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Antimicrobial activity of some novel 1-(1,3,4-oxadiazol-2-yl)-*1H*-benzo[d]imidazolele substituted derivatives

***Neetu Soni, Namrata Soni and Pushpraj Gupta**

Department of Pharmaceutical Sciences, Faculty of Health Sciences, Sam Higginbottom Institute of Technology and Sciences, Naini, Allahabad, (U.P.) 211007, India

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ABSTRACT

In this study 12 benzmidazoles bearing oxadiazole moiety were synthesized in order to investigate their possible antibacterial and anti-fungal activities. Derivatives of benzimidazole were synthesized by nucleophilic substitution of 1H benzimidazoles with ethylchloroformate to yield acetate. The resulting acetate on the treatment with hydrazine hydrate and further with substituted carboxylic acid in the presence of phosphorous oxy chloride afforded corresponding oxadiazole derivatives. The structures of all compounds were established by IR, ^{1}HNMR, ^{13}C NMR and mass spectral data. Almost all newly synthesized compounds showed moderate to good antimicrobial activity.

Keywords: benzmidazoles, oxadiazole , Antibacterial activity, Antifungal activity

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INTRODUCTION

Benzimidazole heterocyclics are great importance in their biological as well as synthetic approach of medicinal chemistry. Derivatives of benzimidazoles nucleus showed remarkable biological activity as antitubercular[1,2], antihypertensive [3], GABA modulator[4], antitumor [5], antimicrobial including anti-HIV [6, 7, 8]. Oxadiazole is associated with various pharmaceutical and biological activities. It displays pronounced antifungal [9] and antimycobacterial [10] activities. Here light on some rationally designed compounds with biologically active antimicrobial having benzimidazole and oxadiazole moiety. It would be worthwhile to synthesize some new benzimidazole derivatives bearing oxadiazole.

MATERIALS AND METHODS

All melting points were determined by open capillary tube and were uncorrected. The Infrared spectra were recorded in KBr on Shimadzu FT-IR 157 spectrophotometer. ^{1}H NMR spectra were measured in DMSO-D_6 or $CDCl_3$ solutions on a Perkin–Elmer EM 300 MHz spectrometer using TMS as internal standard. The mass spectra were recorded on a JEOL JMS-D 300 spectrometer operating at 70 eV. The elemental analysis was carried out by using Elementar Vario EL III element analyser. Reactions were routinely monitored by thin-layer chromatography (TLC) on Silica Gel.

Methods of synthesis [11, 12, 13]

Synthesis of 1H-benzimidazole (2): 1H-benzimidazole was prepared by heating 0.24 mol of *o*-phenylenediamine in round bottomed flask with 0.48 mol of 90% formic acid on water bath at 100^{o}C for 2h, cooled, added 10% NaOH solution slowly with constant stirring until the mixture is just alkaline to litmus. Filtered off the product at the pump, cooled and washed with ice cold water, recrystallized with hot water, yield 90%, mp 171-173^{o} C.

Synthesis of ethyl 1H-benzo[d]imidazole-1-carboxylate (3): An equimolar solution of of 1H-benzimidazole (2) (1.18g, 0.01mol) and ethylechloroformate (0.95ml, 0.01mol) in dry acetone (4ml) in the presence of K_2CO_3 (1g) was refluxed on a water bath for 6h. The solvent was removed by vacuum distillation and the residue was dried and recrystallized from chloroform to give (3). Yield 90% , mp 170^{o}C.

Synthesis of 1H-benzo[d]imidazole-1-carbohydrazide(4): Compound (3) (1.9g, 0.01mol) dissolved in methanol (50ml) and 99% hydrazine hydrate (1ml) was refluxed for 4-5h. The reaction mixture was cooled and solid was filtered off, washed with methanol to obtain (4). Yield 85%, mp 180^{o}C.

