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SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF INDOLE DERIVATIVE BEARING THE PYRAZOLE MOIETY

Imaduddin Quazi [*1], V. Girija Sastry [2] and Javed Akhtar Ansari [3]

Department of Pharmaceutical Chemistry [1], Faculty of Pharmacy, MESCO College of Pharmacy (Affiliated to Osmania University), Hyderabad - 50006, TS, India.
Department of Pharmaceutical Chemistry [2], Faculty of Pharmacy, University College of Pharmaceutical Sciences, Andhra University, Visakhapatnam, AP, India.
Department of Pharmacology [3], Faculty of Pharmacy, Mesco College of Pharmacy, (Affiliated to Osmania University), Hyderabad - 50006, India.

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Correspondence to Author:
Quazi Imaduddin

Senior Assistant Professor Mesco College of Pharmacy karwan Road Hyderabad (TS) - 500006, India.

E-mail: qimadh@gmail.com

ABSTRACT: Series of 1 of 1-[(3,5 diphenyl substituted) -4,5-dihydro-1H-pyrazol-1-yl]-2-(3H-indol-3-yl) ethan-1-one (5a-5j) derivatives were synthesized by the reaction between indole 3 acetic acid hydrazide and various chalcones (3a-3j). The Chalcones were prepared by Claisen-Schmidt condensation reaction in which substituted aromatic aldehydes was treated with simple acetophenone(aromatic ketones) in presence of 20% base(NaOH) and indole 3 acetic acid hydrazide was prepared by reaction between 3 indole acetic acid with hydrazide. The synthesized new compounds were identified by spectral studies and elemental analysis, and were evaluated in vitro for their antimicrobial activity using standard agar diffusion method and using four bacterial strains (*Bacillus, Pseudomonas, Escherichia coli* and *Staphylococcus*) and two fungal strains (*Sclerotium rolfsii* & *Macrophomina phaseolina*) most of compounds such 5c.5a,5b,5f,5g i.e 1-[5-(4-Chloro phenyl)-3-phenyl-4,5-dihydro-1H-pyrazol-1-yl] - 2 - (3H-indol-3-yl) ethan-1-one (5c), 1-(3, 5-diphenyl-4,5-dihydro-1H-pyrazol-1-yl) -2-(3H-indol-3-yl) ethan-1-one (5a), 1-[5-(4-methoxyphenyl)-3-phenyl-4,5-dihydro-1H-pyrazol-1-yl]-2-(3H-indol-3-yl) ethan - 1-one(5b), 1-[5-(4 dimethyl amino phenyl)-3-phenyl-4,5-dihydro-1H-pyrazol-1-yl]-2-(3H-indol-3-yl)ethan-1-one(5e), 1-[5-(4 Hydroxyl 3 Methoxy phenyl)-3-phenyl-4,5-dihydro-1H-pyrazol-1-yl]-2-(3H-indol-3-yl)ethan-1-one(5g). Shows good activity against gram positive and gram negative bacteria. All the compound exhibits moderate to average antifungal activity.

INTRODUCTION: It has been delineated that the morbidity, mortality, and costs connected to the healing of infectious diseases have been amplified by antimicrobial resistance. The multiple resistance in bacterial strains that have propagated so widely has never been at anytime of such great importance.

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The increased use of antibiotics, extensive movement of people, and increased industrial and economic development are the important factors constraining this hazard [1]. The rapid global pre-eminent issue is the resistance of pathogenic microorganisms to approachable antibiotics, anxiolytics, sedatives, hypnotics and anti-convulsants. Secondly, the primary and opportunistic fungal infections persist to increase very quickly as the number of resistant patients is amplifying [2]. The multiple biological and pharmacological properties of heterocyclic compounds have evoked recognition [3]. The delineation of new compounds to treat resistant

bacteria has become of the most significant aim of antibacterial research currently. This is because the antibiotic resistance as a consequence of improper and irrational utilization of antimicrobial medicines, renders suitable conditions for resistant bacteria to become prominent. As a result of this resistance of pathogenic bacteria towards available antibiotics happens to be a worldwide problem [4]. The pyrazole moiety is a resourceful lead molecule in the pharmaceutical progress and has a broad range of biological activities antibacterial, antifungal and pharmacological activities such as anti-inflammatory, antitubercular, anticancer, Analgesic [5]. Pyrazole moiety fused indole also shows the potent antibacterial activity [6]. It has been reported that indole derivatives bearing pyrazole nucleus are good antioxidant [6]. Indole derivatives such as indole -2-carboxamide are potent and broad spectrum antivral agents [7].

A large number of heterocyclic compounds containing the indole ring are associated with diverse pharmacological properties such as Analgesic, Antiallergic, Antibacterial, Anticonvulsant, Antifungal, Antihistaminic, Anti-inflammatory, Anticancer, Anthelminthic, Anti hypertensive, Cardiovascular, Antioxidant [8]. The present investigation was undertaken to develop an efficient method for synthesizing indole derivatives having pyrazoline moiety can be potent anti microbial agent.

MATERIALS AND METHODS: The used chemicals were supplied by S.D. Fine Chemicals, Spectrochem lab awra (India). Melting points were determined by open tube capillary process and are uncorrected.

