Pharmaceutical Significance Of Oxotungsten And Oxochromium Complexes Of Schiff Bases Derived From Thiosemicarbazones

Abstract

The thiosemicarbazones of bis(5-chlorosalicylaldehyde), bis(trifluoroacetylacetone), and their complexes with oxotungsten and oxochromium have been produced as metal complexes. These complexes have been identified by their IR, electronic, molar, and magnetic moment spectra. These studies have shown that the metal ion is surrounded by an octahedral geometry. Additionally, the complexes were examined for potential medicinal uses.

Microbial agents acquiring drug resistant tendencies,have infected human beings,this research explores synthesis and characterization of these Schiff base metal complexes showing biological properties and were evaluated for their in-vitro anti-microbial activity.Antibacterial activity was examined by agar plate diffusion technique.Antifungal properties were examined by the radial growth method using agar-agar culture.The results show that activity increases on chelation.This activity is affected by the nature of substituents.This in relation to the lipophilicity of the ligands and their membrane permeability,is a key factor in determining their entry inside the cell.

Keywords—Chromium complexes, tungsten complexes, Schiff base, thiosemicarbazide

Introduction

"Schiff bases are the condensation products of primary amines and compounds containing carbonyl groups,the compounds carrying imine or azomethine (–C=N–) functional group and these exhibit useful biological activities such as antimicrobial,anticarcinogenic, antioxidant, and antitumour activities.In recent years, it is a matter of great interest amongst the medical microbiologists,to combat microbial resistance.Schiff bases and their metal complexes have been screened to show prolific antimicrobial and antifungal properties" [1].

In continuation of our earlier reports [2] on "the medicinal significance of Schiff bases and their metal complexes,the present communication reports the synthesis of some new complexes of Schiff bases derived from condensation of 5-chlorosalicyldehyde,terephthaldehyde,2,4-pentanedione and trifluoroacetyl acetone with thiosemicarbazide".Thecomplexeswerecharacterizedontheb asisoftheir micro analytical data,elementalanalysis,melting points,IR, UV-Vis spectra and magnetic moment properties. The magnetic moment data suggests pairing of electrons.Theinfraredspectrumofthecomplexes showed stretching due to ν(C=N) and ν(C=S)[3].Schiff bases are first reported by Schiff. Schiff bases have gained potency in medicinal and pharmaceutical fields due to biological activities like anti-inflammatory[4-7],analgesic[5-8],antimicrobial[9-10],anticonvulsant[11],antitubercular[12],anticancer[13-14],antioxidant[15]. "Azomethine linkage[16] and cell process mechanism [17-18].Studies enlightened that metal complexes show greater biological activity than free organic compounds [19,20]. Proliferation of biological activity was reported by implementation of transition metals into Schiff bases" [21,45] . Schiff bases play an influencing role in development of inorganic biochemistry.[22-26]

1. Material and methods

A. Preparation of Schiff bases

Schiff baseswere synthesized by the condensation of respective aldehyde and ketone with thiosemicarbazide in the ratio of 2:1 in ethanolic solution.[27].0.91 gm of the thiosemicarbazide was dissolved in ethanol and refluxed for 30 min.Weighed quantity of each reagent is added to the flask.Reaction mixture was heated for 6h.The crystals of the ligand were obtained and were purified by recrystallization in ethanol.[2]

B. Preparation of metal complexes

Oxotungsten and oxochromium complexes were synthesized by the addition of salt solution in methanol/ethanolic solution of ligand in DMSO/THF.The precipitate thus obtained was washed with DMSO/THF and dried over fused $CaCl_2$.

Metal complexes were prepared by refluxing their ethanolic solution for 24h.The precipitate thus obtained was filtered and washed with hot ethanol and then with hot benzene and dried over anhydrous calcium chloride.

UNDER PEER REVIEW

Preparation of oxochromium complexes

A methanolic solution of chromium tri chloride was added in small quantities with stirring to a hot solution of the ligands in methanol.The pH of the solution mixture was adjusted to 5.0 with NaOAc buffer,in 1:1:3/4 molar ratio and stirring continued for 10-15 minutes.