Synthesis for 5- substituted 1-(1,3,4-oxadiazol-2-yl)-1H-benzo[d]imidazole(5a-l)
General method: A solution of hydrazide (4) (1.6g, 0.01mol) and corresponding acid (0.01mol) in $POCl_3$ (30ml) was refluxed to 18-20h. Excess solvent was removed by steam distillation and the solution poured on ice with stirring and the product was precipitated by neutralization by ammonia, filtered, washed with water and recrystallized by chloroform to get respective oxadiazole. **Scheme 1** [16]

(5-(1H-benzo[d]imidazol-1-yl)-1,3,4-oxadiazol-2-yl)methanamine(5a):
Yield 50%, IR (KBr) cm^{-1}: 3226 (N-H), 3169(C-H), 1555 (C=N), 1494(C=C), 1296 (C-N), 960 (C-C), 1082 (C-H), 792 (C-H), 825(C-H),^{1}H-NMR (DMSO-d_6) δ ppm: 2.0(s, 2H-NH_2), 3.82 (s, 2H- CH_2), 8.18 (s,-N-CH-N) 7.26-7.70 (m, 4H, Ar-H), **^{13}C**-NMR (500 Hz, DMSO, δ in ppm); 43(NH_2-CH_2), 115.6,123.05, 135.2. 138.9, 143.2 (benzimidazole), 155.54, 172.65 (oxa). TOF-MS ES+1.55e3, m/z: 201.03(100%), 215(43%), 216(10%).

4-(5-(1H-benzo[d]imidazol-1-yl)-1,3,4-oxadiazol-2-yl)-3-hydroxybenzenesulfonic acid (5b):
IR (KBr) cm^{-1}: 3426 (S=O), 3169(S-OH), 1555 (C=N), 683, 1494(C=C), 1296 (C-N), 960 (C-C), 1082 (C-H), 792 (C-H), 825(C-H),^{1}H-NMR (DMSO-d_6) δ ppm: 2.0(s, 1H, S-OH), 5.00 (s, 1H, Ar-O-H) 7.26-7.34 (m, 4H, benzimidazole, Ar-H), 8.00 (s, 1H, benzimidazole,- N-CH-N), 7.46, 7.55, 7.59(m, 3H, Ar, sulphosalisylic acid) **^{13}C**-NMR (500 Hz, DMSO, δ in ppm); 115.3, 123.0, 135.2, 138.9,(Ar-benzimidazole), 143.2, (-N-CH-N, benzimidazole), 155.54 (C_5, oxa), 172.65 (C_2, oxa), 114.1. 116.0, 121.2, 130.2 (Ar- sulphosalisylic acid), 151.2(C_4, Ar- sulphosalisylic acid), 164.5(C_1, Ar- sulphosalisylic acid) TOF-MS ES+1.55e3, 288.4 (100%), 358(24%), 359(5.7%)

1-(5-(pyridin-4-yl)-1,3,4-oxadiazol-2-yl)-1H-benzo[d]imidazole(5c):
IR (KBr) cm^{-1}; 3058 (N-H), 1603 (C=N), 1494 (C=C), 1279(C-N), 1177(C-C), 1103(C-H), 781(C-H), 870(C-H), 701(C-H).^{1}H-NMR (DMSO-d_6) δ ppm; 7.26-7.70 (m, 4H, benzimidazole, Ar-H), 8.08 (s, 1H, benzimidazole,- N-CH-N), 7.65, 8.48 (m, 4H, 4-pyridine), **^{13}C**-NMR (500 Hz, DMSO, δ in ppm); 115.5, 123.4, 135.7, 138.0,(Ar-benzimidazole), 147.3, (-N-CH-N, benzimidazole), 152.54 (C_5, oxa), 164.6 (C_2, oxa), 121.4, 143.7, 149.8 (4-pyridine), TOF-MS ES+1.55e, 202 (100%), 263(14%), 264 (20%).

1-(5-(4-nitrophenyl)-1,3,4-oxadiazol-2-yl)-1H-benzo[d]imidazole(5d):
IR (KBr) cm^{-1}; 3167 (N-H), 1466 (C=C), 2949 (C-H), 1589 (N-H), 1625 (C=N), 1424 (C-N), 1162 (C-C), 1084 (C-C), 1261 (C-H), 954 (C-H), 855 (C-H), 839 (C-H). ^{1}H-NMR (DMSO-d_6) δ ; 7.30-7.82 (m, 4H, benzimidazole, Ar-H), 8.38 (s, 1H, benzimidazole,- N-CH-N), 7.75, 8.35 (m, 4H, NO_2benzene), ^{13}C-NMR (500 Hz, DMSO, δ in ppm);); 115.5, 123.4, 135.8, 138.0,(Ar-benzimidazole), 143.5, (-N-CH-N, benzimidazole), 155.5 (C_5, oxa), 164.6 (C_2, oxa), 121.4, 128.4, 132.8, 143.7 (NO_2 – benzene), TOF-MS ES: 287(100%), 307 (32%), 308 (12%).

