CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
https://doi.org/10.5281/zenodo.7362000

Available online at: http://www.iajps.com *Review Article*

A VERSATILE HYDRAZONES SCHIFF BASE AND METAL COMPLEXES OF PHARMACOLOGICAL APPLICATION AND BIOLOGICAL ACTIVITIES: A REVIEW

Gajanan Dongare
Department of Chemistry,
Shri Shivaji Science and Arts College, Chikhli-443201
Affiliated to Sant Gadge Baba Amravati University, Amravati-444602.MS, India

Abstract:
The development of hydrazones Schiff base have been shown a wide variety of biological activities viz. antimicrobial, anticonvulsant, antidepressant, anti-inflammatory, analgesic, antiplatelet, antimalarial, anticancer, antifungal, antitubercular, antiviral, cardio protective etc., The hydrazones consist of azomethine (H-C=NH-) imines possess and deals with an important type of compounds for the new drug development. The researchers have been synthesized, and assay the microbial activities of hydrazones, hydrazone derivatives and its metal complexes. This review has targeted to explore the diversity of hydrazones in biological sciences.

Keyword- *Hydrazones, Schiff bases, metal complexes, biological activity.*

Corresponding author:
Gajanan Dongare,
Department of Chemistry,
Shri Shivaji Science and Arts College, Chikhli-443201
Affiliated to Sant Gadge Baba Amravati University,
Amravati-444602.MS, India
phone: +919422712054; email: infogmdongare@gmail.com

QR code

Please cite this article in press as ***Gajanan Dongare****,* ***A Versatile Hydrazones Schiff Base And Metal Complexes Of Pharmacological Application And Biological Activities: A Review****, Indo Am. J. Pharm. Sci, 2017; 4(04).*

INTRODUCTION:

Hydrazones related to aromatic aldehydes and ketones and belong to a class of organo compounds with the structure, R` C = NNH_2. These compounds displayed its biological and medicinal and pharmacological significance Viz.,s antimicrobial, anti-inflammatory, analgesic, antifungal, anti-tubercular, antiviral, anticancer, antiplatelet, antimalarial, anticonvulsant, cardio protective, antihelmintic, antiprotozoal, These compounds contain (>C = N-) bond, which contain a lone pair of electrons with the functional nitrogen atom[1-5]. The nitrogen atoms of acts as the nucleophile in hydrazone and the carbon atom has both electrophilic as well as nucleophilic character. The α-hydrogen of hydrazones is more potent than that of acidic ketones. The Schiff bases are of primary amines is condensation products from carbonyl compounds and reported by Schiff in 1864. The structural feature of compounds is the azomethine group with a general formula (R-HC=N-R) where R and R1 are alkyl, aryl, cyclo alkyl or heterocyclic groups which may be variously substituted. These compounds are also known as anils, imines or azomethine. The several studies have been showed that the presence of a lone pair of electrons in sp^2 hybridized orbital of N-atom in the azomethine group displaying the chemical and biological importance. The preparation, flexibility in donation, and the special property of >C=N group Schiff bases are generally excellent chelating agents especially when a functional group like –OH is present close to the azomethine group to form chelating ring with the metal ion [5-10].

The versatility of hydrazone ligands and biological, analytical applications of their complexes reflecting the investigations in this area which are highly desirable [10-11].Considering the importance associated with their biological, pharmacological and medicinal properties, for the synthesis of heterocyclic compounds are present herein.

