International Journal of Pharmacy
Journal Homepage: http://www.pharmascholars.com

Research Article **CODEN: IJPNL6**

Synthesis and evaluation of 2-substituted thiadiazole Schiff bases

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ABSTRACT

A series of 1, 3, 4-thiadiazole schiff bases were synthesized and characterized by IR and ^{1}H NMR, ^{13}C NMR spectral data. The compounds were evaluated for antibacterial activity against gram-positive and gram-negative bacteria. Insilico screening was carried aiming to present potential selective activities as enzyme inhibitors and kinase inhibitors. These activities were suggested by the score values using molinspiration cheminformatics program.

Keywords: 1, 3, 4-thiadiazole, molinspiration cheminformatics program, schiff bases

INTRODUCTION

Thiadiazoles constitute a class of heteroaromatic compound containing two heteroatoms (sulphur and nitrogen). The structural moiety is found in natural products and an essential skeleton in medicinal compounds .1, 3, 4 thiadiazole represent an important heterocyclic system due to their pharmacological activities. They possess wide range of therapeutic activities like antimicrobial[(1)], antifungal[(2)], diuretics[(3)], antiepileptic[(4)], antiulcer[(5)], anticonvulsant[(6)], anti-inflammatory[(7)] ,anticonvulsant[(8)] etc. Thiadiazoles weresynthesized from thiosemicarbazide or hydrazide by methods like conventional [(9)], ultrasound or microwave using catalyst like sulphuric acid, polyphosphoricacid, phosphorous oxy chloride and hydrochloric acid. The thiadiazole heterocyclic ring that has been reported to date illustrates different approaches to the challenge of preparing these bioactive products and allows the synthesis of many novel chemical derivatives.

MATERIALS AND METHODS

Materials and Instruments: Materials and reagents were obtained from commercial suppliers (Merck grade) and were used without further purification. Progress of the reaction and purity of the compounds was checked on thin layer chromatography (TLC) plates (Silica Gel G). Melting points were determined on GallenKamp (MFB-600) melting point apparatus and were uncorrected. IRspectra were recorded in KBr discs on a Bruker analyzer. ^{1}H NMR and ^{13}CNMR spectra were recorded on a Bruker (400 MHz) and (125 MHz) spectrometer (chemical shifts in ppm) in DMSO using TMS as internal standard.

Typical Procedure For The Synthesis Of 2-Substituted 1, 3, 4-Thiadiazole Schiff Bases(4-21):
Step-1(4): Thiosemicarbazide (0.01moles) was dissolved in minimal quantity of water. To this vanillin (0.02moles) was added, mixed thoroughly and phosphorous oxy chloride was added drop by drop until the compound precipitates out. The product obtained was transferred to ice cold water and filtered under vacuum.

Step-2(5-21): Thiadiazole obtained in step1 was condensed with various aldehydes under basic conditions. The components were continuously stirred until the base gets precipitated .The product was transferred to ice cold water, filtered under suction and recrystallized with rectified spirit. The compounds were identify by physical characterization such as M.P, TLC.The complete experimental work of 2 -substituted 1, 3, 4-

thiadiazole Schiff bases were illustrated under **Scheme-1.**

4-(5-amino-1, 3, 4thiadiazol-2-yl)-2-methoxy phenol (4): Reactiontime: 30min; %yield:56.17%; R_f:0.56(ethylacetate:hexane1:1); M.P(^{0}c):178^{0}C; IR(KBr, V_{max},Cm^{-1}):3458(-NH_2), 3225(OH),3051(C-C),1512(C=N), 610 (C-S).;^{1}HNMR(400MHZ,MeOD): 2.58(NH_2),3.88(0-CH_3),5.94(OH),6.9,7.1,7.3(CH-protons).^{13}CNMR (125MHZ,MeOD) :56.17 (O-CH_3),113.31,113.89, 121.57, 125.80,149.13,150.18(Ar-protons),159.24, 167.47,(N-C-S).

