ISSN: 2320 - 4230

Journal of Drug Discovery and Therapeutics
Available Online at www.jddt.in
CODEN: - JDDTBP (Source: - American Chemical Society)
Volume 3, Issue 28, May, 2015, 39-44

Research Article

SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL SCREENING OF NOVEL SERIES OF BIS-IMIDAZO[1,2-a]PYRIDINE DERIVATIVES

Gollapalli Naga Raju[1], Karumudi Bhavya Sai*[2], Jagarlamudi Rajarajeswari[2], Varanasi Vasanthi Krishna Priya, Pendyala Vandana[1], Rama Rao Nadendla[1]

[1]Department of Pharmaceutical Analysis
[2]Department of Pharmacy Practice
Chalapathi Institute of Pharmaceutical Sciences, Guntur, India.

Received 04 May 2015; Accepted 16 May 2015

ABSTRACT

A novel series of Bis-imidazo[1,2-a]pyridine derivatives were synthesized from 2-(4-Fluorophenyl)-6-methyl*H*-imidazo[1,2-*a*]pyridine. All the synthesized compounds have been characterized by using elemental analysis, FT-IR, ^{1}H NMR, ^{13}C NMR spectroscopy and further supported by mass spectroscopy. Purity of all the compounds has been checked on thin layer chromatographic plate and HPLC technique. All the synthesized compounds were tested for their antibacterial and antifungal activity (MIC) *in vitro* by broth dilution method with two Gram-positive bacteria, two Gram-negative bacteria and two fungal strains. The biological activities of the synthesized compounds have been compared with standard drugs Ampicillin and Greseofulvin. The compounds exhibited significant antibacterial and moderate antifungal activities. These compounds can be further exploited to get the potent lead compounds. The detailed synthesis and the antimicrobial screening of the new compounds are reported.

Keywords: Imidazo[1,2-a]pyridine, Antibacterial activity, Antifungal activity.

INTRODUCTION

Imidazo[1,2-a]pyridines, a novel class of pharmaceutical compounds exhibit a broad range of biological activities. Besides, imidazo[1,2-a]pyridine scaffold is found in a number of marketed drug formulations, such as zolimidine (an antiulcer drug), zolpidem (ahypnotic drug), and alpidem (a nonsedative anxiolytic). As a result, numerous reports have described the structural modifications of this scaffold with the aim of developing novel therapeutic agents. Bis imidazo[1,2-*a*]pyridine derivatives are important intermediates in organic synthesis, especially in the synthesis of biologically active and medicinally useful agents. For instance, they are widely used in the synthesis of cyclin-dependent kinases (CDK) inhibitors, sleep inducers, anticonvulsant agents, etc. It has long been known that imidazo [1, 2-a] pyridine derivatives exhibited diverse biological activities like antibacterial [1, 2], Antitumor [3, 4], Antiinflammatory [5, 6], antiviral [7, 8], anti malarial [9,] antifungal [10, 11], antimicrobial [12], antiprotozoal [13, 14] and antitubercular[15] agents.

Considering the above observations and in connection to previous publications involving the synthesis of new biologically active heterocycles. Thus the efficient synthesis novel series of Bis-imidazo[1,2-a]pyridine derivatives compounds still represent highly pursued target.

EXPERIMENTAL

Material and Methods:

Melting points were determined in open capillary tubes and are uncorrected. Formation of the compounds was checked by TLC on silica gel-G plates of 0.5 mm thickness and spots were located by iodine and UV light. All compounds were purified by recrystallization with suitable organic solvents. IR spectra were recorded on Brooker-ALPHA FT-IR instrument using KBr pellet method. Mass spectra were recorded on Shimadzu GC-MS-QP-2010 model using direct inlet probe technique. ^{1}H NMR and ^{13}C NMR was determined in $CDCl_3$ solution on a Bruker Ac 400 MHz spectrometer. Purity of the synthesized compounds was checked by HPLC Agilent. The results are in agreements with the structures assigned. Elemental analysis of the all the synthesized compounds was carried out on Euro EA 3000 elemental analyzer and the results are in agreements with the structures assigned.

