Short communication

Synthesis of New Series of Pyrazole and Imidazole Derivatives and their Antimicrobial Activity

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Abstract

New series of pyrazole derivatives 3-(furan-2-yl)-4-(5-hydroxy-4*H*-pyrazol-3-yl)-*N*-phenylbutanamide **1**–**5** and imidazole derivatives 3-(furan-2-yl)-3-(1*H*-imidazol-1-yl)-*N*-phenylpropanamide **6**–**10** were synthesized by the Mannich base method. Synthesized compounds **1**–**10** were confirmed by IR, ^{1}H NMR, ^{13}C NMR, Mass and elemental analysis and further screened for antimicrobial activity.

Keywords: Pyrazole derivative, Imidazole derivatives, Mannich condensation, Antibacterial activity, Antifungal activity.

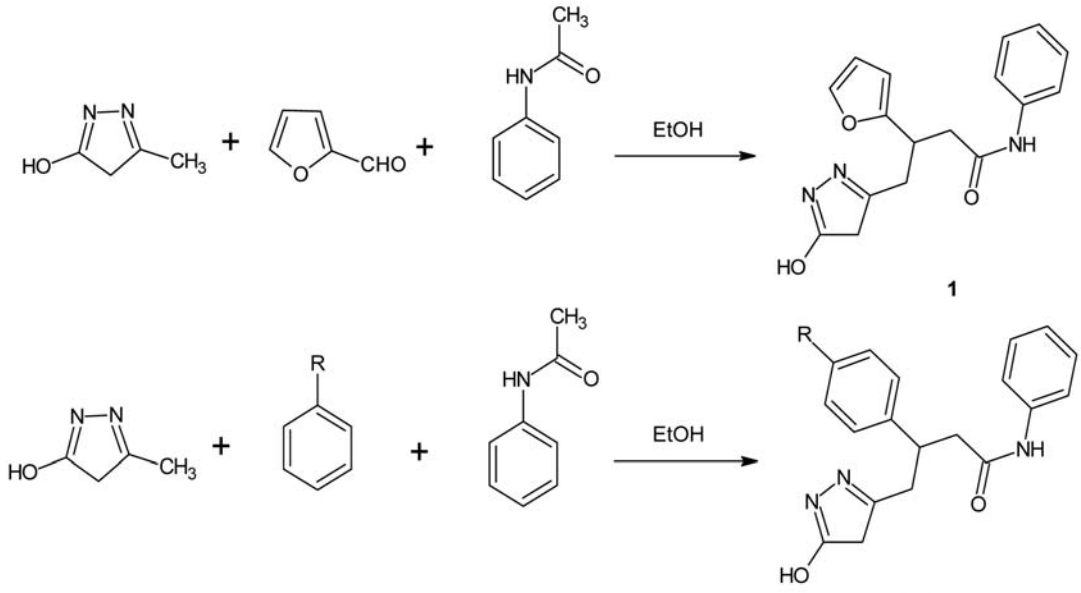
1. Introduction

In recent years serious attention has been directed toward the discovery and development of new antimicrobial drugs. Pyrazoles show important biological activity such as antimicrobial,[1–3] anticoagulant activities,[4–6] anti-inflammatory,[7–9] antirheumatic[13,14] and anti-inflammatory[15] activities. Also imidazole and their derivatives represent an important class of heterocyclic compounds and many naturally occurring imidazoles are known to possess biological activity.[16] A number of antifungal imidazole agents has been studied and now they are used in clinical practice such as miconazole and bifonazole.[17] The imidazole nucleus is also a major component of a variety of drugs such as angiotensin II receptor antagonists, oral anti-inflammatory agents, protein kinase inhibitors and fungicides.[18] Imidazole derivatives have many pharmacological properties and play important roles in biochemical processes.[19] Many of the substituted imidazoles are inhibitors, used as fungicides and herbicides, plant growth regulators and therapeutic agents.[20] Imidazoles are frequently found as part of a large number of medicinally significant substances.[21,22] Imidazole derivatives possess a broad spectrum of pharmacological activities such as anticonvulsant,[23] antiparkinson[24] and monoamineoxidase (MAO) inhibitory[25] activity. Indeed, Mannich reaction is of considerable importance for the synthesis and modification of biologically active compounds.[26,27] Mannich bases have several biological activities such as antimicrobial,[28–32] cytotoxic,[33,34] and anticancer.[35,36] In the present study, a new series of pyrazole and imidazole derivatives have been synthesized and screened for the antimicrobial activity.

