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SYNTHESIS, CHARACTERISATION, AND ANTI-OXIDANT ACTIVITY OF SOME NITROGEN-CONTAINING MOIETIES AS POSSIBLE ANTIMICROBIAL AGENTS

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ABSTRACT

Novelnitrogen-containing moieties were prepared and analyzed by various techniques like NMR and mass spectrometry. The antimicrobial and anti-oxidant behaviors of novel moieties have been screened. The synthesized moieties are better antimicrobial activities. The moieties 1-5 are the greatest antioxidant reagents in the DPPH process. The IC50 standards are 0.13, 0.14, 0.11, 0.16, and 0.11 µg/Ml, respectively. Compound 3, 5 (IC50 = 0.11 µg/mL) was the most potent compound with $–OCH_3$ and $–CH_3$ groups as substituents showing good antioxidant activity even at very low concentrations. The particulars of synthetic methods, spectroscopic data, and biological results are recorded.

Keywords: Heterocyclic compounds, NMR, Antibacterial, Antifungal, Anti-oxidant.

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INTRODUCTION

Imidazole moieties have exhibited a diversity of pharmaceutical behavior[1-3] and act an essential function in the biochemical process. The nucleus construction of imidazole was established as a structural division of a lot of significant natural molecules like histamine and biotin as well as numerous drug moieties.[4] Heterocyclic moieties have novel therapeutic activities, kinase,[5] herbicides[6], and plant-growth regulators.[7] Furthermore, current intelligence points out that hetero moieties are cytotoxic,[8] anticonvulsants,[9] anti-inflammatories,[10] analgesic[11], and efficient self-consciousness of protein–protein communications.[12,13] Antimicrobial, antioxidant, and cytotoxic behavior of heterocyclic moieties have been screened. An outstanding antibacterial action for all the experienced bacteria with negligible inhibitory concentration range between 21.9 and 43.8 µg/mL.[14-16]

EXPERIMENTAL

Production of Substituted Imidazoles(1-5)

A combination of Diketone (1 mmol), aldehyde (1 mmol), substituted aryl amine (1 mmol), NH_4OAc (1mmol), and Boron trifluoride (1 mol%) set aside beneath stirring was at 80 °C. After the achievement of the result, the response combination was frozen; dissolve in acetone, and filtered. The manufactured goods were purified by column chromatography with benzene: ethyl acetate as the eluent (Scheme-1).

Spectral Measurements

The 1H and 13C NMR spectra of moieties 1-5 were recorded at space hotness with a Bruker 400 NMR spectrometer at 400 MHz. The mass spectra were recorded with a Thermo Fischer LC-Mass spectrometer in FAB mode.

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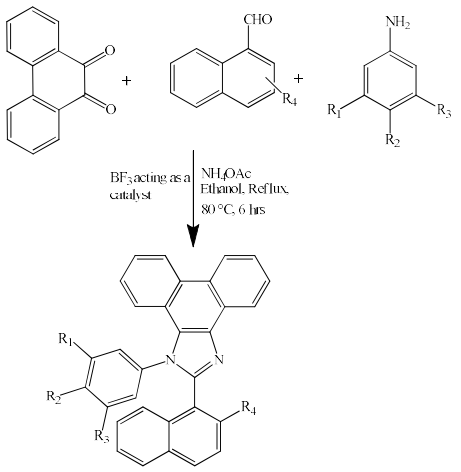
Anti-Oxidant Activity

DPPH Radical Scavenging Assets

The without-charge radical scavenging movement of the moieties was evaluated by DPPH for the earlier report.[17] Briefly a 0.0001M solution of DPPH in DMSO was prepared and 10mL of this solution was additional to 100mL of the solutions of all compounds in DMSO at various concentrations (100µL, 200µL, 300µL, and 400µL). The mixtures were shaken vigorously and permitted to situate at space hotness for 30 min, and their absorption was deliberate at 516 nm. Ascorbic acid was second-hand as a reference. Inferior absorbance standards of response combination point out superior free-of-charge radical scavenging movement. The potential to scavenge the DPPH fundamental was intended by:

DPPH scavenge consequence (% inhibition) = [A0-At/ A0] x100



Compd.	R_1	R_2	R_3	R_4
1	H	H	H	H
2	H	$-CH_3$	H	H
3	H	$-OCH_3$	H	H
4	$-CH_3$	H	$-CH_3$	H
5	H	H	H	-OH

Scheme-1: Synthetic Route of N-Containing Compounds

Anti-bacterial Activity

Preparation of Inoculums

Sub-culture

Staphylococcus aureus; Escherichia Coli; Bacillus cereus; Klebsiella pneumonia and *P. aeruginosa* were inoculated in tapering flasks containing 100 mL of sterile nutrient broth. The tapering flasks were incubating 37 ± 2 ˚C for one day.

