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Review Article

REVIEW OF BIOLOGICAL ACTIVITIES OF HYDRAZONES

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ABSTRACT

Hydrazones possess an azomethine –NHN=CH group and are considered as derivatives of aldehydes and ketones in which the oxygen atom has been replaced by the NNH_2 functional group. These are widely studied molecules owing to their ease of preparation and diverse pharmacological potential. This has led researchers to synthesize different heterocyclic compounds bearing hydrazones. Medicinal chemists across the world have done immense work on hydrazones and developed agents with better activity and low toxicity profiles. Following different synthetic protocols and through proper SAR studies differently substituted hydrazones have been developed and found to be active against different pharmcological targets. They are known to possess different biological activities viz. antimicrobial, anti-inflammatory, anticancer, antimalarial etc. These observations have been guiding for the development of new hydrazones that possess varied biological activities. The review aims at highlighting the diverse biological activities of hydrazones.

Key words: Azomethine, Hydrazones, Pharmacological Potential

INTRODUCTION

Hydrazones are a class of organic compounds which possess the structure $R_1R_2C=NNH_2$. They are related to ketone and aldehyde in which oxygen has been replaced with NNH_2 group. These azometine -NHN=CH- proton constitute an important class of compounds for new drug development. Hydrazones are formed by the reaction of hydrazine or hydrazide with aldehydes and ketones. They act as reactants in various important reactions such as hydrazone iodination, Shapiro reaction and Bamford-Stevans reaction to form vinyl compounds. They act as intermediate in Wolff-Kishner reaction. Hydrazones can also be synthesized by the Japp-Klingemann reaction (from β-ketoacids or β-ketoester's and aryldiazonium salts). The N,N'-dialkyl type of hydrazones can be hydrolysed, reduced and oxidized this leads to the formation of amines by reduction of N-N bond. The C=N double bond in hydrazones are important compounds in drug design as they act as ligands for metal complexes, organocatalysis and synthesis of organic compounds.

The C=N bond of hydrazone and terminal nitrogen atom containing a lone pair of electron is responsible for the physical and chemical properties. The C-atom in hydrazone has both electrophilic and nucleophilic character and both the N-atoms are nucleophilic although the amino type nitrogen is more reactive. Due to these properties hydrazones are widely used in organic synthesis. The chemical structure of hydrazone derivatives were showed in figure 1-4.

BIOLOGICAL ACTIVITY

Antimicrobial activity

The overuse of chemicals against various infectious diseases has led to rapid emergence of resistivity against different bacteria. Therefore, the search for antimicrobials is a never ending task. Consequently, there has been an immense research on hydrazones as antibacterial agents. Sharma *et al.* (2011) reported the antibacterial activity of hydrazine derivatives (**1**) against various bacterial strains. Hydrazine derivatives (**2, 3**) synthesized by Jubie *et al.* (2010) are promising antibacterial agents. Ozkay *et al.* (2010) synthesized novel benzimidazole derivatives bearing hydrazone

moiety (**4**) and evaluated their antibacterial activity against different bacterial strains. Novel chloropyrrole derivatives of aroylhydrazone (**5**) developed by Rane *et al.* (2010) have been evaluated for antibacterial activity against different bacterial strains. Edress *et al. (2010)* synthesized some hydrazonoyl substituted pyrimidinones (**6, 7**) and evaluated their antibacterial activity. Govindasami *et al.* (2011) synthesized vanillin based hydrazine derivatives (**8, 9**) and reported their antibacterial activity specifically against *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Ajani *et al.* (2010) have reported the antibacterial activity of 2-quinoxalinone-3-hydazine derivative (**12**) against different bacterial strains. Lee *et al.* (2012) synthesized various hydrazones (**13, 14**) as selective inhibitors of *Staphylococcus aureus* β-ketoacyl carrier proteinsynthase III. The compound was found to have an MIC of 1-2μg/mL. Aryloxyacetic acid hydrazide (**15**) having promising antibacterial activity with MIC of 4.1-16.5μg/mL against an array of bacterial strains has been reported by Wahab *et al. (*2012). Rasras *et al.* (2010) synthesized various cholic acid based hydrazones (**22**) and screened them as antibacterials. The best compound among the series is reported to have MIC of 2μg/mL and 3.9μg/mL against *Escherichia faecalis* and *Escherichia coli*. Anthraquinone based hydrazones (**23**) synthesized by Gouda *et al.* (2010) are reported to have promising bacteriostatic activity against *P. auriginosa*. Kumar *et al.* (2010) synthesized various benzyledine-hydrazides (**24**) and reported their bactericidal activity against *S. aureus*. The agent is reported to have a MIC of 1.5μM/mL. Abdel-Wahab *et al.* (2011) synthesized different hydrazone bearing imidazoles (**25**). The synthesized compounds were screened for their antibacterial activity against numerous bacterial strains. Vijesh *et al.* (2010) synthesized 2,4- disubstituted thiazoles (**26**). The compound has a MIC value ranging between 1.6μg/mL and 3.1μg/mL when tested against different strains.