Pureness of the compounds was checked on thin layer chromatography (TLC) plates (silica gel G) in the solution system toluene-ethyl formate-formic acid (5:4:1, v/v/v)and N-hexane-ethylacetate (4:1, v/v), the spots were to be found under iodine vapors and UV light. IR spectra were obtained on a Shimadzu spectrometer (KBr pellets). ^{1}HNMR spectroscopy were recorded on a Avance- 300 MHz spectrometer using TMS as internal standard in DMSO-d6/ CDCl3 and mass spectra under electron impact conditions (EI) were recorded at 70 eV ionizing voltage and are presented as m/z.

Experimental Procedure:

Synthesis of (2E)-3-(substituted phenyl)-1-phenylprop-2-en- 1-one (3A – 3 J): Derivatives were synthesized by condensing acetophenone with appropriate substituted aromatic aldehydes according to Claisen-Schmidt condensation [9-15]. To a solution of acetophenone (0.01 mole) in ethanol (100ml), there was added solution of aromatic aldehyde (0.01 mole) in ethanol (100) (if doesn't dissolve warm it), it was stirred for 2-3 minutes. After 10 minutes drop by drop 10% of KOH solution was added till turbidity was formed (don't add excess) stirring was continued till the solid separated. Product was filtered and was washed with water. In case if product was not obtained stirring was continued for 10-12 hours. After that, it was kept in the refrigerator for 6-7 hours. Then, it was acidified with hydrochloric acid (10%) and allowed it to stand at room temperature. Solid separated was collected, dried and crystallized with the suitable solvent (ethanol).

Synthesis of (2E)-3-(substituted phenyl)-1-phenylprop-2-en- 1-one (3A – 3 J) (2E)-1, 3-diphenylprop-2-en-1-one (3A): White solid, (60 % yield); mp= 55 ˚C IR: (KBR cm^{-1}): υ=3058 (CH), 1660 (C=O). ^{1}HNMR (DMSO-d6), δ (ppm): 7.54(1H ×2, d J = 6Hz, 7.8Hz CH=HC), 7.6-8. (10 H, m, Ar-H). EI-MS: m/z: 208 (m+1)

Anal Calcd for $C_{15}H_{12}O$ (208.25): C, 86.51; H, 5.81. Found C, 86.61; H, 5.80.

(2E)-3-(4-methoxyphenyl)-1-phenylprop-2-en-1-one (3 B). White solid, (75 yield); mp= 80 ˚C IR: (KBR cm^{-1}): υ = 3030 (CH), 1654(C=O).^{1} HNMR (DMSO-d_6), δ (ppm): 6.9 (1H× 2 d J = 6.39Hz, 6.68Hz CH=CH), 7.5-8. (9H, m, Ar- H), 3.88 (3 H s, CH_3). EI-MS: m/z: 239 (m+1).

Anal Calcd for C_{16} H_{14} 0_2 (238.38): C, 80.65; H, 5.92. Found C, 80.40; H, 5.89.

(2E) - 3 - (4-chlorophenyl)-1-phenylprop-2-en-1-one (3C): White solid, (65% yield); mp= 85˚C; IR: (KBr cm^{-1}): υ = 3030 (CH), 1676 (C=O). ^{1}HNMR (DMSO-d $_6$), δ (ppm): 7.5 (1H× 2, d J = 8.4Hz, 8.1Hz CH=CH), 7.7-8.16 (9 H, m, Ar-H). EI-MS: m/z: 242 (m+1)

Anal Calcd for $C_{15}H_{11}0Cl$ (242.70): C, 74.23; H, 4.57. Found C, 74.44; H, 4.57.

4 (2E)-3-(2-chlorophenyl)-1-phenylprop-2-en-1-one (3D): White solid, (75 yield); mp= 80˚C; IR: (KBr cm^{-1}): υ = 3030 (CH), 1676 (C=O), ^{1}HNMR (DMSO-d_6), *δ* (ppm): 7.56 (1H× 2, d *J*= 8.3Hz, 8.1Hz HC=CH) ,7.52-8.1 (9H,m, Ar-H). EI-MS: m/z: 242 (m+1).

Anal Calcd for $C_{15}H_{11}0Cl$ (242.70): C, 74.23; H, 4.57. Found C, 74.44; H, 4.57.

(2E)-3-(2-4-chlorophenyl)-1-phenylprop-2-en-1-one (3E): Yellow solid, (55% yield); mp= 70˚CIR: (KBr cm^{-1}): υ = 3030 (CH), 1676 (C=O). ^{1} HNMR (DMSO-d_6), *δ* (ppm): 7.57 (1H× 2, d *J*= 8.2Hz, 8.0 Hz CH=CH), 7.7-8 (8H, m, Ar-H). EI-MS: m/z: 278 (m+1).

Anal Calcd for $C_{15}H_{10}Cl_2O$ (277.14): C, 65.01; H, 3.64. Found: C, 64.77; H, 3.61.

(2E)-3-[4-(dimethylamino)phenyl]-1phenylprop-2-en-1-one (3F). Yellowish –white Solid, (63% yield); mp= 90 ˚C IR: (KBr cm^{-1}): υ = 3030 (CH), 1660 (C=O). ^{1} HNMR (DMSO-d_6), *δ* (ppm): 6.7 (1H × 2, d *J*= 8.7Hz, 7.2Hz CH=CH), 7.323-8 (9H, m, Ar-H), 3.3 (6H,s, N $(CH3)_2$). EI-MS: m/z: 252 (m+1).

