ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Synthesis, Charectrrization of Indole Having Tetrazol - 1, 3, 4 - Oxadiazole Derivatives and Evaluation of their Antibacterial and Antifungal Activities.

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ABSTRACT

This research work has been aimed to the synthesis of some new derivatives of 1-(5-((5-chloro-3-(1-(pyridine-4-yl)-4-(1-(4-substituted phenyl)-1H-tetrazol-5-yl) -1H-pyrazol-3-yl)-1H-indol-1-yl)methyl)-2-(4-substituted phenyl)-2-methyl-1,3,4-oxadiazol-3(2H)-yl)ethanone (5a-g) were prepared from 2-(5-chloro-3-(1-(pyridine-4-yl)-4-(1-(4-substituted phenyl)-1H-tetrazol-3-yl)-1H-Indol-1-yl) -N′-(1-(4-substituted phenyl) ethylidene) acetohydrazide(4a-g). A mixture (4 a-g) having phenyl ethylidene acetohydrazide which on reacted with excess of acetic anhydride was refluxed for 3 hours to get corresponding 1,3,4-oxadiazole derivatives (5 a-g). The structure of the newly synthesized products were charecterized by IR, NMR, Mass and elemental analysis for carbon,hydrogen and nitrogen. All the compounds were evaluated for anti-bacterial and anti-fungal activity. Some of these compounds showed good antibacterial and good antifungal activity compared with standard compounds.

Key words: 1,3,4-oxadiazole, hydrazine hydrate , sodium azide , acetic anhydride, anti-fungal, anti-bacterial activity.

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ISSN: 0975-8585

INTRODUCTION

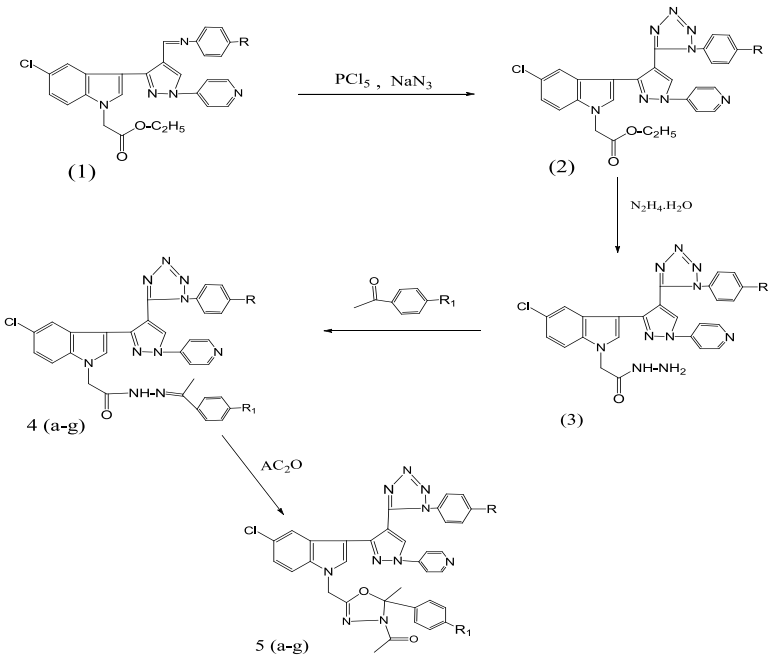
Heterocyclic chemistry is one of the most valuable source of novel compounds with diverse biological activity. The heterocyclic molecules which possess indole, tetrazol and 1,3,4-oxadiazole moieties exhibit wide range of biological activities. Indole is a popular component of fragrances and the precursor to many pharmaceuticals.indole moiety is very small but is fascinated by scientists because of the diverse biological activities by not only indole but its various substituted derivatives as well. Indole derivatives constitute an important class of therapeutic agents in medicinal chemistry including antiviral,antitumor, analgesic, anti-inflammatory, antimicrobial, antifungal activities, etc.

Tetrazole and their derivatives possess broad spectrum of biological activity inboth medicinal and pharmaceutical, such as antimicrobial [1], antibacterial [2], antifungal [3], analgesic [4], anti-inflammatory [5], antinociceptive [6], antitubercular activity [7], and anticancer [8], antiviral [9,10]. This nitrogen-rich ring system is used inpropellants [11], explosives [12], and pharmaceuticals [13].

1,3,4-Oxadiazole derivatives are reported to show broad spectrum of biological activities [14] like antibacterial [15], antitubercular [16], vasodialatory [17], antifungal [18], anti-inflammatory [19], anticonvulsant [20], cytotoxic [21], anaesthetic [22], analgesic [23], anticancer [24] activities.

