Research Article

Synthesis and Biological Evaluation of some Newer Aryl Imidazoles as Potential Antimicrobial and Anthelmintic Agents

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Accepted on: 02-07-2015; **Finalized on:** 31-08-2015.

ABSTRACT

In the present study we have made an attempt to synthesize novel imidazoles and evaluate them as potential therapeutic agents for antimicrobial and anthelmintic activity. First, Pyridine-3-amine was condensed with heteryl aldehydes to afford corresponding Schiff's base. The Schiff's base further on treatment with NH_4OAC and isatin yielded corresponding aryl imidazoles. The synthesized compounds were analyzed by physical and analytical data. The synthesized compounds were evaluated for their anthelmintic and antimicrobial activity. All the synthesized substituted imidazoles have shown moderate to good anthelmintic activity. The synthesized imidazoles possessed significant antimicrobial activity against gram +ve bacteria *S. aureus & B. subtilis* and gram –ve bacteria *E. coli & K. pneumoniae* and antifungal activity against *A. niger & C. albicans*.

Keywords: Aryl imidazoles, Anthelmintic activity, Antimicrobial activity.

INTRODUCTION

Syntheses of heterocyclic compounds from readily available reagents by simple and efficient methods are the major requirements of heterocyclic chemistry. A survey of the pertinent literature reveals that, imidazole derivatives possess diverse biological activities apart from their synthetic interests. They are reported to exhibit pharmacological activities such as antimicrobial[1,2], anthelmintic[3,4], cognitive enhancers[5,6], anticancer[7-10], and anti-inflammatory activities[11]. Some of the best selling therapies today contain this versatile heterocycle in their core structures.

Therefore, it would be difficult to underestimate the importance of imidazole in the pharmaceutical industry.

In 1858, Debus reported the reaction between glyoxal and ammonia, ever since this reaction became a novel route to the syntheses of imidazoles. Later, a number of articles have described the syntheses of various imidazoles[12-21].

RESULTS AND DISCUSSION

The results and discussion pertaining to the synthesis of Schiff's bases and finally substituted imidazoles are as follows:

First, the primary aromatic was condensed with heteryl aldehydes afforded the corresponding Schiff's base. To prepare aryl imidazoles, the Schiff's base was further treated with ammonium acetate and isatin (cyclization steps involving diketone) in the presence of glacial acetic acid as a solvent, gave a corresponding aryl imidazoles 1b—8b **(Table 1)**. On the basis of above facts (as depicted in the introduction) that the novel series of synthesized derivative of aryl imidazoles containing indole moiety may yield compounds with high therapeutic potential.

Structures of all the newly synthesized compounds were confirmed by FTIR, ^{1}H NMR and Mass spectral analysis. The IR spectra of the newly synthesized compounds showed the presence of characteristic absorption bands in the region 3310-3350 cm^{-1} for N-H in NH_2, 3012-3096 cm^{-1} for aromatic C-H stretching, 1500-1600 cm^{-1} for C=N stretching respectively. ^{1}H NMR spectra of synthesized compounds showed the characteristic peaks in the region 6.67-7.80 ppm for aromatic protons and 10.1-11.0 ppm for N-H.

The synthesized compounds were screened for *in vitro* antibacterial activity using gram +ve bacteria *S. aureus & B. subtilis* and gram –ve bacteria *E. coli & K. pneumoniae*. Compounds showed significant antibacterial activity against gram +ve bacteria. Compounds showed moderate antibacterial activity against gram –ve bacteria **(Table 2)**. The synthesized compounds were screened for *in vitro* antifungal activity using *A. niger & C. albicans.* Compound showed significant antifungal activity **(Table 3)**.

Anthelmintic activity of the synthesized novel imidazoles was carried out against three different species of earthworms *M. konkanensis* and *Eudrilus* at 4mg/ml concentration. All the novel imidazoles showed moderate to good activity at 100mg in tween 80 (0.5%) and distilled water. Comparison of anthelmintic data **(Table 4)** revealed that derivative 1b, 2b, 3b, 6b and 8b possessed higher activity against *M. konkanensis* species in comparison to standard Mebendazole. 1b, 2b, 3b, 4b, 6b, and 8b possessed higher activity against *Eudrilus* species in comparison to standard Mebendazole.

