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Synthesis and antimicrobial activity of some new pyrazoline derivatives bearing sulfanilamido moiety

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ABSTRACT

In the present study, a series of new pyrazoline derivatives bearing sulfanilamido moiety were synthesized and obtained in good yields. The chemical structures of the compounds were elucidated by spectral data (FT-IR, MS, UV-VIS and NMR). The synthesized compounds 41-70 were screened for their antimicrobial activity and compared with controls. The *in vitro* antibacterial activity of compounds 41-45 and 48-57 was checked against two Gram positive microorganisms (*S. aureus* and *S. mutans*) and three Gram negative microorganisms (*E. coli*, *K. pneumonia* and *P. aureginosa*), their antifungal activity was checked against *C. albicans*. The preliminary results showed that these compounds had moderate activity against the tested organisms. Compounds 41, 48, 51 and 56 exhibited promising antimicrobial activity against *S. aureus* compared to standard drug Ampicilin. Final synthesized compounds 58-70 were tested against two Gram positive (*S. aureus* and *B. subtilis*) and two Gram negative (*E. coli* and *P. aureginosa*) microorganisms, their activity against *C. albicans* was also checked and they did not exhibit any antimicrobial activity.

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1. Introduction

2-Pyrazolines (4,5-dihydro-1*H*-pyrazole) are an important class of five-membered heterocyclic compounds and were found to be vital building blocks in medicinal chemistry and led to the discovery of a number of bioactive derivatives [1,2]. 2-Pyrazolines were considered as a cyclic hydrazine moiety [3]. It exhibits the monoamino character and hence is more stable than the rest of the reduced forms. 2-pyrazolines were the most frequently studied form of pyrazolines because they have a considerably easy route of synthesis and rich biological activities [4]. As follows from the X-ray diffraction analysis, it has the structure of the five-membered dihydropyrazole ring, has an envelope conformation [5]. Carbon atom No. 5 in heterocyclic ring is deviated from the almost planar system of the other four atoms of the ring [6].

Derivatives of pyrazolines have played a crucial role in the history of heterocyclic chemistry and been used as important pharmacores and synthons in field of organic chemistry in drug designing [7,8]. Pyrazoline derivatives were found to have potential antipyretic-analgesic, muscle relaxant, psycho analeptic, tranquillizing, antiepileptic, antidepressant, anti-inflammatory, insecticidal and antimicrobial and antihypotensive activities. Their derivatives were also found to exhibit cytotoxic activity, inhibitory activity of platelet aggregation, herbicidal activity and cannabinoid type 1 receptor (CB1) modulators [9-11].

Biological activity potency associated with pyrazolines has made them popular synthetic target. Keeping these observations in mind, we decided to synthesis some new pyrazolines derivatives bearing sulfanilamido moiety and evaluating their biological activities as antimicrobial agents.

2. Experimental

2.1. Materials and methods

All reagents were used as purchased from commercial suppliers without further purification. Melting points were determined by using Fisher-Johns 6200 melting point

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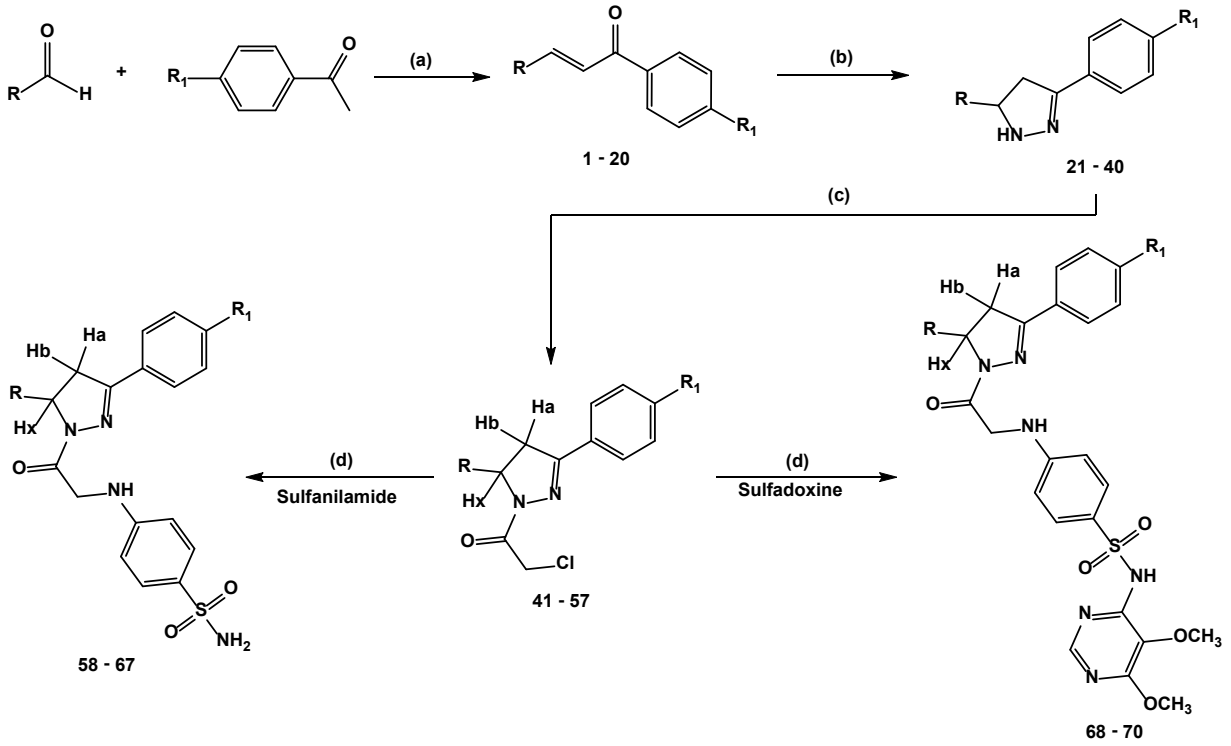

1, 21, 41, 58: R = C_6H_5, R^1 = H
2, 22, 42, 59: R = *p*-ClC_6H_4, R^1 = H
3, 23, 43, 60, 68: R = *p*-$Me_2NC_6H_4$, R^1= H
4, 24, 44, 61: R = Cinnamyl phenyl, R^1= H
5, 25, 45, 62: R = Furyl, R^1 = H
6, 26, 46: R = C_6H_5, R^1 = *p*-Br
7, 27: R = *p*-ClC_6H_4, R^1 = *p*-Br
8, 28: R = *p*-$Me_2NC_6H_4$, R^1 = *p*-Br
9, 29: R = Cinnamyl phenyl, R^1 = *p*-Br
10, 30, 47: R = Furyl, R^1 = *p*-Br
11, 31, 48: R = C_6H_5, R^1 = *p*-NO_2
12, 32, 49: R = *p*-ClC_6H_4, R^1 = *p*-NO_2
13, 33, 50: R = *p*-$Me_2NC_6H_4$, R^1 = *p*-NO_2
14, 34, 51: R = Cinnamyl phenyl, R^1 = *p*-NO_2
15, 35, 52, 63: R = Furyl, R^1 = *p*-NO_2
16, 36, 53, 64, 69: R = C_6H_5, R^1 = *p*-CH_3
17, 37, 54, 65: R = *p*-ClC_6H_4, R^1 = *p*-CH_3
18, 38, 55, 66, 70: R = *p*-$Me_2NC_6H_4$, R^1 = *p*-CH_3
19, 39, 56: R = Cinnamyl phenyl, R^1 = *p*-CH_3
20, 40, 57, 67: R = Furyl, R^1 = *p*-CH_3

Reagents and conditions: (a) 10% aqueous sodium hydroxide solution, ethanol, str. rt, 4 h. (b) hydrazine hydrate, ethanol, reflux, 8 h; (c) chloroacetyl chloride, dry toluene, Et_3N, str. 6 h; (d) anhydrous K_2CO_3, DMF, stirring under reflux.