MATERIALS AND METHODS

Melting points were determined in open capillary tubes on Mel-Temp apparatus and are uncorrected(in degree celsius) .Columnchromatography was performed on silica gel with different solvent systems as eluents to afford the pure compound. TLC was performed on aluminium sheet of silica gel $60F_{254}$,E-Merk,Germany using iodine as visualizing agent. The Infra Red Spectra of the compounds were recorded in KBr pellets on FT-IR(perkin-Elmer 1000 units)instrument . All ^{1}H and ^{13}C-NMR spectra were recorded on a varian XL-300 Spectrometer operating at 300MHz for ^{1}H-NMR and 75 MHz for ^{13}C-NMR. The ^{1}H-NMR spectra were recorded using TMS as an internal standard(Chemical shifts in δ_{ppm}). The compounds were dissolved in DMSO-d_6 and Chemical shifts were referenced to TMS (^{1}H and ^{13}C-NMR). Mass spectral data was recorded on FAB-MS instrument at 70ev with direct inlet system. Elemental analysis were recorded on a Carlo Erba 1108 elemental Analyser, Central Drug Research Institute, Lucknow, India.



Scheme-I Synthetic route for target compounds

Compound	5a	5b	5c	5d	5e	5f	5g
R1	-H	$-CH_3$	$-OCH_3$	4-Cl	4-Br	$4-NO_2$	$-CF_3$
R	$-CF_3$	$-CF_3$	$-CF_3$	$-CF_3$	$-CF_3$	$-CF_3$	$-CF_3$

ISSN: 0975-8585

The structures of the newly synthesized compounds were supported by physical data (**Table-1**) and following spectral analysis.

Table - I

Comp	R	R^1	M.P.	Yield (%)	Molecular Formula	Elemental Analysis Found , Calculated(%)				Rf
						C(%)	H(%)	N(%)	O(%)	
5a	$-CF_3$	-H	161-63	65%	$C_{36}H_{26}ClF_3N_{10}O_2$	59.67 (59.80)	3.46 (3.62)	19.21 (19.37)	4.27 (4.43)	0.57
5b	$-CF_3$	$-CH_3$	156-58	64%	$C_{37}H_{28}ClF_3N_{10}O_2$	60.16 (60.29)	3.66 (3.83)	18.87 (19.00)	4.18 (4.34)	0.60
5c	$-CF_3$	OCH_3	145-47	62%	$C_{37}H_{28}ClF_3N_{10}O_3$	58.84 (59.01)	3.56 (3.75)	18.39 (18.60)	6.16 (6.37)	0.63
5d	$-CF_3$	4-Cl	166-68	66%	$C_{36}H_{25}Cl_2F_3N_{10}O_2$	56.92 (57.08)	3.15 (3.33)	18.33 (18.49)	4.07 (4.22)	0.55
5e	$-CF_3$	4-Br	164-66	67%	$C_{36}H_{25}BrClF_3N_{10}O_2$	53.76 (53.91)	3.02 (3.14)	17.29 (17.46)	3.82 (3.99)	0.53
5f	$-CF_3$	4-NO_2	187-89	70%	$C_{36}H_{25}ClF_3N_{11}O_4$	56.14 (56.29)	3.15 (3.28)	19.89 (20.06)	8.15 (8.33)	0.48
5g	-CF3	4-CF3	180-82	68%	$C_{37}H_{25}ClF_6N_{10}O_2$	56.06 (56.17)	3.04 (3.19)	17.56 (17.71)	3.88 (4.04)	0.51

RESULTS AND DISCUSSION

The target compounds were synthesized via the route as shown in Scheme above. The synthon required for thesynthesis of the target molecules was prepared by a reported method, filtered and recrystallized from ethanol. For all the synthesized compounds, the progress of the reaction was monitored by TLC with hexane, ethylacetate (7:3) as mobile phase. All the synthesized structures showed satisfactory result. The chemical shift values of the synthesized compounds were full agreement with the number of protons present in it.

Procedure for the synthesis of Ethyl-2-(5-chloro-3-(1-(pyridine-4yl)-4-(1-(4-substituted phenyl)-1H-tetrazol-5-yl)-1H-Indol-1-yl)acetate (2)

Schiff base (1) (20 mmol ,11.03g) and PCl_5 (0.03mol) was heated at 100^0C for 1h. When the evalution of fumes of HCl ceased , excess of PCl_3 was removed under reduced pressure and the residual imidoyl chloride was treated with an ice-cold solution of sodium azide(25mmol) and excess of sodium acetate in water (20 mol) and acetone (25 ml) with stirring. Stirring was continued for overnight. The progress of the reaction was monitored by TLC using hexane and ethyl acetate (7:3) solvent mixture as an elutent . After completion of the reaction , the solvent acetone was removed under reduced pressure.The remaining aqueous portion was extracted with $CHCl_3$ and dried to get compound (2) with a yield of 70% .