Synthesis of 2-(4-Fluorophenyl)-6-methyl*H*-imidazo[1,2-*a*]pyridine: A solution of 5-methylpyridin-2-amine (1.08 g, 0.01 mol) in methanol (10 ml) was added to 2-chloro-1-(4-fluorophenyl)ethanone (1.72 g, 0.01 mol) and the reaction mixture was refluxed with stirring for 6 hour in the presence of catalytic amount of triethylamine. After the completion of reaction, cool the content, the solid separated was filtered and dried *in vacuo*. Yield 68%, M.P

*Corresponding author: Karumudi Bhavya Sai |E-mail: rajaneeraja@gmail.com

192^{0}C, Anal. Calcd. For $C_{14}H_{11}FN_2$: Require: C, 74.32, H, 4.90, N, 12.38 %; Found: C, 74.30, H, 4.89, N, 12.35%. MS: *m/z* = 226.

General procedure for the preparation of Bis imidazo[1,2-a]pyridine derivatives (BIP-1 TO BIP-10): To a mixture of 2-(4-fluorophenyl)-6-methyl*H*-imidazo[1,2-*a*]pyridine (4.52 g, 0.02 mol) and aromatic aldehydes (0.01 mol) in acetic acid (4 ml), sodium acetate 1.0 g was added and refluxed for 24 hour (monitoring by TLC). After cooling to room temperature, the reaction mixture was diluted with water and made basic with saturated sodium carbonate solution. The solution was extracted with dichloromethane and the organic layer was dried over anhydrous Na_2SO_4. After the solvent was evaporated, the residue was chromatographed on silica gel (eluent 6 : 4 = E.A. : Hexane) to give analytical pure products. The physical constants of the product are recorded in Table-1.

2-(4-Fluorophenyl)-3-((2-(4-fluorophenyl)-6-methyl*H*-imidazo[1,2-*a*]pyridin-3-yl)(*p*-tolyl) methyl)-6-methyl*H*-imidazo[1,2-*a*]pyridine(BIP-1): Purity by HPLC: 87 %; IR (KBr): 3069 (Ar, C-H str), 2920 (C-H str), 2862 (C-H str), 1616 (C=N str), 1534 (Ar, C=C str), 1464 (Ar, C=C str), 1340 (C-H ban), 1179 (C-N str), 1089 (C-F), 845 (C-H o.p. ban) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 2.34 (s, 3H, CH_3), 2.44 (s, 6H, CH_3), 5.34 (s, 1H, CH), 7.03-7.05 (m, 2H, ArH), 7.08-7.16 (m, 4H, ArH), 7.20-7.24 (m, 2H, ArH), 7.51-7.52 (d, *J*=7.16 Hz, 2H, ArH), 7.53-7.55 (d, *J*=9.2 Hz, 2H, ArH), 7.72-7.80 (m, 4H, ArH), 7.88-7.92 (m, 2H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 18.15, 21.74, 40.49, 107.54, 115.57, 115.78, 116.63, 122.41, 123.36, 127.59, 127.67, 28.31, 129.76, 144.30, 144.55, 163.91; MS: *m/z* = 554 [M]$^+$; Anal. Calcd for $C_{36}H_{28}F_2N_4$: C, 77.96; H, 5.09; N, 10.10. Found: C, 76.31; H, 4.87; N, 10.03%.

2-(4-Fluorophenyl)-3-((2-(4-fluorophenyl)-6-methyl*H*-imidazo[1,2-*a*]pyridin-3-yl) (thiophen-2-yl)methyl)-6-methyl*H*-imidazo[1,2-*a*]pyridine (BIP-2): Purity by HPLC: 84 %; IR (KBr): 3068, 2977, 2823, 1600, 1576, 1435, 1377, 1150, 1067, 840 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 2.52 (s, 6H, CH_3), 5.41 (s, 1H, CH), 6.54- 6.56 (m, 1H, ArH), 6.81-6.87 (m, 1H, ArH), 6.99-7.07 (m, 1H, ArH), 7.11-7.18 (m, 4H, ArH), 7.19-7.23 (m, 2H, ArH), 7.31-7.58 (m, 2H, ArH), 7.74-7.79 (m, 4H, ArH), 7.95- 7.99 (m, 2H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 19.17, 41.12, 104.24, 111.40, 111.78, 112.90, 126.67, 126.80, 127.44, 129.04, 139.64, 140.46, 146.93, 147.14, 164.33; MS: *m/z* = 546 [M]$^+$; Anal. Calcd for $C_{33}H_{24}F_2N_4S$: C, 72.51; H, 4.43; N, 10.25. Found: C, 71.78; H, 4.38; N, 10.07%.