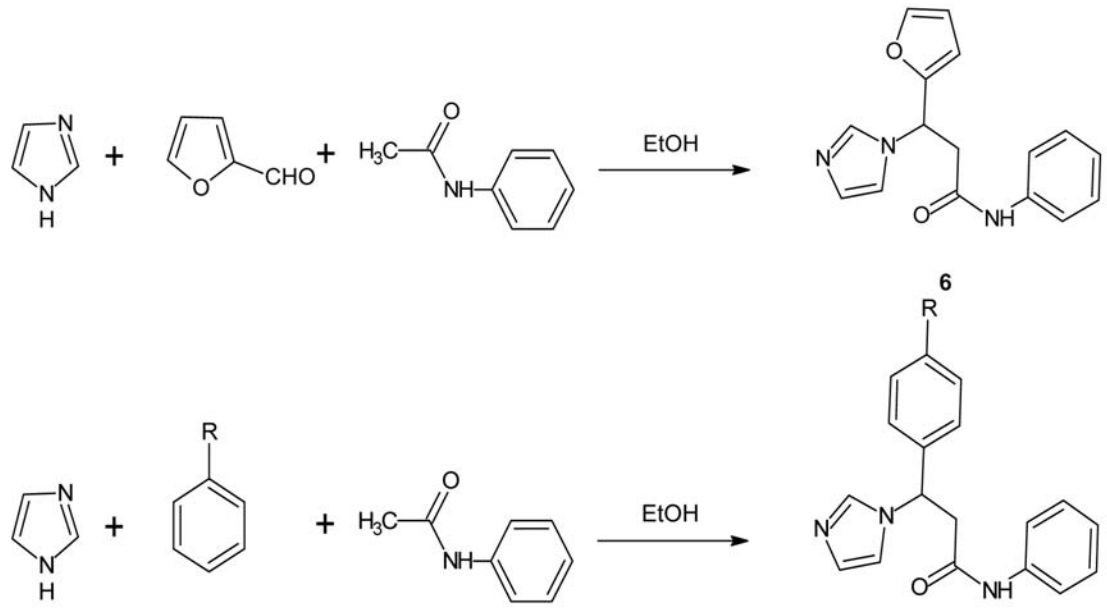
2. Results and Discussion

2. 1. Chemistry

The compounds **1**–**10** were synthesized by the Mannich base method (Schemes 1 and 2). Physicochemical data of compounds **1**–**10** are given in Table 1. Compounds were confirmed by recording the IR, ^{1}H NMR, ^{13}C NMR and elemental analyses. The IR spectrum of compound **1** shows absorption bands at 669 and 1649 cm^{-1} corresponding to an aromatic C–Hstr and NHCO groups respectively. The ^{1}H NMR spectrum of compound **1** shows singlets at δ 10.21, 3.21 and 2.60 corresponding to CONH, -CH- and C$\underline{H}_2$-CO-NH protons, respectively. ^{13}C NMR spectrum of compound **1** shows peaks at δ 172.9, 31.9 and 33.0 corresponding to CONH, -N-CH- and $\underline{C}H_2$-CO-NH carbons, respectively. Mass spectrum (Figure **1**) of compound **1** shows a molecular ion peak at *m/z* 311.42 (M^+, 12%), which confirmed the molecular mass of compound **1**, mass spectral fragmentation pattern of **1** is shown in Scheme 3.



Scheme 1. Synthesis of pyrazole derivatives **1–5**



Scheme 2. Synthesis of imidazole derivatives **6–10**

Table 1. Physicochemical characterization of compounds **1–10**

Compd. No.	R	Molecular formula	m.w.	Yield (%)
1	–	$C_{17}H_{17}N_3O_3$	311.33	82
2	–H	$C_{19}H_{19}N_3O_2$	321.37	80
3	–Cl	$C_{19}H_{18}ClN_3O_2$	355.81	76
4	–OH	$C_{19}H_{19}N_3O_3$	337.37	77
5	$–NO_2$	$C_{19}H_{18}N_4O_4$	366.37	79
6	–	$C_{16}H_{15}N_3O_2$	281.30	87
7	–H	$C_{18}H_{17}N_3O$	291.34	89
8	–Cl	$C_{18}H_{16}ClN_3O$	325.79	79
9	–OH	$C_{18}H_{17}N_3O_2$	307.34	84
10	$–NO_2$	$C_{18}H_{16}N_4O_3$	336.34	82

The IR spectrum of compound **6** shows absorption bands at 641 and 1640 cm^{-1} corresponding to aromatic CHstr and NHCO groups, respectively. The ^{1}H NMR spectrum of compound **6** shows singlets at δ 10.35, 5.41 and 3.42 corresponding to CONH, -CH- and -C<u>H</u>-CO-NH protons, respectively. ^{13}C NMR spectrum of compound **6** shows peaks at δ 173.2, 53.8 and 38.6 corresponding to CONH, N-CH- and <u>C</u>H_2-CH- carbons, respectively. Mass spectrum (Figure 2) of compound **6** shows a molecular ion peak at *m/z* 281.76 (M^+, 27%), which confirmed the molecular mass of compound **6**, mass spectral fragmentation pattern of compound **6** shown is shown in Scheme 4.