Procedure for the synthesis of 2-(5-chloro-3-(1-(pyridine-4-yl)-4-(1-(4-substituted phenyl)-1H-tetrazol-3-yl)-1H-Pyrazol-3-yl)-1H-indol-1-yl) acetohydrazide (3)

A solution of Ethyl-2-(5-chloro-3-(1-(pyridine-4yl)-4-(1-(4-substituted phenyl)-1H- tetrazol -5-yl)-1H-Indol-1-yl)acetate (2) (11mmol, 7g) and hydrazine hydrate (15mmol) in ethanol (20ml) was refluxed for 5 hours. The reaction mixture was cooled and poured on to ice cold water with stirring. The progress of the reaction was monitored by TLC with hexane:ethyl acetate(7:3) as elutent. The separated solid was filtered, washed with water and recrystallized from ethanol to afford corresponding acetohydrazide (3) with a yield of 68% .

Procedure for the synthesis of 2-(5-chloro-3-(1-(pyridine-4-yl)-4-(1-(4-substituted phenyl)-1H-tetrazol-3-yl)-1H-Indol-1-yl)-N'-(1-(4substitutedphenyl)ethylidene)aceto hydrazide (4a-g)

To a solution of 2-(5-chloro-3-(1-(pyridine-4-yl)-4-(1-(4-substituted phenyl)-1H-tetrazol-3-yl)-1H-Pyrazol-3-yl)-1H-indol-1-yl) acetohydrazide (3) (0.001mol) in hot methanol (25ml), acetophenone (0.003mol) and a drop of glacial acetic acid were added. The solid that separated on refluxing for 4hrs was filtered wash with cold methanol and recrystallised from methanol to give compound (4a) with a yield of 65% . The above reaction of (3) with acetophenone has been extended to P-methyl, P-methoxy, P-chloro, P-bromo,P-nitro,P-trifluoromethyl acetophenone to get compounds (4b-g).

Procedure for the synthesis of 1-(5-((5-chloro-3-(1-(pyridine-4-yl)-4-(1-(4-substituted phenyl)-1H-tetrazol-5-yl)1H-pyrazol-3-yl)1H-indol-1-yl)methyl)-2-(4-substitutedphenyl)-2-methyl-1,3,4-oxadiazol-3(2H)-yl) ethanone (5a-g)

A mixture of 4a (0.001mol) and excessive acetic anhydride (3mmol) was refluxed for 3hrs. The excessive acetic anhydride was distilled off and the residue was poured on to crushed ice. The progress of the reaction was monitored by TLC with hexane:ethyl acetate(7:3) as elutent.The solid thus obtained was filtered, washed with water and recrystallised from methanol to furnish (5a) with a yield of 65% . The cyclization reaction was extended to other tetrazoles (5b-g) and in each case the respective (substituted) R_1= P-$CH_3C_6H_4$, P-$OCH_3C_6H_4$, P-ClC_6H_4, P-BrC_6H_4, P-$NO_2C_6H_4$, P-$CF_3C_6H_4$.

The structure of these newly synthesised compounds (5 a-g) were based on the charecterised by their elemental analysis and spectral data (IR, ^{1}H-NMR, ^{13}C-NMR).

Physical, Analytical and Spectral data for the target compounds : (5 a-g)

Characterization of 1-(5-((5-chloro-3-(1-(pyridin-4-yl)-4-(1 -(4-(trifluoromethyl)phenyl)-1H-tetrazol-5-yl)-1H-pyrazol-3-yl)-1H-indol-1-yl)methyl)-2-methyl-2-phenyl-1,3,4-oxadi azol-3(2H)-yl)ethanone (5a)