Scheme 1. The synthetic route for the preparation of compounds 1-70.

apparatus and were uncorrected (Fisher Scientific Company, USA). The purity of final compounds was checked on pre-coated TLC silica gel $60F_{254}$, with different solvent system and visualizing the spots in ultraviolet light (model UVGL-58 multiband UV.254-365 NM, Upland, CA91786, USA).

FT-IR spectra were recorded on a Shimadzu FT-IR-4100 spectrophotometer. UV-Vis spectroscopic data were recorded on Shimadzu UV-3101PC spectrophotometer, and mass spectra were recorded on GC/MS Shimadzu QP-2010 Plus mass spectrometer. Nuclear magnetic resonance (^{1}H NMR) spectra were recorded using Bruker 400 MHz NMR instrument. Chemical shift values are reported in ppm relative to tetramethyl silane (TMS) as internal reference in DMSO-d_6 and peak multiplicities are designed as follows: s, singlet; d, doublet; t, triplet; m, multiplet.

2.2. Synthesis

2.2.1. Synthesis of α,β-unsaturated carbonyl derivatives (1-20)

A mixture of various substituted aromatic aldehydes (0.05 mol), substituted aromatic acetophenone (0.05 mol) and sodium hydroxide 10% in ethanol (30 mL) was stirred at room temperature until the mixture is so thick that stirring is no longer effective (3-5 h), the reaction mixture was removed and kept in refrigerator overnight. The resulting solid was filtered, washed with cold water until the washings are neutral to litmus. The crude α,β-unsaturated carbonyl derivative, was air dried, recrystallized from ethanol and was taken for the next step (Scheme 1).

2.2.2. Synthesis of 3,5-diaryl-2-pyrazoline derivatives (21-40)

A mixture of appropriate α,β-unsaturated carbonyl derivative (0.03 mol) and hydrazine hydrate (0.06 mol) in ethanol (30 mL) were refluxed for 8 h. The reaction mixture was cooled and kept in refrigerator overnight. The resulting solid was filtered and crude pyrazoline after drying and recrystallized from ethanol was taken for the next step (Scheme 1).

2.2.3. General method for the synthesis of 1-(chloroacetyl)-3,5-diaryl-2-pyrazolines derivatives (41-57)

3,5-Diaryl-2-pyrazoline (0.025 mol) and triethylamine (0.025 mol) were dissolved in dry toluene (30 mL) with constant stirring. Later, the mixture was cooled in an ice bath, and chloroacetyl chloride (0.025 mol) was added drop wise with stirring. The reaction mixture thus obtained was further agitated for 3 h at room temperature. The precipitate was

filtrated, the solvent was evaporated to dryness under reduced pressure, and the solid obtained was recrystallized from ethanol (Scheme 1).

2-Chloro-1-(3, 5-diphenyl-4, 5-dihydro-1H-pyrazol-1-yl) ethan-1-one (**41**): Color: Pale yellow powder. Yield: 46 %. M.p.: 130-132 °C. R_f value: 0.75. FT-IR (KBr, ν, cm^{-1}): 1757 (C=O), 1665 (C=N), 1443 (aromatic C=C). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.17 (dd, 1H, $J_{Ha,Hb}$= 18.2 Hz, $J_{Ha,Hx}$= 4.72 Hz, Ha), 3.87 (dd, 1H, $J_{Hb,Ha}$= 18.2 Hz, $J_{Hb,Hx}$= 11.72 Hz, Hb), 4.68 (d, 1H, *J* = 13.8 Hz, CO-CH), 4.77 (d, 1H, *J* = 13.8 Hz, CO-CH) 5.57 (dd, 1H, $J_{Hb,Hx}$= 11.72 Hz, $J_{Ha,Hx}$= 4.64 Hz, Hx), 7.22-7.84 (m, 10H, Ar-H). MS (EI, *m/z* (%)): 298 (M^+, 100). UV/VIS (DMSO, λ_{max}, nm): 300, 293.

2-Chloro-1-[5-(4-chlorophenyl)-3-phenyl-4,5-dihydro-1H-pyrazol-1-yl]ethan-1-one (**42**): Color: Light yellow powder. Yield: 48%. M.p.: 128-130 °C. R_f value: 0.72. FT-IR (KBr, ν, cm^{-1}): 1668 (C=O), 1599 (C=N), 1573 (aromatic C=C). ^{1}H^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.19 (dd, 1H, $J_{Ha,Hb}$= 18.24 Hz, $J_{Ha,Hx}$ = 4.88 Hz, Ha), 3.87 (dd, 1H, $J_{Hb,Ha}$ = 18.28 Hz, $J_{Hb,Hx}$ = 11.76 Hz, Hb), 4.67 (d, 1H, *J* = 13.84 Hz, CO-CH), 4.77 (d, 1H, *J* = 13.84 Hz, CO-CH), 5.58 (dd, 1H, $J_{Hb,Hx}$ = 11.76 Hz, $J_{Ha,Hx}$ = 4.84 Hz, Hx), 7.26-7.83 (m, 9H, Ar-H). MS (EI, *m/z* (%)): 332 (M^+, 86.9). UV/VIS (DMSO, λ_{max}, nm): 349.

2-Chloro-1-{5-[4-(dimethylamino) phenyl]-3-phenyl-4,5-dihydro-1H-pyrazol-1-yl} ethan-1-one (**43**): Color: Yellow powder. Yield: 64%. M.p.: 130-132 °C. R_f value: 0.53. FT-IR (KBr, ν, cm^{-1}): 1664 (C=O), 1612 (C=N), 1565 (aromatic C=C). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 2.85 (s, 6H, CH_3-N), 3.14 (dd, 1H, $J_{Ha,Hb}$ = 18.16 Hz, $J_{Ha,Hx}$ = 4.44 Hz, Ha), 3.80 (dd, 1H, $J_{Hb,Ha}$ = 18.16 Hz, $J_{Hb,Hx}$ = 11.59 Hz, Hb), 4.64 (d, 1H, *J* = 13.72 Hz, CO-CH), 4.72 (d, 1H, *J* = 13.72 Hz, CO-CH), 5.45 (dd, 1H, $J_{Hb,Hx}$ = 11.56 Hz, $J_{Ha,Hx}$ = 4.4 Hz, Hx), 6.66 (d, 2H, *J* = 8.72 Hz, Ar-H), 7.03 (d, 2H, *J* = 8.72 Hz, Ar-H) 7.48-7.83 (m, 5H, Ar-H). MS (EI, *m/z* (%)): 341 (M^+, 61.1). UV/VIS (DMSO, λ_{max}, nm): 350, 265.

2-Chloro-1-{3-phenyl-5-[(E)-2-phenylethenyl]-4, 5-dihydro-1H-pyrazol-1-yl}ethan-1-one (**44**): Color: Pale yellow powder. Yield: 49%. M.p.: 136-138 °C. R_f value: 0.70. FT-IR (KBr, ν, cm^{-1}): 1748 (C=O), 1666 (C=N), 1599 (aromatic C=C). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.25 (dd, 1H, $J_{Ha,Hb}$ = 18 Hz, $J_{Ha,Hx}$ = 4.68 Hz, Ha), 3.65 (dd, 1H, $J_{Hb,Ha}$ = 17.96Hz, $J_{Hb,Hx}$ = 11.32 Hz, Hb), 4.67 (d, 1H, *J* = 13.84 Hz, CO-CH), 4.73 (d, 1H, *J* = 13.72 Hz, CO-CH), 5.19-5.25 (m, 1H, Hx), 6.30 (dd, 1H, $J_{α\text{-}H,β\text{-}H}$ = 15.88 Hz, $J_{α\text{-}H,Hx}$ = 7.08 Hz, α-H), 6.57 (d, 1H , *J* = 15.88 Hz, β-H), 7.32-7.83 (m, 10H, Ar-H). MS (EI, *m/z* (%)): 324 (M^+, 54.6). UV/VIS (DMSO, λ_{max}, nm): 351.

