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Research

Antimicrobial Screening of Some Heterocyclic Compounds in DMSO Solutions

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Abstract

Some novel heterocyclic compounds such as thiazolidinones, dihydropyrazoles and oxazolines, have been synthesized and their structure confirmation was done by spectroscopic techniques such as IR, NMR and mass. The antimicrobial screening of the synthesized compounds was done in DMSO and DMF.

Key Words: Thiazolidinones; Dihydropyrazoles; Oxazolines; DMSO; Antibacterial Activity; Antifungal Activity

Introduction

The molecular manipulation of promising lead compounds is still a major line of approach to new drugs. Molecular manipulations involves the efforts to combine the separate groups of similar activity into one compounds, thus making structural changes into the compound leading to changes in the biological activity.

Biological activity spectrum of a compound represents the pharmacological effects, physiological and biochemical mechanisms of action, specific toxicity that can be revealed in compound's interaction with biological system. Further, it describes the intrinsic properties of the compound, which depends on its structure.

Heterocyclic compounds are the most important class of organic compounds which are found to possess interesting biological activities [1-8]. Some of these heterocycles also exist in natural drugs [9-12].

Some of important heterocycleic compounds such as thiazolidinones, dihydropyrazoles and oxazolines have always attracted researchers because of their efficiency towards various pharmacological usages. These heterocycles are known to possess valuable bioactivities like, anti-inflammatory [13], antitumor [14], cytotoxic [15], anticancer [16], antibacterial [17], anti-HIV [18], insecticidal [19], fungicidal [20], tuberculostatic [21], anthelmintic [22], antiproliferative [23], antimalarial [24], anticonvulsunt [25], analgesic [26], antidiabatic [27], antidepressant [28], antiamoebic [29], antiarrythmic [10], cardiovascular [30] etc.

In view of the biological/pharmacological significance of these heterocycles, in the present work, some new nitrogen, sulphur and oxygen containing heterocyclic compounds are synthesized. The synthesized derivatives are of thiazolidinones, dihydropyrazoles and oxazolines and their structures were elucidated on the basis of IR, MASS and 1H NMR spectral data. All the compounds have been screened for their in-vitro biological activity in DMSO by agar well diffusion method.

Experimental

Synthesis of Dihydropyrazoles

Synthesis of Substituted Chalcones: In a methanolic solution of equimolar substituted aldehydes and substituted acetophenones, 3-4 drops of saturated sodium hydroxide solution (as a catalyst) was added and the solution was stirred for 24 hours. After the completion of reaction, the reaction mass was filtered and washed with chilled methanol. Similarly, other compounds are also prepared using different aldehydes.

Synthesis of 6-Chloro-4-Phenylchroman-2-One: To an equimolar mixture of cinnamic acid and p-chloro phenol, catalytic amount of concentrated H_2SO_4 was added with stirring and the reaction mixture was heated at 120°-125°C for 3-4 hours. The reaction mixture was then cooled

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up to 80°C. To this solution, a binary mixture of toluene and water (50:50) was added and solution was stirred for 30 minutes. The toluene layer was separated and washed with saturated sodium bicarbonate solution and water. The resulting toluene layer was then dried using sodium sulphate under vacuum. To the resulting oily mass, isopropyl alcohol was added and stirring was done for 30 minutes at 0-5° C. The product was filtered, washed with chilled iso-propyl alcohol and dried to give 6-chloro-4-phenylchroman-2-one.

Synthesis of Methyl 3-(2-(Benzyloxy)-5-Chlorophenyl)-3-Phenyl Propanoate: A mixture of 6-chloro-4-phenylchroman-2-one, potassium carbonate, benzyl chloride, sodium iodide, acetone and methanol was heated with stirring. After the completion of reaction, solvent was removed under vacuum. To the reaction mixture, a binary mixture of dichloromethane and water (50:50) was added and the resulting solution was stirred for 30 minutes. The organic layer was separated and dried using sodium sulphate and distilled completely under vacuum to get oily residue of 3-(2-(benzyloxy)-5-chlorophenyl)-3-phenylpropanoate.

Synthesis of 3-(2-(Benzyloxy)-5-Chlorophenyl)-3-Phenyl Propane Hydrazide: To a methanolic solution of 3-(2-(benzyloxy)-5-chlorophenyl)-3-phenylpropanoate, hydrazine hydrate was added and the resulting mixture was refluxed for 10-12 hours. The reaction mass was then filtered and washed with chilled methanol to give pure product.

Synthesis of 3-(2-Benzyloxy)-5-Chlorophenyl)-1-(3-(4-Chlorophenyl)-5-(P-Tolyl)-4,5-Dihydro-1H-Pyrazol-1yl)-3-Phenylpropan-1-One: To an equimolar mixture of 3-(2-benzyloxy)-5-chlorophenyl)-3-phenyl propane hydrazide and different substituted chalcones, small amount of glacial acetic acid was added with stirring. The reaction mixture was refluxed on oil bath for 12 hours. The mixture was then poured into crushed ice to give solid product. The solid mass was filtered and purified by column chromatography using eluent hexane: ethyl acetate (7:3). Similarly other compounds were also prepared with different chalcones.

Synthesis of Oxadiazoles

Synthesis 0f 2-(2-(2-(Benzyloxy)-5-Chlorophenyl)-2-Phenylethyl)-5-(O Tolyl)-1, 3, 4-Oxa Diazole: An equimolar mixture of 3-(2-(benzyloxy)-5-chlorophenyl)-3-phenyl propane hydrazide (synthesized above) and different aryl acids in phosphorous oxychloride was refluxed for 10-12 hours at 100°C with continue stirring. After completion of the reaction, reaction was poured in to ice and neutralized with saturated sodium bicarbonate solution. The product was extracted in ethyl acetate. The organic extract was washed with water and the resulting crude product was purified by column chromatography.

Synthesis of Thiazolidinones

In equimolar solution of 4-((1H-1,2,4-triazol-1yl)methyl) aniline and different substituted aromatic aldehydes in methanol, catalytic amount of glacial acetic acid was added and the reaction mixture was heated with stirring for 10-12 hrs. After the completion of reaction, the reaction mass was filtered, washed with chilled methanol and then dried to give substituted azomethines. The other compounds were prepared similarly by treating with corresponding aldehydes.

A solution of azomethine (synthesized above) and 2-merccapto acetic acid (1:3 ratio) in toluene was refluxed for 10-12 hours in a dean-stark assembly with continuous stirring. After completion of the reaction, the content was cooled to room temperature and then neutralized with sodium bicarbonate solution. The organic extract was washed with water (2 x 10 ml), dried using sodium sulphate and distilled completely under vacuum and give yellow colored product which is thiazolidinone.

The formation of synthesized compounds was checked by thin-layer chromatography and accomplished on 0.2-mm pre coated plates of silica gel G60 F_{254} (Merck). Visualization was made with UV light (254 and 365nm) or with an iodine vapor.

The melting point of all the synthesized compounds was determined in open capillary tubes and was uncorrected. The characterization of all these compounds was done by IR, NMR and mass spectral data. The IR spectra were recorded on Shimadzu FT-IR-8400 instrument using KBr pellet method. The Mass spectra were recorded on Shimadzu GC-MS-QP-2010 model using direct inlet probe technique. ^{1}H NMR and ^{13}C NMR was determined in DMSO solution on a Bruker Ac 400 MHz spectrometer.

Antimicrobial Screening

The antibacterial and antifungal activities of all synthesized compounds were studied in DMSO. All the synthesized compounds were recrystallized prior to use.

The solvent DMSO was also purified before use by standard method [31]. For all the compounds, agar well diffusion method was used.

Test Microorganisms

The synthesized compounds were tested for its antibacterial activity against three Gram positive bacteria Stephylococcus aureus ATCC29737, Bacillus cereus ATCC11778 and Micrococcus flavus ATCC10240 and three Gram negative bacteria Escharichia coli NCIM2931, Salmonella tuphimurrium ATCC23564 and Proteus mirabilis NCIM2241 and two antifungal strains Candida glabrata NCIM3448 and Candida neoformans NCIM3542 The microorganisms were obtained from National Chemical Laboratory (NCL), Pune, India and were maintained at 4°C on nutrient agar slants.

Preparation of Test Compounds

The solutions were prepared at a concentration of 1 mg/µl for all the compounds. This is the minimum inhibitory concentration (MIC) which was observed by experiment using different concentrations of compounds in DMSO.