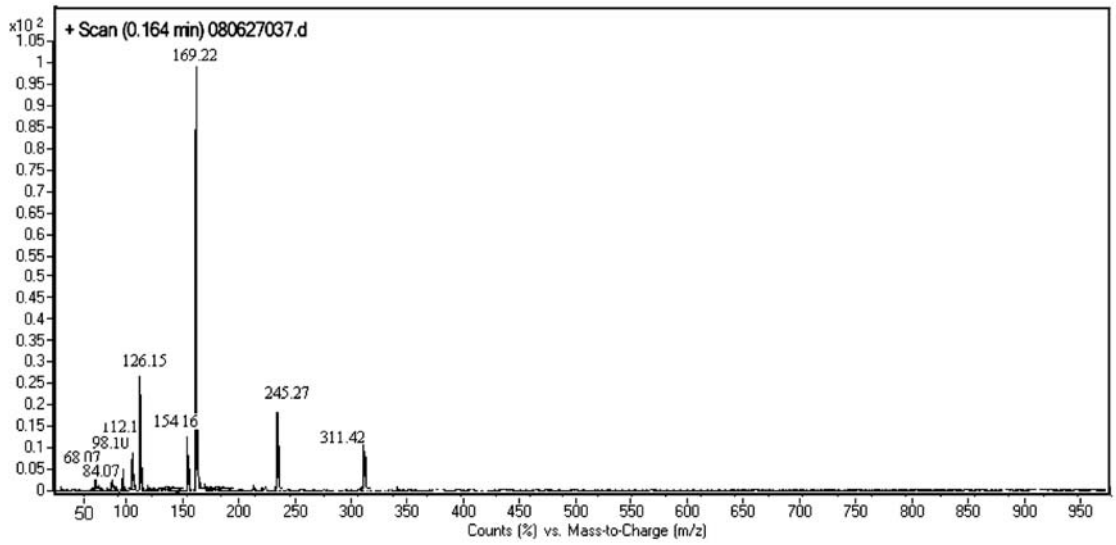
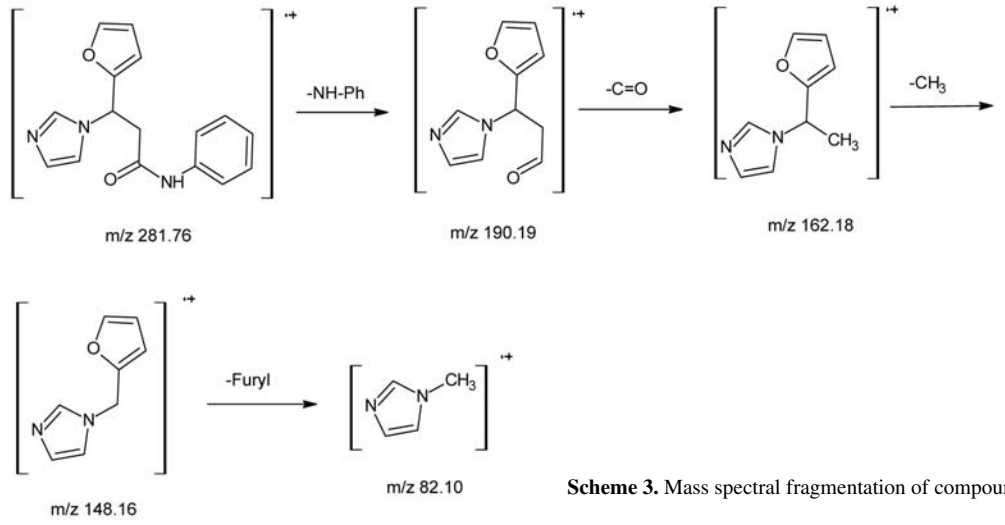