Tuberculosis is a chronic infection caused by different strains of *Mycobacterium tuberculosis*. The bacterium affects almost any organ but the favorite site is lung. The activity of the newer agents is mostly tested against virulent H37Rv strain. Few hydrazone derivatives (**27**) synthesized by Raja *et al.* (2010) have been screened and reported to have MIC of 6.3μg/mL. 4-hydroxy-8-trifluromethyl-quinoline derivatives (**31**) with a MIC of 0.625μg/mL have been reported by Thomas *et al.* (2011). Vavrikova *et al.* (2011) synthesized fluorine-containing hydrazones (**32**) with a MIC of 0.5μg/mL and a selectivity index of 1268.6 Pavan *et al.* (2010) synthesized some hydrazines (**35**) with promising results. Ferrocenyl hydrazones (**38, 39**) with a MIC of 0.75 and 0.7μmol/L have been reported by Maguene *et al.* (2011) Mahajan *et al.* (2011) synthesized ferrocene-based hydrazone derivatives (**43**) with significant potential. Eswaran *et al.* (2010) synthesized hydrazones (**44**) with a MIC of 6.25μg/mL. Jordao *et al.* (2011) synthesized hydrazone derivatives (**45**) with antitubercular activity. The compound is reported to have MIC of 2.5μg/mL. Fungal species are known to cause many superficial and systemic infections in humans, plants as-well-as livestock. Hydrazone derivatives (**49**) synthesized by Ozdemir *et al.* (2010) after being screened against different *Candida spp* have been reported to have promising antifungal potential.

Viruses are obligate parasites which require cellular machinery of the host to prosper. They are capable of causing immense harm to host. Hydrazone derivatives (**53, 54**) synthesized by Jin *et al.* (2010) have been reported to have EC_{50} value of 0.6 and 0.4μM respectively against HIV1-CA.

Analgesic and Anti-inflammatory activity

Much work has been done describing the analgesic and anti-inflammatory potential of hydrazides. Harnandez *et al.* (2012) reported analgesic and anti-inflammatory activity of furoxanyl-N-acylhydrazones (**55, 56**). Rajitha *et al.* (2011) evaluated the anti-inflammatory activity of some aryl hydrazones (**58**) and got good results. Moldovan *et al.* (2011) synthesized various hydrazone derivatives (**60**) and reported them to have promising *in-vivo* anti-inflammatory activity. El-Sayed *et al.* (2011) synthesized hydrazone derivatives (**62**) with selective COX-2 inhibition. The compound is reported to have an ED_{50} value of 0.2 mmol/Kg.

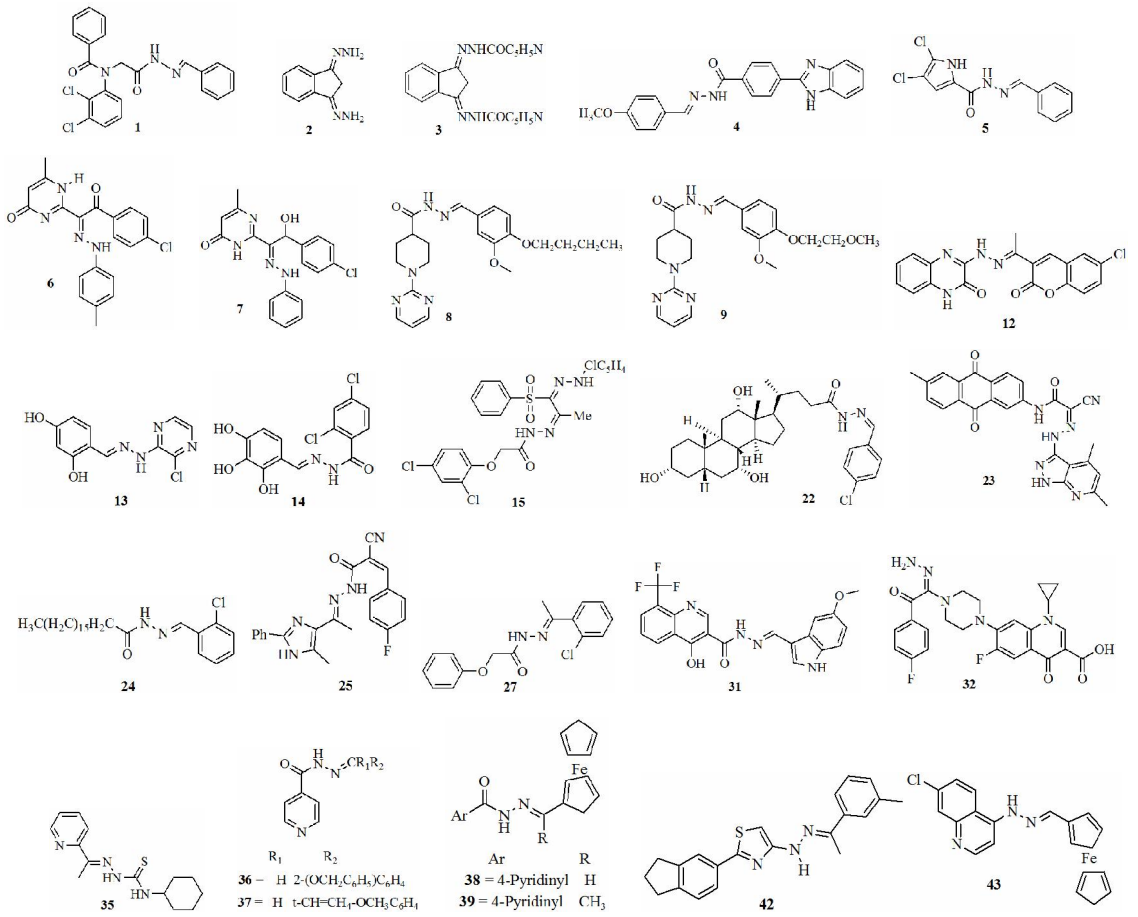

Figure 1. Chemical structure of hydrazone derivatives no.1-42

Benzo-thiophene derivatives (**66**) with inhibition of 50.2% have been developed by Isloor *et al.* (2010).

