Journal of Drug Design and Medicinal Chemistry
2015; 1(1): 1-11
Published online September 29, 2015 (http://www.sciencepublishinggroup.com/j/jddmc)
doi: 10.11648/j.jddmc.20150101.11

A Review on the Medicinal Importance of Pyridine Derivatives

Ataf Ali Altaf[1, *], Adnan Shahzad[2], Zarif Gul[2], Nasir Rasool[1], Amin Badshah[3], Bhajan Lal[4], Ezzat Khan[2]

[1]Department of Chemistry, Government College University, Faisalabad, Pakistan
[2]Department of Chemistry, University of Malakand, Dir Lower, Pakistan
[3]Department of Chemistry, Quaid-i-Azam University, Islamabad, Pakistan
[4]Departmen of Energy Systems Engineering, Sukkur Institute of Business Administration, Pakistan

Email address:
atafali_altaf@yahoo.com (A. A. Altaf)

To cite this article:
Ataf Ali Altaf, Adnan Shahzad, Zarif Gul, Nasir Rasool, Amin Badshah, Bhajan Lal, Ezzat Khan. A Review on the Medicinal Importance of Pyridine Derivatives. *Journal of Drug Design and Medicinal Chemistry.* Vol. 1, No. 1, 2015, pp. 1-11. doi: 10.11648/j.jddmc.20150101.11

Abstract: Pyridine and its derivatives are the important chemical compounds with tremendous applications in the various fields. In this review we have summarized the medicinal and non-medicinal uses of number of pyridine derivatives. Pyridine derivatives have been reported for variety of biological activities and numbers of the compounds are in clinical uses. Pyridine derivatives also have increasing importance for modern medicinal applications.

Keywords: Pyridine Derivatives, Medicinal Use, Synthesis of Pyridines, Characterization of Pyridines

1. Introduction

Pyridine is a basic heterocyclic organic compound with the chemical formula C_5H_5N. In many aspects it can be related to well established and very fundamental aromatic molecule, benzene, with one C-H group replaced by a nitrogen atom. Pyridine has a conjugated system of six π-electrons exactly as benzene has, that are delocalized over the heterocyclic ring. The molecule is planar in nature and follows Hückel criteria for aromaticity.

2. Historical Background of Pyridine

The name pyridine is derived from the Greek word and is the combination of two words "pyr" means fire and "idine" is used for aromatic bases. The first pyridine base was isolated in 1846 by Anderson, picoline (Compound 1). After quit a long time its structure was determined by Wilhelm Körner in 1869 and James Dewar in 1871, independently. It was suggested that the structure of pyridine might be analogous to quinoline and naphthalene. It was concluded that pyridine has been derived from benzene and its structure might be obtained by replacing a CH moiety with a nitrogen atom. In the year 1876, William Ramsay synthesized this compound by combining acetylene and hydrogen cyanide, a red-hot iron-tube furnace was used to carry out the reaction. It was the ever first synthesis of a hetero-aromatic compound. Pyridine became an interesting target in 1930 with the importance of niacin for the treatment of dermatitis and dementia [1]. Niacin is pyridine derivative as represented in figure 1, Compound 2.

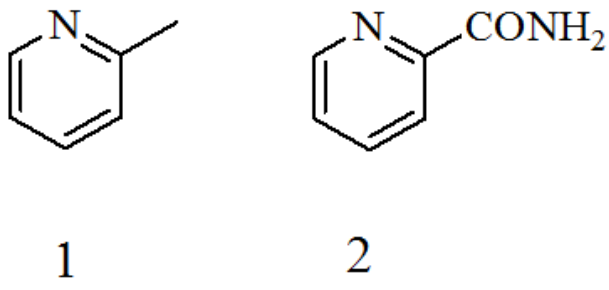
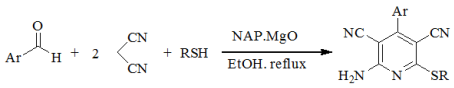


Figure 1. *Pyridine derivatives, Picoline and Niacin.*

Nitrogen containing six membered aromatic pyridine and its derivatives abundantly exist in nature and they play a vital role in the field of heterocyclic chemistry [2]. Such compounds are widely used for many applications in medicinal science as listed below.

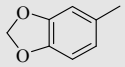
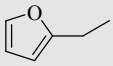
3. Synthesis of Different Derivatives of Pyridine

(1) On-pot Synthesis of Pyridines Catalyzed by NAP-MgO [3]

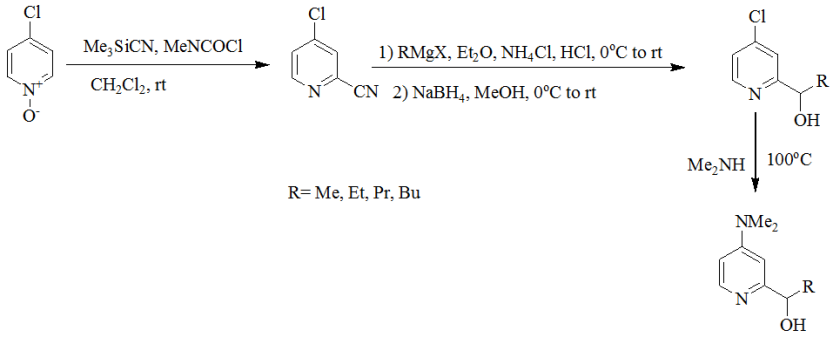


Scheme 1. *On-pot synthesis of pyridine derivatives (P1-P16) catalyzed by NAP-MgO.*

Table 1. *One-pot synthesis of pyridines catalyzed by NAP-MgO.*

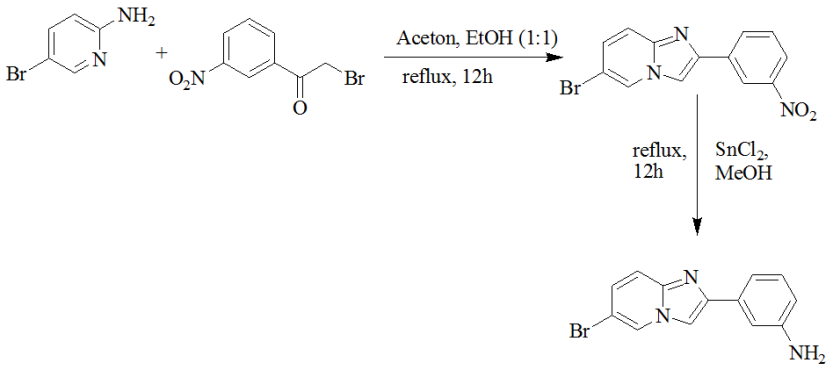
Entry	Ar	R	Time(h)	Product P[b]	Yield(%)[c]
1	C_6H_5	C_6H_5	2	P1	64
2	4-MeO–C_6H_4	C_6H_5	6	P2	61
3	4-Me–C_6H_4	C_6H_5	6	P3	59
4	4-NO_2–C_6H_4	C_6H_5	2	P4	52
5	4-Cl–C_6H_4	C_6H_5	2	P5	49
6	4-OH–C_6H_4	C_6H_5	7	P6	64
7	4-HOOC–C_6H_4	C_6H_5	2	P7	50
8		C_6H_5	9	P8	48
9		C_6H_5	4	P9	69
10	C_6H_5	4-MeC_6H_4	4	P10	65
11	4-MeO–C_6H_4	4-Me–C_6H_4	8	P11	59
12	C_6H_5	4-Cl–C_6H_4	5	P12	50
13	C_6H_5	C_6H_5–CH_2	4	P13	44
14	4-Me-C_6H_4	C_6H_5–CH_2	7	P14	41
15	4-MeO–C_6H_4		8	P15	56
16	4-Cl–C_4H_4		6	P16	52