2-(4-Fluorophenyl)-3-((2-(4-fluorophenyl)-6-methyl*H*-imidazo[1,2-*a*]pyridin-3-yl) (phenyl)methyl)-6-methyl*H*-imidazo[1,2-*a*]pyridine (BIP-3): IR (KBr): 3099, 2975, 2849, 1599, 1557, 1439, 1366, 1134, 1054, 842 cm^{-1}; MS: *m/z* = 541 [M+1]$^+$; Anal. Calcd for $C_{35}H_{26}F_2N_4$: C, 77.76; H, 4.85; N, 10.36. Found: C, 77.17; H, 4.71; N, 10.23%.

2-(4-Fluorophenyl)-3-((2-(4-fluorophenyl)-6-methyl*H*-imidazo[1,2-*a*]pyridin-3-yl)(4- nitrophenyl)methyl)-6-methyl*H*-imidazo[1,2-*a*]pyridine (BIP-4): IR (KBr): 3081, 2966, 2843, 1634, 1584, 1446, 1366, 1240, 1138, 1031 cm^{-1}; MS: *m/z* = 585 [M]$^+$; Anal. Calcd for $C_{35}H_{25}F_2N_5O_2$: C, 71.79; H, 4.30; N, 11.96. Found: C, 70.70; H, 4.17; N, 11.79%.

3-((4-Chlorophenyl)(2-(4-fluorophenyl)-6-methyl*H*-imidazo[1,2-*a*]pyridin-3-yl) methyl)-2-(4-fluorophenyl)-6-methyl*H*-imidazo[1,2-*a*]pyridine (BIP-5): IR (KBr): 3087, 2988, 2867, 1616, 1558, 1467, 1346, 1135, 1021, 720 cm^{-1}; MS: *m/z* = 577 [M+2]$^+$; Anal. Calcd for $C_{35}H_{25}ClF_2N_4$: C, 73.10; H, 4.38; N, 9.74. Found: C, 72.18; H, 4.26; N, 9.66%.

4-(Bis(2-(4-fluorophenyl)-6-methyl*H*-imidazo[1,2-*a*]pyridin-3-yl)methyl)benzenamine (BIP-6): IR (KBr): 3490, 3073, 2973, 2864, 1611, 1567, 1454, 1386, 1138, 1036 cm^{-1}; MS: *m/z* = 556 [M+1]$^+$; Anal. Calcd for $C_{35}H_{27}F_2N_5$: C, 75.66; H, 4.90; N, 12.60. Found: C, 75.18; H, 4.77; N, 12.43%.

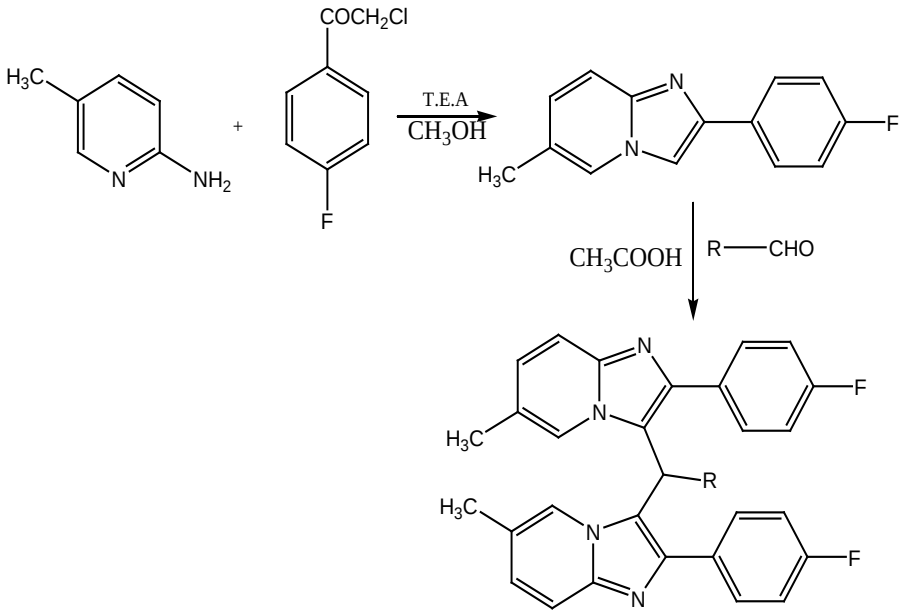
2-(4-Fluorophenyl)-3-((4-fluorophenyl)(2-(4-fluorophenyl)-6-methyl*H*-imidazo[1,2- *a*]pyridin-3-yl)methyl)-6-methyl*H*-imidazo[1,2-*a*]pyridine (BIP-7):IR (KBr): 3090, 2961, 2853, 1614, 1546, 1467, 1369, 1129, 1043 cm^{-1}; MS: *m/z* = 558 [M]$^+$; Anal. Calcd for $C_{35}H_{25}F_3N_4$: C, 75.26; H, 4.51; N, 10.03. Found: C, 74.83; H, 4.25; N, 9.83%.