The contents were refluxed for 5h and observed for change in colours.The solid complexes that separated were filtered and washed with aqueous methanol and dried over P_4O_{10} in vacuum, yellow needle shaped crystals appeared.

Preparation of oxotungsten complexes

The complex was synthesized by digesting a mixture of the ethanolic solution (50mL) of the ligands and the metal in the ratio of 1: 2 and acidified aqueous sodium tungstate (2mmol) solution(50mL) on the water bath for 1½ hours. Brown complex was formed which was then filtered, washed with hot water and ethanol and dried in vacuum.

2. Analytical studies

Elemental Analysis

It was carried out at R.S.I.C.,Dept.,C.D.R.I., Lucknow.The complexes were analysed for metal and chlorine content by standard procedure.The values obtained are given in table -1.

Conductivity measurement

Conductivity measurements were carried out at Philips conductivity bridge model PR 9500 with a dip type conductivity cell at Department of Chemistry, Bareilly College, Bareilly.The conductances of the complexes were measured in DMF and MeOH at 10-3 M dilution at 30°C.The values obtained are given in table -2.

I.R. Studies

The infra red studies[34-35] of ligand and it's metal complexes were recorded in Perkin-Elmer spectrophotometer model 651(US) in KBr as well as Nuzol phase from 4000 cm-1 to 200cm-1at R.S.I.C.,Dept.,C.D.R.I., Lucknow.
The values obtained are given in table -2.

Magnetic susceptibility

Magnetic susceptibility of the complexes was determined by Gouy's method at the Dept. of Chemistry, University of Roorkee[35].The sample tube was calibrated with copper sulphate.The diamagnetic corrections were made.The values obtained are given in table -2.

UNDER PEER REVIEW

Table-1 Analytical and physical data of the ligands and the complexes

Compound	% of Metal (Found/Calcd.)	% of Hydrogen (Found/Calcd.)	% of Carbon (Found/Calcd.)	%of Nitrogen (Found/Calcd.)	%of Sulphur (Found/ Calcd.)	% of Chlorine (Found/Calcd.)
bis (5-chlorosalicylaldehyde) thiosemicarbazone oxotungsten(IV)chloride	38.15 (38.20)	3.67 (4.80)	20.22 (20.12)	9.54 (9.0)	12. 98 (12.2)	7.50 (7.61)
bis(terephthaldicarboxaldehyde) thiosemicarbazone oxotungsten(IV)chloride	28.50 (29.50)	3.09 (3.21)	39.50 (40.49)	9.80 (10.39)	8.50 (7.92)	8.51 (8.60)
bis (2,4- pentanedione) thiosemicarbazone oxotungsten(IV)chloride	42.10 (41.17)	3.06 (4.70)	27.01 (26.56)	11.01 (11.63)	9.02 (8.86)	7.13 (7.14)
bis (trifluoroacetylacetone) thiosemicarbazone oxotungsten(IV)chloride	30.21 (30.09)	2.67 (2.02)	22.01 (23.70)	11.01 (11.63)	9.02 (8.86)	7.00 (7.50)
bis (5- chlorosalicyldehyde) oxochromium (V)chloride	26.67 (25.90)	1.66 (2.70)	31.22 (30.19)	8.00 (7.99)	9.98 (10.0)	7.90 (7.81)
bis (terephthaldicarboxaldehyde) thiosemicarbazone oxochromium(V)chloride	17.57 (18.29)	2.55 (2.78)	56.50 (56.65)	12.33 (11.81)	8.80 (9.40)	7.00 (7.3)
bis (2,4- pentanedione) thiosemicarbazone oxochromium(V)chloride	20.55 (19.23)	3.98 (3.31)	40.0 (41.01)	12.00 (13.14)	9.50 (10.0)	9.33 (9.6)
bis (trifluoroacetylacetone) thiosemicarbazone oxochromium(V)chloride	39.04 35.90	1.93 (2.21)	43.09 (40.82)	8.00 (8.40)	6.00 (6.0)	7.00 (7.10)