Anal Calcd for $C_{17}H_{17}NO$ (251.32): C, 81.24; H, 6.82; N, 5.57. Found: C, 80.95; H, 6.74.

(2E)-3-(4-hydroxy-3-methoxyphenyl) – 1 -phenyl prop-2-en-1-one (3G). White solid, (80 yield); mp= 87˚C; IR: (KBr cm^{-1}): υ = 3030 (CH), 1676 (C=O), 3455(OH). ^{1} HNMR (DMSO-d_6), *δ* (ppm): 6.71 (1H× 2, d *J*=8.2Hz, 7.3Hz HC=CH) ,7.51-8 (8H,m, Ar-H), 10.19 (1 H, s ,OH), 3.4(3 H, s, OCH_3). EI-MS: m/z: 255 (m+1).

Anal Calcd for $C_{16}H_{14}O_3$ (254.28): C, 75.57; H, 5.55. Found: C, 75.36; H, 5.52.

(2E)-3-(4-bromophenyl)-1-phenylprop - 2 - en-1-one (3 H). Pink solid, (80 % yield); mp= 85 ˚C; IR: (KBr cm^{-1}): υ = 3030 (CH), 1676 (C=O). ^{1}HNMR (DMSO-d_6), *δ* (ppm): 7.55 (1H× 2, d *J*= 6.1Hz, 7.89Hz CH=CH), 7.7-8.2 (9H, m, Ar-H). EI-MS: m/z: 288 (m+1).

Anal Calcd for $C_{15}H_{11}0Br$ (287.15): C, 62.74; H, 3.86. Found: C, 62.55; H, 3.84.

(2E)-1-phenyl-3-(3,4,5-trimethoxyphenyl) prop-2-en-1-one (3 I). White solid, (70 yield); mp= 108 ˚C; IR: (KBr cm^{-1}): υ = 3030 (CH), 1676 (C=O). ^{1}HNMR (DMSO-d_6), δ (ppm): 7.1 (1H × 2, d *J*= 6.40Hz, 6.68Hz CH=CH), 7.51-8 (7H, m, Ar-H), 3.23 (9H, s, OCH_3). EI-MS: m/z: 299 (m+1).

Anal Calcd for $C_{18}H_{18}0_4$ (298.33): C, 72.47; H, 6.08. Found: C, 72.30; H, 6.06.

(2E)-3-(4-nitrophenyl)-1-phenylprop-2-en-1-one (3 J). Red solid, (85 yield); mp= 80˚C; IR: (KBr cm^{-1}): υ = 3030 (CH), 1676 (C=O), 1380 (N-O). ^{1}HNMR (DMSO-d_6), *δ* (ppm): 7.55 (1H× 2, d *J*=7.5Hz, 7.2Hz CH=CH), 7.58 -8 (9H,m, Ar-H). EI-MS: m/z: 254 (m+1)

Anal Calcd for $C_{15}H_{11}N0_3$ (253.25): C, 71.14; H, 4.38; N, 5.53. Found: C, 70.92; H, 4.33; N, 5.51.

Synthesis of 3 Indole acetic hydrazide (4):0.001 mole of 3 indole acetic acid was dissolved in 100ml of absolute alcohol and 3 drops of sulphuric acid were added, refluxed it for 18 hours. Then TLC was taken and compared with starting compound using N-hexane-ethyl acetate (4:1) ratio. After completion of reaction content was neutralized with $NaHCO_3$ (Esterification reaction) filtered it to remove the salt, after that 0.003 mole hydrazine hydrate was added to above Ester and refluxed for 15 hours. Product was obtained by filtration and recrystallized it from ethanol to give pure compound [16-19]. As white solid (75% yield); mp = 142˚C; IR: (KBr cm^{-1}): υ = 3029 (CH), 1673 (C=O), 3374(N-H) ^{1}HNMR (DMSO-d_6), *δ* (ppm): 3.73 (s 2H CH_2), 3.5 (s 1H, CH), 2.4 (s, 2H, NH), 7.51(s, 1H, NH), 10.87 (s 1H NH), 7.02-7.4 (4H,m, Ar-H).

Anal Calcd for $C_{10}H_{11}N_3O_3$ (189.21) C, 63, 47; H, 5.85; N, 22.20. Found: C, 63.23; H, 5.83; N, 22.12.

Synthesis of 1-[(3,5-diphenyl substituted)-4,5-dihydro-1H-pyrazol-1-yl] - 2 - (3H-indol-3-yl) ethan-1-one (5 A- 5J): 0.001M of indole 3 acetic hydrazide was reacted with 0.001M of (2*E*)-3-(substituted)-1-phenylprop-2-en-1-one (chalcones 3A-3J) in 30 ml of glacial acetic acid. Mixture was refluxed for 24 hour. Excess of solvent was removed under reduced pressure. Reaction mixture was cooled and poured onto crushed ice (30g).

Product obtained was filtered and recrystallized from methanol.[20-21]

1-(3, 5-diphenyl-4,5-dihydro-1H-pyrazol-1-yl)-2-(3H-indol-3-yl)ethan-1-one(5A): White solid (70%yield); mp 135 ˚C; IR: (KBR cm^{-1}): υ = 3391(C-H),1701(C=O). ^{1}HNMR (DMSO-d $_6$), δ (ppm): 3.6(2H s- CH_2), 4.822 (1H, s –CH), 2.48(2H s- CH_2), 3.2 (1H s-CH) 7.49 (1H, s, CH) 6.88-7.33 (14 H, m, Ar-H). EI-MS: m/z: 380 (m+1).

