ejpmr, 2017,4(12), 511-517

SJIF Impact Factor 4.161

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

SYNTHESIS, CHARACTERIZATION, ANTIMICROBIAL AND COMPUTATIONAL STUDIES OF SOME SULFONAMIDE DERIVATIVES POSSESSING THIADIAZOLE AND INDOLE NUCLEUS

Mohammad Arshad*

College of Medicine, Al-Dawadmi, Shaqra University, Kingdom of Saudi Arabia.

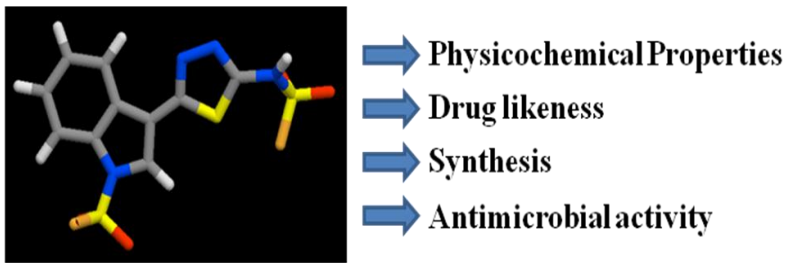
***Corresponding Author: Mohammad Arshad**

College of Medicine, Al-Dawadmi, Shaqra University, Kingdom of Saudi Arabia.

Article Received on 21/10/2017 **Article Revised on 12/11/2017** **Article Accepted on 02/12/2017**

ABSTRACT

The synthesis of N-{5-[1-(substituted-phenylsulfonyl)-1H-indol-3-yl]-1, 3, 4-thiadiazol-2-yl}-substituted-benzenesulfonamide (1-5), was performed followed by the computational screening.



The synthesized analogues were the evaluated for the antimicrobial assessment against Gram (+ve & -ve) pathogens such as *S. aureus, S. epidermidis, P. mirabilis* and *E. coli.* The findings portrayed that all the component were in compliance with the Lipinski Rule of Five and the bioactivity score is in active zone. The synthesized analogues showed better activity than the "Ciprofloxacin".

1. INTRODUCTION

Our regular effort in search for new antimicrobial therapeutic agents is still in demand due to the development of antimicrobial drug resistance to the available antimicrobial agents and the recent microbial infection.[1-2] Aromatic Heterocyclic compounds have been contributed a lot in medicinal chemistry. Especially, the synthesis of five membered heterocyclic compounds has been aimed by the researchers due to their potential physiological functions.[3-5] Our continuous contribution to find out new chemotherapeutic agents possessing the heterocyclic nucleus like tetrazole[6], pyrimidine[7, 8], pyrazoline[9-12], triazole[13], thiadiazole[14], triazine[15, 16], oxadiazole.[17-19] Heterocyclic nucleus, especially thiadiazole attracted more attention by the researcher for the preparation of new antimicrobial chemotherapeutic agents with different route for action. Literature survey revealed the tremendous biological activities of the thiadiazole derivatives such as Antimicrobial[20-23], anti-inflammatory[24-27], anticonvulsants[28, 29], antioxidant[30], anticancer[31], antifungal.[32] The indole nucleus has been a part of variety of antimicrobial agents.[33-38] On the other hand the various biological importances of the component with sulfony group have been noticed.[39-47] Recently, the study reported the synthesis of sulfonamide analogues containing the pyrimidine nucleus were assessed for antiamoebic and cytotoxicity.[7] Considering the importance of these functional moieties we designed the structure containing all the important part as discussed and it was thought that these structures will work together for the enhancement in therapeutic effect.

2. Experimental

2.1. Chemistry

2.1.1. General procedure for the synthesis 5-(1H-indol-3-yl)-1,3,4-thiadiazol-2-amine

The equivalent amount like 10 mmoles, of the indole-3-carboxylic acid and thiosemicarbazide was taken in a 100 mL round bottom flask, added the five ml of H_2SO_4 and put on refluxing for five hours. After completion the mixture was mixed with crushed ice to generate ppt that was separated, filtered and purified by ethanol.