(2) Synthesis of DMAP [4-(N,N-dimethylamino) Pyridine] Derivative [4]



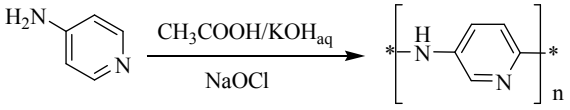
Scheme 2. *Synthesis of DMAP [4-(N,N-dimethylamino)pyridine] derivatives.*

(3) Synthesis of a novel Series of Imidazo Pyridine Derivatives [5]



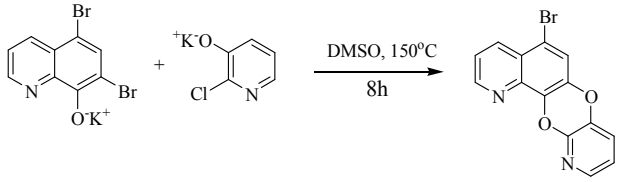
Scheme 3. *Synthesis of a novel series of imidazo pyridine derivatives.*

(4) Oxidative Polycondensation Reaction of 3-Aminopyridine [6]



Scheme 4. *Oxidative polycondensation reaction of 3-aminopyridine.*

(5) Synthesis of Pyridine-Quinoline Hybrid [7]



Scheme 5. *Synthesis of pyridine-quinoline hybrid.*

4. Characterization of Pyridine Derivatives

UV-Visible spectroscopy; The pyridine derivatives give different characteristic bands in the region of 362-460 nm owing to the presence of various substituents also known as chromophores attached to main pyridine ring. The presence of these chromospheres which are electron donor in nature, show absorption in the range of 391-460 nm, if the chromophores are electron accepter then the observed absorption is in the region of 362-415 nm. The presence of electron donor chromophores e.g. methoxy moiety at position C-4 and C-3,4 give bathochromic shift (red) but acceptor e.g. nitro moiety chromophores are responsible for hypsochromic (blue) shift [8, 9].

FT-IR Spectroscopy; The FT-IR is very important characterization techniques used to characterize chemical compounds in solid as well as in liquid state. This technique provides useful information regarding geometry and other aspects of chemical compounds. Since the pyridine molecule contains various functionalities, its IR spectrum gives characteristic peaks corresponding to groups present therein i.e., $\nu_{C=N}$ 1570-1654 cm^{-1}, $\nu_{C=C}$ 1593-1597 cm^{-1}, $\nu_{C=O}$ 1681-1700 cm^{-1} [10-12].

NMR-spectroscopy; Substitution of certain group on six member heterocyclic aromatic ring of pyridine cause changes in chemical schift value of all proton and carbon atoms of ring. Signals corresponding to a particular ^1H present in pyridine molecule (figure 2) appear in the range of 6.5-9.2 ppm [10, 12-16] the electron donating group like aromatic group at position 3 at pyridine ring the 1HNMR appears in range of (8.05-9.00) when there is carbonyl group is present between pyridine and other aromatic group at position 3 the proton of pyridine appear at (7.56-9.00) the proton at position 2 is most deshielded among the other proton of pyridine ring [12]. The presences of amide functionality at position 2 so the hydrogen will appear at (8.29-8.37) [13]. when bulky group i.e. R present at position 2 to nitrogen the proton appear in range (7.66-8.74) the proton at position 6 is most deshielded to 8.74 but the presence of R at position 3 the proton of pyridine ring appear at (7.60-9.2) the proton at position 2 is most deshielded to 9.2. And when this group present at position 4, para to nitrogen the proton appears in range of 7.94-8.82 [17]. the presence of R' at position 3 the proton is appear at (7.63-9.17) the proton which is most deshielded is at position 2 at 9.17ppm [18].

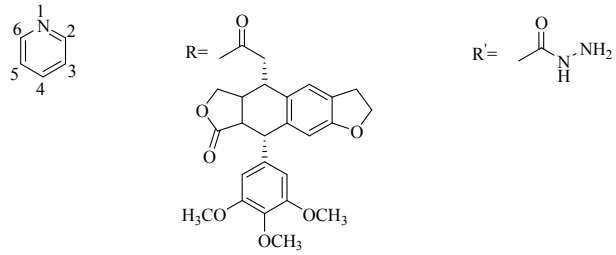


Figure 2. *Representative example for NMR spectral discussion.*

When R_1 and R_2 are present at position 3 the proton of pyridine appear at (7.58-9.11) the most deshielded proton in both case is at position 2. In case of R_1 it appears at 9.11 and in case of R_2 at 9.2ppm [19].

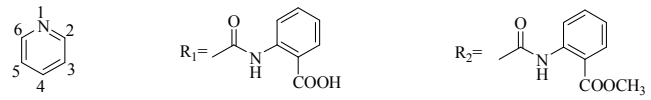


Figure 3. *Representative example for HNMR spectral discussion.*

The presence of R= CONHN=CHPhR (figure 4) at position 3 the hydrogen of pyridine ring appear in range of 7.42-8.98ppm and the proton at position 2 is most deshielded [20].

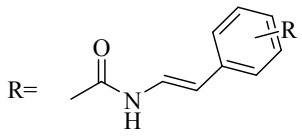


Figure 4. *Representative example for ^{13}CNMR spectral discussion.*

^{13}C-NMR signals of pyridine carbons appears in the range of 121-165 ppm [14, 16] The presence of above R group the carbon of pyridine ring appear in range of (130-149) the carbon at position 3 and 5 are more deshielded to 149 [20].

XRD SINGLE CRYSTAL ANALYSIS; The single crystal analysis show that the distance between C-N lies in the range of 1.337-1.342 Å [13, 16, 21, 22].

5. Biological Application

5.1. Anti-microbial

Pyridine derivatives such as di-acylhydrazine (Compound 3) and acyl(arylsulfonyl)hydrazine (Compound 4) possess exciting antibacterial activities against gram negative bacteria

E. coli and gram positive bacteria S. albus as compared to standard drug streptomycine sulphate. They have also been tested as herbicides against C. dactylon, C. rotundus, E. crusgalli, E. hirta, C. argentia, E. indica, and T. procumbens. Antifungal activities of the same compounds against A. niger and A. teniussiama using Griseofulvin as a standard have also been investigated [23].

Figure 5. *Structural representation of N-(3, 5, 6-Trichloro-2-pyridyloxyacetyl)-N'-aroylhydrazines, 3 and N-(3,5,6-Trichloro-2-pyridyloxyacetyl)-N'-arylsulfonylhydr-azines, 4.*

Compound of type 5 is a hybrid derived from pyridine as precursor. It consists of hdrophelic and lipophilic parts and it has been tested for its antimicrobial activity [24].