Incubation of Nutrient Agar Petri Dishes

The strength was considered by inoculating 0.2 mL at every intensity to solidify nutrient intermediate by stretch plate technique after incubation at 37 ± 2˚C for one day. The information on attractive colonies on the dishware was counted. The seeded broth was then properly watery to have 105-107 microorganisms cfu/mL. This was elected as the functioning stock and second-hand for the antibacterial study.

Production of Solutions for Test Moieties

Solutions of assessment compounds are arranged by dissolving the identical DMSO in a precise gravity pot and stored in a refrigerator. The investigation moieties were arranged at a consideration of 200 µg/mL. Likewise, the normal solutions of Ciprofloxacin were second-hand, respectively at meditation 200 µg/mL for the least amount of inhibitory concentration.

Determination of Antibacterial Activity

Nutrient agar dishware was ready beneath a sterilized situation and incubated all night to notice pollution. 0.2 mL of functioning store culture was transferred into split nutrient agar dishware and extends systematically by a glass source. Whatman No.1 discs impregnated with the investigation moieties dissolve in DMSO (200 µg/mL) for regarding a half hour. Commercially accessible medicine disc (Ciprofloxacin 10 µg/disc) was second-hand as a positive standard. Negative pedals were also equipped by impregnating the disc of identical dimension on the inoculate agar dishware and incubating at 37 ± 2˚C for concerning 18-24 h. The antibacterial movement was evaluated by determining the district of embarrassment beside the investigation organism.

Antifungal

Fungal is, *Trichoderma viride, Clodosorium, Candida albicans, Aspergillus flavus,* and *Aspergillus Niger, Flucazonal* was second-hand as a standard drug.

Production of Culture Media

The subculture and the feasible calculation were accepted by the same process used for antibacterial study except for the heat, which should be maintained at 27 ± 3˚C for concerning 72 h. Likewise, for disc spreading performance, Petri dishware was incubated at 27 ± 3˚C for concerning 72 h.

RESULTS AND DISCUSSION

***In-vitro* Antibacterial Movement**

The preliminary antimicrobial movement of moieties 1-5 is scrutinized using the disc diffusion method, and DMSO is utilized as a control. Ciprofloxacin as well as Flucazonalare were employed as a standard for microbial studies. The moieties 1-5 were tested for their antibacterial movement touching selected pathogens. The imidazole 1-5 derivatives exhibited a wide spectrum of antibacterial movement besides all the experienced organisms as shown in Table-1. The replacement of methyl group at six bonded heterocyclic rings usually enlarged their antiseptic movement. Moiety 1 lacking any substituent of the aryl group of imidazole ring exerted moderate antibacterial movement beside the bacterial strains. The methyl substituent in compounds 2, and 4 expressed an appreciable movement alongside all the strains. The substitution of the –CH3 cluster in the parasite of the aryl assembly through the –OCH3 functionality in compounds 3, and 4 exhibits outstanding activity against *K.pneumoniae, B.cerus, E.coli, P. aeruginosa,* and *S. aureus* (Fig.-1).

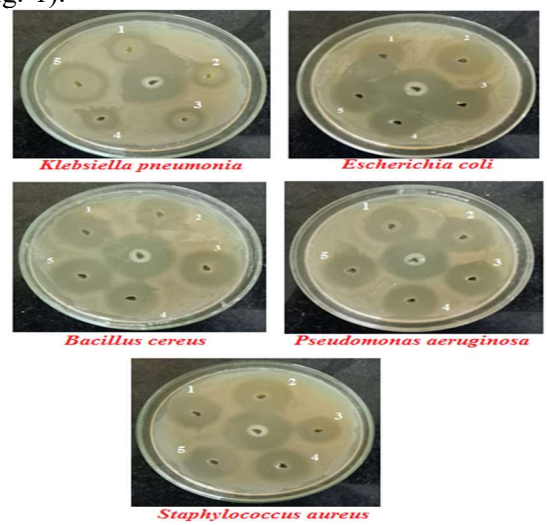


Fig.-1: Region Inhibition of Moieties 1-5 Against Antibacterial Strains

Table-1: Antibacterial Movement of Imidazole Moieties (1-5)