1-(5-phenyl-1,3,4-oxadiazol-2-yl)-1H-benzo[d]imidazole(5e):
IR (KBr) cm^{-1}; 3069 (N-H), 1612 (C=N), 1486 (C=C), 1282(C-N), 1165(C-C), 1112(C-H), 780(C-H), 868(C-H),797(C-H).^{1}H-NMR (DMSO-d_6) δ ppm; 7.14-7.85 (m, 4H, benzimidazole, Ar-H), 8.90 (s, 1H, benzimidazole,- N-CH-N), 7.48, 7.32, 7.22 (m, 5H, benzene), ^{13}C-NMR (500 Hz, DMSO, δ in ppm);); 112.5, 121.4, 136.8, 139.0,(Ar-benzimidazole), 145.5, (-N-CH-N, benzimidazole), 155.8 (C_5, oxa), 168.0 (C_2, oxa), 126.0, 127.8, 128.5, 129.5 (benzene), TOF-MS ES+1.55e3, (M^+); 212 (100), 262 (18%), 263 (12%).

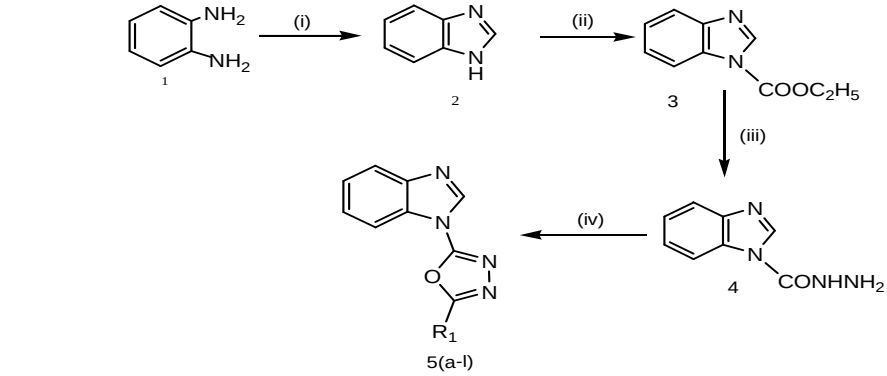
1-(5-(2-chlorophenyl)-1,3,4-oxadiazol-2-yl)-1H-benzo[d]imidazole(5f):
IR (KBr) cm^{-1}; 3166 (N-H), 1467 (C=C), 2939 (C-H), 1549 (N-H), 1675 (C=N), 1474 (C-N), 1132 (C-C), 1074 (C-C), 1265 (C-H), 964 (C-H), 865 (C-H), 839 (C-H). ^{1}H-NMR (DMSO-d_6) δ ppm; 7.26 -7.70 (m, 4H, benzimidazole, Ar-H), 8.06 (s, 1H, benzimidazole,- N-CH-N), 7.16, 7.20, 7.33, 7.42 (m, 4H,Cl- benzene), ^{13}C-NMR (500 Hz, DMSO, δ in ppm); 115.3, 123.6, 135.8, 138.0,(Ar-benzimidazole), 143.2, (-N-CH-N, benzimidazole), 153.8 (C_5, oxa), 164.7 (C_2, oxa), 127.7, 128.9, 129.4, 132.7, 136.9 (Cl-benzene), TOF-MS ES; 212 (100), 296 (35%), 297 22%).