Yield 65%, M.P: 161-63 ^{0}C , **IR(KBR)**: **δ** 3042cm^{-1}(=CH aromatic str.),1698cm^{-1} (C=O of carbonyl group), 1645&1232(1,3,4-oxadiazole),1620cm^{-1}(characteristic of C=N), 1450-1520cm^{-1}, (characteristic of indol nucleus), 1410-1460 cm^{-1}(stretching vibration of pyridine ring), 1108-1135(characteristic of tetrazole),1140cm^{-1}(N-N),678 cm^{-1}(characteristic of C-Cl nucleus) respectively. **^{1}H-NMR(300 MHz, DMSO-d_6)** δppm**:** 8.10(s,1H,N-CH gp.), 7.10-8.40(m,17H,of indol nucleus,-C_6H_5 phenyl nucleus and -$C_6H_4CF_3$ and C_6H_4N), 5.25(s,2H,-NCH_2),2.45(s,3H, CH_3-C=O),1.85(s,3H,-CH_3). **^{13}C-NMR spectra (75MHz,DMSO-d_6)** δ : 129.5, 111.5, 121.7, 125.8,122.5, 112.5, 134.7,130.2, 121.3, 137.6, 103, 163.5, 131.5, 135.2, 123.5,131,124.5,146.9,113.9,149.9,60,158,91,169, 24, 28,143, 127,129,126.7 corresponding to C1, C2, C3, C4, C5, C6, C7, C8, C9, C10, C11,C12,C13,C14&C18, C15 & C17,C16, C19, C20,C21 &C24, C22& C23,C25,C26,C27,C28, C29, C30, C31, C32& C36, C33 & C35, C34 carbon atoms respectively. **Mass**(m/z):722.19,**Anal.Calcd.For** $C_{36}H_{26}ClF_3N_{10}O_2$: C 59.67%, H 3.46 %, N 19.21%, O 4.27% Found: C 59.80%, H 3.62%, N 19.37%, O 4.43% .

Characterization of 1-(5-((5-chloro-3-(1-(pyridin-4-yl)-4-(1-(4-(trifluoromethyl)phenyl)-1H-tetrazol-5-yl)-1H-pyrazol-3-yl)-1H-indol-1-yl)methyl)-2-methyl-2-(p-tolyl)-1,3,4-oxa diazol-3 (2H) -yl)ethanone (5b)

Yield 64%, M.P: 156-58 ^{0}C , **IR(KBR): δ** 3040cm^{-1}(=CH aromatic str.),1695cm^{-1} (C=O of carbonylgroup),1645&1232(1,3,4-oxadiazole),1622cm^{-1}(characteristic of C=N), 1460-1510 cm^{-1}(characteristic of indol nucleus), 1415-1450 cm^{-1}(stretching vibration of pyridine ring), 1110-1130(characteristic of tetrazole),1143cm^{-1}(N-N),676cm^{-1}(characteristic of C-Cl nucleus) respectively. **^{1}H-NMR (300MHz,DMSO-d6) δ ppm:** 8.08(s,1H,N-CH gp.),7.10-8.40(m, 16H,of indol nucleus,-C_6H_4 phenyl nucleus and -$C_6H_4CF_3$ and C_6H_4N), 5.24(s,2H,-NCH_2),2.45(s,3H, CH_3-C=O), 1.85(s,3H,-CH_3),2.23(s,3H,-CH_3 attached to phenyl ring).

^{13}C-NMR spectra(75MHz, DMSO-d6) δ : 129.5, 111.5, 121.7, 125.8,122.5, 112.5, 134.7, 130.2, 121.3, 137.6, 103, 163.5,131.5,135.2,123.5,131,124.5,146.9,113.9,149.9,60, 158,91, 169, 24, 28, 140,127,128.8,136.4, 22 these signals are due to C1, C2, C3, C4, C5, C6, C7, C8,C9,C10,C11,C12,C13,C14&C18,C15&C17,C16,C19,C20,C21&C24,C22&C23,C25,

C26,C27,C28,C29,C30,C31,C32&C36,&C35,C34,C37 carbon atoms respectively. **Mass** (m/z):736.21, Anal. Calcd. For $C_{37}H_{28}ClF_3N_{10}O_2$: C 60.16%, H 3.66 %, N 18.87%, O 4.18% Found: C 60.29%, H 3.83%, N 19.00%, O 4.34% .

Characterization of 1-(5-((5-chloro-3-(1-(pyridin-4-yl)-4-(1-(4-(trifluoromethyl)phenyl)-1H-tetrazol-5-yl)-1H-pyrazol-3-yl)-1H-indol-1-yl)methyl)-2-(4-methoxyphenyl)-2-methyl -1,3,4-oxadiazol-3(2H)-yl)ethanone (5c)

