Available online at www.derpharmachemica.com

ISSN 0975-413X
CODEN (USA): PCHHAX

Der Pharma Chemica, 2016, 8(15):207-212
(http://derpharmachemica.com/archive.html)

Synthesis and Biological evaluation of new 4-amino tetrazolo[1,5-*a*]quinoline

Priya M. Madalageri[a]*, V. Rajinikanth[a], Sakey Ravindra[a], K. Mahesh Kumar[b] and O. Kotresh[c]

[a]*Department of Physics, University of South Africa, Johannesburg-1709, South Africa*
[b]*Department of Civil and Chemical Engineering, University of South Africa, Johannesburg-1709, South Africa*
[c]*Department of Chemistry, Karnatak Science College, Dharwad-580001, Karnataka, India*

ABSTRACT

A series of new 4-amino tetrazolo[1,5-a]quinolones ***4(a-o)*** *are synthesised from 4-chloro tetrazolo[1,5-a]quinolines. The synthesized compounds were characterized through FT-IR, Mass spectrometry, ^{1}H NMR and ^{13}C NMR. These synthesized compounds have been screened for antimicrobial activity against S. aureus, E. coli and A. niger, A. alternata. Compounds* ***(4a, 4e, 4f, 4g, 4j, 4m)*** *were highly active against S.aureus and E. coli with less MIC.*

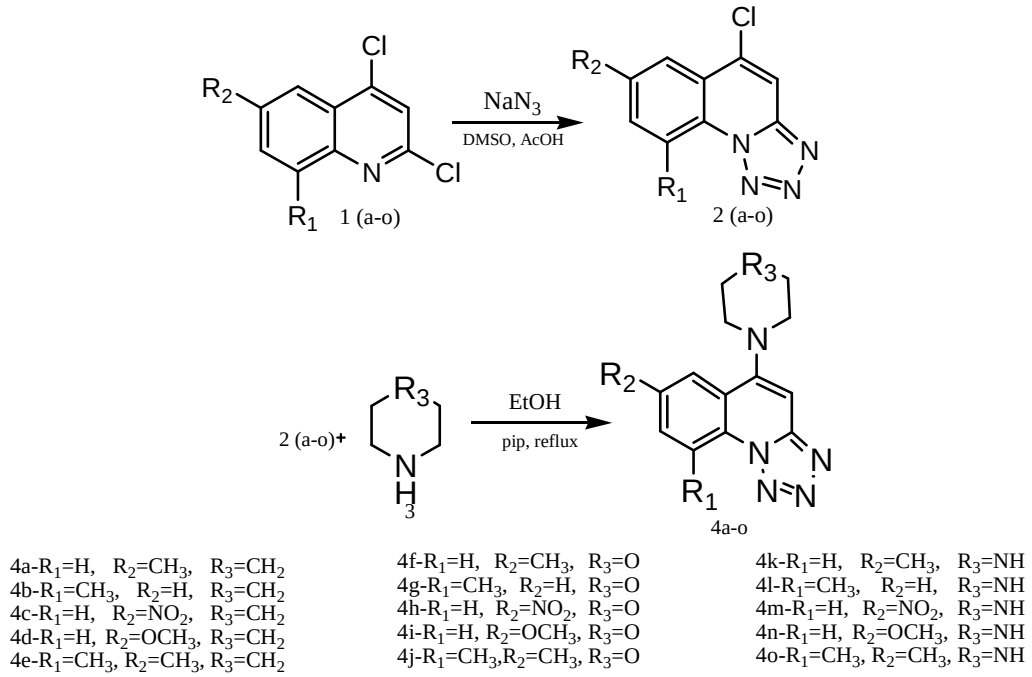
Keywords:4-amino tetrazolo[1,5-*a*]quinolones, 4-chloro tetrazolo[1,5-*a*]quinolones, Antimicrobial Studies.

INTRODUCTION

Tetrazoles are increasingly popular functionality with wide-ranging applications. Over the past few years, the interest in tetrazole chemistry has been rapidly increasing, mainly due to the role played by these heterocyclic compounds in medicinal chemistry for example, as HIV, sartane drug family, in coordination chemistry as ligand), in material science as polymers, and explosive agents[1].