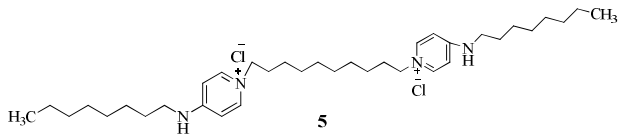


Figure 6. *Structure of pyridinium derivative, Octenidiene used as antibacterial agent.*

The thienopyridine and other pyridine derivatives compounds of type 6-14 also possess good antimicrobial i.e. antibacterial activity has been showed against gram positive bacteria S. aureus and are also efficient against gram negative E. coli, P. aeruginesa and P. vulgaris [25].

A series of pyrimidine derivatives are easily accessible such as compounds of type 15 and 16, Figure 5. They also show antimicrobial activity and the maximum zone of inhibition has been observed against bacteria *E. coli. S. aureus, S. typhi and B. subtitlis*. Compound of type 17 has also tested to show good activity against *E. coli*. Compounds 18 shows remarkable efficiency to fight against *S. Aureus,* while those represented by formula 19 and 20 are active to control *S. typhi*. The compound of type 20 has shown modest activity against *B. subtilis* compared with standard drug [26]. In below listed compounds, Figure 7 the excellent activity is observed probably due to the presence of halogens added to one or more of the bonded benzene ring(s).

Some Schiff base ligands of type 1-phenyl-2,3-dimethyl-4-salicylalidene pyrazole-5-one, are easy in respect of synthesis, they have the ability to couple with metal center such as Cu^{2+}, Ni^{2+}, Zn^{2+} and Fe^{3+}. These ligands in free state and their metal complexes both show antibacterial and antifungal activities even better than some the well-established antibiotics [27].

The compound, 3-hydroxypyridine-4-ones and 3-hydroxy-pyran-4-ones containing pyridine ring are active against *Staphylococcus aureus*, *Aspergilus niger* and *Candida albicans* [28].

The 3-substitutedmethylene-2*H*-thiopyrano [2,3-*b*]pyridin-4(3*H*)-ones type compounds were obtained to be tested for their antifungal activity in vitro, and it was concluded that all compounds are antifungal. The compound 21 showed comparable activity with Fluconazole against *M. gypseum* and *C. Krusei*, it showed moderate activity against *C. glabrata* [29]. A series of chiral pyridine carboxamides are accessible possessing linear and macro cyclic structures. The screening tests for antibacterial and antifungal activities were observed to be positive. Results revealed that compounds 22-27 possess antimicrobial activities almost comparable to reference drug ketaconazole. Compounds of type 24-28 were observed for their antibacterial activities having similar level to commonly used drug Ciprofloxacin [13].

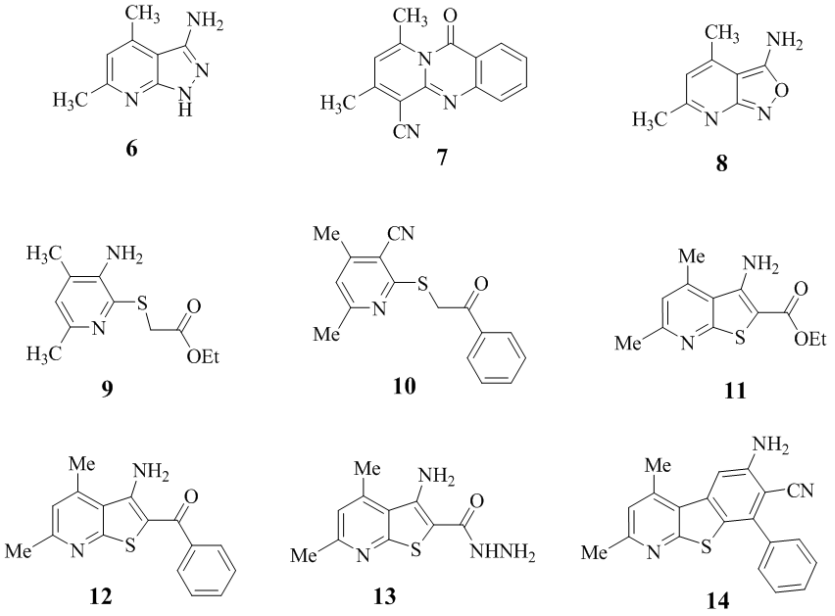


Figure 7. *Representative examples of antimicrobial compounds containing pyridine as basic unit.*

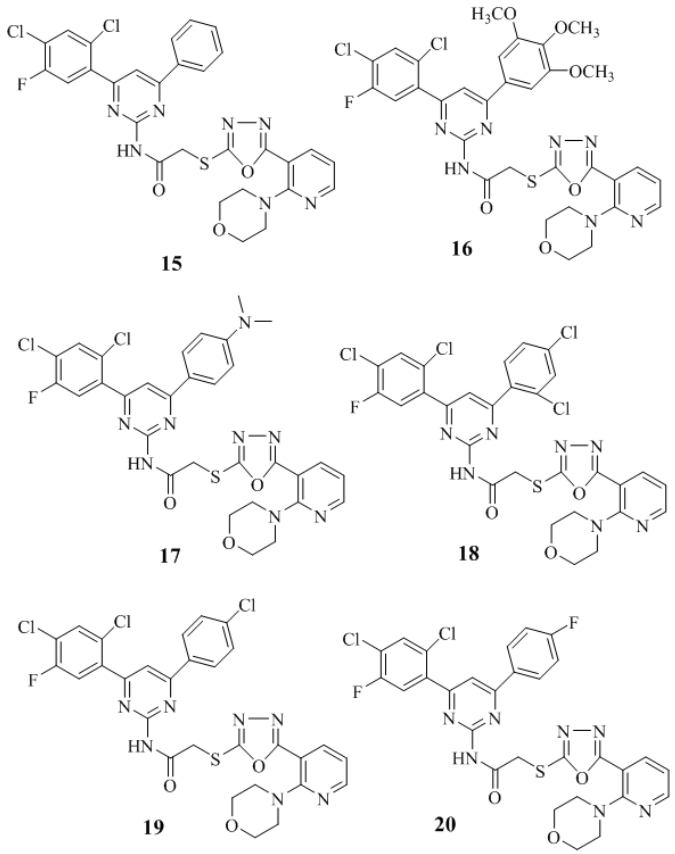


Figure 8. *Oxadiazole substituted Pyridine derivatives active against various bacteria.*