MATERIALS AND METHODS

^{1}H spectra were recorded on Bruker DRX-400 (400 MHZ, FT NMR) spectrometer using tetramethylsilane as internal standard and the chemical shifts are reported in δ units.

Mass spectra were recorded on LC-MS (Schimadzu-2010AT) under Electro Spray Ionization (ESI) technique. IR spectra (λ_{max} in cm^{-1}) were recorded on Perkin-Elmer infrared-283 FTIR spectrometer. Elemental analyses were recorded on Elementar Vario EL spectrometer. All chromatographic purification was performed with silica gel 60 (230–400 mesh), whereas all TLC (silica gel) development was performed on silica gel coated (Merck Kiesel 60 F254, 0.2 mm thickness) sheets. All chemicals were purchased from Aldrich Chemical Ltd (Milwaukee, WI, USA). Solvents used for the chemical synthesis acquired from commercial sources were of analytical grade, and were used without further purification unless otherwise stated.

In view of these observations and in continuation of our endeavour to develop better and potent antimicrobial and anthelmintic agents new series of novel imidazoles were synthesized as follows:

General procedure for the preparation of Schiff's bases (1a- 8a) Step-I.

Equimolar amounts (0.01 M) of pyridine-3-amine and substituted aromatic aldehydes were transferred to a 250 ml round bottom flask containing 15 ml glacial acetic acid and refluxed for 6 h. The reaction mixture was allowed to cool to give product. The reactions were monitored through TLC. The completed reactions were taken directly for the preparation of imidazoles.

General procedure for the preparation of aryl imidazoles (1b- 8b) Step-II.

Isatin (0.01M) was transferred along with excess of ammonium acetate (0.1 M) into a flask containing the Schiff's base (~0.01M) obtained by step-I. The reaction mixture was stirred and refluxed on heating plate with magnetic stirrer for about 11-14 h. The reaction was monitored through TLC.

The reaction mixture was poured into 250 ml of water to remove ammonium acetate and acetic acid then it was filtered and dried in hot air oven. The crude product was washed with 2 x 20 ml of benzene to remove traces of any unreacted isatin and products were recrystallized by ethyl acetate.

Methodology for Biological Activity

Antibacterial activity studies

The synthesized aryl imidazole derivatives were screened for their antibacterial activity against two gram positive bacterial strains *B. subtilis*, *S. aureus* and two gram negative bacterial strains *K. pneumonia*, *E. coli* by using modified Kirby–Bauer disc diffusion method[22,23]. Minimum inhibitory concentration (MIC) values of test compounds were determined by tube dilution technique[24]. All the synthesized compounds were dissolved separately to prepare a stock solution of 1mgml_1 using *N*,*N*-dimethylformamide (DMF). Stock solution was aseptically transferred and suitably diluted with sterile broth medium to have seven different concentrations of each test compound ranging from 200 to 3.1mgml_1 in different test tubes. All the tubes were inoculated with one loopful of one of the test bacteria. The process was repeated with different test bacteria and different samples. Tubes inoculated with bacterial cultures were incubated at 37 °C for 18 h and the presence/absence of growth of the bacteria was observed. From these results, MIC of each test compound was determined against each test bacterium. A spore suspension in sterile distilled water was prepared from 5-dold culture of the test bacteria growing on nutrient broth media. About 20 ml of the growth medium was transferred into sterilized petri plates and inoculated with 1.5 ml of the spore suspension (spore concentration 6_104 spores ml_1). Filter paper disks of 6 mm diameter and 2 mm thickness were sterilized by autoclaving at 121 °C (15 psi) for 15 min. Each petri plate was divided into five equal portions along the diameter to place one disc. Three discs of test sample were placed on three portions together with one disc with reference drug ciprofloxacin and a disk impregnated with the solvent (DMF) as negative control. Test sample and reference drugs were tested at the concentration of 10mgml_1. The petri plates inoculated with bacterial cultures were incubated at 37 °C for 18 h. Diameters of the zones of inhibition (mm) were measured and the average diameters for test sample were calculated in triplicate sets. The diameters obtained for the test sample were compared with that produced by the standard drug ciprofloxacin given in table 2.

Anti Fungal Activity Studies by Disk diffusion method

Cultivation of microorganisms

The cultures will be obtained from the Dept. of Microbiology, IVRI, Bareilly. The following fungal cultures will be used for the study. The fungal cultures will be sub cultured in Sabouraud's broth medium and incubated under aerobic condition at 25°C for 48 hrs. These cultures will be used for the test.