3-((4-Bromophenyl)(2-(4-fluorophenyl)-6-methyl*H*-imidazo[1,2-*a*]pyridin-3-yl) methyl)-2-(4-fluorophenyl)-6-methyl*H*-imidazo[1,2-*a*]pyridine (BIP-8): IR (KBr): 3088, 2976, 2858, 1606, 1568, 1434, 1374, 1144, 1046, 840 cm^{-1}; MS: *m/z* = 619 [M]$^+$; Anal. Calcd for $C_{35}H_{25}BrF_2N_4$: C, 67.86; H, 4.07; N, 9.04. Found: C, 67.33; H, 3.83; N, 9.00%.

2-(4-Fluorophenyl)-3-((2-(4-fluorophenyl)-6-methyl*H*-imidazo[1,2-*a*]pyridin-3-yl)(4-methoxyphenyl)methyl)-6-methyl*H*-imidazo[1,2-*a*]pyridine (BIP-9): IR (KBr): 3087, 2973, 2851, 1600, 1587, 1446, 1379, 1099, 1063 cm^{-1}; MS: *m/z* = 570 [M]$^+$; Anal. Calcd for $C_{36}H_{28}F_2N_4O$: C, 75.77; H, 4.95; N, 9.82. Found: C, 75.15; H, 4.58; N, 9.53%.

4-(Bis(2-(4-fluorophenyl)-6-methyl*H*-imidazo[1,2-*a*]pyridin-3-yl)methyl)phenol (BIP-10):
IR (KBr): 3440, 3082, 2946, 2864, 1609, 1579, 1446, 1378, 1149, 1081 cm^{-1}; MS: *m/z* = 557 [M+1]$^+$; Anal. Calcd for $C_{35}H_{26}F_2N_4O$: C, 75.52; H, 4.71; N, 10.07. Found: C, 74.67; H, 4.47; N, 9.84%.

Scheme 1: Synthesis of novel series of Bis-imidazo[1,2-a]pyridine derivatives



Bis imidazo[1,2-a]pyridine derivatives (BIP-1 TO BIP-10)

Table 1: Physical constants of synthesized novel series of Bis-imidazo[1,2-a]pyridine derivatives

Comp	Substitution (R)	M.F	M.W	M.P (^{0}C)
BIP-1	*p*-Tolyl	$C_{36}H_{28}F_2N_4$	554.63	161-163
BIP-2	Thiophen-2-yl	$C_{33}H_{24}F_2N_4S$	546.63	192-193
BIP-3	Phenyl	$C_{35}H_{26}F_2N_4$	540.60	175-177
BIP-4	4-Nitrophenyl	$C_{35}H_{25}F_2N_5O_2$	585.60	209-211
BIP-5	4-Chlorophenyl	$C_{35}H_{25}ClF_2N_4$	575.04	203-204
BIP-6	4-Aminophenyl	$C_{35}H_{27}F_2N_5$	555.61	185-187
BIP-7	4-Fluorophenyl	$C_{35}H_{25}F_3N_4$	558.59	173-175
BIP-8	4-Bromophenyl	$C_{35}H_{25}BrF_2N_4$	619.50	226-228
BIP-9	4-ethoxyphenyl	$C_{36}H_{28}F_2N_4O$	570.63	157-159
BIP-10	4-Hydroxyphenyl	$C_{35}H_{26}F_2N_4O$	556.60	177-178