Anal Calcd for $C_{25}H_{21}N_3O$ (379.45): C, 79.13; H, 5.58; N, 11.07. Found: C, 79.01; H, 5.56; N, 11.05.

1-[5-(4-methoxyphenyl)-3-phenyl- 4, 5 - dihydro-1H-pyrazol-1-yl]-2-(3H-indol-3-yl)ethan-1 - one (5B). White solid (yield 80); mp=120 ˚C; IR: (KBr cm^{-1}): υ=1665(C=O), 3364 (CH). ^{1}HNMR (DMSO-d $_6$), δ (ppm) : 3.8 (2H,s CH2), 5.5(1H,s CH), 2.48 (2H,s,CH2), 3.2(1H,S,CH) 7.50(1H,s CH), 3.7 (3H, S, OCH $_3$), 7- 8 (13H,m, Ar-H proton). EI-MS: m/z: 409 (m+1).

Anal Calcd for $C_{26}H_{23}N_3O$ (409.47): C, 76.26; H, 5.66, N, 10.26. Found: C, 76.35; H, 5.66; N, 10.27.

1-[5-(4-Chloro phenyl)-3-phenyl-4,5-dihydro-1H-pyrazol-1-yl]-2-(3H-indol-3-yl)ethan - 1 - one (5 C): White Solid (yield 85%); mp 170 ˚C; IR: (KBr cm^{-1}): υ = 17O4(C=O), 3390,(C-H), 794(C-CL). ^{1}HNMR (DMSO-d $_6$), δ (ppm): 3.34 (2H, s,CH_2), 4.8 (1H, s, CH), 2.48 (2H,s, CH_2), 3.34(1 H,s CH) , 7.50 (1H,s CH), 7.56-8 , (13H,m, Ar-H). EI-MS: m/z =: 414 (m+1)

Anal Calcd for $C_{25}H_{2O}ClN_3O$ (413.89) C, 72.55; H, 4.57; N, 10.15. Found: C, 72.52; H, 4.83; N, 10.15

1-[5-(2-Chloro phenyl)-3-phenyl-4, 5 - dihydro-1H-pyrazol-1-yl]-2-(3H-indol-3-yl) ethan-1-one (5D): White solid (55% yield); mp 180˚C; IR: (KBr cm^{-1}): υ = 1698(C=O), 3391(C-H) 783 (C-CL). ^{1}HNMR (DMSO-d $_6$), δ (ppm): 3.6(2H, s, CH_2), 4.5 (1H, s, CH), 2.48(2 H, s, CH_2), 3.33(1Hs CH), 7.50(1H,s CH) , 6.94- 8 (13 H,m, Ar-H). EI-MS m/z: 414 (m+1).

Anal Calcd for $C_{25}H_{2O}ClN_3O$ (413.89) C, 72.55; H, 4.57; N, 10.15. Found: C, 72.52; H, 4.83; N, 10.15.

1-[5-(2,4 dichloro phenyl)-3-phenyl-4,5-dihydro-1H-pyrazol-1-yl]-2-(3H-indol-3-yl)ethan - 1 - one (5E): Whitish yellow (yield 60%) ; mp 210 ˚C; IR: (KBr cm^{-1}): υ= 1671(C=O), 3391(CH), 793(C-CL).^{1}HNMR (DMSO-d $_6$), δ (ppm): 3.4(2H, s, CH_2), 5.1 (1H,s.CH), 2.46 (2H,s, CH_2), 3.3 (1 H,s, CH), 7.52(1H,s, CH), 6.5 - 7.5 (12 H, m, Ar-H). EI-MS: m/z: 449(m+1).

Anal Calcd for $C_{25}H_{19}Cl_2N_3O$ (448.34): C, 66.97; H, 4.27; N, 9.37. Found: C, 66.87; H, 4.26; N, 9.35.

1-[5-(4 dimethyl amino phenyl)-3-phenyl-4,5-dihydro-1H-pyrazol-1-yl]-2-(3H - indol - 3-yl) ethan-1-one(5F) . Whitish yellow (yield 75%) ; mp 115 ˚C; IR: (KBr cm^{-1}): υ = 1701(C=O), 3393 (CH),1248 (N-H). ^{1}HNMR (DMSO-d $_6$), δ (ppm): 3.46(2 H, s, CH2), 4.5 (1H, s.CH), 2.48 (2H,s, CH_2), 3.3(1H,s,CH) , 7.5 (1H,s,CH,), 3.03 (6, H,s, N (CH_3)$_2$, 6.5 to 7.5 (13H,m, Ar-H). EI-MS: m/z: 423 (m+1).

Anal Calcd for $C_{27}H_{26}N_4O$ (422.52): C, 76.75; H, 6.20; N, 13.26. Found: C, 76.66; H, 6.18; N, 13.24.

