Available online at www.derpharmachemica.com

ISSN 0975-413X
CODEN (USA): PCHHAX

Der Pharma Chemica, 2016, 8(14):39-52
(http://derpharmachemica.com/archive.html)

Synthesis and antimicrobial activity of 1-[(3,5-diphenyl substituted)-4,5-dihydro-*1H*-pyrazol-1-yl]-2-(*3H*-indol-3-yl) ethan-1-one derivatives

Imaduddin Quazi[1]*, V. Girija Sastry[2], Javed Akhtar Ansari[3] and S. H. Rizwan[4]

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

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 synthesized new compounds were identify by spectral studies and elemental analysis, and were evaluated in vitro for their antimicrobial activity.

Key words: Antimicrobial, antifungal, chalcone, 3 indole acetic hydrazide, indole, pyrazoline.

INTRODUCTION

The microbial pathogens enter into the host through the mucosal surfaces of intestinal,respiratory and genitourinary tract which are the major sites of microbially induced diseases.

Mucosal infections with microbial pathogens can result in a range of disease manifestations that range from mild and self-limited to fulminate and fatal, or can be chronic and disturbing. [1]. Urinary Tract Infections (UTIs) is a disease caused by the occurrence and growth of microorganism in the urinary tract and is perhaps the single common bacterial infection found in human beings[2]. The rate of morbidity- and mortality by bacterial and fungal infections has amplified globally mostly in developing countries due to the cases of antibacterial and antifungal drug resistance. It comprises severe problems such as strong resistance of microorganisms to a various number of antimicrobial agents such as β-lactam antibiotics,macrolides, quinolones and vancomycin[3]. Pyrazoles and their various derivatives are important biological agents and a major amount of research activity has been intended towards this class. Particularly, they are used as antitumor, antibacterial, antifungal, antiviral, antiparasitic, anti-tubercular and insecticidal agent [4]. The simple doubly unsaturated compound containing two nitrogen and three carbon atoms in the ring, with the nitrogen atoms adjacent, is known as pyrazole[5]. With these considerations in mind, 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.

3. 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.[4-10]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 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 [11]. As white solid (75% yield); mp = 142 ˚C;

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.[12,13]

4. BIOLOGICAL ACTIVITY

4.1. ANTIMICROBIAL ACTIVITY

4.1a 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 37oC[21].

In MIC range of concentrations were tested. The zone of inhibition was recorded in centimeters

4.1b 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.[21]

RESULTS AND DISCUSSION

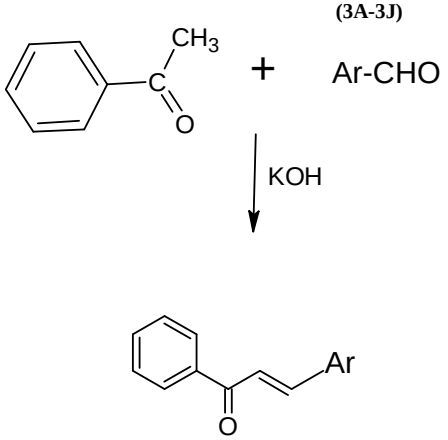
Synthesis 2E)-3-(substituted phenyl)-1-phenylprop-2-en- 1-one (3A – 3 J) The present compound such as (2E)-3-(substituted phenyl)-1-phenylprop-2-en-1-one 3A – 3 J was prepared by Claisen-Schmidt condensation reaction in which substituted aromatic benzaldehyide is reacted with simple aromatic ketone (acetophenone) 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 20-27. 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 -8 ppm 20,21. 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 [31] 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-1*H*-pyrazol-1-yl]-2-(3*H*-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-1*H*-pyrazol-1-yl]-2-(3*H*-indol-3-yl)ethan-1-one The structure of all compounds has been supported by different spectral data (IR, ^{1}H 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). ^{1}H NMR spectra compound (5A) display singlet at δ = 3.6ppm and 4.88ppm for (C 4' CH_2 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' CH_2 and C 5' CH) was also confirmed on the basis of literature [21, 28] in all 10 newly synthesized compounds i.e. (5A-5J).Both analytical and spectral data (IR and ^{1}H 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.

Scheme 1: Synthesis of chalcones ((2E)-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)

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˚C IR: (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.

(2*E*)-3-[4-(dimethylamino)phenyl]-1-phenylprop-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.