S. No.	Bacteria	Region of inhibition mm in width				
		1	2	3	4	5
1.	*Klebsiella pneumonia*	13	12	12	11	22
2.	*Escherichia coli*	13	15	17	19	18

3.	*Bacillus cereus*	20	19	21	20	22
4.	*Pseudomonas aeruginosa*	19	22	21	22	22
5.	*Staphylococcus aureus*	17	20	16	19	20

**Ciprofloxacin*

***In-vitro* Antifungal Movement**

In-vitro antifungal movement of moieties 1-5 were examined beside the fungal strain viz., *Trichoderma viride, Clodosorium, Candida albicans, Aspergillus flavus,* and *Aspergillus niger, Flucazonal* was old as a standard drug. Compound 1, and 2 heterocyclic rings have minimum inhibitory movement beside every strain. The substitution of $–CH_3$, $-OCH_3$, and –OH in the place of aryl groups 3, 4, and 5 exerted remarkable activities against fungal strains. MIC of antifungal values is reproduced in Table-2. From Table-2, it is obvious that compound 3, exhibits outstanding antifungal movement (Fig.-2).

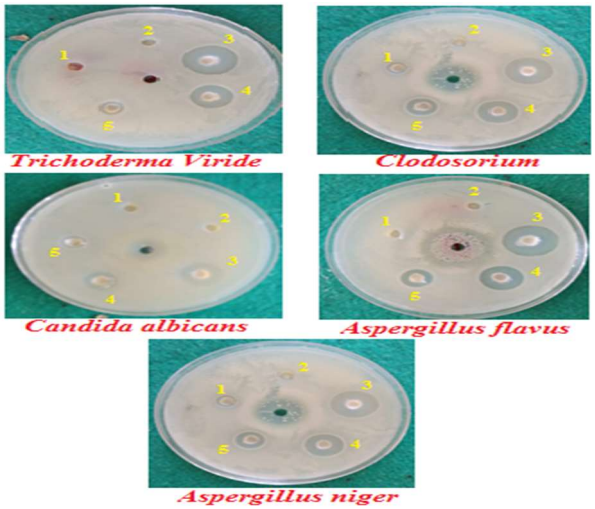


Fig.-2: Zone of Inhibition of Moieties 1-5 Against Antifungal

Table-2: Antifungal Behavior of Imidazole Moieties (1-5)

S. No.	Fungi	Region of inhibition mm in width				
		1	2	3	4	5
1.	*Trichoderma Viride*	4	3	20	16	8
2.	*Clodosorium*	3	2	19	16	13
3.	*Candida albicans*	2	2	16	14	9
4.	*Aspergillus flavus*	3	3	21	19	14
5.	*Aspergillus niger*	3	2	20	19	15

**Flucazonal*

***In-vitro*Antioxidant Behavior in DPPH Radical Method of the Moieties 1-5**

DPPH essential scavenging movement inference is a normal assessment for the resolve of antioxidant action and offers a quick practice for broadcasting the essential scavenging performance of precise compounds. A newly arranged DPPH solution exhibits an incorporation maximum at 517 nm. When an antioxidant is there in the normal molecule, it resolves to quench the DPPH free radical and exchange them for dark DPPH or a substituted analog of hydrazine will ensue in a reduction in absorbance. Hence, it will encourage a quick decrease in absorbance, which constructs the compound's additional potent antioxidant action. The proportion association of D in the MSO result of imidazole moieties 1-5 were compared with the interior normal Ascorbic acid. Moieties 1-5 with IC50 values 0.13, 0.14, 0.11, 0.16, and 0.11 µg/mL respectively (Table-3). Compound 3, 5 (IC50 = 0.11 µg/mL) was the majority powerful amalgam with $–OCH_3$ and –CH3 groups as substituent performance superior antioxidant movement even at extremely small concentrations. While, moieties 1, 2, and 4 show moderate activity, The graphical illustration of proportion inhibition at a dissimilar concentration of moieties 1-5 are revealed in Fig.-3. The IC50 importance of moieties 1-5 is shown in Fig.-4.