Table-2 Analytical and physical data of the ligands and the complexes

Compound Colour	Molar inductance ($\Omega^{-1}cm^2$ mol^{-2})		M=O/M-Cl	υ (C=S) cm^{-1} L-M shift	Magnetic Moment (B.M.)	M.P (°C) L/C	υ(C=N) cm^{-1} L-M shift
	DMF	Me OH					
$[(CSALTSC)_2WOCl4]$ Dark brown	6.77	8.0	300/700	1800-1600	1.50	201/230	1625-1600
$[(TALDICTSC)_2WOCl4]$ Yellow	4.99	7.5	312/712	1500-1401	1.20	212/225	1630-1610
$[(PDIOTSC)_2$ $WOCl4]$ Brownish yellow	6.20	6.0	310/707	1500-1300	1.02	215/237	1500-1457
$[(TFAATSC)_2WOCl4]$ Dirty yellow	8.33	8.7	330/711	1615-1500	1.57	210/240	1525-1497
$[(CSALTSC)_2CrOCl]$ Yellowish brown	7.82	6.0	323/720	1500-1405	2.82	240/255	1515-1500
$[(TALDICTSC)$ $_2CrOCl]$ Brown	6.91	7.9	315/705	1628-1600	2.56	256/265	1600-1595
$[(PDIOTSC)$ $_2CrOCl]$ Yellowish pink	6.74	8.6	325/715	1630-1610	1.08	230/245	1650-1640
$[(TFAATSC))$ $_2CrOCl]$ Yellowish white	7.60	8.2	301/700	1576-1550	2.20	240/248	1590-1480

Table-3 Antibacterial screening at 2 µg disc (Zone formation in mm) MIC(µg ml^{-1})

Compound	*S. aureus(mm)*	*B.subtilis(mm)*
$[(CSALTSC)_2WOCl4]$ Dark brown	9.0	8.0
$[(TALDICTSC)_2WOCl4]$ Yellow	6.0	8.0
$[(PDIOTSC)_2 WOCl4]$ Brownish yellow	7.0	8.9
$[(TFAATSC)_2WOCl4]$ Dirty yellow	8.9	8.7
$[(CSALTSC)_2CrOCl]$ Yellowish brown	10.9	10.0
$[(TALDICTSC)_2CrOCl]$ Brown	10.7	11.3
$[(PDIOTSC)_2CrOCl]$ Yellowish pink	9.3	11.0
$[(TFAATSC))_2CrOCl]$ Yellowish white	9.6	10.0

Antimicrobial Screening

in vitro[40]antifungal activity[11,12,13] was evaluated by the radial growth method using agar disc method against various species using distilled water,glucose,starch and agar-agar adding a requisite amount of the compound after being dissolved in DMF so as to obtain certain final concentrations.

in-vitro[40] antibacterial study: A solution of all the complexes were prepared in DMSO[28] in such a manner that 20µL contained 40 µg of the sample.Filter paper discs were taken in a petri dish and the solution was applied on the disc with the help of a micro pipette.Thus disc containing 40 µg of sample was prepared.With the use of sterile forceps, the sample-impregnated disc were gently placed on solidified agar plates seeded with the organisms to guarantee contact with the media. For 24 hours, the plates were placed in a refrigerator set at 4°C so that the substances absorbed into the discs would have enough time to diffuse into the media.The plates were then incubated for 24 hours at 370°C. After a 24-hour incubation period, the complexes' antibacterial efficacy was assessed by measuring the zone of inhibition on a transparent scale in terms of millimeters.The results are shown in tables 3 (antibacterial) and 4 (fungicidal), respectively.

Table-4 Response of the test compound(1mg/ml) against fungi

Compound	*Rhizopus species* (conc.in ppm)			*Aspergillus species* (conc. in ppm)		
	200	100	50	200	100	50
$[(CSALTS)_2 WOCl4]$	60	56	45	65	78	46
$[(TALDICTSC)_2 WOCl4]$	67	55	40	66	65	42
$[(PDIOTSC)_2 WOCl4]$	65	50	45	75	58	45
$[(TFAATSC)_2WOCl4]$	85	49	44	80	67	43
$[(CSALTSC)_2CrOCl]$	71	58	46	71	70	35
$[(TALDICTSTSC)_2 CrOCl]$	88	56	41	80	55	41
$[(PDIOTSC)_2 CrOCl]$	60	63	43	77	49	42
$[(TFAA TSC)_2CrOCl]$	70	53	37	76	49	38

UNDER PEER REVIEW

Results and discussion

All the complexes formed were found to be soluble in ethanol and insoluble in water. The molar conductance of all complexes of oxotungsten and oxochromium are found to be of non conductive nature (4.9-8.6 $\Omega^{-1}cm^2$ mol) in DMF and MeOH indicating the non electrolytic nature of the complexes.

