Original Article

"Synthesis of Novel Potential, Substituted Thiazolidinone, Azetidinone, Deriv-atives Containing Substituted, Triazole, Indole Moiety and Their Screening Effect as Antifungal, Biological Activity"

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Abstract

3-chloro-4-(substitutedphenyl)-1-(3-(methylthio)-5-((5-nitro-1H-indole-1-yl) methyl)-4H-1,2,4-triazol-4-yl)azetidin-2-one 6(a-e), and 2-(substituted phenyl)-3-(3-(methylthio)-5-((5-nitro-1H-indol-1-yl)methyl)-4H-1,2,4-triazol-4-yl)thiazolidin-4-one7(a-e) were prepared through systematic path way. Compounds 6 (a-e) were contain indole, triazole units while compounds 7(a-e) were possesses effective indole, triazole and thiazolidinone moiety. Both the compounds series 6(a-e) , and 7(a-e) were show valuable characteristics and efficacy as anti-fungal and antibacterial .These drugs derivatives were also show better inhibition activities as compare to standard drugs .These drugs were also represent less side effect. Synthesis of novel heterocyclic compounds and its derivative were very useful in medicinal chemistry, biological and, pharmacological aspects. So all these triazole, azetidinone and thiazolidinone derivatives were exhibited better useful properties.

Keywords: Indole, Triazole, Azetidinone, Thiazolidinone, Antifungal Activity, Griseofulvin.

Introduction

In earlier and present time, we are seeing different life treating infection cause through fungal, bacterial infections in our surrounding. Thiazolidinone, azetidinone, triazole, indole moiety containing drug derivatives are useful in the field of modern medicinal chemis-try.Thiazolidinone drug derivatives exhibit different biological activity like antimicrobial, anti-bacterial, antifungal etc. Thiazolidinone moiety containing drugs was function as antimicrobial 1-2, antifungal 3, 4, 5. It was also representing biologically active nucleus 6,7,8,9, anticonvulsant (antiepileptic) 10 and antibacterial nature10 -11. This moiety was also work as antimicrobial and insecticidal activity. Azetidinone derivative was exhibited beneficial properties in the biological system.

Azetidinone derivatives were used as notropic, antidepressant agent 12 .It was also exhibited an-timicrobial activity 12-14, desire efficacy, antibacterial and antifungal 15. It was also work as an-ticonvulsant, anti-inflammatory and antibacterial16. Triazole derivatives was showed biological significance17 triazole nucleus molecules were also exhibited various protective function against diseases. Triazole nucleus were show the properties as protective ulcergenic18 antifungal 20 antifungal and antitubucular activity21,,26,29 .It was showed various biological active 23, antifungal and anti bacterial24 antiproliferative activity25, antimicrobial 27, cytotoxic activity.

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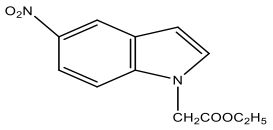
Indole also showed activity as antimicrobial and insecticidal 30.These derivatives which contain small ring heterocyclic, electro negative atom in ring e.i N, S, O, chloro were also show better results due to their effectivity. So these derivatives were used in biological and pharmaceutical system. Their activity rate was also affected with various hetro atoms and formatted different ring. The older drugs were showed high frequency of renal toxicity and several adverse effects. However, in this research work some novel drug derivatives were synthesised. These deriva-tives of compounds 6(a-e) and 7(a-e) which shown the better antifungal activity with less side effects.

MATERIAL AND METHOD:

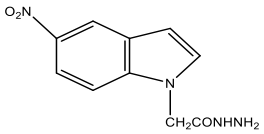
In these syntheses different reagents were used directly. A desire reagent was dissolve in proper suitable solvents at ordinary temperature. The reaction was completed at different required condition. Melting points were recorded by ordinary glass capillary tube in Buchi melting point apparatus it may be incorrect. The homogeneity of all newly synthesized portions was checked. Purity and completion of Reaction was checked, by using ordinary (TLC) plate. TLC plate was coated with silica gel- G. The spots were visualized on TLC by spotting, drying and put it in iodine chamber. This plate was as comes in contact with iodine vapor, visualize the clear spot. Different portion of elemental parts of the synthesis compounds were determined by Perkin Elmer2400 elemental analyzer and results were found within the ±4% of theoretical value. The (IR) (KBr pellet) spectra were recorded on a spectrum by FTIR. The Brucker (300)DPX was help to predict and recorded of 1H NMR values and the chemical shift(values) are expressed in ppm (δ) scale using tetra methyl silane as an internal standard , it was use in CDCl3 solvent. EXPERIMENTAL:

1: Synthesis of compound N indolyl acetate or ethyl 2-(5-nitro-1H-indol-1-yl) acetate (1):



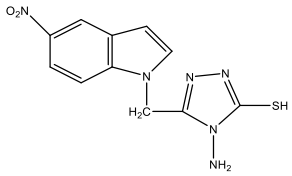
Take the reagent 5-nitro indole (0.01mol) in 100 ml RBF. These reagents were AR grade (CDH) batch 2020. Now, ethyl chloroacetate (0.01) mol was added in it drop wise with carefully and it was stirring slowly. Dry acetone (12 ml) solvent was added in this RBF. All the contents of this mixture were mixed properly with gentle shaking. Approximate, 1g amount of anhydrous K2CO3 was added. This mixture content was stirred and refluxed on magnetic stirrer for16 h. Progress of the reaction was monitored by ordinary TLC plate coated with silica Gel .The reac-tion mixture was obtained, poured into 100ml ice cold water. After pouring, crystal of com-pound was formed .This desire ester was extracted with ether. The solid compound was ob-tained, washed with water and dried. The final indole ester product was obtained. The yield of the compound was appxi. 82 %. Analytical value and Spectral data are given in table 1 & 2 re-spectively.

2: Synthesis of N indolyl acetate hydrazine or 2-(5-nitro-1H-indol-1-yl) acetohydrazide (2):



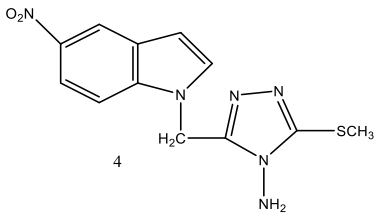
The mixture of compound (1) indolyl ester (0.01mol) and hydrazine hydrate (0.01mol) was tak-en in a RBF. This mixture content was stirred for some time and it was continuous refluxed on a water bath for 13 hr. Progress of the reaction was monitored by ordinary TLC plate coated with silica gel G. In the confirmation of progress of the reaction, eluent 4:1 toluene and ethyl acetate was used. After completion of the reaction it was put aside for some time to cool down the temperature and it was transfer into a beaker containing approximately250 ml ice cold wa-ter. Put aside the content for some time to grow the crystal and finally put it in refrigerator (not freezer) overnight. The crystal of the compound was obtained. These crystals were washed, dried and recrystallised with ethanol to obtained final product with 81% yield. Data and analyt-ical value are given table.