Tetrazoles are a class of heterocycles with a wide range of applications, and they are receiving considerable attention [2]. This functional group is regarded as biologically equivalent to the carboxylic acid in medicinal chemistry, [3] such as polydentate aromatic N-donor ligands in coordination chemistry, and in various material sciences, including specialty explosives, information recording systems, and photography[4,5]

This tetrazole is used in MTT assay to quantify the respiratory activity of live cells in cell culture, although it kills cells in the process [6,7].Tetrazoles and its derivatives are used for biological activities such as antibacterial, anti-inflammatory, antifungal, antiviral, antitubercolous, cyclo-oxygenase inhibitors, antinociceptive, hypoglycemic and anticancer activities. They are used as catalyst in the synthesis of phosphonates [8] There is considerable and continuing interest in the chemistry of five-member N-heterocycles [9] Five-member nitrogen heterocycles are structural fragments of a series of biologically active compounds, [10] pesticides,[11] corrosion inhibitors, pigments,[12] products of petroleum refining, [13-15] and other industrial chemicals. The tetrazolic acid fragment –CN_4H has similar acidity to the carboxylic acid group –CO_2H, and the two are almost isosteric, but the former is metabolically more stable [16,17]. Hence, replacement of – CO_2H groups by –CN_4H in biologically active molecules is a research area of major interest [18]. It is this property that makes it possible to use tetrazole as isosteric substituents of various functional groups in the development of biologically active substances. Tetrazoles are an increasingly popular functionality with wide ranging applications. Interest in tetrazole chemistry over the past few years has been increasing rapidly, mainly as a result of the role played by this heterocyclic functionality in medicinal chemistry as these offer a more favorable pharmacokinetic.



4a-R_1=H, R_2=CH_3, R_3=CH_2
4b-R_1=CH_3, R_2=H, R_3=CH_2
4c-R_1=H, R_2=NO_2, R_3=CH_2
4d-R_1=H, R_2=OCH_3, R_3=CH_2
4e-R_1=CH_3, R_2=CH_3, R_3=CH_2

4f-R_1=H, R_2=CH_3, R_3=O
4g-R_1=CH_3, R_2=H, R_3=O
4h-R_1=H, R_2=NO_2, R_3=O
4i-R_1=H, R_2=OCH_3, R_3=O
4j-R_1=CH_3,R_2=CH_3, R_3=O

4k-R_1=H, R_2=CH_3, R_3=NH
4l-R_1=CH_3, R_2=H, R_3=NH
4m-R_1=H, R_2=NO_2, R_3=NH
4n-R_1=H, R_2=OCH_3, R_3=NH
4o-R_1=CH_3, R_2=CH_3, R_3=NH

Scheme 1 Synthesis of 4-amino tetrazolo-quinolines 4(a-o)

MATERIALS AND METHODS

Melting points were determined in open capillaries and are uncorrected. The FT-IR spectra were recorded on Nicolet Impact 5200 USA FT-IR using KBr pellets. ^{1}H NMR spectra in DMSO-$d_6$solution were recorded on Bruker 300-MHz NMR spectrometer. The mass spectra were recorded on Shimadzu Japan QP2010 S model spectrometer and elemental analyses were carried out using Heraus CHN rapid analyzer. All the compounds gave satisfactory elemental analysis. 7-carbethoxyamino-4-bromomethyl coumarin was prepared by Pechman condensation using 3-carbethoxyamino phenol. The purity of the compounds was checked by thin layer chromatography (TLC) on silica gel plate.

Synthesis of 7-methyl-5-(piperdin-1-yl)tetrazolo[1,5-*a*]quinoline (4a)

A mixture of (3.0 mmol) of proper chloro derivative **2(a-o)**, secondary amine **3** (30.0 mmol) and ethanol (100 mL) was stirred at room temperature for 2 h. The progress of the reaction was monitored by TLC. The solution obtained was poured into water (250 mL) and the mixture exhaustively extracted with chloroform. The combined extracts, after drying and removal of solvents, afforded an oily or nearly solid residue which, in most cases, treated with a little ethyl ether to give pure compound**4**which was then crystallized from the suitable solvents.