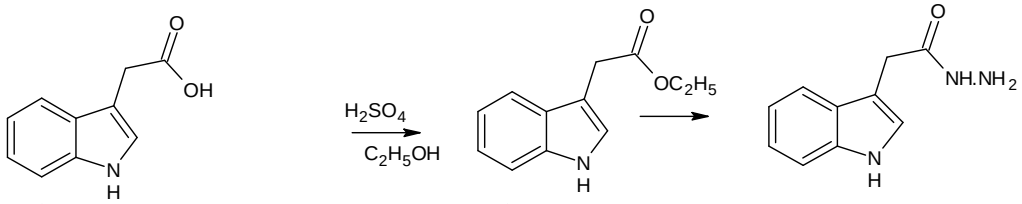
(2*E*)-3-(4-hydroxy-3-methoxyphenyl)-1-phenylprop-2-en-1-one (3 G). White solid, (80 yield) ; mp= 87˚C; IR: (KBr cm^{-1}): υ = 3030 (CH), 1676 (C=O), 3455(OH). ^{1} HNMR (DMSO-d_6), δ (ppm): 6.71 (1H× 2, d *J*=8.2Hz, 7.3Hz HC=CH) ,7.51-8 (8H,m ,Ar-H), 10.19 (1 H, s ,OH), 3.4(3 H, s, OCH_3). EI-MS: m/z: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

(2*E*)-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.

(2*E*)-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.

(2*E*)-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.

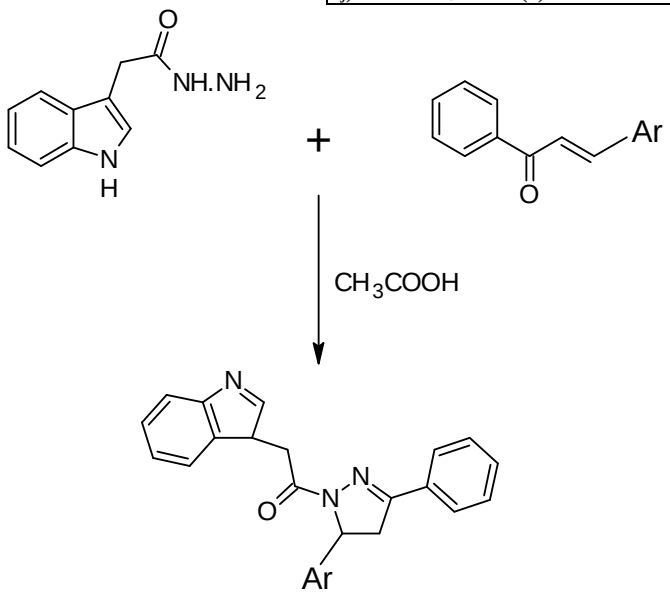
Scheme 2: Synthesis of 3 Indole acetic hydrazide (4)



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). EI-MS: m/z: 189 (m+1). 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.

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)



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-methoxy phenyl)-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 Methoxyphenyl)-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-(4 Bromo 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-dihydro-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 (2 H,s, CH_2), 3.38(1 H,s ,CH) , 7.5 (1H,s, -CH) , 3.85 (9 H, 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.

Antimicrobial activity

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 & Macrophomina phaseolina)at different concentrations. The screening results indicate that the compounds 5a,5c,5d,5e,5f,5g,5h .Exhibited potent antibacterial activities against tested strains i.e Escherichia coli. And moderately active against other strain such as Bacillus, Pseudomonas, and Staphylococcus and compound 5j is weak active compound a against gram positive. Which has shown in table1Among all compounds. where as 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.