1-(5-(4-chlorophenyl)-1,3,4-oxadiazol-2-yl)-1H-benzo[d]imidazole(5g):
IR (KBr) cm^{-1}; 3167(N-H), 1650 (C=N), 3001 (C-H), 1261(C-N), 536 (C-Br), 1560 (C=C), 1573(C=C), 1162 (C-C), 1084 (C-C),1065 (C-H), 778 (C-H), 696 (C-H), 677 (C-H). ^{1}H-NMR (DMSO-d_6) δ ppm; 7.26 -7.70 (m, 4H, benzimidazole, Ar-H), 8.08 (s, 1H, benzimidazole,- N-CH-N), 7.33, 7.42 (m, 4H,Cl- benzene), ^{13}C-NMR (500 Hz, DMSO, δ in ppm); 116.3, 123.0, 135.6, 138.3,(Ar-benzimidazole), 145.2, (-N-CH-N, benzimidazole), 152.9 (C_5, oxa), 165.9 (C_2, oxa), 124.3, 128.7, 129.4, 129.4, 134.3, (Cl-benzene), TOF-MS ES; 220 (100), 296 (56%), 297 (34%).

(Z)-1-(5-styryl-1,3,4-oxadiazol-2-yl)-1H-benzo[d]imidazole(5h):
IR (KBr) cm^{-1}; 3408 (N-H), 2934 (C-H) 1626 (C=N), 2934(C-H), 1281(C-N), 1611 (C=C), 1094 (C-H), 813 (C-H), 863 (C-H), 1205 (C-C). ^{1}H-NMR (DMSO-d_6) δ ppm; 7.26 -7.70 (m, 4H, benzimidazole, Ar-H), 8.08 (s, 1H, benzimidazole,- N-CH-N), 7.14, 7.21, 7.30, (m, 5H ,Ar- styryl), 6.56 (s, 4H, CH-Ar) ^{13}C-NMR (500 Hz, DMSO, δ in ppm); 115.3, 123.0, 135.6, 138.3,(Ar-benzimidazole), 143.2, (-N-CH-N, benzimidazole), 152.9 (C_5, oxa), 165.9 (C_2, oxa), 126.4, 128.7, (Ar- styryl), 133.4, 135.2 (CH-Ar)TOF-MS ES; 201 (100%), 288 (12%), 289 (42%).

4-(5-(1H-benzo[d]imidazol-1-yl)-1,3,4-oxadiazol-2-yl)benzenamine(5i):
IR (KBr) cm^{-}3067 (N-H), 1465 (C=C), 2938 (C-H), 1564 (N-H), 1433 (C-N), 1209 (C-C), 1615 (C=N), 1270 (C-C), 1047 (C-H), 960(C-H), 858 (C-H), 840 (N-H), ^{1}H-NMR (DMSO-d_6) δ ppm; 7.26 -7.70 (m, 4H, benzimidazole, Ar-H), 8.08 (s, 1H, benzimidazole,- N-CH-N), 6.52, 7.73 (m, 4H ,-NH_2-Ar), 4.0(s, 2H, NH_2) ^{13}C-NMR (500 Hz, DMSO, δ in ppm; 152.9 (C_5, oxa), 164.9 (C_2, oxa), 116.2, 116.8, 128.3 (Ar- NH_2), 148.4(C-NH_2)TOF-MS ES; 234 (100%), 277 (18%), 278 (12%).

1-(1,3,4-oxadiazol-2-yl)-1H-benzo[d]imidazole(5j):
IR (KBr) cm^{-} 3167 (N-H), 1485 (C=C), 3038 (C-H), 1504 (N-H), 1439 (C-N), 1212(C-C), 1613 (C=N), 1295(C-C), 1043 (C-H), 958(C-H), 860 (C-H), 834 (N-H). ^{1}H-NMR (DMSO-d_6) δ ppm: 7.26-7.70 (m, 4H, Ar-H), **^{13}C**-NMR (500 Hz, DMSO, δ in ppm); 115.3, 123.0, 135.2. 138.9, 143.2 (benzimidazole), 155.54, 172.65 (oxa). TOF-MS ES+1.55e3, m/z: 105 (100%), 186(15%), 187(34%).