BIOLOGICAL EVALUATION

Preparation of Culture Media: Nutrient broth was used as growth medium for bacteria and Saubouraud dextrose broth for fungi. Nutrient broth was prepared by dissolving 13gm of dehydrated powder (HI-media) in 100ml of distilled water. Saubouraud dextrose broth was prepared by dissolving 4gm of dextrose and 1gm of peptone in 100ml of distilled water. The media were sterilized by autoclaving at 15lbs pressure for 20 minutes.

Preparation of Stock Culture: Stock cultures were obtained by aseptically transferring a loopful of test organisms to 100ml of sterile broth and incubated for 24 hours at 37^{0}C.

Standardization of Stock Culture: Stock cultures were placed in the incubator (37^{0}C for bacteria and 24^{0}C for fungi) and shaken well. One ml of stock cultures was aseptically transferred to 9 ml of sterile water containing 0.05% tween 80. This was mixed with using a cyclomixer and serially diluted from 10^{-1} to 10^{-10}. From each dilution,

0.2ml was taken and spread on sterile nutrient agar plates for bacteria and Sabouraud dextrose agar plates for fungi, which were incubated for 18 hours. After incubation, the numbers of colonies in the plate were counted. The number of colonies for a plate that was formed from the maximum dilute tube was noted. The number of microorganisms in stock were then calculated and expressed as colony forming units per ml (cfu/ml). By back calculation the stock culture was found to contain 15×10^8 cfu/ml.

Preparation of Working Stock Culture: Stock culture (0.1ml) was diluted with nutrient broth (100ml) and Sabouraud dextrose broth (100ml) respectively to obtain 10^5 cfu/ml. This was then used for further *in vitro* screening.

Preparation of Drug Dilutions: Solutions of the title compounds in DMSO (1mg/ml) were prepared and used for screening their antimicrobial activity.

Antimicrobial Screening: Synthesized compounds were subjected to antimicrobial screening by estimating the minimum inhibitory concentration (MIC) by adopting serial dilution technique. Test was carried out on four bacterial strains, namely *Staphylococcus aureus* (MTCC 96), *Staphylococcus pyogenus, Pseudomonas aeruginosa* (MTCC 1688), *Escherichia coli* (MTCC 443) and two fungal strains, namely *Candida albicans* (MTCC 227) and *Aspergilla niger* (MTCC 282).

Determination of MIC: The study involved a series of six assay tubes for each title compound against each microorganism. The entire test was done in duplicate. To the first assay tube, 1.8ml of seeded broth and 0.2ml of title compound (1mg/ml) was added and mixed thoroughly and the two fold serial dilution was done up to the sixth tube containing 1 ml of seeded broth. The additions of the drug solution and serial dilution were done under strict aseptic conditions. Solvent control, negative control (growth control) and drug control were maintained during the experiment. The assay tubes were incubated at 37^0C and 25^0C respectively for 24 hours for bacteriae and fungi. The lowest concentration, which apparently caused complete inhibition of growth of microorganisms, was considered as the minimum inhibitory concentration (MIC).The MIC values of the test compounds are recorded in Table-2.

Table 2: Antimicrobial activity of novel series of Bis-imidazo[1,2-a]pyridine derivatives

Compound	Minimal Inhibitory Concentration (µg/ml)					
	Antibacterial Activity				Antifungal activity	
	S.aureus	***S.pyogenus***	***E.coli***	***P.aeruginosa***	***C.albicans***	***A.niger***
BIP-1	250	500	100	500	250	500
BIP-2	200	100	250	100	200	1000
BIP-3	50	100	100	100	1000	500
BIP-4	250	250	500	500	500	250
BIP-5	200	250	100	250	250	500
BIP-6	500	250	200	100	200	250
BIP-7	100	500	125	500	500	1000
BIP-8	250	100	500	200	1000	500
BIP-9	250	200	200	200	500	200
BIP-10	125	100	250	100	250	250
Ampicillin	250	100	100	100	NT	NT
Greseofulvin	NT	NT	NT	NT	500	100

