>	22
16)	Zn (II)	ZnSO <sub>4</sub>	Interferes
17)	Al (III)	AlCl <sub>3</sub>	36
18)	Pd (II)	PdCl <sub>2</sub>	Interferes
19)	K(II)	KCl	64

**Fig 1. Absorption Spectra of Pyridoxal isonicotinoyl hydrazone (PIH)**

**Structure of Ni (II)- Pyridoxal isonicotinoyl hydrazone (PIH)****REFERENCES**

1. Sahu R, Sondhi SM, Gupta B. *Talanta*, 1995, 42(3), 401.
2. Naik MN, Thakkar NV, *Indian J. Chem.*, 1995, 34(5), 410.
3. Singh RB, Jain P, Singh RP, *Talanta*, 1982, 29, 77.
4. Mehrotra RC, Wilkinson G, Gillard RD, McCleverty JA, *Comprehensive Coordinate Chemistry*,
5. Baligar RS, Revankar VK, *J. Serb. Chem. Soc.*, 2006, 71(12), 1301.
6. Dey K, Chakaraborty K, Bhattacharya PK, Bandopadhyaya D, Nag SK, Bhowmick R, *Indian Chem. Soc.*, 1999, 38, 1173.
7. Raman N, Ravichandran S, Thangaraja C. *J. Chem. Sci.*, 2004, 4, 116.
8. Rasstagi DK, Sahani SK, Rana VB, Due SK. *Indian J. Chem.*, 1978, 16, 86.
9. Dilwarth JR. *Coord. Chem. Rev.*, 1976, 21, 29.
10. Kotyal M, Dutt Y, *Talanta*, 1975, 22, 151.
11. Garg BS, Singhand PK, Garg SK. *Indian J. Chem.*, 1991, 30A, 979-981.
12. Al-Macrosaur LQ, Dayam R, Taheri T, Witvrouw M, Debyser Z, Neamati N, Discovery of Novel No. cytotoxic salicylhydrazine containing HIV-1 integrase Inhibitors. *Biorg. Med. Chem. Lett.* 2007, 1, 6472-6475.
13. Kueukguzel SG, Mazi A, Sahin F, Ozturk S, Stables JJ, Synthesis and biological activities difulunisal hydrazide-hydrazones. *Eur. J. Med. Chem.*, 2003, 38, 1005-1013.
14. Hanna ML, Tarasow TM, Perkins J. Mechanistic differences between in vitro assays for hydrazone based small molecule Inhibitors of antrax lethal factor *Biorg. Med. Chem.*, 2007, 35, 50-58.
15. Salgin-Goksen U, Gokhan N, Goktas O, Koysal Y, Kille E, Trik S, Aktay G, Ozalp M, Synthesis of thiosemicarbazides, 1,2,4-triazole-5(4H)-thiones, 1,3,4-thiadiazoles and hydrazones containing methyl-2-benzoxazolones-synthesis, analgesic anti-inflammatory and antimicrobial activities, *Biorg. Med. Chem.*, 2007 15, 5738-5751.
16. Roma G, Braccio MD, Grossi G, Mattioli F, Ghia M, 1,8-naphthyridines IV.9-substituted. N,N-dialkyl-5-alkylamino or cycloalkyl amino)[1,2,4] triazolo[4,3-a] [1,8] naphthyridine-6-carboxamide, new compounds with antiaggressive and potent anti-inflammatory activities. *Eur. J. Med. Chem.*, 2008, 35, 1021-1035.
17. Kucukguzel SG, Mazi M, Sahin F, Ozturk S, Stables F., J. Synthesis and biological activities of difulunisal hydrazide-hydrazones, *Eur. J. Med. Chem.*, 2003, 39, 1005-1013.