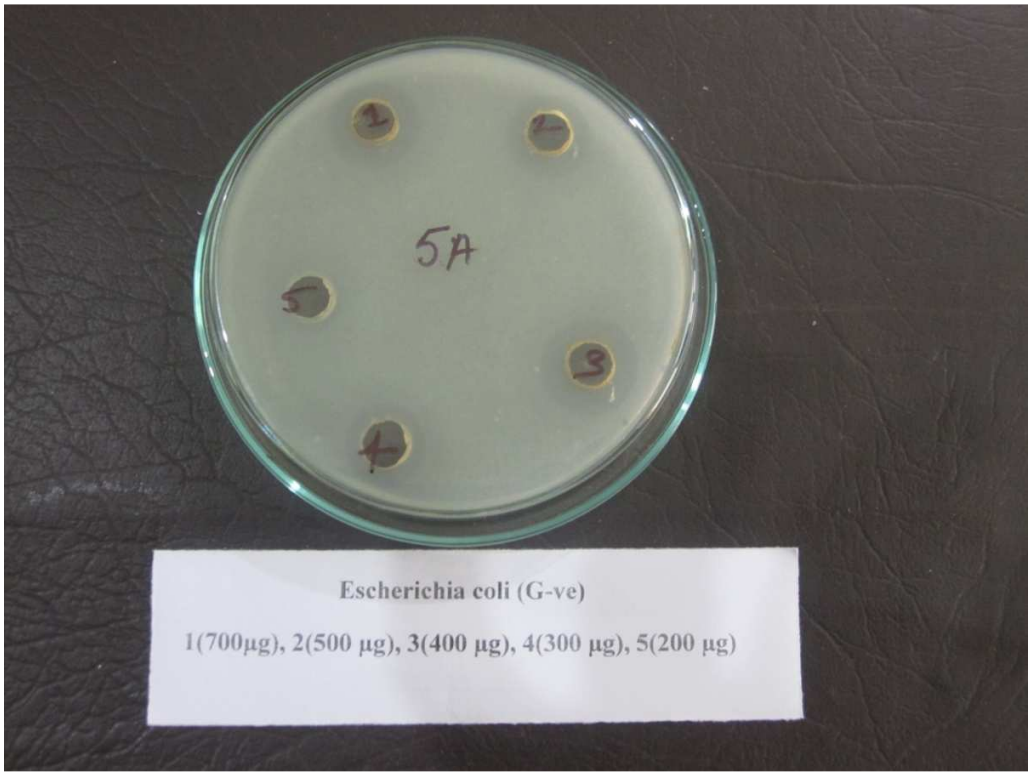
Table 1 antibacterial activity

compound	Ar	Concentration In µg	Zone of Inhibition in cm			
			Bacillus	**Pseudomonas**	**Escherichia coli**	**Staphylococcus**
5a	C_6H_5	700	**0.5**	**-**	**0.5**	**0.4**
		500	**0.3**	**-**	**0.4**	**0.3**
		400	**0.2**	**-**	**0.5**	**0.3**
		300	**0.1**	**-**	**0.3**	**0.2**
5b	$C_6H4OCH3(4)$	700	**0.3**	**0.1**	**0.1**	**0.3**
		500	**0.2**	**-**	**-**	**0.2**
		400	**0.1**	**-**	**-**	**-**
		300	**-**	**-**	**-**	**-**
5c	$C_6H_4CL(4)$	700	**0.7**	**0.1**	**0.5**	**0.5**
		500	**0.5**	**0.1**	**0.4**	**0.4**
		400	**0.3**	**-**	**0.3**	**0.3**
		300	**0.2**	**-**	**0.2**	**0.3**
5d	$C_6H_4CL(2)$	700	**0.5**	**0.1**	**0.3**	**0.4**
		500	**0.4**	**-**	**0.3**	**0.3**
		400	**0.3**	**-**	**0.2**	**0.2**
		300	**0.2**	**-**	**0.2**	**0.2**
5e	$C_6H_3CL(2)(4)$	700	**0.4**	**0.2**	**0.5**	**0.6**
		500	**0.3**	**0.1**	**0.4**	**0.5**
		400	**0.2**	**-**	**0.3**	**0.5**
		300	**0.1**	**-**	**0.2**	**0.4**
5f	$C_6H_4N(CH3)_2(4)$	700	**0.2**	**0.2**	**0.3**	**0.5**
		500	**0.1**	**0.1**	**0.3**	**0.4**
		400	**0.1**	**-**	**0.2**	**0.3**
		300	**-**	**-**	**-**	**0.2**
5g	$C_6H_3OCH_3,OH(3,4)$	700	**0.5**	**-**	**0.4**	**0.5**
		500	**0.3**	**-**	**0.5**	**0.5**
		400	**0.2**	**-**	**0.3**	**0.4**
		300	**0.1**	**-**	**-**	**0.3**
5h	$C_6H_4Br(4)$	700	**0.3**	**o.1**	**0.3**	**0.5**
		500	**0.2**	**-**	**0.2**	**0.4**
		400	**0.1**	**-**	**0.2**	**0.3**
		300		**-**		**0.2**
5i	$C_6H_2OCH_3(3,4.5)$	700	**0.4**	**-**	**0.1**	**0.4**
		500	**0.2**	**-**	**-**	**0.3**
		400	**0.1**	**-**	**-**	**0.2**
		300	**-**	**-**	**-**	**0.1**
5j	$C_6H_4\ NO_2\ (4)$	700	**0.2**	**0.1**	**0.1**	**0.5**
		500	**0.1**	**0.1**	**0.1**	**-**
		400	**o.1**	**-**	**-**	**-**
		300	**-**	**-**	**-**	**-**
Control	Streptomicin		1.2	1.4	0.3	0.6