Preparation of the Plates and Microbiological Assay

The test organism was activated by inoculating a loop full of the strain in 25 ml of Nutrient broth/ Sabouraud Dextrose Broth and kept overnight on a rotary shaker. Mueller Hinton agar and Sabouraud Dextrose Agar medium were used for antibacterial and antifungal activity respectively. The assay was performed by agar well diffusion method [32,33]. 200 µl inoculums (1×10^8 cfu/ml) was introduced into molten Muller Hinton agar/ Sabouraud Dextrose agar and poured into Petri dishes when temperature was reached to 40 – 42°C. The media was solidified and wells were prepared in the seeded agar plates with the help of a cup borer (8.5 mm). 100 µl of the test compound (20 mg/ml DMSO) was introduced into the well and the plates were incubated at 37/28°C for 24 /48 h for bacteria and fungi, respectively. Dimethyl sulfoxide (DMSO) was taken as a negative control. All the tests were performed in triplicate under strict aseptic conditions. The microbial growth was determined by measuring the diameter of the zone of inhibition in mm.

Results and Discussion

The physical constants of all the synthesized compounds are given in Tables 1-3 and general structures of synthesized compounds are given in Figure 1.

Spectral Data

3-(2-benzyloxy)-5-chlorophenyl)-1-(5-(2-chlorophenyl)-3(4-fluorophenyl)-4,5-dihydro--1H- pyrazol-1yl)-3-phenylpropan-1-one (PAB-301). mp 162-164°C; IR (KBr): 3030(Ar, C-H str), 2956(C-H str), 2821(C-H str), 1692(C=O str), 1616(Ar, C=C str), 1563(Ar, C=C str), 1535(Ar, C=C str), 1479(C-H ben), 1078(C-O-C str), 1030(C-F str),736(C-Cl str) cm^{-1}; MS: m/z = 623 $[M]^+$

3-(2-(benzyloxy)-5-chlorophenyl)-1-(3-(4-nitrophenyl)-5-(p-tolyl)-4,5-dihydro-1H-pyrazol-1-yl)-3-phenylpropan-1-one (PAB-302). mp 154-156°C; IR (KBr): 3026(Ar, C-H str), 2914(C-Hstr), 1662(C=O str), 1613(Ar, C=C str), 1551(Ar, C=C str), 1533(Ar, C=C str), 1472(C-H ben), 1076(C-O-C str), 734(C-Cl str) cm^{-1}; MS: m/z = 630 $[M]^+$

3-(2-(benzyloxy)-5-chlorophenyl)-1-(5-(4-fluorophenyl)-3-(3-nitrophenyl)-4,5-di hydro- 1H- pyrazol-1-yl)-3-phenylpropan-1-one (PAB-303). mp 145-147°C; IR (KBr): 3061(Ar, C-H str), 1666(C=O str), 1626(Ar, C=C str), 1535(Ar, C=C str), 1479(C-H ben), 1020(C-O-C str), 1030(C-F str), 734(C-Cl str) cm^{-1}; MS: m/z = 634 $[M]^+$

3-(2-benzyloxy)-5-chlorophenyl)-1-(3-(4-chlorophenyl)-5-(3,4-dimethoxyphenyl)-4,5-dihydro-1H-pyrazol-1-yl)-3-phenylpropan-1-one (PAB-304). mp 178-180°C; IR (KBr) : 3029(Ar, C-H str), 2959(C-H str), 2829(C-H str), 1662(C=O str), 1617(Ar, C=C str), 1563(Ar, C=C str), 1535(Ar, C=C str), 1443(C-H ben), 1078(C-O-C str), 1030(C-F str),739(C-Cl str) cm^{-1}; MS: m/z = 665 $[M]^+$

3-(2-(benzyloxy)-5-chlorophenyl)-1-(5-(4-fluorophenyl)-3-(4-nitrophenyl)-4,5-di hydro-1H-pyrazol-1-yl)-3-phenylpropan-1-one (PAB-305). mp 170-172°C; IR (KBr): 3064(Ar, C-H str), 1668(C=O str), 1599(Ar, C=C str), 1404(C-H ben), 1012(C-O-C str), 1028(C-F str), 734(C-Cl str) cm^{-1}; MS: m/z = 634 $[M]^+$

3-(2-(benzyloxy)-5-chlorophenyl)-1-(3-(2-nitrophenyl)-5-(4-nitrophenyl)-4,5-dihydro -1H-pyrazol-1-yl)-3-phenylpropan-1-one (PAB-306). mp 149-151°C; IR (KBr): 3069(Ar, C-H str), 2969(C-H str), 2822(C-H str), 1669(C=O str), 1616(Ar, C=C str), 1539(Ar, C=C str), 1476(C-H ben), 1026(C-O-C str), 739(C-Cl str) cm^{-1}; MS: m/z = 661 $[M]^+$

3-(2-(benzyloxy)-5-chlorophenyl)-1-(3-(4-chlorophenyl)-5-phenyl-4,5-dihydro-1H-pyrazol-1-yl)-3-phenylpropan-1-one (PAB-307). mp 138-140°C; IR (KBr): 3079(Ar, C-H str), 2967(C-H str), 2842(C-H str), 1661(C=O str), 1636(Ar, C=C str), 1519(Ar, C=C str), 1472(C-H ben), 1023(C-O-C str), 750 (C-H ben), 729(C-Cl str) cm^{-1}; MS: m/z = 605 $[M]^+$

3-(2-(benzyloxy)-5-chlorophenyl)-1-(3-(4-chlorophenyl)-5-(2-nitrophenyl)-4,5-dihydro-1H pyrazol-1-yl)-3-phenylpropan-1-one (PAB-308). mp 161-163°C; IR (KBr): 3067(Ar, C-H str), 1676(C=O str), 1636(Ar, C=C str), 1532(Ar, C=C str), 1473(C-H ben), 1028(C-O-C str), 745(C-H ben), 734(C-Cl str) cm^{-1}; MS: m/z = 650 $[M]^+$

3-(2-(benzyloxy)-5-chlorophenyl)-1-(5-(3,4-dimethoxyphenyl)-3-(4-fluorophenyl)-4,5-dihydro-1H-pyrazol-1-yl)-3-phenylpropan-1-one (PAB-309). mp 140-142°C; IR (KBr): 3025(Ar, C-H str), 2956(C-H str), 2829(C-H str), 1666(C=O str), 1617(Ar, C=C str), 1573(Ar, C=C str), 1532(Ar, C=C str), 1453(C-H ben), 1071(C-O-C str), 1023(C-F str), 736(C-Cl str) cm^{-1}; MS: m/z = 649 $[M]^+$

3-(2-(benzyloxy)-5-chlorophenyl)-1-(5-(2-nitrophenyl)-3-phenyl-4,5-dihydro-1H-pyrazol-1-yl)3-phenylpropan-1-one (PAB-310). mp 147-149°C; IR (KBr): 3073(Ar, C-H str), 2963(C-H str), 2862(C-H str), 1667(C=O str), 1626(Ar, C=C str), 1520(Ar, C=C str), 1471(C-H ben), 1025(C-O-C str), 750(C-H ben), 739(C-Cl str) cm^{-1}; MS: m/z = 616 $[M]^+$

3-(2-(benzyloxy)-5-chlorophenyl)-1-(3-(4-chlorophenyl)-5-(p-tolyl)-4,5-dihydro-1H-pyrazol-1-yl)-3-phenylpropan-1-one (PAB-311). mp 167-169°C; IR (KBr): 3043(Ar, C-H str), 2922(C-H str), 2847(C-H str), 1606(C=O str), 1529(Ar, C=C str), 1466(C-H ben), 1022(C-O-C str), 750 (C-H ben), 729(C-Cl str) cm^{-1}; ^{1}H NMR (400 MHz, DMSO): δ ppm 2.45 (s, 3H, $-CH_3$), 3.0-3.04 (d, 2H, $-CH_2$), 3.54-3.59 (d, 2H, $-CH_2$), 3.93 (t, 1H,-CH), 4.93-5.01(m, 3H, $-CH_2$-CH),6.58-6.62 (dd, 2H, ArH), 6.84-6.88 (t, 4H, ArH), 6.97-7.35 (m,7H, ArH), 7.42-7.51 (m, 7H, ArH), 8.05 (s, 1H, ArH). 13C NMR (100 MHz, DMSO): δ ppm 20.47, 36.63, 43.41, 44.63, 56.28, 61.64, 108.46, 114.13, 117.43, 119.28, 119.80, 124.11, 129.29, 130.19, 132.77, 134.38, 141.49, 143.20, 152.48, 155.79, 168.52. MS: m/z = 619 $[M]^+$

3-(2-(benzyloxy)-5-chlorophenyl)-1-(5-(4-chlorophenyl)-3-phenyl-4,5-dihydro-1H-pyrazol-1-yl)-3-phenylpropan-1-one (PAB-312.) mp 164-166°C; IR (KBr): 3069(Ar, C-H str), 2967(C-H str), 2832(C-H str),

1667(C=O str), 1631(Ar, C=C str), 1519(Ar, C=C str), 1474(C-H ben), 1022(C-O-C str), 743(C-H ben), 732(C-Cl str) cm^{-1}; MS: m/z = 605 $[M]^+$