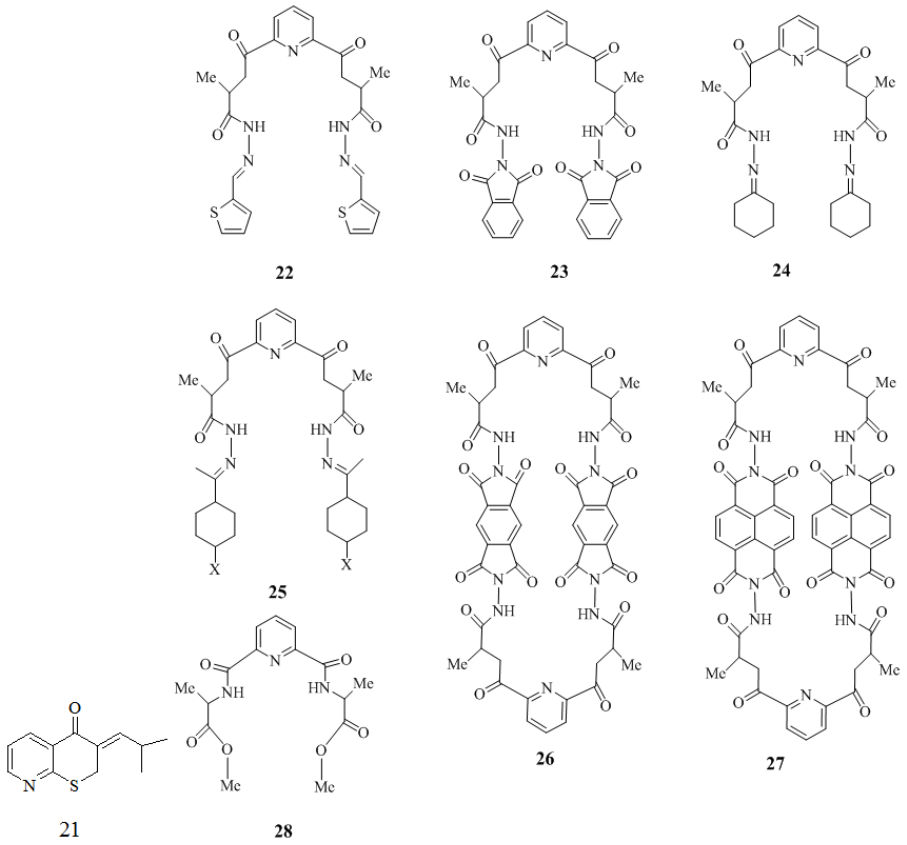


Figure 9. *Macro-cyclic and open chain 2,6-substituted pyridine derivatives as antibacterial agents.*

The pyridine containing benzothiazolylamino group substituted at position 2 and carboxylic functionality are synthetic derivatives and have been checked for their biological activities. Experimental data obtained regarding their antimicrobial activities show that they have weak to modest activities[30]. These results show that substituents have greater influence on biological activities of pyridine derivatives.

Pyrazoline, Pyridine, and Pyrimidine derivatives linked to Indole moiety were obtained as conversion product of synthetic chalcone. These conversion products were screened out for antitumor activities in addition to antimicrobial activities, results thus obtained showed moderate to high bactericidal activity against *Staphylococcus aureus and Pseudomonas aeroginosa*, the ciprofloxacin was used as standard. Some of compounds were good fungicidal agents, their activity was recorded close to nystin, against *Fusarium*. Almost all the screened compounds were found to have moderate activity against *Candidaalbicans* [31].

A group of penta substituted pyridine derivatives containing quinoline moiety were designed in the laboratory, and were subjected for tests in order to investigate their antimicrobial activities (against Bacillus subtilis, Clostridium tetani, Streptococcus pneumonia, gram positive and Escherichia coli, Salmonella typhi, Vibrio cholera gram negative bacteria), and two fungal stains were also taken into consideration (A. fumigatus, Candida albicans). Most of the compounds under observation were found active against these microorganisms. A small amount of these compounds were most effective against V. cholerae and E. coli [32]. Another family of pyridine derivatives was synthesized and was reported that they show comparable antifungal activities to standard drugs Fluconazole and Gieseofulvin [33]. Chiral tricyclic and macro cyclic derivatives of the compound pyridine show high antimicrobial activities than the established standard compounds ampicillin and chloramphenicol [34]. The activity of some other derivatives was compared with ampicillin as standard, and these derivatives were proved to have good antimicrobial activity [35].

The anti-fungal activity of pyridine containing compound i.e., *N*-(pyridine-2-methyl)-2-(4-chlorophenyl)-3-methylbutanamide was determined to have good antifungal activities [21]. The triazoles substituted pyridine derivatives were obtained with greater ease and their antibacterial, antifungal, anti-inflammatory activities were studied. The data obtained from the experiments suggested that all compounds exhibit mild to good antibacterial and antifungal activities. It was pointed out that compounds having free NH_2 at 4-position show highest antibacterial activity. The activities/efficiency against bacteria may also be linked to the triazoles ring system. Interestingly, these compounds were more efficient against bacteria compared with fungi. Some of the compounds were reported to have anti-inflammatory activity [36].

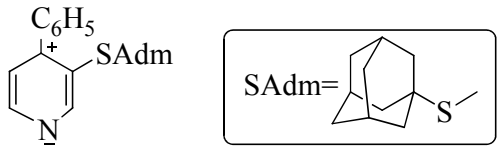
5.2. Anti-viral

Influenza B-Mass virus: The Oxime derivatives of thiazolo[5,4-*b*]pyridine exhibit activity against *influenza B-Mass* virus. The oxime derivatives of pyridine and naphthiridine have high activity against HIV. Recently it has been reported that oximes of naphthiridine also show antibacterial activity. Oximes-Pyridine derivatives are used as antidotes against poisoning by organophosphorus compounds [37].

Anti-viral (HCV): Hydarzone of 3 and 4-acetyl pyridine along with anti-tumor activity are also capable to inhibit the replication of HCV both RNA(+) and RNA(-) stran [38]. Bi Pyridinyl derivatives complex with ruthenium display anti-viral activity against heptitas C-virus (HCV) [39].

5.3. Antioxidant

Some thiopyridine derivatives are antioxidant (SOD) in addition to their cytotoxic (DPPH) activities, these activities are quite attractive, particularly compounds 29 shown highest SOD and DPPH activities. The SOD and DPPH activities are strongly related to the structure of the compounds. The QSAR studies show that dipole moment and elcetrophilic index were the most significant descriptors for correlating the molecular structure of compounds with their respective SOD activities. Results indicated that molecules with high dipole moment and elcetrophilic index values also had high SOD activity. Those compounds which have lowest atomic polarizability (MATS4p) have highest DPPH activity [40].



29

Figure 10. *Representative example of antioxidant.*

5.4. Anti-Diabetic

The pyridine derivatives containing thiazolidinones exhibit antidiabetic activities using GOD-POD method. The results reveal that some of these compounds show very effective anti-diabetic activities, few among these compounds showed appreciable anti-diabetic activity and these findings could lead to the development of novel class of anti-diabetic drugs in coming time [44].

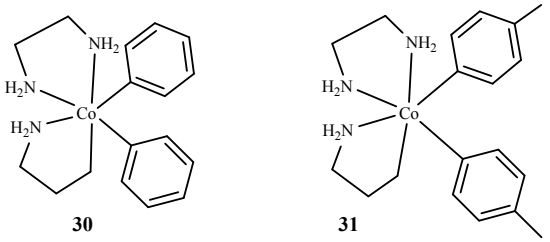
5.5. Anti-Cancer Activities

Metal complexes of Cu(II) with Schiff base 2-[N-(a-picolyl)-amino]-benzophenone on pzridine particularly brominated products have highest cytotoxity and show very good antitumor activity [22]. Compounds of pyrazoline, pyridine and pyrimidine coupled with indole functionality were obtained in reasonable pure form and were found to

have excellent activity against tumor cells [31].