3: Synthesis of Compound,4-amino-5-((5-nitro-1H-indol-1-yl) methyl)-4H-1, 2,4-triazole-3-thiol (3) :



Take the mixture of compound 2nd (0.01 mol), KOH (1.0 mol) and CS2 (1.5 mol) in RBF and it was dissolved in methanol (15 ml). The mixture content was stirred vigorously for 2-3 hr. and some excess solution of hydrazine hydrate was added. The mixture was refluxed further for 4.5 hr. The completion of the reaction was confirmed by TLC plate which was coated with silica gel G. Proper confirmation and visualisations of spots were performed in iodine chamber. After completion of refluxing, some extra solvent was removed. It was cool down by putting aside for some time and it was neutralised by concentrated HCl solution. The solid crystal was obtained, it was filter with water and crystallised from appropriate solvent to obtained desire compound (3). Data and analytical value are given in table1,2.

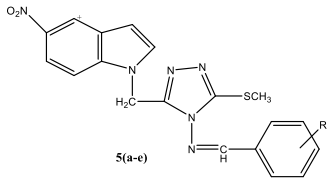
4: 3-(methylthio)-5-((5-nitro-1H-indol-1-yl) methyl)-4H-1, 2, 4-triazol-4-amine (4):



4

Take the mixture of compound 3rd (0.01mol) in RBF and methyl iodide (0.01mol) was added. These reagents (AR grade Merck) were used. The reaction mixture was stirred vigorously and it was refluxed for 2-3 hr. The completion of reaction was confirmed by ordinary TLC plate. The extra solvent was distilled off and now it was cool to room temperature. This content mixture was transfer into cold ice water for crystallization. The solid crystals were obtained .These crystals were washed with distilled water and it was dried. These crystals were recrystallised with appropriate solvent to obtained compound 4. Data and analytical value are given table 1,2.

5: General Procedure of Synthesis of N-(3-(methylthio)-5-((5-nitro-1H-indol-1-yl) me-thyl)-4H-1, 2, 4-triazol-4-yl)-1-phenylmethanimine Compound 5a-5e:

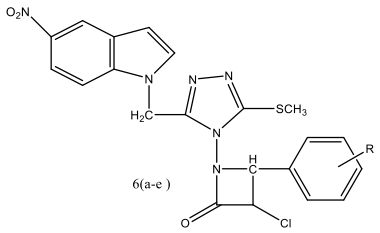


5(a-e)

5a: The derivative of compound 4 (0.01 mol) was taken in RBF and it was dissolved in proper required methanol solvent. The benzaldehyde (0.01mol) was added in this solution. This mix-ture content was stirred for some time to proper mixing and this reaction mixture was refluxed 3-4 hr. After refluxing, extra solvent was removed. The content was put aside for some time to grow the proper crystal. The solid crystal of desire compound was obtained 5a.

The following compounds (5b-5e) were prepared using a similar procedure described as com-pound 5a. The physical, spectral data (values) of derivatives (5a-5e) was given in table 1and 2 below respectively.

6- General Procedure of Synthesis of 3-chloro-1-(3-(methylthio)-5-((5-nitro-1H-indol-1-yl) methyl)-4H-1, 2, 4-triazol-4-yl)-4-phenylazetidin-2-one compound 6a -6e. :

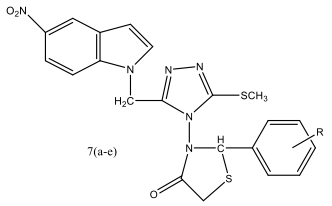


6(a-e)

6a :Take a mixture of compound, derivatives of Schiff base 5a (0.01mol) in dioxin (50 ml) in RBF of 100 ml and chloro acetyl chloride (0.015 mol) was added drop wise with continuous stirring in presence of triethyl amine (.008 mol). This reaction mixture was stirred at 0.00C and mixture further stirred at room temperature for some time, then kept aside for overnight. This mixture was poured into cold ice water. The solid crystal was obtained. This derivative was washed, and dried. These crystals were recrystallised with appropriate solvent to obtained com-pounds 6a. Physical and chemical analysis was performed for this compound. Data and analyt-ical value were given in table1,2.

The following compounds (6b-6e) were also prepared using a similar procedure described to compound 6a. The physical, spectral data (values) of derivatives (6b-6e) was given in table 1, 2 respectively.

7: A general process of synthesis of compound 3-(3-(methylthio)-5-((5-nitro-1H-indol-1-yl) methyl)-4H-1, 2, 4-triazol-4-yl)-2-phenylthiazolidin-4-one. 7(a-e):



7(a-e)

Take the solution of compound of Schiff base 5a (0.01mol) and thioglycollic acid (0.01 mol) in N, N dimethyl formamide (17 ml) with a pinch of anhydrous ZnCl2 in RBF. This mixture con-tent was mixed properly by stirring. Now it was refluxed for 4-5.Hour. The progress of the re-action was checked with the help of TLC using ethyl acetate: toluene 1:4 as an eluent. Excess solvent was separated through distilled off. Mixture was cool down, and then resulting portion was poured into crushed ice water and put it for formation of crystal at overnight. The crystal were obtained. These crystals were filtered, washed and dried. These crystals were recrystal-lised from ethanol, yield of the compound 7a was 65%. Data and analytical value are given ta-ble1

The following compounds (7b-7e) were prepared using a similar procedure described to com-pound 7a. The physical, spectral data (values) of derivatives (7b-7e) was given in table 1&2 re-spectively.