7-methyl-5(piperidin-1-yl)tetrazolo[1,5-a]quinoline (4a)

Dark yellow solid (ethyl acetate+Chloroform), m.p. 182 ^{o}C, yield 74%; IR (KBr, υ in cm^{-1}) 1660.4 (C=N); 1466.4 (C-N); ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 1.72-4.49 (*m*, 10H, pip, CH_2's), 2.52 (*s*, 3H, CH_3), 6.73 (*s*, 1H, 3-CH), 7.99-9.05 (*m*, 3H, Ar H); MS *m/z*: 267 [M^+]; Anal. Calc. for $C_{15}H_{17}N_5$; C, 67.39; H, 6.41; N, 26.20; Found: C, 67.34; H, 6.46; N, 26.23.

9-methyl-5(piperidin-1-yl)tetrazolo[1,5-a]quinoline (4b)

Dark yellow solid (ethyl acetate+Chloroform), m.p. 176 ^{o}C, yield 78%; IR (KBr, υ in cm^{-1}) 1658.4 (C=N); 1453.4 (C-N); ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 1.73-4.52 (*m*, 10H, pip, CH_2's), 2.56 (*s*, 3H, CH_3), 6.69 (*s*, 1H, 3-CH), 7.83-9.27 (*m*, 3H, Ar H); MS *m/z*: 267 [M^+]; Anal. Calc. for $C_{15}H_{17}N_5$; C, 67.39; H, 6.41; N, 26.20; Found: C, 67.33; H, 6.42; N, 26.21.

7-nitro-5(piperidin-1-yl)tetrazolo[1,5-a]quinoline (4c)

Pale yellow solid (ethyl acetate), m.p. 169 ^{o}C, yield 73%; IR (KBr, υ in cm^{-1}) 1658.7 (C=N); 1457.3 (C-N); ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 1.79-4.67 (*m*, 10H, pip, CH_2's), 6.73 (*s*, 1H, 3-CH), 7.68-8.72 (*m*, 3H, Ar H); MS *m/z*: 298 [M^+]; Anal. Calc. for $C_{14}H_{14}N_6O_2$; C, 56.37; H, 4.73; N, 28.17; Found: C, 56.35; H, 4.72; N, 28.19.

7-methoxy-5(piperidin-1-yl)tetrazolo[1,5-a]quinoline (4d)
Dark brown solid (ethyl acetate+Chloroform), m.p. 175 ^{o}C, yield 73%; IR (KBr, υ in cm^{-1}) 1662.8 (C=N); 1451.2 (C-N); ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 1.78-4.28 (*m*, 10H, pip, CH_2's), 3.64 (*s*, 3H, OCH_3), 6.83 (*s*, 1H, 3-CH), 7.79-8.52 (*m*, 3H, Ar H); MS *m/z*: 283 [M^+]; Anal. Calc. for $C_{15}H_{17}N_5O$; C, 63.59; H, 6.05; N, 24.72; Found: C, 63.57; H, 6.02; N, 24.74.

7,9-dimethyl-5(piperidin-1-yl)tetrazolo[1,5-a]quinoline (4e)
Dark yellow solid (ethyl acetate+ethanol), m.p. 163 ^{o}C, yield 76%; IR (KBr, υ in cm^{-1}) 1646.7 (C=N); 1427.7 (C-N); ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm:1.78-4.62 (*m*, 10H, pip, CH_2's), 2.45, 2.53 (*s*, 6H, CH_3), 6.73 (*s*, 1H, 3-CH), 7.73-8.71 (*m*, 2H, Ar H); MS *m/z*: 281 [M^+]; Anal. Calc. for $C_{16}H_{19}N_5$; C, 68.30; H, 6.81; N, 24.89; Found: C, 68.33; H, 6.84; N, 24.86.

7-methyl-5-morpholinotetrazolo[1,5-a]quinoline (4f)
Dark brown solid (ethyl acetate), m.p. 172 ^{o}C, yield 77%; IR (KBr, υ in cm^{-1}) 1658.3 (C=N); 1443.3 (C-N); ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 3.25-4.29 (*m*, 8H, mor, CH_2's), 2.42 (*s*, 3H, CH_3), 6.62 (*s*, 1H, 3-CH), 7.62-8.66 (*m*, 3H, Ar H); MS *m/z*: 269 [M^+]; Anal. Calc. for $C_{14}H_{15}N_5O$; C, 62.44; H, 5.61; N, 26.01; Found: C, 62.41; H, 5.63; N, 26.03.