2-acetylpyridine derivative's, 2-benzoxazolylhydrazon have anti-tumor activity and if acetyl group is replace by acyl group then it have excellent inhibitor of leukemia, colon and ovarian cancer cell line [41]. Palladium and zinc complexes of 2-acetyl pyridine thiosemicarbazone have good anti-tumor activity against human cell with less cytotoxicity and are potential candidates as anti-tumor agents for future [42]. Cd complex with 2,6-diacetyl pyridine have anti-tumor activity against C6 glioma cell line and could be potential tool to treat drugs-resistant brain tumor [43]. Hydrozne of 3 and 4-acetylpyridine display excellent growth inhibition at a different concentration in all cancer cell line [38].

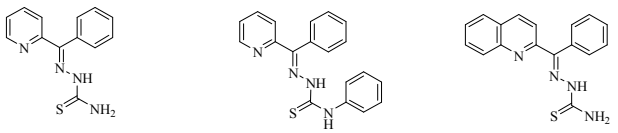
Many ligands derived from pyridine (pyridine based) when coupled with metals, the resulted complexes exhibit high cytotoxicity and have proved to be antitumor agents. Among metals Cu(II) complexes have shown promising activities. The cytotoxicity of complexes could be linked to the substituent on the aromatic ring. The maximum cytotoxicity was found when aromatic ring is rich in bromine. When the activities were compared with the standard drug, it came out that the compound under trial was even better than 5-Fluorouracil [22]. The cobalt(III) pyridine complexes of type 30 and 31, Figure 10, efficiently interact with DNA and can bind the two strand of the DNA in an effective manner. The anticancer activity of complex 30 is even better than 31. These complexes containing Co(III) ion have the ability to photocleavage the plasmid DNA pBR322 when irradiated at 365 nm [15].



30 31

Figure 11. *Heterolyptic cobalt(III) complexes possessing remarkable anticancer activities.*

Thiosemicarbazone derivatives analogous to quinoline and isoquinolines which contain benzoylpyridine thiosemicarbazones are easy to synthesize. When such compounds were checked for cytotoxic activities. They were found to exhibit moderate to good cytotoxicity against HuCCA-1, HepG2, A549 and MOLT-3 human cancer cells. Benzoylpyridine thiosemicarbazones of type 32 and 33 and of of the quinoline analogues, 34 showed antimalarial activity in the range of mild to good. It is suggested that some in these compounds particularly 33 is potential anticancer and antimalarial agents [45]. The pyridine derivatives containing substituents at 2- and (or) 6-position including heterocyclic substituents were obtained. The biological (anticancer) screening of these compounds show that they have good anticancer activity even better than those of references, 5-flurouracil (5-FU) and doxorubicin (DOX) [46].



32 33 34

Figure 12. *Thiosemicarbazones derived from pyridine as anticancer drugs.*

N-substituted thiosemicarazone derivatives of acetyl pyridine, imino pyridine.[47] and their complexes with gallium(III) and iron(III) exhibit excellent anti-cancer activity against two human cancer cell line 41M and SK-BR-3 and their cytotoxicity mostly depend on central metal ions, gallium increase the cytotoxicity while iron decrease but ligand itself is more cytotoxic as compare to the central metal ions so metal ions interaction to the ligand decrease cytotoxicity [47-49].

Thiosemicarbazone of 2-acetyl pyridine derivativies are iron chelator due to this properties it is the most potent anti preliferative agent [50, 51]. Indol derivative of quinoline and their complexes with ruthenium and osmium have anti preliferative activity against human cell line A549(non-small cell lung cancer), SW480 (colon-adeno carcinoma) and CH1 (ovarian carcinoma).[52] 2-acetyl pyridine thhiosemicarbazone and terpyridinyl complex with copper show anti preliferative activity which are best as compare to the ligand itself.[53, 54] Novel 2-acetyl pyridine thiosemicrbazone complex of organo platiniumII, both ligand and complexe exhibit anti-tumor activity against human tumor cell line (HT-29 and Hu Tu-80). Complex have high anti proliferative property with IC_{50}=1.2 while ligand have 8.5 so complex is potential anti-tumor agent.[55]

Platinium complex with thiosemicarbazone of 2-acetyl pyridine and 4-acetyl pyridine exhibit excellent anti-proliferative activity against human cells with IC50 value in μM rang best than commercial anti-tumor drugs cis-platin so these new compounds are considered as a potential anti-tumor agents.[56] Zn complex of thiosemicarbazone of 2-acetyl pyridine containing 1-(4-florophenyl)-piprazinyl ring display excellent anti-proliferative activity with IC50 value 26-90nM against all cell line than cis-platin with IC50 2-17μM.[57]

Complex of ruthenium II with thiosemicarbazone of 2-acety pyridine are the first water soluble anti-proliferative activity against overian carcinoma cell line 41M with IC50 0.87μM and against breast cancer cell line SK-BR-3 with IC50 value 39μM.[58] Trisubstituted pyridine bearing substituents at 2-, 4- and 6-position containing 5, 6-dihydrobenzo[h]quonoline were experimentally obtained and were subjected to biological tests for topo I and II (topoisomerase I and II) inhibition. Topo I and II are enzymes responsible to control alteration occur in DNA structure. The results thus obtained showed that four of these compounds 42-45 in the entire series were significantly active in topo I inhibition in reasonable (100 μM) concentration. The activity showed by these compounds was proved to be comparable to Camptothecin and etoposide, which as well-known topo I and II inhibitors. The compound of type 39 is the most

effective topo I inhibitor. These compounds contain substituents such as 2-thienyl, 2- or 3-furyl, or 3-thienyl at 2- or 4-position on central pyridine. The crucial role in topo I or II inhibitory activity, observed for these compounds is regarded as a function of these functional groups. In addition to inhibitory activity these compounds were examined for their cytotoxicity, which indicates that they show moderate cytotoixcity. The optimal level of IC_{50} values was in the range of 10–60 μM, this level is approximately ten times lesser potent than the standard [65].

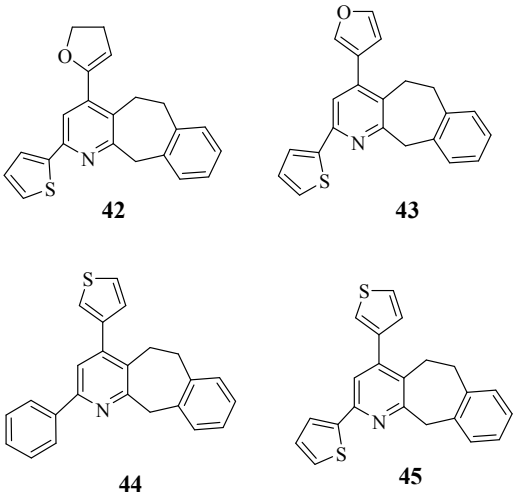


Figure 17. *Topoisomerase I and II inhibitors.*

Copper(II) complex of nitrogen containing heterocyclic thiosemicarabazone inhibite topo isomeraseII and proliferatin of breast cancer cell line.[66] 4-pyridyl anilinothioaazol (PAT) is used intreatment of renal cell carcinomas against Von Hippel Lindall (VHL) tumor activated and this will provide to a novel chemotype a target aproch for treatment of RCC [69].