Table 1 Physical and Elemental data:

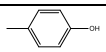
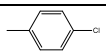
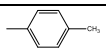
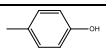
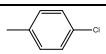
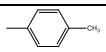
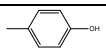
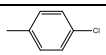
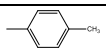
Compound N O	R- Group And Position	Molecular Formula	Functional Group R, Position	Molecular Weight (G)	Mp ^{0}C	Yield	Recrystalised Solvent	Theoretical Elemental Values / Calculated Elemental Values		
								C %	H%	N%
1	-	$C_{12}H_{12}N_2O_4$	-	248.08		82	ethanol	58.06/58.04	4.87/4.89	11.29/11.28
2	-	$C_{10}H_{10}N_4O_3$	-	234.22		80	methanol	51.28/51.26	4.30/4.28	23.92/23.93
3	-	$C_{11}H_{10}N_6O_2S$	-	290.30		72	methanol	45.51/45.50	3.47/3.46	28.95/28.95
4	-	$C_{12}H_{12}N_6O_2S$	-	304.33		68	ethanol	47.36/47.35	3.97/3.95	27.62/27.60
5a		$C_{19}H_{16}N_6O_2S$	H	392.44		72	ether	58.15/58.13	4.11/4.10	21.42/21.40
5b		$C_{19}H_{16}N_6O_3S$	4-OH	408.44		70	ether	55.87/55.89	3.95/3.94	20.58/20.56
5c		$C_{19}H_{15}ClN_6O_2S$	4-Cl	426.88		65	ethanol	53.46/53.45	3.54/3.54	19.69/19.70
5d		$C_{19}H_{16}N_6O_3S$	2-OH	408.44		68	methanol	55.87/55.56	3.95/3.94	20.58/20.58
5e		$C_{20}H_{18}N_6O_2S$	4-CH_3	406.46		69	ethanol	59.10/59.11	4.46/4.45	20.68/20.67
6a		$C_{22}H_{18}ClN_5O_3S$	H	467.93		72	acetone	56.47/56.44	3.88/3.87	14.97/14.98
6b		$C_{22}H_{18}ClN_5O_4S$	4-OH	483.93		71	methanol	54.60/54.62	3.75/3.73	14.47/14.45
6c		$C_{22}H_{17}Cl_2N_5O_3S$	4-Cl	502.37		64	ethanol	52.60/52.58	3.41/3.40	13.94/13.95
6d		$C_{22}H_{18}ClN_5O_4S$	2-OH	483.93		62	DMF-water	54.60/54.59	3.75/3.76	14.47/14.46
6e		$C_{23}H_{20}ClN_5O_3S$	4-CH_3	481.96		70	methanol	57.32/57.33	4.18/4.19	14.53/14.50
7a		$C_{21}H_{18}N_6O_3S_2$	H	466.53		58	ether	54.06/54.03	3.89/3.90	18.01/18.00
7b		$C_{21}H_{18}N_6O_4S_2$	4-OH	482.53		63	ethanol	52.27/52.26	3.76/3.75	17.42/17.41
7c		$C_{21}H_{17}ClN_6O_3S_2$	4-Cl	500.98		59	ethanol	50.35/50.37	3.42/3.40	16.78/16.77
7d		$C_{21}H_{18}N_6O_4S_2$	2-OH	482.53		54	acetone	52.27/52.25	3.76/3.75	17.42/1740
7e		$C_{22}H_{20}N_6O_3S_2$	4-CH_3	480.56		60	ethanol	54.99/54.97	4.20/4.19	17.49/17.48

Table 2: Spectral Analysis:

S.NO.	Compound	IR(KBr)cm^{-1}	^{1}H NMR ($CDCl_3$) δ ppm
1	$C_{12}H_{12}N_2O_4$	1600 (C=C), 1620 -1532 N=O C-NO_2 Stretching,1745 C=O str ,3041 H-C-Ar str, 1702 C-H str in methylene.1200 C-O ester.	δ 5.4 ,1×1H (s, =C-H) , δ 7.3 ,4×1H (d, =C-H Ar) , δ 1.1 ,2×1H (s, -CH_2), δ 1.2 ,1×2H (q, -CH_2), δ 2.2 ,1×3H (t, -CH_3) .
2	$C_{10}H_{10}N_4O_3$	1604 (C=C – Ar), 1619 -1531 N=O C-NO_2 Stretching,1740 C=O str ,3042 H-C-Ar str, 1700 C-H str in methylene .3500 N-H str.	δ 5.2 ,1×1H (s, =C-H) , δ 7.1 ,4×1H (d, =C-H Ar) , δ 1.2 ,1×2H (s, -N-C-H), δ 4.1 ,1×1H (t, -NH), δ 4.2 ,1×2H (d, -NH_2) .