Figure 1. Mass spectrum of compound **1**



Scheme 3. Mass spectral fragmentation of compound **1**

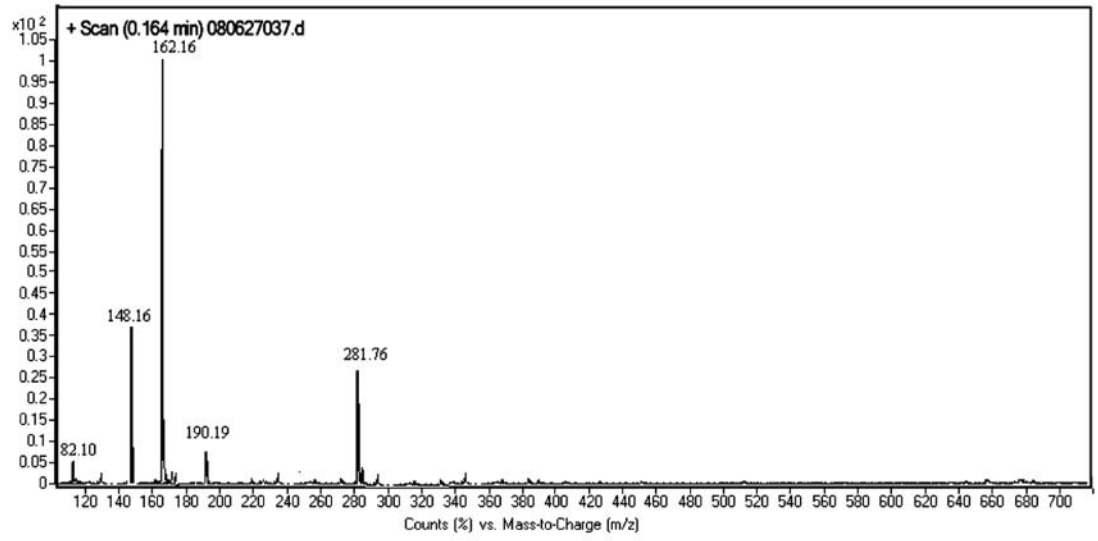
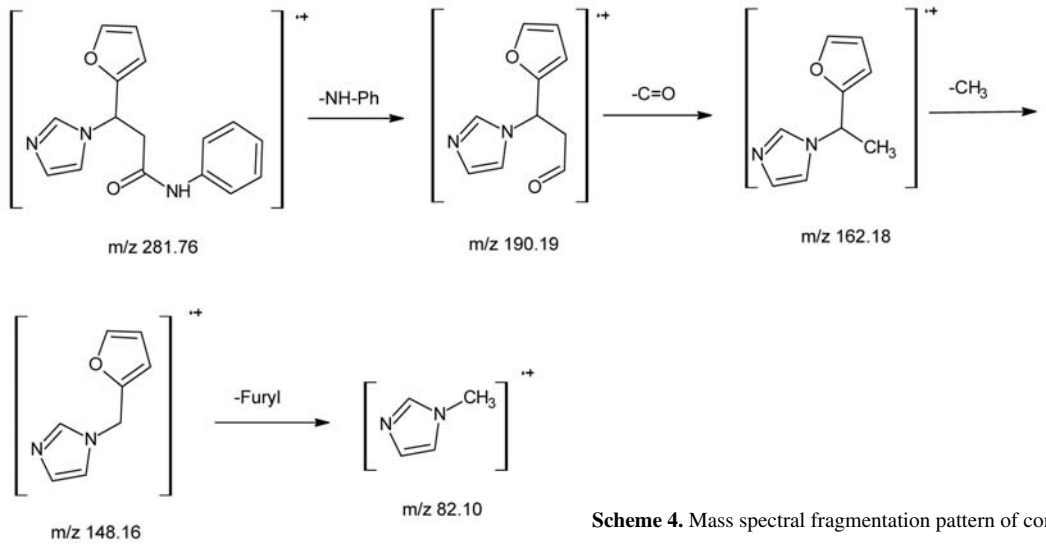


Figure 2. Mass spectrum of compound **6**



Scheme 4. Mass spectral fragmentation pattern of compound **6**

2. 2. Biological Screening

2. 2. 1. Antibacterial Activity

The bacterial zones of inhibition (in mm) for *Escherichia coli* and *Staphylococcus aureus* for compounds **1**–**10** are summarized in Table 2. Compound **6** was found to be highly active against *S. aureus* as compared with ciprofloxacin.

Table 2. Antibacterial activity of compounds **1–10**

Compounds No	*E. coli*	*S. aureus*
1	10	13
2	8	16
3	12	20
4	10	14
5	8	19
6	0	26
7	12	16
8	15	8
9	10	12
10	15	20
Standard	20	24

The compounds were used at concentration 100 μg/mL, ciprofloxacin used as the standard. Zone of inhibition measured in mm

2. 2. 2. Antifungal Activity

The zones of inhibition (in mm) for *Aspergillus niger* and *Candida albicans* for compounds **1**–**10** are summarized in Table 3. Compound **1** has equipotent activity against *C. albicans* as compared with standard clotrimazole.

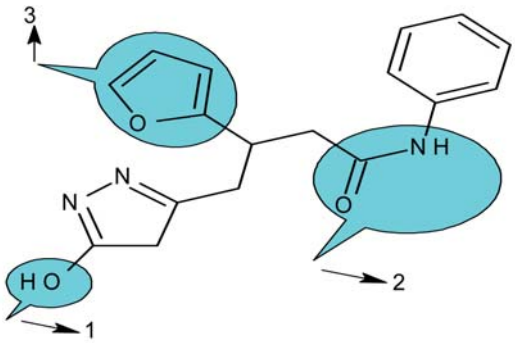
Table 3. Antifungal activity of compounds **1–10**

Compounds No.	*A. niger*	*C. albicans*
1	15	22
2	8	16
3	12	10
4	6	12
5	13	21
6	24	10
7	12	8
8	15	12
9	16	19
10	8	18
Standard	23	25