Yield 62%, M.P: 145-47 ^{0}C , **IR(KBR): δ** 3045cm^{-1}(=CH aromatic str.),1680cm^{-1} (C=O of carbonyl group), 1645&1232(1,3,4-oxadiazole),1455-1510cm^{-1},(characteristic of indol nucleus), 1420-1465 cm^{-1}(stretching vibration of pyridine ring), 1108-1130(characteristic of tetrazole),675 cm^{-1} (characteristic of C-Cl nucleus) respectively. **^{1}H-NMR (300MHz,DMSO-d_6) δ** ppm**:** 8.07(s,1H,N-CH gp.),7.10-8.40(m,16H,of indol nucleus,-C_6H_4 phenyl nucleus and -$C_6H_4CF_3$ and C_6H_4N), 5.24(s,2H,-NCH_2),2.45(s,3H, CH_3-C=O), 1.82(s,3H,-CH_3), 3.83 (s, 3H,-OCH_3 attached to phenyl ring). **^{13}C-NMR spectra(75MHz, DMSO-d6) δ** : 129.5, 111.5,121.7,125.8,122.5,112.5,134.7, 130.2, 121.3, 137.6, 103, 163.5, 131.5, 135.2, 123.5, 131, 124.5, 146.9, 113.9, 149.9, 60,158,91, 169,24,28, 135, 128, 114.1, 158.6, 55.8 these signals are due to C1, C2, C3, C4, C5, C6, C7, C8, C9, C10, C11, C12, C13, C14&C18,C15&C17,C16 ,C19, C20,C21&C24,C22& C23, C25, C26, C27, C28, C29, C30, C31,C32&C36,C33&C35,C34,C37 carbon atoms respectively. **Mass** (m/z): 752.21, **Anal.Calcd.For $C_{37}H_{28}ClF_3N_{10}O_3$**: C 58.84% , H 3.56 %, N 18.39%, O 6.16% Found: C 59.01%, H 3.75%, N 18.60%, O 6.37% .

Characterization of 1-(5-((5-chloro-3-(1-(pyridin-4-yl)-4-(1-(4-(trifluoromethyl)phenyl)-1H-tetrazol-5-yl)-1H-pyrazol-3-yl)-1H-indol-1-yl)methyl)-2-(4-chlorophenyl)-2-methyl-1,3,4-oxadiazol-3(2H)-yl)ethanone (5d)

Yield 66%, M.P: 166-68 ^{0}C , **IR(KBR): δ** 3042cm^{-1}(=CH aromatic str.),1690cm^{-1} (C=O of carbonyl group), 1640&1230(1,3,4-oxadiazole), 1622cm^{-1}(characteristic of C=N), 1445-1525cm^{-1}, (characteristic of indol nucleus), 1415-1450 cm^{-1}(stretching vibration of pyridine ring), 1105-1140 cm^{-1} (characteristic of tetrazole), 677 cm^{-1} (characteristic of C-Cl nucleus) respectively. **^{1}H-NMR(300MHz,DMSO-d6)δppm:** 8.09(s,1H,N-CH gp.), 7.10-8.40(m, 16H, of indol nucleus,-C_6H_4Cl nucleus and -$C_6H_4CF_3$ and C_6H_4N), 5.24(s,2H,-NCH_2),2.45(s,3H, CH_3-C=O), 1.86(s,3H,-CH_3). **^{13}C-NMR spectra(75MHz, DMSO-d6)δ**: 129.2, 111.2, 121.7, 125.8,122.5, 112.5, 134.7,130.2, 121.3, 137.6, 103, 163.5, 131.5, 135.2,123.5, 131, 124.5, 146.9, 113.9, 149.9, 60,158,91, 169, 24, 28, 141, 125.4, 128.6, 132.3 these signals are due to C1, C2, C3, C4, C5, C6, C7, C8, C9, C10, C11,C12, C13, C14&C18, C15& C17,C16, C19, C20, C21& C24,C22&C23,C25,C26,C27,C28,C29,C30,C31, C32& C36, C33 &C35,C34 carbon atoms respectively. **Mass**(m/z): 756.15, **Anal. Calcd. For $C_{36}H_{25}Cl_2F_3N_{10}O_2$:** C 56.92%, H 3.15 %, N 18.33%, O 4.07% Found: C 57.08%, H 3.33%, N 18.49%, O 4.22%.

Characterization of 1-(2-(4-bromophenyl)-5-((5-chloro-3-(1-(pyridin-4-yl)-4-(1-(4(tri fluoromethyl)phenyl)-1H-tetrazol-5-yl)-1H-pyrazol-3-yl)-1H-indol-1-yl)methyl)-2methyl -1,3,4-oxadiazol-3(2H)-yl)ethanone (5e)