(i) HCOOH (ii) $ClCOOC_2H_5$ (iii) EtOH, $NH_2NH_2.H_2O$ (iv) R_1COOH, $POCl_3$

$R_{1=}$a) $-CH_2NH_2$ b) c) d) e) f) g) h) i) j) -H k) l) $ClCH_2$-

Scheme 1. Synthesis of benzimidazole derivatives

1-(5-(1H-benzo[d]imidazol-1-yl)-1,3,4-oxadiazol-2-yl)ethanol(5k):
IR (KBr) cm^{-1}; 3256 (N-H), 1467 (C=C), 2967 (C-H), 1549 (N-H), 1675 (C=N), 1468 (C-N), 1132 (C-C), 1074 (C-C), 1265 (C-H), 964 (C-H), 865 (C-H), 839 (C-H). ^{1}H-NMR (DMSO-d_6) δ ppm: 1.49 (CH_3) 2.0 (OH), 4.68 (CH), 7.26-7.70 (m, 4H, Ar-H), **^{13}C**-NMR (500 Hz, DMSO, δ in ppm); 22.6 (CH_3), 71.8, (-CH-OH) 115.3, 123.0, 135.2. 138.9, 143.2 (benzimidazole), 155.54, 172.65 (oxa), TOF-MS ES+1.55e3, m/z: 201 (100%), 230(25%), 231(10%).

1-(5-(chloromethyl)-1,3,4-oxadiazol-2-yl)-1H-benzo[d]imidazole(5l):
IR (KBr) cm¯3067 (N-H), 1465 (C=C), 2938 (C-H), 1564 (N-H), 1613 (C=N), 1295(C-C), 1043 (C-H), 958(C-H), 860 (C-H), 834 (N-H).). ^{1}H-NMR (DMSO-d_6) δ ppm: 4.64 (CH_2), 7.26-7.70 (m, 4H, Ar-H), **^{13}C**-NMR (500 Hz, DMSO, δ in ppm); 44.7 (CH_3), 115.3, 123.0, 135.2. 138.9, 143.2 (benzimidazole), 155.54, 172.65 (oxa), TOF-MS ES+1.55e3, m/z: 214 (100%), 234(25%), 235(10%).

Antimicrobial activity study [14, 15]: The antibacterial activity of synthesized compounds (5a-l) were determined by using agar diffusion method against three gram positive bacteria [*Staphylococcus aureus* (NCIM-2079) *Bacillus subtilis* (NCIM-2063) *Bacillus cerus* (NCIM-2156)] and three gram negative bacteria [*Escherichia coli* (NCIM-2065), *Proteus vulgaris* (NCIM-2027) *Pseudomonas aeruginosa* (NCIM-2036)]

Fungi *Aspergillus fumigates*, (NCIM-2081*), Candida albicans*, (NCIM-2087) *Aspergillus niger* (NCIM-2191) were used to test antifungal activity. The compounds (5a-l) were dissolved in sterile DMSO at concentrations 25-200 µg/ml; uniform holes (6mm) were made in the agar plate by the help of a sterile borer and 0.2ml of the solution was filled in the hole of the agar plate seeded with the test microorganism and a blank with sterile DMSO was carried out as a negative control. Cefixime was used as standard for antibacterial activity and Fluconazole for antifungal activity. To evaluate the activity of synthesized compounds against bacteria and fungi, the diameter of the inhibitory zone around the hole was measured after incubation.

Antibacterial activity of the synthesized compounds was tested by agar diffusion method under standard conditions using Mueller Hinton medium as described by NCCLS. Agar plates were inoculated with a standardized suspension of microorganism tested and incubated at 37°C for 24 hours. Antifungal activity was evaluated in Potato Dextrose Agar medium (PDA), inoculated plates were incubated at 28 ± 2 ^{o}C for 7 days. The diameters of inhibition zones (in mm) of triplicate sets were measured and results were reported in **Table 2, Table 3.**