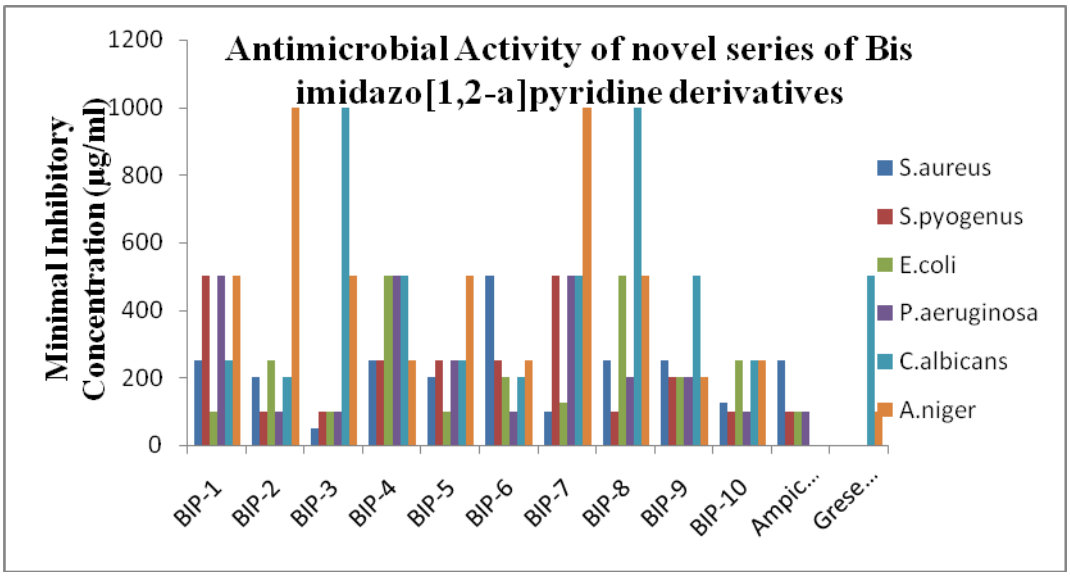


Figure 1: Antimicrobial activity of novel series of Bis-imidazo[1,2-a]pyridine derivatives

RESULTS AND DISCUSSION:

A solution of 5-methylpyridin-2-amine to 2-chloro-1-(4-fluorophenyl)ethanone in presence of methanol and refluxed with stirring for 6 hour in the presence of catalytic amount of triethylamine gives 2-(4-Fluorophenyl)-6-methyl*H*-imidazo[1,2-*a*]pyridine. The solution of 2-(4-Fluorophenyl)-6-methyl*H*-imidazo[1,2-*a*]pyridine and aromatic aldehydes in acetic acid, sodium acetate the titled compounds.

The data recorded in Table 2 indicated that compounds **BIP-3, BIP-7 and BIP-10** are more potent towards the *Staphylococcus aureus.* Compounds **BIP-2 and BIP-5** are moderately potent towards the *Staphylococcus aureus.* Compounds **BIP-2**, **BIP-3, BIP-8** and **BIP-10** moderately potent towards the *Streptococcus pyogenes.* Compounds **BIP-1, BIP-3** and **BIP-5** are moderately potent towards the *Escherichia coli.* Compounds **BIP-2**, **BIP-3, BIP-6** and **BIP-10** are moderately potent towards the *Pseudomonas aeruginosa.* All these compounds are compared with the standard reference (Ampicillin) for their antibacterial activities. Compounds **BIP-1**, **BIP-2, BIP-7** and **BIP-8** are more potent towards the *Candida albicans.* All these compounds are compared with the standard reference (Greseofulvin) for their antifungal activities.

CONCLUSION:

In this study, novel series of Bis imidazo[1,2-a]pyridine derivatives were synthesized and evaluated for their antimicrobial activities. Results revealed that the compounds exhibited significant *in-vitro* activity. Compounds **BIP-2**, **BIP-3, BIP-5** and **BIP-10** are more potent against all the bacterial strains. Compounds **BIP-1**, **BIP-2, BIP-7** and **BIP-8** are more potent against all the fungal strains. Remaining compounds also showed moderate to weak antimicrobial activities. The study would be a fruitful matrix for the development of novel series of Bis imidazo[1,2-a]pyridine derivatives for further bio-evaluation.