The oxotungsten (IV) chloride and oxochromium (V) chloride complexes show magnetic moment values in the range of 1.20-2.82 B.M. which corresponds to the diamagnetic nature of these complexes.

The electronic spectral bands [6,7] of the present oxotungsten (IV) complexes show similar absorption peaks. The spectral bands at 16060-12900 cm^{-1} indicated octahedral environment for these complexes. A moderately intense band observed in the region of 14000-14560 cm^{-1} has been assigned to unresolved band resulting from dxy→dyz, dxz($2B_2 \rightarrow 2E_1$) and the third band at 20600-26000 cm^{-1} may either be assigned to the transaction dxz→ dz_2 ($2B_2 \rightarrow 2A_1$) which emerge from the low energy charge transfer.

Thecomplexesweresubjectedtochemical analysis and results for the proposed complexes fall in the expected range of experimentally calculated values.

The IR spectra of the ligands indicated two bands i.e., n(C=N) n(C=S)[35],which on complexation, shifted to lower frequencies clearly indicated the coordination through nitrogen of (C=N) group and sulphur of (C=S) group [10].

The IR spectra of the complexes also exhibited more bands which may be due to (M=O)stretching at ~300 $cm^{-1}$and (M- Cl) at ~ 700cm^{-1}stretching(Table- 2.)

Pharmaceutical significance

Antibacterial[14,15] and antifungal [16,28] activities of the schiff bases and their metal complexes have been reported here.

Complexes have been evaluated for their antifungal activities against *rhizopus* and *aspergillus* species at various concentrations[28-34].The MIC values were listed in table-4.Antibacterial activities are observed (table-3) as zones in mm.S.*aureus* and *aspergillus* species showed prominent activity.Anticarcinogenic[17,18] antifungal, and antitubercular [19-20] properties of the complexes are well known.All the complexes were screened for antibacterial and antifungal activities as shown in tables 3 and 4, respectively.Schiff bases are known to be potent chelating agents[41-44] showing analgesic properties[5-8],antimicrobial[9-10],anticonvulsant[11] antitubercular[12], anticancer[13,14],antioxidant[15].and anti-inflammatory properties[36-40]

Conclusion

Schiff bases have been widely explored for their biological,medicinal and catalytic applications.Recently discovered compounds inthis category are gaining pharmaceutical importance.Schiff base complexes have promising antimicrobial properties. Further investigatory studies demand analyses of the SAR and mode of action in clinical applications.

References

1. View at: Publisher Site | Google Scholar

P. G. Avaji, C. H. Vinod Kumar, S. A. Patil, K. N. Shivananda, and C. Nagaraju, "Synthesis, spectral characterization, in-vitro microbiological evaluation and cytotoxic activities of novel macrocyclic bis hydrazone," European Journal of Medicinal Chemistry, vol. 44, no. 9, pp. 3552–3559, 2009.

2. Charu,and H.L.Saxena, International J.,IAPS,13,2009

3 Hodnett E.M, and Dunn WJ, J.Med. Chem.13: 768(10) (1970).

4. Syamal A, Ahmad S, &Gupta B K,Rev.Chim.Minor 20(2): 181-5 (1983).

A.B.P. Lever." Electronic Spectroscopy".2nd ed., Elsevier, Amsterdam, 1984:B.N Figgis." Comprehensive

5. K.Nakamoto."Infrared Spectra of Inorganic and Coordination compounds," Wiley, New Tork 1963.

6. R.Crickshank J.P Duguid B.P Mermion and R.H.A Swain,"Medical Microbiology", J.H Quested Gen Microbial...1966,45,14.

Patil S, Kulkarni A and Vasant H, Inorg, Chem.Acta 95: 195 (1984).