2-Chloro-1-[5-(furan-2-yl)-3-phenyl-4,5-dihydro-1H-pyrazol-1-yl]ethan-1-one (**45**): Color: Light brown powder. Yield: 51%. M.p.: 136-138 °C. R_f value: 0.69. FT-IR (KBr, ν, cm^{-1}): 1669 (C=O) , 1599 (C=N), 1501 (aromatic C=C). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.40 (dd, 1H, $J_{Ha,Hb}$ = 18.04 Hz, $J_{Ha,Hx}$ = 4.72 Hz, Ha), 3.74 (dd, 1H, $J_{Hb,Ha}$ = 18.04 Hz, $J_{Hb,Hx}$ = 11.8 Hz, Hb), 4.65 (d, 1H, *J* = 14 Hz, CO-CH), 4.70 (d, 1H, *J* = 14.04 Hz, CO-CH), 5.67 (dd, 1H, $J_{Hb,Hx}$ = 11.76 Hz, $J_{Ha,Hx}$ = 4.72 Hz, Hx), 6.38-6.42 (m, 2H, furan-H), 7.47-7.52 (m, 3H, Ar-H), 7.58 (d, 1H, *J* = 1.60 Hz, furan-H), 7.82-7.85 (m, 2H, Ar-H). MS (EI, *m/z* (%)): 288 (M^+, 93.4). UV/VIS (DMSO, λ_{max}, nm): 347.

1-[3-(4-Bromophenyl)-5-phenyl-4,5-dihydro-1H-pyrazol-1-yl]-2-chloroethan-1-one (**46**): Color: Pale yellow powder. Yield: 54%. M.p.: 122-124 °C. R_f value: 0.29. FT-IR (KBr, ν, cm^{-1}): 1683 (C=O), 1589 (C=N), 1490 (aromatic C=C). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.17 (dd, 1H, $J_{Ha,Hb}$ = 18.24 Hz, $J_{Ha,Hx}$ = 4.8 Hz, Ha), 3.86 (dd, 1H, $J_{Hb,Ha}$ = 18.24 Hz, $J_{Hb,Hx}$ = 11.8 Hz, Hb), 4.67 (d, 1H, *J*= 13.84 Hz, CO-CH), 4.77 (d, 1H, *J* = 13.84 Hz, CO-CH), 5.57 (dd, 1H, $J_{Hb,Hx}$ = 11.72 Hz, $J_{Ha,Hx}$ = 4.76 Hz, Hx), 7.22-7.37 (m, 5H, Ar-H), 7.67 (d, 2H, *J* = 8.56 Hz, Ar-H), 7.75 (d, 2H, *J* = 8.56 Hz, Ar-H). MS (EI, *m/z* (%)): 376 (M^+, 75.1). UV/VIS (DMSO, λ_{max}, nm): 299, 293.

1-[3-(4-Bromophenyl)-5-(furan-2-yl)-4,5-dihydro-1H-pyrazol-1-yl]-2-chloroethan-1-one (**47**): Color: White powder. Yield: 50%. M.p.: 128-130 °C. R_f value: 0.31. FT-IR (KBr, ν, cm^{-1}): 1678 (C=O), 1589 (C=N), 1500 (aromatic C=C). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.39 (dd, 1H, $J_{Ha,Hb}$ = 18.12 Hz, $J_{Ha,Hx}$ = 4.84 Hz, Ha), 3.73 (dd, 1H, $J_{Hb,Ha}$ = 18.08 Hz, $J_{Hb,Hx}$ = 11.8 Hz, Hb), 4.65 (d, 1H, *J* = 14.08 Hz, CO-CH), 4.70 (d, 1H, *J* = 14.04 Hz, CO-CH), 5.68 (dd, 1H, $J_{Hb,Hx}$ = 11.8 Hz, $J_{Ha,Hx}$ = 4.84Hz, Hx), 6.39-6.42 (m, 2H, furan-H), 7.58 (d, 1H, *J* = 0.72 Hz, furan-H), 7.69 (d, 2H, *J* = 8.56 Hz, Ar-H), 7.76 (d, 2H, *J* = 8.52 Hz, Ar-H). MS (EI, *m/z* (%)): 367 (M^+, 16.4). UV/VIS (DMSO, λ_{max}, nm): 300, 255.

2-Chloro-1-[3-(4-nitrophenyl)-5-phenyl-4,5-dihydro-1H-pyrazol-1-yl] ethan-1-one (**48**): Color: Yellow powder. Yield: 65%. M.p.: 136-138 °C. R_f value: 0.43. FT-IR (KBr, ν, cm^{-1}): 1672 (C=O), 1577 (C=N), 1515 (aromatic C=C). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.25 (dd, 1H, $J_{Ha,Hb}$ = 18.36 Hz, $J_{Ha,Hx}$ = 4.96 Hz, Ha), 3.93 (dd, 1H, $J_{Hb,Ha}$ = 18.32 Hz, $J_{Hb,Hx}$ = 11.92 Hz, Hb), 4.72 (d, 1H, *J* = 13.96 Hz, CO-CH), 4.82 (d, 1H, *J* = 14 Hz, CO-CH), 5.63 (dd, 1H, $J_{Hb,Hx}$ = 11.88 Hz, $J_{Ha,Hx}$ = 4.96 Hz, H_{5a}), 7.24-7.38 (m, 4H, Ar-H), 8.05 (d, 2H, *J* = 8.88 Hz, Ar-H), 8.30 (d, 2H, *J* = 8.88 Hz, Ar-H). MS (EI, *m/z* (%)): 343 (M^+, 56.9). UV/VIS (DMSO, λ_{max}, nm): 350.

2-Chloro-1-[5-(4-chlorophenyl)-3-(4-nitrophenyl)-4,5-dihydro-1H-pyrazol-1-yl]ethan-1-one (**49**): Color: Pale yellow powder. Yield: 61%. M.p.: 160-162 °C. R_f value: 0.30. FT-IR (KBr, ν, cm^{-1}): 1667 (C=O), 1598 (C=N), 1513 (aromatic C=C). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.27 (dd, 1H, $J_{Ha,Hb}$ = 18.36 Hz, $J_{Ha,Hx}$ = 5.16 Hz, Ha), 3.92 (dd, 1H, $J_{Hb,Ha}$ = 18.36Hz, $J_{Hb,Hx}$ = 11.99 Hz, Hb), 4.71 (d, 1H, *J* = 14 Hz, CO-CH), 4.81 (d, 1H, *J* = 14 Hz, CO-CH), 5.63 (dd, 1H, $J_{Hb,Hx}$ = 11.92 Hz, $J_{Ha,Hx}$ = 5.2 Hz, Hx), 7.28 (d, 2H, Ar-H), 7.40 (d, 2H, Ar-H), 8.04 (d, 2H, Ar-H), 8.30 (d, 2H, Ar-H). MS (EI, *m/z* (%)): 378 (M^+, 17). UV/VIS (DMSO, λ_{max}, nm): 300.

2-Chloro-1-{5-[4-(dimethylamino)phenyl]-3-(4-nitrophenyl)-4,5-dihydro-1H-pyrazol-1-yl}ethan-1-one (**50**): Color: Red powder. Yield: 52%. M.p.: 196-198 °C. R_f value: 0.50. FT-IR (KBr, ν, cm^{-1}): 1673 (C=O), 1608 (C=N), 1566 (aromatic C=C). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 2.87 (s, 6H, CH_3-N), 3.22 (dd, 1H, $J_{Ha,Hb}$ = 18.28 Hz, $J_{Ha,Hx}$ = 4.76 Hz, Ha), 3.86 (dd, 1H, $J_{Hb,Ha}$ = 18.24 Hz, $J_{Hb,Hx}$ = 11.8, Hz, Hb), 4.68 (d, 1H, *J* = 13.88 Hz, CO-CH), 4.77 (d, 1H, *J* = 13.88 Hz, CO-CH), 5.51 (dd, 1H, $J_{Hb,Hx}$ = 11.68 Hz, $J_{Ha,Hx}$ = 4.68 Hz, Hx), 6.71-8.34 (m, 8H, Ar-H). MS (EI, *m/z* (%)): 386 (M^+, 55.1). UV/VIS (DMSO, λ_{max}, nm): 301, 265.