RESULTS AND DISCUSSION

Chemistry
The reaction sequence for different title compounds is outlined in **scheme 1**. The starting material 1H-benzo[d]imidazole **2** was prepared according through the reaction of o-phenylenediamine with formic acid . The structure of compound **2** was confirmed by comparison of its physical and spectral data with the reported one. Compound **2** yielded ethyl 1H-benzo[d]imidazole-1-carboxylate **3.** The structure of compound **3** was confirmed by proton NMR and elemental analysis. ^{1}H NMR spectra revealed the multiplet at δ 7.26-7.70 ppm corresponding to the four aromatic protons, 8.06 ppm for (–N-CH=N -). The appearance of signals at δ 4.20 ppm (-CH_2), 1.30 ppm (-CH_3) in - $COOC_2H_5$, confirms the formation of ester. This was also confirmed by IR spectra which shows a broad band at 1730 cm^{-1} due to ester and at 1635cm^{-1} (-C=N). Compound **3** on treatment with hydrazine hydrate resulted in the formation of 1H-benzo[d]imidazole-1-carbohydrazide **4.** IR spectrum of compound 4 showed >C= O band for amide at 1654cm^{-1} , -C =N stretch at 1648 cm^{-1} . H-1 NMR at δ 7.26-7.70 ppm due to aromatic ring, δ 8.0 ppm for sec amide (NH) and δ 2.04 ppm for NH_2 confirms the structure of 4. Compound 4 on the treatment with different carboxylic acid and phosphorous oxychloride yielded the 1-[(5-substituted-1,3,4-oxadiazole-2-yl)]-1H benzimidazole (5a-l). All the spectral data of compounds (5a-l) were in accordance with assumed structures.

Melting points were determined by open capillary method and were uncorrected (Table 1). The IR spectra (in KBr pellets) were recorded on a Shimadzu FT-IR 157 spectrophotometer. 1H NMR spectra were recorded on a Perkin–Elmer EM 300 MHz spectrometer using TMS as internal standard. The mass spectra were recorded on a JEOL JMS-D 300 spectrometer operating at 70 eV. Reactions were routinely monitored by thin-layer chromatography (TLC) on Silica Gel.

Antimicrobial activity test
All the synthesized compounds 5a-l were screened for their in vitro antimicrobial activity against the standard strains of pathogenic microorganism including Gram positive bacteria (Staphylococcus aures, Bacillus subtilis and Bacillus cerus), Gram negative bacteria (Escherichia coli, Proteus vulgaris, and Pseudomonas aeruginosa) and fungal strains (Candida aibicans, Aspergillus fumigates, Aspergillus niger). Solutions of the synthesized compounds (25, 50 100, 200 µg/ml) and standard drugs (Ciprofloxacin & Fluconazole)(25 µg/ml) were prepared in

DMSO. The diameter of zone of inhibition (in mm) was measured and results are reported in **Table 1 and Table 2** at 100 µg/ml concentration.

Table 1. Characterization data of (5a-l)

Compound	R	Molecular formulae	% Yield	MP (^{0}C)
5a	$-CH_2NH_2$	$C_{10}H_9N_5O$	60	160 – 62
5b	$-C_6H_3(OH)(SO_3H)$	$C_{15}H_{10}N_4O_5S$	89	172 – 74
5c	$-C_5H_4N$	$C_{14}H_9N_5O$	50	167- 69
5d	$4\text{-}NO_2C_6H_4$	$C_{15}H_9N_5O_3$	55	178- 80
5e	$-C_6H_5$	$C_{15}H_{10}N_4O$	70	196 – 98
5f	$2\text{-}ClC_6H_5$	$C_{15}H_9N_4OCl$	45	188 – 90
5g	$4\text{-}ClC_6H_5$	$C_{15}H_9N_4OCl$	46	196 – 98
5h	$-CH=CH-C_6H_5$	$C_{17}H_{12}N_4O$	49	159 – 61
5i	$4\text{-}NH_2C_6H_5$	$C_{15}H_{11}N_5O$	43	179 – 81
5j	H	$C_9H_6N_4O$	46	193 – 95
5k	$-CH(OH)(CH_3)$	$C_{14}H_{10}N_4O_2$	71	186 – 88
5l	$-CH_2Cl$	$C_{10}H_7N_4OCl$	67	194- 96