7. J.PSoovill.D.LKlayman and C.F Franhino .J. Med Chem...1982,25,1261.

8. R.Crickshank J.P Duguid B.P Mermion and R.H.A Swain,"Medical Microbiology", Churchill Livingstone, London and New York, 1975.2.190.

9. P.Courvalin-,Am. Chem.Soc. Microbiol.News,1992,85,368

10. C.J Ballhausen and A.B, Gray, *Inorg,, Chem,* 1962, 111,.Selbin J, Co-ord Chem. Rev.

11. Sun, Y.; Lu, Y.; Bian, M.; Yang, Z.; Ma, X.; Liu, W. Pt(II) and Au(III) complexes containing Schiff-base ligands: A promising source for antitumor treatment. Eur. J. Med. Chem., 2021, 211, 113098. http://dx.doi.org/10.1016/j.ejmech.2020.113098 PMID: 33348237

UNDER PEER REVIEW

12. Shiju, C.; Arish, D.; Bhuvanesh, N.; Kumaresan, S. Synthesis,
characterization, and biological evaluation of Schiff baseplatinum(II) complexes. Spectrochim. Acta A Mol. Biomol. Spec

13. View at: Google Scholar

B. S. Sathe, E. Jaychandran, V. A. Jagtap, and G. M. Sreenivasa, "Synthesis characterization and anti-inflammatory evaluation of new fluorobenzothiazole schiff's bases," International Journal of Pharmaceutical Research and Development, vol. 3, no. 3, pp. 164–169, 2011.

14. View at: Google Scholar

S. M. Sondhi, N. Singh, A. Kumar, O. Lozach, and L. Meijer, "Synthesis, anti-inflammatory, analgesic and kinase (CDK-1, CDK-5 and GSK-3) inhibition activity evaluation of benzimidazole/benzoxazole derivatives and some Schiff's bases," Bioorganic and Medicinal Chemistry, vol. 14, no. 11, pp. 3758–3765, 2006.

15. View at: Publisher Site | Google Scholar

A. Pandey, D. Dewangan, S. Verma, A. Mishra, and R. D. Dubey, "Synthesis of schiff bases of 2-amino-5-aryl-1,3,4-thiadiazole and its analgesic, anti-inflammatory, anti-bacterial and anti-tubercular activity," International Journal of ChemTech Research, vol. 3, no. 1, pp. 178–184, 2011.

16. View at: Google Scholar

C. Chandramouli, M. R. Shivanand, T. B. Nayanbhai, B. Bheemachari, and R. H. Udupi, "Synthesis and biological screening of certain new triazole schiff bases and their derivatives bearing substituted benzothiazole moiety," Journal of Chemical and Pharmaceutical Research, vol. 4, no. 2, pp. 1151–1159, 2012.

17. View at: Google Scholar

R. P. Chinnasamy, R. Sundararajan, and S. Govindaraj, "Synthesis, characterization, and analgesic activity of novel schiff base of isatin derivatives," Journal of Advanced Pharmaceutical Technology and Research, vol. 1, no. 3, pp. 342–347, 2010.

18. View at: Publisher Site | Google Scholar

K. Mounika, B. Anupama, J. Pragathi, and C. Gyanakumari, "Synthesis, characterization and biological activity of a Schiff base derived from 3-ethoxy salicylaldehyde and 2-amino benzoic acid and its transition metal complexes," Journal of Scientific Research, vol. 2, no. 3, pp. 513–524, 2010.

19. View at: Google Scholar

P. Venkatesh, "Synthesis, characterization and antimicrobial activity of various schiff bases complexes of Zn(II) and Cu(II) ions," Asian Journal of Pharmaceutical and Health Sciences, vol. 1, no. 1, pp. 8–11, 2011.

20. View at: Google Scholar

T. Aboul-Fadl, F. A. Mohammed, and E. A. Hassan, "Synthesis, antitubercular activity and pharmacokinetic studies of some Schiff bases derived from 1- alkylisatin and isonicotinic acid hydrazide (INH)," Archives of Pharmacal Research, vol. 26, no. 10, pp. 778–784, 2003.