Preparation of paper disk

Paper disk of 6 mm diameter and 2 mm thickness will be used for the test. These disks Will be found to absorb 0.02 ml of the solvent (DMF). These disks will be sterilized by autoclaving at 121°C (15lbs psig) for 15 minutes. All the samples will tested at 50μg level. To obtain this sample solution containing 2500 μg/ml (25 mg/10 ml) will prepared in sterile DMF and 0.2 ml each of the solution will be added into bottle containing 10 disks. Disk containing 25 μg/disk of griseofulvin will be taken as standard. All the solutions will be prepared using aseptic precautions.

All the synthesized compounds will be dissolved separately to prepare a stock solution containing 1000 μg/ml of DMF. 32 mg of different synthesized compounds will dissolved in 2 ml of the DMF and 1 ml of this solution will be aseptically transferred to the sterile nutrient broth

medium and made up to 16 ml with sterile nutrient media, thus 1 ml of the resulted solution gives 1000 µg/ml. 1 ml of the above solution will be transferred to 1 ml of DMF to give half the concentration of first. Thus successive concentrations like 250, 125, 62.5 and so will be prepared in a similar manner up to 6 dilutions from sixth one ml of the solution are discarded.

The tubes will be mixed well after each addition. All the tubes will be inoculated with one loopful of one the test organism. The process will be repeated with different test organism. A positive control and a negative control will also prepared to confirm the nutritive property and sterility, respectively of the prepared medium. The tubes will be incubated at 25°C for 48 hours. The presence or absence of growth of organism will be observed after incubation given in table 3.

Scheme 1

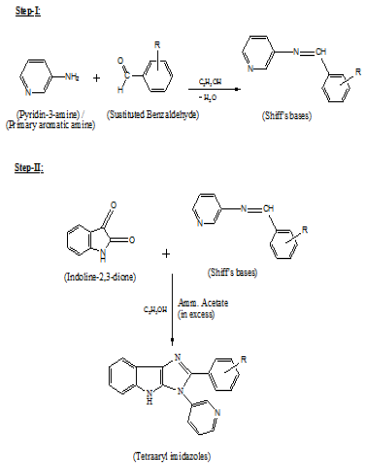
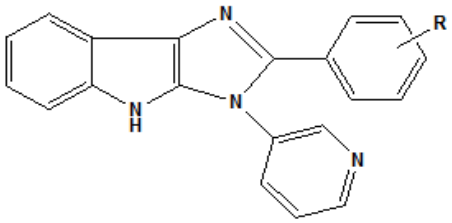


Table 1: Data of all Synthesized Novel Imidazoles (1b-8b)



(1b-8b)

Compound name	R	Molecular Formula	Molecular Weight	Reaction Time (hr)	% Yield
1b	3-nitro	$C_{20}H_{13}N_5O_2$	355.35	11.5	61.86
2b	2-hydroxy	$C_{20}H_{14}N_4O$	326.35	12	58.24
3b	3-hydroxy	$C_{20}H_{14}N_4O$	326.35	12.5	63.34
4b	2-chloro	$C_{20}H_{13}ClN_4$	344.8	13.5	65.05
5b	4-chloro	$C_{20}H_{13}ClN_4$	344.8	13	64.32
6b	3-chloro	$C_{20}H_{13}ClN_4$	344.8	14	63.36
7b	4-nitro	$C_{20}H_{13}N_5O_2$	355.35	12	61.25
8b	3-methoxy	$C_{21}H_{16}N_4O$	340.38	13.5	67.60

Table 2: (Antimicrobial Activity) Antibacterial Data of All Synthesized Aryl Imidazoles Compounds Screened against Various Bacterial Strains.

Compound name	Diameter of zone of inhibition (mm) Bacterial strains			
	Gram (+ve)		Gram (-ve)	
	S. aureus	*B. subtilis*	*E. coli*	*K. pneumoniae*
1b	5.9 (50)	6.9(50)	7.2(50)	8.1(50)
2b	5.1 (25)	5.5 (25)	8.1 (50)	8.9 (50)
3b	8.6 (25)	8.4 (25)	9.2 (12.5)	9.5 (12.5)
4b	13.1 (50)	12.5 (25)	11.9 (25)	12.5 (6.2)
5b	9.1 (25)	8.8 (50)	7.6 (100)	7.8 (100)
6b	5.7 (100)	5.9 (100)	6.6 (50)	6.9 (50)
7b	12.5 (50)	12.1 (25)	11.9 (25)	11.6 (25)
8b	11.9 (50)	11.3 (25)	10.9 (100)	10.7 (50)
control	-	-	-	-
Ciprofloxacin	18 (12.5)	19 (6)	19 (12.5)	17 (6)

Values in bracket are MIC values (µg ml^{-1}).