2-Chloro-1-{3-(4-nitrophenyl)-5-[(E)-2-phenylethenyl]-4,5-dihydro-1H-pyrazol-1-yl}ethan-1-one (**51**): Color: Yellow powder. Yield: 71%. M.p.: 142-144 °C. R_f value: 0.42. FT-IR (KBr, ν, cm^{-1}): 1684 (C=O), 1573 (C=N), 1510 (aromatic C=C). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.32 (dd, 1H, $J_{Ha,Hb}$ = 18.04 Hz, $J_{Ha,Hx}$ = 4.96 Hz, Ha), 3.70 (dd, 1H, $J_{Hb,Ha}$ = 18.08 Hz, $J_{Hb,Hx}$ = 11.44 Hz, Hb), 4.71 (d, 1H, *J* = 14 Hz, CO-CH), 4.77 (d, 1H, *J* = 14.04 Hz, CO-CH), 5.25-5.31 (m, 1H, Hx), 6.32 (dd, 1H, $J_{α\text{-}H,β\text{-}H}$ = 15.88 Hz, $J_{α\text{-}H,Hx}$ = 7.28 Hz, α-H), 6.60 (d, 1H, *J* = 15.88 Hz, β-H), 7.23-7.45 (m, 5H, Ar-H), 8.05-8.34 (m, 4H, Ar-H). MS (EI, *m/z* (%)): 369 (M^+, 32.4). UV/VIS (DMSO, λ_{max}, nm): 295, 255.

2-Chloro-1-[5-(furan-2-yl)-3-(4-nitrophenyl)-4,5-dihydro-1H-pyrazol-1-yl]ethan-1-one (**52**): Color: Yellow powder. Yield: 72%. M.p.: 162-164 °C. R_f value: 0.18. FT-IR (KBr, ν, cm^{-1}): 1667 (C=O), 1597 (C=N), 1573 (aromatic C=C).^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.48 (dd, 1H, $J_{Ha,Hb}$ = 18.16 Hz, $J_{Ha,Hx}$ = 5.00 Hz, Ha), 3.80 (dd, 1H, $J_{Hb,Ha}$ = 18.16 Hz, $J_{Hb,Hx}$ = 11.88 Hz, Hb), 4.69 (d, 1H, *J* = 14.16 Hz, CO-CH), 4.75 (d, 1H, *J* = 14.16 Hz, CO-CH), 5.74 (dd, 1H, $J_{Hb,Hx}$ = 11.92 Hz, $J_{Ha,Hx}$ = 4.96 Hz, Hx), 6.42-6.43 (m, 2H, *J* = 1.24 Hz, furan-H), 7.59 (d, 1H, *J* = 0.72 Hz, furan-H), 8.07-8.33 (m, 4H, Ar-H). MS (EI, *m/z* (%)): 333 (M^+, 79). UV/VIS (DMSO, λ_{max}, nm): 294, 254.

2-Chloro-1-[3-(4-methylphenyl)-5-phenyl-4, 5-dihydro-1H-pyrazol-1-yl] ethan-1-one (**53**): Color: Pale yellow powder. Yield: 64%. M.p.: 118-120 °C. R_f value: 0.60. FT-IR (KBr, ν, cm^{-1}): 1750 (C=O), 1664 (C=N), 1442 (aromatic C=C). ^{1}H NMR

(400 MHz, DMSO-d_6, δ, ppm): 2.35 (s, 3H, CH_3), 3.14 (dd, 1H, $J_{Ha,Hb}$ = 18.16 Hz, $J_{Ha,Hx}$ = 4.64 Hz, Ha), 3.84 (dd, 1H, $J_{Hb,Ha}$ = 18.2 Hz, $J_{Hb,Hx}$ = 11.76 Hz, Hb), 4.66 (d, 1H, *J* = 13.76 Hz, CO-CH), 4.76 (d, 1H, *J* = 13.8 Hz, CO-CH), 5.55 (dd, 1H, $J_{Hb,Hx}$ = 11.68 Hz, $J_{Ha,Hx}$ = 4.6 Hz, Hx), 7.21-7.36 (m, 7H, Ar-H), 7.70 (d, 2H, *J* = 8.16 Hz, Ar-H). MS (EI, *m/z* (%)): 312 (M^+, 100). UV/VIS (DMSO, λ_{max}, nm): 300.

2-Chloro-1-[5-(4-chlorophenyl)-3-(4-methylphenyl)-4, 5-dihydro-1H-pyrazol-1-yl]ethan-1-one (**54**): Color: Light yellow powder. Yield: 62%. M.p.: 138-140 °C. R_f value: 0.56. FT-IR (KBr, ν, cm^{-1}): 1684 (C=O), 1667 (C=N), 1603 (aromatic C=C). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 2.35 (s, 3H, CH_3), 3.14 (dd, 1H, $J_{Ha,Hb}$ = 18.24 Hz, $J_{Ha,Hx}$ = 4.8 Hz, Ha), 3.83 (dd, 1H, $J_{Hb,Ha}$ = 18.2Hz, $J_{Hb,Hx}$ = 11.76 Hz, Hb), 4.65 (d, 1H, *J* = 13.8 Hz, CO-CH), 4.75 (d, 1H, *J* = 13.8 Hz, CO-CH), 5.55 (dd, 1H, $J_{Hb,Hx}$ = 11.72 Hz, $J_{Ha,Hx}$ = 4.76 Hz, Hx), 7.24-7.30 (m, 4H, Ar-H), 7.39 (d, 2H, *J* = 8.44 Hz, Ar-H), 7.69 (d, 2H, *J* = 8.12 Hz, Ar-H). MS (EI, *m/z* (%)): 346 (M^+, 100). UV/VIS (DMSO, λ_{max}, nm): 298, 266.

2-Chloro-1-{5-[4-(dimethylamino)phenyl]-3-(4-methyl phenyl)-4,5-dihydro-1H-pyrazol-1-yl}ethan-1-one (**55**): Color: Light brown powder. Yield: 46%. M.p.: 134-136 °C. R_f value: 0.47. FT-IR (KBr, ν, cm^{-1}): 1673 (C=O), 1613 (C=N), 1524 (aromatic C=C). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 2.36 (s, 3H, CH_3), 2.85 (s, 6H, CH_3-N), 3.11 (dd, 1H, $J_{Ha,Hb}$ = 18.12 Hz, $J_{Ha,Hx}$ = 4.36 Hz, Ha), 3.76 (dd, 1H, $J_{Hb,Ha}$ = 18.08 Hz, $J_{Hb,Hx}$ = 11.56 Hz, Hb), 4.62 (d, 1H, *J* = 13.72 Hz, CO-CH), 4.70 (d, 1H, *J* = 13.68 Hz, CO-CH), 5.43 (dd, 1H, $J_{Hb,Hx}$ = 11.48 Hz, $J_{Ha,Hx}$ = 4.32 Hz, Hx), 6.65 (d, 2H, *J* = 8.72 Hz, Ar-H), 7.01 (d, 2H, *J* = 8.72 Hz, Ar-H), 7.28 (d, 2H, *J* = 8.00 Hz, Ar-H), 7.70 (d, 2H, *J* = 8.12 Hz, Ar-H). MS (EI, *m/z* (%)): 355 (M^+, 74.6). UV/VIS (DMSO, λ_{max}, nm): 295, 255.