Table 2 antifungal activity

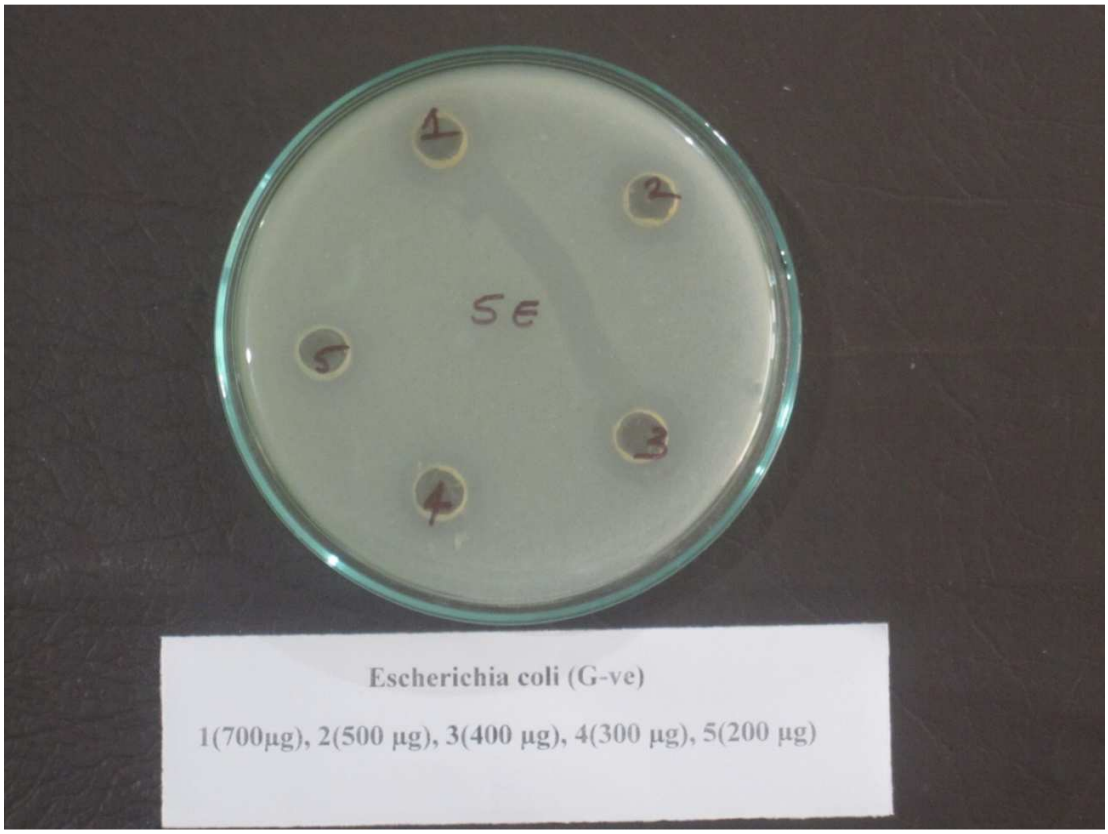
Serial No.	Compound	Sclerotium rolfsii Zone of inhibition (cm)	Macrophomina phaseolina Zone of Inhibition (Cm)
1	5A	0.6	1.1
2	5B	0.5	1.0
3	5C	1.5	1.0
4	5D	0.7	1.0
5	5E	1.4	0.9
6	5F	1.0	1.6
7	5G	0.1	0.4
8	5H	0.4	1.5
9	5I	1.3	0.0
10	5J	0.9	1.5
control	Indofil-M 45	2.4	2.6