Anticancer activity

Cancer is a lethal group of diseases with a high level of penetrating potency affecting almost every organ of the body. Al-Said *et al.* (2011) synthesized compounds (**67**) active against human breast cancer cell lines MCF7. Hassan *et al.* (2011) synthesized pyrazole based hydrazone derivatives (**69**) with potential to treat breast carcinoma. Kendall *et al.* (2012) evaluated some derivatives (**70**) as PI3K p110α inhibitors. P13K are signaling proteins in different cell types responsible for phosphorylation of lipids in cell membranes. Kumar *et al.* (2012) synthesized various bis(indolyl) based hydrazones (**72, 73**) active against multiple cancer cell lines. Effenberger *et al.* (2010) reported a hydrazone derivative (**75**) with potent activity against HL-60 leukaemia and 518A2 melanoma. Acylhydrazones (**79**) by Cui *et al.* (2010) have been reported to have potent activity against the human promyelocytic leukemic cells (Hl-60). Copper based hydrazone derivatives (**82**) are reported to act against integrin β4 in H322 lung carcinoma cell lines by Fan *et al.* (2010). Palladium based hydrazones (**86**) by Abu-Surrah *et al.* (2010) have been reported to be active against human head and neck squamous carcinoma cell lines SQ20B and SCC-25. 2-phenylindole based hydrazone (**87**) synthesized by El-Nakkady *et al.* (2012) have been developed against breast carcinoma cell lines and reported to have an IC_{50} of 1.60nM.

Central Nervous System Activity

Hydrazones are reported to have activity against various illnesses' of central nervous system. Hydrazones (**88**) synthesized by

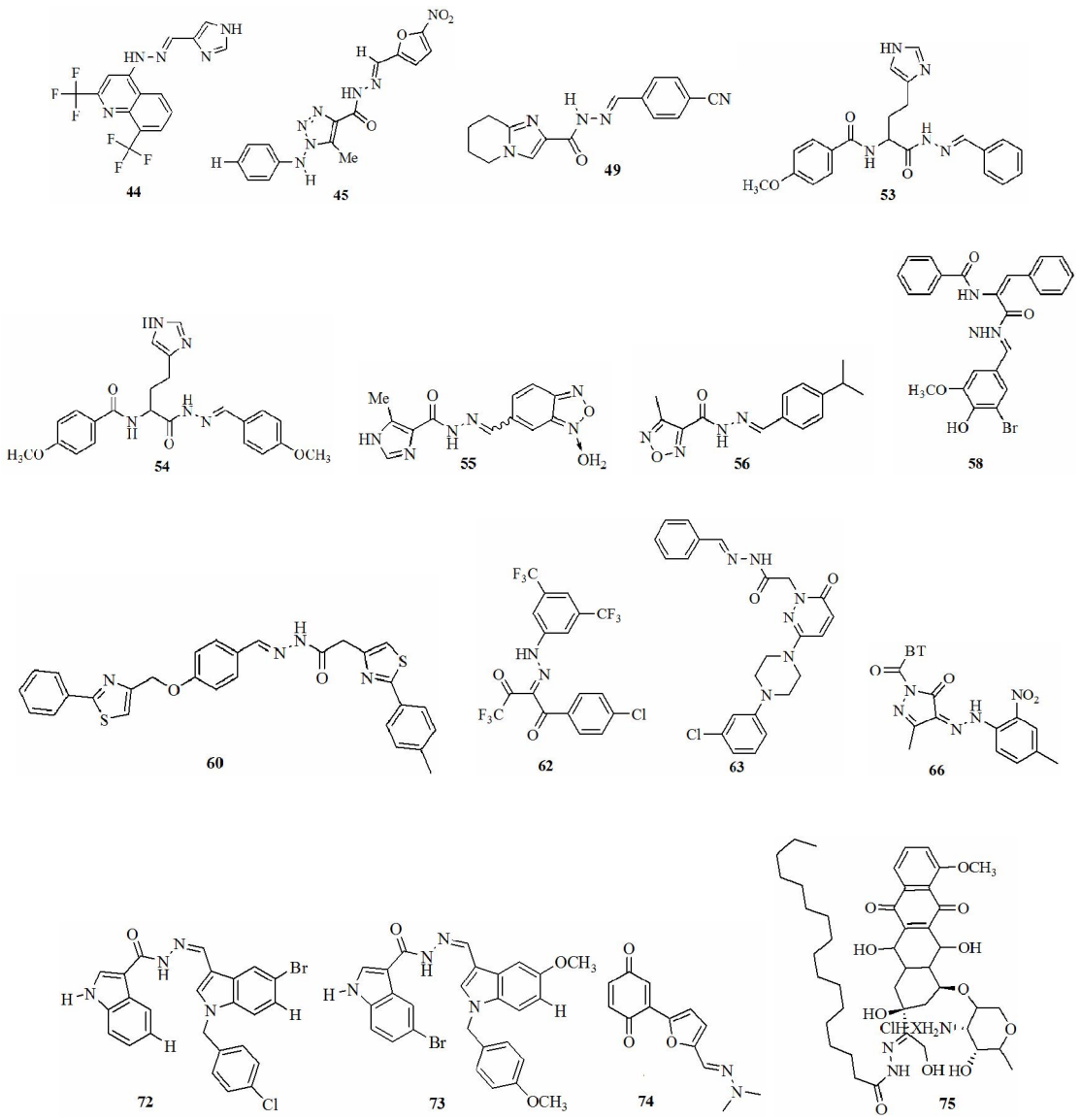

Figure 2. Chemical structure of hydrazone derivatives no.44-75

Gage *et al.* (2011) have been evaluated for inhibition of PDE10A- a phosphodiesterase responsible for neurological and psychological disorder such as Parkinson's, Schizophrenia and Huntington's disease. Kaushik *et al.* (2010) reported the anticonvulsant potential of some hydrazone derivatives (**91, 92**) having long duration of action and a rapid onset of action.