Table 3: Antifungal Activity

Compound name	Diameter of zone of inhibition (mm) Fungal strains	
	A. niger	*C. albicans*
1b	10	11
2b	12	12
3b	18	19
4b	19	19
5b	11	12
6b	18	17
7b	11	15
8b	12	15
Control	-	-
Griseofulvin	23	23

Table 4: Anthelmintic Activity

Compound No.	Mean paralyzing time (min)		Mean death time (min)	
	M. konkanensis	*Eudrilus*	*M. konkanensis*	*Eudrilus*
1b	15.50 ± 0.50	20.50 ± 0.50	22.33 ± 1.52	28.50 ± 0.50
2b	14.16 ± 1.25	20.33 ± 0.76	23.16 ± 0.76	28.83 ± 0.76
3b	15.37 ± 0.57	20.16 ± 0.57	24.33 ± 0.57	29.16 ± 0.76
4b	26.66 ± 0.57	19.50 ± 0.50	33.66 ± 0.57	27.66 ± 0.57
5b	32.66 ± 0.57	26.33 ± 0.57	39.16 ± 0.76	39.83 ± 0.76
6b	16.83 ± 0.76	20.00 ± 1.00	23.33 ± 0.57	29.33 ± 0.57
7b	38.16 ± 1.75	27.83 ± 0.76	45.66 ± 0.57	41.33 ± 0.57
8b	15.33 ± 0.57	20.33 ± 1.52	22.33 ± 0.57	29.00 ± 1.00
Control	-	-	-	-
Mebendazole	18.22 ± 1.00	20.83 ± 0.76	25.37 ± 1.00	29.33 ± 1.52

Anthelmintic studies

Anthelmintic activity studies were carried out against two different species of earthworms *M. konkanensis* and *Eudrilus* at 2 mg ml^{-1} concentration using Garg and Atal method[25]. Suspensions of samples were prepared by triturating synthesized compounds (100 mg) with Tween 80 (0.5%) and distilled water and the resulting mixtures were stirred using a mechanical stirrer for 30 min. The suspensions were diluted to contain 0.2% w/v of the test samples. Suspension of reference drug, mebendazole, was prepared with the same concentration in a similar way. Three sets of five earthworms of almost similar sizes (2 inch in length) were placed in Petri plates of 4 inch diameter containing 50 ml of suspension of test sample and reference drug at RT.

Another set of five earthworms was kept as control in 50 ml suspension of distilled water and Tween 80 (0.5%). The paralyzing and death times were noted and their mean was calculated for triplicate sets.

The death time was ascertained by placing the earthworms in warm water (50 °C) which stimulated the movement, if the worm was alive. The results are given in table 4.

3,4-Dihydro-2-(3-Nitrophenyl)-3-(pyridine-3yl)imidazo[4,5-*b*]indole (1b, $C_{20}H_{13}N_5O_2$)

Mp (°C): 130; R_f value: 0.76; IR (KBr): 3322.12 (N–H), 3082.04 (Ar C-H), 1595.09 (C=N), 1546.22 (C=C), 1402.15 (NO_2), 1151.42 (C-N), 858.77 (C-N stretching for NO_2), cm^{-1}; ^{1}H NMR (DMSO-d_6): δ = 7.12-8.48 (m, 12H, Ar-H), 10.1 (s, 1H, N-H, D_2O exchangeable) ppm; MS (ESI) m/z: M+1 peak found, 355.96 (M+1 peak calculated, 355.35); Anal. Calcd. for: C, 67.60; H, 3.69; N, 19.71; O, 9.00. Found: C, 67.48; H, 3.57; N, 19.68; O, 8.97.

