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Antifungal activity of newly synthesized nucleosides containing [1,3,4] oxadiazole-2(3H) one core

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Abstract: *In the present study various nucleoside derivatives were synthesized by condensing differently substituted [1,3,4] Oxadiazole-2(3H) one with β-D-1,2,3,4,6-penta-O-acetylglucopyranosyl followed by deacetylation. Structure of obtained compounds has been established by using tools like IR, 1HNMR, and elemental analysis. The compounds have been evaluated for their antifungal behavior against fungi such as Aspergillus flavus, Aspergillus niger and Fusarium oxysporum. The disk diffusion methodology was applied for the values of minimum inhibitory concentration using well known antifungal agent fluconazole as reference standard in cases of all the studies done.*

Keywords: *Antifungal Agent, Nucleosides, Oxadiazole, Fluconazole*

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I. Introduction

Oxadiazoles, a member of azole family are a five membered heterocyclic compounds having one oxygen and two nitrogen in a ring, exist in three stable isomeric forms 1,2,4-oxadiazole, 1,2,5-oxadiazole and 1,3,4-oxadiazole. Out of three isomers, 1,3,4-oxadiazole have various biological activities such as antifungal[1-8], antibacterial[9-14], anticancer[15-19], anti-inflammatory[20-24], antiviral[25,26], antihypoglycemic [27], antipyretic [28], Antihypertensive [29,30] . Therefore, they attracted much attention of chemist to synthesize new compounds having 1,3,4-oxadiazole nucleus as a main constituent.

Nucleosides are glucosamine consisting of a nucleobase and sugar moiety. In a nucleoside, a nucleobase is bound to the sugar via a β-glycosidic linkage. Nucleosides have been reported to possess various biological activities such as antifungal [31-38], anti-viral [38-45], anti-bacterial [46-50], anti-cancer [51-56], anti-inflammatory [57-59] and anti-oxidant [60].

On the basis of above facts, it was thought of interest to couple differently substituted 1,3,4-oxadiazole with β-D-1,2,3,4,6-penta-O-acetylglucopyranosyl to get novel nucleosides having potent antifungal activity.

II. Materials and Methods

All the chemicals used in the synthesis were indented from sigma-Aldrich (Merck) India. Melting points of synthesized compounds were determined by Jindal SM capillary melting point apparatus and have been reported without any correction. The purity of the compounds were also monitored by TLC (Thin layer chromatography) for which silica gel (Merck, 350 mesh size) was used for coating the chromatographic plates. IR spectra in KBr and 1H NMR spectra in DMSO-d_6 of various compounds reported in this present study were recorded by SAIF, Panjab University Chandigarh using Perkin-Elmer 881Infrared spectrophotometer for IR spectra and Bruker Advance II 400 MH_z for recording 1H-NMR spectra. Biological activity in particular antifungal activity have been evaluated by disk diffusion method against three pathogenic fungi viz *Aspergillus niger (A. niger), Aspergillus flavus (A. flavus)) and Fusarium oxysporum (F. oxysporum)* using fluconazole as a reference standard, which is well known potent antifungal agent.

III. Experimental

3.4 General Procedure: Substituted benzohydrazide 2(a-k)

4-methyl benzoic acid (0.07 mole) was dissolved in 100 ml of n-butanol. The reaction mass was cooled below 10^0C and added drop wise 8 ml of conc. H_2SO_4. The reaction mass was allowed to attain room temperature followed by reflux for about 7-8 h by using Dean-stark apparatus. The reaction mass was allowed to attain room temperature and addition of saturated solution of sodium carbonate to separate out organic layer. Organic layer obtained was washed with water and was concentrated up to 20-30 ml by applying vacuum distillation. Hydrazine hydrate (0.2 mole) and 70ml methanol was added into the obtained concentrated organic layer and

further refluxed for 9 hrs. The reaction mass was cooled and poured into the water. The product obtained was filtered and washed with water and purified by recrystallization from ethanol.

4-methyl benzohydrazide (2a): Yield: 78%; mp: 195-199 ^{o}C; Rf value: 0.67; Anal. Cald. For $C_8H_{10}N_2O$: C: 63.98, H: 6.71, N: 18.65, Found: C: 63.93, H: 6.74, N: 18.67.

4-methyl-3-nitro benzohydrazide (2b): Yield: 89%; mp: 201-205 ^{o}C; Rf value: 0.70; Anal. Cald. For $C_8H_9N_3O_3$: C: 49.23, H: 4.65, N: 21.53, Found: C: 49.28, H: 4.59, N: 21.55.

4-methyl-3,5-dinitrobenzohydrazide (2c): Yield: 69%; mp: 179-181 ^{o}C; Rf value: 0.71; Anal. Cald. For $C_8H_8N_4O_5$ C: 40.01, H: 3.36, N: 23.33, Found: C: 40.07, H: 3.34, N: 23.31.

3-bromo-4-methylbenzohydrazide (2d): Yield: 85%; mp: 234-236 ^{o}C; Rf value: 0.59; Anal. Cald. For $C_8H_9N_2OB_r$: C: 41.95, H: 3.96, N: 12.23 Found: C: 41.89, H: 3.99, N: 12.25.

3-methyl benzohydrazide (2e): Yield: 67%; mp: 122-125 ^{o}C; Rf value: 0.77; Anal. Cald. For: $C_8H_{10}N_2O$: C: 63.98, H: 6.71, N: 18.65 Found: C: 63.93, H: 6.75, N: 18.63.

3-methyl-4-nitrobenzohydrazide (2f): Yield: 87%; mp: 245-248 ^{o}C; Rf value: 0.65; Anal. Cald. For: $C_8H_9N_3O_3$: C: 49.23, H: 4.65, N: 21.53 Found: C: 49.19, H: 4.70, N: 21.50.

4-bromo-3-methylbenzohydrazide (2g): Yield: 75%; mp: 240-243 ^{o}C; Rf value: 0.63; Anal. Cald. For $C_8H_9N_2OB_r$: C: 41.95, H: 3.96, N: 12.23 Found: C: 41.93, H: 3.94, N: 12.33.

2-methylbenzohydrazide (2h): Yield: 89%; mp: 118-120 ^{o}C; Rf value: 0.67; Anal. Cald. For $C_8H_{10}N_2O$: C: 63.98, H: 6.71, N: 18.65 Found: C: 63.95, H: 6.69, N: 18.69.

2-methyl-3-nitrobenzohydrazide (2i): Yield: 69%; mp: 221-223 ^{o}C; Rf value: 0.59; Anal. Cald. For $C_8H_9N_3O_3$: C: 49.23, H: 4.65, N: 21.53 Found: C: 49.20, H: 4.69, N: 21.51.

2-methyl-3,5-dinitrobenzohydrazide (2j) : Yield: 75%; mp: 218-219^{o}C; Rf value: 0.61; Anal. Cald. For $C_8H_8N_4O_5$: C: 40.01, H: 3.36, N: 23.33, Found: C: 39.96, H: 3.34, N: 23.39.

3-bromo-2-methyl benzohydrazide (2k): Yield: 64%; mp: 178-180 ^{o}C; Rf value: 0.76; Anal. Cald. For $C_8H_9N_2OB_r$: C: 41.95, H: 3.96, N: 12.23 Found: C: 41.88, H: 4.00, N: 12.26.

3.5 General Procedure: 5-(Aryl)-1,3,4-oxadiazole-2-(3H) one 3(a-k)

4-methylbenzohydrazide (0.01mole) and N, N-Carbonyldiimidazole (CDI) (0.015mole) was dissolved in 15 mL of dioxane. The reaction mixture was initially stirred at room temperature for about 1 h and then refluxed for 12 h. The reaction mass was distilled to skip of dioxane and added distilled water into it. The product thus obtained filtered, washed, recrystallized from ethanol.