Antidepressant activity of hydrazones (**93**) has been reported by *de Oliveira et al.* (2011). Catto *et al.* (2010) reported the in-*vitro* β-amyloid aggregation inhibition of hydrazone derivatives (**96**) with an IC_{50} of 23μM.

Antiprotozoal activity

Protozoal diseases are highly prevalent in tropical countries affecting human and animal populations' and causing suffering and death. Caputto *et al.* (2011) reported the inhibitory activity of hydrazones (**98, 99**) against cruzipen- a major cysteine protease of *T.cruzi*. Hayat *et al.* (2010) reported the *in-vitro* antiamoebic activity of hydrazones (**102, 103**) against the HM1:IMSS strain of *Entamoeba histolytica*. The compounds are reported to have IC_{50} value of 0.03 and 0.04μM respectively. Vaio *et al.* (2009) synthesized hydrazone derivatives (**106, 107**) and described

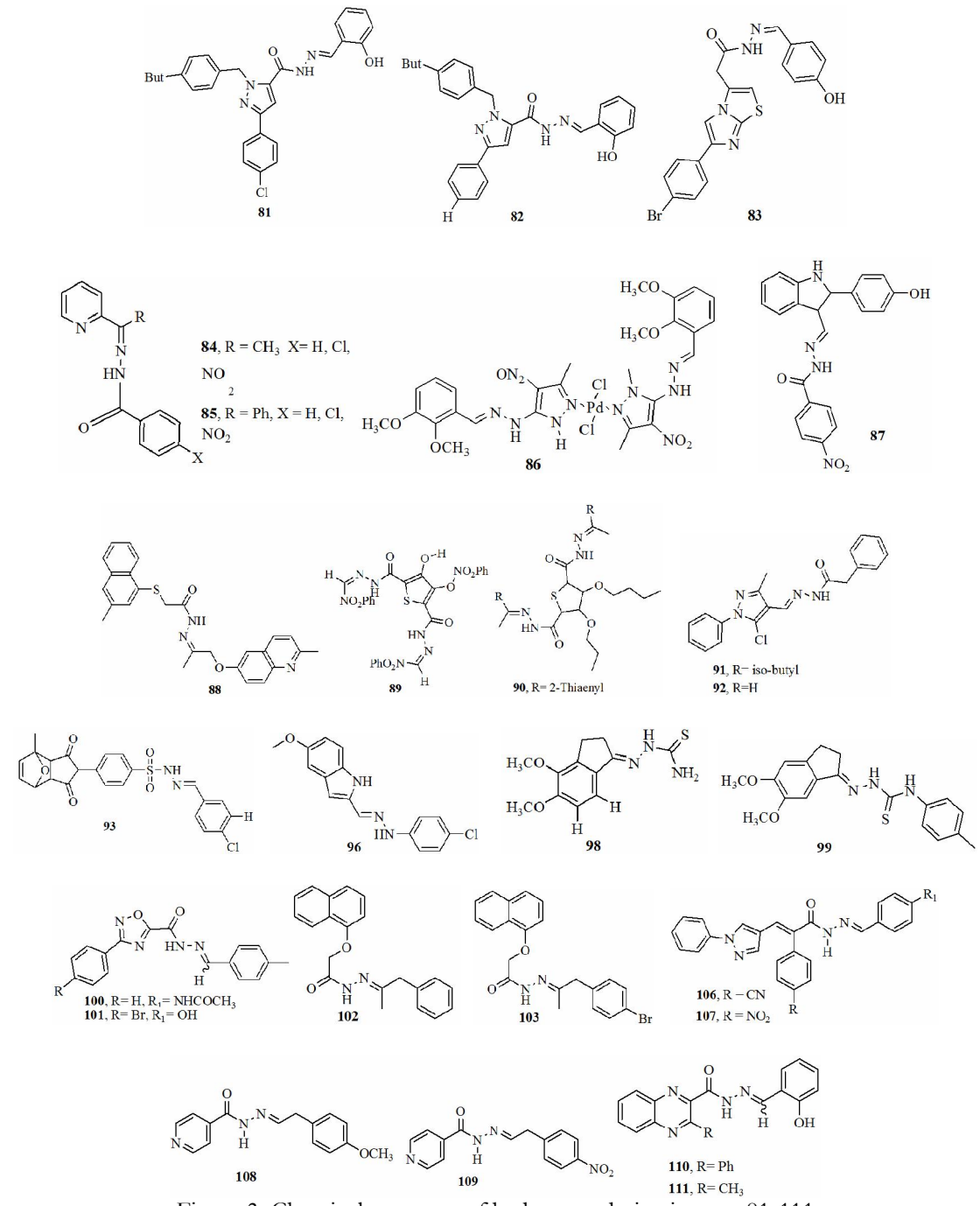

Figure 3. Chemical structure of hydrazone derivatives no.81-111

them to be of high utility in Chagas disease. Siddiqui *et al.* (2012) described the antiamoebic activity of hydrazone derivatives (**108, 109**). Romeiro *et al.* (2009) developed hydrazone derivatives (**110, 111**) as cruzin inhibitors. Aponte *et al.* (2010) evaluated the anti-trypanosomal activity of hydrazone derivatives (**112**).

Miscellaneous activity

In addition to the mentioned activities hydrazines are also reported to have other activities, as mentioned below:

Antioxidant activity

Oxidation reactions are crucial for sustenance of life but they can also be damaging.