3-(2-(benzyloxy)-5-chlorophenyl)-1-(3-(4-bromophenyl)-5-(4-fluorophenyl)-4,5-dihydro-1H-pyrazol-1-yl)-3-phenylpropan-1-one (PAB-313). mp 175-177°C; IR (KBr): 3059(Ar, C-H str), 2961(C-H str), 2822(C-H str), 1667(C=O str), 1631(Ar, C=C str), 1529(Ar, C=C str), 1472(C-H ben), 1032(C-O-C str), 1023(C-F str), 740(C-H ben), 733(C-Cl str), 575(C-Br str) cm^{-1}; MS: m/z = 667 $[M]^+$

3-(2-(benzyloxy)-5-chlorophenyl)-1-(3-(4-chlorophenyl)-5-(4-nitrophenyl)-4,5-di hydro-1H-pyrazol-1-yl)-3-phenylpropan-1-one (PAB-314). mp 180-182°C; IR (KBr): 3062(Ar, C-H str), 1679(C=O str), 1639(Ar, C=C str), 1542(Ar, C=C str), 1475(C-H ben), 1029(C-O-C str), 741(C-H ben), 731(C-Cl str) cm^{-1}; MS: m/z = 650 $[M]^+$

3-(2-(benzyloxy)-5-chlorophenyl)-1-(5-(4-chlorophenyl)-3-(4-fluorophenyl)-4,5-dihydro -1H-pyrazol-1-yl)-3-phenylpropan-1-one (PAB-315). mp 144-146°C; IR (KBr): 3069(Ar, C-H str), 2963(C-H str), 2826(C-H str), 1677(C=O str), 1635(Ar, C=C str), 1527(Ar, C=C str), 1474(C-H ben), 1039(C-O-C str), 1027(C-F str), 740(C-H ben), 732(C-Cl str) cm^{-1}; MS: m/z = 623 $[M]^+$

3-(2-(benzyloxy)-5-chlorophenyl)-1-(3-(4-fluorophenyl)-5-(4-nitrophenyl)-4,5-dihydro-1H-pyrazol-1-yl)-3-phenylpropan-1-one (PAB-316). mp 135-137°C; IR (KBr): 3052(Ar, C-H str), 1677(C=O str), 1634(Ar, C=C str), 1541(Ar, C=C str), 1476(C-H ben), 1037(C-O-C str), 1022(C-F str), 743(C-H ben), 731(C-Cl str) cm^{-1}; MS: m/z = 634 $[M]^+$

3-(2-(benzyloxy)-5-chlorophenyl)-1-(3-(4-chlorophenyl)-5-(4-fluorophenyl)-4,5-dihydro-1H-pyrazol-1-yl)-3-phenylpropan-1-one (PAB-317). mp 161-163°C; IR (KBr): 3068(Ar, C-H str), 2965(C-H str), 2829(C-H str), 1674(C=O str), 1632(Ar, C=C str), 1521(Ar, C=C str), 1475(C-H ben), 1035(C-O-C str), 1028(C-F str), 742(C-H ben), 735(C-Cl str) cm^{-1}; MS: m/z = 623 $[M]^+$

3-(2-(benzyloxy)-5-chlorophenyl)-1-(3-(4-chlorophenyl)-5-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazol-1-yl)-3-phenylpropan-1-one (PAB-318). mp 174-176°C; IR (KBr): 3021(Ar, C-H str), 2953(C-H str), 2822(C-H str), 1662(C=O str), 1619(Ar, C=C str), 1579(Ar, C=C str), 1531(Ar, C=C str), 1455(C-H ben), 1072(C-O-C str), 1021(C-F str), 737(C-Cl str) cm^{-1}; MS: m/z = 635 $[M]^+$

3-(2-(benzyloxy)-5-chlorophenyl)-1-(3-(4-fluorophenyl)-5-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazol-1-yl)-3-phenylpropan-1-one (PAB-319). mp 162-164°C; IR (KBr): 3029(Ar, C-H str), 2957(C-H str), 2826(C-H str), 1666(C=O str), 1611(Ar, C=C str), 1572(Ar, C=C str), 1533(Ar, C=C str), 1453(C-H ben), 1071(C-O-C str), 1024(C-F str), 733(C-Cl str) cm^{-1}; MS: m/z = 619 $[M]^+$

3-(2-(benzyloxy)-5-chlorophenyl)-1-(5-(4-fluorophenyl)-3-phenyl-4,5-dihydro-1H-pyrazol-1-yl)-3-phenylpropan-1-one (PAB-320). mp 150-152°C; IR (KBr): 3024(Ar, C-H str), 2955(C-H str), 2820(C-H str), 1660(C=O str), 1613(Ar, C=C str), 1572(Ar, C=C str), 1531(Ar, C=C str), 1443(C-H ben), 1077(C-O-C str), 1022(C-F str), 731(C-Cl str) cm^{-1}; MS: m/z = 589 $[M]^+$

2-(2-(2-(benzyloxy)-5-chlorophenyl)-2-phenylethyl)-5-(4-methoxyphenyl)-1, 3, 4-

oxadiazole (PAB-401) mp 182-184°C; IR (KBr): 3055(Ar, C-H str), 2959(C-H str), 2838(C-H str), 1611(Ar, C=C str), 1553(Ar, C=C str), 1528(Ar, C=C str), 1452(C-H ben), 1237(C-C str), 1080(C-O-C str), 1034(C-O-C str), 748(C-Cl str) cm^{-1}; MS: m/z = 496$[M]^+$

2-(2-(2-(benzyloxy)-5-chlorophenyl)-2-phenylethyl)-5-(4-bromophenyl)-1,3,4-oxadiazole (PAB-402) mp 160-162°C; IR (KBr): 3045(Ar, C-H str), 2955(C-H str), 2818(C-H str), 1616(Ar, C=C str), 1553(Ar, C=C str), 1528(Ar, C=C str), 1462(C-H ben), 1230(C-Cstr), 1078(C-O-C str), 1044(C-O-C str), 768(C-Cl str), 728(C-Br str) cm^{-1}; MS: m/z = 545 $[M]^+$

2-(2-(2-(benzyloxy)-5-chlorophenyl)-2-phenylethyl)-5-(4-chlorophenyl)-1,3,4 oxadiazole (PAB-403). mp 158-160°C; IR (KBr): 3040(Ar, C-H str), 2953(C-H str), 2813(C-H str), 1614(Ar, C=C str), 1548(Ar, C=C str), 1534(Ar, C=C str), 1461(C-H ben), 1222(C-Cstr), 1071(C-O-C str), 1033(C-O-C str), 745(C-Cl str) cm^{-1}; MS: m/z =501 $[M]^+$

2-(2-(2-(benzyloxy)-5-chlorophenyl)-2-phenylethyl)-5-(p-tolyl)-1,3,4-oxadiazole (PAB-404). mp 172-174°C; IR (KBr): 3035(Ar, C-H str), 2949(C-H str), 2858(C-H str), 1543(Ar, C=C str), 1521(Ar, C=C str), 1462(C-H ben), 1247(C-C str), 1063(C-O-C str), 1032(C-O-C str), 745(C-Cl str) cm^{-1}; MS: m/z = 480 $[M]^+$

2-(2-(2-(benzyloxy)-5-chlorophenyl)-2-phenylethyl)-5-phenyl-1,3,4-oxadiazole (PAB-405). mp 138-140°C; IR (KBr): 3043(Ar, C-H str), 2941(C-H str), 2848(C-H str), 1553(Ar, C=C str), 1527(Ar, C=C str), 1474(C-H ben), 1246(C-C str), 1073(C-O-C str), 1029(C-O-C str), 748(C-Cl str), cm^{-1}; MS: m/z = 466 $[M]^+$

2-(2-(2-(benzyloxy)-5-chlorophenyl)-2-phenylethyl)-5-(2,4-dichlorophenyl)-1,3,4-oxadiazole (PAB-406). mp 147-149°C; IR (KBr): 3065(Ar, C-H str), 2951(C-H str), 2835(C-H str), 1631(Ar, C=C str), 1551(Ar, C=C str), 1523(Ar, C=C str), 1452(C-H ben), 1237(C-C str), 1070(C-O-C str), 1064(C-O-C str), 749(C-Cl str) cm^{-1}; MS: m/z =535[M $]^+$

2-benzyl-5-(2-(2-(benzyloxy)-5-chlorophenyl)-2-phenylethyl)-1,3,4-oxadiazole (PAB-407). mp 122-124°C; IR (KBr): 3032(Ar, C-H str), 2937(C-H str), 2839(C-H str), 1546(Ar, C=C str), 1522(Ar, C=C str), 1476(C-H ben), 1073(C-O-C str), 1031(C-O-C str), 735(C-Cl str) cm^{-1}; MS: m/z = 480 $[M]^+$

