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Synthesis, characterization and evaluation of 3-acetylindole derivatives as potential antifungal agents

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Abstract
In the present study a series of novel 3-acetylindole derivatives were synthesized by reacting 3-acetylindole and benzaldehyde. The synthesized 3-acetylindole derivatives were characterized physicochemically, by elemental analysis and spectral (IR and ^{1}H-NMR) analysis. The synthesized compounds were screened for their *in-vitro* antifungal activity against *Candida albicans, Rhizopus oligosporus, Gibberella fuzikuroi and Asperigillus niger* by cup plate method. The results revealed that five compounds namely NK-3, NK-8, NK-11, NK-13 and NK-14 have better or equal antifungal activity compared to the standard fluconazole.

Keywords: Antifungal, indole, benzaldehyde, Cup-plate method

1. Introduction
Antimicrobials have been designed to inhibit or kill the infecting organism without having measurable effect on the recipient [1]. The clinically available antifungal agents can be divided into four categories- the polyenes (e.g., Amphotericin B and Nystatin) [2], echinocandins (e.g., Caspofungin and Micafungin) [3], antimetabolites (e.g., 5-fluorocytosine) [4], and azoles (e.g., Fluconazole, Voriconazole and Itraconazole) [5]. Azole antifungal agents are used as first-line antifungal drugs. They act by inhibiting fungal lanosterol 14α-demethylase (CYP51), which plays a central role in ergosterol biosynthesis [6-8]. Among these agents, fluconazole, the first triazole alcohol antifungal drug has narrow antifungal spectrum and has suffered severe drug resistance [9, 10]. In the search for better antifungal compounds, the structure of fluconazole has been modified, and a variety of its analogues like Itraconazole, Voriconazole, and Ketoconazole were developed [11-13]. However, they have narrow antifungal spectrum, low bioavailability and faced the problem of drug resistance [14]. Thus there is need to develop better antifungal agents to overcome these shortcomings.
Indole is a bicyclic heterocyclic system having m.p. 52-54 °C, molecular weight 117.151g/mol with empirical formula C_8H_7N in which the pyrrole ring is fused with benzene ring at α, β-position.
Various medicinal activities of compounds having indole nucleus is reported *viz* insecticidal of 5-iodoindole [15], anti-viral activities of isatin and indole oximes and anti-inflammatory activity of indole-3-acetic acid [16-18], fungicidal activity of the oxime derivatives of 2-substituted indoles and 3-substituted indoles [19], antibacterial activity of 3-aryl/ 3-heteroaryl substituted indoles, antioxidant activity of a series of 3-pyranyl indole derivatives [20], *in vitro* antitubercular activity of indoleamide derivatives [21], anticancer [22] of indole-2-carbohydrazides and thiazolidinyl-indole-2-carboxamide derivates etc.
3-Acetylindole derivatives are also reported to have various pharmacological activities, for example, *N*-arylsulfonyl-3-acetylindoles and oxobutenoic substituted-3-acetylindole acids were reported as anti-HIV agent [23-24], hetroaryl substituted-3-acetylindole were reported as anti-inflammatory and antibacterial activity [25]. Antileishmanial activity of derivative of bis(indolyl)-pyridines were reported [26].
In the present study 3-acetylindole derivatives were synthesized, characterized and evaluated for antifungal activity.

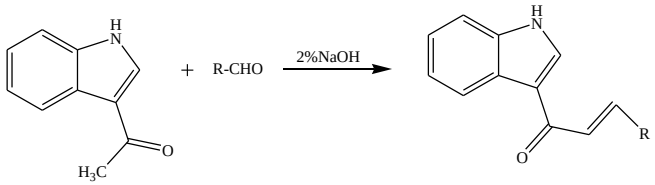
2. Material and Methods
2.1 Experimental
All the commercially available reagent grade chemicals of Merck and Sigma Aldrich were used as received. Purity of the compound and progress of the reaction were monitored by thin

layer chromatography (TLC) using by Ultra-violet (UV) light detector and/or by exposure to iodine vapors chamber. The melting point ranges of newly synthesized compounds were determined using visual melping point apparatus of Lab India model MR-VIS 10230308. Infra-red (IR) spectra were recorded using Bruker Alpha 1005151/06 ATIR spectrophotometer. Nuclear Magnetic Resonance (^{1}H-NMR) spectra were recorded on a Bruker using $CDCl_3$ or DMSO at 300MHz or 400MHz respectively. The Chemical shift values are reported in parts per million (ppm) relative to Tetra methyl silane as internal reference.