NMR Spectral Details

2-(Naphthalen-1-yl)-1-phenyl-1H-phenanthro[9,10-d]imidazole (1)

^1H ^{13}C NMR (400 MHz, $CDCl_3$): δ 8.87 (d, J = 7.6 Hz, 1H), 8.81 (d, J = 8.3 Hz, 1H), 8.74 (d, J = 7.7 Hz, 1H), 7.98 (d, J = 5.7 Hz, 1H),7.82 (d, J = 7.7 Hz, 2H), 7.75 (t, 1H), 7.68 (t, 1H), 7.52 (t, 1H), 7.49-7.43 (m, 3H), 7.34-7.29 (m, 6H). 121.87, 122.89, 123.01, 123.18, 124.16, 124.48, 125.02, 125.65, 126.02, 126.17, 126.34, 126.88, 127.38, 127.44, 128.05, 128.15, 128.34, 128.49, 129.28, 129.48, 129.55, 129.73, 133.21, 133.47, 137.38, 138.04, 150.48. MS: m/z. 420.80 $[M^+]$

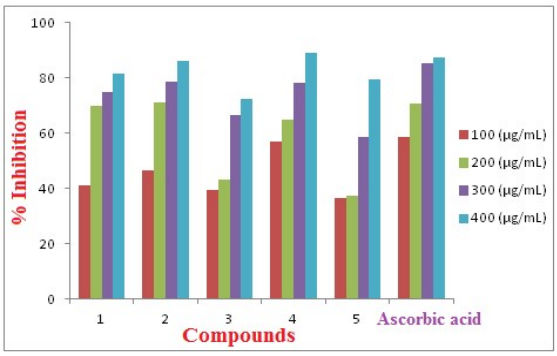


Fig.-3: The Percentage Inhibition at Diverse Concentration of Moieties 1-5

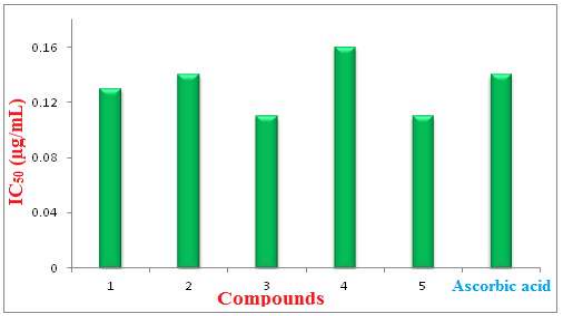


Fig.-4: IC_{50} Assessment of the Moieties 1-5

Table-3: In-vitro Anti-Oxidant Behavior in DPPH Radical Method of the Moieties 1-5

Compounds	% Inhibition at dissimilar concentrations				IC_{50} (µg/mL)
	100 µL	200 µL	300 µL	400 µL	
1	40.99	69.74	75.03	81.61	0.13
2	46.68	71.04	78.45	86.34	0.14
3	39.48	43.29	66.73	72.26	0.11
4	57.05	64.69	78.17	88.94	0.16
5	36.69	37.50	58.78	79.42	0.11
Ascorbic acid	58.68	70.60	85.41	87.50	0.14

2-(Naphthalen-1-yl)-1-p-tolyl-1H-phenanthro[9,10-d]imidazole(2)

^1H ^{13}C NMR (400 MHz, $CDCl_3$): δ 2.33 (s, 3H), 8.89 (d, J = 7.8 Hz, 1H), 8.78 (d, J = 8.6 Hz, 1H), 8.72 (d, J = 8.2 Hz, 1H), 7.97 (d, J = 7.5 Hz, 1H), 7.82 (d, J = 8.1 Hz, 2H), 7.19 (d, J = 7.8 Hz, 2H), 7.11 (d, J = 8.2 Hz, 2H), 7.73 (t, 1H), 7.66 (t, 1H), 7.54 (t, 1H), 7.42 (q, 3H) 7.34-7.25 (m, 4H). 21.31, 121.11, 122.87, 123.12, 123.20, 124.14, 124.50, 124.70, 125.00, 125.10, 125.62, 126.04, 126.14, 126.35, 126.83, 127.38, 127.53, 127.77, 128.15, 128.34, 128.39, 129.28, 129.47, 129.67, 130.20, 133.23, 133.44, 133.76, 135.32, 137.27, 139.29, 150.63. MS: m/z. 434.10 $[M^+]$.

1-(4-Methoxyphenyl)-2-(naphthalen-1-yl)-1H-phenanthro[9,10-d] imidazole (3)

^1H ^{13}C NMR (400 MHz, DMSO): δ 3.73 (s, 3H), 8.97 (d, J = 8.6 Hz, 1H), 8.92 (d, J = 8.4 Hz, 1H), 8.67 (d, J = 7.5 Hz, 1H), 7.86 (d, J = 8.1 Hz, 1H), 7.76 (d, J = 7.4 Hz, 1H), 7.56 (d, J = 8.0 Hz, 1H), 7.39 (t, 1H), 7.22 (d, J = 8.3 Hz, 1H), 6.96 (d, J = 8.4 Hz, 2H), 7.97 (t, 2H), 7.68 (t, 2H), 7.56-7.43 (m, 5H).