5-(4-methylphenyl)-1,3,4-oxadiazole-2(3H)one (3a): Yield: 63%; mp: 215-217^{o}C; Rf value: 0.73; IR (KBr, cm^{-1}): 1182 (NCO), 1582 (C=N), 1604 (C=C), 1682 (C=O), 3336 (NH); 1H NMR (400 MHz, DMSO-d6) δ ppm: 2.36 (s, 3H, CH_3), 7.21 (s, 1H, NH), 7.32-7.34 (d, 2H, Ar-H), 7.67-7.69 (d, 2H, Ar-H); Anal. Cald. For $C_9H_8N_2O_2$: C: 61.36, H: 4.58, N: 15.90 Found: C: 61.30, H: 4.64, N: 15.87.

5-(4-methyl-3-nitrophenyl)-1,3,4-oxadiazole-2(3H)one (3b): Yield: 66%; mp: 221-223 ^{o}C; Rf value: 0.66; IR(KBr, cm^{-1}): 1180 (NCO), 1582 (C=N), 1606 (C=C), 1683 (C=O), 3334 (NH); 1H NMR (400 MHz, DMSO-d6) δ ppm: 2.34 (s, 3H, CH_3), 7.20 (s, 1H, NH), 7.66-7.68 (d, 1H, Ar-H), 8.19-8.20 (d, 1H, Ar-H), 8.11 (s, 1H, Ar-H); Anal. Cald. For $C_9H_7N_3O_4$: C: 48.87, H: 3.19, N: 19.00 Found: C: 48.82, H: 3.15, N: 19.06.

5-(4-methyl-3,5-dinitrophenyl)-1,3,4-oxadiazole-2(3H)one(3c): Yield: 69%; mp: 224-227 ^{o}C; Rf value: 0.70; IR (KBr, cm^{-1}): 1182 (NCO), 1585 (C=N), 1602 (C=C), 1685 (C=O), 3340 (NH); 1H NMR (400 MHz, DMSO-d6) δ ppm: 2.32 (s, 3H, CH_3), 7.21 (s, 1H, NH), 8.74 (s, 2H, Ar-H); Anal. Cald. For $C_9H_6N_4O_6$: C: 40.61, H: 2.27, N: 21.05 Found: C: 40.57, H: 2.23, N: 20.10.

5-(3-bromo-4-methylphenyl)-1,3,4-oxadiazole-2(3H)one (3d): Yield: 70%; mp: 220-222 ^{o}C; Rf value: 0.71; IR (KBr, cm^{-1}): 1182 (NCO), 1578 (C=N), 1608 (C=C), 1680 (C=O), 3339 (NH); 1H NMR (400 MHz, DMSO-d6) δ ppm: 2.35 (s, 3H, CH_3), 7.22 (s, 1H, NH), 7.15-7.16 (d, 1H, Ar-H), 7.81(s, 1H, Ar-H), 7.91-7.92 (d, 1H, Ar-H); Anal. Cald. For $C_9H_7N_2O_2B_r$: C: 42.38, H: 2.77, N: 10.98 Found :C: 42.44, H: 2.70, N:10.95.

5-(3-methylphenyl)-1,3,4-oxadiazole-2(3H)one(3e): Yield: 55% mp: 228-230 ^{o}C Rf value: 0.86; IR (KBr, cm^{-1}): 1179 (NCO), 1587 (C=N), 1607 (C=C), 1671 (C=O), 3330 (NH); 1H NMR (400 MHz, DMSO-d6) δ ppm: 2.31 (s, 3H, CH_3), 7.32 (s,1H, NH), 7.20-7.75 (m, 3H, Ar-H), 7.60 (s, 1H, Ar-H) Anal. Cald. For $C_9H_8N_2O_2$: C: 61.36, H: 4.58, N: 15.90, Found: C: 61.42, H: 4.54, N: 15.84.

5-(3-methyl-4-nitrophenyl)-1,3,4-oxadiazole-2(3H)one (3f) Yield: 61%; mp: 223-225 ^{o}C; Rf value: 0.74; IR (KBr, cm^{-1}):1181 (NCO), 1584 (C=N), 1609 (C=C), 1668 (C=O), 3316 (NH); 1H NMR (400 MHz, DMSO-d6) δ ppm: 2.34 (s, 3H, CH_3), 7.17 (s, 1H, NH), 7.89-7.90 (d, 1H Ar-H), 7.91 (s,1H, Ar-H), 8.19-8.20 (d, 1H, Ar-H); Anal. Cald. For $C_9H_7N_3O_4$: C: 48.87, H: 3.19, N: 19.00 Found: C: 48.81, H: 3.15, N: 19.08.

5-(4-bromo-3-methylphenyl)-1,3,4-oxadiazole-2(3H)one (3g): Yield: 64%; mp: 218-220 ^{o}C Rf value: 0.76; IR (KBr, cm^{-1}): 1179 (NCO), 1584 (C=N), 1598 (C=C), 1662 (C=O), 3299 (NH); 1H NMR (400 MHz, DMSO-d6) δ ppm: 2.34 (s, 3H, CH_3), 7.21 (s, 1H, NH), 7.34 (s, 1H, Ar-H), 7.45-7.46 (d, 1H, Ar-H), 7.34 (s, 1H, Ar-H), 7.50-7.52(d, 1H, Ar-H); Anal. Cald. For $C_9H_7N_2O_2B_r$: C: 42.38, H: 2.77, N: 10.98 Found: C: 42.44, H: 2.66, N: 10.90.

5-(2-methylphenyl)-1,3,4-oxadiazole-2(3H)one (3h): Yield: 64%; mp: 202-204^{o}C; Rf value: 0.66; IR (KBr, cm^{-1}): 1185 (NCO), 1581 (C=N),1608 (C=C), 1665 (C=O), 3323 (NH), 1H NMR (400 MHz, DMSO-d6) δ ppm: 2.39 (s, 3H, CH_3), 7.20 (s, 1H, NH), 7.27-7.69 (m ,4H, Ar-H); Anal. Cald .For $C_9H_8N_2O_2$: C: 61.36, H: 4.58, N: 15.90 Found: C: 61.29, H: 4.64, N: 15.83.

5-(2-methyl-3-nitrophenyl)-1,3,4-oxadiazole-2one (3i): Yield: 69%; mp: 238-240 ^{o}C; Rf value: 0.79; IR (KBr, cm^{-1}): 1187 (NCO), 1582 (C=N), 1609 (C=C), 1651 (C=O), 3331 (NH); 1H NMR (400 MHz, DMSO-d6) δ ppm: 2.36 (s, 3H, CH_3), 7.25 (s, 1H, NH), 7.99-8.20 (m, 3H, Ar-H); Anal. Cald. For $C_9H_7N_3O_4$: C: 48.87, H: 3.19, N: 19.00 Found: C: 48.79, H: 3.23, N: 18.97.