21. View at: Google Scholar

R. Miri, N. Razzaghi-asl, and M. K. Mohammadi, "QM study and conformational analysis of an isatin Schiff base as a potential cytotoxic agent," Journal of Molecular Modeling, vol. 19, no. 2, pp. 727–735, 2013.

22. View at: Publisher Site | Google Scholar

S. M. M. Ali, M. Abul Kalam Azad, M. Jesmin et al., "In vivo anticancer activity of Vanillin semicarbazone," Asian Pacific Journal of Tropical Biomedicine, vol. 2, no. 6, pp. 438–442, 2012.

23. View at: Google Scholar

D. Wei, N. Li, G. Lu, and K. Yao, "Synthesis, catalytic and biological activity of novel dinuclear copper complex with Schiff base," Science in China B, vol. 49, no. 3, pp. 225–229, 2006.

24. View at: Publisher Site | Google Scholar

K. N. Venugopala and B. S. Jayashree, "Synthesis of carboxamides of 2′-amino-4′-(6-bromo-3-coumarinyl) thiazole as analgesic and antiinflammatory agents," Indian Journal of Heterocyclic Chemistry, vol. 12, no. 4, pp. 307–310, 2003.

25. View at: Google Scholar

K. Vashi and H. B. Naik, "Synthesis of novel Schiff base and azetidinone derivatives and their antibacterial activity," European Journal of Chemistry, vol. 1, pp. 272–276, 2004.

26. View at: Publisher Site | Google Scholar

Z. H. Chohan, M. Praveen, and A. Ghaffar, "Structural and biological behaviour of Co(II), Cu(II) and Ni(II) metal complexes of some amino acid derived Schiff-bases," Metal-Based Drugs, vol. 4, no. 5, pp. 267–272, 1997.

27. View at: Google Scholar

F. Tisato, F. Refosco, and G. Bandoli, "Structural survey of technetium complexes," Coordination Chemistry Reviews, vol. 135-136, pp. 325–397, 1994.

28.View at: Google Scholar

A. Jarrahpour, D. Khalili, E. De Clercq, C. Salmi, and J. M. Brunel, "Synthesis, antibacterial, antifungal and antiviral activity evaluation of some new bis-Schiff bases of isatin and their derivatives," Molecules, vol. 12, no. 8, pp. 1720–1730, 2007.

29.View at: Publisher Site | Google Scholar

A. Bhattacharya, V. C. Purohit, and F. Rinaldi, "Environmentally friendly solvent-free processes: novel dual catalyst system in Henry reaction," Organic Process Research and Development, vol. 7, no. 3, pp. 254–258, 2003.

30. View at: Publisher Site | Google Scholar

C. R. Prakash and S. Raja, "Synthesis, characterization and in vitro antimicrobial activity of some novel 5-substituted Schiff and Mannich base of isatin derivatives," Journal of Saudi Chemical Society, 2011.

31. View at: Publisher Site | Google Scholar

N. B. Patel and J. C. Patel, "Synthesis and antimicrobial activity of Schiff bases and 2-azetidinones derived from quinazolin-4(3H)-one," Arabian Journal of Chemistry, vol. 4, no. 4, pp. 403–411, 2011.

32. View at: Publisher Site | Google Scholar

S. Malladi, A. M. Isloor, S. Isloor, and D. S. Akhila, "Synthesis, characterization and antibacterial activity of some new pyrazole based Schiff bases," Arabian Journal of Chemistry, vol. 6, no. 3, pp. 335–340, 2013.

33. View at: Publisher Site | Google Scholar

H. H. Essa, F. Kandil, and A. Falah, "Synthesis and identification of schiff bases and biological activity new study," Iraqi Journal of Science, vol. 53, no. 2, pp. 230–240, 2012.

34. View at: Google Scholar

V. A. Shelke, S. M. Jadhav, V. R. Patharkar, S. G. Shankarwar, A. S. Munde, and T. K. Chondhekar, "Synthesis, spectroscopic characterization and thermal studies of some rare earth metal complexes of unsymmetrical tetradentate Schiff base ligand," Arabian Journal of Chemistry, vol. 5, pp. 501–507, 2012.