Acknowledgement

The authors are grateful to Department of Pharmaceutical Analysis, Chalapathi Institute of Pharmaceutical Sciences, Guntur for providing facilities to perform this research work.

REFERENCES:

1. Nimmala Srinivas Rao et al, Synthesis and antibacterial activity of novel imidazo[1,2-a]pyrimidine and imidazo[1,2-a]pyridine chalcones derivatives, Der Pharma Chemica, 2012, 4 (6):2408-2415.
2. Bharagava et al. Ionic Liquid Promoted Synthesis Of 2-Phenylimidazo [1,2-A]Pyridine Derivatives And Their Antibacterial Screening, Int J Pharm Pharm Sci, Vol 6, Issue 6, 553-557.
3. Lukasik PM et al, Synthesis and biological evaluation of imidazo[4,5-b]pyridine and 4-heteroaryl-pyrimidine derivatives as anti-cancer agents, Eur J Med Chem. 2012 Nov;57:311-22.
4. R. Chekkara et al, Theoretical studies on benzimidazole and imidazo[1,2-a]pyridine derivatives as Polo-like kinase 1 (Plk1) inhibitors: Pharmacophore modeling, atom-based 3D-QSAR and molecular docking approach, Journal of Saudi Chemical Society (2014).

5. Nimmala Srinivas Rao et al, Synthesis and antibacterial activity of novel imidazo[1,2-a] pyrimidine and imidazo[1,2-a]pyridine chalcones derivatives, Der Pharma Chemica, 2012, 4 (6):2408-2415.

6. Valentina et al, Synthesis, Docking Studies And Biological Evaluation Of Some Newly Substituted-5-(2 - Methyl Imidazo [1,2-A] Pyridin-3 -Yl) -2,5 - Dihydro - 1,3,4 - Thiadiazol-2-Amines, Int J Pharm Pharm Sci, Vol 5, Suppl 3, 872-876

7. Chaouni-Enabdallah A et al, 3-Benzamido, ureido and thioureidoimidazo[1,2-a]pyridine derivatives as potential antiviral agents, Chem Pharm Bull (Tokyo). 2001 Dec;49(12):1631-5.

8. Mavel S et al, Synthesis of imidazo[1,2-a]pyridine derivatives as antiviral agents, Arzneimittel for schung. 2001;51(4):304-9.

9. Kelly Chibale et al, Antimalarial Pyrido[1,2-*a*]benzimidazoles, *J. Med. Chem.*, 2011, *54* (13), pp 4581–4589

10. R. Saddik et al, Synthesis, antibacterial and antifungal activity of some new imidazo [1,2-a]pyridine derivatives, Der Pharmacia Lettre, 2014, 6 (4):343-348.

11. GOKTAS¸ et al, Synthesis of novel imidazo[1,2-a]pyridines and evaluation of their antifungal activities, Turk J Chem (2014) 38: 581 – 591.

12. Vivek D. Bobade et al, Synthesis and antimicrobial studies of 2-(5-substituted)-1, 3, 4- oxadiazole-2-yl)-H-imidazo [1, 2, α] pyridine derivatives, J. Chem. Pharm. Res., 2014, 6(7):102-108.

13. Ismail MA et al, Synthesis and antiprotozoal activity of novel bis-benzamidino imidazo[1,2-a]pyridines and 5,6,7,8-tetrahydro-imidazo[1,2-a]pyridines, Bioorg Med Chem. 2008 Jan 15;16(2):683-91.

14. Marhadour S et al, Synthesis and biological evaluation of 2,3-diarylimidazo[1,2-a]pyridines as antileishmanial agents, Eur J Med Chem. 2012 Dec;58:543-56

15. Jose G et al, Synthesis, molecular docking and anti-mycobacterial evaluation of new imidazo[1,2-a]pyridine-2-carboxamide derivatives, Eur J Med Chem. 2015 Jan 7;89:616-27