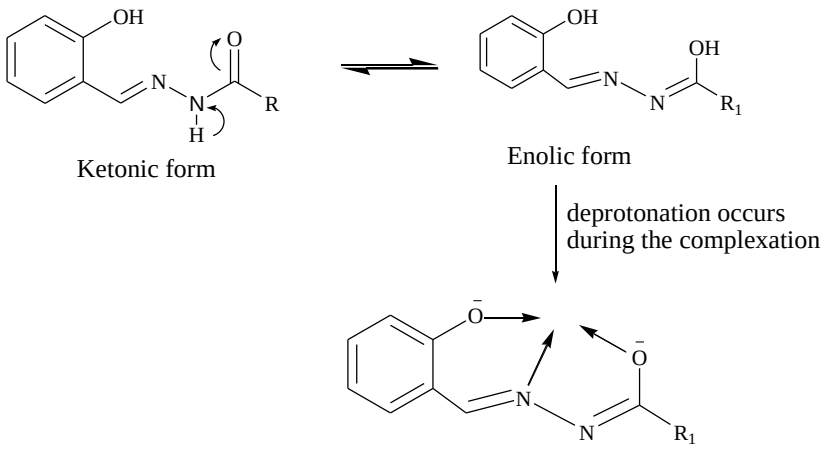


Fig.1 Tautomeric form of tridentate hydrazone

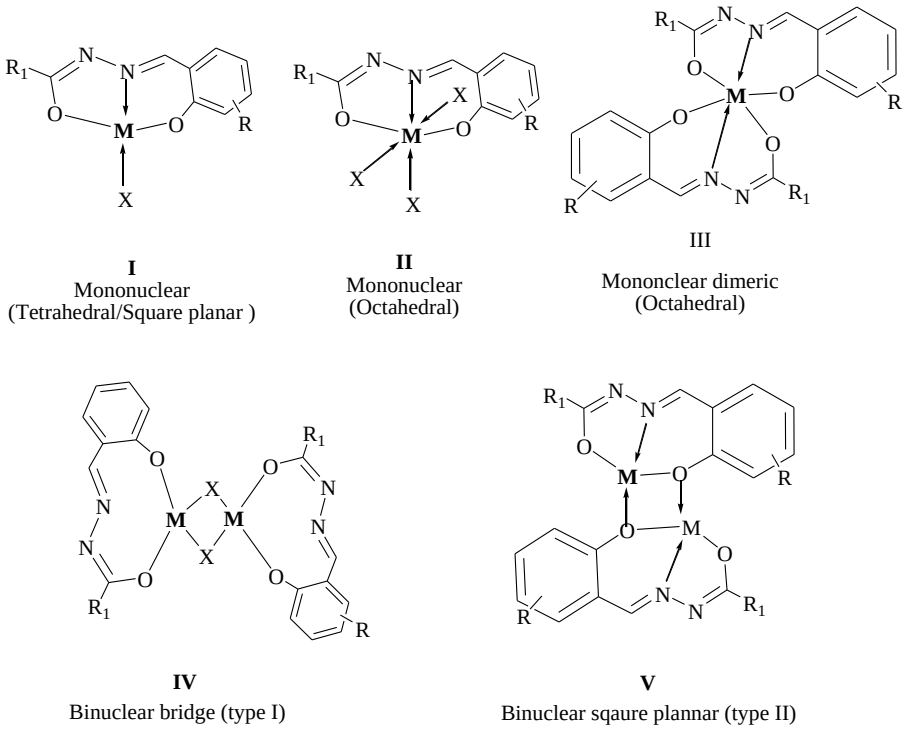
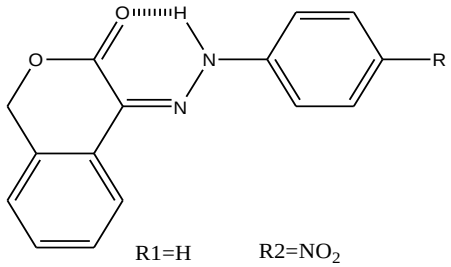


Fig.2 Types of coordination mode in aroyl tridentate hydrazones

The hydrazone ligands imparts their own functionality and can tune a unique properties of the overall in the complexation due to the structure and bonding. The hydrazone and their derivatives are highly important because of these ligands developed due to their diverse chelating ability, structural flexibility and pharmacological activities such as antimicrobial, anti-inflammatory, analgesic, antifungal, antiviral, anticancer and anti-tuberculosis. In addition to this, some transition metal complexes are important in catalysis, materials synthesis, photochemistry and biological systems [12-18]The medicinal inorganic chemistry can exploit the unique properties of metal ions for the designing of new hydrazone drugs. The hydrazone and their complexes were used in the medicinal purposes due to the metal-ligand interactions influence ligand exchange reactions. Hydrazone compounds was synthesized by coupling methods and now using in medical biotechnology to couple drugs to targeted antibodies e.g. antibodies against the certain type of cancer cell. The phenomenon in which hydrazone bond is stable at neutral pH in the blood stream, but is bond destroyed in the acidic condition of lysosomes of the cell. The drug is thereby released in the cell where it is exerts in its function [19-21].

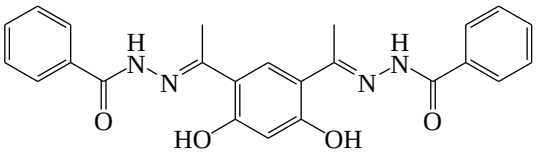
The Schiff base have been synthesized the photochromic compounds in which compounds was activated in the respective wavelengths with the thermal relaxation half-lives ($\tau_{1/2}$), which was essential optimization and modulation of the properties in various types of applications [22].