Antibacterial activity images

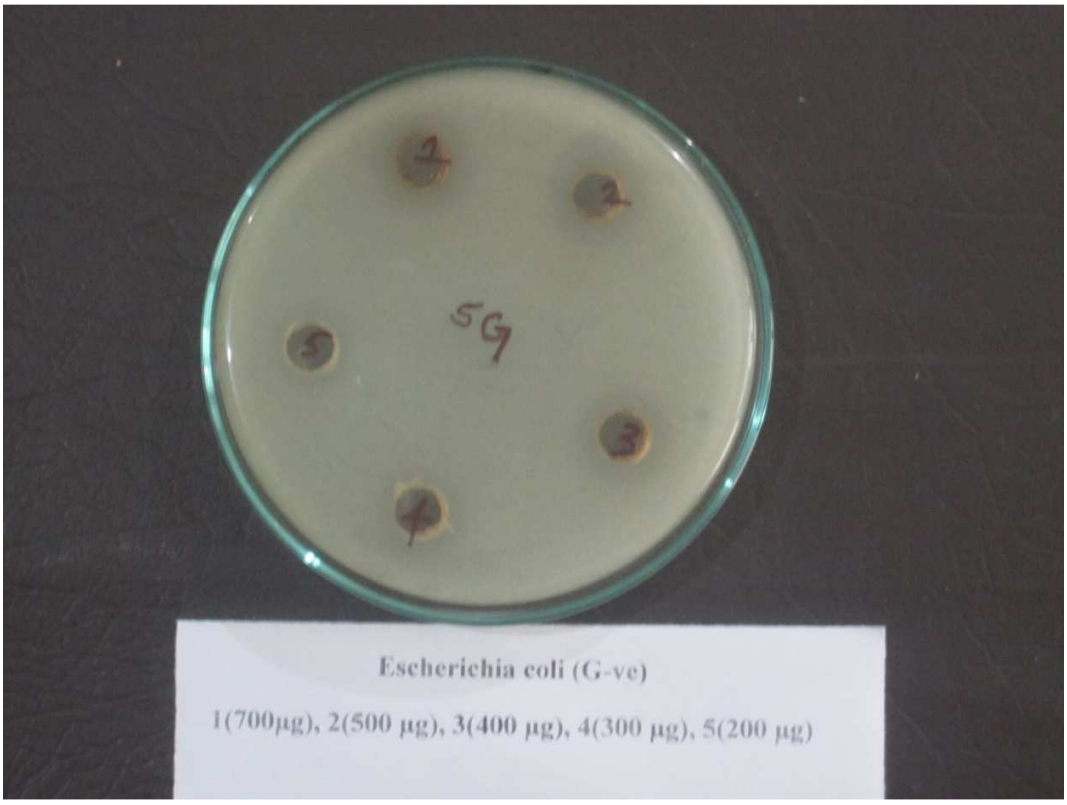


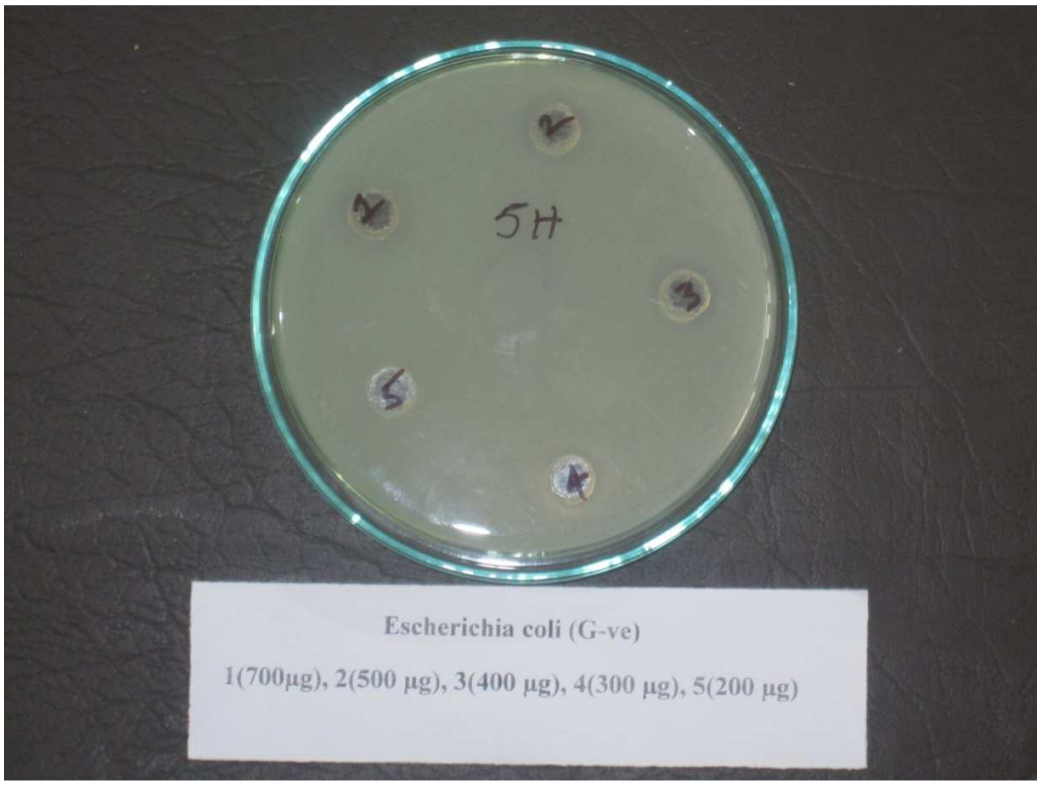

5c
Escherichia coli (G-ve)
1(700µg), 2(500 µg), 3(400 µg), 4(300 µg), 5(200 µg)