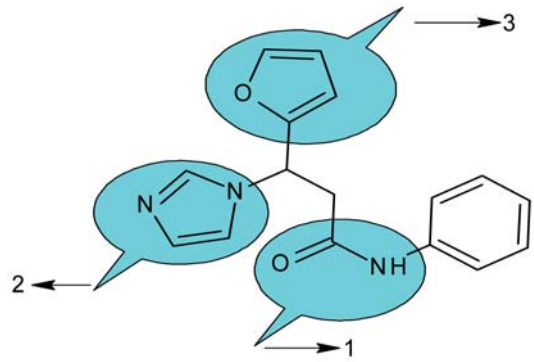
The compounds were used at concentration 100 μg/mL, clotrimazole used as the standard. Zone of inhibition measured in mm.

2. 2. 3. Structural Activity Relationship

The OH and NHCO groups in compounds **6**–**10** have significance for antibacterial activity but for the majority of the compounds, though the compound **6** having furyl and imidazole rings along with OH and NHCO groups exhibits the highest activity against *S. aureus* compared with standard ciprofloxacin. Also antifungal screening for the compound **6** showed its high activity against *A. niger* compared with standard clotrimazole, whereas the compound **1** has equipotent activity against *C. albicans* compared with the standard clotrimazole. A rough comparison of the structure with the activity shows the imidazole derivatives to possess a higher potential biological activity compared with the pyrazole derivatives.



Compound **1**



Compound **6**

3. Experimental

3. 1. Chemistry

Melting points were recorded in open capillary tubes and are uncorrected. The IR spectra was recorded in KBr on a FT-IR Shimadzu 8201pc (4000–400 cm^{-1}) and ^1H NMR and ^{13}C NMR on Bruker DRX-300 MHz. Elemental analysis (C, H, and N) were undertaken using an Elemental analyzer model vario EL III. The purity of the compounds was checked by thin layer chromatography (TLC) with silica gel plates.

3. 1. 1. General procedure for the synthesis of compounds 1–10

3-(Furan-2-yl)-4-(5-hydroxy-4*H*-pyrazol-3-yl)-*N*-phenylbutanamide (1)

To prepare the solution of 5-methyl-4*H*-pyrazol-3-ol (9.8 g, 0.1 mol), acetanilide (13.5 g, 0.1 mol) and furaldehyde (9.6 g, 0.1 mol) in ethanol, the reaction mixture was refluxed for 3 h. The reaction mixture were cooled and poured into ice-cold water. The precipitated material was obtained in a few minutes. The precipitate was collected by filtration, dried and recrystallised from absolute ethanol. Using above procedure was followed by all the remaining compounds **2**–**5**.

m.p. 167 °C; IR (cm^{-1}): υ 3423 (C-OH), 1649 (CONH), 669 (CH); ^1H NMR (DMSO-d_6): δ 2.21 (s,1H, OH), 1.60 (s, 2H, CH in pyrazole), 1.82 (d, 2H, CH_2), 3.21 (tt, 1H, CH), 2.60 (d, 2H, CH_2-CO), 10.21 (s, 1H, CONH), 7.19–7.61 (m, 5H, Ph), 7.58 (d,1H, pyrazole), 6.42 (dd, 1H, furyl), 6.12 (d,1H, furyl); ^{13}C NMR (DMSO-d_6): 172.9 (CONH), 164.8 (C-OH), 31.8 (CH_2 in pyrazole), 164.2 (C-CH_2-C-), 39.8 (-CH_2-CH-), 31.9 (-CH-), 33.0 (-CH-CH_2-CO-NH), 138.5, 128.9, 121.8, 128.1 (Ph), 156.0, 141.5, 110.0, 121.1 (furyl ring). MS (*m/z*): 311.42 (M^+, 20%), 245.27, 169.22 (100%), 154.16, 126.15, 112.12, 98.10, 84.07, 68.07. Elemental analysis: Calculated for C, 65.58; H, 5.50; N, 13.50%; Found: C, 65.50; H, 5.54; N, 13.58%.

4-(5-Hydroxy-4*H*-pyrazol-3-yl)-*N*,3-diphenylbutanamide (2)

m.p. 154 °C; IR (cm^{-1}): υ 3420 (C-OH), 1647 (CONH), 642 (CH); ^1H NMR (DMSO-d_6): δ 2.31 (s, 1H, OH), 1.54 (s, 2H, CH_2 in pyrazole), 1.80 (d, 2H, CH_2), 3.49 (tt, 1H, CH), 2.66 (d, 2H, CH_2-CO), 10.11 (s, 1H, CONH), 7.45–7.61 (dd, 4H, NH-Ph), 7.20–7.34 (m, 5H, Ph); ^{13}C NMR(DMSO-d_6): 173.6 (CONH), 163.2 (C-OH), 31.8 (CH_2 in pyrazole), 163.6 (C-CH_2-C-), 39.2 (CH_2-CH-), 32.5 (C-CH-), 33.6 (-CH-CH_2-), 138.5, 128.9, 121.8, 128.1 (Ph), 125.5, 126.1, 123.7, 142.8 (Ph ring). MS (*m/z*): 321.72 (M^+, 34%), 245.27, 169.21 (100%), 154.19, 110.98, 98.01, 85.21, 68.18. Elemental analysis: Calculated for C, 71.01; H, 5.96; N, 13.12%; Found: C, 71.11; H, 5.90; N, 13.12%.