2-Chloro-1-{3-(4-methylphenyl)-5-[2-phenylethenyl]-4, 5-dihydro-1H-pyrazol-1-yl}ethan-1-one (**56**): Color: Pale yellow powder. Yield: 65%. M.p.: 108-110 °C. R_f value: 0.62. FT-IR (KBr, ν, cm^{-1}): 1751 (C=O), 1671 (C=N), 1608 (aromatic C=C). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 2.35 (s, 3H, CH_3), 3.20 (dd, 1H, $J_{Ha,Hb}$ = 18.00 Hz, $J_{Ha,Hx}$ = 4.72 Hz, Ha), 3.59 (dd, 1H, $J_{Hb,Ha}$ = 17.96Hz, $J_{Hb,Hx}$ = 11.28 Hz, Hb), 4.65 (d, 1H, *J* = 13.80 Hz, CO-CH), 4.71 (d, 1H, *J* = 13.84 Hz, CO-CH), 5.16-5.22 (m, 1H, Hx), 6.28 (dd, 1H, $J_{\alpha\text{-}H,\beta\text{-}H}$ = 15.88 Hz, $J_{\alpha\text{-}H,Hx}$ = 7.08 Hz, α-H), 6.57 (d, 1H, *J* = 15.88 Hz, β-H), 7.22-7.34 (m, 5H, Ar-H), 7.42 (d, 2H, *J* = 7.40 Hz, Ar-H), 7.69 (d, 2H, *J* = 8.08 Hz, Ar-H). MS (EI, *m/z* (%)): 338 (M^+, 75.8). UV/VIS (DMSO, λ_{max}, nm): 296.

2-Chloro-1-[5-(furan-2-yl)-3-(4-methylphenyl)-4,5-dihyd ro-1H-pyrazol-1-yl]ethan-1-one (**57**): Color: Pale yellow powder. Yield: 56%. M.p.: 124-126 °C. R_f value: 0.64. FT-IR (KBr, ν, cm^{-1}): 1683 (C=O), 1604 (C=N), 1563 (aromatic C=C). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 2.36 (s, 3H, CH_3), 3.36 (dd, 1H, $J_{Ha,Hb}$ = 18.04Hz, $J_{Ha,Hx}$ = 4.72 Hz, Ha), 3.71 (dd, 1H, $J_{Hb,Ha}$ = 18.00 Hz, $J_{Hb,Hx}$ = 11.76 Hz, Hb), 4.63 (d, 1H, *J* = 14.00 Hz, CO-CH), 4.68 (d, 1H, *J* = 13.96 Hz, CO-CH), 5.65 (dd, 1H, $J_{Hb,Hx}$ = 11.68 Hz, $J_{Ha,Hx}$ = 4.72 Hz, Hx), 6.37-6.42 (m, 2H, furan-H), 7.29 (d, 2H, *J* = 8.00 Hz, Ar-H), 7.57 (d, 1H, *J* = 0.84 Hz, furan-H), 7.71 (d, 2H, *J* = 8.12 Hz, Ar-H). MS (EI, (*m/z* (%)): 302 (M^+, 100). UV/VIS (DMSO, λ_{max}, nm): 300.

2.2.4. General method for the synthesis of 1-(subistituted aminoacetyl) -3,5-diaryl-2-pyrazolines derivatives (58-70)

A mixture of 10 mmol sulfanilamide or sulfadoxine, 10 mmol of 1-(chloroacetyl)-3,5-diaryl-2-pyrazolines, and appropriate amount of potassium carbonate anhydrous was stirred under reflux in 10 mL of dry DMF. Reaction was followed by thin layer chromatography (TLC), the mixture obtained after time complete was poured in crushed ice. The products were separated by filtration, washed with water, ethanol, and dried. Recrystallization from ethanol/dioxane rendered desired products in pure form (Scheme 1).

4-((2-(3, 5-Diphenyl-4, 5-dihydro-1H-pyrazol-1-yl)-2-oxoeth yl)amino)benzene sulfonamide (**58**): Color: White powder. Yield: 70%. M.p.: 200-202 °C. R_f value: 0.62. FT-IR (KBr, ν, cm^{-1}): 3482-3392 (NH_2), 3232 (NH), 1660 (C=O), 1625 (C=N), 1395-1155 (SO_2), 1594 (aromatic C=C). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.10 (dd, 1H, $J_{Ha,Hb}$ = 18.12 Hz, $J_{Ha,Hx}$ = 4.72 Hz, Ha), 3.80 (dd, 1H, $J_{Hb,Ha}$ = 18.16 Hz, $J_{Hb,Hx}$ = 11.80 Hz, Hb), 4.02 (d, 2H, *J* = 6.00 Hz, CO-CH_2), 5.44 (dd, 1H, $J_{Hb,Hx}$ = 11.76 Hz, $J_{Ha,Hx}$ = 4.64 Hz, Hx), 5.95 (s, 2H, NH_2), 6.58 (d, 2H, *J* = 8.68 Hz, Ar-H), 7.13 (d, 2H, *J* = 7.16 Hz, Ar-H), 7.24 (t, 1H, NH), 7.32-7.78 (m, 10H, Ar-H). MS (EI, *m/z* (%)): 434 (M^+, 15.4). UV/VIS (DMSO, λ_{max}, nm): 291, 276.

4-((2-(5-(4-Chlorophenyl)-3-phenyl-4,5-dihydro-1H-pyrazol-1-yl)-2-oxoethyl)amino) benzene sulfonamide (**59**): Color: White powder. Yield: 75%. M.p.: 198-200 °C. R_f value: 0.55. FT-IR (KBr, ν, cm^{-1}): 3479-3375 (NH_2) , 3224 (NH), 1651 (C=O), 1593 (C=N), 1396-1153 (SO_2), 1500 (aromatic C=C). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.11 (dd, 1H, $J_{Ha,Hb}$ = 18.24 Hz, $J_{Ha,Hx}$ = 4.72 Hz, Ha), 3.80 (dd, 1H, $J_{Hb,Ha}$ = 18.20 Hz, $J_{Hb,Hx}$ = 11.80 Hz, Hb), 4.01 (d, 2H, *J*= 5.72 Hz, CO-CH_2), 5.44 (dd, 1H, $J_{Hb,Hx}$ =11.72 Hz, $J_{Ha,Hx}$ = 4.54 Hz, Hx), 5.95 (s, 2H, NH_2), 6.58 (d, 2H, *J*= 8.48 Hz, Ar-H), 7.16 (d, 2H, *J*= 8.24 Hz, Ar-H), 7.31 (t, 1H, NH), 7.36-7.77 (m, 9H, Ar-H). MS (EI, *m/z* (%)): 468 (M^+, 16.8). UV/VIS (DMSO, λ_{max}, nm): 286, 271.

4-((2-(5-(4-(Dimethylamino)phenyl)-3-phenyl-4, 5-dihydro-1H-pyrazol-1-yl)-2-oxoethyl)amino)benzene sulfonamide (**60**): Color: Pale yellow powder. Yield: 57%. M.p.: 110-112 °C. R_f value: 0.71. FT-IR (KBr, ν, cm^{-1}): 3441-3363 (NH_2), 3228 (NH), 1651 (C=O), 1600 (C=N), 1392-1153 (SO_2), 1523 (aromatic C=C). ^{1}H^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 2.84 (s, 6H, CH_3-N), 3.07 (dd, 1H, $J_{Ha,Hb}$ = 18.12 Hz, $J_{Ha,Hx}$ = 4.36 Hz, Ha), 3.73 (dd, 1H, $J_{Hb,Ha}$ = 18.08 Hz, $J_{Hb,Hx}$ = 11.60 Hz, Hb), 3.92-4.04 (m, 2H, CO-CH_2), 5.33 (dd, 1H, $J_{Hb,Hx}$ = 11.52 Hz, $J_{Ha,Hx}$ = 4.32 Hz, Hx), 5.95 (s, 2H, NH_2), 6.59 (dd, 2H, *J* = 8.60 Hz, Ar-H), 6.94 (d, 2H, *J* = 8.60 Hz, Ar-H), 7.25 (t, 1H, NH), 7.45-7.77 (m, 9H, Ar-H). MS (EI, *m/z* (%)): 477 (M^+, 100). UV/VIS (DMSO, λ_{max}, nm): 292, 267.