2-(3,4-dihydro-3-(pyridin-3-yl)imidazo[4,5-b]indol-2-yl)phenol (2b, $C_{20}H_{14}N_4O$)

Mp (°C): 124; R_f value: 0.72; IR (KBr): 3570.42 (O-H), 3330.71 (N–H), 3080.17 (Ar C-H), 1560.10 (C=N), 1546.22 (C=C), 1195.78 (C-N), cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 7.12-8.48 (m, 12H, Ar-H), 10.1 (s, 1H, N-H, D_2O exchangeable), 4.9 (s, 1H, OH, D_2O exchangeable) ppm; MS (ESI) m/z: M+1 peak found, 326.01 (M+1 peak calculated, 326.35);

Anal. Calcd. for: C, 73.61; H, 4.32; N, 17.17; O, 4.09. Found: C, 73.59; H, 4.29; N, 17.12; O, 4.05.

3-(3,4-dihydro-3-(pyridin-3-yl)imidazo[4,5-b]indol-2-yl)phenol (3b, $C_{20}H_{14}N_4O$)

Mp (°C): 127; R_f value: 0.70; IR (KBr): 3570.42 (O-H), 3330.71 (N–H), 3080.17 (Ar C-H), 1560.10 (C=N), 1546.22 (C=C), 1195.78 (C-N), cm^{-1}; ^1H NMR (DMSO-d_6): δ = 7.12-8.48 (m, 12H, Ar-H), 10.1 (s, 1H, N-H, D_2O exchangeable), 4.9 (s, 1H, OH, D_2O exchangeable) ppm; MS (ESI) m/z: M+1 peak found, 326.01 (M+1 peak calculated, 326.35); Anal. Calcd. for: C, 73.61; H, 4.32; N, 17.17; O, 4.09. Found: C, 73.59; H, 4.29; N, 17.12; O, 4.05.

2-(2-chlorophenyl)-3,4-dihydro-3-(pyridin-3-yl)imidazo[4,5-b]indole (4b, $C_{20}H_{13}ClN_4$)

Mp (°C): 152; R_f value: 0.69; FTIR (KBr): 3328.83 (N–H), 3063.62 (Ar C-H), 1569.66 (C=N), 1543.76 (C=C), 1151.42 (C-N), 756.04 (C-Cl) cm^{-1}; ^1H NMR (DMSO-d_6): δ = 7.12-8.48 (m, 12H, Ar-H), 10.1 (s, 1H, N-H, D_2O exchangeable) ppm; MS (ESI) m/z: M+1 peak found, 344.02 (M+1 peak calculated, 344.8); Anal. Calcd. for: C, 69.67; H, 3.80; Cl, 10.28; N, 16.25. Found: C, 69.63; H, 3.76; Cl, 10.22; N, 16.20.

2-(4-chlorophenyl)-3,4-dihydro-3-(pyridin-3-yl)imidazo[4,5-b]indole (5b, $C_{20}H_{13}ClN_4$)

Mp (°C): 148; R_f value: 0.67; FTIR (KBr): 3328.83 (N–H), 3063.62 (Ar C-H), 1569.66 (C=N), 1543.76 (C=C), 1151.42 (C-N), 756.04 (C-Cl) cm^{-1}; ^1H NMR (DMSO-d_6): δ = 7.12-8.48 (m, 12H, Ar-H), 10.1 (s, 1H, N-H, D_2O exchangeable) ppm; MS (ESI) m/z: M+1 peak found, 344.02 (M+1 peak calculated, 344.8); Anal. Calcd. for: C, 69.67; H, 3.80; Cl, 10.28; N, 16.25. Found: C, 69.63; H, 3.76; Cl, 10.22; N, 16.20.

2-(3-chlorophenyl)-3,4-dihydro-3-(pyridin-3-yl)imidazo[4,5-b]indole (6b, $C_{20}H_{13}ClN_4$)

Mp (°C): 154; R_f value: 0.68; FTIR (KBr): 3328.83 (N–H), 3063.62 (Ar C-H), 1569.66 (C=N), 1543.76 (C=C), 1151.42 (C-N), 756.04 (C-Cl) cm^{-1}; ^1H NMR (DMSO-d_6): δ = 7.12-8.48 (m, 12H, Ar-H), 10.1 (s, 1H, N-H, D_2O exchangeable) ppm; MS (ESI) m/z: M+1 peak found, 344.02 (M+1 peak calculated, 344.8); Anal. Calcd. for: C, 69.67; H, 3.80; Cl, 10.28; N, 16.25. Found: C, 69.63; H, 3.76; Cl, 10.22; N, 16.20.