5-(1H-indol-3-yl)-1,3,4-thiadiazol-2-amine: Yield: 90 %; m.p. 110-112 ^{0}C: Yellow crystals; Anal. calc. for $C_{10}H_8N_4S$: C 55.54, H 3.73, N 25.91, found C 55.55, H 3.75, N 25.88; FT-IR (cm^{-1}): 3390 (NH_2), 3280 (N–H), 2897 (C–H); ^{1}H NMR (DMSO-d6) (ppm): 10.931 (s, 1H,

NH), 9.608 (s, 2H, NH_2), 7.880-7.8918 (d, 2H, CH), 7.092-7.127 (m, 3H, CH), 6.980-7.044 (m, 3H, CH); ESI-MS (m/z): [M^+ + 1]: 217.12 (217.05).

2.1.2. General procedure for the synthesis of compounds 1-5.

5-(1H-indol-3-yl)-1,3,4-thiadiazol-2-amine, sulfonyl chloride and 10 % NaOH solution in a round bottom were refluxed for six hours. After the formation of product the reaction mixture was then added to the crushed ice to yield precipitate.

N-{5-[1-(phenylsulfonyl)-1H-indol-3-yl]-1,3,4-thiadiazol-2-yl}benzenesulfonamide (1): Yield: 80%; m.p. 131-133: Creamy crystals; Anal. calc. for $C_{22}H_{16}N_4O_4S_3$: C 53.21, H 3.25, N 11.28, found C 53.22, H 3.26, N 11.27; FT-IR (cm^{-1}): 3316 (N–H), 2895 (C–H), 1561 SO_2 Asym.), 1572 (SO_2 Asym.), 1021 (SO_2 Sym.), 1028 (SO_2 Sym.); ^{1}H NMR (DMSO-d6) (ppm): 10.931 (s, 1H, NH), 8.930 (s, 1H, CH), 7.960-7.991 (d, 2H, CH), 7.835-7.870 (d, 2H, CH), 7.630-7.661 (d, 2H, CH), 7.512-7.543 (d, 2H, CH), 7.439-7.488 (m, 2H, CH), 7.095-7.125 (m, 3H, CH), 6.983-7.038 (m, 3H, CH); ESI-MS (m/z): [M^+ + 1]: 497.06 (497.04).

N-{5-[1-(4-methylphenylsulfonyl)-1H-indol-3-yl]-1,3,4-thiadiazol-2-yl}-4-methylbenzenesulfonamide (2): Yield: 79 %; m.p. 128-131 ^{0}C: Creamy crystals; Anal. calc. for $C_{24}H_{20}N_4O_4S_3$: C 54.94, H 3.84, N 10.68, found C 54.96, H 3.82, N 10.66; FT-IR (cm^{-1}): 3317 (N–H), 2891 (C–H), 1569 SO_2 Asym.), 1577 (SO_2 Asym.), 1018 (SO_2 Sym.), 1020 (SO_2 Sym.); ^{1}H NMR (DMSO-d6) (ppm): 11.111 (s, 1H, NH), 8.942 (s, 1H, CH), 7.953-7.959 (d, 2H, CH), 7.792-8.082 (d, 2H, CH), 7.580-7.623 (d, 2H, CH), 7.437-7.471 (d, 2H, CH), 7.337-7.384 (d, 2H, CH), 6.993-7.028 (d, 2H, CH), 2.537 (s, 3H, CH_3), 2.529 (s, 3H, CH_3); ESI-MS (m/z): [M^+ + 1]: 525.09 (525.07).

N-{5-[1-(4-methoxyphenylsulfonyl)-1H-indol-3-yl]-1,3,4-thiadiazol-2-yl}-4-methoxybenzenesulfonamide (3): Yield: 83%; m.p. 130-132 ^{0}C: Creamy crystals; Anal. calc. for $C_{24}H_{20}N_4O_6S_3$: C 51.79, H 3.62, N 10.07, found C 51.75, H 3.68, N 10.11; FT-IR (cm^{-1}): 3307 (N–H), 2888 (C–H), 1563 SO_2 Asym.), 1570 (SO_2 Asym.), 1026 (SO_2 Sym.), 1033 (SO_2 Sym.); ^{1}H NMR (DMSO-d6) (ppm): 11.327 (s, 1H, NH), 8.763 (s, 1H, CH), 8.365-8.390 (d, 2H, CH), 8.175-8.203 (d, 2H, CH), 7.917-7.958 (d, 2H, CH), 7.874-7.900 (d, 2H, CH), 7.439-7.470 (d, 2H, CH), 7.217-7.253 (d, 2H, CH), 3.778 (s, 3H, OCH_3), 3.789 (s, 3H, OCH_3); ESI-MS (m/z): [M^+ + 1]: 557.10 (557.06).