Table: 2 Antibacterial activity of synthesized compounds

Compound[a]	Zone of inhibition in mm					
	B.s	S.a	B.c	P.v	E.c	P.a
5a	13 ± 0.04	11 ± 0.03	15 ± 0.02	13 ± 0.02	11 ± 0.05	14 ± 0.05
5b	14 ± 0.03	12 ± 0.03	15± 0.04	15 ± 0.02	12 ± 0.05	12 ± 0.04
5c	13 ± 0.02	14 ± 0.04	11± 0.03	14 ± 0.03	9 ± 0.05	15 ± 0.04
5d	09 ± 0.05	11 ± 0.04	10± 0.04	8 ± 0.03	13 ± 0.05	13 ± 0.04
5e	10 ± 0.03	11 ± 0.05	14± 0.04	13 ± 0.03	12 ± 0.03	16 ± 0.03
5f	15 ± 0.02	13 ± 0.03	11± 0.04	17 ± 0.03	10 ± 0.03	13 ± 0.03
5g	12 ± 0.05	11 ± 0.04	13± 0.05	9 ± 0.05	12 ± 0.03	14 ± 0.03
5h	13 ± 0.01	11 ± 0.05	9± 0.02	12 ± 0.04	10 ± 0.03	14 ± 0.02
5i	15 ± 0.03	12 ± 0.01	16± 0.05	16 ± 0.05	12 ± 0.05	15 ± 0.01
5j	14 ± 0.04	12 ± 0.01	15± 0.01	15 ± 0.03	13 ± 0.05	14 ± 0.01
5k	15 ± 0.05	11 ± 0.02	14± 0.03	14 ± 0.02	12 ± 0.03	15 ± 0.01
5l	16 ± 0.02	14 ± 0.05	14± 0.05	13 ± 0.02	13 ± 0.02	14 ± 0.03
Cifexime	19 ± 0.01	18 ± 0.05	22± 0.02	22 ± 0.01	20 ± 0.04	21 ± 0.04

Symbols: S.a: Staphylococcus aureus B.s: Bacillus subtilis B.c: Bacillus cerus
E.c: Escherichia coli P.v: Proteus vulgaris P.a: Pseudomonas aeruginosa.
[a] Cifexime (25 µg/ml) was used as positive reference; synthesized compounds (100 µg/ml)

Table: 3 - Antifungal activity of synthesized compounds

Compound[a]	Zone of inhibition in mm		
	C. a	A.f.	A.n
5a	19 ± 0.04	19 ± 0.04	18± 0.04
5b	16 ± 0.03	15 ± 0.03	19 ± 0.03
5c	18 ± 0.02	14 ± 0.02	19 ± 0.02
5d	19 ± 0.05	13 ± 0.05	17 ± 0.05
5e	16 ± 0.03	17 ± 0.03	14 ± 0.03
5f	17 ± 0.02	19 ± 0.02	13 ± 0.02
5g	17 ± 0.05	13 ± 0.05	12 ± 0.05
5h	19 ± 0.01	13 ± 0.01	18 ± 0.01
5i	18 ± 0.03	18 ± 0.03	15 ± 0.03
5j	16 ± 0.04	14 ± 0.04	16 ± 0.04
5k	15 ± 0.05	18 ± 0.05	17 ± 0.05
5l	18 ± 0.02	16 ± 0.02	18 ± 0.02
Fluconazole	21 ± 0.01	19 ± 0.01	21 ± 0.01

Symbols: C.a : Candida aibicans A.f : Aspergillus fumigatus
A.n : Aspergillus niger
[a] Fluconazole (25 µg/ml) was used as positive reference and synthesized compounds (100 µg/ml)

CONCLUSION

Several (1,3,4-oxadiazol-2-yl)-1H-benzo[d]imidazolele (5a-l) synthesized and structures were confirmed by IR, ^{1}H NMR, ^{13}C NMR and Mass spectral studies. The pharmacological study was undertaken to evaluate the effect of substituents on the antimicrobial activity. All synthesized compounds exhibit good antibacterial activity against Gram positive and Gram negative bacteria. Compounds showed moderate antifungal activity. compound 5f, 5i have good activity against B. subtilis, B. cerus and P. aeruginosa. Compounds 5a , 5b, 5j found to be good active against

E. coli. On the other hand all the synthesized compounds show very good activity against fungal strains specially Aspergillus and C. albicans.

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