Yield 67%, M.P: 164-66 ^{0}C , **IR(KBR): δ** 3046cm^{-1}(=CH aromatic str.),1688cm^{-1} (C=O of carbonyl group), 1640&1230(1,3,4-oxadiazole), 1620cm^{-1}(characteristic of C=N), 1450-1520cm^{-1}, (characteristic of indol nucleus), 1410-1460 cm^{-1}(stretching vibration of pyridine ring), 1108-1135(characteristic of tetrazole), 676 cm^{-1} (characteristic of C-Cl nucleus) respectively. **^{1}H-NMR (300MHz,DMSO-d_6)** δppm**:** 8.09(s,1H,N-CH gp.), 7.10-8.40(m, 1H, of indol nucleus,-C_6H_4Br nucleus and -C_6H_4 CF_3 and C_6H_4N), 5.24(s,2H,-NCH_2), 2.45(s, 3H,CH_3-C=O), 1.86(s,3H,-CH_3). **^{13}C-NMR spectra(75MHz, DMSO-d_6) δ** : 129.3, 111.2, 121.7, 125.8,122.5, 112.5, 134.7,130.2, 121.3, 137.6, 103, 163.5, 131.5, 135.2, 123.5, 131, 124.5, 146.9, 113.9, 149.9, 60,158,91, 169, 24, 28, 141.6, 129.1, 131.4, 121.1 these signals are due to C1,C2,C3,C4,C5,C6,C7,C8,C9,C10,C11,C12,C13,C14&C18,C15&C17,C16, C19, C20,C21&C24,C22&C23,C25,C26,C27,C28,C29,C30,C31,C32&C36,C33&C35,C34 carbon atoms respectively.**Mass**(m/z): 800.10, **Anal. Calcd. For $C_{36}H_{25}BrClF_3N_{10}O_2$** : C 53.76%, H 3.02 %, N 17.29%, O 3.82% Found: C 53.91%, H 3.14%, N 17.46%, O 3.99% .

Characterization of 1-(5-((5-chloro-3-(1-(pyridin-4-yl)-4-(1-(4-(trifluoromethyl)phenyl)-1H-tetrazol-5-yl)-1H-pyrazol-3-yl)-1H-indol-1-yl)methyl)-2-methyl-2-(4-nitrophenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (5f)

Yield 70%, M.P:187-89 ^{0}C ,**IR(KBR): δ** 3044cm^{-1}(=CH aromatic str.),1697cm^{-1} (C=O of carbonylgroup), 1640&1230(1,3,4-oxadiazole), 1620cm^{-1}(characteristic of C=N), 1460- 1530 cm^{-1}(characteristic of indol nucleus), 1413-1465 cm^{-1}(stretching vibration of pyridine ring),1140cm^{-1}(N-N) , 1106-1130(characteristic of tetrazole), 678 cm^{-1} (characteristic of C-Cl nucleus) respectively. **^{1}H-NMR (300MHz,DMSO-d_6) δ ppm:** 8.10(s,1H,N-CH gp.), 7.10-8.40(m,16H,of indol nucleus,-$C_6H_4NO_2$ nucleus and -C_6H_4 CF_3 and C_6H_4N), 5.25(s,2H,-

NCH_2),2.45(s,3H,CH_3-C=O), 1.89(s,3H,-CH_3).**^{13}C-NMR spectra(75MHz, DMSO-d6) δ** : 129.2, 111.3, 121.7, 125.6,122.5, 112.5, 134.7,130.2, 121.3, 137.6, 103, 163.5, 131.5, 135.2,123.5, 131, 124.5, 146.9, 113.9, 149.9, 60,158,91, 169, 24, 28, 148.7, 127.8, 123.7, 146. these signals are due to C1,C2,C3,C4,C5,C6,C7,C8,C9,C10,C11,C12,C13,C14&C18,C15&C17, C16,C19,C20,C21&C24,C22&C23,C25,C26,C27,C28,C29,C30,C31,C32&C36,C33&C35, C34 carbon atoms respectively. **Mass**(m/z): 767.17, **Anal. Calcd. For $C_{36}H_{25}ClF_3N_{11}O_4$** : C 56.14%, H 3.15 %, N 19.89%, O 4.27% Found: C 56.29%, H 3.28%, N 20.06 %, O 8.33 % .

Characterization of 1-(5-((5-chloro-3-(1-(pyridin-4-yl)-4-(1-(4-(trifluoromethyl)phenyl)-1H-tetrazol-5-yl)-1H-pyrazol-3-yl)-1H-indol-1-yl)methyl)-2-methyl-2(4(trifluoromethyl) phenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (5g)