5D
Escherichia coli (G-ve)
1(700µg), 2(500 µg), 3(400 µg), 4(300 µg), 5(200 µg)

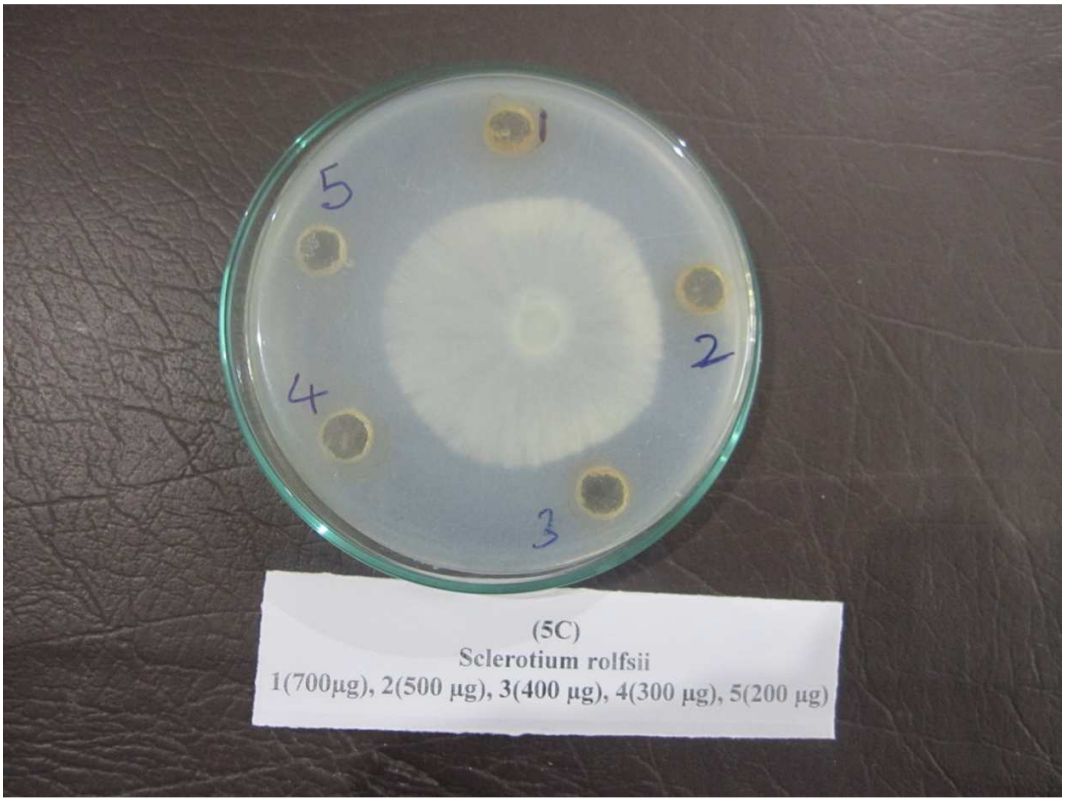

1
2
5E
5
3
4
Escherichia coli (G-ve)
1(700µg), 2(500 µg), 3(400 µg), 4(300 µg), 5(200 µg)