N-{5-[1-(4-bromophenylsulfonyl)-1H-indol-3-yl]-1,3,4-thiadiazol-2-yl}-4-bromobenzenesulfonamide (4): Yield: 80%; m.p. 137-139 ^{0}C: Creamy crystals; Anal. calc. for $C_{24}H_{14}Br_2N_4O_4S_3$: C 40.38, H 2.16, N 8.56, found C 40.34, H 2.10, N 8.52; FT-IR (cm^{-1}): 3301 (N–H), 2888 (C–H), 1555 SO_2 Asym.), 1563 (SO_2 Asym.), 1015 (SO_2 Sym.), 1023 (SO_2 Sym.); ^{1}H NMR (DMSO-d6) (ppm): 10.931 (s, 1H, NH), 8.557 (s, 1H, CH), 8.193-8.212 (d, 2H, CH), 7.911-7.947 (d, 2H, CH), 7.801-7.835 (d, 2H, CH), 7.659-7.690 (d, 2H, CH), 7.321-7.357 (d, 2H, CH), (d, 2H, CH); ESI-MS (m/z): [M^+ + 1]: 656.88 (656.85).

N-{5-[1-(4-chlorophenylsulfonyl)-1H-indol-3-yl]-1,3,4-thiadiazol-2-yl}-4-chlorobenzenesulfonamide (5): Yield: 78 %; m.p.133-135 ^{0}C: Creamy crystals; Anal. calc. for $C_{22}H_{14}Cl_2N_4O_4S_3$: C 46.73, H 2.50, N 9.91, found C 46.75, H 2.51, N 9.90; FT-IR (cm^{-1}): 3321 (N–H), 2885 (C–H), 1558 SO_2 Asym.), 1566 (SO_2 Asym.), 1027 (SO_2 Sym.), 1035 (SO_2 Sym.); ^{1}H NMR (DMSO-d6) (ppm): 11.129 (s, 1H, NH), 8.757 (s, 1H, CH), 8.531-8.578 (d, 2H, CH), 8.310-8.357 (d, 2H, CH), 8.195-8.211 (d, 2H, CH), 8.091-8.111 (d, 2H, CH), 7.835-7.863 (d, 2H, CH), 7.437-7.469 (d, 2H, CH); ESI-MS (m/z): [M^+ + 1]: 564.91 (564.96).

2.2. Antimicrobial screening

The antimicrobial assessment for the synthesized compounds (1-5), was carried out against the pathogens (gram positive & negative) employing disc diffusion method with minor modification as described in.[48-52]

2.3. Computational studies

The calculation of drug likeness and the physicochemical properties was achieved by the software can be found at www.molinspiration.com, and the complete route is discussed in.[53-55]