R1=H R2=NO_2

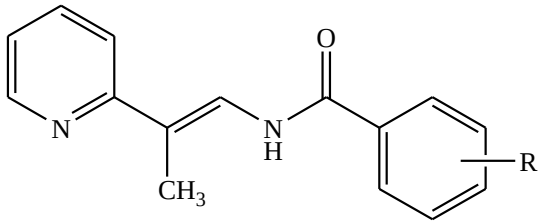
Fig.3

The deprotonation coordination in the present case increases the basic character of the nitrogen atom in the structure thus improving the emission [23].



BIOLOGICAL ACTIVITY:

Hydrazone and its derivatives was very important class of ligands because of their physiological activity, coordinative capability and applications in analytical and medicinal chemistry [24].



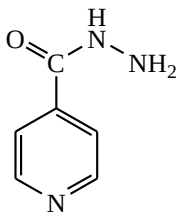
Acetyl pyradine benzoyl hydrazone

The Schiff bases have also been developed as chemical sensors extensively in environmental monitoring and clinical analysis during the past two decades and liquid membrane transport of metal ions [25-29].The coordinating ability of hydrazide based Schiff bases are attractive as they can coordinate to the metal ions while acting as bidentate, tridentate or tetradentate depending upon their coordinating functionalities like NO, ONO, N_2O_4 etc. The ternary metal complexes of hydrazone with Cr(III), Fe(III) and La(III) ions was reported for their significant antimicrobial activity when tested against specific microbes [117-119].Their strong coordinating properties of Schiff based towards 3d transition metals have been stimulated research in recent years as resulting complexes further enhance most of the pharmacological properties and enzymatic inhibitors[30-34].

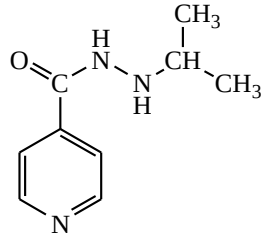
Hydrazones containing an azomethine (-CH=N<) have been demonstrated significant role in the field of medicinal chemistry therapeutic applications such Alzheimer disease (AD) common neurodegenerative disorder of the central nervous system (AD) is associated with memory loss, difficulties in thinking, problem-solving, speaking or language and many other cognitive disorders. The therapies are only effective transiently in the early stage of disease. In search of new therapeutic agents 1,4-oxazepine analogues have been patented as anti-*β*-secretases inhibitors [35-37]

Antidepressant activities:

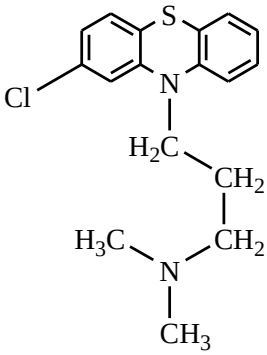
The modern treatment of mental depression have been started with the availability of monoamine oxidase (MAO) inhibitors and tricyclic antidepressants. These drugs was contributed to the early development of psychopharmacology to improve the anti-tuberculous action of the hydrazine derivative of isoniazid and later to the synthesis of iproniazide (V-VIII). The first modern antidepressant introduced was based on three unexpected actions of the drug i.e. monoamine oxidase (MAO), reversal of reserpine-induced sedation, and the presence of psychostimulation as a clinical side effect in man [38-40].



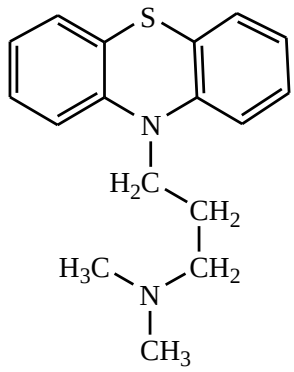
Isonicotinohydrazide
(Isonizid)
(a)



N'-isopropylisonicotinohydrazide
(Iproniazid)
(b)



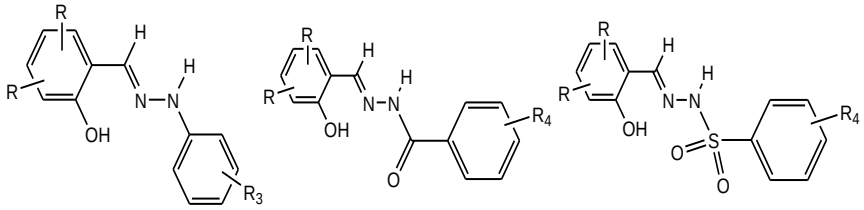
chloropromazine
(A)



Imipramine
(B)

BIOLOGICAL ACTIVITIES EVALUATION

The salicylaldehydes hydrazones and hydrazides was shown as potent inhibitors of fungal growth with low cell toxicity in mammalian proposed for future the therapeutic uses.