Yield 68%, M.P: 180-82 ^{0}C , **IR(KBR): δ** 3041cm^{-1}(=CH aromatic str.),1698cm^{-1} (C=O of carbonyl group), 1640&1230(1,3,4-oxadiazole), 1620cm^{-1}(characteristic of C=N), 1450-1520cm^{-1}, (characteristic of indol nucleus), 1410-1460 cm^{-1}(stretching vibration of pyridine ring),1140cm^{-1}(N-N) ,1108-1135 (characteristic of tetrazole), 677 cm^{-1} (characteristic of C-Cl nucleus) respectively. **^{1}H-NMR (300MHz,DMSO-d6) δ ppm:** 8.10(s,1H,N-CH gp.), 7.10-8.40(m,16H,of indol nucleus and -C_6H_4 CF_3 and C_6H_4N), 5.24(s,2H,-NCH_2), 2.45(s, 3H,CH_3-C=O), 1.87(s,3H,-CH_3).**^{13}C-NMR spectra(75MHz, DMSO-d6)δ**: 129.3,111.3,121.7, 125.6, 122.5,112.5,134.7,130.2,121.3,137.6,103,163.5,131.5,135.2,123.5,131,124.5,146.9,113.9, 149.9,60,158,91,169,24,28,150,127.2,124.9,129,124.1 these signals are due to C1, C2, C3, C4, C5, C6, C7, C8, C9, C10, C11, C12, C13, C14& C18, C15&C17, C16, C19, C20, C21 & C24,C22&C23,C25,C26,C27,C28,C29,C30,C31,C32&C36,C33&C35,C34,C37carbon atoms respectively. **Mass** (m/z) :790.18, **Anal. Calcd. For $C_{37}H_{25}Cl\ F_6N_{10}O_2$:** C 56.06%, H 3.04 %, N 17.56%, O 3.88% Found: C 56.17%, H 3.19%, N 17.71 %, O 4.04% .

Biological Screening Antimicrobial activity test

The newly synthesized compounds 1-(5-((5-chloro-3-(1-(pyridin-4-yl)-4-(1-(4-substituted phenyl) -1H-tetrazol-5-yl) -1H-pyrazol-3-yl) -1H-indol-1-yl) methyl) -2-methyl-2-substituted phenyl-1,3,4-oxadiazol-3(2H)-yl)ethanone(5a-g) were screened for their antimicrobial studies against anti bacterial and anti fungal activity by Disc Diffusion method[25]. The synthesized compounds were used at the concentration of 250µg/mL and 500µg/mL DMSO as a solvent[26]. The amoxicillin 10 µg/disc, cefaclor 30 µg/disc and ketaconazole 50 µg/mL were used as standards.

Table II: Antimicrobial activity by disc diffusion method for 1,3,4-oxadiazoles

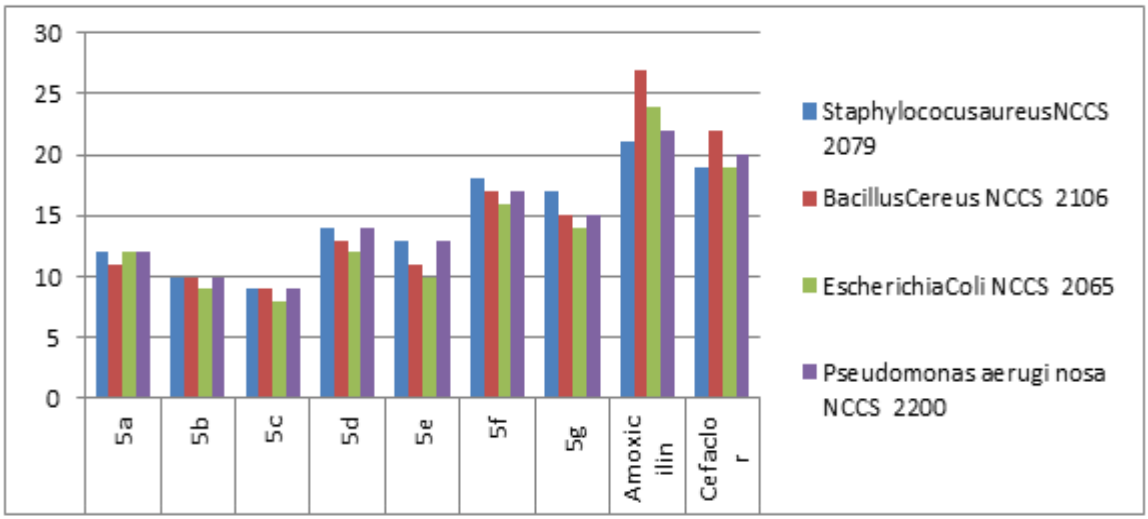
S.NO.	Compd.	Zone of Inhibition (mm)					
		Anti-bacterial activity				**Anti-fungal activity**	
		Staphylococus aureus NCCS 2079	Bacillus Cereus NCCS 2106	Escherichia Coli NCCS 2065	Pseudomonas aerugi nosa NCCS 2200	Aspergillus niger NCCS 1196	Candida albicans NCCS 3471
1)	5a	12	11	12	12	14	16
2)	5b	10	10	09	10	11	14
3)	5c	09	09	08	09	12	13
4)	5d	14	13	12	14	16	19
5)	5e	13	11	10	13	14	17
6)	5f	18	17	16	17	20	21
7)	5g	17	15	14	15	19	20
8)	Amoxi cillin	21	27	24	22	---------	--------
9)	Cefaclor	19	22	19	20	---------	--------
10)	Ketoco nazol	--------	---------	----------	----------	23	26