3. RESULTS AND DISCUSSION

The novel investigation dealt with the preparation, characterization, drug likeness, physic-chemical calculation, antimicrobial assessment of the analogues possessing thiadiazole, indole and sulfony group in its structure. The synthesis of the compounds (1-5), was carried out by the two steps synthetic route represented in the Figure-1, The first step deals with the preparation of 5-(1H-indol-3-yl)-1,3,4-thiadiazol-2-amine by reacting indole-3-carboxylic acid with thiosemicarbazide followed by addition of H_2SO_4, under reflux. The final compounds (1-5) was obtained by the reaction of 5-(1H-indol-3-yl)-1,3,4-thiadiazol-2-amine with corresponding sulfonyl chloride with some drops of NaOH and refluxing. The structures of the prepared compounds were confirmed by the spectroscopic analysis like FT-IR, ^{1}H-NMR, elemental analysis, melting point and mass spectroscopy. The presence of FT-IR bands at 3390 cm^{-1}, 3280 cm^{-1} and 2897 cm^{-1} due to NH_2, NH and Ar-CH, simultaneously the absence of bands at or about 1700 due to the C=O of indole-3-carboxylic acid strongly recommended the formation of 5-(1H-indol-3-yl)-1,3,4-thiadiazol-2-amine. The absence of bands at 3390 cm^{-1}, 3280 cm^{-1} for NH_2 and NH and the presence of bands at 3301-3327 cm^{-1}, 1015-1035 cm^{-1} and 1555-1577 cm^{-1} due to NH, SO_2 (Sym.) and SO_2 (Asym.) respectively. Besides FT-IR data the ^{1}H-NMR also used for confirming the structure of the synthesized compounds. The synthesis of 5-(1H-indol-3-yl)-1,3,4-thiadiazol-2-

amine was confirmed by the presence of singlet at 10.931 ppm and 9.608 ppm due to NH and NH_2 and the absence of singlet for COOH proton. On the other hand the singlet in the range 10.931-11.327 ppm and 8.557-8.942 ppm due to NH and N-CH-C proton and the absence of singlets due to NH and NH_2 in the range 10.931 ppm and 9.608 ppm. The prepared analogues are analyzed to assess the parameters such as drug likeness and physicochemical. All the calculated analogues were found to portray excellent bioactivity and physicochemical properties Table-1. The zone of inhibition was calculated by the halo zone test and the disc diffusion method with modification and the results are tabled as Table-2, Figure-2. Using gram positive and gram negative pathogens the antimicrobial studies were performed and the findings exhibited that the prepared compounds possessed the antimicrobial potential better than the standard drug "Ciprofloxacin".

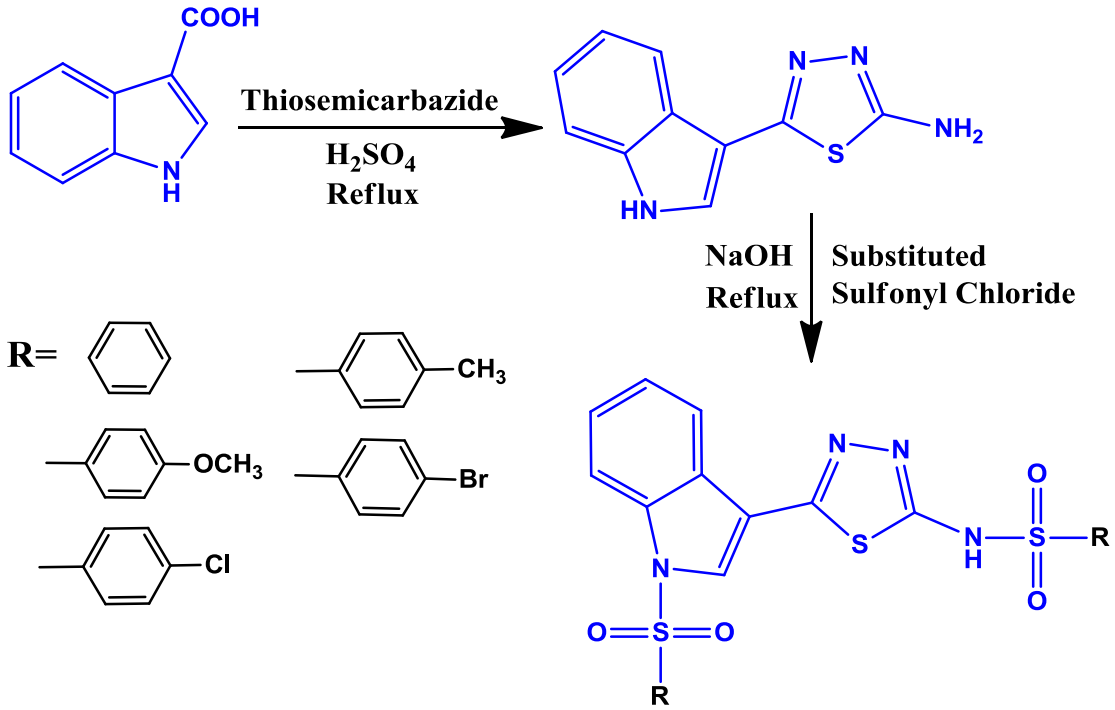


Figure 1: Systematic route adopted for the synthesis of compounds 1-5.