4-((2-Oxo-2-(3-phenyl-5-styryl-4, 5-dihydro-1H-pyrazol-1-yl)ethyl)amino)benzene sulfonamide (**61**): Color: Yellow powder. Yield: 42%. M.p.: 140-142 °C. R_f value: 0.68. FT-IR (KBr, ν, cm^{-1}): 3464-3360 (NH_2), 3236 (NH), 1654 (C=O), 1597 (C=N), 1388-1149 (SO_2), 1504 (aromatic C=C). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.17 (dd, 1H, $J_{Ha,Hb}$ = 17.84 Hz, $J_{Ha,Hx}$ = 4.56 Hz, Ha), 3.98-3.99 (m, 1H, Hb), 4.62 (m, 2H, CO-CH_2), 5.11-5.15 (m, 1H, Hx), 5.94 (s, 2H, NH_2), 6.29 (m, 2H, α-H & β-H), 6.44-7.76 (m, 14H, Ar-H), 7.25 (s, 1H, NH). MS (EI, *m/z* (%)): 460 (M^+, 6.8). UV/VIS (DMSO, λ_{max}, nm): 293.

4-({2-[5-(Furan-2-yl)-3-phenyl-4, 5-dihydro-1H-pyrazol-1-yl]-2-oxoethyl}amino)benzene-1-sulfonamide (**62**): Color: Yellow powder. Yield: 40%. M.p.: 184-186 °C. R_f value: 0.55. FT-IR (KBr, ν, cm^{-1}): 3471-3371 (NH_2), 3224 (NH), 1658 (C=O), 1597 (C=N), 1311-1153 (SO_2), 1507 (aromatic C=C). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.67-3.71 (m, 1H, Ha), 3.93-3.98 (m, 1H, Hb), 4.54 (m, 2H, CO-CH_2), 5.54-5.56 (m, 1H, Hx), 5.94 (s, 2H, NH_2), 6.28-7.79 (m, 12H, Ar-H), 7.35 (s, 1H, NH). MS (EI, *m/z* (%)): 424 (M^+, 15.1). UV/VIS (DMSO, λ_{max}, nm): 349, 287.

4-((2-(5-(Furan-2-yl)-3-(4-nitrophenyl)-4, 5-dihydro-1H-pyrazol-1-yl)-2-oxoeth yl)amino)benzene sulfonamide (**63**): Color: Yellow powder. Yield: 45%. M.p.: 190-192 °C. R_f value: 0.58. FT-IR (KBr, ν, cm^{-1}): 3448-3383 (NH_2), 3240 (NH), 1670 (C=O), 1631 (C=N), 1342-1153 (SO_2), 1597 (aromatic C=C). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.10-3.17 (m, 1H, Ha), 3.72 (dd, 1H, $J_{Hb,Ha}$ = 18.12 Hz, $J_{Hb,Hx}$ = 11.84 Hz, Hb), 3.97-4.01 (m, 2H, CO-CH_2), 5.59 (dd, 1H, $J_{Hb,Hx}$ = 11.8 Hz, $J_{Ha,Hx}$ = 4.72 Hz, Hx), 5.94 (s, 2H, NH_2), 6.32-8.33 (m, 11H, Ar-H), 7.21 (s, 1H, NH). MS (EI, *m/z* (%)): 469 (M^+, 4.7). UV/VIS (DMSO, λ_{max}, nm): 288, 279.

Table 1. Antimicrobial activities of synthesized chloroacetyl pyrazolines.

Compound	Diameter of zone of inhibition (mm) *					
	Gram negative bacteria			Gram positive bacteria		Fungi
	E. coli.	*K. pneumonia*	*P. aeruginosa*	*S. aureus*	*S. mutans*	*C. albicans*
41	19	10.3	-	34	-	14.6
42	13	16	-	10	8.6	15.3
43	23	24.3	-	21	18	14.3
44	-	11.3	11	19	-	12.6
45	-	12.3	-	-	-	13.6
48	11.3	11.3	-	32	19.6	18.6
49	-	11.6	-	27	29	15.3
50	15	12.6	-	-	23.6	10.3
51	-	-	-	33	-	16.3
52	-	-	-	-	-	12.3
53	-	19.3	-	14	22	16.3
54	-	12.3	-	28	-	15.3
55	19	22.3	13	24	22	11.6
56	-	-	-	34	-	16.6
57	-	-	-	-	-	13.6
Gentamicin	35	35	30	-	-	-
Ampicilin	-	-	-	30	35	-
Nystatin	-	-	-	-	-	20

* "-": no activity.

4-((2-Oxo-2-(5-phenyl-3-(p-tolyl)-4, 5-dihydro-1H-pyrazol-1-yl)ethyl)amino)benzene sulfonamide (**64**): Color: White powder. Yield: 59%. M.p.: 210-212 °C. R_f value: 0.59. FT-IR (KBr, ν, cm^{-1}): 3448-3356 (NH_2), 3217 (NH), 1670 (C=O), 1635 (C=N), 1311-1153 (SO_2), 1597 (aromatic C=C). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 2.35 (s, 3H, CH_3), 3.06 (dd, 1H, $J_{Ha,Hb}$ = 18.16 Hz, $J_{Ha,Hx}$ = 4.64 Hz, Ha), 3.77 (dd, 1H, $J_{Hb,Ha}$ = 18.12 Hz, $J_{Hb,Hx}$ = 11.76 Hz, Hb), 4.00 (d, 2H, J = 6.00 Hz, CO-CH_2), 5.42 (dd, 1H, $J_{Hb,Hx}$ = 11.68 Hz, $J_{Ha,Hx}$ = 4.64 Hz, Hx), 5.94 (s, 2H, NH_2), 6.57 (d, 2H, J = 8.68 Hz, Ar-H), 7.12 (d, 2H, J = 7.12H z, Ar-H), 7.28 (t, 1H, NH), 7.30-7.67 (m, 9H, Ar-H). MS (EI, *m/z* (%)): 448 (M^+, 19.4). UV/VIS (DMSO, λ_{max}, nm): 294

4-((2-(5-(4-Chlorophenyl)-3-(p-tolyl)-4, 5-dihydro-1H-pyrazol-1-yl)-2-oxo ethyl) amino)benzene sulfonamide (**65**): Color: Yellow powder. Yield: 48%. M.p.: 216-218 °C. R_f value: 0.45. IR (KBr, ν, cm^{-1}): 3448-3367 (NH_2), 3213 (NH), 1651(C=O), 1597 (C=N), 1319-1149 (SO_2), 1492 (aromatic C=C). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 2.34 (s, 3H, CH_3), 3.10-3.13 (m, 1H, Ha), 3.76-3.87 (m, 1H, Hb), 4.00 (d, 2H, CO-CH_2), 5.42-5.58 (m, 1H, Hx), 5.95 (s, 2H, NH_2) 6.59-7.95 (m, 12H, Ar-H), 7.35 (t, 1H, NH). MS (EI, *m/z* (%)): 482 (M^+, 16.3). UV/VIS (DMSO, λ_{max}, nm): 293, 291, 276.