2-methoxy-4-[(5-methylidene amino)-1, 3, 4-thiadiazole-2-yl] phenol (5)
Reactiontime:30min;%yield:58.2 %;R_f:0.61(ethylacetate:hexane1:1);M.P(^{0}c):155 ^{0}C ;IR(KBr,V_{max},Cm^{-1}):3220(OH),3017(C-C),1518(C=N),618(C-S);^{1}HNMR(400MHZ,MeOD):3.88 (CH_3):6.00(OH):6.92(N-CH_2):6.87,7.10,7.15, 7.34(CH-protons);^{13}CNMR(125MHZ,MeOD): 56.17(O-CH_3), 113.31,113.89,121.57, 125.80,149.13, 150.18(Ar-protons), 159.24, 167.47,(N-C-S).

2-methoxy-4-{5-[(E)-phenylmethylidene) amino]-1, 3, 4-thiadiazol-2-yl} phenol (6)
Reactiontime:30min;%yield:47.8%;R_f:0.46(ethylacetate:hexane1:1);M.P(^{0}c):180^{0}C;IR(KBr,V_{max},Cm^{-1}):3190(OH),3017(C-C),1518(C=N),618(C-S),1596(C=C).;^{1}HNMR(400MHZ,MeOD): 3.88 (OCH_3):6.01(OH):8.31(N-CH_2):6.92,7.15,7.32(CH-protons):7.32,7.56,7.45(Ar-(m))^{13}CNMR (125MHZ,MeOD):56.17(O-CH_3),113.31,113.89,121.57,125.80,149.13,150.18(Ar protons), 159.24 , 167.47,(N-C-S).

4-{5-[(E)-[4-hydroxy phenylmethylidene] amino]-1, 3, 4-thiadiazol-2-yl} 2-methoxy phenol (7)
Reactiontime:30min;%yield:62.6 %;R_f:0.55 (ethylacetate:hexane1:1);M.P(^{0}c):110^{0}C;IR(KBr, V_{max},Cm^{-1}):3232(OH),3048(C-C),1512(C=N),610.62(C-S),1586(C=C);^{1}HNMR(400MHZ ,MeOD):6.00(OH(s)):3.88(O-CH_3(S)):8.32(N--CH_2);9.89(Ar-OH):6.85,7.15,7.34(CH-protons) ^{13}CNMR(125MHZ,MeOD):56.17(O-CH_3),113.31,113.89,121.57,125.80,149.13,150.18(Ar-protons),159.24, 167.47,(N-C-S).

2-methoxy-4-{5-[(E)-[(4-nitrophenyl) methylidene] amino]-1, 3, 4-thiadiazol-2-yl} phenol (8)
Reactiontime:30min;%yield:73%;R_f:0.63(ethylacetate:hexane1:1);M.P(^{0}c):80^{0}C;IR(KBr, V_{max},Cm^{-1}):3214(OH),3014(C-C),1510(C=N),617(C-S),1542(C=C)1635(Ar NO_2).;^{1}HNMR (400 MHZ,MeOD):3.88(OCH_3),6.00(OH),8.34(N-CH_2),6.90,7.41,7.66(CH-protons),7.34,7.35(Ar-protons)^{13}CNMR(125MHZ,MeOD):56.17(O-CH_3),113.31,113.89,121.57, 125.80,149.13, 150.18 (Ar-protons), 159.24, 167.47,(N-C-S).

4-{5-[(E)-[(4-chlorophenyl) methylidene) amino]-1, 3, 4thiadiazol-2-yl}-2-methoxy phenol (9)
Reactiontime:30min;%yield:46.3%;R_f:0.43(ethylacetate:hexane1:1);M.P(^{0}c):130^{0}C;IR(KBr, V_{max},Cm^{-1}):3214(OH),3048(C-C),1513(C=N),615(C-S),1590(C=C),1296(Ar-Cl);^{1}HNMR (400 MHZ ,MeOD):3.88(OCH_3),6.00(OH),8.34(N-CH_2),6.90,7.41,7.66(CH-protons), 7.59,7.96(Ar-protons)^{13}CNMR(125MHZ,MeOD):56.17(O-CH_3),113.31,113.89,121.57,125.80, 149.13,150.18 (Ar-protons),159.24, 167.47,(N-C-S).