Table 1: Representing the Physicochemical property and the bioactivity score for the compounds (1-5) and standard.

Physicochemical property score	Components					
	1	2	3	4	5	STANDARD
miLogP	4.46	5.36	4.58	6.08	5.82	-0.071
TPSA	111.03	111.03	129.50	111.03	111.03	74.569
Natoms	33	35	37	35	35	24.0
MW	496.60	524.65	556.65	654.39	565.49	331.347
nON	8	8	10	8	8	6
nOHNH	1	1	1	1	1	2
Nviolations	0	2	1	2	2	0
Nrotb	6	6	8	6	6	3
Volume	385.29	418.41	436.38	421.06	412.36	285.460
Bioactivity score	Components					
	1	2	3	4	5	STANDARD
GPCR ligand	-0.10	-0.12	-0.12	-0.17	-0.10	0.12
Ion channel modulator	-0.43	-0.47	-0.50	-0.47	-0.42	-0.04
Kinase inhibitor	0.09	0.05	0.05	0.05	0.07	-0.07
Nuclear receptor ligand	-0.34	-0.34	-0.31	-0.40	-0.34	-0.19
Protease inhibitor	-0.19	-0.22	-0.21	-0.26	-0.21	-0.21
Enzyme inhibitor	0.12	0.07	0.07	0.06	0.09	0.28

Table 2: Representing the effects of compounds (1-5), on growth of microorganism & Minimum Inhibitory Concentration.

S. No.	Effect of compounds on microorganism			
	Gram positive		Gram negative	
	S. aureus	*S. epidermidis*	*E. coli*	*P. mirabilis*
1	21.33±0.10	22.11±0.24	23.67±0.22	22.12±0.14
2	21.48±0.34	21.44±0.14	22.92±0.43	21.92±0.20
3	21.80±0.18	22.08±0.32	23.41±0.33	21.78±0.31
4	22.26±0.28	21.22±0.20	23.83±0.17	22.42±0.33
5	21.43±0.26	22.74±0.18	22.66±0.43	21.77±0.18
Ciprofloxacin	21.39±0.21	22.87±0.37	23.69±0.81	22.34±0.21
S. No.	**Minimum Inhibitory Concentration (µg/ml)**			
	Gram positive		**Gram negative**	
	S. aureus	***S. epidermidis***	***E. coli***	***P. mirabilis***
1	6.25	3.125	6.25	12.5
2	6.25	3.125	6.25	12.5
3	6.25	3.125	6.25	12.5
4	6.25	3.125	6.25	12.5
5	6.25	3.125	6.25	12.5
Ciprofloxacin	6.25	3.125	6.25	12.5