2-(5-(2-(2-(benzyloxy)-5-chlorophenyl)-2-phenylethyl)-1,3,4-oxadiazol-2-yl)phenyl acetate (PAB-408). mp 176-178°C; IR (KBr): 3042(Ar, C-H

str), 2932(C-H str), 2831(C-H str), 1687(C=O str), 1556(Ar, C=C str), 1532(Ar, C=C str), 1465(C-H ben), 1063(C-O-C str), 1032(C-O-C str), 737(C-Cl str) cm^{-1}; MS: m/z = 524 $[M]^+$

2-(2-(2-(benzyloxy)-5-chlorophenyl)-2-phenylethyl)-5-(2-chloro-5-nitrophenyl)-1,3,4-oxadiazole (PAB-409). mp 184-186°C; IR (KBr): 3054(Ar, C-H str), 2934(C-H str), 2857(C-H str), 1542(N=O str), 1521 (Ar, C=C str), 1469(C-H ben), 1053(C-O-C str), 747(C-Cl str) cm^{-1}; MS: m/z = 546 $[M]^+$

2-(2-(2-(benzyloxy)-5-chlorophenyl)-2-phenylethyl)-5-(2-chlorophenyl)-1,3,4 oxadiazole (PAB-410). mp 145-147°C; IR (KBr): 3039(Ar, C-H str), 2945(C-H str), 2863(C-H str), 1535(Ar, C=C str), 1521(Ar, C=C str), 1467(C-H ben), 1062(C-O-C str), 1042(C-O-C str), 744(C-Cl str) cm^{-1}; MS: m/z =501 $[M]^+$

2-(2-(2-(benzyloxy)-5-chlorophenyl)-2-phenylethyl)-5-(3-chlorophenyl)-1,3,4-oxadiazole (PAB-411). mp 152-154°C; IR (KBr): 3037(Ar, C-H str), 2949(C-H str), 2860(C-H str), 1532(Ar, C=C str), 1530(Ar, C=C str), 1464(C-H ben), 1060(C-O-C str), 1038(C-O-C str), 738(C-Cl str) cm^{-1}; MS: m/z =501 $[M]^+$

2-(2-(2-(benzyloxy)-5-chlorophenyl)-2-phenylethyl)-5-(3-nitrophenyl)-1,3,4-oxadiazole (PAB-412) mp 133-135°C; IR (KBr): 3043(Ar, C-H str), 2954(C-H str), 2856(C-H str), 1540(N=O str), 1533(Ar, C=C str), 1514(Ar, C=C str), 1469(C-H ben), 1053(C-O-C str), 1042(C-O-C str), 743(C-Cl str) cm^{-1}; MS: m/z = 511 $[M]^+$

2-(2-(2-(benzyloxy)-5-chlorophenyl)-2-phenylethyl)-5-(3,4-dimethoxyphenyl)-1,3,4-oxadiazole (PAB-413). mp 130-132°C; IR (KBr): 3034(Ar, C-H str), 2966(C-H str), 2854(C-H str), 1565(Ar, C=C str), 1531(Ar, C=C str), 1453(C-H ben), 1079(C-O-C str), 1054(C-O-C str), 737(C-Cl str) cm^{-1}; MS: m/z = 527 $[M]^+$

2-(2-(2-(benzyloxy)-5-chlorophenyl)-2-phenylethyl)-5-(o-tolyl)-1,3,4-oxadiazole (PAB-414). mp 166-168°C; IR (KBr): 3001(Ar, C-H str), 2933(C-H str), 2850(C-H str), 1632(Ar, C=C str), 1585(Ar, C=C str), 1533(Ar, C=C str), 1457(C-H ben), 1093(C-O-C str), 1010(C-O-C str), 748(C-Cl str) cm^{-1}; ^1H NMR (400 MHz, DMSO): δ ppm 2.51 (s, 3H, $-CH_3$), 2.89-3.03 (dd, 2H, $-CH_2$), 4.41 (t, 1H,-CH), 4.75 (s, 2H,$-CH_2$), 8.15-8.17 (d, 2H, ArH) 6.96-7.00 (t, 3H, ArH), 7.14-6.7.25 (m, 4H, ArH), 7.44-7.46 (d, 2H, ArH), 7.57-7.59 (d, 3H, ArH), 8.04 (m, 3H, ArH), 8.15-8.17 (d, 2H, ArH). 13C NMR (100 MHz, DMSO): δ ppm 21.92, 37.86, 38.01, 69.12, 117.65, 118.98, 123.22, 129.91, 133.22, 140.17, 141.14, 148.84, 163.91, 164.21. MS: m/z =480 $[M]^+$

4-(5-(2-(2-(benzyloxy)-5-chlorophenyl)-2-phenylethyl)-1,3,4-oxadiazol-2-yl)phenol (PAB-415). mp 128-130°C; IR (KBr): 3635(O-H str), 3043(Ar, C-H str), 2941(C-H str), 2853(C-H str), 1543(Ar, C=C str), 1521(Ar, C=C str), 1475(C-H ben), 1063(C-O-C str), 1032(C-O-C str), 737(C-Cl str) cm^{-1}; MS: m/z =482 $[M]^+$

2-(2-(2-(benzyloxy)-5-chlorophenyl)-2-phenylethyl)-5-(m-tolyl)-1,3,4-oxadiazole (PAB-416). mp 174-176°C; IR (KBr): 3043(Ar, C-H str), 2963(C-H str), 2843(C-H str), 1626(Ar, C=C str), 1533(Ar, C=C str), 1510(Ar, C=C str), 1459(C-H ben), 1073(C-O-C str), 1054(C-O-C str), 750(C-Cl str) cm^{-1}; MS: m/z =480 $[M]^+$

2-(5-(2-(2-(benzyloxy)-5-chlorophenyl)-2-phenylethyl)-1,3,4-oxadiazol-2-yl)phenol (PAB-417). mp 148-150°C; IR (KBr): 3623(O-H str), 3012(Ar, C-H str), 2941(C-H str), 2843(C-H str), 1540(Ar, C=C str), 1497(Ar, C=C str), 1479(C-H ben), 1065(C-O-C str), 1035(C-O-C str), 739(C-Cl str) cm^{-1}; MS: m/z = 482 $[M]^+$

2-(2-(2-(benzyloxy)-5-chlorophenyl)-2-phenylethyl)-5-(2-chlorobenzyl)-1,3,4-oxadiazole (PAB-418). mp 133-135°C; IR (KBr): 3032(Ar, C-H str), 2936(C-H str), 2852(C-H str), 1536(Ar, C=C str), 1510(Ar, C=C str), 1465(C-H ben), 1053(C-O-C str), 1042(C-O-C str), 743(C-Cl str) cm^{-1}; MS: m/z = 515 $[M]^+$

2-(5-(2-(2-(benzyloxy)-5-chlorophenyl)-2-phenylethyl)-1,3,4-oxadiazol-2-yl)-5-((2-chlorophenoxy)methyl)phenol (PAB-419). mp 118-120°C; IR (KBr): 3636(O-H str), 3032(Ar, C-H str), 2921(C-H str), 2876(C-H str), 1556(Ar, C=C str), 1532(Ar, C=C str), 1465(C-H ben), 1067(C-O-C str), 1039(C-O-C str), 749(C-Cl str) cm^{-1}; MS: m/z = 531 $[M]^+$

2-(2-(2-(benzyloxy)-5-chlorophenyl)-2-phenylethyl)-5-((4-chlorophenoxy)methyl)-1,3,4-oxadiazole (PAB-420). mp 126-128°C; IR (KBr): 3043(Ar, C-H str), 2941(C-H str), 2853(C-H str), 1543(Ar, C=C str), 1521(Ar, C=C str), 1475(C-H ben), 1063(C-O-C str), 1032(C-O-C str), 737(C-Cl str) cm^{-1}; MS: m/z = 531 $[M]^+$

3-(4-((1H-1,2,4-triazol-1-yl)methyl)phenyl)-2-(4-chlorophenyl) thiazolidin-4-one (PAB-501). mp 127-129°C; IR (KBr): 3109(Ar, C-H str), 2995(C-H str), 2914(C-H str), 2877(C-H str), 1685 (C=O str), 1608(Ar, C=C str), 1514(Ar, C=C str), 1502(Ar, C=C str), 1489(C-H ben), 1421(C-H ben), 1371(C-H ben), 1255(Ar, C-H ben), 744(C-Cl str) cm^{-1}; MS: m/z = 370 $[M]^+$