1-[5-(4 Hydroxyl 3 Methoxy phenyl)-3-phenyl-4,5-dihydro-1H-pyrazol-1-yl]- 2 - (3H-indol-3-yl) ethan-1-one(5G). White (yield 65%); mp 160 ˚C IR: (KBr cm^{-1}): υ=1660(C=O), 3397(CH), 3455 (OH). ^{1}HNMR (DMSO-d $_6$), δ (ppm): 3.6(2H, s, CH_2,), 4.54 (1 H,s, CH), 2.49(2H,s, CH_2), 3.5 (1H,s,CH), 7.5(1H,s, CH), 3.8 (3 H,s, OCH_3), 10.81 (1H,s, OH),6.603- 7.49 (12H,m, Ar-H). Mass: EI-MS m/z: 426 (m+1).

Anal Calcd for $C_{26}H_{23}N_3O_3$ (425.47): C, 73.39; H, 5.45, N, 9.88. Found: C, 73.30; H, 5.43; N, 9.86.

1-[5-(4Bromo phenyl)-3-phenyl-4,5-dihydro-1H-pyrazol-1-yl]-2-(3H-indol-3-yl) ethan - 1-one (5H): White (yield 80%); mp 240 ˚C; IR: (KBr cm^{-1}) : υ= 1660(C=O), 2915 (CH),684(C-Br). ^{1}HNMR (DMSO-d $_6$), δ (ppm): 3.70 (2 H,s, CH_2), 3.85 (1 H,s, CH), 2.49 (2H,s, CH_2), 3.6(1H,s H), 7.49 (1H,s,CH), 7.2 to 8.1 (13H,m, Ar-H). Mass: EI-MS m/z: 459 (m+1).

Anal Calcd for $C_{25}H_{20}BrN_3O$ (458.34: C, 65.51; H, 4.4; N, 9.17. Found: C, 65.54; H, 4.38; N, 9.15.

1-[5-(3, 4, 5 methoxy phenyl)-3-phenyl-4,5-di hydro-1H-pyrazol – 1 - yl] - 2 - (3H-indol-3-yl) ethan-1-one(5I): White (yield 73%) ; mp 190 ˚C; IR: (KBr cm^{-1}): υ = 1660 (C=O), 2991 (CH).

^{1}HNMR (DMSO-d $_6$), δ (ppm): 3.7 (2 H,s,CH_2), 4.13 (1 H,s ,CH), 2.49(2H,s, CH_2), 3.38(1 H,s ,CH), 7.5 (1H,s, -CH), 3.85 (9H, s, OCH3), 7.52 - 8.16 (11H,m, Ar –H). Mass: EI-MS m/z: 467(m+1).

Anal Calcd for $C_{28}H_{27}N_3O_4$ (469.53): C, 71.62; H, 4.4; N, 9.17. Found: C, 72.01; H, 4.52; N, 8.99.

1-[5-(4 Nitro phenyl)-3-phenyl-4,5-dihydro-1H-pyrazol-1-yl]-2-(3H-indol-3-yl)ethan-1-one(5J): Brown solid (yield 85); mp 130 ˚C IR: (KBr cm^1): υ = 1654 (C=O) ,2915 (CH) ,1331(N-0). ^{1}HNMR (DMSO-d $_6$), δ (ppm): ^{1}HNMR (DMSO-d $_6$), δ (ppm): 3.36 (2H,s,CH_2) 3.9 (1 H,s-CH) 2.51 (2 H,s, CH_2), 7.58 (1 H,s CH), 3.6 (1H,s,CH), 7.58 - 8.3 (13H,m, Ar-H). MASS: EI-M S m/z: 425 (m+1).

Anal Calcd for $C_{25}H_{20}N_4O_3$ (424.45): C, 70.74; H, 4.75; N, 13.20. Found: C, 70.65; H, 4.74; 13.18.

RESULTS AND DISCUSSION: Synthesis 2E)-3-(substituted phenyl)-1-phenylprop-2-en- 1-one (3A – 3 J) The present compound such as (2E)-3-(substituted phenyl)-1-phenylprop-2-en-1-one 3A – 3 J was prepared by Claisen-Schmidt condensation reaction in which substituted aromatic benzaldehyide is reacted with simple aromatic ketone (acetophenone) in the presence of 20% alkali such as sodium hydroxide or potassium hydroxide, where the two above component's were stirred in the solvent such as ethanol for 10 minutes. After that, alkali was added drop by drop until product was Separated [9-15]. Detailed analysis of 1H NMR, IR, and Mass spectral data of all compound has been describe in this paper.

The IR spectrum compound 3A showed stretching bands at υ= 3058 cm-1 (CH), υ=1660 cm-1 (C=O), υ= 1571 (CH=CH), υ = 1448 (C=C), υ=1217 (C-O-C), υ= 748 cm-1 mono substituted benzene. 1H NMR Spectrum of compound 3A displays two signals i.e. doublet at δ =7.4 ppm which is attributed to (- CH=CH) and also multiplets of ten aromatic proton at δ 7.5-8ppm [12-15]. Mass spectrum revealed a molecular ion peak at m/z 243 (m+1). Similarly, by using the above procedure 10 new derivatives i.e (3A, 3B, 3C, 3D, 3E, 3F, 3G, 3H, 3I, 3J) were prepared and their structure was established on the basis of elemental analysis and spectral data. The required indole 3 acetic acid hydrazine(4) is prepared by procedure as describe in literature [16] 0.001 Mole of indole 3 acetic acid was dissolved in 100 ml absolute ethanol. 3 drops of sulphuric acid were added and refluxed for 18 hours. After completion of reaction (esterification) 0.003 mole of hydrazine hydrate was added and refluxed for 15 hours. Product was obtained by filtration. The structure of compound 4 was confirmed by spectral data of (IR, 1HNMR Mass). IR Spectra compound stretching band at υ = 3029 cm-1 (CH), υ=1673 cm-1 (C=O), υ= 3374 cm-1 (N-H), 1H NMR of compound (4), exhibited singlet at 2.4, 8.11, 10.8 confirmed with the –NH2 NH and NH Protons of hydrazide [31]. Mass spectrum supports the molecular weight of the compound (4) i.e. m/z peak at 189 (m+1).