4-{5-[(E)-[(2-hydroxyphenyl) methylidene] amino]-1, 3, 4-thiadiazo-2-yl}-2-methoxy phenol (10)
Reactiontime:30min;%yield:54.6%;R_f:0.43(ethylacetate:hexane1:1);M.P(^{0}c):140^{0}C;IR(KBr, V_{max},Cm^{-1}):3234(OH),3052(C-C),1512(C=N),612(C-S), 1593(C=C).;^{1}HNMR(400MHZ,MeOD) :3.88(OCH_3),8.40(N-CH_2),6.00(OH),5.65,6.93(Ar-OH),7.16(CH-protons),7.32,7.42(Ar-protons)^{13}CNMR(125MHZ,MeOD):56.17(O-CH_3),113.31,113.89,121.57,125.80,149.13, 150.18(Ar-protons),159.24, 167.47,(N-C-S).

2-methoxy-4-{5-[(E)-[(4-methoxy phenyl) methylidene] amino]-1, 3, 4 thiadiazol-2-yl phenol (11)
Reactiontime:30min;%yield:61.3%;R_f:0.63(ethylacetate:hexane1:1);M.P(^{0}c):180-185^{0}C;IR (KBr,V_{max},Cm^{-1}):3230(OH),3042(C-C),1505(C=N),603(C-S),1582(C=C);^{1}HNMR(400MHZ, MeOD):3.88(OCH_3):3.80(ArOCH_3):6.00(OH):8.32(NCH_3):7.07,7.15,7.32,(CH_2-protons): 7.15, 7.89,7.32,(Ar-CH)^{13}CNMR(125MHZ,MeOD):56.17(O-CH_3),113.31,113.89,121.57,125.80, 149.13, 150.18(Ar-protons),159.24, 167.47(N-C-S).

4-{5-[(E)-[(4-hydroxy-3-methoxy phenyl) methylidene] amino] thiadiazol-2-yl}-2-methoxy phenol (12)
Reactiontime:30min;%yield:46.5%;R_f:0.3(ethylacetate:hexane1:1);M.P(^{0}c):132^{0}C;IR(KBr, V_{max},Cm^{-1}):3233(OH),3051(C-C),1512(C=N),1588(C-S),611(N=CH_2),.;^{1}HNMR(400MHZ, MeOD):3.86(OCH_3):3.86(AR-OCH_3):36.00(OH):6.15(AR-OH):8.32(N-CH_2),7.02,7.32,7.15 (CH-protons):6.92,7.15,7.32(Ar-

protons)^{13}CNMR(125MHZ,MeOD):56.17(OCH_3),113.31, 113.89, 121.57, 125.80,149.13,150.18(Ar-protons),159.24, 167.47,(N-C-S).

4-{5-(E)-[(3-bromophenyl) methylidene] amino]-1, 3, 4 thiadiazol-2-yl}-2- methoxy phenol (13)

Reactiontime:30min;%yield:51.3%;R_f:0.58(ethylacetate:hexane1:1);M.P(^{0}c):150^{0}C;IR (KBr,V_{max},Cm^{-1}):3232(OH),3148(C-C),1526(C=N),617(C-S),3648(N=CH_2),1594(C=C),671 (Ar -Br);^{1}HNMR(400MHZ,MeOD):3.88(OCH_3):6.01(OH):8.33(N-CH_2):6.93,7.12,7.37(CH-protons) :7.59,7.57,7.60(Ar-protons)^{13}CNMR(500MHZ,MeOD):56.17(O-CH_3) , 113.31,113.89, 121.57, 125.80,149.13,150.18(Ar-protons),159.24, 167.47,(N-C-S).

2-methoxy -4-{5-[(E)-{(3-nitro phenyl) methylidene] amino]-1, 3, 4- thiadiazol-2-yl} phenol (14)

Reactiontime:30min;%yield:56.4%;R_f:0.58(ethylacetate:hexane1:1);M.P(^{0}c):92^{0}C;IR(KBr, V_{max},Cm^{-1}): 3291(OH),3014(C-C),1510(C=N),1542(C-S), 1542 (C=C),3670(Ar-NO_2).;^{1}HNMR (400MHZ,MeOD):3.88(OCH_3):6.00(OH):6.90,7.41,7.65(CH-protons):8.25(N-CH_2): 8.09 ,8.36 ,8.50(Ar-protons)^{13}CNMR(125MHZ,MeOD):56.17(O-CH_3),113.31,113.89,121.57,125.80, 149.13, 150.18(Ar-protons),159.24, 167.47,(N-C-S).