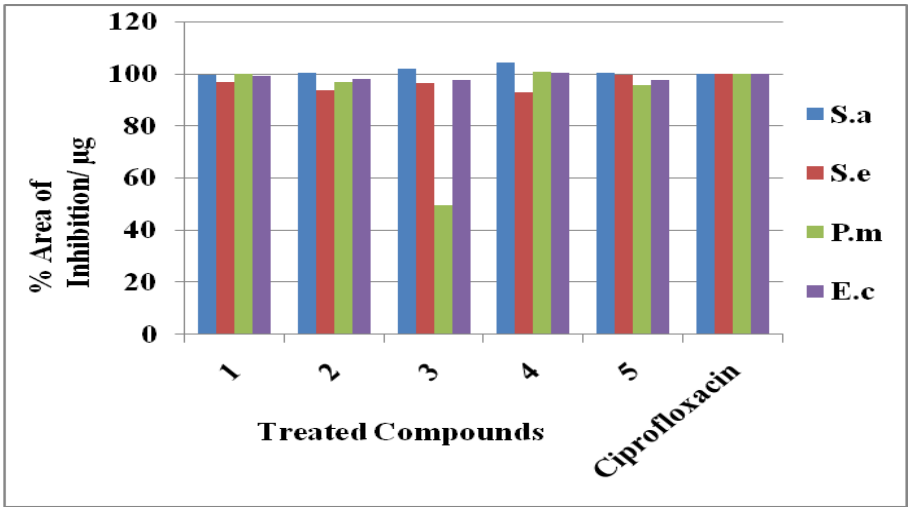


Figure 2: Representing the percent area of inhibition per microgram of compounds and ciprofloxacin.

4. CONCLUSION

The sulfonamide analogues with possessing indole and thiadiazole nucleus were designed and calculated the activity score and physicochemical property. Only the components with bioactivity score in the zone for active compounds were synthesized and assessed for antimicrobial potential. The synthesized analogues were found express the better antimicrobial potential than the Ciprofloxacin.

ACKNOWLEDGEMENT

Dr. Mohammad Arshad is highly thankful to Dr. Feras Al-Marshad, the dean college of medicine Al-Dawadmi, Shaqra University, Kingdom of Saudi Arabia.

REFERENCES

1. F.C. Tenover, L.C. McDonald, Vancomycin-resistant Staphylococci and Enterococci: epidemiology and control. Curr. Opin. Infect. Dis, 2005; 18: 300-305.
2. K.R. Babu, B. Eeshwaraiah, D. Aravind, H.M. Meshram, R.M. Raju, A. Bhattacharya, R. Bandichhor, Synthesis of quinoline analogues: search for antimalarial agents. Monatsh. Chem, 2008; 39: 179-181.
3. W. Bauer, W.M.M. Kirby, J.C. Sherris, M. Turck, Antibiotics susceptibility testing by a standardized single disk method. Am. J. Clin. Pathol, 1966; 45: 493-496.
4. Hetzhein, A., Mockel, K., Adv. Heterocycl. Chem, 1996; 7: 183.
5. Sandstrom, J., Adv. Heterocycl. Chem, 1968; 9: 165.
6. M. Arshad, A. R. Bhat, S. Pokharel, E. J. Lee, F. Athar, I. Choi, Synthesis, Characterization and Anticancer Screening of Some Novel Piperonyl-Tetrazole Derivatives, European Journal of Medicinal Chemistry, 2014; 71: 229-236.
7. A. R. Bhat, M. Arshad, E. J Lee, S. Pokharel, I. Choi, F. Athar, Synthesis, Characterization and Antiamoebic activity of N-(pyrimidine-2-