4-((2-(5-(4-(Dimethylamino)phenyl)-3-(p-tolyl)-4, 5-dihydro-1H-pyrazol-1-yl)-2-oxoethyl)amino)benzene sulfonamide (**66**): Color: Yellow powder. Yield: 39%. M.p.: 118-120 °C. R_f value: 0.72. FT-IR (KBr, ν, cm^{-1}): 3452-3363 (NH_2), 3213 (NH), 1651 (C=O), 1597 (C=N), 1311-1153 (SO_2), 1519 (aromatic C=C). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 2.35 (s, 3H, CH_3), 2.84 (s, 6H, CH_3-N), 3.04-3.08 (m, 1H, Ha), 3.69 (dd, 1H, $J_{Hb,Ha}$ = 18.00 Hz, $J_{Hb,Hx}$ = 11.52 Hz, Hb), 3.95 (m, 2H, CO-CH_2), 5.31 (dd, 1H, $J_{Hb,Hx}$ = 11.44 Hz, $J_{Ha,Hx}$ = 4.20 Hz, Hx), 5.94 (s, 2H, NH_2), 6.59 (dd, 4H, J = 8.64, 15.96 Hz, Ar-H), 6.93 (d, 2H, J = 8.640 Hz, Ar-H), 7.23 (t, 1H, NH), 7.26-7.29 (m, 2H, Ar-H), 7.44 (d, 2H, J = 8.60 Hz, Ar-H), 7.64 (d, 2H, J = 8.00 Hz, Ar-H). MS (EI, 70 ev) (*m/z*): 491 (M^+, 100). UV/VIS (DMSO, λ_{max}, nm): 294, 267.

4-((2-(5-(Furan-2-yl)-3-(p-tolyl)-4, 5-dihydro-1H-pyrazol-1-yl)-2-oxoethyl)amino)benzene sulfonamide (**67**): Color: Yellow powder. Yield: 51%. M.p.: 202-204 °C. R_f value: 0.62. FT-IR (KBr, ν, cm^{-1}): 3444-3356 (NH_2), 3213 (NH), 1654 (C=O), 1597 (C=N), 1315-1153 (SO_2), 1504 (aromatic C=C). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 2.36 (s, 3H, CH_3), 3.40 (m, 1H, Ha), 3.89 (m, 1H, Hb), 4.62 (s, 2H, CO-CH_2), 5.19 (m, 1H, Hx), 5.95 (s, 2H, NH_2), 6.27-7.68 (m, 11H, Ar-H), 7.29 (t, 1H, NH). MS (EI, *m/z* (%)): 438 (M^+, 11.4). UV/VIS (DMSO, λ_{max}, nm): 280, 276.

N-(5,6-Dimethoxypyrimidin-4-yl)-4-((2-(5-(4-(dimethyl amino)phenyl)-3-phenyl-4, 5-dihydro-1H-pyrazol-1-yl)-2-oxo ethyl)amino) benzene sulphonamide (**68**): Color: Yellow powder. Yield: 50%. M.p.: 168-170 °C. R_f value: 0.67. FT-IR (KBr, ν, cm^{-1}): 3398 (NH), 1662 (C=O), 1597 (C=N), 1338-1157 (SO_2), 1523 (aromatic C=C). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 2.85 (s, 6H, CH_3-N), 3.66 (s, 3H, OCH_3), 3.13 (dd, 1H, $J_{Ha,Hb}$ = 17.88 Hz, $J_{Ha,Hx}$ = 4.36 Hz, Ha), 3.82-3.87 (m, 1H, Hb), 4.00 (s, 3H, OCH_3), 4.33-4.44 (m, 2H, CO-CH_2), 4.76-4.78 (t, 1H, NH-CH_2), 5.44-5.47 (m, 1H, Hx), 6.63-7.87 (m, 14H, Ar-H). MS (EI, *m/z* (%)): 615 (M^+, 4.7). UV/VIS (DMSO, λ_{max}, nm): 294, 265.

N-(5,6-Dimethoxypyrimidin-4-yl)-4-((2-oxo-2-(5-phenyl-3-(p-tolyl)-4, 5-dihydro-1H-pyrazol-1-yl)ethyl)amino)benzene sulfonamide (**69**): Color: Yellow powder. Yield: 47%. M.p.: 192-194 °C. R_f value: 0.32. FT-IR (KBr, ν, cm^{-1}): 3425 (NH), 1658 (C=O), 1600 (C=N), 1330-1118 (SO_2), 1519 (aromatic C=C). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 2.34 (s, 3H, CH_3), 3.62 (s, 3H, OCH_3), 3.13-3.15 (m, 1H, Ha), 3.78-3.80 (m, 1H, Hb), 3.85 (s, 3H, OCH_3), 4.42-4.49 (m, 2H, CO-CH_2), 4.83 (t, 1H, NH-CH_2), 5.52-5.59 (m, 1H, Hx), 6.27-7.95 (m, 14H, Ar-H). MS (EI, *m/z* (%)): 583 (M^+, 4.40). UV/VIS (DMSO, λ_{max}, nm): 294.

N-(5,6-Dimethoxypyrimidin-4-yl)-4-((2-(5-(4-(dimethylamino)phenyl)-3-(p-tolyl)-4, 5-dihydro-1H-pyrazol-1-yl)-2-oxoethyl) amino)benzene sulfonamide (**70**): Color: Yellow powder. Yield: 40%. M.p.: 184-186 °C. R_f value: 0.61. FT-IR (KBr, ν, cm^{-1}): 3394 (NH), 1658 (C=O), 1312 (C=N), 1130-1157 (SO_2), 1597 (aromatic C=C). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 2.35 (s, 3H, CH_3), 2.84 (s, 6H, CH_3-N), 3.01-3.05 (m, 1H, Ha), 3.65-3.66 (m, 1H, Hb), 3.83 (s, 3H, OCH_3), 4.00 (s, 3H, OCH_3), 4.39-4.42 (m, 2H, CO-CH_2), 4.73 (t, 1H, NH-CH_2), 5.41-5.45 (m, 1H, Hx), 6.64-7.68 (m, 13H, Ar-H). MS (EI, *m/z* (%)):629 (M^+, 5.3). UV/VIS (DMSO, λ_{max}, nm): 295, 265.

2.3 Antimicrobial activity

The synthesized 2-pyrazoline derivatives **41**-**70** were screened for their *in vitro* antimicrobial activity against some bacteria employing the disk-diffusion technique. Chloroacetyl pyrazoline derivatives (**41**-**45** and **48**-**57**) was tested against different strains of bacteria, *Escherichia coli* (ATCC 3008), *Klebsiella pneumonia* (ATCC 4415), *Pseudomonas aeruginosa* (ATCC 27853), *Staphylococcus aureus* (ATCC 6538), *Streptococcus mutans* (ATCC 25175) and anti fungal activity against *Candida albicans* (ATCC 10231), compared with standard drug gentamicin, ampicilin and nystatin (Table 1). Micro dilution technique was used to obtain the minimum inhibitory concentrations (MICs) for compound derivatives (**41**-**45** and **48**-**57**), it was determined using 6-well microtiter plates (Table 2).

Table 2. Determination of minimum inhibition concentration (MIC) *.

Compound	Minimum inhibition concentration, µg/mL					
	Gram negative bacteria			Gram positive bacteria		Fungi
	E. coli	*K. pneumonia*	*P. aeruginosa*	*S. aureus*	*S. mutans*	*C. albicans*
41	62.5	-	-	31.2	-	250
42	-	62.5	-	-	-	250
43	31.2	31.2	-	31.5	125	125
44	-	-	-	125	-	-
45	-	-	-	-	-	125
48	-	-	-	31.2	250	125
49	-	-	-	31.2	-	500
50	250	-	-	-	31.2	-
51	-	-	-	15.6	-	62.5
52	-	-	-	-	-	-
53	-	62.5	-	-	125	125
54	-	-	-	31.2	-	250
55	62.5	-	-	31.2	31.2	-
56	-	-	-	-	15.6	125
57	-	-	-	-	-	250

* "-": no activity.

1-(Subistituted-aminoacetyl)-3,5-diaryl-2-pyrazolines derivatives (58-70) was tested against *Escherichia coli* (ATCC 25922), *Pseudomonas aeruginosa* (ATCC 27853), *Bacillus subtilis* (NCTC 8236), *Staphylococcus aureus* (ATCC5923) to obtain their anti-bacterial activity and *Candida albicans* (ATCC 7596) for their anti-fungal activity.