4-{5-[(E)-{[4-(dimethylamino) phenyl] methylidene] amino]-1, 3, 4 thiadiazol-2-yl}-2-methoxy phenol (15)

Reactiontime:30min;%yield:58.3%;R_f:0.55(ethylacetate:hexane1:1);M.P(^{0}c):139^{0}C;IR(KBr, V_{max},Cm^{-1}):3234(OH),3048(C-C),1513(C=N),612(C-S),3667(N=CH_2),1593(C=C).^{1}HNMR (400MHZ,MeOD):3.88(OCH_3):3.02(NCH_3):8.33(N-CH_2):6.01(OH):7.32,7.15,6.92(CH-protons):6.74,7.06,6.80(Ar-protons)^{13}CNMR(125MHZ,MeOD):56.17(O-CH_3),113.31, 113.89, 121.57, 125.80,149.13,150.18(Ar-protons),159.24, 167.47,(N-C-S).

2-methoxy-4-{5-[(E)-[(3,4,5 tri methoxy phenyl) methylidene] amino] -1,3,4 thiadiazol-2-yl}phenol (16)

Reactiontime:30min;%yield:49.8 %;R_f:0.75(ethylacetate:hexane1:1);M.P(^{0}c):132 ^{0}C; IR(KBr,V_{max},Cm^{-1}): 3234(OH),3048(C-C),1513(C=N),612(C-S), 3667(N=CH_2), 1593 (C=C).^{1}HNMR (400MHZ,MeOD):3.88(OCH_3),3.02(NCH_3),8.33(N-CH_2), 6.01(OH) :7.32,7.15,6.92(CH-protons):6.74,7.06,6.80(Ar-protons) ^{13}CNMR(125MHZ,MeOD): 56.17(O-CH_3),113.31,113.89, 121.57, 125.80,149.13,150.18(Ar-protons),159.24, 167.47,(N-C-S).

4-{5-[(E)-[(2, 4-dimethoxy phenyl) methylidene] amino] -1,3,4 thiadiazol-2-yl}-2-methoxy phenol (17)

Reactiontime:30min ;%yield:51.3%;R_f:0.63(ethylacetate:hexane1:1);M.P(^{0}c):136^{0}C; IR (KBr,V_{max},Cm^{-1}): 3234(OH),3048(C-C),1513(C=N),612(C-S),3667(N=CH_2), 1593(C=C).;^{1}H NMR (400MHZ,MeOD):3.88(OCH_3):3.75,3.86(Ar-OCH_3):6.01(OH): 8.34 (NCH_2): 7.15,6.92,7.32(CH-protons):6.93,6.91(Ar-protons):^{13}CNMR (125MHZ, MeOD): 56.17 (O-CH_3),113.31,113.89, 121.57, 125.80,149.13,150.18(Ar-protons),159.24, 167.47,(N-C-S).

4-{5-[(E)-[(3, 4 dimethoxy phenyl) methylidene amino]-1,3,4 thiadiazol-2-yl}-2-methoxy phenol (18)

Reactiontime:30min;%yield:39.6 %;R_f:0.63 (ethylacetate:hexane1:1);M.P(^{0}c):98 ^{0}C; IR(KBr, V_{max},Cm^{-1}): 3230(OH),3148(C-C),1513(C=N),612(C-S), 1593(C=C) ;^{1}HNMR (400MHZ ,MeOD):3.88(OCH_3):3.75,3.86(Ar-OCH_3):6.01(OH):8.34(N-CH_2): 7.15, 6.92,7.32(CH-protons):6.93,6.91(Ar-protons):^{13}CNMR(125MHZ,MeOD):56.17(O-CH_3), 113.31, 113.89, 121.57, 125.80,149.13,150.18(Ar-protons),159.24, 167.47,(N-C-S).

4-{5-[(E)-(4-hydroxy 3,5 –dimethoxy phenyl)methylidene] amino] 1,3,4 thiadiazol-2-yl} -2-methoxy phenol (19)

Reactiontime:30min ;%yield:42.1 %;R_f:0.7 (ethylacetate:hexane1:1);M.P(^{0}c):142^{0}C; IR(KBr, V_{max},Cm^{-1}): 3234(OH),3048(C-C),1513(C=N),612(C-S), 1593(C=C).; ^{1}HNMR (400MHZ ,MeOD): 3.88(OCH_3):3.82(Ar-OH):8.43(N-CH_2: 5.99(OH): 6.92,7.12,7.34(OH-protons) :6.92,7.12,7.34(OH-protons):6.41,6.65,8.22(Ar-protons) ^{13}CNMR (125MHZ,MeOD): 56.17(O-CH_3),113.31,113.89, 121.57, 125.80,149.13,150.18(Ar-protons), 159.24, 167.47,(N-C-S).