3	$C_{11}H_{10}N_6O_2S$	1603 (C=C – Ar), 1618 -1522 N=O C-NO_2 Stretching,1654 C=N str ,785 -C-S str,	δ 5.3 ,1×1H (s, =C-H) , δ 7.2 ,4×1H (d, =C-H Ar) , δ 1.6 ,1×1H (s, -SH), δ 1.2 ,1×2H (q, -CH_2), δ 4.3 ,1×2H (s, -NH_2) .
4	$C_{12}H_{12}N_6O_2S$	1601 (C=C – Ar), 1619 -1523 N=O C-NO_2 Stretching,1655 C=N str ,3061 C-H str,1615 N-N str ,2585=C-S , 782 -C-S,	δ 5.2 ,1×1H (s, =C-H Ar) , δ 7.2 ,4×1H (d, =C-H Ar) , δ 4.2 ,1×2H (s, -NH_2), δ 1.3 ,1×2H (s, -CH_2), δ 2.2 ,1×3H (s, -CH_3) .
5a	$C_{19}H_{16}N_6O_2S$	1602(C=C – Ar), 1619 -1524 N=O C-NO_2 Stretching,1655 C=N str ,3048 C-H str,1616 N-N str ,2580=C-S , 783 -C-S,	: δ 5.5 ,1×1H (s, =C-H Ar) , δ 7.1 ,4×1H (d, =C-H Ar) , δ 1.2 ,1×2H (s, -CH_2), δ 2.2 ,1×3H (s, S-CH_3), δ 3.2 ,1×1H (s, =C-H) ,), δ 7.5 ,5×1H (m, C-H Ar) .
5b	$C_{19}H_{16}N_6O_3S$	1603(C=C – Ar), 1618 -1520 N=O C-NO_2 Stretching,1657 C=N str ,3051 C-H str,1613 N-N str ,2583=C-S , 782 -C-S, 3400, O-H	δ 5.4 ,1×1H (s, =C-H Ar) , δ 7.0 ,4×1H (d, =C-H Ar) , δ 1.1 ,1×2H (s, -CH_2), δ 2.3 ,1×3H (s, S-CH_3), δ 3.3 ,1×1H (s, =C-H) ,), δ 7.1 ,4×1H (m, C-H Ar) , δ 6.7 ,1×1H (s,p O-H Ar) .
5c	$C_{19}H_{15}ClN_6O_2S$	1600 (C=C – Ar), 1617 -1521 N=O C-NO_2 Stretching,1650 C=N str ,3047 C-H str,1612 N-N str ,2581=C-S , 781 -C-S, 749 C-Cl	δ 5.3 ,1×1H (s, =C-H Ar) , δ 6.9 ,4×1H (d, =C-H Ar) , δ 1.0 ,1×2H (s, -CH_2), δ 2.0 ,1×3H (s, S-CH_3), δ 3.1 ,1×1H (s, =C-H) ,), δ 7.0 ,2×1H (d, C-H Ar) , δ 6.8 2×1H (d,CCl- C-H Ar) .
5d	$C_{19}H_{16}N_6O_3S$	1603(C=C – Ar), 1620 -1523 N=O C-NO_2 Stretching,1648 C=N str ,3046 C-H str,1614 N-N str ,2584=C-S , 780 -C-S, 3401, O-H	δ 5.6 ,1×1H (s, =C-H Ar) , δ 7.2 ,4×1H (d, =C-H Ar) , δ 1.3 ,1×2H (s, -CH_2), δ 2.1 ,1×3H (s, S-CH_3), δ 3.2 ,1×1H (s, =C-H) ,), δ 7.0 ,3×1H (d, C-H Ar) , δ 6.9, 1×1H (d, C-H Ar) , δ 6.6, 1×1H (m, C-OH Ar) .
5e	$C_{20}H_{18}N_6O_2S$	1604(C=C – Ar), 1618 -1523 N=O C-NO_2 Stretching,1656 C=N str ,3057 C-H str,1613 N-N str ,2585=C-S , 783 -C-S,	δ 5.7 ,1×1H (s, =C-H Ar) , δ 7.3 ,4×1H (d, =C-H Ar) , δ 1.5 ,1×2H (s, -CH_2), δ 2.2 ,1×3H (s, S-CH_3), δ 3.4 ,1×1H (s, =C-H) ,), δ 7.3 ,4×1H (d, C-H Ar) , δ 2.4, 3×1H (s,C- CH_3 Ar)
6a	$C_{22}H_{18}ClN_5O_3S$	1603(C=C – Ar), 1615 -1518 N=O C-NO_2 Stretching,1653 C=N str ,3058 C-H str,1617 N-N str ,2580=C-S , 784 -C-S, 1715 C=O , 750 C-Cl, 1650 C-N	δ 5.4 ,1×1H (s, =C-H Ar) , δ 7.3 ,4×1H (d, =C-H Ar) , δ 1.3 ,1×2H (s, -CH_2), δ 2.3 ,1×3H (s, S-CH_3), δ 3.4 ,1×1H (d, CHCl) ,), δ 7.4 ,5×1H (m, C-H Ar) .
6b	$C_{22}H_{18}ClN_5O_4S$	1602(C=C – Ar), 1616 -1517 N=O C-NO_2 Stretching,1652 C=N str ,3057 C-H str,1616 N-N str ,2579=C-S , 782 -C-S, 1718 C=O 751 C-Cl, 1647 C-N	δ 5.3 ,1×1H (s, =C-H Ar) , δ 7.2 ,4×1H (d, =C-H Ar) , δ 1.2 ,1×2H (s, -CH_2), δ 2.4 ,1×3H (s, S-CH_3), δ 3.6 ,1×1H (d, CHCl) ,), δ 6.8 ,4×1H (m, C-H Ar) , δ 6.7 ,1×1H (s, C-OH Ar) .
6c	$C_{22}H_{17}Cl_2N_5O_3S$	1601(C=C – Ar), 1614 -1520 N=O C-NO_2 Stretching,1650 C=N str ,3053 C-H str,1615 N-N str ,2580=C-S , 781 -C-S, 1714 C=O 748 C-Cl, 1643 C-N	δ 5.2 ,1×1H (s, =C-H Ar) , δ 7.0 ,4×1H (d, =C-H Ar) , δ 1.1 ,1×2H (s, -CH2), δ 2.1 ,1×3H (s, S-CH3), δ 3.3 ,1×1H (d, CHCl) ,), δ 6.6 ,4×1H (m, C-H Ar) .
6d	$C_{22}H_{18}ClN_5O_4S$	1602(C=C – Ar), 1618 -1522 N=O C-NO_2 Stretching,1651 C=N str ,3054 C-H str,1617 N-N str ,2585=C-S , 783 -C-S, 1716 C=O ,749 C-Cl,1644 C-N	δ 5.4 ,1×1H (s, =C-H Ar) , δ 7.1 ,4×1H (d, =C-H Ar) , δ 1.2 ,1×2H (s, -CH_2), δ 2.2 ,1×3H (s, S-CH_3), δ 3.5 ,1×1H (d, CHCl) ,), δ 6.7 ,4×1H (m, C-H Ar) , δ 6.6 ,1×1H (s,2 C-OH Ar) .
6e	$C_{23}H_{20}ClN_5O_3S$	1602(C=C – Ar), 1619 -1524 N=O C-NO_2 Stretching,1652 C=N str ,3055 C-H str,1616 N-N str ,2582=C-S , 784 -C-S, 1719 C=O , 752 C-Cl, 1648 C-N.	δ 5.6 ,1×1H (s, =C-H Ar) , δ 7.3 ,4×1H (d, =C-H Ar) , δ 1.4 ,1×2H (s, -CH_2), δ 2.3 ,1×3H (s, S-CH_3), δ 3.7 ,1×1H (d, CHCl) ,), δ 6.9 ,4×1H (m, C-H Ar) , δ 2.5, 3×1H (s,C- CH_3 Ar) .
7a	$C_{21}H_{18}N_6O_3S_2$	1604(C=C – Ar), 1669 -1530 N=O C-NO_2 Stretching,1647 C-N str ,3048 C-H str,1614 N-N str ,2577=C-S , 785 -C-S, 1714 C=O 748 C-Cl, 1643 C-N	5.5 ,1×1H (s, =C-H Ar) , δ 5.7 ,4×1H (d, =C-H Ar) , δ 1.2 ,1×2H (s, -CH_2), δ 2.3 ,1×3H (s, S-CH_3), δ 2.4 ,1×1H (s, CH) ,), δ 4.5,1×2H (s, C-CH_2S) , δ 6.5, 5×1H (m,CH Ar) .
7b	$C_{21}H_{18}N_6O_4S_2$	1605(C=C – Ar), 1665 -1532 N=O C-NO_2 Stretching,1653 C-N str ,3051 C-H str,1615	5.7 ,1×1H (s, =C-H Ar) , δ 5.6 ,4×1H (d, =C-H Ar) , δ 1.4 ,1×2H (s, -CH_2), δ 2.4 ,1×3H (s, S-