5-(2-methyl-3,5-dinitrophenyl)-1,3,4-oxadiazole-2(3H)one(3j): Yield: 63%; mp: 253-254 ^{o}C; Rf value: 0.81; IR (KBr, cm^{-1}): 1179 (NCO), 1581 (C=N), 1602(C=C), 1649 (C=O), 3312 (NH); 1H NMR (400 MHz, DMSO-d6) δ ppm : 2.36 (s, 3H, CH_3), 7.24 (s, 1H, NH), 7.49 (s, 1H, Ar-H), 8.74 (s, 1H, Ar-H); Anal. Cald. For $C_9H_6N_4O_6$; C: 40.61 H: 2.27, N: 21.05 Found: C: 40.69, H: 2.20, N: 20.97

5-(3-bromo-2-methylphenyl)-1,3,4-oxadiazole-2(3H)one (3k) Yield: 69%; mp: 224-226 ^{o}C; Rf value: 0.79; IR(KBr,cm^{-1}): 1181 (NCO), 1580 (C=N), 1616 (C=C), 1667 (C=O), 3321 (NH); ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm : 2.37 (s, 3H, CH_3), 7.22 (NH), 7.46-7.75 (m, 3H, Ar-H); Anal. Cald .For $C_9N_2O_2H_7B_r$: C: 41.53, H: 2.69, N: 10.76 Found C: 41.44, H: 2.60, N: 10.67.

3.6 General Procedure: 5-(Aryl)-3-(β-D-2,3,4,6-tetra-O-acetylglucopyranosyl)-1,3,4-oxadiazole-2(3H)one 4(a-k)

5-(4-methylphenyl)-1,3,4-oxadiazole-2(3H)one (0.005mole), β-D-1,2,3,4,6-penta-O-acetylglucopyranosyl (0.015mole) and 0.4g of iodine was dissolved in 10 mL of dioxane. The reaction mass was refluxed for 4h. The reaction mass was cooled and added saturated solution of sodium thiosulphate (15 mL) to remove excess iodine. The desired product thus obtained was filtered, washed with water and crystallized from ethanol. The product formed was dissolved in 15 mL of dry methanol and 1mL of freshly prepared solution of $NaOCH_3$ ($NaOCH_3$ solution was prepared by adding 0.1g of sodium in 20mL of dry CH_3OH) in a closed vessel. The mixture was allowed to stand for 3h with occasional shaking. The solution was neutralized by adding dilute hydrochloric acid. The product thus precipitated was filtered and recrystallized from ethanol.

5-(4-methylphenyl)-3-(β-D-2,3,4,6-tetra-O-acetylglucopyranosyl)-1,3,4-oxadiazole-2(3H)one (4a): Yield: 38%; mp: 250-252^{o} C; Rf value: 0.86; IR (KBr, cm^{-1}): 1183 (NCO), 1583 (C=N), 1604 (C=C), 1686 (C=O), 3660 (OH); 1H NMR (400 MHz, DMSO-d6) δ ppm: 2.36 (s, 3H, CH_3), 3.00-3.61 (m,10H, pyranose), 6.21-6.22 (d, 1H, NCH), 7.32-7.34 (d, 2H, Ar-H), 7.67-7.69 (d, 2H, Ar-H), Anal. Cald. For $C_{15}H_{18}N_2O_7$: C: 53.25 H: 5.36 N: 8.28 Found: C: 53.19 H: 5.38 N: 8.26.

5-(4-methyl-3-nitrophenyl)-3-(β-D-2,3,4,6-tetra-O-acetylglucopyranosyl)-1,3,4-oxadiazole-2(3H)one (4b): Yield: 41%; mp: 255-257 ^{o}C; Rf value: 0.89; IR (KBr, cm^{-1}): 1182 (NCO),1580 (C=N),1604 (C=C), 1682 (C=O), 3660 (OH), 1H NMR (400 MHz, DMSO-d6) δ ppm: 2.36 (s, 3H, CH_3), 3.05-3.64 (m, 10H, pyranose), 6.19-6.20 (d, 1H, NCH), 7.33-7.34 (d, 1H Ar-H), 8.03-8.04 (d, 1H, Ar-H), 8.35 (s, 1H, Ar-H) Anal. Cald. For $C_{15}H_{17}N_3O_9$: C: 47.00 H: 4.47 N: 10.96 Found: C: 47.05 H: 4.42 N: 10.93

5-(4-methyl-3,5-dinitrophenyl)-3-(β-D-2,3,4,6-tetra-O-acetylglucopyranosyl)-1,3,4-oxadiazole-2(3H)one (4c): Yield: 35%; mp: 245-246 ^{o}C; Rf value: 0.84; IR (KBr, cm^{-1}):1185 (NCO), 1579 (C=N), 1606 (C=C), 1684 (C=O), 3665 (OH); NMR (400, MHz, DMSO-d6) δ ppm: 2.37 (s, 3H, CH_3), 3.09-3.63 (m, 10H, pyranose), 6.13-6.14 (d, 1H, NCH), 8.76 (s, 2H, Ar-H) ; Anal. Cald. For $C_{15}H_{16}N_4O_{11}$: C: 42.06 H: 3.77 N: 13.08 Found C: 42.00 H: 4.03 N: 13.02.

5-(3-bromo-4-methylphenyl)-3-(β-D-2,3,4,6-tetra-O-acetylglucopyranosyl)-1,3,4-oxadiazole-2(3H)one (4d): Yield: 41%; mp: 245-246 ^{o}C; Rf value:0.80;IR (KBr,cm^{-1}): 1180 (NCO), 1581 (C=N), 1605 (C=C), 1683 (C=O), 3659 (OH), 1H NMR(400 MHz, DMSO-d6) δ ppm: 2.34 (s, 3H, CH_3), 3.11-3.70 (m,10H, pyranose), 6.16-6.17(d,1H, NCH), 7.13-7.15 (d, 1H, Ar-H), 7.79 (s, 1H, Ar-H), 7.91-7.92(d, 1H, Ar-H); Anal. Cald. For $C_{15}H_{17}N_2O_7B_r$: C: 43.18 H: 4.11 N: 6.71 Found: C: 43.10 H: 4.15 N: 6.67.

5-(3-methylphenyl)-3-(β-D-2,3,4,6-tetra-O-acetylglucopyranosyl)-1,3,4-oxadiazole-2(3H)one(4e): Yield: 36%; mp: 210-212 ^{o}C; Rf value: 0.81; IR (KBr, cm^{-1}): 1184 (NCO), 1578 (C=N), 1601 (C=C), 1683 (C=O), 3660 (OH); 1H NMR (400 MHz, DMSO-d6) δ ppm: 2.30 (s, 3H, CH_3), 3.08-3.67 (m,10H, pyranose), 6.14-6.15 (d, 1H, NCH), 7.19-7.76 (m, 3H, Ar-H), 7.62 (s, 1H, Ar-H), Anal. Cald. For $C_{15}H_{18}N_2O_7$ C: 53.25 H: 5.36 N: 8.28 Found: C: 53.20 H: 5.40 N: 8.25.

5-(3-methyl-4-nitrophenyl)-3-(β-D-2,3,4,6-tetra-O-acetylglucopyranosyl)-1,3,4-oxadiazole-2(3H)one (4f): Yield: 35%; mp: 247-248 ^{o}C; Rf value: 0.79; IR (KBr, cm^{-1}): 1179 (NCO), 1580 (C=N), 1602 (C=C), 1688 (C=O), 3659 (OH); 1H NMR (400 MHz, DMSO-d6) δ ppm: 2.64 (s, 3H, CH_3), 3.12-3.69 (m, 10H, pyranose), 6.18-6.19 (d, 1H, NCH), 7.90-7.91 (d, 1H, Ar-H), 7.90 (s,1H, Ar-H), 8.18-8.19 (d, 1H, Ar-H) ; Anal. Cald. For $C_{15}H_{17}N_3O_9$: C: 47.00 H: 4.47 N: 10.96 Found: C: 46.93 H: 4.49 N: 10.89