2-methoxy-4-{5-[(E)-propylidene amino] 1, 3, 4-thiadiazol-2-yl} phenol (20)

Reactiontime:30min ;%yield: 50.9%;R_f: 0.53(ethylacetate:hexane1:1);M.P(^{0}c):148 ^{0}C;IR (KBr,V_{max},Cm^{-1}): 3225(OH),3051(C-C),1512(C=N),610(C-S).;^{1}HNMR(400MHZ, MeOD): 3.88(0CH_3);3.86(Ar-OCH_3): 6.01(OH):8.34(NCH_2): 7.09,6.13,7.53 (CH-protons):

7.39, 7.40,7.42, (Ar-protons)^{13}CNMR(125MHZ,MeOD):56.17(O-CH_3),113.31,113.89, 121.57, 125.80,149.13, 150.18(Ar-protons),159.24, 167.47,(N-C-S).

4-{5-[(E)-(furan-2-ylmethylidiene) amino]-1, 3, 4 thiadiazol-2-yl}-2-methoxy phenol (21)

Reactiontime:30min;%yield:48.3%;R_f:0.58(ethylacetate:hexane1:1);M.P(^{0}c):184 ^{0}C;IR (KBr,V_{max},Cm^{-1}): 3236(OH),3053(C-C),1514(C=N),611(C-S),3669(N=CH_2). ;^{1}HNMR (400MHZ, MeOD):3.88(OCH_3),3.86(Ar-OCH_3);5.98(OH),8.54(Ar-OH),8.13(N-CH_2)7.35, 7.06, 6.92,(CH-protons):6.63,6.92,(Ar-OH)^{13}CNMR(125MHZ,MeOD): 56.17(O-CH_3),113.31,113.89, 121.57, 125.80,149.13,150.18(Ar-protons),159.24, 167.47,(N-C-S).

INSILICO EVALUATION:

Insilico evaluation was carried out by molinspiration, web based software [10] [11] to obtain parameters such as drug likeness and bioactive scores. Molinspiration cheminformatics program presents specific activity scores for each of these six receptor classes (GPCR ligand, ion channel modulator, kinase inhibitor, nuclear receptor ligand, protease inhibitor and enzyme inhibitor). The drug likeness score and the calculated value of various parameters of the isolated compounds (4-21) were represented in **Table 2** and the bioactive scores in **Table 3**.

ANTIBACTERIAL ACTIVITY:

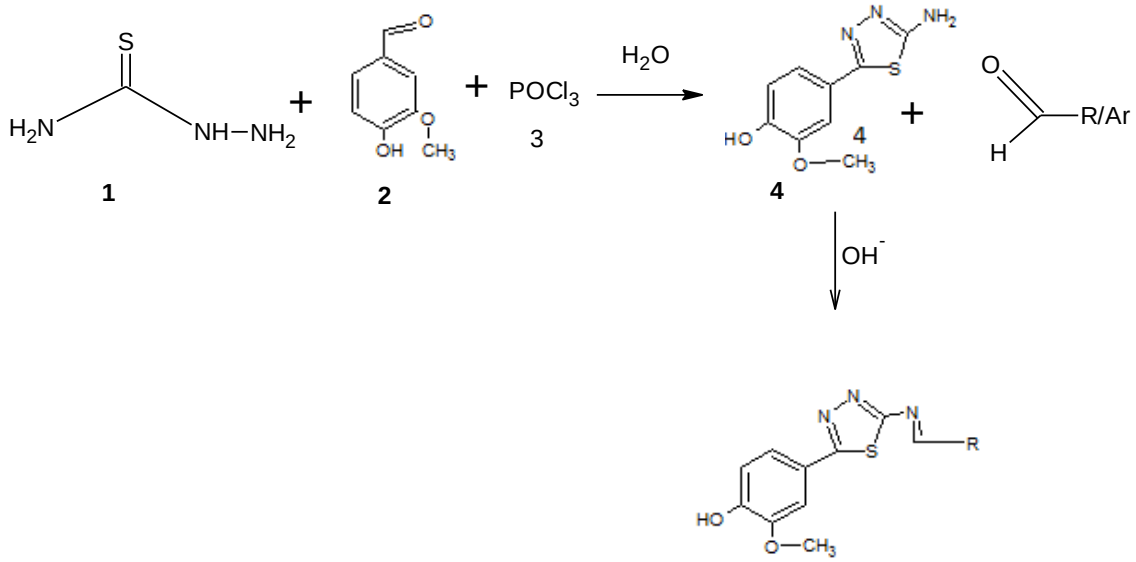
Cup plate method [12] [13] [14] using Mueller-Hinton agar medium was employed to study the preliminary antibacterial activity of compounds (4-21) against *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Bacillus subtilis*. The agar media was purchased from HI-media laboratories limited, Mumbai, India. Preparation of nutrient broth, subculture, base layer medium, agar medium and peptone water was done as per the standard procedure .Each test compound (5mg) was dissolved in 5ml of dimethyl formamide. Benzyl Penicillin was employed as reference standard (1000µg/ml) to compare the results. All the compounds were tested at a concentration of 0.15ml (100µg) level and DMF as control did not show any inhibition. The medium was inoculated at one percent level using 18hrs old cultures of the test organism mentioned above aseptically into sterile Petri dishes and allowed to set at room temperature for about 30 minutes. The test and standard solutions were added into cups, left for 90 minutes in a refrigerator for diffusion. After incubation for 24 hours at 37 °c, the plates were examined for inhibition zones. The results were tabulated in **table-4**