3,4-Dihydro-2-(4-Nitrophenyl)-3-(pyridine-3yl)imidazo[4,5-*b*]indole (7b, $C_{20}H_{13}N_5O_2$)

Mp (°C): 134; R_f value: 0.74; IR (KBr): 3322.12 (N–H), 3082.04 (Ar C-H), 1595.09 (C=N), 1546.22 (C=C), 1402.15 (NO_2), 1151.42 (C-N), 858.77 (C-N stretching for NO_2), cm^{-1}; ^1H NMR (DMSO-d_6): δ = 7.12-8.48 (m, 12H, Ar-H), 10.1 (s, 1H, N-H, D_2O exchangeable) ppm; MS (ESI) m/z: M+1 peak found, 355.96 (M+1 peak calculated, 355.35); Anal. Calcd. for: C, 67.60; H, 3.69; N, 19.71; O, 9.00. Found: C, 67.48; H, 3.57; N, 19.68; O, 8.97.

3,4-dihydro-2-(3-methoxyphenyl)-3-(pyridin-3-yl)imidazo[4,5-b]indole (8b, $C_{21}H_{16}N_4O$)

Mp (°C): 165; R_f value: 0.79; FTIR (KBr): 3350.76 (N–H), 3072.39 (Ar C-H), 2925.81 (Ali. C-H), 1593.09 (C=N), 1547.22 (C=C), 1236.29 (C-N), 1149.50 (C-O-C) cm^{-1}; ^1H NMR (DMSO-d_6): δ = 3.7 (s, 3H, OCH_3), 7.12-8.48 (m, 12H, Ar-H), 10.1 (s, 1H, N-H, D_2O exchangeable) ppm; MS (ESI) m/z: M+1 peak found, 340.02 (M+1 peak calculated, 340.38); Anal. Calcd. for: C, 74.10; H, 4.74; N, 16.46; O, 4.70. Found: C, 74.07; H, 4.70; N, 16.43; O, 4.68.

Acknowledgement: Authors are thank full to the sophisticated analytical instrumentation facility (SAIF), Punjab University, Chandigarh, Punjab India for providing the elemental and spectral analysis of the compounds. Authors are also thanks full to Director I.V.R.I. for their support in biological activity.

REFERENCES

1) Aridoss G, Balasubramanian S, Parithiban S, Kabilan S, Synthesis and *in vitro* microbiological evaluation of imidazo(4,5-b)pyridinylethoxypiperidones, Eur J Med Chem, 41, 2006, 268-275.

2) Benkil K, Demirayak S, Gundogdu KN, Kiraz N, Iscan G, Ucucu U, Synthesis and antimicrobial activities of some imidazole substituted indoles, Ind J Chem, 43 B, 2004, 174-179.

3) Reddy S, Nagaraj A, Srinivas A, Synthesis and nematicidal activity of 2-(1H)-benzo [d]imidazol-2-ylmethyl)-4-aryl-1-thia-4-azaspiro[4.5]decan-3-one, Ind J Chem, 47, 2008, 787-791.

4) Kowalski P, Nowak K, Szpakiewicz B, Synthesis and prediction of bioactivity of new nitroimidazole derivatives, J Heterocycl Chem, 42, 2005, 883-888.

5) Chamber MS, Atack JR, Broughton HB, Collinson N, Reeve AJ, MacLeod AM, Identification of a novel, selective GABA(A) alpha5 receptor inverse agonist which enhances cognition, J Med Chem, 46, 2003, 2227-2240.

6) Pinza M, Farina C, Cerri A, Synthesis and pharmacological activity of a series of dihydro-1H-pyrrolo[1,2-a]imidazole-2,5(3H,6H)-diones, a novel class of potent cognition enhancers, J Med Chem, 36, 1993, 4214-4220.

7) Brana MF, Cacho M, Garcia MA, Yuste M, Ramos A, Synthesis, antitumor activity, molecular modeling, and DNA binding properties of a new series of imidazonaphthalimides. J Med Chem, 45, 2002, 5813-5816.

8) Suthakaran R, Nagarajan G, Suganthi K, Kannan M, Velrajan G, Synthesis and antitumor activity of 4-aryl/alkyl 2"-D aldo sugar disubstituted bis benzimidazoles, Ind J Heterocycl Chem, 15, 2005, 173-176.