Synthesis of 1-[(3,5-diphenyl substituted)-4,5-dihydro-1H-pyrazol-1-yl]-2-(3H-indol-3-yl)ethan-1-one 5A-5J was done from procedure as describe in literature [21] were (2E)-3-(substituted phenyl)-1-phenylprop-2-en-1-one (chalcone) was reacted with 3 indole acetic hydrazide in presence of glacial acetic acid, refluxed for 24 hours to form new indole derivative such as, 1-[(3,5-diphenyl substituted)-4,5-dihydro-1H-pyrazol-1-yl]-2-(3H-indol-3-yl)ethan-1-one

The structure of all compounds has been supported by different spectral data (IR, 1H NMR, Mass). For example, compound (5A) IR spectra show characteristic absorption band at υ = 1701 cm-1, and υ=3391 cm-1 which assigned for (C=O) and (CH). 1H NMR spectra compound (5A) display singlet at δ = 3.6ppm and 4.88ppm for (C 4' CH2 and C 5' CH), and also multiplets of aromatic proton at δ = 7.5 to 8ppm. Mass spectrum of compound (5A) molecular ion peak at m/z =380 which is in agreement with its molecular weight. Singlet of (C 4' CH2 and C 5' CH) was also confirmed on the basis of Literature [20] in all 10 newly synthesized compounds i.e. (5A-5J). Both analytical and spectral data (IR and 1H NMR) of all synthesized compounds completely supports the purposed structure. Spectra of compounds such as (5A, 5B, 5C, 5D, 5E, 5F, 5G, 5H, 5I, 5J) has been described in experimental section.

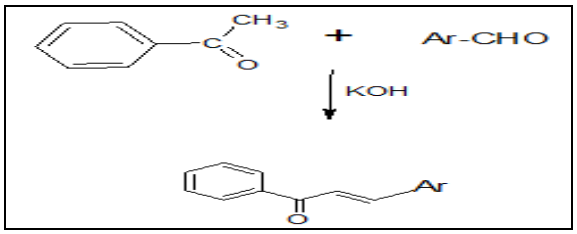
Biological Activity:

Antimicrobial Activity:

Determination of Antibacterial activity by Agar cup method: Antibacterial activity was tested by standard agar diffusion method. Fresh bacterial culture having 5x10-5 colonies was mixed with nutrient agar medium and poured in to plates. Wells were made in the cooled agar plates (1cm).The compounds 10mg were dissolved in 2 ml DMSO and 100µl was loaded in the well. The activity or sensitivity was observed after 24-48 hours incubation at 37˚C [22-23].

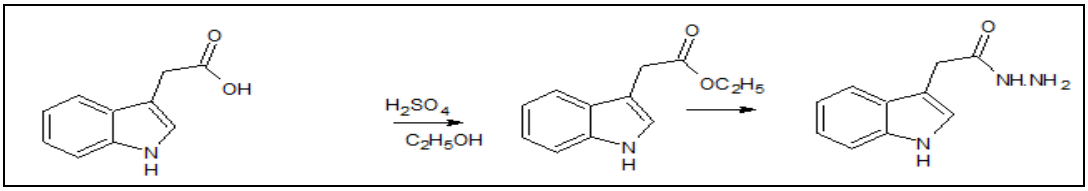
Determination of Antifungal activity by Disc diffusion method: Anti fungal activity studies were carried out using two fungi. Potato Dextrose Agar media was prepared and the fungal plugs were placed in the center of the plate and the compounds were put in the wells surrounding the plug and the zone of inhibition was measured after 72 hours.[22]

1,3-diphenyl (Substituted)prop-2-en-1-one (2E)-1,3-diphenyl (Substituted)prop-2-en-1-one 1-ones (3A-3J):

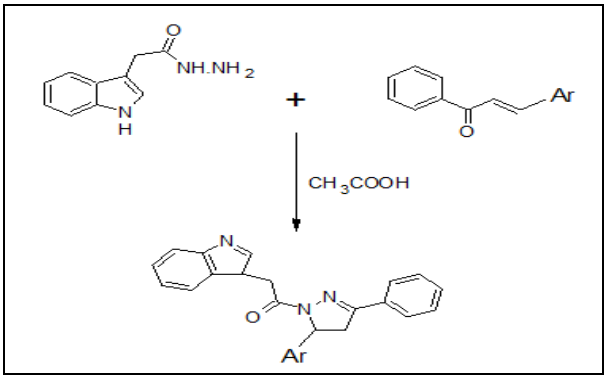


Where	Ar
a)	C_6H_5
b)	$C_6H_4\ OCH_3$ (4)
c)	C_6H_4CL(4)
d)	C_6H_4CL(2)
e)	C_6H_3CL(2,4)
f)	$C_6H_4N(CH_3)_2$
g)	$C_6H_3OCH_3OH$(3,4)
h)	C_6H_4Br(4)
i)	$C_6H_2OCH_3$(3,4.5)
j)	$C_6H_4\ NO_2$ (4)