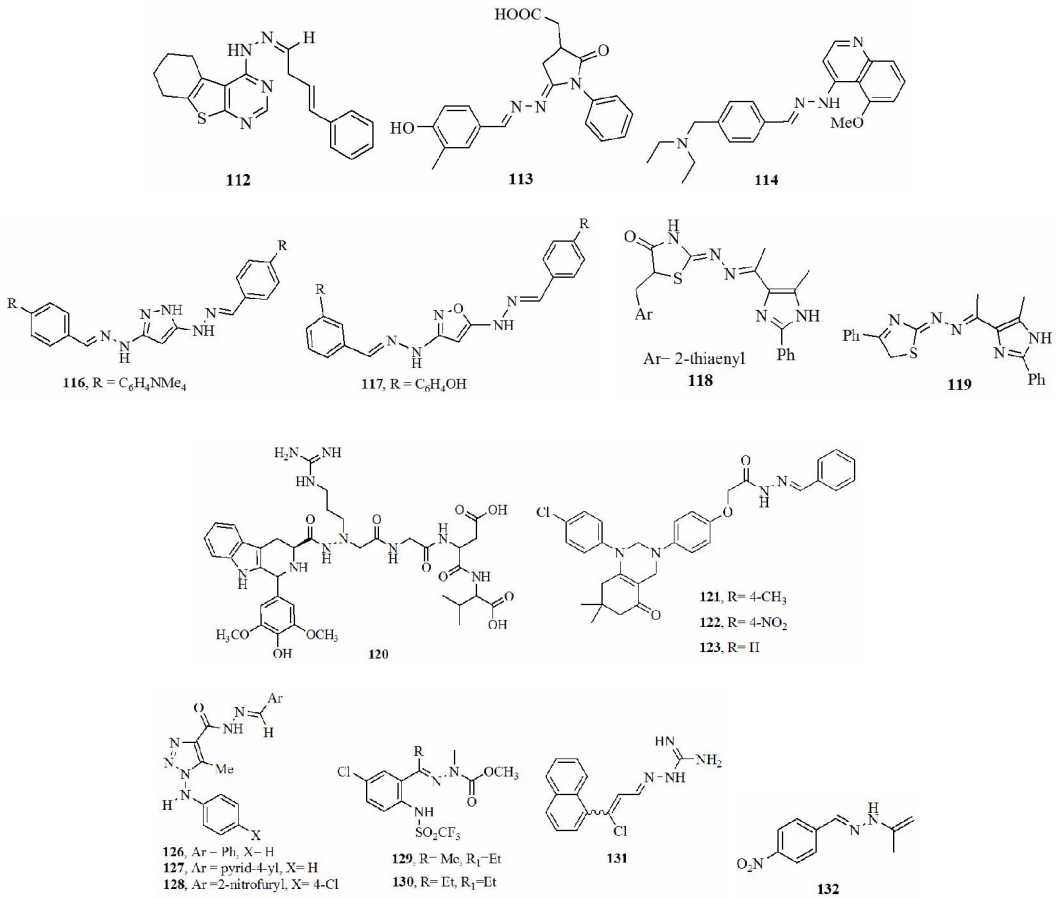

Figure 4. Chemical structure of hydrazone derivatives no.112-132

Oxidative stress is the cause of different pathological states. Hydrazone derivatives (**116, 117**) synthesized by Musad *et al.* (2011) are reported to have radical scavenging activity (RSA) at the concentration of 10μg/mL. Abdel-Wahab *et al.* (2011) evaluated imidazoline based hydrazones (**118, 119**) by 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid (ABTS) assay method and reported them to have promising antioxidant activity.

Cardioprotective activity

Despite the intensive drug research cardiovascular diseases still remain the leading cause of mortalities worldwide. El-Sabbagh *et al.* (2010) synthesized octahydroquinazoline-hydrazones (**121, 122, 123**) and reported them to be potential hypotensive agents. The activity was attributed to α-blockage. The chemical structure of hydrazone derivatives no.112-132 were showed in figure 4.

Antiplatelet activity

Antiplatelets decrease platelet aggregation, hold back the formation of thrombus. Jordao *et al.* (2009) synthesized hydrazone derivatives (**126, 127, 128**) and evaluated them for *in-vitro* antiplatelet activity.

Antiparasitic activity

Ali *et al.* (2010) evaluated the *in-vitro* anti parasitic activity of hydrazone derivatives (**129, 130**) against *Ctenocephalides felis* and *Rhipicephalus sanguineus*as. LD_{50} of 0.39 and 0.28μg/tick has been reported.

Aslam *et al.* (2011) synthesized hydrazone derivatives (**132**) as urease inhibitors. Urease catalyzes the hydrolysis of urea to ammonia and carbamate. This is beneficial for the pathogenesis of urolithiasis, pyelonephrities, ammonia and hepatic encephalopathy, hepatic coma and urinary catheter encrustation.

CONCLUSION

The review highlights the use of hydrazones as lead for development of newer agents. As mentioned the moiety possesses an array of activity. With proper synthesis and structure activity relationship, potential compounds can be designed with different biological activity.

REFERENCES

Abdel-Wahab FB., Awad AEG., and Badria AF., 2011, Synthesis, antimicrobial, antioxidant, anti-hemolytic and cytotoxic evaluation of new imidazole-based heterocycles, *Eur. J. Med. Chem.*, **46**, 1505-1511.

Abdel-Wahab FB., Khidre ER. and Awad AEG. 2012, Regioselective synthesis and antimicrobial activities of some novel aryloxyacetic acid derivatives, *Eur. J. Med. Chem.*, **50**, 55-62.