2.2 Synthesis

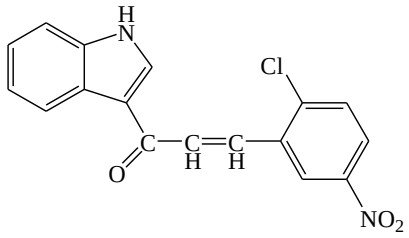
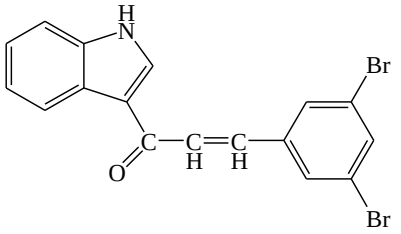
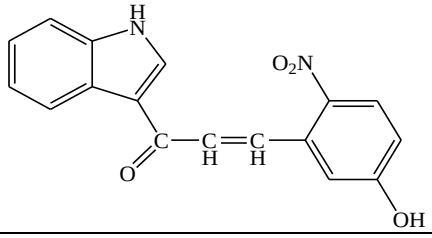
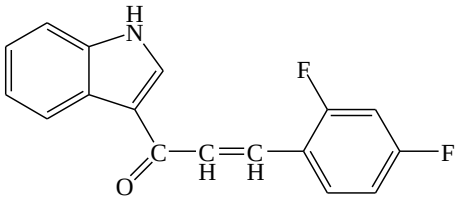
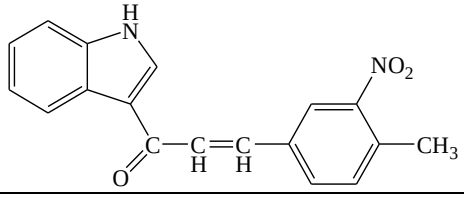
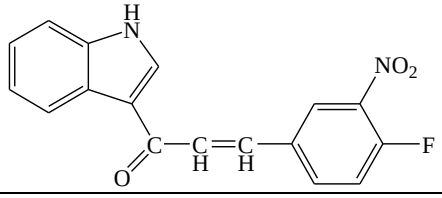
The title compounds were synthesized using synthetic strategy described in Scheme 1.

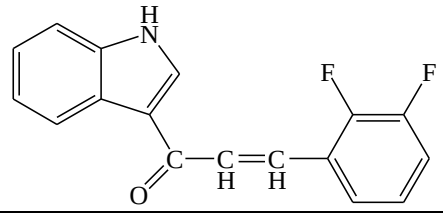
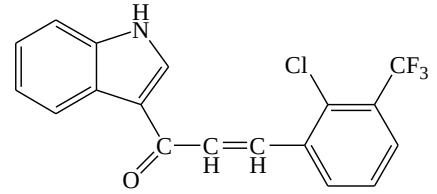
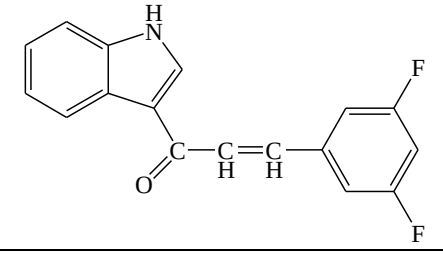
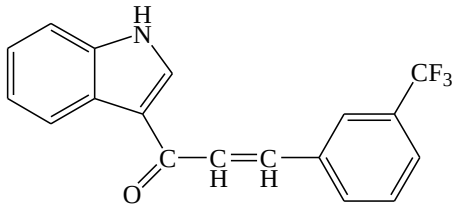
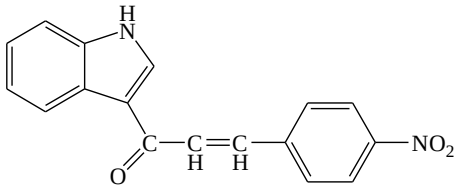
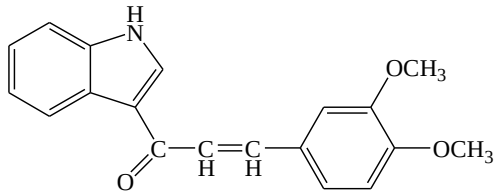
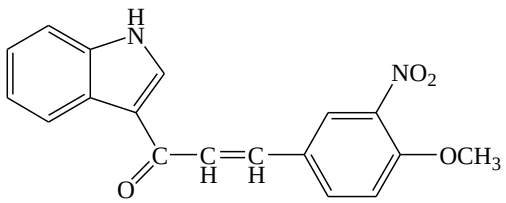
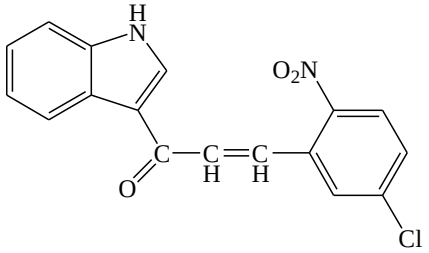
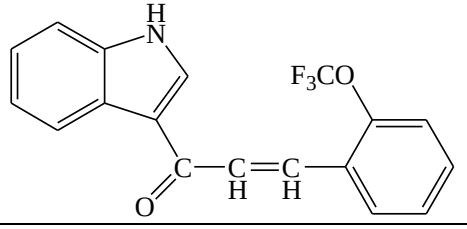
Scheme 1