3-(4-((1H-1,2,4-triazol-1-yl)methyl)phenyl)-2-(2,5-dimethoxyphenyl) thiazolidin-4-one (PAB-502). mp 136-138°C; IR (KBr): 3043(Ar, C-H str), 2964(C-H str), 2911(C-H str), 2838(C-H str), 1676(C=O str), 1613(Ar, C=C str), 1552(Ar, C=C str), 1429(C-H ben), 1384(C-H ben), 1303(C-H ben), 1219(Ar, C-H ben), 1178(Ar, C-H ben), 1139(Ar, C-H ben), 1107(Ar, C-H ben), 1026(C-O-C str), 1016(Ar, C-H ben), 956(Ar, C-H ben) cm^{-1}; MS: m/z = 396 $[M]^+$

3-(4-((1H-1,2,4-triazol-1-yl)methyl)phenyl)-2-(4-nitrophenyl) thiazolidin-4-one (PAB-503). mp 121-123°C; IR (KBr): 3105(Ar, C-H str), 2993(C-H str), 2916(C-H str), 2872(C-H str), 1689 (C=O str), 1602(Ar, C=C str), 1536(N=O str), 1515(Ar, C=C str), 1487(C-H ben), 1422(C-H ben), 1376(C-H ben), 1251(Ar, C-H ben) cm^{-1}; MS: m/z = 381 $[M]^+$

3-(4-((1H-1,2,4-triazol-1-yl)methyl)phenyl)-2-(4-bromophenyl)

thiazolidin-4-one (PAB-504). mp 114-116°C; IR (KBr): 3019(Ar, C-H str), 2945(C-Hstr), 2914(C-H str), 2877(C-H str), 1689 (C=O str), 1603(Ar, C=C str), 1514(Ar, C=C str), 1505(Ar, C=C str), 1481(C-H ben), 1422(C-H ben), 1372(C-H ben), 1254(Ar, C-H ben), 575(C-Br str)cm^{-1}; MS: m/z = 415 $[M]^+$

3-(4-((1H-1,2,4-triazol-1-yl)methyl)phenyl)-2-(4-methoxyphenyl) thiazolidin-4-one (PAB-505). mp 130-132°C; IR (KBr): 3107 (Ar, C-H str), 2960 (C-H str), 2912 (C-H str), 2837 (C-H str), 1666 (C=O str), 1610(Ar, C=C str), 1512(Ar, C=C str), 1464(Ar, C=C str), 1429 (C-H ben), 1388 (C-H ben), 1342(C-H ben), 1303(C-H ben), 1253(Ar, C-H ben), 1219(Ar, C-H ben), 1178(Ar, C-H ben), 1139(Ar, C-H ben), 1107(Ar, C-H ben), 1026(C-O-C str), 1016(Ar, C-H ben), 956(Ar, C-H ben) cm^{-1}; ^1H NMR (400 MHz, DMSO δ ppm 3.72 (s, 3H, -OCH_3), 3.79-3.93 (dd, 2H, -CH_2), 5.30 (S, 2H,-CH_2), 6.22 (s, 1H,-CH), 6.76-6.78 (t, 2H, ArH) 7.14-7.24 (m, 6H, ArH), 7.86 (s, 1H, CH), 8.32 (s, 1H, CH). ^{13}C NMR (100 MHz, DMSO): δ ppm 32.97, 51.82, 54.76, 64.00, 113.69, 125.54, 128.14, 130.63, 133.55, 137.16, 143.46, 151.41, 159.28, 170.30. MS: m/z = 366 $[M]^+$

3-(4-((1H-1,2,4-triazol-1-yl)methyl)phenyl)-2-(2-nitrophenyl) thiazolidin-4-one(PAB-506). mp 114-116°C; IR (KBr): 3109(Ar, C-H str), 2995(C-H str), 2914(C-H str), 2877(C-H str), 1685 (C=O str), 1608(Ar, C=C str), 1539(N=O str), 1514(Ar, C=C str), 1489(C-H ben), 1421(C-H ben), 1371(C-H ben) cm^{-1}; MS: m/z = 381 $[M]^+$

3-(4-((1H-1,2,4-triazol-1-yl)methyl)phenyl)-2-(4-hydroxyphenyl) thiazolidin-4-one (PAB-507). mp 130-132°C; IR (KBr): 3635(O-H str), 3035(Ar, C-H str), 2953(C-H str), 2917(C-H str), 2878(C-H str), 1669 (C=O str) 1600(Ar, C=C str), 1515(Ar, C=C str), 1487(C-H ben), 1427(C-H ben), 1356(C-H ben), 1251(Ar, C-H ben) cm^{-1}; MS: m/z = 352 $[M]^+$

3-(4-((1H-1,2,4-triazol-1-yl)methyl)phenyl)-2-(3-nitrophenyl) thiazolidin-4-one (PAB-508). mp 141-143°C; IR (KBr): 3103(Ar, C-H str), 2991(C-H str), 2914(C-H str), 2872(C-H str), 1669 (C=O str), 1602(Ar, C=C str), 1536(N=O str), 1515(Ar, C=C str), 1488(C-H ben), 1432(C-H ben), 1376(C-H ben) cm^{-1}; MS: m/z = 381 $[M]^+$

3-(4-((1H-1,2,4-triazol-1-yl)methyl)phenyl)-2-(4-fluorophenyl) thiazolidin-4-one (PAB-509). mp 148-150°C; IR (KBr): 3029(Ar, C-H str), 2940(C-H str), 2914(C-H str), 2877(C-H str), 1679 (C=O str), 1607(Ar, C=C str), 1511(Ar, C=C str), 1521(Ar, C=C str), 1471(C-H ben), 1412(C-H ben), 1372(C-H ben), 1254(Ar, C-H ben), 1024 (C-F str)cm^{-1}; MS: m/z = 354 $[M]^+$

3-(4-((1H-1,2,4-triazol-1-yl)methyl)phenyl)-2-(p-tolyl)thiazolidin-4-one(PAB-510). mp 147-149°C; IR (KBr): 3013(Ar, C-H str), 2951(C-H str), 2913(C-H str), 2872(C-H str), 1669 (C=O str), 1602(Ar, C=C str), 1515(Ar, C=C str), 1454(C-H ben), 1432(C-H ben), 1376(C-H ben) cm^{-1}; MS: m/z = 350 $[M]^+$

Antimicrobial Studies

All the inhibition results are plotted after subtracting the zone of inhibition for the solvent DMSO (i.e., control).

Dihydropyrazole Derivatives (PAB 301-PAB-320)

Figure 2 shows the inhibition of dihydropyrazole derivatives (PAB 301-PAB-320) against Gram positive bacteria. It is observed from Fig. 2 that against B. Cereus. PAB-314 showed maximum inhibition whereas PAB-305 showed minimum inhibition. For M. flavus, only few compounds exhibited inhibition and PAB-311 showed maximum inhibition. Against M. flavus, PAB-317 showed minimum inhibition whereas against S. aureus, PAB-308 exhibited maximum inhibition, which is followed by PAB-312.

All these dihydropyrazole derivatives contain the same moiety but different side chains as shown in Table 1.Thus, the extent of inhibition depends on substitutions. PAB-314 containing p- chloro and p-nitro group groups at R_1 and R positions respectively affects B. Cereus to maximum extent. When one of these groups is present with some other functional group as in PAB-304, PAB-307, PAB-308, PAB-311, PAB-317 and PAB-318), the inhibition is considerably reduced. However, against M. flavus, PAB-311 containing p-chloro and p-methyl group is found to be most effective whereas against S. aureus, PAB-308 containing p-chloro and o-nitro groups at R_1 and R positions respectively is more effective. Thus, against the studied Gram positive bacteria, mostly compounds containing p-chloro groups at R_1 position are found to be more effective.

Figure 3 shows the inhibition of dihydropyrazole derivatives (PAB 301-PAB-320) against Gram negative bacteria. Against E. Coli, PAB-305 exhibited maximum inhibition whereas minimum is observed for PAB-307. PAB-314 could inhibit P. Mirabilis to maximum extent in comparison to other compounds whereas PAB-306 showed maximum inhibition against S. Tuphimurrium. Some of the compounds had no effect on S. Tuphimurrium. PAB-305 contains p-nitro and p-fluoro groups at R_1 and R positions respectively, which is found to be more effective against E. Coli. PAB-314 containing p- chloro and p-nitro group groups at R_1 and R positions respectively affects P. Mirabilis to maximum extent whereas o-nitro and p-nitro groups at R_1 and R positions (as in PAB-306) could affect S. Tuphimurrium more effectively. Thus, against the studied Gram negative bacteria, compounds containing p-nitro groups are more effective.

Against fungal strains, it is observed from Figure 4 that all the studied compounds could not inhibit C. Glabrata. However, against C. Neoformans, some compounds exhibited inhibition and PAB-307 and PAB-318 showed maximum inhibition. PAB-307 contains p-chloro and p-aryl groups at R_1 and R positions respectively whereas PAB-318 contains p-chloro and p-methoxy groups at R_1 and R positions respectively. Thus, for fungal strain C. Neoformans, again compounds with p-chloro groups

are effective with p-aryl and p-methoxy groups in combination.