Abu-Surrah AS., Safieh KAA., Ahmadb IM., Abdalla MY., Ayoub MT., Qaroush AK., and Abu-Mahtheieh AM. 2010, New palladium (II) complexes bearing pyrazole-based Schiff base ligands: Synthesis, characterization and cytotoxicity, *Eur. J. Med. Chem.*, **45**, 471-475.

Ajani OO., Obafemi CA., Nwinyi OC., and Akinpelu DA. 2010, Microwave assisted synthesis and antimicrobial activity of 2-quinoxalinone-3-hydrazone derivatives, *Bioorg. Med. Chem.*, **18**, 214-221.

Ali A., Fisara P., Freemont JA., Kyi S., Meyer AG., Andrew G., Riches A.G., Sargent RM., Sawutz DG., Turner KA., Winzenberg KN., and Yang Q. 2010, Discovery of ectoparasiticidal hydrazono-trifluoro-methanesulfonanilides, *Bioorg. Med. Chem. Lett.,* **20**, 649-652.

Al-Said MS., Bashandy MS., Al-qasoumi SI., and Ghorab MM., 2011, Anti-breast cancer activity of some novel 1,2-dihydropyridine, thiophene and thiazole derivatives, *Eur. J. Med. Chem.*, **46**, 137-141.

Aponte JC., Vaisberg AJ., Castillo D., Gonzalez G., Estevez Y., Arevalo J., Quiliano M., Zimic M., Verastegui M., Malaga E., Juan RHG., Bustamante B., Tarleton RL., Wang Y., Franzblau SG., Pauli GF., Sauvain M., and Hammond GB., 2010, Trypanoside, anti-tuberculosis, leishmanicidal, and cytotoxic activities of tetrahydrobenzothienopyrimidines, *Bioorg. Med. Chem.,* **18**, 2880-2886.

Aslam MAS., Mahmood S., Shahid M Saeed A., and Iqbal J. 2011, Synthesis, biological assay in vitro and molecular docking studies of new Schiff base derivatives as potential urease inhibitors, *Eur. J. Med. Chem.*, **46**, 5473-5479.

Belskaya NP., Dehaen W., and Bakulev VA. 2010, Synthesis and properties of hydrazones bearing amide, thioamide and amidine functions, ARKIVOC, **1**, 275-332.

Caputto ME., Fabian LE., Benitez D., Merlinoz A., Rios N., Cerecetto H., Moltrasio GY., Moglioni AG., Gonzalez, M., and Finkielsztein LM., 2011, Thiosemicarbazones derived from 1-indanones as new anti-Trypanosoma cruzi agents, *Bioorg. Med. Chem.,* **19**, 6818-6826.

Catto M., Aliano R., Carotti A., Cellamare S., Palluotto F., Purgatorio R., Stradis A.D., and Campagna F., 2010, Design, synthesis and biological evaluation of indane-2-arylhydrazinylmethylene-1,3-diones and indol aryldiazenylmethylene-3-ones as β-amyloid aggregation inhibitors, *Eur. J. Med. Chem.*, **45**, 1359-136.

Corey EJ., and Enders D., 1976, Applications of N,N-dimethylhydrazones to synthesis. Use in efficient, positionally and stereochemically selective C瑁C bond formation, oxidative hydrolysis to carbonyl compounds, *Tetrahedron Lett.*, **17**, 3-6.

Corey EJ., and Enders D., 1976, Synthetic routes to polyfunctional molecules via metallated N,N-dimethylhydrazones, *Tetrahedron Lett.*, **17**, 11-14.

Cui Z., Li Y., Ling Y., Huang J., Cui J., Wang R., and Yang X., 2010, New class of potent antitumor acylhydrazone derivatives containing furan, *Eur. J. Med. Chem.*, **45**, 5576-5584.

de Oliveira KN., Costa P., Santin JR., Mazzambani L., Burger C., Mora C., Nunes RJ., and de-Souza MM., 2011, Synthesis and antidepressant-like activity evaluation of sulphonamides and sulphonyl-hydrazones, *Bioorg. Med. Chem.*, **19**, 4295-4306.

Edrees MM., Farghaly TA., El-Hag, AAF., Abdalla, M.M., 2010, Antimicrobial, antitumor and 5 α-reductase inhibitor activities of some hydrazonoyl substituted pyrimidinones, *Eur. J. Med. Chem.*, **45**, 5702-5707.

Effenberger K., Breyer S. and Schobert R. 2010, Modulation of doxorubicin activity in cancer cells by conjugation with fatty acyl and terpenyl hydrazones, *Eur. J. Med. Chem.*, **45**, 1947-1954.

El-Nakkady SS., Hanna MM., Roaiah HM., and Ghannam IAY., 2012, Synthesis, molecular docking study and antitumor activity of novel 2-phenylindole derivatives, *Eur. J. Med. Chem.*, **47**, 387-398.

El-Sabbagh OI., Shabaan MA., Kadry HH. and Al-Din ES. 2010, New octahydro-quinazoline derivatives: Synthesis and hypotensive activity, *Eur. J. Med. Chem.*, **45**, 5390-5396.

El-Sayed MAA., Abdel-Aziz NI., Abdel-Aziz NAM., El-Azab AS., Asiri YA. and Tahir KEHE. 2011, Design, synthesis, and biological evaluation of substituted hydrazone and pyrazole derivatives as selective COX-2 inhibitors, molecular docking study, *Bioorg. Med. Chem.,***19**, 3416-3424.

Eswaran S., Adhikari AV., Chowdhury IH., Pal, NK. and Thomas KD. 2010, New quinoline derivatives: Synthesis and investigation of antibacterial and antituberculosis properties, *Eur. J. Med. Chem.*, **45**, 3374-3383.