RESULTS AND DISCUSSION:

The results represented in **Table 2** fulfil Lipinski's rule and show good drug likeness score. **Table 3** showing specific activity scores for each of six receptor classes represents that all the compounds exbhited moderately active kinase and enzyme inhibition. Compounds **16** and **19** showed increased kinase and enzyme inhibition. The results of antibacterial activity revealed that all the compounds exhibited moderate to good antibacterial activity. Compounds **7,10,16,20** showed maximum activity against gram positive and gram negative organisms.

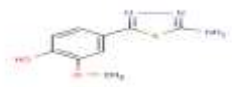
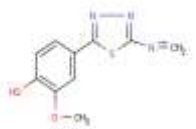
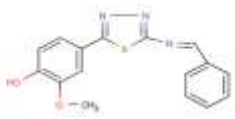
The structure-activity relationship studies based on the above results clearly indicate that a hydroxyl and methoxy substitution to the aryl group of thiadiazole is responsible for significant inhibitory activity. The results also indicate the rise in inhibition with the increase in the number methoxy substitution on the aryl ring. The results clearly revealed the contribution of electron releasing groups and electron withdrawing groups on the aryl substituted thiadiazole ring in determining the activity.

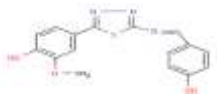
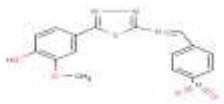
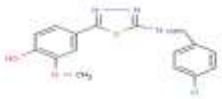
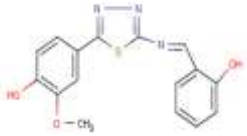
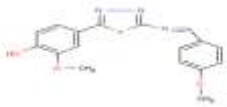
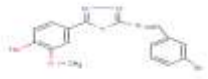
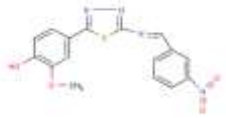
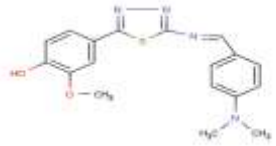
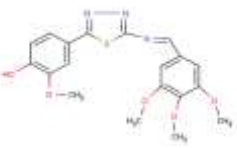
SCHEME-1



R= 5 HCHO
6 C_6H_5CHO
7 $C_6H_4(OH)CHO$
8 $C_6H_4(NO_2)CHO$
9 $C_6H_4(Cl)CHO$
10 $C_6H_4(O\text{-}OH)CHO$
11 $C_6H_4(O\text{-}OCH_3)CHO$
12 $C_6H_3(P\text{-}OH)m\text{-}OCH_3CHO$
13 $C_6H_4(P\text{-}Br)CHO$
14 $C_6H_4(m\text{-}NO_2)CHO$
15 $C_6H_5(N\text{-}(CH_3)_2)CHO$
16 $C_6H_2(3, 4,5\ OCH_3)CHO$
17 $C_6H_3(2, 4\ OCH_3)\ CHO$
18 $C_6H_3(3,4\ OCH_3)CHO$
19 $C_6H_2(P\text{-}OH)(3,5OCH_3)CHO$
20 CH_3CH_2CHO
21 $C_4H_3(O)CHO$