9-methyl-5-morpholinotetrazolo[1,5-a]quinoline (4g)
Dark brown solid (ethanol), m.p. 178 ^{o}C, yield 81%; IR (KBr, υ in cm^{-1}) 1646.2 (C=N); 1439.7 (C-N); ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 3.38-4.56 (*m*, 8H, mor, CH_2's), 2.45 (*s*, 3H, CH_3), 6.58 (*s*, 1H, 3-CH), 7.73-8.69 (*m*, 3H, Ar H); MS *m/z*: 269 [M^+]; Anal. Calc. for $C_{14}H_{15}N_5O$; C, 62.44; H, 5.61; N, 26.01; Found: C, 62.43; H, 5.65; N, 26.04.

7-nitro-5-morpholinotetrazolo[1,5-a]quinoline (4h)
Dark yellow solid (ethanol+chloroform), m.p. 182 ^{o}C, yield 69%; IR (KBr, υ in cm^{-1}) 1649.4 (C=N); 1438.3 (C-N); ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 3.41-4.63 (*m*, 8H, mor, CH_2's), 6.67 (*s*, 1H, 3-CH), 7.82-8.82 (*m*, 3H, Ar H); MS *m/z*: 300 [M^+]; Anal. Calc. for $C_{13}H_{12}N_6O_3$; C, 52.00; H, 4.03; N, 27.99; Found: C, 52.03; H, 4.05; N, 27.94.

7-methoxy-5-morpholinotetrazolo[1,5-a]quinoline (4i)
Dark yellow solid (chloroform), m.p. 185 ^{o}C, yield 78%; IR (KBr, υ in cm^{-1}) 1663.0 (C=N); 1427.7 (C-N); ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 3.39-4.27 (*m*, 8H, mor, CH_2's), 3.92 (*s*, 3H, OCH_3) 6.61 (*s*, 1H, 3-CH), 7.30-8.92 (*m*, 3H, Ar H); MS *m/z*: 285 [M^+]; Anal. Calc. for $C_{14}H_{15}N_5O_2$; C, 58.94; H, 5.30; N, 24.55; Found: C, 58.93; H, 5.32; N, 24.56.

7,9-dimethyl-5-morpholinotetrazolo[1,5-a]quinoline (4j)
Dark yellow solid (ethanol+chloroform), m.p. 176 ^{o}C, yield 75%; IR (KBr, υ in cm^{-1}) 1656.4 (C=N); 1449.4 (C-N); ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 3.52-4.58 (*m*, 8H, mor, CH_2's), 2.34, 2.57 (*s*, 6H, CH_3), 6.72 (*s*, 1H, 3-CH), 7.83-8.43 (*m*, 2H, Ar H); MS *m/z*: 283 [M^+]; Anal. Calc. for $C_{15}H_{17}N_5O$; C, 63.59; H, 6.05; N, 24.72; Found: C, 63.56; H, 6.07; N, 24.71.

7-methyl-5-(piperazin-1-yl)tetrazolo[1,5-a]quinoline (4k)
Dark yellow solid (ethanol+chloroform), m.p. 169 ^{o}C, yield 72%; IR (KBr, υ in cm^{-1}) 1647.8 (C=N); 1462.5 (C-N); 3342.2 (N-H) ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 1.73 (*s*, 1H, NH D_2O exchangeable), 2.51 (*b*, 4H, CH_2), 4.36 (*b*, 2H, CH_2), 4.43 (*b*, 2H, CH_2), 2.57 (*s*, 3H, CH_3), 6.82 (*s*, 1H, 3-CH), 7.83-8.43 (*m*, 3H, Ar H); MS *m/z*: 268 [M^+]; Anal. Calc. for $C_{14}H_{16}N_6$; C, 62.67; H, 6.01; N, 31.32; Found: C, 62.63; H, 6.04; N, 31.34.

9-methyl-5-(piperazin-1-yl)tetrazolo[1,5-a]quinoline (4l)
Dark yellow solid (ethanol+chloroform), m.p. 167 ^{o}C, yield 76%; IR (KBr, υ in cm^{-1}) 1647.4 (C=N); 1453.7 (C-N); 3347.9 (N-H) ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 1.75 (*s*, 1H, NH D_2O exchangeable), 2.54 (*b*, 4H, CH_2), 4.38 (*b*, 2H, CH_2), 4.38 (*b*, 2H, CH_2), 2.53 (*s*, 3H, CH_3), 6.82 (*s*, 1H, 3-CH), 7.86-8.53 (*m*, 3H, Ar H); MS *m/z*: 268 [M^+]; Anal. Calc. for $C_{14}H_{16}N_6$; C, 62.67; H, 6.01; N, 31.32; Found: C, 62.64; H, 6.03; N, 31.36.