5-(4-bromo-3-methylphenyl)-3-(β-D-2,3,4,6-tetra-O-acetylglucopyranosyl)-1,3,4-oxadiazole-2(3H)one (4g): Yield: 36%; mp: 256-257 ^{o}C; Rf value: 0.85; IR (KBr, cm^{-1}): 1183 (NCO), 1583 (C=N),1602 (C=C), 1687 (C=O), 3662 (OH); 1H NMR (400 MHz, DMSO-d6) δ ppm: 2.35 (s, 3H, CH_3), 3.03-3.66 (m,10H, pyranose),

6.09-6.10 (d,1H, NCH), 7.32 (s, 1H, Ar-H), 7.43-7.45 (d, 1H, Ar-H), 7.31 (s, 1H, Ar-H), 7.48-7.51 (d, 1H, Ar-H) ; Anal. Cald. For $C_{15}H_{17}N_2O_7B_r$: C: 43.18 H: 4.11 N: 6.71 Found: C: 43.20 H: 4.07 N: 6.73

5-(2-methylphenyl)-3-(β-D-2,3,4,6-tetra-O-acetylglucopyranosyl)-1,3,4-oxadiazole-2(3H)one (4h): Yield: 41%; mp: 249-250 ^oC; Rf value: 0.78; IR (KBr, cm^{-1}): 1181 (NCO), 1586 (C=N), 1603 (C=C), 1681 (C=O), 3658 (OH); 1H NMR(400 MHz, DMSO-d6) δ ppm: 2.35 (s, 3H, CH_3), 3.13-3.68 (m, 10H, pyranose), 6.14-6.16 (d, 1H, NCH), 7.20- 7.67 (m , 4H, Ar-H) , Anal. Cald. For $C_{15}H_{18}N_2O_7$: C: 53.25 H: 5.36 N: 8.28 Found: C: 53.30 H: 5.32 N: 8.24.

5-(2-methyl-3-nitrophenyl)-3-(β-D-2,3,4,6-tetra-O-acetylglucopyranosyl)-1,3,4-oxadiazole-2(3H)one (4i): Yield: 39%; mp: 249-250; Rf value: 0.83; IR (KBr, cm^{-1}): 1180 (NCO), 1585 (C=N), 1604 (C=C), 1684 (C=O), 3662 (OH), 1H NMR (400 MHz, DMSO-d6) δ ppm: 2.36 (s, 3H, CH_3), 3.08-3.69 (m,10H, pyranose), 6.18-6.19 (d,1H, NCH), 8.05-8.19 (m, 3H, Ar-H) Anal. Cald. For $C_{15}H_{17}N_3O_9$: C: 47.00 H: 4.47 N: 10.96 Found C: 46.97 H: 5.01 N: 10.90.

5-(2-methyl-3,5-dinitrophenyl)-3-(β-D-2,3,4,6-tetra-O-acetylglucopyranosyl)-1,3,4-oxadiazole-2(3H)one (4j): Yield: 44%; mp: 278-280 ^oC; Rf value: 0.88; IR (KBr, cm^{-1}): 1181 (NCO), 1581 (C=N),1601 (C=C),1686 (C=O), 3660 (OH); H NMR (400 MHz, DMSO-d6) δ ppm: 2.33 (s, 3H, CH_3), 3.07-3.67 (m, 10H, pyranose) 6.12-6.13 (d,1H, NCH), 8.69 (s, 1H, Ar-H), 9.18 (s, 1H, Ar-H) ; Anal. Cald. For $C_{15}H_{16}N_4O_{11}$: C: 42.06 H: 3.77 N: 13.08 Found C: 41.99 H: 3.71 N: 13.03.

5-(3-bromo-2-methylphenyl)-3-(β-D-2,3,4,6-tetra-O-acetylglucopyranosyl)-1,3,4-oxadiazole-2(3H)one (4k): Yield: 33%; mp: 243-245 ^oC Rf value: 0.89; IR (KBr, cm-1): 1179 (NCO), 1585 (C=N), 1606 (C=C), 1689 (C=O), 3661 (OH); 1H NMR (400 MHz, DMSO-d6) δ ppm: 2.36 (s, 3H, CH3), 3.03-3.41 (m,10H, pyranose), 6.09-6.10 (d, 1H, NCH), 7.22-7.66 (m, 3H, Ar-H); Anal. Cald. For $C_{15}H_{17}N_2O_7B_r$: C: 43.18 H: 4.11 N: 6.71 Found C: 43.15 H: 4.19 N: 6.69.

3.7 Antifungal activity of compounds

The reliability of all the newly synthesized nucleosides 4(a-k) were tested against three pathogenic fungi *A. niger, A. flavus, F. oxysporum* by calculating its minimum inhibitory concentration (MIC) values and compared its activity with well-known antifungal agent fluconazole. Disk diffusion technique was applied for calculating MIC values [61] in Czapex Dox Agar medium. All the compounds were prepared in seven different concentrations 10 mg/mL, 5 mg/mL, 2.5 mg/mL, 1.25 mg/mL, 0.62 mg/mL, 0.31 mg/mL and 0.15 mg/mL by serial dilution method. The stock of the each compound was prepared by dissolving 20 mg in 2 mL of dimethyl sulfoxide (DMSO) that is the concentration of solution is 10mg/mL. Pipette out 1 mL of stock solution and dissolved in 1 mL DMSO to get concentration 5 mg/mL. The same process was repeated for the preparation of 2.5 mg/mL, 1.25 mg/mL, 0.62 mg/mL, 0.31 mg/mL and 0.15 mg/mL.

Cpaxek Dox Agar medium was prepared by dissolving 30g sucrose, 1g K_2HPO_4, 0.5g $MgSO_47H_2O$, 0.5g KCl, 0.01g $FeSO_47H_2O$ and 15g agar-agar in 1000 mL double distilled water then the solution was heated to boil and autoclaved for 1h. The obtained medium was poured into 90 mm sterile petri plate and allowed to solidify. Disks impregnated with test compound were placed on previously inoculated with test fungi and incubated at 37^oC for 48h. The concentration at which a clear ring is formed around the impregnated disk recorded as MIC value for the compound. All the experiments were carried out in triplicate. A control plate was also incubated at 37^oC for 48h.The same procedure was applied to know the MIC values of fluconazole used as standard drug. The results of antifungal studies of tested compounds and fluconazole are given in Table 1.The comparison studies of antifungal activities of all compounds were also showed in the form of bar diagram in Fig.1.

IV. Results and Discussion

The synthetic route for the synthesis of desired compounds are given in Scheme 1.Compounds benzohydrazide 2(a-k) were prepared by the esterification followed by condensation with hydrazine hydrate of differently subsituted benzoic acid 1(a-k) and formation of compounds 2(a-k) were confirmed by thier elemental analysis (C,H,N). Compounds 3(a-k) were prepared by reacting compounds 2(a-k) with CDI in presence of dioxane and resulted compounds were further condensed with β-D-1,2,3,4,6-penta-O-acetylglucopyranosyl followed by deacetylation to get the final desired compounds 4(a-k).

The IR band of compounds 3(a-k) revealed characteristic bands for -NCO at 1179-1187 cm^{-1}, C=N at 1576-1587 cm^{-1}, C=C(aromatic) at 1598-1609 $cm^{-1,}$ C=O at 1649-1683 cm^{-1} and >NH at 3299-3340 cm^{-1}. The IR band of compounds 4(a-k) revealed characteristic bands for -NCO at 1179-1185 cm^{-1}, C=N at 1578-1586 cm^{-1}, C=C(aromatic) at 1600-1606 $cm^{-1,}$ C=O at 1683-1688 cm^{-1} and -OH at 3658-3665 cm^{-1}.