I II III

The Schiff bases especially hydrazide-fydrazone and their metal complexes (II,III) have been reported synthesis, spectral and thermal characterization derived from the novel Schiff bases and studied for their thermal, electrochemical, antimicrobial features, and their effect as catalysts in the oxidation reactions of cyclohexene and styrene. The result of biological activity was revealed that both ligands and their complexes are effective as being antimicrobial and antifungal [41-46].

CONCLUSION:

The hydrazone Schiff bases are one of the most versatile organo compounds having a common integral feature of a variety of medicinal candidates. This review inferred the contribution of Schiff bases to synthesis design, and progress of new lead for the potential biological activities with minimum of side effects. This bioactive pharmacore has also promoting to the researchers in receiving the most suggestive and conclusive assay in the field Schiff bases chemistry in concern of medicinal importance from three decades. The present paper is an attempt to review mostly the biological activities and medicinal significance reported in the current literature with recent research literature survey's.

Acknowledgements

The author are thankful to SGB Amravati University, authorities for providing necessary research facilities and literatures facilities.

Disclosure statement

Declaration of Competing Interest- The author declares that this our original work and we don't have any conflict of interest towards its publication.

REFERENCES:

[1]. D. N. Dhar and C. L. Taploo, "Schiff bases and their applications," Journal of Scientific and Industrial Research, vol. 41, no. 8, pp. 501–506, 1982.

[2]. 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.
[3]. Rao S, Mishra DD, Mourya RV, Nageswara N. Polyhedron. 1997; 16:1825-1829. 8. Singh M, Raghav N. Inter. J Pharm. Pharm. Sci. 2011; 3:26-32.
[4]. 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.
[5]. 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 antitubercular activity," International Journal of ChemTech Research, vol. 3, no. 1, pp. 178–184, 2011.
[6]. 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.
[7]. 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.
[8]. Nasr, T.; Bondock, S.; Youns, M. Anticancer activity of new coumarin substituted hydrazide–hydrazone derivatives. Eur. J. Med. Chem. 2014, 76, 539–548.
[9]. Pavan, F.R.; Maia, P.I.S.; Leite, S.R.A.; Deflon, V.M.; Batista, A.A.; Sato, D.N.; Franzblau, S.G.; Leite, C.Q.F. Thiosemicarbazones, semicarbazones, dithiocarbazates and hydrazide/hydrazones: Anti–Mycobacterium tuberculosis activity and cytotoxicity. Eur. J. Med. Chem. 2010, 45, 1898–1905.
[10]. Z.Q. Liu, Y. M. Ng, P. J. Tiong, R. A. Abu Talip, N. Jasin, V. Y. M. Jong and M. G. Tay, Int. J. Inorg. Chem., 2017, 7520640, 1-9.
[11]. H. S. Seleem, Chem. Cent. J., 2011, 5, 1–8.
[12]. W. R. Algar, D. E. Prasuhn, M. H. Stewart, T. L. Jennings, J. B. Blanco-Canosa, P. E. Dawson and I. L. Medintz, Bioconjug. Chem., 2011, 22, 825–858.
[13]. A. Ramakrishnan, S. S. Chourasiya and P. V. Bharatam, RSC Adv., 2015, 5, 55938–55947.
[14]. N. H. Al-Sha'alan, Molecules, 2007, 12, 1080–1091.
[15]. S. Rodríguez-Hermida, A. B. Lago, R. Carballo, O. Fabelo and E. M. Vázquez-Lõpez, Chem. - A Eur. J., 2015, 21, 6605–6616.
[16]. P. C. Sharma, A. Sinhmar, A. Sharma, H. Rajak and D. P. Pathak, J. Enzyme Inhib. Med. Chem., 2012, 28, 240–266.
[17]. S. M. Mamba, A. K. Mishra, B. B. Mamba, P. B. Njobeh, M. F. Dutton and E. Fosso-Kankeu, Spectro. Acta - Part A: Mole. and Biomol. Spectro., 2010, 77, 579–587.
[18]. N. M. A. Alaghaz, H. A. Bayoumi, Y. A. Ammar and S. A. Aldhlmani, J. Mol. Struct., 2013, 1035, 383–399.
[19]. B. Barta Holló, J. Magyari, S. Armaković, G. A. Bogdanović, M. V. Rodić, S. J. Armaković, J. Molnár, G. Spengler, V. M. Leovac and K. Meszaros Szecsenyi, New J. Chem., 2016, 40, 5885–5895.
[20]. S. Bal and S. S. Bal, Adv. Chem., 2014, 506851, 1–12.
[21]. E. L. Chang, C. Simmers and D. A. Knight, Pharmaceuticals, 2010, 3, 1711–1728.
[22]. D. A. Xavier and N. Srividhya, IOSR J. Appl. Chem., 2014, 7, 1–15.
[23]. W. Qin, S. Long, M. Panunzio and S. Biondi, Molecules, 2013, 18, 12264–12289.
[24]. A. A. El-Asmy, A. Z. Al-Abdeen, W. M. A. El-Maaty and M. M. Mostafa, *Spectrochim. Acta - Part A Mol. Biomol. Spectrosc.*, 2010, **75**, 1516–1522.
[25]. A. Kajal, S. Bala, N. Sharma, S. Kamboj and V. Saini, *Int. J. Med. Chem.*,2014, 761030, 1–11.
[26]. S. S. Tajudeen and G. Kannappan, *Indian J. Adv. Chem. Sci.*, 2016, 4, 40–48.
[27]. K. Kashinath, V. Durg and S. D. Angadi, *Int. J. Res. Pharm. Chem.*, 2014, 4, 557–563.
[28]. G. Verma, A. Marella, M. Shaquiquzzaman, M. Akhtar, M. R. Ali and M. M. Alam, *J. Pharm. Bioallied Sci.*, 2014, 6, 69–80.
[29]. J. Patole, U.Sandbhor, S. Padhye, D. N. Deobagkar, C. E. Anson and A. Powell, *Bioorganic Med. Chem. Lett.*, 2003,13,51–55.
[30]. G. Verma, A. Marella, M. Shaquiquzzaman, M. Akhtar, M. R. Ali and M. M. Alam, *J. Pharm. Bioallied Sci.*, 2014, 6, 69–80.
[31]. M. Albu, V. David and F. Tache, *J.Liq.Chrom. and Related Techn*. 2009, 32, 2569-2583.
[32]. M. Cacic, M. Trkovnik, F. Cacic and E. Has-Schon, *Molecules*, 2006, 11, 134–147.
[33]. M. Alias, H. Kassum and C. Shakir, J. Assoc. Arab Univ. *Basic Appl. Sci*., 2014, 15, 28–34.