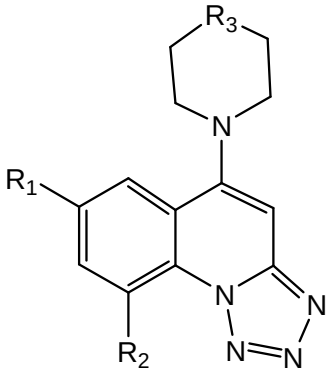
7-nitro-5-(piperazin-1-yl)tetrazolo[1,5-a]quinoline (4m)
Dark yellow solid (ethanol), m.p. 178 ^{o}C, yield 78%; IR (KBr, υ in cm^{-1}) 1647.8 (C=N); 1449.5 (C-N); 3342.7 (N-H) ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 1.76 (*s*, 1H, NH D_2O exchangeable), 2.48 (*b*, 4H, CH_2), 4.41 (*b*, 2H, CH_2), 4.48 (*b*, 2H, CH_2), 6.85 (*s*, 1H, 3-CH), 7.82-8.18 (*m*, 3H, Ar H); MS *m/z*: 299 [M^+]; Anal. Calc. for $C_{13}H_{13}N_7O_2$; C, 52.17; H, 4.38; N, 32.76; Found: C, 52.15; H, 4.35; N, 32.74.

7-methoxy-5-(piperazin-1-yl)tetrazolo[1,5-a]quinoline (4n)
Brown solid (ethanol), m.p. 183 ^{o}C, yield 72%; IR (KBr, υ in cm^{-1}) 1643.4 (C=N); 1438.9 (C-N); 3349.2 (N-H) ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 1.72 (*s*, 1H, NH D_2O exchangeable), 2.49 (*b*, 4H, CH_2), 4.43 (*b*, 2H, CH_2), 4.46 (*b*, 2H, CH_2), 2.47 (*s*, 3H, OCH_3)6.85 (*s*, 1H, 3-CH), 7.64-8.26 (*m*, 3H, Ar H); MS *m/z*: 284 [M^+]; Anal. Calc. for $C_{14}H_{16}N_6O$; C, 59.14; H, 5.67; N, 29.56; Found: C, 59.16; H, 5.65; N, 29.54.

7,9-dimethyl-5-(piperazin-1-yl)tetrazolo[1,5-a]quinoline (4o)
Brown solid (ethanol), m.p. 178 ^{o}C, yield 79%; IR (KBr, υ in cm^{-1}) 1647.2 (C=N); 1442.4 (C-N); 3341.7 (N-H) ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 1.76 (*s*, 1H, NH D_2O exchangeable), 2.42 (*b*, 4H, CH_2), 4.44 (*b*, 2H, CH_2), 4.49 (*b*, 2H, CH_2), 2.31, 2.38 (*s*, 6H, CH_3) 6.88 (*s*, 1H, 3-CH), 7.51-8.16 (*m*, 2H, Ar H); MS *m/z*: 284 [M^+]; Anal. Calc. for $C_{15}H_{18}N_6$; C, 63.81; H, 6.43; N, 29.77; Found: C, 63.83; H, 6.45; N, 29.74.

RESULTS AND DISCUSSION

The following 4-chloro tetrazoloquinolines have been employed during reaction with secondary amines in presence of ethanol was not used in an earlier.



4(a-o)

The IR spectrum of 7-methyl-5(piperidin-1-yl)tetrazolo[1,5-a]quinoline**(4a) (**R_1=CH_3, R_2=H, R_3=CH_2) showed the frequency at 1660.4 cm^{-1} which indicates the C=N peak and 1466.4 cm^{-1} indicates the C-N peak.

The ^{1}H-NMR spectrum of (**4a)** showed the multiplet in the range 1.79-4.49 due to piperidine protons, singlet at 2.52 ppm due to methyl protons, singlet at 6.73 is due to 3-CH proton and multiplet in the range 7.99-9.05 ppm due to aromatic protons. This was further confirmed by its mass spectrum which shows the molecular ion peak *m/z* 267 (M+) which agrees with the molecular weight of the compound.