35. Synthesis, Characterization and Antimicrobial Studies of Co(II) and Mn(II) complexeswith Thiosemicarbazones; IRJMETS, e- ISSN: 2582- 5208; Vol.02/Issue 12/ Dec.2020, IF -5.3

36. View at: Publisher Site | Google Scholar

K. V. Sashidhara, A. Kumar, G. Bhatia, M. M. Khan, A. K. Khanna, and J. K. Saxena, "Antidyslipidemic and antioxidative activities of 8-hydroxyquinoline derived

UNDER PEER REVIEW

novel keto-enamine Schiffs bases," European Journal of Medicinal Chemistry, vol. 44, no. 4, pp. 1813–1818, 2009.

37. View at: Publisher Site | Google Scholar

K. V. Sashidhara, J. N. Rosaiah, G. Bhatia, and J. K. Saxena, "Novel keto-enamine Schiffs bases from 7-hydroxy-4-methyl-2-oxo-2H-benzo[h] chromene-8,10-dicarbaldehyde as potential antidyslipidemic and antioxidant agents," European Journal of Medicinal Chemistry, vol. 43, no. 11, pp. 2592–2596, 2008.

38. View at: Publisher Site | Google Scholar

H. D. Revanasiddappa, K. S. Prasad, L. S. Kumar, and B. Jayalakshmi, "Synthesis and biological activity of new schiff bases containing 4(3H)-quinazolinone ring system," International Journal of ChemTech Research, vol. 2, no. 2, pp. 1344–1349, 2010.

39. View at: Google Scholar

A. Kundu, N. A. Shakil, D. B. Saxena, P. Pankaj, J. Kumar, and S. Walia, "Microwave assisted solvent-free synthesis and biological activities of novel imines (Schiff bases)," Journal of Environmental Science and Health B, vol. 44, no. 5, pp. 428–434, 2009.

40. View at: Publisher Site | Google Scholar

M. J. Hearn, M. H. Cynamon, M. F. Chen et al., "Preparation and antitubercular activities in vitro and in vivo of novel Schiff bases of isoniazid," European Journal of Medicinal Chemistry, vol. 44, no. 10, pp. 4169–4178, 2009.

Jin,R.;Cho,C.S.;Jiang,L.H.;Shim,S.C.

41. A. B. Thomas, R. K. Nanda, L. P. Kothapalli, and S. C. Hamane, "Synthesis and biological evaluation of Schiff's bases and 2-azetidinones of isonicotinyl hydrazone as potential antidepressant and nootropic agents," Arabian Journal of Chemistry, 2011.

42. View at: Publisher Site | Google Scholar

M. A. Bhat and M. A. Al-Omar, "Synthesis, characterization and in vivo anticonvulsant and neurotoxicity screening of Schiff bases of phthalimide," Acta Poloniae Pharmaceutica, vol. 68, no. 3, pp. 375–380, 2011.

43. View at: Google Scholar

A. A. Kulkarni, S. B. Wankhede, N. D. Dhawale, P. B. Yadav, V. V. Deore, and I. D. Gonjari, "Synthesis, characterization and biological behavior of some Schiff's and Mannich base derivatives of anticonvulsant drugs," Arabian Journal of Chemistry, http://dx.doi.org/10.1016/j.arabjc.2012.07.020.

44. View at: Google Scholar

M. M. Aly, Y. A. Mohamed, K. A. M. El-Bayouki, W. M. Basyouni, and S. Y. Abbas, "Synthesis of some new 4(3H)-quinazolinone-2-carboxaldehyde thiosemicarbazones and their metal complexes and a study on their anticonvulsant,analgesic,cytotoxic and antimicrobial activities e Part-1," European Journal of Medicinal Chemistry, vol. 45, no. 8, pp. 3365–3373, 2010.

45. Li QX, Tang HA, Li YZ, Wang M, Wang LF, Xia CG. Synthesis, characterization, and antibacterial activity of novel Mn (II), Co (II), Ni (II), Cu (II), and Zn (II) complexes with vitamin K3-thiosemicarbazone. Journal of inorganic biochemistry. 2000 Jan 30;78(2):167-74.

UNDER PEER REVIEW