ISSN: 0975-8585

Antibacterial activity

The test was performed according to the disk diffusion method adopted with some modifications for the prepared compounds using amoxicillin, and cefaclor as references. The prepared compounds were tested against Gram positive bacteria (*Staphylococcus aureus* NCCS 2079, *Bacillus cereus*NCCS 2106), Gram negative bacteria (*Escherichia coli* NCCS 2065, *Pseudomonas aeruginosa* NCCS 2200). Nutrient agar was used as a culture media and DMSO was used as a solvent control for antibacterial activity.

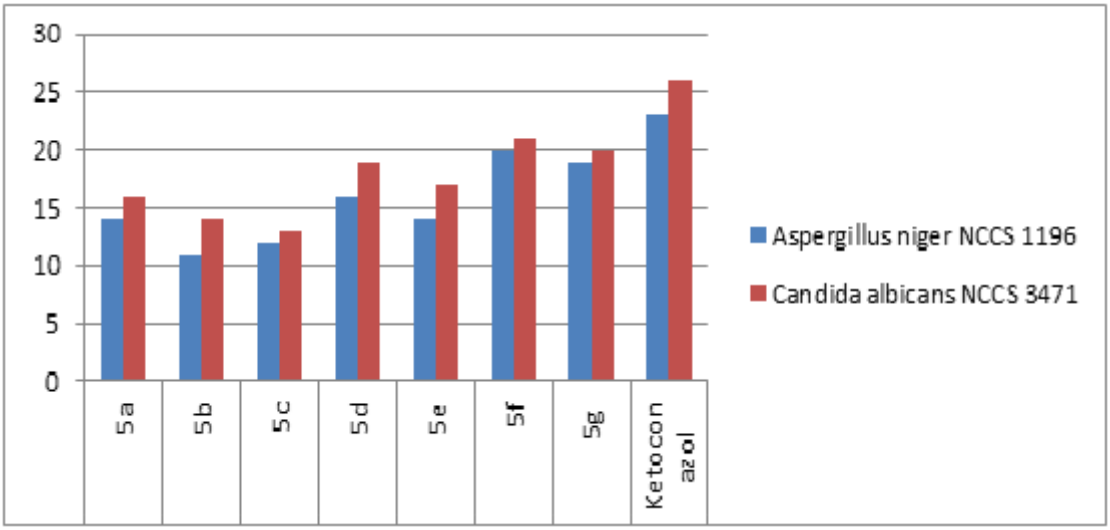
Zone of inhibition with respect standard drugs amoxycillin and cefaclor



Antifungal activity

The antifungal activity of synthesized compounds were studied by disc diffusion method against the organisms of aspergillus niger NCCS 1196,Candida albicans NCCS 3471. Ketoconazol is considered as standered reference compound for antifungal activity. Nutrient agar was used as a culture media and DMSO was used as a solvent control for antifungal activity.

Zone of inhibition with respect standard drug Ketoconazol



In the above series(5 a-g) of compounds P-nitro (5f), P-trifluoro methyl (5g), P-chloro (5d) compounds showed good antibacterial and antifungal activity than the other compounds of the series. More polar groups having compounds are exhibit more activity when compare than less polar compounds.

Substituent's activity -NO_2 > -CF_3 > -Cl > -Br > -H >-CH_3>-OCH_3. Compounds activity 5f > 5g > 5d > 5e > 5a > 5b > 5c.

CONCLUSION

Indol bearing pyrazole ring, besides tetrazol moiety and 1,3,4-oxadiazole group were prepared by the reaction of aceticanhydride with acetohydrazid group. These synthons were purified& charecterized by chromatographic and spectral techniques. Indol derivatives were subjected to antimicrobial evaluation and some of these compounds were found to posses good anti-bacterial and anti-fungal activity.

ACKNOWLEDGEMENTS

The author (P Ashokgajapathiraju) thanks to U G C – S A P and U G C – B S R , New Delhi for financial assistance and also thankful to IICT Hyderabad and CDRI Lucknow for spectral and analytical data.I express my sincere thanks to my Research Supervisor Prof J.Sreeramulu for his valuable guidance. I express my sincere thanks to Prof LK Ravindranath, who is giving valuable suggestions during my research.

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