The IR spectrum of 7-methoxy-5-morpholinotetrazolo[1,5-a]quinoline **(4i) (**R_1=OCH_3, R_2=H, R_3=O) showed the frequency at 1663.0 cm^{-1} which indicates the C=N peak and 1427.7 cm^{-1} due to C-N peak.

The ^{1}H-NMR spectrum of (**4i)** showed the multiplet around 3.39-4.27 ppm due to morpholine protons, singlet at 3.92 ppm due to methoxy protons, singlet at 6.61 ppm due to 3-CH proton, a multiplet in the range 7.30-8.92 ppm due to aromatic protons. This was further confirmed by its mass spectrum which shows the molecular ion peak *m/z* 285 (M+) which agrees with the molecular weight of the compound.

ANTIMICROBIAL STUDIES

Antibacterial screening

The anti-bacterial activity of the synthesised compounds **4(a-o)**were performed in vitro against *Staphylococcus aureus* and *Escherichia coli* by broth micro dilution method [19].

The MIC determination of the tested compounds was investigated in comparison with Ciprofloxacin. Double dilutions of the test compounds and reference drugs were prepared in Muller-Hinton agar. 10 mg of each test compounds were dissolved in 1 mL of (DMSO) separately to prepare stock solution. Further, progressive dilutions with melted Muller-Hinton agar were performed to obtain the required concentrations of 500, 250, 125, 62.5, 31.25, 16, 8, 4, 2, 1 μg/mL. the petri dishes were inoculated with 1-5 x 10^4 colony forming units (cfu/mL) and incubated at 37 ^{o} C for 18 hours.

The minimum inhibitory concentration (MIC) of the tested compound that yield no visible growth on the plate were recorded in Table 1. To ensure that the solvent had no effect on the bacterial growth, a control as performed with a test medium supplemented with DMSO at the same dilutions as used in the experiments.

Antifungal Screening

The anti-fungal activity of compounds **4(a-o)** was performed against the standard strains: *Aspergillus niger* and *Alternaria alternate* in DMSO by broth micro dilution method.

The MIC determination of the tested compounds was investigated in comparison with Amphotericin B by broth micro dilution method. Double dilutions of the test compounds and reference drugs were prepared in Sabouraud's dextrose broth. 10 mg of each test compounds were dissolved in 1 mL of (DMSO) separately to prepare stock solution.

Further, progressive dilutions with melted Sabouraud's dextrose agar were performed to obtain the required concentrations of 500, 250, 125, 62.5, 31.25, 16, 8, 4, 2, 1 µg/mL the petri dishes were inoculated with 1-5 x 10^4 colony forming units (cfu/mL) and incubated at 37 ^{o} C for 18 hours. The minimum inhibitory concentration (MIC) of the tested compound that yield no visible growth on the plate were recorded in Table 1. To ensure that the solvent had no effect on the fungal growth, a control as performed with a test medium supplemented with DMSO at the same dilutions as used in the experiments.

Table 1Results of Antimicrobial activities of compounds 4(a-o)

Antimicrobial Activity of compounds 4(a-o) MICs (µg/mL)				
	Antibacterial Activity		Antifungal Activity	
Compound	***S. aureus***	***E. coli***	***A. niger***	***A. alternata***
4a	08	16	31.25	62.5
4b	250	>500	250	125
4c	62.5	62.5	125	>500
4d	16	31.25	250	125
4e	08	08	31.25	16
4f	16	08	08	31.25
4g	31.25	31.25	04	08
4h	>500	>500	250	125
4i	125	62.5	62.5	125
4j	16	8	31.25	16
4k	31.25	62.5	16	16
4l	31.25	31.25	31.25	62.5
4m	08	08	62.5	31.25
4n	250	125	>500	250
4o	125	125	250	>500
Ciprofloxacin	01	01	--	--
Amphotericin B	--	--	01	01

CONCLUSION

The antibacterial data **(Table 1)** reveled that all the compounds exhibited moderate activity a few of them highly active, and very few of them are inactive against *Staphylococcus aureus* and *Escherichia coli*. Compounds **(4a, 4e, 4f, 4g, 4j, 4m)** were highly active against *S.aureus* and *E. coli* with less MIC. Many compounds exhibited with moderate activity. Highest activity was associated with di-methyl piperidine and 7-nitro piperizine substituents.