2.1.1 General procedure: To a solution of 3-acetylindole(2gm) (0.01 mole) in methanol (50ml), Ar aldehyde (2ml) (0.01 mole) was added in the presence of 2% sodium hydroxide (5ml). The reaction mixture was stirred for 9-10 h at room temperature and then the mixture was poured into ice water. The compound obtained was filtered, washed with water and recrystallized using methanol.

Table 1: List of synthesized compounds

Compound	Structure	IUPAC name
NK-1		3-(2-chloro-5-nitrophenyl)-1-(1*H*-indol-3-yl)prop-2-en-1-one
NK-2		3-(3,5-dibromophenyl)-1-(1*H*-indol-3-yl)prop-2-en-1-one
NK-3		3-(5-hydroxy-2-nitrophenyl)-1-(1*H*-indol-3-yl)prop-2-en-1-one
NK-4		3-(2,4-difluorophenyl)-1-(1*H*-indol-3-yl)prop-2-en-1-one
NK-5		1-(1*H*-indol-3-yl)-3-(4-methyl-3-nitrophenyl)prop-2-en-1-one
NK-6		3-(4-fluoro-3-nitrophenyl)-1-(1*H*-indol-3-yl)prop-2-en-1-one

NK-7		3-(2,3-difluorophenyl)-1-(1*H*-indol-3-yl)prop-2-en-1-one
NK-8		3-(2-chloro-3-(trifluoromethyl)phenyl)-1-(1*H*-indol-3-yl)prop-2-en-1-one
NK-9		3-(3,5-difluorophenyl)-1-(1*H*-indol-3-yl)prop-2-en-1-one
NK-10		1-(1*H*-indol-3-yl)-3-(3-(trifluoromethyl)phenyl)prop-2-en-1-one
NK-11		1-(1*H*-indol-3-yl)-3-(4-nitrophenyl)prop-2-en-1-one
NK-12		3-(3,4-dimethoxyphenyl)-1-(1*H*-indol-3-yl)prop-2-en-1-one
NK-13		1-(1*H*-indol-3-yl)-3-(4-methoxy-3-nitrophenyl)prop-2-en-1-one
NK-14		3-(5-chloro-2-nitrophenyl)-1-(1*H*-indol-3-yl)prop-2-en-1-one
NK-15		1-(1*H*-indol-3-yl)-3-(2-(trifluoromethoxy)phenyl)prop-2-en-1-one

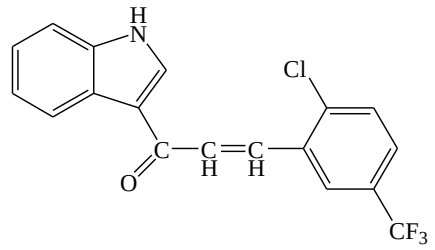
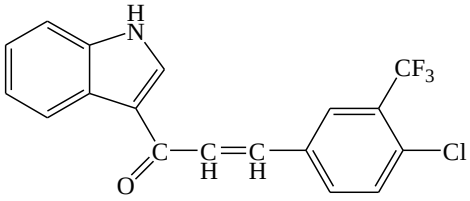
NK-16		3-(2-chloro-5-(trifluoromethyl)phenyl)-1-(1*H*-indol-3-yl)prop-2-en-1-one
NK-17		3-(4-chloro-3-(trifluoromethyl)phenyl)-1-(1*H*-indol-3-yl)prop-2-en-1-one

Table 2: Physical data of synthesized compounds:

S. No.	Compound	Molecular Formula	State	Solubility	%Yield	Melting point
1.	NK-1	$C_{17}H_{11}N_2O_3Cl$	Solid	DMSO	56%	190-193ºC
2.	NK-2	$C_{17}H_{11}NOBr2$	Solid	DMSO	62%	142-145ºC
3.	NK-3	$C_{17}H_{12}N_2O_4$	Solid	DMSO	66%	187-190ºC
4.	NK-4	$C_{17}H_{11}NF_2O$	Solid	DMSO	57%	162-166ºC
5.	NK-5	$C_{18}H_{14}N_2O_3$	Solid	DMSO	70%	189-191ºC
6.	NK-6	$C_{17}H_{11}N_2O_3F$	Solid	DMSO	65%	190-193ºC
7.	NK-7	$C_{17}H_{11}NOF_2$	Solid	DMSO	57%	151-153ºC
8.	NK-8	$C_{18}H_{11}NClF_3O$	Solid	DMSO	69%	170-173ºC
9.	NK-9	$C_{17}H_{11}NOF_2$	Solid	DMSO	64%	150-154ºC
10.	NK-10	$C_{18}H_{12}NOF_3$	Solid	DMSO	66%	160-162ºC
11.	NK-11	$C_{17}H_{12}N_2O_3$	Solid	DMSO	59%	181-183ºC
12.	NK-12	$C_{19}H_{17}NO_3$	Solid	DMSO	68%	159-161ºC
13.	NK-13	$C_{18}H_{14}N_2O_4$	Solid	DMSO	72%	171-174ºC
14.	NK-14	$C_{17}H_{11}N_2O_3Cl$	Solid	DMSO	59%	176-178ºC
15.	NK-15	$C_{18}H_{12}NO_2F_3$	Solid	DMSO	65%	161-164ºC
16.	NK-16	$C_{18}H_{11}NClF3O$	Solid	DMSO	55%	168-170ºC
17.	NK-17	$C_{18}H_{11}NClF_3O$	Solid	DMSO	64%	159-162ºC

Table 3: Spectral study of synthesized compounds:

Compound	IR spectra data	^{1}HNMR spectra data ($CDCl_3$)
NK-1	3271.55 cm^{-1}(Ar-H stretch), 1600.79 cm^{-1}(α,β unsaturated C=O stretch), 1518.89 cm^{-1}(Ar Nitro), 1433.75 cm^{-1} (Ar C-C stretch), 1341.34 cm^{-1} (Ar –N stretch), 1186.79 cm^{-1}-1139.50 cm^{-1}(Ar-Cl stretch), 742.92 cm^{-1}(Ar C-H out of plane).	*δ*11.916(1H, NH), *δ* 8.158(2H, CH=CH), *δ* 7.215-8.141 (7H, Ar-H)
NK-2	3181.48 cm^{-1}(Ar-H stretch), 1696.77 cm^{-1} (α,β unsaturated C=O Stretch), 1433.44 cm^{-1} (Ar C-C stretch), 1240.02 cm^{-1} (Ar –N stretch),1145.88 cm^{-1}(Ar-Br stretch), 749.62 cm^{-1} (Ar C-H out of plane)	*δ* 9.917(1H, NH), 7.688(2H, CH=CH), *δ* 7.286-7.607 (7H, Ar-H).
NK-3	3156.36 cm^{-1}(Ar-OH bonded), 3043.03 cm^{-1}(Ar-H stretch),1612.67 cm^{-1} (α,β unsaturated C=O stretch), 1523.97 cm^{-1}(Ar Nitro), 1432.91 cm^{-1} (Ar C-C stretch), 1314.62 cm^{-1}-1241.27 cm^{-1}(Ar-N stretch), 753.07 cm^{-1}(Ar C-H out of plane)	*δ*11.932(1H, NH), *δ* 8.074(2H,CH=CH), *δ* 7.023-7.492(7H, Ar-H), *δ*6.988(1H, Ar-OH).
NK-4	3161.97 cm^{-1}(Ar-H stretch),1615.17 cm^{-1} (α,β unsaturated C=O stretch), 1432.26 cm^{-1}(Ar C-C stretch), 1315.61 cm^{-1}-1241.68 cm^{-1}(Ar-N stretch), 1241.68 cm^{-1}-1178.18 cm^{-1}(C-F stretch), 753.24 cm^{-1}(Ar C-H out of plane)	*δ* 11.94(1H,NH), *δ* 8.223(2H, CH=CH), *δ* 7.180-7.504(7H, Ar-H).
NK-5	3168.49 cm^{-1}(Ar-H stretch),1615.07 cm^{-1} (α,β unsaturated C=O stretch), 1525.23 cm^{-1}(Ar Nitro), 1435.04 cm^{-1}(Ar C-C stretch), 1316.67 cm^{-1}-1242.19 cm^{-1}(Ar-N stretch), 753.37 cm^{-1}(Ar C-H out of plane)	*δ* 10.059(1H,NH), *δ* 7.956(2H,CH=CH), 7.183-7.555(7H, Ar-H).
NK-6	3165.81 cm^{-1}(Ar-H stretch),1612.77 cm^{-1} (α,β unsaturated C=O stretch), 1536.34 cm^{-1}(Ar –Nitro), 1428.23 cm^{-1}(Ar C-C stretch), 1351.65 cm^{-1}-1285.48 cm^{-1}(Ar-N stretch), 1078.83 cm^{-1}-1011.52 cm^{-1} (C-F stretch), 755.51 cm^{-1}(Ar C-H out of plane)	*δ* 10.014(1H,NH), *δ* 8.119(2H,CH=CH), *δ* 7.179-7.41(7H, Ar-H).
NK-7	3167.26 cm^{-1}(Ar-H stretch),1614.25 cm^{-1} (α,β unsaturated C=O stretch), 1431.38 cm^{-1}(Ar C-C stretch), 1316.68 cm^{-1}-1242.87 cm^{-1}(Ar-N stretch), 1179.17 cm^{-1}-1027.54 cm^{-1}(C-F stretch), 753.27 cm^{-1}(Ar C-H out of plane)	*δ* 8.37(1H, NH), *δ*8.225(2H, CH=CH), *δ* 7.191-7.506(7H, Ar-H).
NK-8	3247.89 cm^{-1}(Ar-H stretch),1596.10 cm^{-1} (α,β unsaturated C=O stretch), 1411.10 cm^{-1}(Ar C-C stretch), 1317.11 cm^{-1}(Ar-N stretch), 1130.54cm^{-1}(Ar-Cl Stretch), 1094.90 cm^{-1}-1014.31cm^{-1}(C-F stretch),798.21 cm^{-1}(Ar C-H out of plane)	^{1}HNMR(DMSO,400MHz)-*δ* 8.6 (1H, NH), *δ* 8.021(2H, CH=CH), *δ* 7.232-7.810(7H, Ar-H).
NK-9	3256.83 cm^{-1}(Ar-H stretch),1614.29 cm^{-1} (α,β unsaturated C=O stretch), 1434.75 cm^{-1}(Ar C-C stretch), 1316.72 cm^{-1}(Ar-N stretch), 1241.18 cm^{-1}-1143.86 cm^{-1}(C-F stretch), 754.34 cm^{-1}(Ar C-H out of plane)	^{1}HNMR(DMSO,400MHz)- *δ* 8.401(1H, NH), *δ* 8.012(2H,CH=CH), 7.031-7.432(7H, Ar-H).