		N-N str ,2581=C-S , 782 -C-S, 1715 C=O, 744 C-Cl, 1640 C-N	CH_3), δ 2.5 ,1×1H (s, CH) ,), δ 4.3,1×2H (s, C-CH_2S) , δ 6.6, 4×1H (m,CH Ar) , δ 6.6 ,1×1H (s, 4C-OH Ar) .
7c	$C_{21}H_{17}ClN_6O_3S_2$	1602(C=C – Ar), 1664 -1528 N=O C-NO_2 Stretching,1646 C-N str ,3050 C-H str,1613 N-N str ,2580=C-S , 781 -C-S, 1714 C=O 748 C-Cl, 1643 C-N	5.5 ,1×1H (s, =C-H Ar) , δ 5.4 ,4×1H (d, =C-H Ar) , δ 1.3 ,1×2H (s, -CH_2), δ 2.2 ,1×3H (s, S-CH_3), δ 2.3 ,1×1H (s, CH) ,), δ 4.1,1×2H (s, C-CH_2S) , δ 6.4, 4×1H (m,CH Ar) .
7d	$C_{21}H_{18}N_6O_4S_2$	1603(C=C – Ar), 1663 -1529 N=O C-NO_2 Stretching,1655 C-N str ,3051 C-H str,1616 N-N str ,2581=C-S , 782 -C-S, 1714 C=O 748 C-Cl, 1643 C-N	5.6 ,1×1H (s, =C-H Ar) , δ 5.5 ,4×1H (d, =C-H Ar) , δ 1.2 ,1×2H (s, -CH_2), δ 2.5 ,1×3H (s, S-CH_3), δ 2.4 ,1×1H (s, CH) ,), δ 4.2,1×2H (s, C-CH_2S) , δ 6.5, 4×1H (m,CH Ar) , δ 6.7 ,1×1H (s, 4C-OH Ar) .
7e	$C_{22}H_{20}N_6O_3S_2$	1604(C=C – Ar), 1660 -1527 N=O C-NO_2 Stretching,1650 C=N str ,3053 C-H str,1617 N-N str ,2580 =C-S , 783 -C-S, 1714 C=O 748 C-Cl, 1643 C-N	δ 5.7 ,1×1H (s, =C-H Ar) , δ 5.6 ,4×1H (d, =C-H Ar) , δ 1.3 ,1×2H (s, -CH_2), δ 2.3 ,1×3H (s, S-CH_3), δ 2.5 ,1×1H (s, CH) , δ 4.4,1×2H (s, C-CH_2S) , δ 6.6, 4×1H (m,CH Ar) , δ 2.4 ,1×3H (s, 4C-CH_3 Ar) .

Table 3 Antifungal activity of compounds 5(a-e), 6(a-e), 7(a-e) :

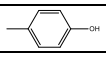
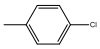
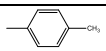
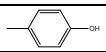
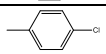
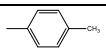
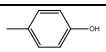
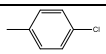
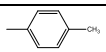
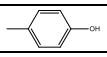
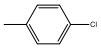
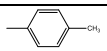
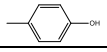
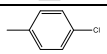
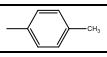
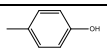
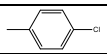
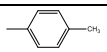
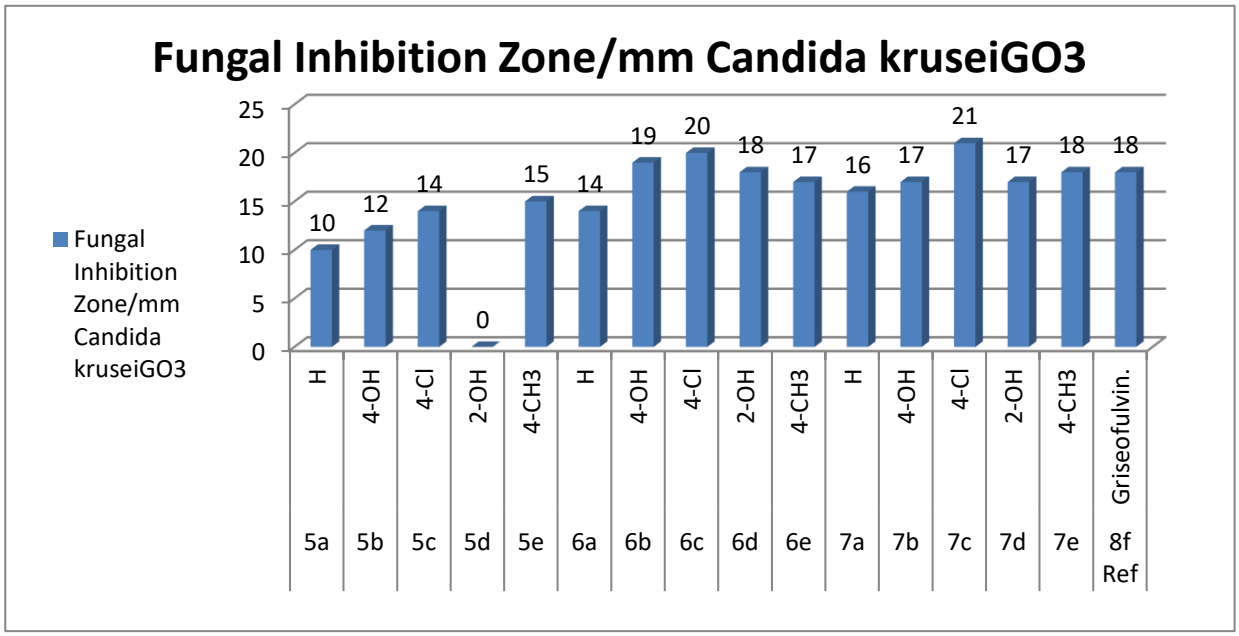
Compounds No	**R Group**	**Compound**	**Functional Group**	**Fungal Inhibition Zone/mm**		
				Candida kruseiGO3	**Candida GlabrataHO5**	**Parapsilosis 22019**
5a		$C_{19}H_{16}N_6O_2S$	H	10	-	12
5b		$C_{19}H_{16}N_6O_3S$	4-OH	12	11	14
5c		$C_{19}H_{15}ClN_6O_2S$	4-Cl	14	14	16
5d		$C_{19}H_{16}N_6O_3S$	2-OH	-	11	-
5e		$C_{20}H_{18}N_6O_2S$	4-CH_3	15	12	13
6a		$C_{22}H_{18}ClN_5O_3S$	H	14	13	15
6b		$C_{22}H_{18}ClN_5O_4S$	4-OH	19	17	20
6c		$C_{22}H_{17}Cl_2N_5O_3S$	4-Cl	20	18	22
6d		$C_{22}H_{18}ClN_5O_4S$	2-OH	18	15	19
6e		$C_{23}H_{20}ClN_5O_3S$	4-CH_3	17	14	16
7a		$C_{21}H_{18}N_6O_3S_2$	H	16	15	20
7b		$C_{21}H_{18}N_6O_4S_2$	4-OH	17	17	22
7c		$C_{21}H_{17}ClN_6O_3S_2$	4-Cl	21	19	24
7d		$C_{21}H_{18}N_6O_4S_2$	2-OH	17	15	19
7e		$C_{22}H_{20}N_6O_3S_2$	4-CH_3	18	15	21
8f	Reference	Griseofulvin.	Ref.	18	16	22