The antifungal screening activity data (Table 1) gives a spectrum of their activity and all of them showed moderate activity against *Aspergillus niger* and *Alternaria alternate*. The antifungal activity data reveal that compounds **4e, 4f, 4g, 4j, 4k** showed excellent activity against the test fungi and nearly equal to the standard amphotericin B.

Acknowledgement

The authors are thankful to the USIC for providing some spectral analyses. The authors are grateful to The Principal, Karnatak Science College for providing necessary facilities for conducting part of this work and they are also thankful for the UNISA.

REFERENCES

[1] Hossein Naeimi, FatemehKiani, Mohsen Moradian, *J Nanopart Res*., **2014**, 16:2590.

[2] (a) Butler, R. N. In Comprehensive Heterocyclic Chemistry; A. R. Katritzky, C. W. Rees, E. F. V. Scriven (Eds.); Pergamon: Oxford, UK, **1996**; vol. 4; (b) Valentina, A.; Gottfried, S. *Angew. Chem., Int. Ed***. 2007**, 46, 8440–8444.

[3] (a) Singh, H.; Chawla, A. S.; Kapoor, V. K.; Paul, D.; Malhotra, R. K. Prog. *Med. Chem***. 1980**, 17, 151–183; (b) Juby, P. F.; Hudyma, T. W.; Brown, M. Steroids, *J. Med. Chem*. **1968**, 11, 111–117.
[4] (a) Wang, L. Z.; Qu, Z. R.; Zhao, H.; Wang, X. S.; Xiong, R. G.; Xue, Z. L. *Inorg. Chem***. 2003**, 42, 3969–3971; (b) Dinca, M.; Dailly, A.; Liu, Y.; Brown, C. M.; Neumann, D. A.; Long, J. R. *J. Am. Chem. Soc.***2006**, 128, 16876–16883.
[5] (a) Ostrovskii, V. A.; Pevzner, M. S.; Kofmna, T. P.; Shcherbinin, M. B.; Tselinskii, I. V. *Targets Heterocycl.Syst.***1999**, 3, 467–526; (b) Koldobskii, G. I.; Ostrovskii, V. A. *Tetrazoles.Usp.Khim*.**1994**, 63, 797–814.
[6] Dahlof B, Deveruex RB, Kjeldsen SE. *Lancet***2002**; 359(9311): 995-1003.
[7]Bhalla Y, Puri E, Monga P, Sapra S. *Innovations in Pharmacy Plane***, 2013**, 1(1): 20-30.
[8] Mohite PB, Bhaskar VH. *Inter J Pharm Tech Res*. **2011**; 3(3): 1557-1566
[9] Wong, Ming Wah, Leung-Toung, Regis,Wentrup. *Curt. J Am Chem Soc*. **1993**; 115(6): 2465-72.
[10] Nelson, David L, Lehninger, Albert Lester, Cox, Michael M. Lehninger principles of biochemistry. Macmillan; **2008**.
[11] Brooks GT, Roberts T. Pesticide Chemistry and Biosciences: The Food Environment Challenge *Royal Society Of Chemistry*, Cambridge; **1999**.
[12]Davarski KA, Khalachev NK, Yankova RZ, Raikov S. *Chem Heterocycl Compd*. **1998**; 34: 568.
[13]Balabin RM, Syunyaev RZ, Karpov SA. *Energy Fuels***2007**; 21: 2460.
[14]Syunyaev Z, Balabin RM, Akhatov IS, Safieva JO. *Energy Fuels, and chemicals. Academic press,* **2009**; 23: 1230.
[15]Balabin RM, Syunyaev RZ. *J. Colloid Interface Sci*.**2008**; 318: 167.
[16]Bugalho SCS, Macoas EMS, Cristiano MLS, Fausto R. *Phys ChemChem Phys*. **2001**; 3(17): 3541.
[17] Singh H, Chawla AS, Kapoor VK, Paul D, Malhotra RK. *Prog Med Chem*. **1980**; 17: 151.
[18]Noda K, Saad Y, Kinoshita A, Boyle TP, Graham RM, Husain A, Karnik SS. *J Biol Chem*. **1995**; 270: 1284628514.
[19] M. Basanagouda, K. Shivshankar, M. V. Kulkarni, Vijaykumar P. Rasal, Harishchandra Patel, Sumit S. Mutha, Ashwini A. Mohite; *European Journal of Medicinal Chemistry*; **2010**, 45, 1151–1157.