[34]. J. Ferraro, *Low Frequency vibration of Inorganic and coordination compound*, I[st] ed., Plenum press, New York,1[st] ed., 1971.
[35]. J. Fujita, K. Nakamoto and M. Kobayashi, *J. Am. Chem. Soc*., 1956, 78, 3963–3965.
[36]. J. Singh and A.Singh, *J. Spectrosc*.,2013, 92318, 1-8.
[37]. O.O. Kehinde, A.A. Joseph, C.O. Ehi-Eromosele, O.T. Siyanbda, A.Kayode, M.A. Mesubi and T. Narender, *J. App. Sci*.,10,2015, 1210-1222.
[38]. M. A. Neelakantan, S. S. Marriappan, J. Dharmaraja, T. Jeyakumar and K. Muthukumaran, *Spectrochim. Acta - Part A Mol. Biomol. Spectrosc*., 2008, 71, 628-635.
[39]. O. A. El-Gammal, G. Abu El-Reash and S. F. Ahmed, Spectrochim. Acta - Part A Mol. Biomol. Spectrosc., 2015, 135, 227–240.
[40]. S. A. Sadeek, M. S. El-attar and S. M. A. El-hamid, *Int. J. Adv. Res.*, 2014, 2, 90–107.
[41]. H. H. Monfared, O. Pouralimardan and C. Janiak, *Chem. Sci.*, 2007, 62, 717–720.
[42]. G. G. Mohamed, M. M. Omar and A. M. Hindy, *Turkish J. Chem.*, 2006, 30, 361 382.
[43]. B. K. Singh, U. K. Jetley, R. K. Sharma and B. S. Garg, *Spectrochim. Acta - PartA Mol. Biomol. Spectrosc.*, 2007, 68, 63–73.
[44]. L. Taghizadeh, M. Montazerozohori, A. Masoudiasl, S. Joohari and J. M. White, *Mater. Sci. Eng. C*, 2017, 77, 229–244.
[45]. G. L. Backes, D. M. Neumann and B. S. Jursic, *Bioorg. and Med.Chem.*, 2014, 22, 4629–4636.
[46]. B. Yadagiri, U. D. Holagunda, R. Bantu, L. Nagarapu, V. Guguloth, S. Polepally and N. Jain, *Bioo.and Med.Chem.Lett.*, 2014, 24, 5041–5044.