5.6. Anti-Malarial Agents

Some compounds 35 and 36 of pyridine quinoline as hybrid molecules were tasted for their anti-malarial activities (against a chloroquine-susceptible strain of Plasmodium falciparum) the results showed that these molecules are poor anti-malarial activity. These compounds give a clue that they can be used as templates for designing new anti-malarial drugs and their activities can be improved. These molecules also showed haem polymerization inhibition (HPIA) activities [7].

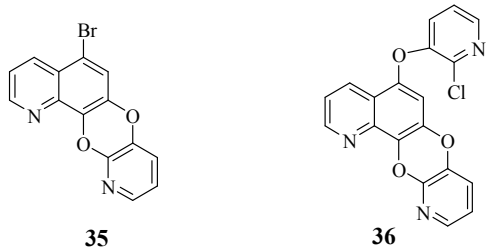


Figure 13. *Macromolecular structures containing pyridine.*

5.7. Anti-Inflammatory Agents

A group of imidazo[1,2-a]pyridine derivatives have been synthesized similar to compound **37**, the same exhibit anti-inflammatory activities [59].

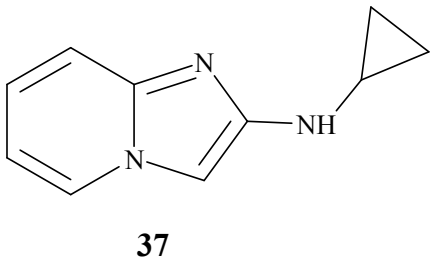


Figure 14. *Pyridine derivative as portent Anti-inflammatory agent.*

2-acetyl pyridine and 4-acetyl pyridine condence with some amide have excellent anti-inflammatory activity [60].

5.8. Analgesic Potency

Some heterocyclic compounds shown in Figure 14, containing pyridine nucleolus were synthesized and tasted for analgesic activity, compounds represented below 38-40 showed comparable analgesic activity to the standard drug (pentazocine). The mecamylamine on heterocyclic ring was observed as activity retardant [12].

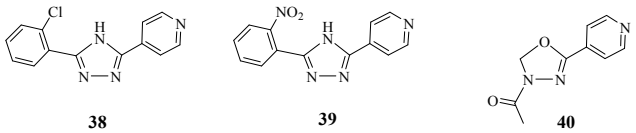


Figure 15. *Pyridine derived compounds used as analgesic.*

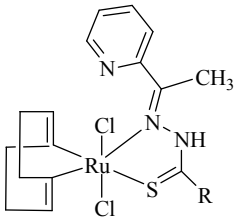
2-acetyl pyridine and 4-acetyl pyridine condence with some amide have excellent anti-inflammatory activity.[60]

5.9. Psychopharmacological Antagonistic

1,10-di(4-octylaminopyridinium-1)decane dichloride $[Cr(ox)_2(2\text{-(aminomethyl)pyridine}]^-$ complex have bioavailability for biomolecules due to its solubility in aqueous medium. The presence of functional group is of prime importance as these groups are capable of establishing bond with other biomolecules. Derivatives of 6-methyl-2-(phenylethynyl)-pyridine (MPEP) possess psychopharmacological antagonistic activities against nicotin [61].

5.10. Anti-Amoebic Agents

Some ligands which is derived from acetyl pyridine have anti-amoebic activity, however, when this ligands is coupled with ruthenium(II) to afford a complex, the anti-amoebic activity drastically increase. The complex 41 show high anti-amoebic activity compared with commercially available standard drug, metronidazole [62].



41

Figure 16. *Ruthenium complex as anti-amoebic agent.*

Bi-nuclear complex of vanadium containing 2-acetylpyridine exhibit execellent ameobocidal activity with IC50 value 1.68-0.40 then commercial drugs metromidazole with IC50 value 1.81 but ligand itself have no activity against amoeba.[62]

Anti-arhythmatic activity; The pyridine and pyrimidine derivatives can easily be fused with thiophine moiety. When the resultant compounds were further tested for antiarrhythmic activities, results revealed that they have antiarrhythmic activity better than Procaine amide and Lidocaine as standard antiarrhythmic agents [64].

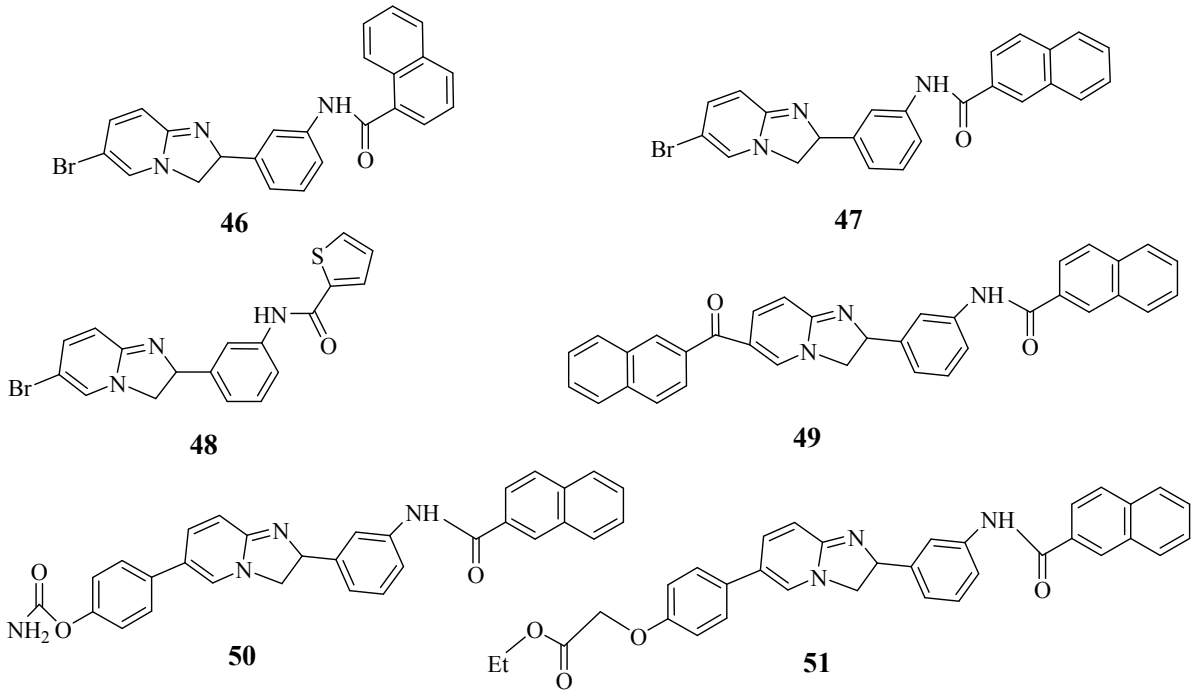
Anti-staphylococcal agents; 3-aminopyridine a derivatives of pyridine undergo polymerization and the resulted polymer show antistaphylococcal activity. Results obtained show that the 3-aminopyridine when applied in free state, was inactive. Its polymer has antistaphylococcal activity small oligomers were found more efficient. It showed that the antibacterial activity of the polymer is molecular weight dependent [6].

5.11. Iron Overload Disease

The pyridine derivative, pyridine-2-carboxaldehydeisonicotinoylhydrazone (PCIH) make considerably stable complex with iron, the resulted compounds is a chelator. The ligands derivatives independently are used as medicine in iron overload disease. Ligands equivalent activities as standard drug, desferrioxamine (DFO) [67].