NK-10	3157.58 cm^{-1}(Ar-H stretch),1612.31 cm^{-1}(α,β unsaturated C=O stretch), 1432.48 cm^{-1}(Ar C-C stretch), 1330.72 cm^{-1}(Ar-N stretch), 1176.16 cm^{-1}-1128.59 cm^{-1}(C-F stretch), 752.21 cm^{-1}(Ar C-H out of plane)	^{1}HNMR(DMSO,400MHz)- δ 8.421(1H,NH), δ 8.001(2H, CH=CH), δ 7.011-7.801(7H, Ar-H).
NK-11	3211.25 cm^{-1}(Ar-H stretch),1626.84 cm^{-1}(α,β unsaturated C=O stretch),1520.92 cm^{-1} (Ar -Nitro), 1439.07 cm^{-1}(Ar C-C stretch), 1343.59 cm^{-1}(Ar-N stretch), 748.57 cm^{-1}(Ar C-H out of plane)	^{1}HNMR(DMSO,400MHz)- δ 8.569(1H,NH), δ 8.094(2H, CH=CH), δ 7.142-7.801(8H, Ar-H).
NK-12	3157.20 cm^{-1}(Ar-H stretch), 2832.36cm^{-1}(O-CH_3 stretch), 1610.47 cm^{-1}(α,β unsaturated C=O stretch), 1430.06 cm^{-1}(Ar C-C stretch), 1343.93 cm^{-1}-1241.67cm^{-1}(Ar-N stretch), 752.69 cm^{-1} (Ar C-H out of plane)	^{1}HNMR(DMSO,400MHz)-δ 8.401(1H,NH), δ 8.099(2H,CH=CH), δ 7.012-7.410(4H, Ar-H), δ 2.512(3H, OCH_3).
NK-13	3064.79 cm^{-1}(Ar-H stretch), 2735.31cm^{-1}(O-CH_3 stretch), 1669.09cm^{-1}(α,β unsaturated C=O stretch), 1512.93cm^{-1}(Ar-Nitro), 1448.19cm^{-1}(Ar C-C Stretch), 1334.50cm^{-1}(Ar-N Stretch), 762.90cm^{-1}(Ar C-H Out of plane)	δ 9.761(1H,NH), δ 7.638(2H, CH=CH), δ 6.633-7.366(7H, Ar-H).
NK-14	3059.76 cm^{-1}(Ar-H stretch), 2735.31cm^{-1}(O-CH_3 stretch), 1605.52cm^{-1}(α,β unsaturated C=O stretch), 1212.22cm^{-1}(Ar-Cl Stretch), (1493.60cm^{-1}(Ar-Nitro), 1448.80cm^{-1}(Ar C-C Stretch), 1336.39cm^{-1}(Ar-N Stretch), 749.94cm^{-1}(Ar C-H Out of plane)	δ 9.873(1H, NH), δ 7.437(2H, CH=CH), δ 5.986-7.419(7H, Ar-H).
NK-15	1690.09cm^{-1}(α,β unsaturated C=O stretch), 1449.01cm^{-1}(Ar C-C Stretch), 1345.03cm^{-1}(Ar-N Stretch), 754.19cm^{-1}(Ar C-H out of plane).	δ 10.170(1HNH), δ 7.260-7.644(8H, Ar-H), δ5.743(2H,CH=CH).
NK-16	2966.88 cm^{-1}(Ar-H Stretch), 1682.13cm^{-1}(α,β unsaturated C=O stretch), 1448.67cm^{-1}(Ar C-C Stretch), 1308.99cm^{-1}(Ar-N Stretch), 1143.30cm^{-1}(Ar-Cl Stretch), 1077.58cm^{-1}(C-F Stretch), 761.22cm^{-1}(Ar C-H Out of plane).	δ 9.981(1H, NH), δ 8.057(2H, CH=CH), δ 7.240-7.846(7H, Ar-H).
NK-17	3063.14 cm^{-1}(Ar-H Stretch), 1664.91cm^{-1}(α,β unsaturated C=O stretch), 1448.12cm^{-1}(Ar C-C Stretch), 1352.59cm^{-1}(Ar-N Stretch), 1201.55cm^{-1}(Ar-Cl Stretch), 1074.73cm^{-1}(C-F Stretch), 752.25cm^{-1}(Ar C-H Out of plane).	δ 9.970(1H,NH), δ 7.472(2H, Ar-H), δ 6.819(2H, CH=CH).

3. Pharmacological Evaluation

3.1 Antifungal Activity

All synthesised compounds were screened for *In vitro* antifungal activity against *Candida albicans*, *Rhizopus oligosporus*, *Gibberella fuzikuroi* and *Asperigillus niger* strain of fungi by cup-plate method [27]. Fluconazole was used as reference antifungal drug.

3.2 Procedure

The Sabouraud agar medium was prepared by dissolving 40 g of dextrose, 10g of peptone, 15g of agar in 1000 ml distilled water. The pH was adjusted to 5.6 with hydrochloric acid. The Sabouraud agar so prepared was allowed to boil, after that it was autoclaved at 121℃, 15 Psig for 30 minutes and cooled to 45-50 ℃. The medium was then inoculated aseptically with 0.5 ml of strains of *Candida albicans*, *Rhizopus oligosporus*, *Gibberella fuzikuroi* and *Asperigillus niger* at room temperature. The petriplates were sterilized by autoclaving. Into each sterile petridish about 15 ml of inoculated molten medium was poured. The plates were left at room temperature for solidification. After solidification, the cups of 6 mm diameter were made by scooping out the medium with the sterilized corn borer and were labelled.

All the synthesized compounds and reference were dissolved in DMSO to get required concentration of 60µg/ml, 80µg/ml and 100µg/ml. The solution of each compound and reference (DMSO) were added separately into each cup. The plates were incubated for period of 48 hours. The diameter of zone of inhibition was measured with the help of antibiotic zone reader.