The 1H NMR spectra of compounds 3(a-k) showed the singlet at δ=7.21-7.32 ppm characteristic for the secondary amine (>NH) and a singlet at δ=2.36-2.39 ppm for methyl proton (-CH_3). Compounds 3(a-k) have showed singlet, doublet and multiplet for aromatic proton depending upon environment. The 1H-NMR spectra of 4(a-k) showed the multiplet at 3.02-3.61 ppm characteristic for -OH proton present in pyranose ring singlet at

δ=2.36-2.38ppm for methyl proton(-CH_3)) doublet at δ=6.09-6.22 ppm for –NCH and singlet, doublet and multiplet for aromatic proton depending upon environment.

The IR bands at 3299-3340 cm^{-1} and 1H-NMR at δ=7.21-7.32ppm for >NH group did not appeared in title compounds 4(a-k) as compared to compounds 3(a-k). This observation including appearance of IR bands at 3658-3665 cm^{-1} of pyranose –OH,) doublet at δ=6.09-6.22 ppm for –NCH and multiplet at δ=3.00-3.70 ppm in 1H-NMR spectra of compounds 4(a-k) clearly indicates that compounds 3(a-k) are condensed with β-D-1,2,3,4,6-penta-O-acetylglucopyranosyl.

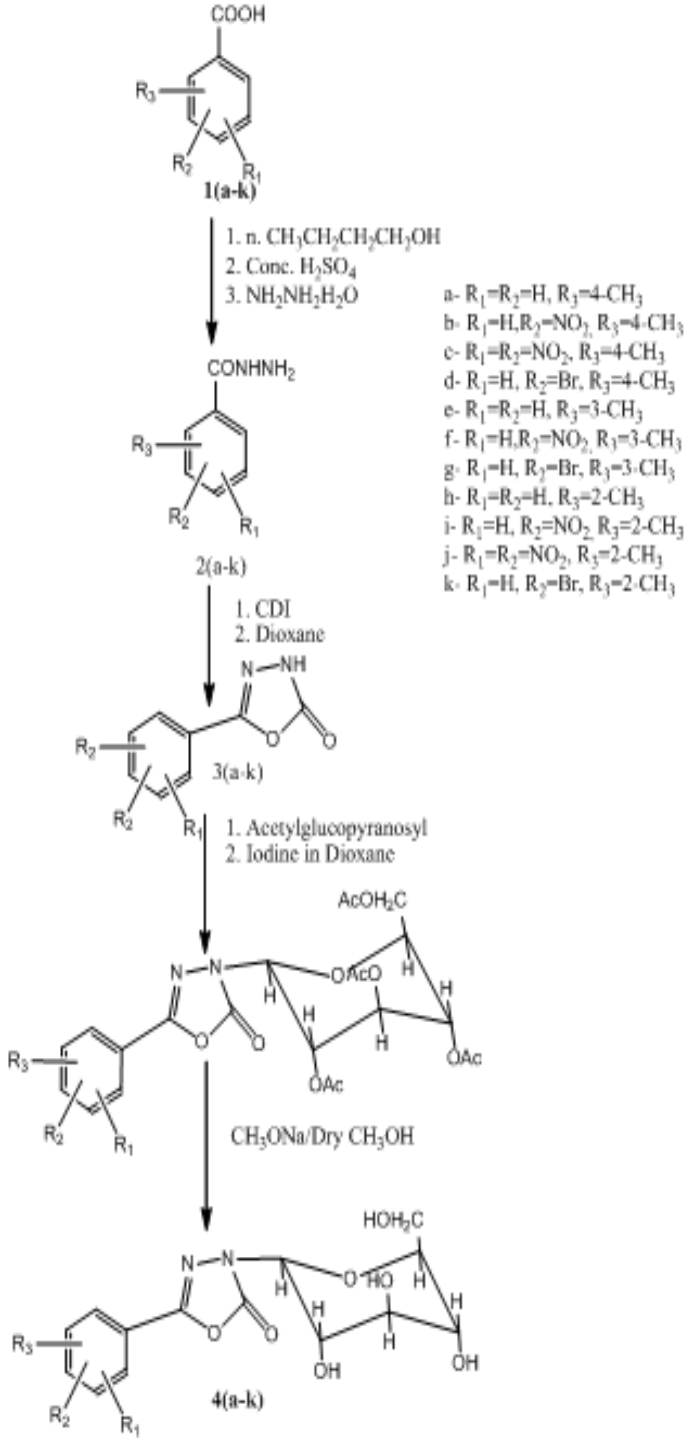
The antifungal data given in Table 1 showed that all the synthesized compounds are active against fungi taken for experiment. Some compounds are as active as reference standard fluconazole and some compounds are less active then reference standard against particular fungi. Compounds 4c, 4f, 4g and 4j are as active as fluconazole against fungi *A. niger* at 0.15mg/mL concentration. Compounds 4a, 4b, 4d, 4e, 4h, 4i, 4k are less active then fluconazole against fungi *A. niger*. For fungi *A. flavus*, compounds 4c, 4d, 4j and 4k are as potent as fluconazole at concentration 0.15mg/mL whereas 4a, 4b, 4e, 4f, 4g, 4h, 4i are less activity then reference standard. Compounds 4d, 4g, 4j are found similar active as fluconazole against *F. oxysporum* at concentration 0.15mg/mL on the other hand 4a, 4b, 4c, 4e, 4f, 4h, 4i and 4k are found less active against *F. oxysporum*.

V. Figures And Tables

Table 1. MIC (mg/mL) values of compounds

Compound	**R_1**	**R_2**	**R_3**	**Structure**	**Antifungal Activity**		
					A. niger	***A. flavous***	***F. oxysporam***
4a	H	H	4-CH_3		2.5	2.5	1.25
4b	H	NO_2	4-CH_3		1.25	1.25	0.62
4c	NO_2	NO_2	4-CH_3		0.15	0.15	0.31
4d	H	Br	4-CH_3		0.31	0.15	0.15
4e	H	H	3-CH_3		0.62	1.25	0.62
4f	H	NO_2	3-CH_3		0.15	0.62	0.31
4g	H	Br	3-CH_3		0.15	0.31	0.15
4h	H	H	2-CH_3		5.0	1.25	0.62
4i	H	NO_2	2-CH_3		0.31	0.62	0.31
4j	NO_2	NO_2	2-CH_3		0.15	0.15	0.15