5.12. Enzyme Inhibition

The benzoimidazole derivatives containing pyridine ring show gastric H+/K+-ATPase inhibitory activity [68]. A series of imidazo[1,2-a]pyridine derivatives were synthesized in which six compounds 46-51 have the ability to inhibit acyl-CoA (cholesterol acyltransferase) [5, 70].



46 **47** **48** **49** **50** **51**

Figure 18. *Acyl-CoA inhibitors derived from pyridine.*

6. Conclusion

Pyridine derivatives are very important chemicals with tremendous biological application. In medicinal applications these compounds share an important part. Pyridine derivatives have moderate to excellent activities against number of biological targets. With changing substituents on the pyridine nucleus the biological targets vary from microbial diseased to viral problems and variety of cancerous cells. Pyridine derivatives target different biological problems by interacting with enzymes, proteins and DNA.

References

[1] Henry, G. D. *Tetrahedron*. 2004, 60, 6043-6061.

[2] Gómez, I.; Alonso, E.; Ramón, D. J.; Yus, M. *Tetrahedron*. 2000, 56, 4043-4052.

[3] Lakshmi Kantam, M.; Mahendar, K.; Bhargava, S. *Journal of Chemical Sciences*. 2010, 122, 63-69.

[4] Busto, E.; Gotor-Fernández, V.; Gotor, V. *Tetrahedron: Asymmetry*. 2005, 16, 3427-3435.

[5] Jin, Y.; Rho, M. C.; Gajulapati, K.; Jung, H. Y.; Boovanahalli, S. K.; Lee, J. H.; Song, G. Y.; Choi, J. H.; Kim, Y. K.; Lee, K. *Bulletin of the Korean Chemical Society* 2009, 30, 1297.

[6] Akgul, C.; Yildirim, M. *Journal of the Serbian Chemical Society*. 2010, 75, 1203-1208.

[7] Narayan Acharya, B.; Thavaselvam, D.; Parshad Kaushik, M. *Medicinal Chemistry Research*. 2008, 17, 487-494.

[8] Jachak, M. N.; Bagul, S. M.; Birari, D. R.; Ghagare, M. G.; Kazi, M. A.; Toche, R. B.; Mathad, V. T. *Journal of fluorescence*. 2010, 20, 787-796.

[9] Toche, R. B.; Kazi, M. A.; Ghotekar, B. K.; Bagul, S. M.; Tantak, C. D.; Jachak, M. N. *Journal of fluorescence*. 2009, 19, 1119-1124.

[10] Drabina, P.; Funk, P.; Růžička, A.; Hanusek, J.; Sedlák, M. *Transition Metal Chemistry*. 2010, 35, 363-371.

[11] El-Essawy, F.; Hawatta, M.; Abdel-Megied, A. E. S.; El-Sherbeny, D. *Chemistry of Heterocyclic Compounds*. 2010, 46, 325-333.

[12] Nigade, G.; Chavan, P.; Deodhar, M. *Medicinal Chemistry Research*. 2010, 1-11.

[13] Al-Salahi, R. A.; Al-Omar, M. A.; Amr, A. E. G. E. *Molecules*. 2010, 15, 6588-6597.

[14] Jun'ichi Uenishi; Hamada, M.; Aburatani, S.; Matsui, K.; Yonemitsu, O.; Tsukube, H. *The Journal of Organic Chemistry*. 2004, 69, 6781-6789.

[15] Nagababu, P.; Kumar, D. A.; Reddy, K. L.; Kumar, K. A.; Mustafa, M. B.; Shilpa, M.; Satyanarayana, S. *Metal-Based Drugs*. 2008, 24, 1-8.

[16] Altaf, A. A.; Badshah, A.; Khan, N.; Marwat, S.; Ali, S. *Journal of Coordination Chemistry*. 2011, 64, 1815-1836.

[17] Liu, Y. Q.; Yang, L.; Tian, X. *Medicinal Chemistry Research*. 2007, 16, 319-330.

[18] Sidhaye, R.; Dhanawade, A.; Manasa, K.; Aishwarya, G. *Curr Pharma Res CPR*. 2011, 1, 135-139.

[19] Ammar, Y. A.; Mohamed, Y.; El-Sharief, A.; El-Gaby, M.; Abbas, S. *Chemical Sciences Journal*. 2011, 2011,

[20] Kumar, P. P.; Rani, B. *International Journal of ChemTech Research*. 2011, 3, 155-160.

[21] Long, C.; Si-Jia, X.; Zhi-Kun, F.; An-Qin, Y.; Yang, X. *Chinese Journal of Structural Chemistry* 2009, 28, 990-994.

[22] Yang, X. T.; Wu, H.; Ma, S. J.; Hu, J. J.; Wang, Y. *Transition Metal Chemistry*. 2011, 1-5.

[23] Chavan, V.; Sonawane, S.; Shingare, M. ; Karale, B. *Chemistry of Heterocyclic Compounds*. 2006, 42, 625-630.

[24] Savchenko, V.; Dorokhov, V.; Yakushchenko, I.; Zyuzin, I.; Aldoshin, S. *Herald of the Russian Academy of Sciences*. 2010, 80, 149-154.

[25] Zav'yalova, V.; Zubarev, A.; Shestopalov, A. *Russian Chemical Bulletin*. 2009, 58, 1939-1944.

[26] Naik, T.; Chikhalia, K. *e-Journal of Chemistry*. 2007, 4, 60-66.

[27] Mashaly, M. M.; Abd-Elwahab, Z. H.; Faheim, A. A. *Journal-Chinese Chemical Society Taipei.* 2004, 51, 901-916.

[28] Sabet, R.; Fassihi, A.; Moeinifard, B. *Research in Pharmaceutical Sciences*. 2009, 2, 103-112.

[29] Zheng, Y.; Ma, Z.; Zhang, X.; Yang, N.; Yang, G. *International Journal of Chemistry*. 2011, 3, 42-46.

[30] Patel, N. B.; Agravat, S. N.; Shaikh, F. M. *Medicinal Chemistry Research*. 2011, 20, 1033-1041.

[31] Nassar, E. *Journal of American Science*. 2010, 6, 338-347.

[32] Makawana, J. A.; Patel, M. P. ; Patel, R. G. *Medicinal Chemistry Research*. 2011, 1-8.

[33] Rajput, C. S.; Sharma, S. *International Journal of Pharma and Bio Sciences*. 2011, 2, 200-209.

[34] Amr, A. E. G. E.; Mohamed, A. M.; Ibrahim, A. A. *Zeitschrift Fur Naturforschung B*. 2003, 58, 861-868.

[35] Mohamed, S. F.; Youssef, M. M.; Amr, A. ; Kotb, E. R. *Scientia pharmaceutica*. 2008, 76, 279-303.

[36] Muthal, N.; Ahirwar, J.; Ahriwar, D.; Masih, P.; Mahmdapure, T.; Sivakumar, T. *Synthesis*. 2010, 2, 2450-2455.

[37] Abele, E.; Abele, R.; Lukevics, E. *Chemistry of heterocyclic compounds*. 2003, 39, 825-865.

[38] El-Hawash, S. A. M.; Abdel Wahab, A. E.; El-Demellawy, M. A. *Archiv der Pharmazie*. 2006, 339, 14-23.