Table 4: Antifungal activity of synthesized compounds and standard drug fluconazole.

Compound	Diameter of zone of inhibition in mm											
	C. albicans			*R. oligosporus*			*A. niger*			*G. fuzikuroi*		
	60µg/ml	80µg/ml	100µg/ml	60µg/ml	80µg/ml	100µg/ml	60µg/ml	80µg/ml	100µg/ml	60µg/ml	80µg/ml	100µg/ml
NK-1	-	12	14	6	8	12	6	8	8	-	-	10
NK-2	-	8	10	-	6	10	-	10	12	-	8	10
NK-3	10	14	24	10	18	24	10	16	22	10	20	28
NK-4	8	10	14	-	8	15	8	10	16	-	10	12
NK-5	10	12	16	-	10	18	14	18	20	8	12	18
NK-6	-	-	10	-	8	12	-	10	14	8	10	14
NK-7	-	10	12	8	10	12	-	16	12	-	12	18
NK-8	14	16	22	12	16	22	10	14	24	10	16	20
NK-9	18	20	22	-	14	16	-	12	14	-	8	14
NK-10	6	10	12	-	8	14	8	10	14	-	6	10
NK-11	-	8	12	10	16	20	-	14	20	10	12	20
NK-12	-	6	10	-	6	8	-	6	8	-	8	12
NK-13	12	18	22	12	18	26	12	18	24	12	18	22
NK-14	10	16	22	8	12	22	10	14	20	12	24	28
NK-15	-	10	12	-	8	14	-	10	14	-	-	14
NK-16	-	14	20	-	12	16	8	12	14	-	12	14
NK-17	10	12	16	10	14	18	10	14	18	8	14	16
Fluconazole	18	22	26	20	24	28	16	20	24	18	26	30

4. Results and Discussion

A series of 3-acetyl indole derivatives were designed, synthesized, characterized and evaluated for their anti-fungal activity. Based on the work done, it can be said that:

I. Yield All compounds were synthesized in appreciable yield.

II. Spectral data were found to be in agreement with assigned structure.

III. Antifungal Activity

Candida albicans

- NK-8 and NK-9 showed equal antifungal activity as compared to standard Fluconazole at 60µg/ml.
- NK-8, NK-9, NK-13 and NK-14 showed equal antifungal activity as compared to standard Fluconazole at 80µg/ml.
- NK-3, NK-8, NK-9, NK-13, NK-14 and NK-16 equal antifungal activity as compared to standard Fluconazole at 100µg/ml.

Comparison amongst the doses

- NK-9 and NK-13 at 80µg/ml showed better antibacterial activity as compared to standard fluconazole at 60µg/ml.
- NK-3, NK-8, NK-14 and NK-16 at 80µg/ml showed equal antibacterial activity as compared to standard fluconazole at 60µg/ml.
- NK-3, NK-8, NK-9, NK-13 and NK-14 at 100µg/ml showed equal antibacterial activity as compared to standard fluconazole at 80µg/ml.
- NK-5, NK-16 and NK-17 at 100µg/ml showed equal antibacterial activity as compared to standard fluconazole at 80µg/ml.

Rhizopus oligosporus

- NK-3, NK-8, NK-11 and NK-13 showed equal antifungal activity as compared to standard Fluconazole at 80µg/ml.
- NK-3, NK-8, NK-11, NK-13 and NK-14 showed equal antifungal activity as compared to standard Fluconazole at 100µg/ml.

Comparison amongst the doses

- NK-3, NK-11 and NK-13 at 80µg/ml showed equal antibacterial activity as compared to standard fluconazole at 60µg/ml.
- NK-3 and NK-13 at 100µg/ml showed better antibacterial activity as compared to standard fluconazole at 80µg/ml.
- NK-8, NK-11 and NK-14 at 100µg/ml showed equal antibacterial activity as compared to standard fluconazole at 80µg/ml.

Asperigillus niger

- NK-3, NK-5, NK-8, NK-13, NK-14 and NK-17 showed equal antifungal activity as compared to standard Fluconazole at 60µg/ml.
- NK-3, NK-5, NK-7 and NK-13 showed equal antifungal activity as compared to standard Fluconazole at 80µg/ml.
- NK-3, NK-5, NK-8, NK-11, NK-13, NK-14 and NK-17 showed equal antifungal activity as compared to standard Fluconazole at 100µg/ml.