4k	H	Br	2-CH_3		0.31	0.15	0.31
Fluconazole					0.15	0.15	0.15



scheme1. Synthetic route for the preparation of titled compounds

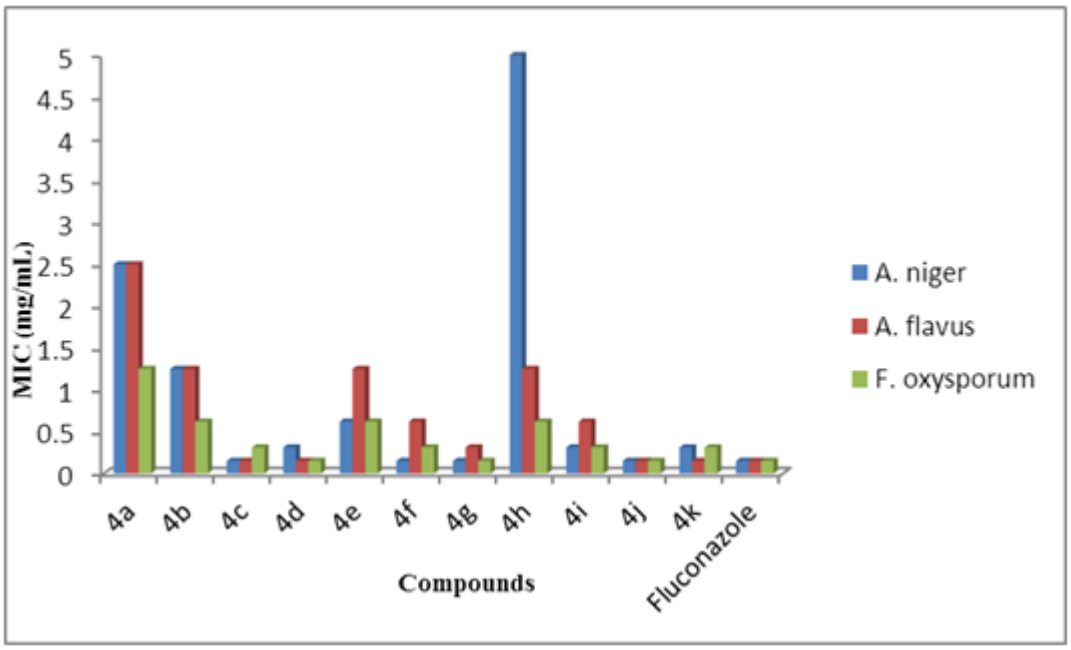


figure1. Antifungal activity of synthesized compounds 4(a-k)

VI. Conclusion

All the synthesized compounds were characterized with the help of elemental analysis, IR and 1H NMR spectra. The spectral data and disappearance of >NH group in the compounds 4(a-k) confirmed that the desire products had formed. The antifungal activity of the synthesized compounds were determined against three pathogenic fungus *A. niger*, *A. flovus*, *F. oxysporum* using fluconazole as reference standard by the disk diffusion method. The antifungal data of compounds have been reported in Table 1 which shows all the compounds are active.

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References

[1]. M.Y. Wani, A. Ahmed, R.A. Shiekh, K.J Al- Ghamgi, A.J. Sobral, Imidazole clubbed 1,3,4-oxadiazole derivatives as potential antifungal agents, *Bioorg Med Chem, 23(15),* 2015, 4172-80.

[2]. A.S. Grewal, S. Redhu, Synthesis Antibacterial and Antifungal Activity of 2,5-Disubstituted-1,3,4-oxadiazole Derivative, *International Journal of Pharm Tech Research, 6 (7),* 2014, 2015-2021.

[3]. P. Sengupta, M. Mal, S. Mandal, J. Singh, T. K. Maity, Evaluation of Antibacterial and Antifungal Activity of some 1, 3, 4 Oxadiazoles, *Iranian Journal of Pharmacology and Therapeutics 7(2),* 2008, 165-167.

[4]. Cai-Jun Chen, Bao-An Song, Song Yang, Guang-Fang Xu, P.S. Bhadury, Lin-Hong Jin, De-Yu Hu, Qian-Zhu Li, Fang Liu, Wei Xue, Ping Lu, Zhuo Chen, Synthesis and antifungal activities of 5-(3,4,5-trimethoxyphenyl)-2-sulfonyl-1,3,4-thiadiazole and 5-(3,4,5-trimethoxyphenyl)-2-sulfonyl-1,3,4-oxadiazole derivatives, *Bioorganic & Medicinal Chemistry, 15(12),* 2007, 3981-3989.

[5]. P. Zoumpoulakis, Ch.Camoutsis, G. Pairas, M. Soković , J. Glamoclija C. Potamitis, A. pitsas, Synthesis of novel sulfonamide-1,2,4-triazoles, 1,3,4-thiadiazoles and 1,3,4-oxadiazoles, as potential antibacterial and antifungal agents. Biological evaluation and conformational analysis studies, *Bioorganic & Medicinal Chemistry 20(4),* 2012, 1569-1583.

[6]. Jaiprakash, N. Sangshetti, A.R. Chabukswar, D.B. Shindea, Microwave assisted one pot synthesis of some novel 2,5- disubstituted 1,3,4-oxadiazoles as antifungal agents, *Bioorganic & Medicinal Chemistry Letters, 21(1),* 2011, 444-448.

[7]. Ming-Zhi Zhang, Nick Mulholl, David Beattie, Dianne Irwin, Yu-Cheng Gu, Qiong Chen Guang-Fu yang, John Clough, Synthesis and antifungal activity of 3-(1,3,4-oxadiazol-5-yl)-indoles and 3-(1,3,4-oxadiazol-5-yl) methyl-indoles, *European Journal of Medicinal Chemistry, 63,* 2013, 22-32.

[8]. B. Kaya Cavusoglu, L. Yurttas, Z. Canturk, The synthesis, antifungal and apoptotic effects of triazole-oxadiazoles against Candida species, *European Journal of Medicinal Chemistry, 144,* 2018, 255-261.

[9]. E. Abdu Musad, R. Mohamed, B. Ali Saeed, B.S. Vishwanath, K.M. Lokanatha Rai, Synthesis and evaluation of antioxidant and antibacterial activities of new substituted bis (1,3,4-oxadiazoles), 3,5-bis (substituted) pyrazoles and isoxazoles, *Bioorganic & Medicinal Chemistry Letters, 21(12),* 2011, 3536-3540.

[10]. Wei-Ming Xu, Fei-Fei Han, Ming He, De-Yu Hu, Jiang He, Song Yang, Bao-An Song, Inhibition of Tobacco Bacterial Wilt with Sulfone Derivatives Containing an 1,3,4-Oxadiazole Moiety, *Journal of Agriculture and Food Chemistry, 60 (4),* 2012,1036–1041.

[11]. Pei Li, Li Shi, Xia Yang, Lei Yang, Xue-Wen Chen, Fang Wu, Qing-Cai Shi, Wei-Ming Xu, Ming He, De-Yu Hu, Bao-An Song, Design synthesis and antibacterial activity against rice bacterial leaf blight and leaf streak of 2,5-substituted-1,3,4-oxadiazole/thiadiazole sulfone derivative, *Bioorganic & Medicinal Chemistry Letters, 24(7),* 2014,1677-1680.

[12]. N.P. Rai, V. Katharigatta, S. Shashikanth, P. N. Arunachalam, Synthesis, characterization and antibacterial activity of 2-[1-(5-chloro-2-methoxy-phenyl)-5-methyl-1H-pyrazol-4-yl]-5-(substituted-phenyl)-[1,3,4]oxadiazoles, *European Journal of Medicinal Chemistry, 44(11),* 2009, 4522-4527.

[13]. Pei Li, Li Shi , Man-Ni Gao, Xia Yang, Wei Xue, Lin-Hong Jin, De-Yu Hu, Bao-An Song, Antibacterial activities against rice bacterial leaf blight and tomato bacterial wilt of 2-mercapto-5-substituted-1,3,4-oxadiazole/thiadiazole derivatives ,*Bioorganic & Medicinal Chemistry Letters, 25(3),* 2015, 481-484.

[14]. Pei Li, Deyu Hu, Dandan Xie, Jixiang Chen, Linhong Jin, Baoan Song, Design Synthesis and Evaluation of New Sulfone Derivatives Containing a 1,3,4-Oxadiazole Moiety as Active Antibacterial Agents, *Journal of Agriculture and Food Chemistry , 66 (12),* 2018, 3093–3100.

[15]. A.S. Aboraia, H.M. Abdel-Rahman, N.M. Mahfouz, Mahmoud A.EL-Gendy, Novel 5-(2-hydroxyphenyl)-3-substituted-2,3-dihydro-1,3,4-oxadiazole-2-thione derivatives: Promising anticancer agents, *Bioorganic & Medicinal Chemistry, 14(4),* 2006, 1236-1246.