3-(4-Chlorophenyl)-4-(5-hydroxy-4*H*-pyrazol-3-yl)-*N*-phenylbutanamide (3)

m.p. 173 °C; IR (cm^{-1}): υ 3423 (C-OH), 1649 (CONH), 669 (CH), 836 (C-Cl); ^1H NMR (DMSO-d_6): δ 2.24 (s,1H, OH), 1.61 (s, 2H, CH in pyrazole), 1.82 (d, 2H, CH_2), 3.43 (tt, 1H, CH), 2.60 (d, 2H, CH_2-CO), 10.21 (s, 1H, CONH), 7.41–7.24 (m, 4H, Ph); ^{13}C NMR (DMSO-d_6): 131.9 (C-Cl), 31.2 (CH_2 in pyrazole ring), 164.2 (C-CH_2-C-), 39.8 (CH_2-CH-), 31.9 (C-CH-), 33.0 (-CH-CH_2-), 72.9 (CONH), 138.5, 128.9, 121.8, 128.1 (Ph), 156.0, 141.5, 110.0, 121.1 (furyl ring). MS (*m/z*): 355.21 (M^+, 42%), 244.91, 169.65 (100%), 154.54, 110.74, 98.22, 85.36, 68.41. Elemental analysis: Calculated for C, 64.13; H, 5.10; N, 11.81%; Found: C, 64.17; H, 5.13; N, 11.79%.

3-(4-Hydroxyphenyl)-4-(5-hydroxy-4*H*-pyrazol-3-yl)-*N*-phenylbutanamide (4)

m.p. 152 °C; IR (cm^{-1}): υ 3423 (C-OH), 1649 (CONH), 669 (CH); ^1H NMR (DMSO-d_6): δ 2.2 (s,1H, OH), 1.66 (s, 2H, CH in pyrazole), 1.82 (d, 2H, CH_2), 3.48 (tt, 1H, CH), 2.60 (d, 2H, CH_2-CO), 10.21 (s, 1H, CONH), 7.19–7.61 (m, 5H, Ph), 7.58 (d,1H, furyl), 6.42 (dd, 1H, furyl), 6.12 (d,1H, furyl); ^{13}C NMR (DMSO-d_6): 155.8 (C-OH), 31.8 (CH_2 in pyrazole ring), 164.2 (C-CH_2-C-), 39.8 (CH_2-CH-), 31.9 (C-CH-), 33.0

(-CH-$\underline{C}H_2$-), 72.9 (CONH), 138.5, 128.9, 121.8, 128.5 (Ph), 135.0, 115.2, 127.6 (Ph). MS (*m/z*): 337.37 (M^+, 21%), 245.65, 169.36 (100%), 153.25, 110.90, 97.91, 86.01, 67.25. Elemental analysis: Calculated for C, 67.64; H, 5.68; N, 12.46%; Found: C, 67.60; H, 5.69; N, 12.40%.

4-(5-Hydroxy-4*H*-pyrazol-3-yl)-3-(4-nitrophenyl)-*N*-phenylbutanamide (5)

m.p. 164 °C; IR (cm^{-1}): υ 3428 (C-OH), 1652 (CONH), 645 (CH), 1581 (C-NO_2); ^{1}H NMR (DMSO-d_6): δ 2.19 (s, 1H, OH), 1.65 (s, 2H, CH in pyrazole), 1.88 (d, 2H, CH_2), 3.39 (tt, 1H, CH), 2.64 (d, 2H, CH_2-CO), 10.11 (s, 1H, CONH), 7.21–7.56 (m, 5H, Ph), 7.56–8.20 (dd, 4H, NO_2-Ph); ^{13}C NMR (DMSO-d_6): 164.0 (C-OH), 30.3 (CH_2 in pyrazole ring), 165.1 ($\underline{C}$-CH_2-C-), 39.0 ($\underline{C}H_2$-CH-), 31.7 (C-$\underline{C}$H-), 33.6 (-CH-$\underline{C}H_2$-), 72.2 (CONH), 148.2, 127.2, 123.8 (Ph), 145.7 ($\underline{C}$-NO_2), 138.4, 128.0, 128.6, 121.1 (-NH-$\underline{Ph}$); MS (*m/z*): 366.41 (M^+, 11%), 245.20, 169.36 (100%), 153.10, 110.20, 98.16, 85.95, 68.26. Elemental analysis: Calculated for C, 62.29; H, 4.95; N, 15.29%; Found: C, 62.32; H, 4.91; N, 15.32%.