18. Cacic M, Trikovnik M, Cacic F, Has-Schon E, Synthesis and antimicrobial activity of some derivatives of (7-hydroxy-2-oxo-2H-chromen-4-yl)-acetic acid hydrazide *Molecules*,2006,11,134-147.
19. Masunari A, Tavares LC, A new class of nifuroxazide analogues : Synthesis of 5-nitrothiophene derivatives with antimicrobial activity against multidrug-resistant *Staphylococcus aureus*. *Bioorg. Med. Chem.*, 2007,15,4229-4236.
20. Metwally KA, Abdel-Aziz LM, Lashine EM, Husseiny MI, Badaway RH, Hydrazones of 2-aryl-quinoline-4-carboxylic acid hydrazides : Synthesis and preliminary evaluation as antimicrobial agents, *Bioorg. Med. Chem.*, 2006, 14, 8675-8682.
21. Anna Senter, Wu M, Peter D, Arming antibodies ; Prospects and challenges for immunoconjugates, *Nature Biotechnology (Nature Publishing Group)* 2005, 23 (9),1137-1146.
22. Radhwan MA, Ragab EA, Sabry NM, El-Shenaway SM, Synthesis and biological evaluation of new 3-substituted indole derivatives as potential anti-inflammatory and analgesic agents. *Bioorg. Med. Chem*, 2007, 15,3832-3841.
23. Nayyar A, Monga V, Malde A, Coutinho E, Jain R, Synthesis, anti-tuberculosis activity and 3D-QSAR study of 4-(adamantan-1-yl)-2-substituted quinolines, *Bioorg, Med, Chem*. 2007,15, 625-640.
24. Badia K, Elcin O, Seda U, Fatma K, Nathalay S, Sevim R, Dimoglo A, Synthesis and Characterisation of novel hydrazide-hydrazones and the study of their structure-antituberculosis activity *Eu. J.Med. Chem*. 2006,41,1253-1261.
25. Manvar A, Malde A, Verma J, Virsodia V, Mishra A, Upadhyay K, Acharya H, Coutinho E, Shah A, Synthesis , anti-tubercular activity and 3D-QSAR study of coumarin-4-acetic acid benzylidene hydrazides. *Eur. J. Med. Chem*. 2008, 41, 754-758.
26. Nayyar A, Monga V, Malde A, Coutinho E, Jain R, Synthesis, anti-tuberculosis activity and 3D-QSAR study of 4-(adamantan-1-yl)-2-substituted quinolines. *Bioorg. Med. Chem*.2007, 15, 626-640.
27. Caffrey CR, Schanz M, Nkemgu-Njinkeng J, Brush M, Hausell E, Cohen FE, Flaherty FE, Mckerrow JH, Steverding D, Screening of acyl hydrazide proteinase inhibitors for antiparasitic activity against *Trypanosoma brucei*. *Int. J. Antimicrob. Agents*.2002, 19, 227-251.
28. Gemma S, Kukreja G, Fattorusso C, Persico M, Romano MP, Altarelli M, Savini L, Campiani G, Fattorusso E, Basilico N, Taramelli D, Yardley V, Butini S, Synthesis of N1- acrylydene-N2- quinoly- and N2- acryldinylhydrazones as potent antimalarial agents active against CQ-resistant *P. falciparum* strains. *Bioorg. Med. Chem. Lett*.2006, 16, 5384-5388.
29. Caffrey CR, Schanz M, Nkemgu-Njinkeng J, Brush M, Hausell E, Cohen FE, Flaherty TM, Mckerrow JS, Steverding D, Screening of acyl hydrazide proteinase inhibitors for antiparasitic activity against *Trypanosoma brucei*. *Int. J. Antimicrob. Agents*. 2002,19, 227-251.
30. Hermes-Lima M , Andrade MS, Jr. *Mol Cell Biochem*. 2008, 228(1-2),73-82.
31. Bell GH, Davidson JN, Scarborough H, Text book of physiology and Biochemistry. E.S. Living stone Ltd., Edinburgh, 1953, 2, 80.
32. Bertrand G, Nakamura H, *Bull. Soc. Chim. Biol.*,1934, 16, 1366.
33. Bernard L, Hawk's physiological chemistry T.M.H. Publishing Company Ltd., New York, 1965, 14, 565.
34. Dixon NE, Gazzola C, Blakey RL, Zerver B, *J. Am. Chem. Soc.*,1975, 97, 4131.
35. Hewit JE, Chemistry and Agriculture special publication No. 36, Chem. Society, London,1979, 91.
36. Welch RM, *J. Plant Nutri.*,1981, 3, 345.
37. Ferreira SL, Santos BF, De Andrade JB, Spinola Costa AC, *Micro Chimica Acta*,1996, 122,109 - 115.
38. Malik AK , Kaul KN , Lark MS, Faube W, Rao AL, Turk J, *J Chem*,2001, 25, 99.
39. Kumar A, Jain M, *Chem Anal*,1992, 39,73.
40. Bansal AK, Nagar M , *J. Indian Chem Soc*, 2006,83, 731.
41. Boladani SN, Tewari M, Agarawal A, Sekhan KC , *J. Anal Chem*, 1994,349, 478.
42. Odashima T, Kohata K ,Yogi K, Ishii H, *Bunseki Kagaku*, 1995,44(2), 135.
43. Praveenkumar A, Raveendr Reddy P, Krishna V, *Indian Journal of Chemistry*,2007,46A, 1625-1629.
44. Sritha B, Sreenivasulu Reddy T, *IOSR Journal of applied Chemistry*, 2014, 7(3), 22-26.
45. Rehana Khanam , Rekha Dashora, *Oriental Journal of Chemistry*, 2014, 30(2), 834-841.
46. Arunabai AK, Chandrsekhar KB, Devanna N, *RASĀYAN J Chemistry*, 2010,3(3),467-472.
47. Barreto WJ, Barreto SR, Scarmino IS, Ishiwaka DN, Fatima MD, *Quim.Nova*, 2010,33(1),109-113.
48. Singh RB, Jain P, Singh RP, *Talanta*,1982, 29, 77.