[16]. D. Kumar , S. Sundaree , E.O. Johnson , K. Shah, An efficient synthesis and biological study of novel indolyl-1,3,4-oxadiazoles as potent anticancer agents, *Bioorganic & Medicinal Chemistry Letters,19(15),* 2009, 4492-4494.

[17]. R. Gudipati, R.N. Reddy Anreddy, S. Manda, Synthesis, characterization and anticancer activity of certain 3-{4-(5-mercapto-1,3,4-oxadiazole-2-yl)phenylimino}indolin-2-one derivatives, *Saudi Pharmaceutical Journal, 19(3),* 2011,153-158,

[18]. M. Rashid, A. Husain, R. Mishra, Synthesis of benzimidazoles bearing oxadiazole nucleus as anticancer agents, *European Journal of Medicinal Chemistry, 54,* 2012,855-866.

[19]. Joana Darc S.Chaves, Luiza Guimarães Tune, Chris Hebertde J. Franco, Thiago Martins Francisco, Charlane Cimini Correa, Silvane MF Murta, Rubens LimaMonte-Neto, HevelineSilva, Ana Paula S Fontes, Mauro V.de Almeida, Novel gold(I) complexes with 5-phenyl-1,3,4-oxadiazole-2-thione and phosphine as potential anticancer and antileishmanial agents, *European Journal of Medicinal Chemistry, 127,* 2017, 727-739.

[20]. E. Palaska, GulayŞahin, PelinKelicen, N.TugbaDurlu , GulcinAltinok, Synthesis and anti-inflammatory activity of 1-acylthiosemicarbazides, 1,3,4-oxadiazoles, 1,3,4-thiadiazoles and 1,2,4-triazole-3-thiones, *Il Farmaco,57(2),* 2002, 101-107.

[21]. M. Akhter, A.H. Bismillah, A. Mohd Ajmal, Aroylpropionic acid based 2,5-disubstituted-1,3,4-oxadiazoles: Synthesis and their anti-inflammatory and analgesic activities, ,*European Journal of Medicinal Chemistry, 44(6),* 2009, 2372-2378.

[22]. S.V. Bhandari, K. G .Bothara, M.K.Raut, A.A Patil A. P. Sarkate, V.J Mokale, Design, Synthesis and Evaluation of Antiinflammatory, Analgesic and Ulcerogenicity studies of Novel S-Substituted phenacyl-1,3,4-oxadiazole-2-thiol and Schiff bases of Diclofenac acid as Nonulcerogenic Derivatives, *Bioorganic & Medicinal Chemistry, 16(4),* 2008, 1822-1831.

[23]. S. Bansal, M. Bala, S. Kumar Suthar, S. Choudhary, S. Bhattacharya, V. Bhardwaj, S. Singla A. Joseph, Design and synthesis of novel 2-phenyl-5-(1,3-diphenyl-1*H*-pyrazol-4-yl)-1,3,4-oxadiazoles as selective COX-2 inhibitors with potent anti-inflammatory activity, *European Journal of Medicinal Chemistry, 80,* 2014, 167-174.

[24]. S. Yatam, R. Gundla, S. Singh Jadav, N.R. Pedavenkatagari, J. Chimakurthy, N. Rani B, T. Kedam, Focused library design and synthesis of 2-mercapto benzothiazole linked 1,2,4-oxadiazoles as COX-2/5-LOX inhibitors, *Journal of Molecular Structure, 1159,* 2018, 193-204.

[25]. Xiuhai Gan, Deyu Hu, Zhuo Chen, Yanjiao Wang, Baoan Song, Synthesis and antiviral evaluation of novel 1,3,4-oxadiazole/thiadiazole-chalcone conjugates , *Bioorganic & Medicinal Chemistry Letters, 27(18),* 2017, 4298-430.

[26]. B.S. kumar, S.P. Vaidyanathan, S.Madhuri, K.P. Elango ,Synthesis and antiviral activity of sulfonohydrazide and 1,3,4-oxadiazole derivatives of 6,6-dimethyl-9-oxo-4,5,6,7,8,9-hexahydropyrazolo[5,1-b] quinazoline, *Antiviral Research,71(1),* 2006,7-14.

[27]. J. B. O'Neal, H. Rosen, P. B. Russell, A. C. Adams, A. Blumenthal Potential Hypoglycemic Agents: 1,3,4-Oxadiazoles and Related Compounds, *Journal of Medicinal Chemistry*, 1962, 5(3),617–626.

[28]. C. Cheptea, V. Sunel, M. Holban, J. Desbrieres, M. Popa, C. Lionte, Enhanced antipyretic activity of new 2,5-substituted 1,3,4-oxadiazoles encapsulated in alginate/gelatin particulated systems, *Cellulose chemistry and technology 46(1-2),* 2012, 19-25.

[29]. C. Cheptea, V. Sunel, M. Holban, J. Desbrieres, M. Popa, C. Lionte, Enhanced antipyretic activity of new 2,5-substituted 1,3,4-oxadiazoles encapsulated in alginate/gelatin particulated systems, *Cellulose chemistry and technology 46(1-2),* 2012, 19-25.

[30]. R. Schlecker, Peter C. Thieme, The synthesis of antihypertensive 3-(1,3,4-oxadiazol-2-yl) phenoxypropanolahines, *Tetrahedron, 44(11),* 1988, 3289-3294.

[31]. R. Kumar, N. Naik, S.C. Patil, S.B. Satyanarayan, Synthesis and Antioxidant, Antibacterial, Antihypertensive Activities of 8-hydroxyquinoline Appended with Oxadiazole and Triazole Rings, *Indo American Journal of Pharmaceutical Research, 49(09),* 2014.

[32]. S.Harada, E. Mizuta , K. Toyokaya, Structure of mildiomycin, a new antifungal nucleoside antibiotic, *Journal of the American Chemical Society,100(15),* 1978, 4895-4897.

[33]. J.B. Behr , T. Gourlian , A. Helimi , G. Guillem , Design synthesis and biological evaluation of hetaryl-nucleoside derivatives as inhibitors of Chitin synthase, *Bioorganic & Medicinal Chemistry,13(10),* 2003, 1713-1716.

[34]. R.W. Binkley, G.D. Hehemann ,W.W. Binkley, Photochemical oxidation of selected nucleosides and related carbohydrates, *The journal of organic chemistry, 43(13),* 1978, 2573–2576.

[35]. F. Benachenhou, G, Gosselin, N. Bounya ,Synthesis of various nucleosides derived from benzothiazole-2-thione as potential antifungal agents, *The jornal of organic chemistry,36(3),* 1988, 607-610.

[36]. R.K. Khare, A.K. Srivastava, H. Singh, Synthesis and fungicidal activity of some 6-aryl-2-(β-D-glucopyranosyl)-3-oxo-2,3-dihydro-1,3,4-oxadiazolo[3,2-b]-1,2,4,6-thiatriazine-1,1-dioxides, *Indian Journal of Chemistry, 44B*, 2005, 163-166.

[37]. R.K. Khare, A.K. Srivastava, H. Singh, Synthesis and fungicidal activity of some -3-(5-aryl-1,3,4-thiadiazol-2-yl)-1-(β-D-glucopyranosyl)-5-alkyl-2-thio-4-imidazalidinones, *Indian Journal of chemistry, 46B*, 2007, 875-879.

[38]. M.P. Anglada, A. Felipe, F.J. Casada, Transport and mode of action of nucleoside derivative used in chemical and antiviral therapies, *Trend in Pharmacological Science,19(10),*1998, 424-430.

[39]. F. Raymond et al, Structure activity relationships of pyrimidine nucleosides as antiviral agents for human immunodeficiency virus type1 **in** peripheral blood mononuclear cells, *Journal of Medicinal Chemistry,32(3),*1989, 612-617.