Comparison amongst the doses

- NK-3, NK-5 and NK-13 at 80µg/ml showed better antibacterial activity as compared to standard fluconazole at 60µg/ml.
- NK-8, NK-11, NK-14 and NK-17 at 80µg/ml showed equal antibacterial activity as compared to standard fluconazole at 60µg/ml.
- NK-3, NK-5, NK-8, NK-11, NK-13 and NK-14 at 100µg/ml showed better antifungal activity as compared to standard fluconazole at 80µg/ml.
- NK-4 and NK-17 at 100µg/ml showed better antifungal activity as compared to standard fluconazole at 80µg/ml.

Gibberella fuzikuroi

- NK-4 and NK-13 showed equal antifungal activity as compared to standard Fluconazole at 60µg/ml.
- NK-3, NK-13 and NK-14 showed equal antifungal activity as compared to standard Fluconazole at 80µg/ml.
- NK-3, NK-8, NK-11, NK-13 and NK-14 showed equal antifungal activity as compared to standard Fluconazole at 100µg/ml.

Comparison amongst the doses

- NK-3, NK-13 and NK-14 at 80µg/ml showed better antibacterial activity as compared to standard fluconazole at 60µg/ml.
- NK-8 and NK-17 at 80µg/ml showed equal antibacterial activity as compared to standard fluconazole at 60µg/ml.
- NK-3 and NK-14 at 100µg/ml showed better antibacterial activity as compared to standard fluconazole at 80µg/ml.
- NK-8, NK-11 and NK-13 at 100µg/ml showed equal antibacterial activity as compared to standard fluconazole at 80µg/ml.

Discussion

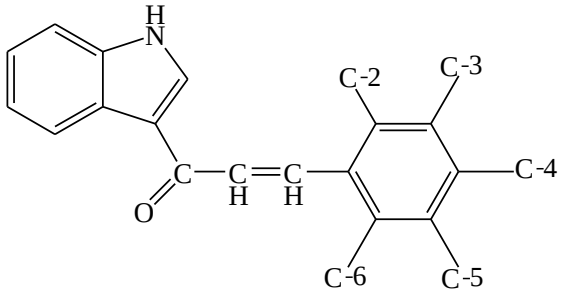


Fig 1: SAR positions of phenyl ring substituted on 2nd position of 3-acetyl indole

Jain S. *et al*. (2016) in his studies on have shown that derivatives of 3-acetyl indole derivatives having electron withdrawing group(nitro group) at C-2 position showed better antifungal activity against standard griseofulvin and Singh C.S. *et al*. (2018) in his studies on 3-acetyl indole derivatives have shown that substitution of electron withdrawing group at C-3(nitro group) or C-4(chloro group) position on the substituted phenyl ring showed good antifungal activity in comparison with standard fluconazole while Wakode S. *et al*. (2017) in his studies on derivatives of 3-acetyl indole have shown that compounds substituted with hydroxyl group at C-4 position on substituted phenyl ring exhibited good antifungal activity fluconazole.

Out of 17 compounds, 6 compounds (NK-3, NK-8, NK-9, NK-13, NK-14 and NK-16) showed better or equal activity against *candida albicans*, 5 compounds (NK-3, NK-8, NK-11, NK-13 and NK-14) exhibited better or equal activity against *Rhizopus oligosporus*, 6 compounds (NK-3, NK-4, NK-8, NK-11, NK-13 and NK-14) showed better or equal activity against *Gibberella fuzikuroi* and 7 compounds (NK-3, NK-5, NK-8, NK-11, NK-13, NK-14 and NK-17) showed better or

equal activity against *Asperigillus niger*. From the results it was observed that the compounds showed a generalized trend of being more or equal active at higher concentration than the standard fluconazole.

NK-3, NK-8, NK-11, NK-13 and NK-14 exhibited better antifungal activity against all four bacterial strains, probably it may be due to the presence of electron withdrawing nitro and trifluoromethyl group at C-2 and C-3 position of the substituted phenyl ring. Thus our study is in concurrence with previous studies of Jain S. *et al*. (2016) and Singh C.S. *et al*.(2018).

5. Conclusion

Amongst all the compounds, NK-3, NK-8, NK-11, NK-13 and NK-14 exhibited better antifungal activity against all four bacterial strains namely, *Candida albicans, Rhizopus oligosporus, Gibberella fuzikuroi* and *Asperigillus niger* due to presence of electron withdrawing group (nitro or trifluoromethyl). These compounds can be further studied for the development of newer antifungal molecules having better antifungal activity. The work can be extended to generate new potential molecules using 3-acetylindole skelton.

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