Thus, in case of studied dihydroxypyrazole derivatives in DMSO solutions, M. flavus is most resistant among three Gram positive bacteria, S. Tuphimurrium is most resistant among three Gram negative bacteria and C. Glabrata is most resistant among the two fungal strains.

Oxadiazole Derivatives (PAB-401-PAB-420)

Figure 5 shows the zone of inhibition of oxadiazole derivatives (PAB-401-PAB-420) against Gram positive bacteria. It is observed from this figure that against B. Cereus, PAB-402 exhibited maximum inhibition and PAB-405 showed minimum inhibition. For M. flavus, PAB-416 exhibited maximum inhibition whereas PAB-413 and PAB-414 showed minimum inhibition. For S. aureus, maximum and minimum inhibitions were exhibited by PAB-411 and PAB-413 respectively.

As evident from Table 2, PAB-402 contains m-bromo benzyl group as side chain whereas in PAB-405, no side chain is in the benzene ring. Thus, it is concluded that when R is benzene ring with side chain, inhibition is higher and it is maximum when side chain is bromo group at para position. Without side chain, compound is not very effective as in case of PAB-405. When methyl group is present at meta position, the compound exhibited maximum inhibition against M. flavus. Against S. aureus, m-chloro group is found to be most effective (as in PAB-411).

Figure 6 shows the zone of inhibition of oxadiazole derivatives (PAB-401-PAB-420) against Gram negative bacteria. It is observed that against E. Coli, P. Mirabilis and S. Tuphimurrium, PAB-406, PAB-403, PAB-412 exhibited maximum inhibition. Against E. Coli, PAB-402 and PAB-415 showed minimum inhibition whereas PAB-420 had no effect at all. Against P. Mirabilis, PAB-407 and PAB-413 exhibited minimum inhibition whereas PAB-403 showed minimum inhibition against S. Tuphimurrium. However, few compounds had no inhibition at all against S. Tuphimurrium. Thus, 2,4-dichloro groups (at ortho and para positions) in PAB-406, p-chloro group as in PAB-403 and m-nitro group (as in PAB-412) are most effective in inhibiting Gram negative bacteria.

Against fungal strains C. Glabrata and C. Neoformans, most of oxadiazole derivatives had no effect at all as shown in Figure 7. However, PAB-403 containing p-chloro group showed maximum inhibition against both fungal strains. Thus, p-chloro group alone as side chain in benzene ring is most effective for selected fungal strains. When other groups are present along with p-chloro group, inhibition is decreased.

Thus, in case of studied oxadiazole derivatives in DMSO solutions, S. aureus is most resistant among three Gram positive bacteria, S. Tuphimurrium is most resistant among three Gram negative bacteria and C. Glabrata is most resistant among the two fungal strains.

Thiazolidinone Derivatives (PAB-501-PAB-510)

Figure 8 [A] shows inhibition against Gram positive bacteria for thiazolidinone derivatives (PAB-501-PAB-510). It is observed that against all the three selected Gram positive bacteria, viz. B. Cereus, M. flavus, S. aureus, PAB-501 exhibited maximum inhibition. Against B. Cereus, PAB-506 and PAB-507 exhibited minimum inhibition. Some compounds such as PAB-503, PAB-506, PAB-507, PAB-508 and PAB-510 could not inhibit M. flavus at all. However, against S. aureus, only PAB-508 showed no inhibition.

Again, in all these compounds central moiety is same but side chains are different (3). Thus, p-chloro group, which is present in PAB-501, is found to be most effective against all the three studied Gram positive bacteria.

In Figure 8 [B], zone of inhibition against Gram negative bacteria for thiazolidinone derivatives (PAB-501-PAB-510) is shown. Against E. Coli and S. Tuphimurrium, PAB-504 exhibited maximum inhibition whereas against P. Mirabilis, both PAB-502 and PAB-503 showed maximum inhibition. Against S. Tuphimurrium, PAB-501, PAB-505, PAB-506 and PAB-508 had no effect at all. As given in Table 3, PAB-504 contains p-bromo group, which is found to be most effective against E. Coli and S. Tuphimurrium. Whereas against P. Mirabilis, 2,5-dimethoxy group (present in PAB-502) is also found to be equally effective as p-nitro group (as in PAB-503).

Figure 8 [C] shows inhibition zones against fungal strains C. Glabrata and C. Neoformans. It is found that for these two fungal strains some of the compound had no effect at all. However, PAB-510 exhibited maximum inhibition against C. Glabrata whereas PAB-508 showed maximum inhibition for C. Neoformans.

Thus, in case of studied thiazolidinone derivatives in DMSO solutions, M. flavus is most resistant among three Gram positive bacteria, S. Tuphimurrium is most resistant among three Gram negative bacteria and C. Neoformans is most resistant among the two fungal strains.

Thus, it is concluded that overall S. Tuphimurrium is most resistant among three Gram negative bacteria for all the three class of heterocyclic compounds. For dihydroxypyrazole and thiazolidinone derivatives, M. flavus is most resistant Gram positive bacteria and C. Neoformans is most resistant fungal strain. However, for oxadiazole derivatives S. aureus is most resistant Gram positive bacteria and C. Glabrata is most resistant fungal strain.

Table 1: Physical constant of dihydropyrazole derivatives

Code	R	R_1	M.F	M.W	Yield (%)	R_f value
PAB-301	2-Cl	4-F	$C_{37}H_{29}Cl_2FN_2O$	623.54	71	0.52
PAB-302	4-NO_2	4-CH_3	$C_{38}H_{32}ClN_3O_4$	630.13	64	0.58
PAB-303	4-F	3-NO_2	$C_{37}H_{29}ClFN_3O_4$	634.10	70	0.54
PAB-304	3,4 di –OCH_3	4-Cl	$C_{39}H_{34}Cl_2N_2O_4$	665.60	62	0.48
PAB-305	4-F	4-NO_2	$C_{37}H_{29}ClFN_3O_4$	634.10	65	0.56
PAB-306	4-NO_2	2-NO_2	$C_{37}H_{29}ClN_4O_6$	661.10	60	0.55
PAB-307	C_6H_5	4-Cl	$C_{37}H_{30}Cl_2N_2O_2$	605.55	58	0.58
PAB-308	2-NO_2	4-Cl	$C_{37}H_{29}Cl\,FN_2O_4$	650.55	66	0.62
PAB-309	3,4 di –OCH_3	4-F	$C_{39}H_{34}Cl_2N_2O_4$	649.15	74	0.51
PAB-310	2-NO_2	C_6H_5	$C_{37}H_{30}Cl_2N_3O_4$	616.10	72	0.60
PAB-311	4-CH_3	4-Cl	$C_{38}H_{32}Cl_2N_2O_2$	619.58	70	0.64
PAB-312	4-Cl	C_6H_5	$C_{37}H_{30}Cl_2N_2O_2$	605.55	61	0.48
PAB-313	4-F	4-Br	$C_{37}H_{29}BrClFN_2O_2$	667.99	67	0.47
PAB-314	4-NO_2	4-Cl	$C_{37}H_{29}Cl_2N_3O_4$	650.55	71	0.51
PAB-315	4-Cl	4-F	$C_{37}H_{29}Cl_2FN_2O_2$	623.54	74	0.56
PAB-316	4-NO_2	4-F	$C_{37}H_{29}ClFN_3O_4$	634.10	69	0.48
PAB-317	4-F	4-Cl	$C_{37}H_{29}Cl_2FN_2O_2$	623.54	63	0.55
PAB-318	4-OCH_3	4-Cl	$C_{38}H_{32}Cl_2N_2O_3$	635.58	70	0.62
PAB-319	4-OCH_3	4-F	$C_{38}H_{32}ClFN_2O_3$	619.12	77	0.58
PAB-320	4-F	C_6H_5	$C_{37}H_{30}ClFN_2O_2$	589.10	76	0.64