Fan CD., Su H., Zhao J., Zhao BX., Zhang SL. and Miao JY. 2010, A novel copper complex of salicylaldehyde pyrazole hydrazone induces apoptosis through up-regulating integrin β-4 in H322 lung carcinoma cells, *Eur. J. Med. Chem.*, **45**, 1438-1446.

Gage JL., Onrust R., Johnston D., Osnowski A., MacDonald W., Mitchell L., Urogdi L., Rohde A., Harbol K., Gragerov, S., Dorman G., Wheeler T., Florio V., and Cutshall NS., 2011, N-Acylhydrazones as inhibitors of PDE10A, *Bioorg. Med. Chem. Lett.*, **21**, 4155-4159.

Gouda MA., Berghot MA., Shoeib AI., and Khalil MA. 2010, Synthesis and antimicrobial of new anthraquinone derivatives incorporating pyrazole moiety, *Eur. J. Med. Chem.*, **45**, 1843-1848.

Govindasami T., Pandey A., Palanivelu N., and Pandey A., 2011, Synthesis, characterization and antibacterial activity of biologically important vanillin related hydrazone derivatives, *Int. J. Org. Chem.*, **1**, 71-77.

Hassan GS., Kadry HH., Abou-Seri SM., Ali, MM., and Mahmoud AEE., 2011, Synthesis and in vitro cytotoxic activity of novel pyrazolo[3,4-d]pyrimidines and related pyrazole hydrazones toward breast adenocarcinoma MCF-7 cell line, *Bioorg. Med. Chem.,* **19**, 6808-6817.

Hayat F., Salahuddin A., Zargan J. and Azam A. 2010, Synthesis, characterization, antiamoebic activity and cytotoxicity of novel 2-(quinolin-8-yloxy) aceto-hydrazones and their cyclized products (1,2,3-thiadiazole and 1,2,3-selenadiazole derivatives), *Eur. J. Med. Chem.*, **45**, 6127-6134.

Hernandez P., Cabrera M., Lavaggi ML., Celano L., Tiscornia I., da Costa TR., Thomson L., Bollati-Fogolin M., Miranda ALP., Lima LM., Barreirod E.J., Gonzalezd M. and Cerecettod H. 2012, Discovery of new orally effective analgesic and anti-inflammatory hybrid furoxanyl N-acylhydrazone derivatives, *Bioorg. Med. Chem.,* **20**, 2158-2171.

Isloor AM., Kalluraya B., and Pai KS., 2010, Synthesis, characterization and biological activities of some new benzo[b] thiophene derivatives, *Eur. J. Med. Chem.*, **45**, 825-830.

Jin CAY., Tan Z., He M., Tian B., Tang S., Hewlett,I., Yang, M., 2010, SAR and molecular mechanism study of novel

acylhydrazone compounds targeting HIV-1, *Bioorg. Med. Chem.*, **18**, 2135-2140.

Jordao AK., Sathler PC., Ferreira VF., Campos VR., de Souza MCBV., Castro HC, H.C., Lannes A., Lourenco A., Rodrigues CR., Bello ML., Lourenco MCS., Carvalho GSL., Almeida MCB. and Cunha AC. 2011, Synthesis, antitubercular activity, and SAR study of N-substituted-phenylamino-5-methyl-1H-1,2,3-triazole-4-carbohydrazides, *Bioorg. Med. Chem.,* **19**, 5605-5611.

Jubie S., Meena S., Ramasheshu KV., Jawahar N. and Vijaykumar S. 2010, Synthesis and biological evaluation of some hydrazones and carbazones of indane 1,3-dione, *Ind. J. Chem*., **49B**,1261-1263.

Kaushik D., Khan SA., Chawla G. and Kumar S. 2010, N'-[(5-chloro-3-methyl-1-phenyl-1H-pyrazol-4-yl) methylene] 2/4-substituted hydrazides: Synthesis and anticonvulsant activity, *Eur. J. Med. Chem.,* **45**, 3943-3949.

Kendall JD., Giddens AC., Tsang KY., Frederick R., Marshall ES., Singh R., Lill CL., Lee WJ., Kolekar S., Chao M., Malik A., Yu S., Chaussade C., Buchanan C., Rewcastle GW., Baguley BC., Flanagan JU., Jamieson SMF. and Denny WA. 2012, Shepherd, P.R., Novel pyrazolo[1,5-a] pyridines as p110α-selective PI3 kinase inhibitors: Exploring the benzenesulfonohydrazide SAR, *Bioorg. Med. Chem.*, **20**, 58-68.

Kumar D., Judge, V., Narang R., Sangwan S., Clercq DE., Balzarini J., and Narasimhan B., 2010, Benzylidene/2-chlorobenzylidene hydrazides: Synthesis, antimicrobial activity, QSAR studies and antiviral evaluation, *Eur. J. Med. Chem.*, **45**, 2806-2816.

Kumar D., Kumar NM., Ghosh S. and Shah K. 2012, Novel bis(indolyl)hydrazide–hydrazones as potent cytotoxic agents, *Bioorg. Med. Chem. Lett.,* **22**, 212-215.

Lee YJ., Jeong WK., Shin S., Lee UJ. and Kim Y. 2012, Discovery of novel selective inhibitors of Staphylococcus aureus β-ketoacyl acyl carrier protein synthase III, *Eur. J. Med. Chem.*, **47**, 261-269.

Maguene GM., Jakhlal J., Ladyman M., Vallin A., Ralambomanana DA., Bousquet T., Maugein J., Lebibi J., and Pelinski L., 2011, Synthesis and antimycobacterial activity of a series of ferrocenyl derivatives, *Eur. J. Med. Chem.*, **46**, 31-38.