3. 1. 2. 3-(Furan-2-yl)-3-(1H-imidazol-1-yl)-N-phenylpropanamide (6)

To prepare the solution of imidazole (6.8 g, 0.1 mol), acetanilide (13.5 g, 0.1 mol) and furaldehyde (9.6 g, 0.1 mol) in ethanol, the reaction mixture was refluxed for 3 h. The reaction mixture were cooled and poured into ice-cold water. The precipitated material was obtained in a few minutes. The precipitate was collected by filtration, dried and recrystallised from absolute ethanol. Using above procedure was followed by all remaining compounds **7**–**10**.

m.p. 198 °C; IR (cm^{-1}): υ 3119 (CH str in Ph ring), 2781 (CH str in furyl), 1640 (CONH), 641 (CH); ^{1}H NMR (DMSO-d_6): δ 6.45 (s, 1H, CH in imidazole ring), 7.84 (s, 1H, CH in imidazole ring), 5.41 (t, 1H, CH), 3.42 (d, 2H, CH_2), 10.35 (s, 1H, CONH), 7.19–7.61 (m, 5H, Ph), 7.56 (d, 1H, furyl), 6.54 (dd, 1H, furyl), 6.37 (d, 1H, furyl); ^{13}C NMR (DMSO-d_6): 137.6 (CH_2 in imidazole ring), 128.6 (CH in imidazole ring), 53.8 (CH), 38.6 ($\underline{C}H_2$-CH-), 173.2 (CONH), 138.6, 121.4, 128.2, 128.0 (Ph), 151.9, 141.6, 110.8, 105.2 (furyl ring). MS (*m/z*): 281.76 (M^+, 17%), 190.19, 162.18 (100%), 148.16, 82.10. Elemental analysis: Calculated for C, 68.29; H, 5.37; N, 14.94%; Found: C, 68.29; H, 5.30; N, 14.96%.

3-(1*H*-Imidazol-1-yl)-*N*,3-diphenylpropanamide (7)

m.p. 195 °C; IR (cm^{-1}): υ 3156 (CH str in Ph ring), 1641 (CONH), 654 (CH); ^{1}H NMR (DMSO-d_6): δ 6.27 (s, 1H, CH in imidazole ring), 7.64 (s, 1H, CH in imidazole ring), 5.97 (t, 1H, CH), 3.41 (d, 2H, CH_2), 10.16 (s, 1H, CONH), 7.43–7.64 (m, 5H, Ph), 7.27–7.40 (m, 5H, Ph); ^{13}C NMR (DMSO-d_6): 136.2 (CH_2 in imidazole ring), 127.3 (CH in imidazole ring), 53.6 (CH), 37.9 ($\underline{C}H_2$-CH-), 171.6 (CONH), 140.9, 128.2, 128.8, 125.8 (Ph), 138.1, 121.8, 128.1, 128.6 (-CONH-$\underline{Ph}$). MS (*m/z*): 291.01 (M^+, 23%), 215.25, 139.25 (100%), 124.14, 110.15, 82.10. Elemental analysis: Calculated for C, 74.20; H, 5.88; N, 14.42%; Found: C, 74.22; H, 5.80; N, 14.44%.

3-(4-Chlorophenyl)-3-(1*H*-imidazol-1-yl)-*N*-phenylpropanamide (8)

m.p. 210 °C; IR (cm^{-1}): υ 3121 (CH str in Ph ring), 1664 (CONH), 654 (CH), 847 ($\underline{C}$-Cl); ^{1}H NMR (DMSO-d_6): δ 6.94 (s, 1H, CH in imidazole ring), 7.41 (s, 1H, CH in imidazole ring), 5.38 (t, 1H, CH), 3.40 (d, 2H, CH_2), 10.34 (s, 1H, CONH), 7.43–7.25 (m, 4H, Ph), 7.19–7.66 (dd, 4H, Ph); ^{13}C NMR (DMSO-d_6): 137.2 (CH_2 in imidazole ring), 127.6 (CH in imidazole ring), 52.9 (CH), 38.3 ($\underline{C}H_2$-CH-), 173.1 (CONH), 131.2($\underline{C}$-Cl), 131.6, 128.6, 129.0 (Ph), 138.6, 122.2, 124.8, 127.9 (-CONH-$\underline{Ph}$). MS (*m/z*): 325.01 (M^+, 46%), 291.34, 139.36 (100%), 124.66, 110.84, 82.41. Elemental analysis: Calculated for C, 66.36; H, 4.95; N, 12.90%; Found: C, 66.32; H, 4.92; N, 12.93%.