9) Andreani A, Burnelli S, Granaiola M, Leoni A, Morigi R, Rambaldi M, Synthesis and antitumor activity of guanylhydrazones from 6-(2,4-dichloro-5-nitrophenyl)imidazo[2,1-b]thiazoles and 6-pyridylimidazo[2,1-b]thiazoles(1), J Med Chem, 49, 2006, 7897-7901.

10) Sztavke K, Rzymowska J, Koziol AE, Synthesis, crystal structure and anticancer activity of novel derivatives of

ethyl 1-(4-oxo-8- aryl-4,6,7,8-tetrahydroimidazo[2,1-c][1,2,4] triazin-3-yl) formate, Eur J Med Chem, 41, 2006, 539-547.

11) Reddy S, Nagaraj A, Srinivas A, Synthesis and nematicidal activity of 2-(1H)-benzo [d]imidazol-2-ylmethyl)-4-aryl-1-thia-4-azaspiro[4.5]decan-3-one, Ind J Chem, 47, 2008, 787-791.

12) Sarshar S, Siev D, Mjalli AMM, Imidazole libraries on solid support, Tetrahedron Lett, 37, 1996, 835-838.

13) Weinmann H, Harre M, Koeing K, Merten E, Tilstam U, Efficient and environmentally friendly synthesis of 2-amino-imidazole, Tetrahedron Lett, 43, 2002, 593-595.

14) Balalaie S, Hashemi MM, Akhbari MA, novel one-pot approach to the synthesis of tetrasubstituted imidazoles under solvent-free condition and microwave irradiation, Tetrahedron Lett, 44, 2003, 1709-1711.

15) Balalaie S, Arabanian A, One-spot synthesis of tetrasubstituted imidazoles by zeolite HY and silica gel under microwave irradiation, Green Chem, 2, 2002, 274-276.

16) Usyatinsky AY, Khemelnitsky YL, Microwave-assisted synthesis of substituted imidazoles on a solid support under solvent-free conditions, Tetrahedron Lett, 41, 2000, 5031-5034.

17) Wolkenberg SE, Wisnoski DD, Leister WH, Wang Y, Zhao Z, Lindsley C, Efficient synthesis of imidazoles from aldehydes and 1,2-diketones using microwave irradiation, Org Lett, 6, 2004, 1453-1456.

18) Kawase M, Saito S, Kurihara T, Convenient synthesis of 4-trifluoromethyl-substituted imidazole derivatives, Chem Pharm Bull, 49, 2001, 461-464.

19) Raghavendra NM, Thampi P, Gurubasavarajaswamy PM, Sriram D, Synthesis and antimicrobial activities of some novel substituted 2-imidazolyl-N-((4-oxo-quinazolin-3(4H)-yl)-acetamides, Chem Pharm Bull, 55, 2007, 1615-1619.

20) Bhaskar VH, Puli K, Sangameswaran B, Jayakar B, Synthesis and antifungal evaluation of (2E)-substituted-2-ethylidene-5,6-diphenylimidazo [2,1-b] [1,3] thiazolo-3-(2H)-ones, Ind J Hetrocycl Chem, 15, 2006, 299-300.

21) Sharma GK, Pathak D, Microwave-Assisted, Solvent-Free and Parallel Synthesis of Some Novel Substituted Imidazoles of Biological Interest, Chem Pharm Bull, 58(3), 2010, 375-380.

22) Kumar BRP, Sharma GK, Srinath S, Noor M, Srinivasa BR, Microwave-assisted, solvent-free, parallel syntheses and elucidation of reaction mechanism for the formation of some novel tetraaryl imidazoles of biological interest, J Heterocycl Chem, 46, 2009, 278-284.

23) Gillespie SH, Medical Microbiology-Illustrated, Butterworth Heinemann Ltd United Kingdom, 1994, 82-93.

24) Skehan P, Stareng R, Scudiero D, Monks A, Mcmahon J, Vistica D, Waren JT, Bokesch H, Kenney S, Michael BR, New colorimetric cytotoxicity assay for anticancer-drug screening, J Nat'l Cancer Inst, 82, 1990, 1107-1112.

25) Garg LC, Atal CK, Anthelmintic activity of Myrsine Africana, Ind J Pharm Sci, 59, 1963, 240-245.

Source of Support: Nil, **Conflict of Interest:** None.

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