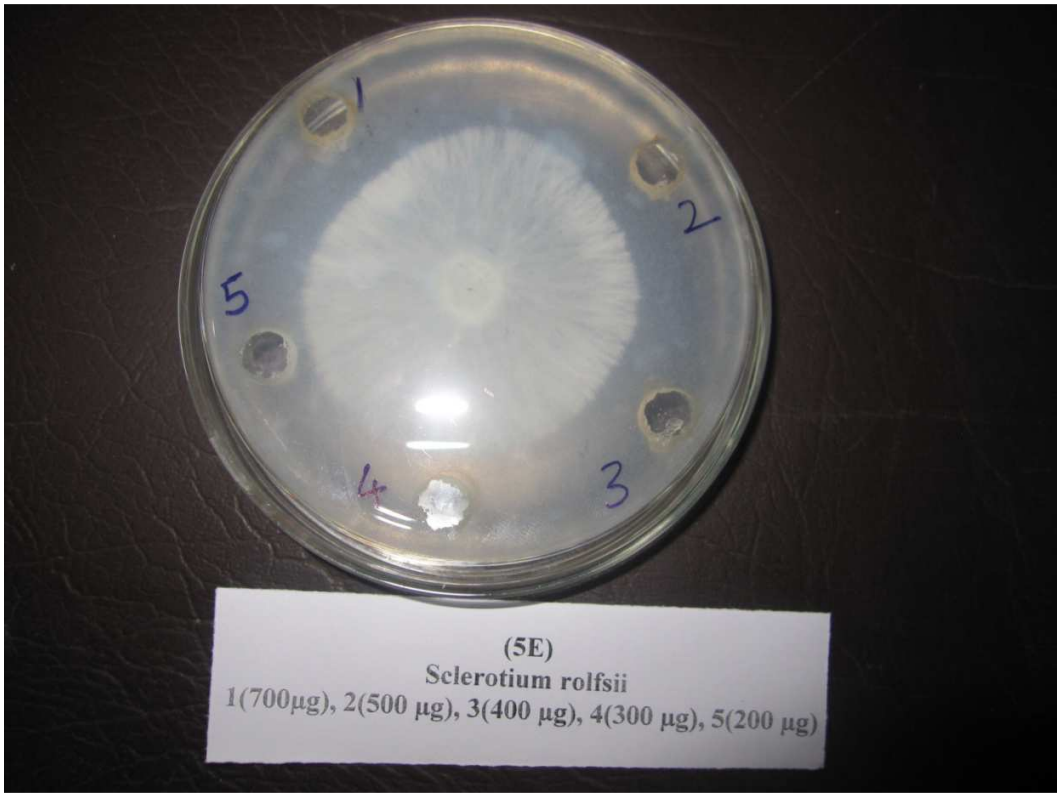

1
2
5F
5
3
4
Escherichia coli (G-ve)
1(700µg), 2(500 µg), 3(400 µg), 4(300 µg), 5(200 µg)


5G
Escherichia coli (G-ve)
1(700µg), 2(500 µg), 3(400 µg), 4(300 µg), 5(200 µg)

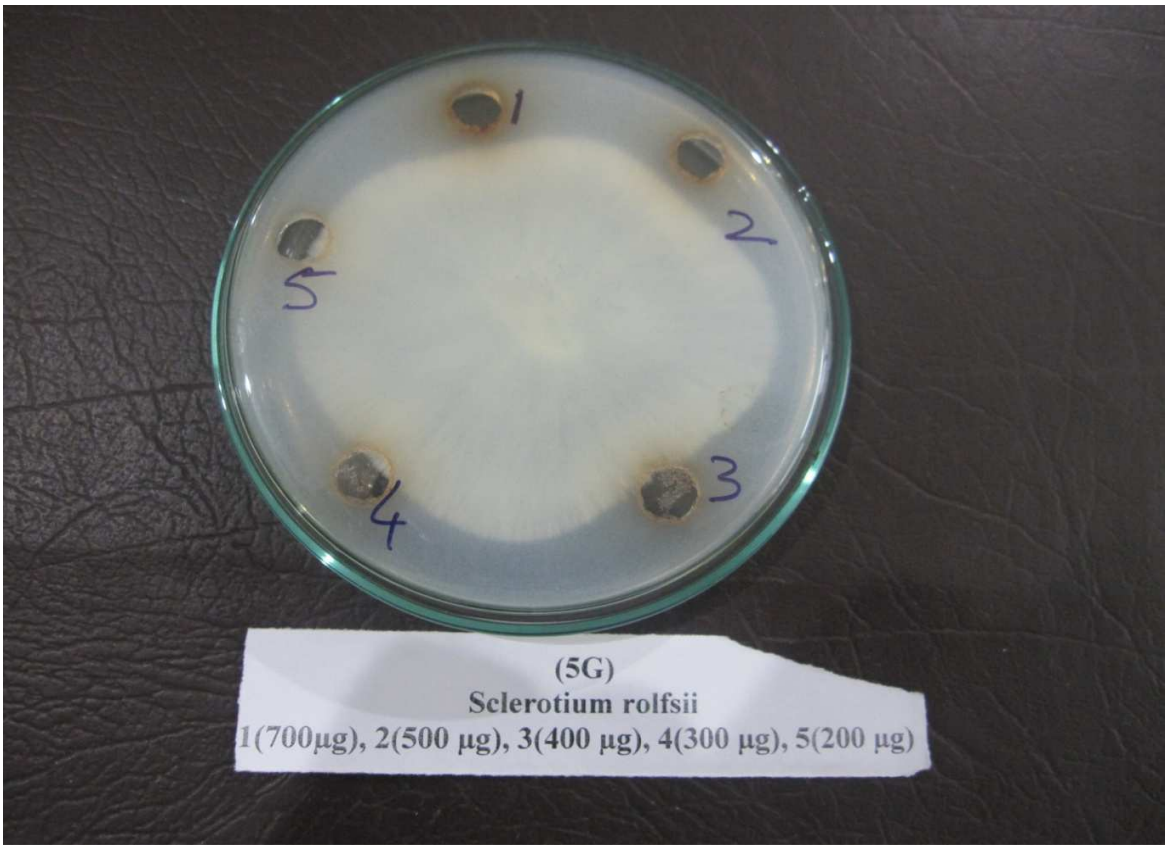

5H
Escherichia coli (G-ve)
1(700µg), 2(500 µg), 3(400 µg), 4(300 µg), 5(200 µg)