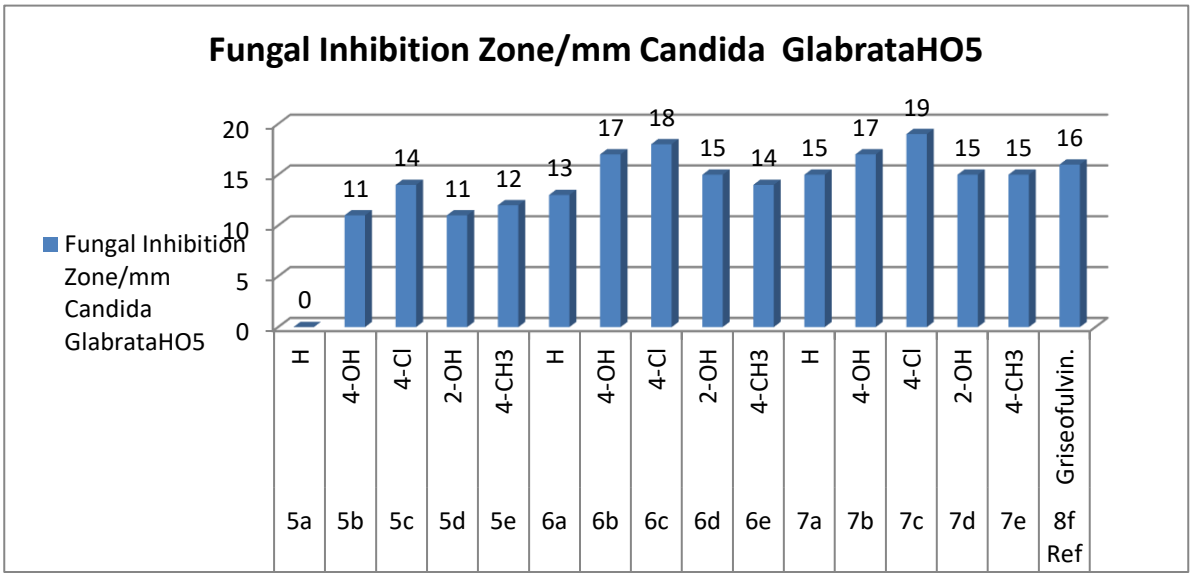
Table 4 Antibacterial activity of compounds 5(a-e), 6(a-e), 7(a-e)

Compounds No	**R Group**	**Compound**	**Functional Group**	**S. Aureus**	**E. coli**
5a		$C_{19}H_{16}N_6O_2S$	H		10

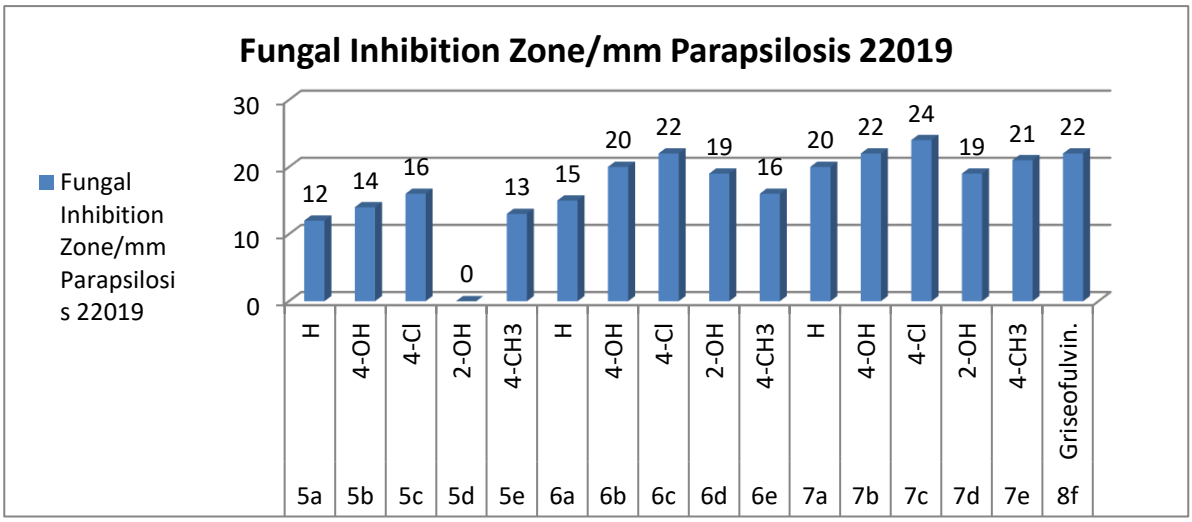
5b		$C_{19}H_{16}N_6O_3S$	4-OH	11	12
5c		$C_{19}H_{15}ClN_6O_2S$	4-Cl	13	13
5d		$C_{19}H_{16}N_6O_3S$	2-OH	11	-
5e		$C_{20}H_{18}N_6O_2S$	4-CH_3	12	13
6a		$C_{22}H_{18}ClN_5O_3S$	H	15	14
6b		$C_{22}H_{18}ClN_5O_4S$	4-OH	17	16
6c		$C_{22}H_{17}Cl_2N_5O_3S$	4-Cl	19	21
6d		$C_{22}H_{18}ClN_5O_4S$	2-OH	15	16
6e		$C_{23}H_{20}ClN_5O_3S$	4-CH_3	17	21
7a		$C_{21}H_{18}N_6O_3S_2$	H	15	16
7b		$C_{21}H_{18}N_6O_4S_2$	4-OH	18	19
7c		$C_{21}H_{17}ClN_6O_3S_2$	4-Cl	20	21
7d		$C_{21}H_{18}N_6O_4S_2$	2-OH	16	19
7e		$C_{22}H_{20}N_6O_3S_2$	4-CH_3	17	18
8f	Reference	Griseofulvin.	Ref	17	20