TABLE-1 GENERAL PROPERTIES

Compound	Structure	IUPAC name	M.W	Melting point(°c)	Elemental composition
4		4-(5-amino-1,3,4thiadiazol-2-yl)-2-methoxy phenol	223	178	C-48.4 H-4.06 N-18.82 O-14.2 S-14.36
5		2-methoxy-4-[(5-methylidene amino)-1,3,4-thiadiazole-2-yl]phenol	235	155	C-51 H-3.68 N-17.86 O-13.2 S-13.63
6		2-methoxy-4-{5-[(E)-phenylmethylidene)amino]-1,3,4-thiadiazol-2-yl}phenol	311	180	C-61.72 H-4.21 N-18.82 O-14.2 S-14.3

7		4-{5-[(E)-[4-hydroxy phenylmethylidene]amino]-1,3,4-thiadiazol-2-yl}2-methoxy phenol	327	110	C-58.7 H-4 N-14.6 O-12.84 S-9.8
8		2-methoxy-4-{5-[(E)-[(4-nitrophenyl)methylidene]amino]-1,3,4-thiadiazol-2-yl}phenol	356	80	C-53.93 H-3.39 N-17.3 O-15.72 S-9
9		4-{5-[(E)-[(4-chlorophenyl)methylidene)amino]-1,3,4thiadiazol-2-yl}-2-methoxy phenol	345	130	C-55.8 H-3.5 N-10.25 O-12.2 S-9.25
10		4-{5-[(E)-[(2-hydroxy phenyl)methylidene]amino]-1,3,4-thiadiazo-2-yl}-2-methoxy phenol	327	140	C-58.7 H-4 N-12.85 O-14.06 S-9.8
11		2-methoxy-4-{5-[(E)-[(4-methoxy phenyl)methylidene]amino]-1,3,4 thiadiazol-2-yl phenol	341	180	C-59.81 H-4.43 N-12.31 O-14.3 S-9.39
12		4-{5-[(E)-[(4-hydroxy-3-methoxy phenyl) methyl dine] amino] thiadiazol-2-yl}-2-methoxy phenol	357.38	132	C-57.13 H-4.23 N-11.76 O-17.23 S-8.097
13		4-{5-(E)-[(3 bromophenyl) methylidene]amino]-1,3,4 thiadiazol-2-yl}-2- methoxy phenol	390	150	C-49.24 H-3.1 N-10.2 O-8.2 S-8.2
14		2-methoxy -4-{5-[(E)-{(3-nitro phenyl) methylidene]amino]-1,3,4- thiadiazol-2-yl}phenol	356	92	C-53.93 H-3.39 N-15.72 O-17.2 S-9
15		4-{5-[(E)-{[4-(dimethyl amino)phenyl]methylidene]amino]-1,3,4 thiadiazol-2-yl}-2-methoxy phenol	354	139	C-61 H-5.12 N-15.81 O-9.03 S-9.05
16		2-methoxy-4-{5-[(E)-[(3,4,5 tri methoxy phenyl) methylidene] amino] -1,3,4 thiadiazol-2-yl}phenol	401	132	C-58.45 H-5.84 N-9.74 O-18.4 S-7.43