[40]. J.T. Wilkowski, K. Roland, Robins, W Robert Sidwell, N Lione, Simon, Design, Synthesis and broad spectrum antiviral activity of 1-beta-D-ribofuranosyl-1,2,4-Triazole-3-Carboxamide and related nucleosides, *Journal of Medicinal Chemistry,15(11),* 1972, 1150-1154.

[41]. W.M. Shannom, G Arnett, L. Westbook, Y.F. Shealy, CAO Dell, R.W. Brookman, Evaluation of carbodine, the carbocyclic analog of cytidine and related carbocyclic analogs of pyrimidine nucleosides for antiviral activity against human influenza type A viruses, *American Society for Microbiology*, *1981*,20(6),769-776.

[42]. KY Hostetler, L M Stuhmiller, H B Henting, H Van den Bosh and DD Richman, synthesis and antiretroviral activity of phospholipid analogs of azidothymidine and other antiviral nucleosides, *Journal of Bioorganic Chemistry*, *265*, 1990, 6112-6117.

[43]. Y Choi, Ling Li, Sue Grill, Elizabeth Gullen, Chang Soo Lee, Giuseppe Gumina, Eisaku, Structure- Activity Relationship of (E)-5-(2-Bromouinyl) uracil and related pyrimidine nucleoside as Antiviral Agenta for Herpes viruses, *Journal of Medicinal Chemistry, 43(13),*2000, 2538-2546.

[44]. S. Singh, R. Srivastava, Prof. Erik De Clercq, Dr. R K Singh, Synthesis and antiviral Properties of Arabino and Ribonucleosides of 1,3-Dicleazaodenine, 4-Nitro-1, 3-dicleaza adenine and Di Ketopiperazine, *Nucleoside Nucleotide Nucleic Acid, 23(12), 2004,* 1815-1824.

[45]. L.D.S. Yadav, S. Singh, Synthesis of antiviral acylic C nucleosides incorporating thiazola-1,3,4-oxa(Thai) diazole or thiazola-1,2,4-triazole structure as nucleobase, *Indian Journal of chemistry,40B(5)*, 2001, 440-442.

[46]. A. Gupte, H. L. Boshoff, D.S. Wilson, J. Nares, N. P. Labella, R.V. Somu, C. Xing, C.E. Barry III , C.C. Aldrich, Inhibition of Siderophore Biosynthesis by 2-Triazole Substituted Analogues of 5'-O-[N-(salicyl) Sulfamoyl] adenosine antibacterial Nucleosides effective against Mycobacterium Tuberculosis, *Journal of Medicinal Chemistry, 51(23),*2008,7495-7507.

[47]. J.Z. Stefanska, R Gralewska, BJ starosciak, Antimicrobial activity of substituted azoles and their nucleosides, *Die Pharmazie,54(12),*1999, 879-884.

[48]. S.N. Sriharsha, Sridharamurthy Satish Sheena Shashikanth, Koteshwara Anandarao Raveesha, Design, Synthesis and antibacterial activity of Novel 1,3-Thiazolidine Pyrimidine nucleoside analogues, *Bioorganic and Medicinal Chemistry, 14(22),*2004, 7476-7481.

[49]. A. Basak, R. Pal, Synthesis of β-Lactum nucleoside Chimera via Kinugasa reaction and evaluation of their antibacterial activity, *Bioorganic and Medicinal Chemistry, 15(8),* 2005, 2015-2018.

[50]. NA Al-Masoudi, A. Yaseen , Al-Soud , Ibrahim A. I. Ali, Synthesis of 1,2,4-Triazole c-Nucleosides from Hydrazonyl chloride and Nitriles, *Nucleosides, Nucleotides and Nucleic acids 26(1),* 2007, 37-43.

[51]. Yoon Sukhee, Sun Min Park, Hwan Mook Kim, Song-Kgu Park, Kiho nee, Chang Woo Lee, Bycang Hyean Kim, C_5-Modified nucleosides exhibiting anticancer activity, *Bioorganic and Medicinal Chemistry, 19(16),* 2009, 4688-4691.

[52]. S.W. Yao , VHC Lopes , F Fernandz , X Garcia-Merax, M. Morales, JE Rodriquiez-Borqies , M.N. Cordeiro , Synthesis and QSAR study of the anticancer activity of some novel indane carbocyclic Nucleosides, *Bioorganic & Medicinal Chemistry ,11(23),* 2003, 4999-5006..

[53]. S. Miura ,S Izuta, DNA Polymerases as targets of anticancer Nucleosides, *Current Drug Targets, 5(2),* 2014,191-195.

[54]. Y Lei, Dehua Zhang, Yang Liu, Guanghui Iian, Hongguang Ce, Synthesis and X Ray structure of New Anticancer Nucleosides Based on 1-[(2-Hydroxyethoxy)-methyl]-5-(Phenylthio)-1H-1,2,4-triazole-3-carboxamide, *Journal of Crystallization Process and Technology, 4,* 2014, 135-139.

[55]. Y Liu, Guanghui Tian, Hongguang Cie xiaoyan Cao, Synthesis and X Ray structure of Important Anticancer Nucleosides Intermediate (2R,3S,4S,5R)-2-(acetoxymethyl)-5-(3-Bromo-5-[methoxy carbonyl]-1H-1,2,4-Triazole-1-yl)Tetrahydrofuran-3,4-diyl Diacetate. *Journal of Crystallization Process and Technology,4,* 2014, 140-144.

[56]. C.I. Tanase, C. Draghici, M. Teodor Caraiu, S. Shova, C. Mathe, F.G. Cocu, C. Enache Maria Maganu, New carbocyclic nucleosides analogues with a bicycle[2,2,1] heptane fragment as sugar Maiety; Synthesis, X-Ray crystallography and anticancer activity, *Bioorganic & Medicinal Chemistry, 22(1),* 2014, 513-522.

[57]. A.B.A. El-Gazzar, HN Hafez, G A M Nawwar, New acyclic nucleosides analogues as potential analgesic, anti-inflammatory, anti-oxidant and anti-microbial derived from pyrimido[4,5-b] quinolones, *European Journal of Medicinal Chemistry*, 44(4), 2009, 1427-1436.

[58]. H N Hafez, Abdel-Rahman, B.A. El-Gazzar, Galal A.M. Nawwar, Synthesis, biological and medicinal significance of S-glycosido-Thieno[2,3-d]-pyrimidine as new anti-inflammatony and analgesic agents, *European Journal of Medicinal Chemistry, , 45(4),* 2010, 1485-1493.

[59]. Sh. H. Abdel-Hafez, HA Saad, MA Mohamed, Synthesis and pharmaclolgical activities of some new selenium containing nucleosides analogues, *Der Pharma Chemica, 4(3),* 2014, 915-925.

[60]. M. M. El Sadek, N. S. Abd El-Dayem, S. Y. Hasan, M. A. Mostafa, G.A. Yacout, Antioxidant and antitumor activities of new synthesized Aromatic C-Nucleoside Derivatives, *Molecules, 19(4),* 2014, 5163-5190.

[61]. E. A. Tendencia, Disk diffusion method, *Laboratory manual of standardized methods for antimicrobial sensitivity tests for bacteria isolated from aquatic animals and environment*, (Tigbauan, Iloilo, Philippines: Aquaculture Department, Southeast Asian Fisheries Development Center, 2004) 13-29.

Shubhra Srivastava. "Antifungal activity of newly synthesized nucleosides containing [1,3,4] oxadiazole-2(3H) one core." IOSR Journal of Applied Chemistry (IOSR-JAC) 11.12 (2018): 73-81.