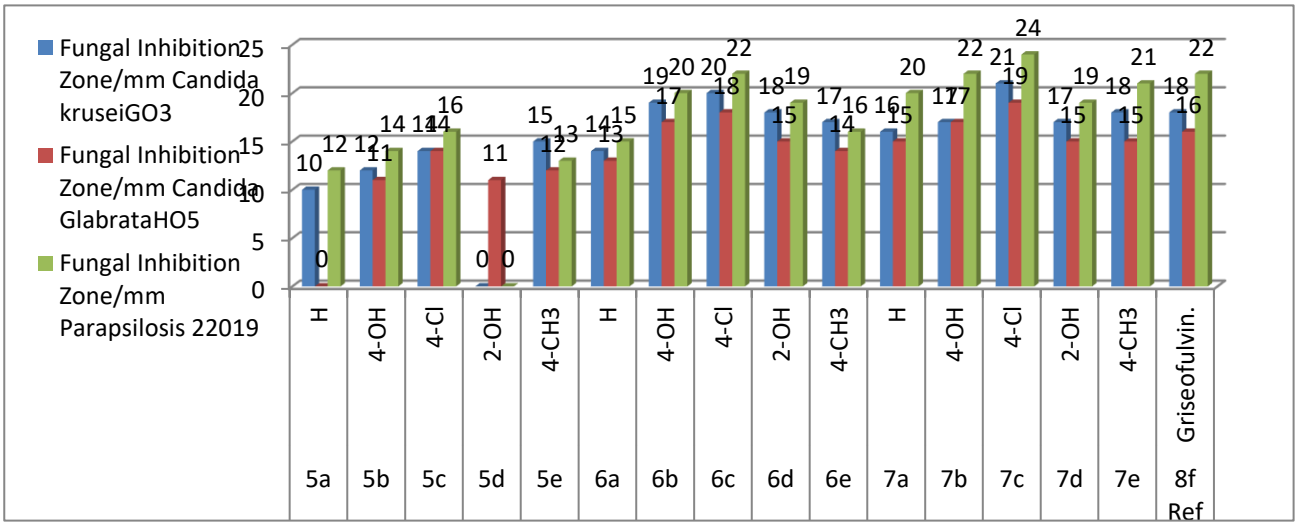
Graph1: Fungal inhibition Zone/mm of 5a-5e, 6a-6e,7a-7e against Krusei GO3



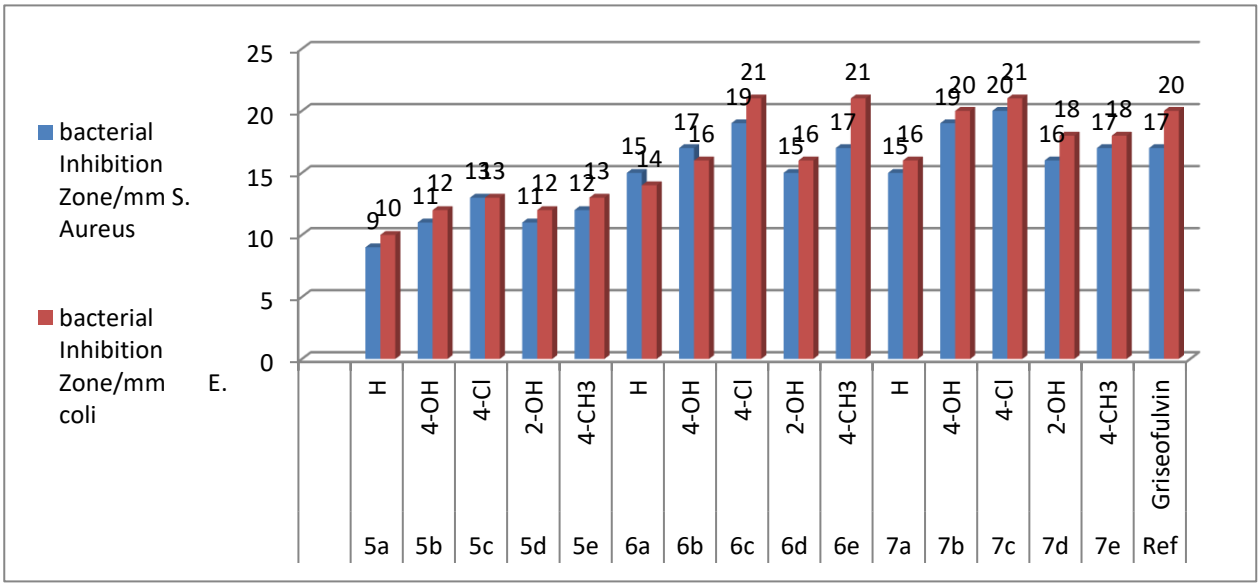
Graph: 2 Fungal inhibition Zone/mm of 5a-5e,6a-6e,7a-7e against Glabrata HO5



Graph3: Fungal inhibition Zone/mm of 5a-5e, 6a-6e, 7a-7e containing various active function groups against Parapsilosis 22019.



Graph 4: Comparative Studies of All Three Stains of compound 5a-5e, 6a-6e, 7a-7e derivatives



Graph: 5 Bacterial inhibition Zone/mm of 5a-5e,6a-6e,7a-7e agains Auerus and E. Coli. Con-taining various function groups

Result and Discussion:

Pharmacological evaluation (Antifungal and antibacterial): Synthesized derivatives were tested for their antifungal and antibacterial activity. First of all, it was incubated with loopful growth culture of the organism activity and it was recorded by disc diffusion method .Take the nutrient agar-agar and it was poured onto the sterilized Petri disc. The plate was incubated at 20-25 0C at 25 hr for antibacterial and 45 hr at 370 C for antifungal. The material was allowed to set 1-1.4 h .The 5% solution of newly synthesized compound was seeded with the help of sterilize syringe. Disc diffusion process was used against Candida krusie GO3, Candida Glabra-ta HO5 and Parapsilosis 22019. The gram +ve staphylococcus aures and E coli and data were recorded in table 4. The standard drugs Griseofulvin were also screen under similar condition and their comparative study was performed.

Fungal activity:

All novel different synthesized derivatives were tested as antifungal in their biological proper-ties. Antifungal properties were confirmed by use of disc diffusion procedure 20 against Can-dida krusei GO3, Candida Glabrata HO5, and Parapsilosis. Inhibition effect of stain confirmed and recorded in (mm). Antifungal property of new synthesized compounds, compared with the standard drugs Griseofulvin.