Scheme 2: Synthesis of 3 Indole acetic hydrazide (4):



Scheme 3: (5A-5J): Synthesis of 1-[(3,5-diphenyl substituted)-4,5-dihydro-1H-pyrazol-1-yl]-2-(3H-indol-3-yl)ethan-1-one (5 A- 5J):



Where 'Ar' is as follows	
a)	C_6H_5
b)	$C_6H_4\ OCH_3$ (4)
c)	C_6H_4CL(4)
d)	C_6H_4CL(2)
e)	C_6H_3CL(2,4)
f)	C_6H_4N(CH3)2
g)	$C_6H_3OCH_3OH$(3,4)
h)	C_6H_4Br(4)
i)	$C_6H_2OCH_3$(3,4.5)
j)	$C_6H_4\ NO_2$ (4)

TABLE 1: ANTIMICROBIAL ACTIVITY RESULTS

Serial No	Compound	Bacillus (zone of inhibition in cm)	Staphylococcus (zone of inhibition In cm)	Escherichia coli (zone of inhibition in cm)	Pseudomonas (zone of inhibition in cm)
1	5A	0.5	0.5	0.3	0.1
2	5B	0.3	0.5	0.1	0.1
3	5C	0.7	0.6	0.3	0.1
4	5D	0.5	0.4	0.2	0.1
5	5E	0.5	0.5	0.3	-
6	5F	0.5	0.4	0.3	-
7	5G	0.5	0.4	0.3	0.1
8	5H	0.3	0.4	0.2	0.1
9	5I	0.5	0.3	0.1	0.1
10	5J	0.2	0.1	0.2	0.1
11	Streptomicin	1.2	1.4	0.3	0.6

TABLE 2: ANTI FUNGAL ACTIVITY

Serial No.	Compound	Sclerotium rolfsii Zone of inhibition (cm)	Macrophomina phaseolina Zone of Inhibition (Cm)
1	5A	0.6	1.1
2	5B	0.5	1.0
3	5C	1.5	1.0
4	5D	0.7	1.0
5	5E	1.4	0.9
6	5F	1.0	1.6
7	5G	0.1	0.4
8	5H	0.4	1.5
9	5I	1.3	0.0
10	5J	0.9	1.5
Control	Indofil-M 45	2.4	2.6

The antimicrobial activity, i.e. antibacterial and antifungal activity of 1-[(3,5diphenyl substituted) 4,5-dihydro-1H-pyrazol-1-yl]-2-(3H-indol - 3 - yl) ethan-1-one (5a-5j) was studied *in vitro* by agar cup & disc diffusion methods respectively against four bacterial strains (*Bacillus, Pseudomonas, Escherichia coli* and *Staphylococcus*) and two fungal strains (*Sclerotium rolfsii* and *Macrophomina phaseolina*) at different concentrations. The screening results indicate that the compounds 5c. Exhibited potent antibacterial activities against tested strains i.e *Bacillus* and *Staphylococcus*. And moderately active against other strain such as *Escherichia coli*, *Pseudomonas,* and other compounds such as 5a, 5b 5d, 5f, 5g exhibit good activity against gram positive bacteria whereas for gram negative bacteria compounds are less active. Which has shown in **Table 1**. Whereas antifungal activity concern compounds 5c, 5e, 5f, 5j and 5i exhibit good activity against fungal strain *Macrophomina phaseolina* and *Sclerotium rolfsii*. Other compounds shows mark antifungal activity against above fungal strain.

CONCLUSION: Novel indole derivatives bearing pyrazoline moiety were synthesized and characterized. The structure of all compounds confirmed using different spectral studies. The antibacterial evaluation of all compounds demonstrates potent to moderate activity compare to standard drug streptomicin, while primary antifungal evaluation of all the compounds shows promising results against all employed strains as campared to standard drug Indofil-M 45.

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REFERENCES:

1. Tabbi A, Kaplancikli ZA, Tebbani D, Yurttas L, Canturk Z, Atli O, Baysal M and Zitounl GL: Synthesis of novel thiazolylpyrazoline derivatives and evaluation of their antimicrobial activities and cytotoxicities, Turkish Journal of Chemistry 2016; 40:641-654.