3. Results and discussion

All the synthesized compounds were isolated in satisfactory yields, α,β-unsaturated carbonyl derivatives (**1**-**20**) 52-97%, 2-pyrazoline derivatives (**21**-**40**) 60-87%, 1-(chloroacetyl)-3,5-diaryl-2-pyrazolines derivatives (**41**-**57**) 46-72% and 1-(substituted aminoacetyl)-3,5-diaryl-2-pyrazolines derivatives (**58**-**70**) 39-75%.

The structures of the synthesized α,β-unsaturated carbonyl derivatives (**1**-**20**) were confirmed by using FT-IR spectroscopy. It showed several characteristic sharp bands in the IR region, where the bands in the range between 1644-1665 cm^{-1} indicated the appearance of the carbonyl C=O group of the formed ketone, which was conjugated to the alkene systems. -C=C- olefein which conjugated to C=O appeared at 1562-1608 cm^{-1}. The absorption band at 1407-1594 cm^{-1} confirms the aromatic -C=C- group.

Resulted α,β-unsaturated carbonyl derivatives undergoes selective cyclization in presence of hydrazine hydrate, in alcohol medium yields 2-pyrazoline derivatives (**21**-**40**). The IR spectra of these compounds show the disappearance of C=C (olefinic) and C=O stretching bands at α,β-unsaturated carbonyl derivatives due to the ring closure and appeared of pyrazoline -NH (3249-3421 cm^{-1}) and C=N stretching (1588-1681 cm^{-1}).

IR spectra of chloroacetyl pyrazoline derivatives (**41**-**57**), which obtained by the reaction of 2-pyrazoline derivatives with chloroacetyl chloride in presence of triethyl amine, showed disappearance of -NH of pyrazoline derivatives and absorption bands in the regions 1664-1757cm^{-1} due to the C=O and 1573-1671 cm^{-1} corresponding to C=N stretching .

Compounds **58**-**67** showed two stretching vibration absorption bands at range 3482-3441 (asym) and 3392-3356 (sym) associated with NH_2, and stretching vibration absorption bands at 3240-3213 cm^{-1} for NH group. All this type of compounds showed two bands at 1396-1311 (asym) and 1155-1149 cm^{-1} due to appearance of SO_2 group.

Compounds **68**-**70** showed absorption band at 3425-3394 cm^{-1} confirms the NH group. Two bands at 1338-1330 (asym) and 1157-1118 cm^{-1} (sym) confirm SO_2 group.

^1H NMR spectra of compounds **58**-**67** showed ABX system due to germinal-vicinal multiple coupling between two protons Ha, Hb and Hx proton of pyrazoline ring. Ha *trans* proton showed doublet of doublets at about δ 3.11-3.48 ppm. Hb *cis* proton appeared at δ 3.65-3.93 ppm as doublet of doublets. Hx proton also showed doublet of doublets at δ 5.19-5.74 ppm due to vicinal coupling with two magnetically non-equivalent protons Ha, Hb. $COCH_2$ methylene protons, present in all compounds, appeared at δ 4.62-4.82 ppm as two doublets. All the other aromatic and aliphatic protons were observed at the expected regions.

Ha proton of compounds **68**-**70** appeared at δ 3.01-3.40, δ 3.57-4.54 Hb proton and δ 5.11-5.59 ppm Hx. The signal for protons attached with carbonyl group appeared at δ 4.01-4.33 ppm. Protons of primary amine showed singlet peak at δ 5.94-5.95 ppm. Proton of secondary amine appeared as triplet or distorted triplet at δ 4.73-7.44 ppm.

Synthesized compounds **41**-**70** were tested for *in vitro* antimicrobial activity by the disk diffusion technique. The antimicrobial screening suggests that the synthesized compounds **41**-**57** showed moderate activity against the tested organisms (Table 1). The compounds **41**, **48**, **51** and **56** tested against *S.aureus*, showed significant antimicrobial activity when compared to standard drug ampicillin.

The preliminary *in vitro* test results of new synthesized compounds **58**-**70** which bearing sulfanilamido moiety was negatives against the five studied microorganisms such as *E. coli, P. aeruginosa*, *B. subtilis, S. aureus* and *C. albicans.* On the bases of these results, we summarized that introduce of sulfonilamide or sulfadoxine moiety in chloroacetylpyrazline derivatives led to complete loss of their antimicrobial activity.

4. Conclusion

In summary, a series of 2-pyrazoline derivatives bearing sulfanilamido moiety have been prepared. Initially, α,β-unsaturated carbonyl derivatives (**1**-**20**) were synthesized via the base-catalyzed Claisene Schmidt condensation of equilmolar quantities of aromatic aldehydes and aromatic ketones in presence of 10% NaOH in ethanol (Scheme 1). Secondly, 3,5-diaryl-2-pyrazoline derivatives (**21**-**40**) were obtained by the cyclization of α,β-unsaturated compounds with hydrazine monohydrate 98% in absolute ethanol. The ring closure reaction of 3,5-diaryl-2-pyrazolines (**21**-**40**) with chloroacetyl chloride afforded 1-(chloroacetyl)-3,5-diaryl-2-pyrazolines derivatives (**41**-**57**). The reaction of chloroacetyl pyrazoline derivatives with aryl amine (sulfanilamide/ sulfadoxine) in dimethylformmaide yielded the final compounds 1-(substituted aminoacetyl)-3,5-diaryl-2-pyrazolines derivatives (**58**-**70**). The purity of the prepared compounds was checked by TLC and the structures are identified by spectral data. Also, the antibacterial and antifungal evaluations of synthesized compounds **41**-**45** and **48**-**70** against different microorganism were reported. Most of

the synthesized compounds **41**-**57** showed moderate antimicrobial activity and no activity observed in synthesized compounds **58**-**70**.

Disclosure statement

Conflict of interests: The authors declare that they have no conflict of interest.
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Sample availability: Samples of the compounds are available from the author.

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References

[1]. Yusuf, M.; Jain, P. *Arab. J. Chem.* **2014**, *7*, 553-596.
[2]. Rani, M.; Yusuf, M. *Eur. J. Chem.* **2012**, *3(4)*, 406-410.
[3]. Gokhan-Kelekci, N.; Koyunoglu, S.; Yabanoglu, S.; Yelekci, K.; Ozgen, O.; Ucar, G.; Erol, K.; Kendi, E.; Yesilada, A. *Bioorg. Med. Chem.* **2009**, *17*, 675-689.
[4]. Shinkar, S. A.; Shetty, V. J.; Jagdale, D. M. *World J. Pharm. Pharm. Sci.* **2015**, *4*, 505-514.
[5]. Shah, S.; Ziauddin, H. M.; Zameer, M.; Khan, T.; Baseer, M. A. *Int. J. Curr. Pharm. Res.* **2011**, *2*, 34-36.
[6]. Karabacak, M.; Altıntop, M. D.; Ciftci, H. I.; Koga, R.; Otsuka, M.; Fujita, M.; Ozdemir, A. *Molecules* **2015**, *20*, 19066-19084.
[7]. Kumar, K. A.; Govindaraju, M. *Int. J. Chem. Tech. Res.* **2015**, *8*, 313-322.
[8]. Ziani, N.; Lamara, K.; Sid, A.; Willem, Q.; Dassonneville, B.; Demonceau, A. *Eur. J. Chem.* **2013**, *4(2)*, 176-179.
[9]. Rahman, Md. A.; Siddiqui, A. A.; *Int. J. Pharm. Sci. Drug Res.* **2010**, *2*, 165-175.
[10]. Khan, S. A.; Asiri, A. M.; Kumar, S.; Sharma, K. *Eur. J. Chem.* **2014**, *5(1)*, 85-90.
[11]. Mahdi, M. F.; Raauf, A. M. R.; Mohammed, N. M. *Eur. J. Chem.* **2015**, *6(4)*, 461-467.