Mahajan A., Kremer L., Louw S., Gueradel Y., Chibale, K., and Biot C., 2011, Synthesis and in vitro antitubercular activity of ferrocene-based hydrazones, *Bioorg. Med. Chem. Lett.,* **21**, 2866-2868.

Moldovan CM., Oniga O., Parvu A., Tiperciuc B., Verite P., Pirnau A., Bojit OCM. and Pop R. 2011, Synthesis and anti-inflammatory evaluation of some new acyl-hydrazones bearing 2-aryl-thiazole, *Eur. J. Med. Chem.*, **46**, 526-534.

Musad EA., Mohamed R., Saeed BA., Vishwanath BS. and Rai KML. 2011, Synthesis and evaluation of antioxidant and antibacterial activities of new substituted bis(1,3,4-oxadiazoles), 3,5-bis(substituted) pyrazoles and isoxazoles, *Bioorg. Med. Chem. Lett*., **21**, 3536–3540.

Ozdemir A., Turan-Zitouni G., Kaplanciklia AZ., Iscan G., Khan S. and Demirci F. 2010, Synthesis and the selective antifungal activity of 5,6,7,8-tetra-hydroimidazo[1,2-a]pyridine derivatives, *Eur. J. Med. Chem.*, **45**, 2080-2084.

Ozkay Y., Tunali Y., Karaca H. and Isikdag I. 2010, Antimicrobial activity and a SAR study of some novel benzimidazole derivatives bearing hydrazone moiety, Eur. J. Med. Chem., **45**, 3293-3298.

Pavan FR., Maia PIS., Leite SRA., Deflon VM., Batista AA., Sato DN., Franzblau S.G. and Leite CQF. 2010, Thiosemicarbazones, semicarbazones, dithiocarbazates and hydrazide/ hydrazones: Anti-Mycobacterium tuberculosis activity and cytotoxicity, *Eur. J. Med. Chem.*, **45**, 1898-1905.

Raja AS., Agarwal AK., Mahajan N., Pandeya, SN. and Ananthan A. 2010, Antibacterial and antitubercular activity of some diphenyl hydrazone and semicarbazone, *Ind. J. Chem*., **49B**, 1384-1388.

Rajitha G., Saideepa N., Praneetha P., 2011, Synthesis and evaluation of N-(α-benzamidocinnamoyl)aryl hydrazone

derivative for anti-inflammatory and antioxidant activities, *Ind. J. Chem.*, **50B**, 729-733.

Rane RA., and Telvekar VN.,2010 Synthesis and evaluation of novel chloropyrrole molecules designed by molecular hybridization of common pharmacophores as potential antimicrobial agents, Bioorg. Med. Chem. Lett., **20**, 5681–5685.

Rasras MJA., Al-Tel HT., Al-Aboudi FA. and Al-Qawasmeh AR., 2010, Synthesis and antimicrobial activity of cholic acid hydrazone analogues, Eur. J. Med. Chem., **45**, 2307-2313.

Rollas S., and Kucukguzel SG., 2007, Biological Activities of Hydrazone Derivatives. Molecules, **12**, 1910-1939.

Romeiro NC., Aguirre G., Hernandez P., González M., Cerecetto H., Aldana I., Silanes SP., Monge A., Barreiro EJ. And Lima LM., 2009, Synthesis, trypanocidal activity and docking studies of novel quinoxaline-N-acylhydrazones, designed as cruzain inhibitors candidates, *Bioorg. Med. Chem.,* **17**, 641-652.

Sharma RN., Sharma KP. and Dikshit SN., 2011, Synthesis, Characterization and biological activities of some new hypophosphorousadducts of acid hydrazones derived from 2-[(N-benzoyl) 2, 3 dichloroanilido] acetohydrazide, Archives of Applied Science Research, **3**, 415-424

Siddiqui SM., Salahuddin A. and Azam A., 2012, Synthesis, characterization and antiamoebic activity of some hydrazone and azole derivatives bearing pyridyl moiety as a promising heterocyclic scaffold, *Eur. J. Med. Chem.*, **49**, 411-416.

Thomas KD., Adhikari, AV., Telkar S., Chowdhury, I.H., Mahmood, R., Pal, K.N., Rowd, G., Sumesh, E. 2011, Design, synthesis and docking studies of new quinoline-3-carbohydrazide derivatives as antitubercular agents, *Eur. J. Med. Chem.*, **46**, 5283-5292.

Uppal G., Bala S., Kamboj S., and Saini M., 2011, Therapeutic Review Exploring Antimicrobial Potential of Hydrazones as Promising Lead, Der Pharma Chemica, **3**, 250-268.

Vaio MAFVD., Freitas ACC., Castro H.C., Albuquerque SD., Cabral LM., Rodrigues CR., Albuquerque MG., Martins RCA., Henriques MGMO., Dias and LRS., 2009, Synthesis, antichagasic in vitro evaluation, cytotoxicity assays, molecular modeling and SAR/QSAR studies of a 2-phenyl-3-(1-phenyl-1H-pyrazol-4-yl)-acrylic acid benzylidene-carbohydrazide series, *Bioorg. Med. Chem.,* **17**, 295-302.

Vavrikova E., Polanc S., Kocevar M., Horvati K., Bosze S., Stolarikova J., Vavrova K. and Vinsova J., 2011, New fluorine-containing hydrazones active against MDR-tuberculosis, *Eur. J. Med. Chem.*, **46**, 4937-4945.

Vijesh AM., Isloor MA., Prabhu V., Ahmad S., and Malladi S., 2010, Synthesis, characterization and anti-microbial studies of some novel 2,4-disubstituted thiazoles, *Eur. J. Med. Chem.*, **45**, 5460-5464.