2. Venkatesh T, Bodke YD, Kenchappa R and Telkar S: Synthesis, Antimicrobial and Antioxidant Activity of Chalcone Derivatives Containing Thiobarbitone Nucleus, Medicinal Chemistry 2016; 6: 440-448.
3. Arisoy M, Arpaci OZ, Onurdag FK and Selda O: Synthesis of some piprazinobenzoxazole derivatives and their antimicrobial property, Indian Journal of Chemistry 2016; 55:240-247.
4. Hafez HN, Abdulrahman G, Alshammari and Gazzar AEL: Facile heterocyclic synthesis and antimicrobial activity of polysubstituted and condensed pyrazolo pyranopyrimidine and pyrazolopyranotriazine derivatives, Acta Pharm 2015; 65: 399–412.
5. Kumar SR, Ibrahim A. Arif B, Ahamed A and Idhayadhulla A: Anti-inflammatory and antimicrobial activities of novel pyrazole analogues, Saudi Journal of Biological Sciences 2016; 23: 614–620.
6. Seham YH: Synthesis, Antibacterial and Antifungal Activity of Some New Pyrazoline and Pyrazole Derivatives, Molecules 2013;18: 2683-2711.
7. Phillip C, Delekta, Craig J, Dobry, Janice A, Sindac, Scott J Barraza, Pennelope K, Blakely, Jianming Xiang, Paul D, Kirchhoff ,Richard F, Keep, David N, Irani, Scott D, Larsen and David J, Millera: Novel Indole-2-Carboxamide Compounds Are Potent Broad-Spectrum Antivirals Active against Western Equine Encephalitis Virus In Vivo, Journal of Virology 2014; 88: 11199-11213
8. G Raju GN, Sai KB, Meghana MS, Chandana K, P.V. Suresh and Nadendla RR: Synthesis, Characterization and biological activity of indole-2-carboxylic acid derivatives, International Journal of Pharmaceutical Chemistry 2015; 5:202-206
9. Rohini RM., Kalpana D, and Simi D: Synthesis of novel phenyl azo chalcone derivatives for antitubercular, anti-inflammatory and antioxidant activity, Der Pharma Chemica, 2015, 7 :77-83.
10. Chauhan R, Kaur N Rajendra, Sharma S and J Dwivedi J: Application of chalcone I synthesis of 1-(1, 5-benzodiazepino) substituted analogues of indole, Rasayan journal of chemistry, 2015; 8: 115-122.
11. Thasneem CK, Biju CR, and Babu G: Synthesis and antimicrobial study of chalcone linked 1,3,4-oxadiazole derivatives, World journal of pharmacy and pharmaceuticals science, 2014; 4: 643-655.
12. ChenYH, Chang CY, Chang CF, Chen PC, Lee YT, ChernYC and Tsai JN: Pro-Angiogenic Effects of Chalcone Derivatives in Zebrafish Embryos in Vivo, Molecules 2015; 20: 12512-12524.
13. Zheng Y, Wang X, Gao S, Ma M, Ren G, Liu H, and Chen X: Synthesis and antifungal activity of chalcone derivatives, Natural Product Research,2015; 29:1804-1810.
14. Chinthala Y, Thakur S, Tirunagari S, Chinde S, Domatti AK, Arigari NK, K V N S S, Alam S, Jonnala KK, Khan F, Tiwari A, and Grover P: Synthesis, docking and ADMET studies of novel chalcone triazoles for anti-cancer and anti-diabetic activity, European Journal of Medicinal Chemistry,2015; 26:564-573.
15. Kamal A, KumarBG, Vishnuvardhan MVPS, Shaik,AB, Reddy VS, Mahesh R, Sayeed IB and Kapureb JS: Synthesis of phenstatin/ isocombretastatin–chalcone conjugates as potent tubulin polymerization inhibitors and mitochondrial apoptotic inducers, Organic & biomolecular chemistry, 2015; 13: 3963-3981.
16. Kuthati Y, Kankala RK, Lin SX, Weng CFand Lee CH: pH-Triggered Controllable Release of Silver-Indole-3 Acetic Acid Complexes from Mesoporous Silica Nanoparticles (IBN-4) for Effectively Killing Malignant Bacteria, Mol Pharm, 2015; 12: 2289-2304.
17. Asmaa S, Salman, Naema A, Mahmoud, Aziem AA, Mona A. Mohamed, and Elsisi DM: Synthesis, Reactions and Antimicrobial Activity of Some New 3-Substituted Indole Derivatives, International Journal of Organic Chemistry, 2015; 5: 81-99.
18. Kumar D, Arun V, Maruthi Kumar N, Acosta G, Noel B,and Shah K: A facile synthesis of novel bis-(indolyl)-1,3,4-oxadiazoles as potent cytotoxic agents, Chem Med Chem 2012; 7: 1915-1920.
19. Kumar D, Narayanam MK, Chang KH, and Shah K. Synthesis of novel indolyl-1,2,4-triazoles as potent and selective anticancer agents, Chemical Biology & Drug Design 2011; 77: 182-188.
20. Quazi I, Sastry VG, Ansari JA and Rizwan SH : Synthesis and antimicrobial activity of 1-[(3,5-diphenylsubstituted)-4,5-dihydro-1H-pyrazol-1-yl]-2-(3H-indol-3-yl)ethan-1-one derivatives, Der Pharma Chemica, 2016; 8 :39-52.
21. Zhang YL, Qin YJ, Tang DJ, Yang MR, Li BY, Wang YT, Cai HY, Wang BZ and Zhu HL: Synthesis and Biological Evaluation of 1-Methyl-1H-indole-Pyrazoline Hybrids as Potential Tubulin Polymerization Inhibitors, Chem Med Chem 2016 ; 11: 1446-1458.
22. Hassan SY: Synthesis, Antibacterial and Antifungal Activity of Some New Pyrazoline and Pyrazole Derivatives, molecules 2013; 18: 2683-2711.

Singh A, Parmar V, Saraf VSK : Studies on Some New Triazolothiadiazoles Derivatives Incorporating Benzofuran Moiety, Der Pharma Chemica 2016; 8:1-5.

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