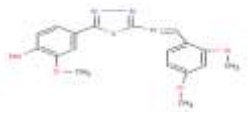
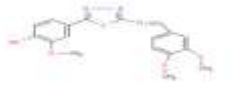
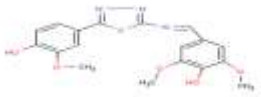
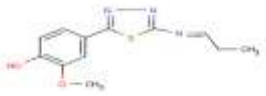
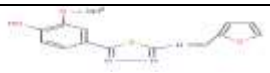
17		4-{5-[(E)-[(2,4-dimethoxy phenyl) methylidene] amino] -1,3,4 thiadiazol-2-yl}-2-methoxy phenol	371	136	C-37.40 H-4.61 N-11.31 O-17.2 S-8.3
18		4-{5-[(E)-[(3,4 dimethoxy phenyl) methylidene amino]-1,3,4 thiadiazol-2-yl}-2-methoxy phenol	371	138	C-37.40 H-4.61 N-11.31 O-17.2 S-8.3
19		4-{5-[(E)-(4-hydroxy 3,5 –dimethoxy phenyl)methyl dine] amino] 1,3,4 thia diazol -2-yl} -2-methoxy phenol	387	142	C-55.21 H-4.42 N-20.04 O-10.85 S-8.28
20		2-methoxy-4-{5-[(E)-propylidene amino]1,3,4-thiadiazol-2-yl} phenol	263	148	C-54.74 H-4.98 N-15.9 O-12.3 S-12.18
21		4-{5-[(E)-(furan-2-ylmethylidiene)amino]-1,3,4 thiadiazol-2-yl}-2-methoxy phenol	301.32	184	C-55.8 H-3.8 N-13.95 O-15.3 S-10.64

Table-2 MOLECULAR PROPERTIES

COMPOUND	Log p	TPSA	NON	NOHNH	Nviolation	Vol
4	1.395	81.26	5	3	0	182.703
5	3.44	67.61	5	1	0	266.08
6	2.96	87.83	6	2	0	274.101
7	3.404	113.43	8	1	0	289.41
8	4.123	67.61	5	1	0	279.61
9	3.385	87.83	6	2	0	274.101
10	3.501	76.85	6	1	0	291.629
11	1.863	67.61	5	1	0	194.989
12	2.784	97.01	7	2	0	299.64
13	4.23	67.61	5	1	0	283.969
14	3.38	113.43	8	1	0	289.418
15	3.54	70.84	6	1	0	311.989
16	3.076	95.31	8	1	0	342.721
17	3.418	97.07	7	2	0	292.64
18	3.091	86.071	7	1	0	317.175
19	2.8	106.306	8	2	0	325.193
20	3.288	67.61	5	1	0	244.84
21	2.702	80.75	6	1	0	247.651

TABLE-3 BIO ACTIVE SCORES

compound	GPCR	Ion channel	Kinase	Nuclear receptor	Protease	Enzyme
4	-0.95	-0.93	-0.26	-1.12	-1.12	-0.32
5	-0.73	-1.05	-0.26	-0.59	-0.88	-0.35
6	-0.66	-0.98	-0.21	-0.48	-0.80	-0.32
7	--0.78	-0.98	-0.36	-0.60	-0.88	-0.43
8	-0.68	-1.01	-0.26	-0.56	-0.86	-0.38
9	-0.68	-1.10	-0.24	-0.54	-0.77	-0.35
10	-0.65	-0.97	-0.24	-0.50	-0.76	-0.33
11	-0.86	-0.98	-0.44	-0.74	-1.17	-0.39
12	-0.63	-0.94	-0.23	-0.48	-0.73	-0.31
13	-0.80	-1.10	-0.32	-0.69	-0.96	-0.43
14	-0.79	-1.00	-0.36	-0.60	-0.88	--0.45
15	-0.62	-0.95	-0.18	-0.48	-0.76	-0.33
16	-0.57	-0.85	-0.20	-0.48	-0.67	-0.28
17	-0.63	-1.04	-0.23	-0.46	-0.69	-0.32
18	-0.60	-0.90	-0.22	-0.46	-0.70	-0.30
19	-0.59	-0.87	-0.19	-0.46	-0.67	-0.26
20	-0.58	-0.92	-0.39	-0.55	-0.86	-0.17
21	-0.83	-1.19	-0.58	-0.82	-1.10	-0.51

TABLE-4 ANTIBACTERIAL ACTIVITY

Zone of Inhibition in mm Per mg of compound				
compound		staphylococcus aureus	E.coli	pseudomonas aeroginosa
4	15	16	17	14
5	14	16	17	14
6	17	20	21	17
7	21	25	26	20
8	15	17	18	14
9	17	12	13	15
10	24	22	23	25
11	16	13	14	15
12	13	17	18	14
13	16	15	16	17
14	17	15	16	20
15	19	15	16	13
16	23	26	27	21
17	14	21	22	15
18	17	11	12	27
19	17	15	16	18
20	24	24	25	24
21	14	18	19	16
STD	26	24	27	24

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