3-(4-Hydroxyphenyl)-3-(1*H*-imidazol-1-yl)-*N*-phenylpropanamide (9)

m.p. 110 °C; IR (cm^{-1}): υ 3235 (C-OH), 3210 (CH str in Ph ring), 1652 (CONH), 710 (CH); ^{1}H NMR (DMSO-d_6): δ 9.41 (s, 1H, Ph-O$\underline{H}$), 6.57 (s, 1H, CH in imidazole ring), 7.95 (s, 1H, CH in imidazole ring), 5.36 (t, 1H, CH), 3.51 (d, 2H, CH_2), 10.16 (s, 1H, CONH), 6.69–7.12 (m, 4H, Ph), 7.17–7.65 (dd, 4H, Ph); ^{13}C NMR (DMSO-d_6): 136.4 (CH_2 in imidazole ring), 128.6 (CH in imidazole ring), 53.9 (CH), 37.6 ($\underline{C}H_2$-CH-), 172.3 (CONH), 154.6 ($\underline{C}$-OH), 136.2, 115.8, 128.5 (Ph), 138.9, 121.0, 128.1, 128.9 (-CONH-$\underline{Ph}$). MS (*m/z*): 307.21 (M^+, 56%), 291.45, 139.01 (100%), 124.77, 110.81, 82.36. Elemental analysis: Calculated for C, 70.34; H, 5.55; N, 13.67%; Found: C, 70.37; H, 5.55; N, 13.60%.

3-(1*H*-Imidazol-1-yl)-3-(4-nitrophenyl)-*N*-phenylpropanamide (10)

m.p. 122 °C; IR (cm^{-1}): υ 3108 (CH str in Ph ring), 2766 (CH str in furyl), 1652 (CONH), 669 (CH), 1586 (C-NO_2); ^{1}H NMR (DMSO-d_6): δ 6.44 (s, 1H, CH in imidazole ring), 7.80 (s, 1H, CH in imidazole ring), 5.46 (t, 1H, CH), 3.47 (d, 2H, CH_2), 10.27 (s, 1H, CONH), 7.17–7.61 (m, 4H, Ph), ^{13}C NMR (DMSO-d_6): 136.9 (CH_2 in imidazole ring), 128.1 (CH in imidazole ring), 53.0 (CH), 37.1 ($\underline{C}H_2$-CH-), 172.6 (CONH), 139.1, 128.6, 128.9, 121.6 (NO_2-Ph), 123.0, 128.4, 128.2 (-CONH-$\underline{Ph}$). MS (*m/z*): 336.28 (M^+, 41%), 291.76, 139.87 (100%), 124.13, 110.06, 82.47. Elemental analysis: Calculated for C, 16.66; H, 4.79; N, 64.28%; Found: C, 64.28; H, 4.73; N, 16.60%.

3. 2. Biological Screening

3. 2. 1. *In vitro* Antibacterial Screening

The compounds **1**–**10** were screened for *in vitro* antibacterial activity against *S. aureus* (ATCC-25923), *E.*

coli (ATCC-25922), by disc diffusion method[37,38] performed using Mueller–Hinton agar (Hi-Media) medium. Each compound was tested at the concentration of 100 ìg/mL in DMSO. Ciprofloxacin was used as the standard. The zone of inhibition was measured after 24 h incubation at 37 °C for 24 h.

3. 2. 2. *In vitro* Antifungal Screening

The compounds **1**–**10** were screened for *in vitro* antifungal activity *A. niger*, *C. albicans*, using an disc diffusion method[39,40] with Sabouraud's dextrose agar (Hi-Media) medium. Each compound was tested at the concentration of 100 ìg/mL in DMSO. Clotrimazole was used as the standard. The zone of inhibition was measured after 24 h incubation at 37 °C.

4. Conclusion

New series of pyrazole and imidazole derivatives **1**–**10** were synthesized by the Mannich base method and screened for antimicrobial activity. Among these, compound **6** has high antibacterial activity against *S. aureus* compared with the standard ciprofloxacin and high antifungal activity against *A. niger* compared with the standard clotrimazole. The synthesized compounds could be extended to the testing for various other pharmacological activities.

5. Acknowledgment

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6. References

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Povzetek

S pomočjo Mannichove metode smo pripravili novi seriji pirazolskih derivatov 3-(furan-2-il)-4-(5-hidroksi-4*H*-pirazol-3-il)-*N*-fenilbutanamidov **1**–**5** in imidazolskih derivatov 3-(furan-2-il)-3-(1*H*-imidazol-1-il)-*N*-fenilpropanamidov **6**–**10**. Strukture pripravljenih spojin **1**–**10** smo potrdili z IR, ^{1}H NMR, ^{13}C NMR, masno spektroskopijo in z elementno analizo. Spojine smo tudi testirali za morebitne antimikrobne aktivnosti.