[39] Vrábel, M.; Hocek, M.; Havran, L.; Fojta, M.; Votruba, I.; Klepetářová, B.; Pohl, R.; Rulíšek, L.; Zendlová, L.; Hobza, P.; Shih, I. h.; Mabery, E.; Mackman, R. *European Journal of Inorganic Chemistry*. 2007, 2007, 1752-1769.

[40] Worachartcheewan, A.; Prachayasittikul, S.; Pingaew, R.; Nantasenamat, C.; Tantimongcolwat, T.; Ruchirawat, S.; Prachayasittikul, V. *Medicinal Chemistry Research*. 2011, 1-9.

[41] Easmon, J.; Pürstinger, G.; Thies, K.-S.; Heinisch, G. ; Hofmann, J. *Journal of Medicinal Chemistry*. 2006, 49, 6343-6350.

[42] Kovala-Demertzi, D.; Alexandratos, A.; Papageorgiou, A.; Yadav, P. N.; Dalezis, P.; Demertzis, M. A. *Polyhedron*. 2008, 27, 2731-2738.

[43] Illán-Cabeza, N. A.; Jiménez-Pulido, S. B.; Martínez-Martos, J. M.; Ramírez-Expósito, M. J. ; Moreno-Carretero, M. N. *Journal of Inorganic Biochemistry*. 2009, 103, 1176-1184.

[44] Firke, S.; Firake, B.; Chaudhari, R.; Patil, V. *Asian Journal of Research in Chemistry*. 2009, 2, 157-161.

[45] Pingaew, R.; Prachayasittikul, S.; Ruchirawat, S. *Molecules*. 2010, 15, 988-996.

[46] Bassyouni, F. A.; Tawfik, H. A.; Soliman, A. M.; Rehim, M. A. *Research on Chemical Intermediates*. 2011, 1-20.

[47] Kowol, C. R.; Berger, R.; Eichinger, R.; Roller, A.; Jakupec, M. A.; Schmidt, P. P.; Arion, V. B.; Keppler, B. K. *Journal of Medicinal Chemistry*. 2007, 50, 1254-1265.

[48] Kowol, C. R.; Trondl, R.; Heffeter, P.; Arion, V. B.; Jakupec, M. A.; Roller, A.; Galanski, M.; Berger, W.; Keppler, B. K. *Journal of Medicinal Chemistry*. 2009, 52, 5032-5043.

[49] Li, R.-Y.; Wang, B.-W.; Wang, X.-Y.; Wang, X.-T.; Wang, Z.-M.; Gao, S. *Inorganic Chemistry*. 2009, 48, 7174-7180.

[50] Richardson, D. R.; Kalinowski, D. S.; Richardson, V.; Sharpe, P. C.; Lovejoy, D. B.; Islam, M.; Bernhardt, P. V. *Journal of Medicinal Chemistry*. 2009, 52, 1459-1470.

[51] Basha, M. T.; Chartres, J. D.; Pantarat, N.; Akbar Ali, M.; Mirza, A. H.; Kalinowski, D. S.; Richardson, D. R.; Bernhardt, P. V. *Dalton Transactions*. 2012,

[52] Filak, L. K.; Mühlgassner, G.; Bacher, F.; Roller, A.; Galanski, M.; Jakupec, M. A.; Keppler, B. K.; Arion, V. B. *Organometallics*. 2010, 30, 273-283.

[53] Jansson, P. J.; Sharpe, P. C.; Bernhardt, P. V.; Richardson, D. R. *Journal of Medicinal Chemistry*. 2010, 53, 5759-5769.

[54] Maity, B.; Roy, M.; Banik, B.; Majumdar, R.; Dighe, R. R. ; Chakravarty, A. R. *Organometallics*. 2010, 29, 3632-3641.

[55] Ali, A. A.; Nimir, H.; Aktas, C.; Huch, V.; Rauch, U.; Schäfer, K.-H.; Veith, M. *Organometallics*. 2012, 31, 2256-2262.

[56] Kovala-Demertzi, D.; Galani, A.; Kourkoumelis, N.; Miller, J. R.; Demertzis, M. A. *Polyhedron*. 2007, 26, 2871-2879.

[57] Stanojkovic, T. P.; Kovala-Demertzi, D.; Primikyri, A.; Garcia-Santos, I.; Castineiras, A.; Juranic, Z.; Demertzis, M. A. *Journal of Inorganic Biochemistry*. 2010, 104, 467-476.

[58] Grguric-Sipka, S.; Kowol, C. R.; Valiahdi, S.-M.; Eichinger, R.; Jakupec, M. A.; Roller, A.; Shova, S.; Arion, V. B.; Keppler, B. K. *European Journal of Inorganic Chemistry*. 2007, 2007, 2870-2878.

[59] Márquez-Flores, Y. K.; Campos-Aldrete, M. E.; Salgado-Zamora, H.; Correa-Basurto, J.; Meléndez-Camargo, M. E. *Medicinal Chemistry Research*. 2011, 1-8.

[60] Sondhi, S. M.; Dinodia, M.; Kumar, A. *Bioorganic & Medicinal Chemistry*. 2006, 14, 4657-4663.

[61] Kita, E.; Lisiak, R. *Transition Metal Chemistry*. 2010, 35, 441-450.

[62] Bharti, N.; Maurya, M. R.; Naqvi, F.; Azam, A. *Bioorganic & Medicinal Chemistry letters*. 2000, 10, 2243-2245.

[63] Maurya, M. R.; Agarwal, S.; Abid, M.; Azam, A.; Bader, C.; Ebel, M.; Rehder, D. *Dalton Transactions*. 2006, 937-947.

[64] Amr, A. G. E. S.; Abdel-Hafez, N. A. S.; Mohamed, S. F.; Abdalla, M. M.; Dokki, C. E. *Turkish Journal of Chemistry*. 2009, 33, 421-432.

[65] Lim, J. T.; Piazza, G. A.; Han, E. K.-H.; Delohery, T. M.; Li, H.; Finn, T. S.; Buttyan, R.; Yamamoto, H.; Sperl, G. J.; Brendel, K. *Biochemical Pharmacology*, 1999, 58, 1097-1107.

[66] Zeglis, B. M.; Divilov, V.; Lewis, J. S. *Journal of Medicinal Chemistry*. 2011, 54, 2391-2398.

[67] Chaston, T. B.; Richardson, D. R. *Journal of Biological Inorganic Chemistry*. 2003, 8, 427-438.

[68] Cho, S. Y.; Kang, S. K.; Kim, S. S.; Cheon, H. G.; Choi, J. K.; Yum, E. K. *Bulletin-Korean Chemical Society*. 2001, 22, 1217-1223.

[69] Hay, M. P.; Turcotte, S.; Flanagan, J. U.; Bonnet, M.; Chan, D. A.; Sutphin, P. D.; Nguyen, P.; Giaccia, A. J.; Denny, W. A. *Journal of Medicinal Chemistry*. 2009, 53, 787-797.

[70] López-Martínez, M.; Salgado-Zamora, H.; San-Juan, E. R.; Zamudio, S.; Picazo, O.; Campos, M. E.; Naranjo-Rodriguez, E. B. *Drug Development Research*. 2010, 71, 371-381.