Antibacterial activity: All the newly derivatives are tested against the gram +ve staphylococ-cus aures and E coli micro organism.

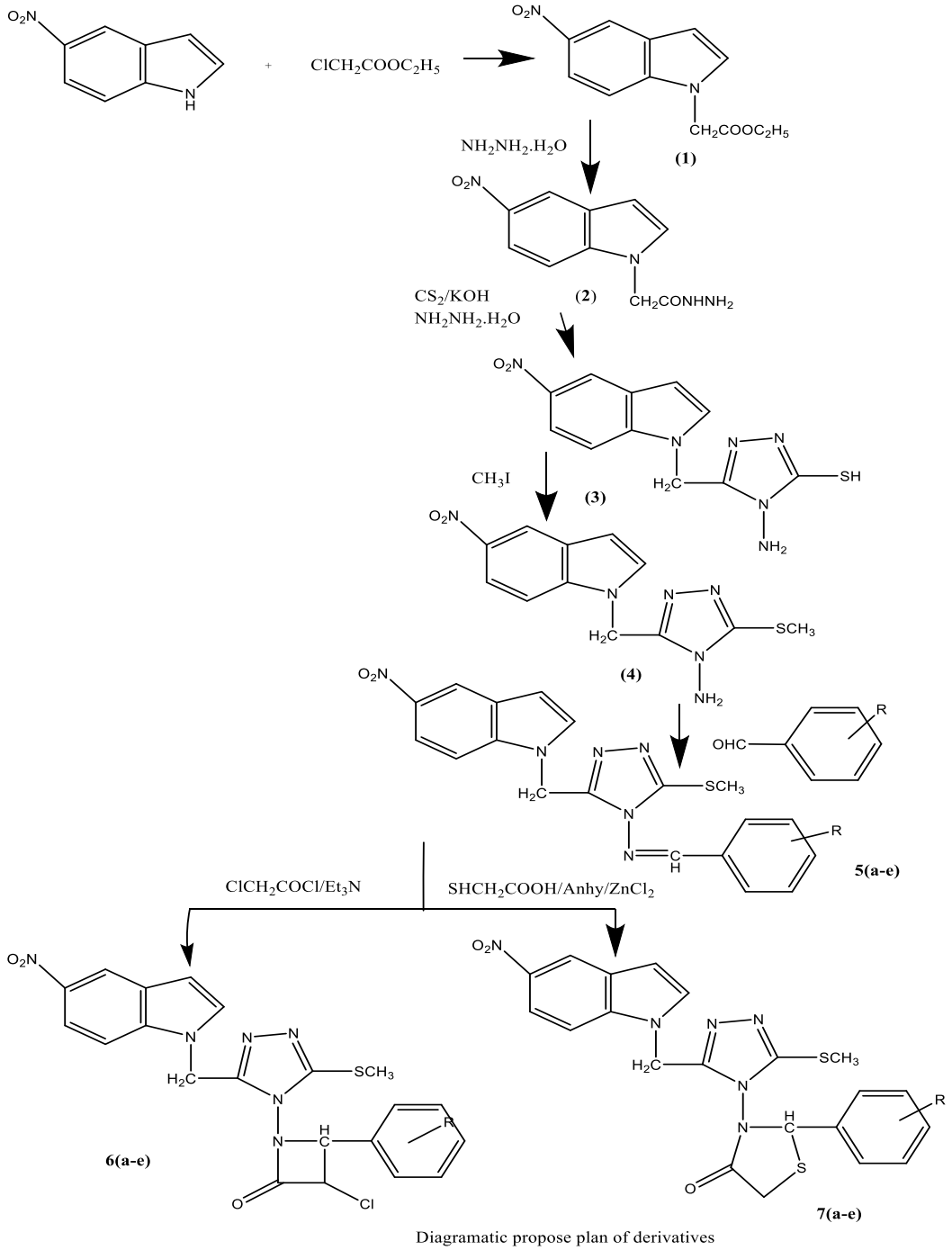
Table -3 and 4 pertaining to the antifungal, antibacterial activity, data of 6a-6e azetidinone, 7a-7e thiazolidinone indicates that these compounds showed antifungal activity. Amongst aze-tidenones of these compounds 6b, 6c, and thiazolidine 7b, 7c were found to be relatively more effective against all three stains of fungi showing a zone of inhibition, respectively. It was no-ticed from the data that other substitutes of compounds, were also showed better activity against organism. In similar pattern, compounds 6c, 6d, 7c, 7d thiazolidinone derivatives was also show the antifungal, antibacterial activity. While other similar compound 6a, 6b 6e 7a, 7b 7e were also exhibited moderate Activity.

Conclusion

Newly novel synthesised drugs derivatives of azetidenone, thiazolidinone containing triazole, indole moiety were exhibited the better results to protect from different class of diseases. These drugs were very useful to protect from alive organism as compare to earlier synthesis drug and it may represent activity against different fungal and bacterial disease. Thiazolidinone, azet-idinone linkage enhances the activity of novel drugs and decrease the toxicity. 4–chloro azet-idinone derivatives 6c, 20 mm,18mm ,22 mm and 4-Chloro substituted thiazolidinone 7c, 21mm, 19mm, and 24mm were shown the better antifungal activity against C. krusei GO3, Glabarata HO5 , Parapsilosis respectively and it was comperare with standared drug gresioful-vin. These were show antibacterial activity 6c, 19 mm, 21mm and 7c 20mm, 21mm as compare with standard drug Griseofulvin. The derivatives of azetidinone, aromatics substituted- OH , at 2 position 6d -11mm and at 4,OH 6b ,19mm,17mm,20mm and 6e, 4-CH3 position 17mm,14mm,16mm, which represent the moderate antifungal activity, respectively . while The derivatives of thiazolidinone, aromatics substituted- OH , at 2 position 7d-17 mm 15mm, 19mm and at 4,OH 7b ,17mm,17mm,22mm and 7e, 4-CH3 position

18mm,15mm,21mm, which represent the moderate antifungal activity, respectively.

Graph -1 ,2,3,4 represent the proper value of inhibition zone. 1st Graph represent the anti fun-gal activity against C Krusie GO3 while Graph 2 show the affectivity against Candida glabrata HO5 while Graph 3 represent the antifungal properly against stain Parapsilosis . Study of de-rivatives ,Graph 4 indicates comparative study and information of its affectivity against various antifungal stain . Graph 5 indicates study of antibacterial.



Diagramatic propose plan of derivatives

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