Antifungal activity images






1
2
3
4
5
(5F)
Sclerotium rolfsii
1(700µg), 2(500 µg), 3(400 µg), 4(300 µg), 5(200 µg)


1
2
3
4
5
(5G)
Sclerotium rolfsii
1(700µg), 2(500 µg), 3(400 µg), 4(300 µg), 5(200 µg)

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 .

Acknowledgment
The author (Quazi Imaduddin) wishes to express his thanks to Indian Institute of Chemical Technology Hyderabad, India for spectral study and Kalam institute (Hyderabad) for performing antimicrobial activity.

REFERENCES

[1] M. F. Kagnoff , L. Eckmann, *J Clin Invest*.,**1997** ,100, 6
[2] U.P. Sharma ,U. Bidwai, *Int.J.Curr.Microbiol.App.Sci* .,**2013,**2, 97.
[3] Y. Didem, A.Oztekin, D.Aylin, T.Ozden , K.Emrah , Z.O Feza , M.S. Sami Serin, *Afr. J. Microbiol. Res.*,**2013,** 7 ,1709.
[4] L.A.R.François, S.Ranjiv, J.M.Khush, Abrams, L. Bruno, *EMBO Rep*., **2000,** 1, 353.
[5] M.A.Ali, M.S.Yar, *Eur .J Med .Chem***, 2007**, 42, 268.
[6] M.S. Yar , M.M Abdullah , A.Husain , M.ABhakht , De.E Clercq , *J Enzyme Inhib Med Chem.*, 2009, 24,949.
[7] M.A. Ali , M.S.yar ,A.A Siddiqui, *Eur J Med Chem*, **2007,** 42 ,75.
[8] M.S. Yar , M.ABakht , A.ASiddiqui ,M.M Abdullah , De.E Clercq ,*J Enzyme Inhib Med Chem.* **2009** ,24 ,876.
[9] V.K.Tirlapur, Q.Imaduddin,R.H.Udupi,Y.R. Prasad, *Indian J.Heterocyclic Chem.*,**2008** ,18 ,65.
[10] M.R.Ahmed, V.G.Sastry, S.N.Bano, Ravichandra,M.Raghavendra, *Rasayan. J. chem.*,**2011,** 4, 289.
[11] N. Siddiqui, M. S.Alam, W. Ahsan, *Acta Pharm.*, 58 **2008** 445.
[12] M.S. Yar, M.A Ali, D. Sriram, P.Yogeeswari, *Acta Pol Pharm.*, **2006**, 63, 491.
[13] M.A.Ali, M.S. Yar , *Eur .J Med .Chem*.,**2007,** 42, 268.
[14] S.M. Hipparagi, M.D Bhanushali, *J. Sci. Society.*, **2013,** 40 80.
[15] R.S.Keri, K. Chand, T. Ramakrishnappa, B.M. Nagaraja, *Arch. Pharm. Chem., Life Sci*, **2015,** 348, 299.
[16] G.C.Ustundag, D.Satana, G. Ozhan, G.Capan, *J .Enzyme Inhib .Med .Chem*.,**2016,** 31, 369.
[17] A.Itareanu, A.M. Zbancioc, C.Tuchiluş, M.Balan, U.Stanescu, G.Tataringa, *Rev Med Chir Soc Med Nat.,* **2015**, 119, 180.
[18] M.S.Yar, M.M. Abdullah, J.Majeed, *Int. Sch. Sci. Res. Innov.*, **2009,** 3, 167.
[19] I.S Krishnanjaneyulu,G.Saravanan, J.Vamsi, P. Supriya, J.U.Bhavana, S.M.V. Kumar, *Adv. Pharm .Technol Resv.*, **2014** , 5, 21.
[20] A.B.FWahab, A.H.A.Aziz, E.M.C.Ahmed , *Arch .Pharm .(Weinheim*).,**2008 ,** 341, 734.
[21] A. Singh, V. Parmar, S.K.Saraf, *Der Pharma Chemica*, **2016,** 8,1