Table 2: Physical constant of oxadiazole derivatives

Code	R	M.F	M.W	Yield (%)	R_f
PAB-401	4-$OCH_3C_6H_4$	$C_{30}H_{25}ClN_2O_3$	496.98	71	0.65
PAB-402	4-Br C_6H_4	$C_{29}H_{22}BrClN_2O_2$	545.85	62	0.70
PAB-403	4-Cl C_6H_4	$C_{29}H_{22}Cl_2N_2O_2$	501.40	59	0.62
PAB-404	4-CH_3 C_6H_4	$C_{30}H_{25}ClN_2O_2$	480.98	70	0.68
PAB-405	C_6H_5	$C_{29}H_{23}ClN_2O_2$	466.96	64	0.71
PAB-406	2,4 di Cl C_6H_3	$C_{29}H_{21}Cl_3N_2O_2$	535.85	61	0.60
PAB-407	C_7H_7	$C_{30}H_{25}ClN_2O_2$	480.98	56	0.58
PAB-408	2-$OCOCH_3C_6H_4$	$C_{31}H_{25}ClN_2O_4$	524.99	55	0.72
PAB-409	2-Cl, 5-$NO_2C_6H_4$	$C_{29}H_{21}Cl_2N_3O_4$	546.40	58	0.64
PAB-410	2-Cl C_6H_4	$C_{29}H_{22}C_{l2}N_2O_2$	501.40	62	0.62
PAB-411	3-Cl C_6H_4	$C_{29}H_{22}Cl_2N_2O_2$	501.40	65	0.54
PAB-412	3-NO_2 C_6H_4	$C_{29}H_{22}ClN_3O_4$	511.96	55	0.57
PAB-413	3,4 di OCH_3	$C_{31}H_{27}ClN_2O_4$	527.01	73	0.71
PAB-414	2-CH_3 C_6H_4	$C_{30}H_{25}ClN_2O_2$	480.98	75	0.62
PAB-415	4-OH C_6H_4	$C_{29}H_{23}ClN_2O_3$	482.96	68	0.55
PAB-416	3-CH_3 C_6H_4	$C_{30}H_{25}ClN_2O_2$	480.98	70	0.58
PAB-417	2-OH C_6H_4	$C_{29}H_{23}ClN_2O_3$	482.96	65	0.60
PAB-418	2-Cl C_7H_6	$C_{30}H_{24}Cl_2N_2O_2$	515.43	59	0.56
PAB-419	2-Cl C_7H_6O	$C_{30}H_{24}Cl_2N_2O_3$	531.43	54	0.59
PAB-420	4-Cl C_7H_6O	$C_{30}H_{24}Cl_2N_2O_3$	531.43	66	0.67

Table 3: Physical constant of thiazolidinone derivatives

Code	R	M.F	M.W	Yield (%)	R_f
PAB-501	4-Cl	$C_{18}H_{15}ClN_4OS$	370.86	72	0.43
PAB-502	2,5diOCH_3	$C_{20}H_{20}N_4O_3S$	396.46	68	0.37
PAB-503	4-NO_2	$C_{18}H_{15}N_5O_3S$	381.41	59	0.46
PAB-504	4-Br	$C_{18}H_{15}BrN_4OS$	415.31	63	0.52
PAB-505	4-OCH_3	$C_{19}H_{18}N_4O_2S$	366.44	70	0.48
PAB-506	2-NO_2	$C_{18}H_{15}N_5O_3S$	381.41	61	0.61
PAB-507	4-OH	$C_{18}H_{16}N_4O_2S$	352.41	57	0.59
PAB-508	3-NO_2	$C_{18}H_{15}N_5O_3S$	381.41	53	0.52
PAB-509	4-F	$C_{18}H_{15}FN_4OS$	354.40	64	0.47
PAB-510	4-CH_3	$C_{19}H_{18}N_4OS$	350.44	60	0.58

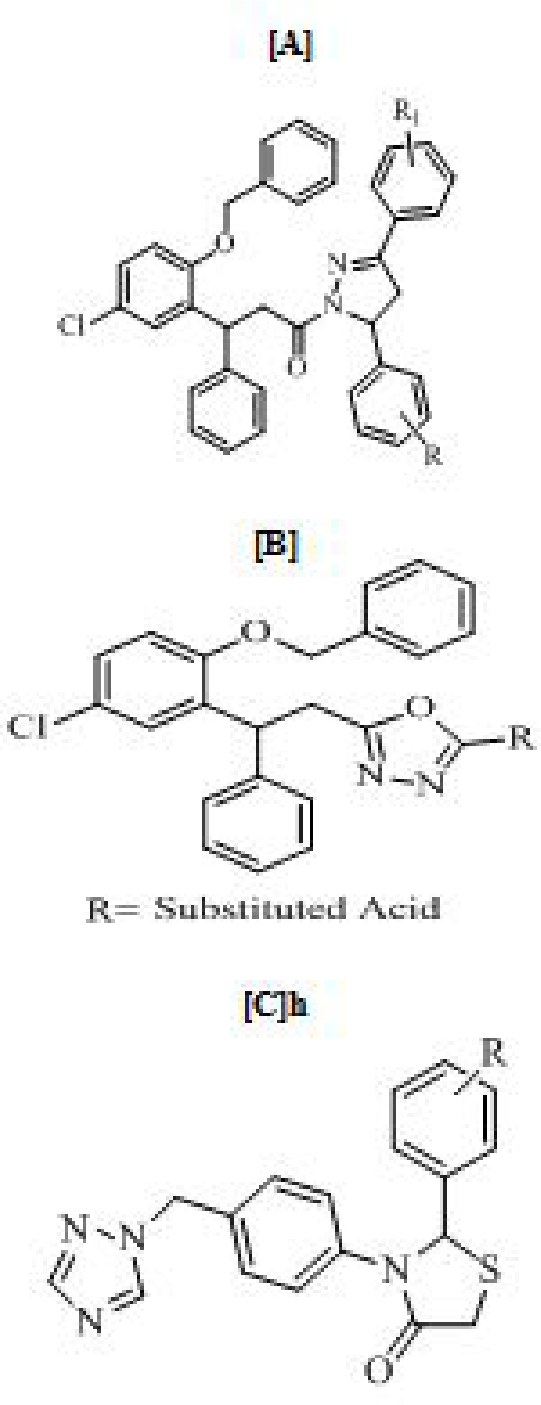


Figure 1: General structure of [A] dihydropyrazole, [B] oxadiazole and [C] thiazolidinone derivatives

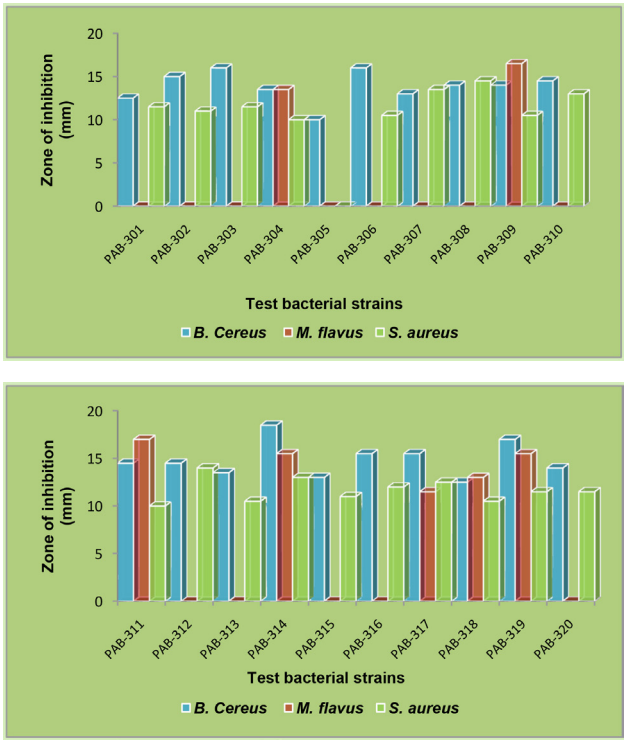


Figure: 2: Antibacterial activity of dihydropyrazole compounds against Gram positive bacteria

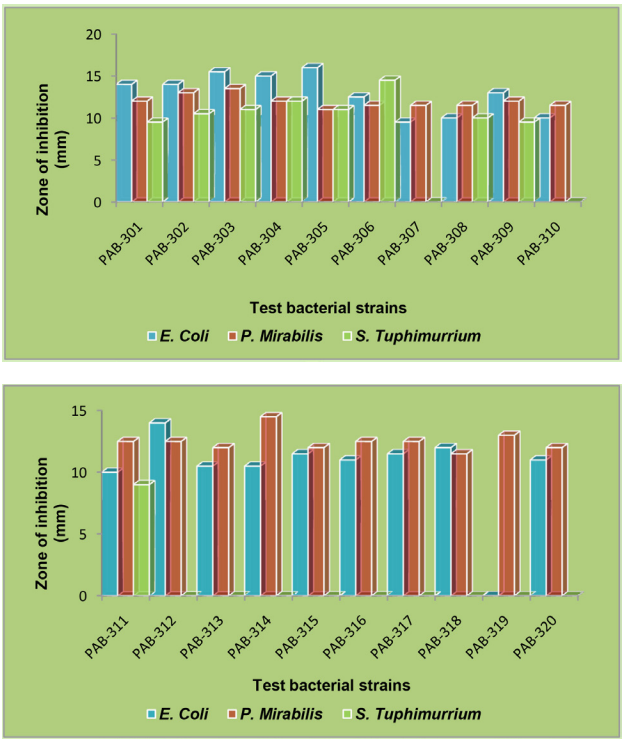


Figure3: Antibacterial activity of dihydropyrazole compounds against Gram negative bacteria