55.28, 114.62, 120.27, 121.98, 122.59, 123.66, 124.42, 124.67, 125.19, 125.60, 125.78, 126.20, 126.69, 126.82, 126.86, 127.24, 127.42, 127.64, 128.04, 128.09, 128.29, 128.41, 129.50, 129.52, 129.72, 129.95, 132.35, 132.76, 136.28, 150.47, 159.47. m/z. 450.50 [M^+].

1-(3,5-Dimethylphenyl)-2-(naphthalen-1-yl)-1H-phenanthro[9,10-d] imidazole (4)

^{1}H &^{13}C NMR (400 MHz, DMSO): δ 2.17 (s, 6H), 8.97 (d, J = 8.1 Hz, 1H), 8.93 (d, J = 8.2 Hz, 1H), 8.65 (d, J = 7.8 Hz, 1H), 7.99 (t, 2H), 7.92 (d, J = 7.6 Hz, 1H), 7.78 (d, J = 7.2 Hz, 1H), 7.75 (d, J = 6.6 Hz, 2H), 7.08 (s, 1H), 7.18 (t, 2H), 7.36-7.41 (m, 3H),7.60-7.48 (m, 3H). 20.54, 120.36, 121.99, 122.45, 123.66, 124.42, 124.66, 125.22, 125.44, 125.66, 125.83, 126.06, 126.22, 126.33, 126.71, 126.76, 127.00, 127.23, 127.45, 127.62, 127.90, 128.04, 128.29, 128.40, 129.54, 131.01, 132.28, 132.75, 136.27, 137.28, 138.90, 150.06. MS: m/z. 448.60 [M^+].

1-(1-phenyl-1H-phenanthro[9,10-d]imidazol-2-yl)naphthalen-2-ol (5)

^{1}H &^{13}C NMR (400 MHz, DMSO): δ, 13.99 (s, 1H), 8.95 (d, J= 8.5 Hz, 1H), 8.89 (d, J = 9.1 Hz, 1H), 8.79 (d, J = 8.9 Hz, 1H), 8.12 (d, J = 8.1 Hz, 1H), 7.89 (d, J = 7.4 Hz, 2H), 7.76 (t, J = 8.9 Hz, 1H), 7.72 (t, J = 8.2 Hz, 1H), 7.63 (t, J = 7.7 Hz, 1H), 7.52 (q, J = 8.1 Hz, 3H), 7.40 – 7.39 (m, 6H), 121.07, 122.89, 123.01,123.18, 124.16, 124.48, 125.02, 125.65, 126.02, 126.17, 126.34, 126.88, 127.38, 127.44, 128.05, 128.15, 128.34, 128.49, 129.28, 129.48, 129.55, 129.73, 133.21, 133.47, 137.38, 138.04, 150.48. MS: m/z. 436 [M^+].

CONCLUSION

The antibacterial behavior of methyl substituent in compounds 2, and 4 expressed an appreciable movement besides all the strains. The substitute of the –CH_3 cluster in the parasite of the aryl cluster through the –OCH_3 functionality in moieties 3, and 4 exhibits outstanding activity against *K. pneumoniae, B.cerus, E.coli, P. aeruginosa,* and *S. aureus*. The antifungal actions of –CH_3, -OCH_3, and –OH substituted position of aryl groups 3, 4, and 5 exerted remarkable activities against fungal strains. From the observation compound, 3 exhibits tremendous antifungal activity. Anti-oxidant of moieties 1-5 with IC_{50} standards are 0.13, 0.14, 0.11, 0.16, and 0.11 µg/mL, respectively. Moieties 3, and 5 (IC_{50} = 0.11 µg/mL) was the majority powerful amalgam with –OCH_3 and –CH_3 group as substituent performance of superior antioxidant movement even at extremely small concentration, While moieties 1, 2, and 4 showed moderate activity.

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CONFLICT OF INTERESTS

The authors declare that there is no conflict of interest.

AUTHOR CONTRIBUTIONS

All the authors contributed significantly to this manuscript, participated in reviewing/editing and approved the final draft for publication.The research profile of the authors can be verified from their ORCID ids, given below:

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