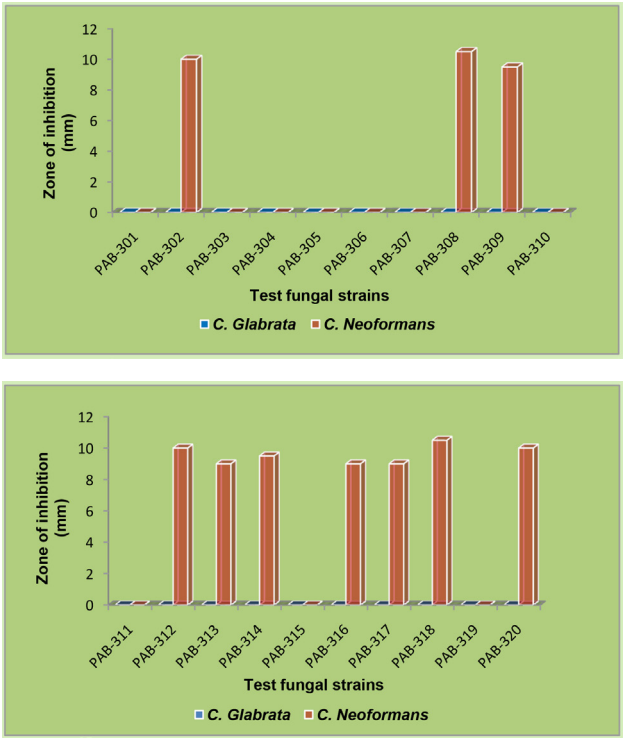


Figure 4: Antifungal activity of dihydropyrazole compounds

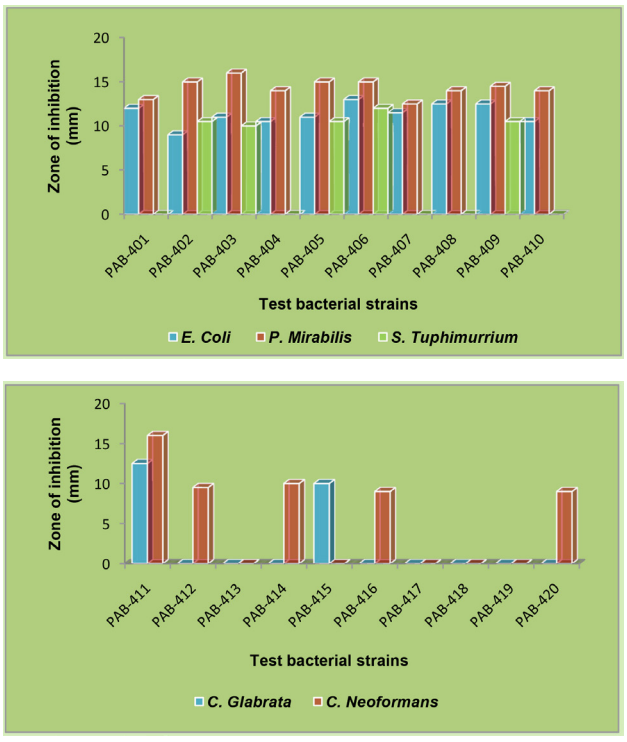


Figure 6: Antibacterial activity of oxadiazole compounds against Gram negative bacteria

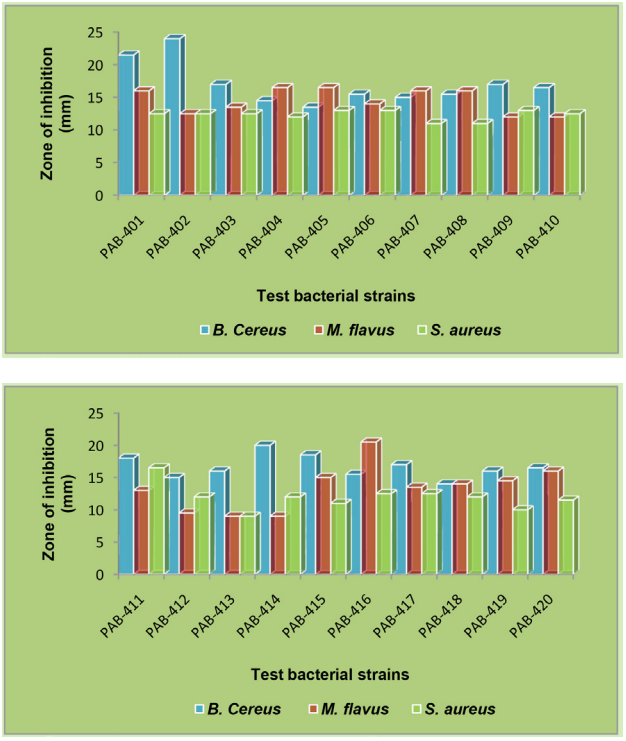


Figure 5: Antibacterial activity of oxadiazole compounds against Gram positive bacteria

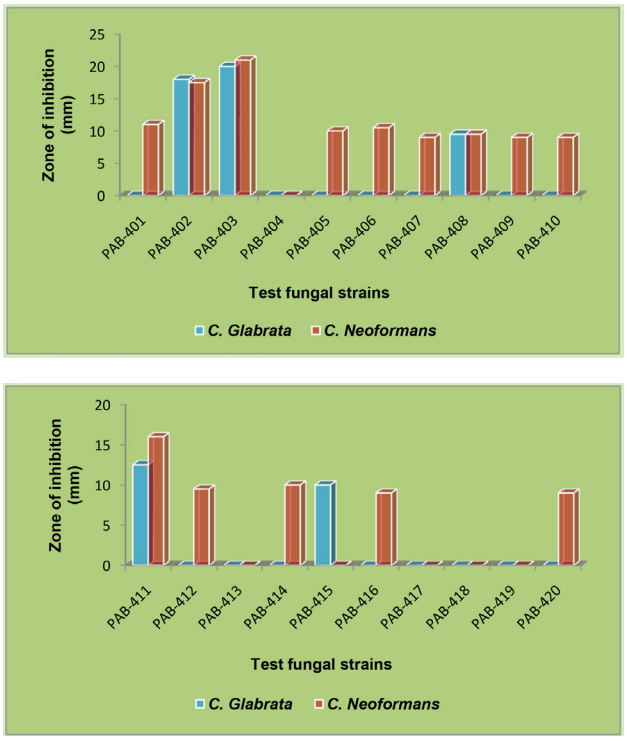
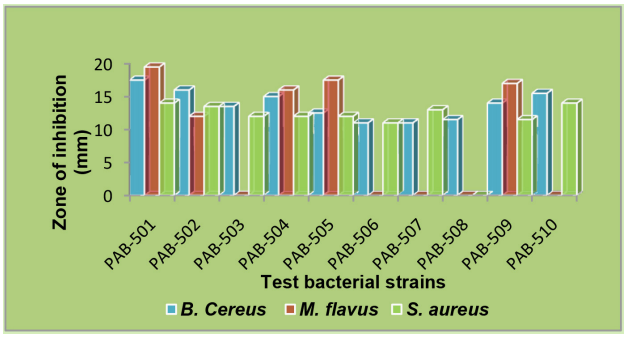
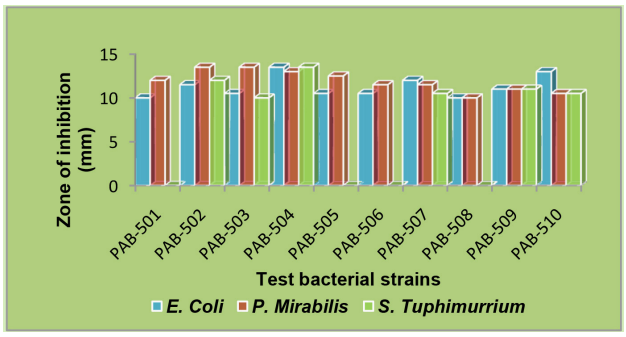


Figure 7: Antifungal activity of oxadiazole compounds



A



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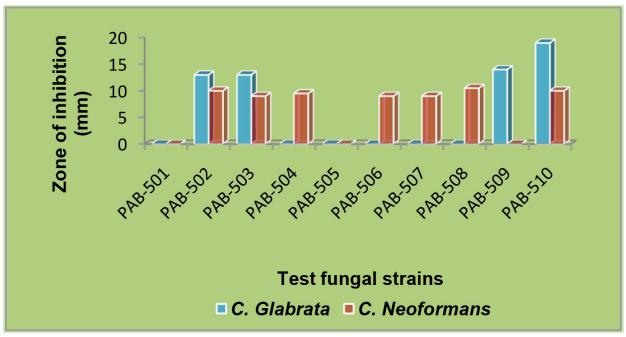

C

Figure 8: Antibacterial activity of thiazolidinone compounds against [A] Gram positive bacteria, [B] Gram negative bacteria and [C] fungal strains.

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