yl)benzenesulfonamide Derivatives, Chemistry & Biodiversity, 2013; 10: 2267-2277.
8. E. A. Alodeani1, M. A. Izhari, M. Arshad, Pharmacological potential and medicinalimportance of pyrimidine derivatives, 2014; 1: 504-527.
9. M. Arshad, Tazeem, A R Bhat, F. Athar, Heterocyclic Azoles and their biological application as antimicrobials, Journal of Natural Science, Biology and Medicine, 2011; 2: 1-156.
10. E. A. Alodeani, M. Arshad, M. A. Izhari, Burn skin pathogens: Isolation, identification and antimicrobial activity pattern against pyrazole derivatives, American Journal of Pharm Tech research, 2015; 5: 150-158.
11. Tazeem, M. Arshad, A R Bhat, F. Athar, Synthesis, characterization of heterocyclic compounds and their application as antibacterial therapeutic agents, Journal of Natural Science, Biology and Medicine, 2011; 2: 1-156.
12. Tuhfa, M. Y. Wani, M. Arshad, Tazeem, F. Athar, Chalcone scaffold: Synthesis, modification, characterization, molecular properties and screening against microbes, Journal of Natural Science Biology and Medicine, 2011; 2: 1-156.
13. M. Arshad, An insight to the synthetically obtained triazole possessing numerous biological activities, International Journal of Pharmacy and Pharmaceutical Sciences, 2014; 9: 16-24.
14. M. Arshad, 1, 3, 4-oxadiazole nucleus with versatile pharmacological applications: a review**,** IJPSR, 2014; 5: 1124-1137.
15. M. Arshad, A. R. Bhat, K. K. Hoi, I. Choi, F. Athar, Synthesis, characterization and antibacterial screening of some novel1,2,4-triazine derivatives, Chinese Chemical Letters, 2017; 28: 1559-1565.
16. M. Arshad, Recent development in the synthesis and biological activity of heterocyclic compounds with triazine nucleus, International Journal of Pharmaceutical Sciences and Research, 2014; 5: 149-162.
17. M. Arshad, T. A. Khan, Recent advances in the synthesis and biological activity of heterocyclic compounds possessing oxadiazole nucleus, International Journal of Pharma Sciences and Research, 2014; 5: 149-162.
18. M. Arshad, 1, 3, 4-Oxadiazole nucleus with versatile pharmacological applications: A Review, International Journal of Pharmaceutical Sciences and Research, 2014; 5: 1000-1013.
19. M. Arshad, T. A. Khan, Recent advances in the synthesis and biological activity of heterocyclic compounds possessing oxadiazole nucleus, International Journal of Pharma Sciences and Research, 2014; 5: 149-162.
20. V. Bhardwaj, Malleshappa N. Noolvi, S. Jalhan, Harun M. Patel, Synthesis, and antimicrobial evaluation of new pyridine imidazo [2,1b]-1,3,4-thiadiazole derivatives, Journal of Saudi Chemical Society, 2016; 20: s406-s410.
21. M. Gür, N. Şener, H. Muğlu, M. S. Çavuş, O. E. Özkan, F. Kandemirli, İ. Şener, New 1,3,4-thiadiazole compounds including pyrazine moiety: Synthesis, structural properties and antimicrobial features, Journal of Molecular Structure, 2017; 1139: 111-118.
22. A. Saeed, A. Mumtaz, Novel isochroman-triazoles and thiadiazole hybrids: Design, synthesis and antimicrobial activity, Journal of Saudi Chemical Society, 2017; 186-192.
23. M. N. Noolvi, Harun M. Patel, S. Kamboj, S. S. Cameotra, Synthesis and antimicrobial evaluation of novel 1,3,4-thiadiazole derivatives of 2-(4-formyl-2-methoxyphenoxy) acetic acid, Arabian Journal of Chemistry, 2016; 9: s1283-s1289.
24. A.A. Kadi, N.R. El-Brollosy, O.A. Al-Deeb, E.E. Habib, T.M. Ibrahim, A.A. El-Emam, Synthesis, antimicrobial, and antiinflammatory activities of novel 2-(1-adamantyl)-5-substituted- 1,3,4-oxadiazoles and 2-(1-adamantylamino)-5-substituted-1,3,4- thiadiazoles. Eur. J. Med. Chem, 2007; 42: 235–242.
25. M.D. Mullican, M.W. Wilson, D.T. Connor, C.R. Kostlan, D.J. Schrier, R.D. Dyer, Design of 5-(3,5-di-tert-butyl-4-hydroxyphenyl)-1,3,4-thiadiazoles, 1,3,4-oxadiazoles, and 1,2,4-triazoles as orally-active, nonulcerogenic, antiinflammatory agent. J. Med. Chem, 1993; 36: 1090-1099.
26. Y. Song, D.T. Connor, A.D. Sercel, R.J. Sorenson, R. Doubleday, P.C. Unangst, B.D. Roth, V.G. Beylin, R.B. Gilbertson, K. Chan, D.J. Schrier, A. Guglietta, D.A. Bornemeier, R.D. Dyer, Synthesis, structure-activity relationships, and in vivo evaluations of substituted di-tert-butylphenols as a novel class of potent, selective, and orally active cyclooxygenase-2 inhibitors. 2. 1,3,4-and 1,2–4-thiadiazole series. J. Med. Chem, 1999; 42: 1161-1169.
27. A.A. Bekhit, T. Abdel-Aziem, Design, synthesis and biological evaluation of some pyrazole derivatives as anti-inflammatory antimicrobial agents. Bioorg. Med. Chem, 2004; 12: 1935-1945.
28. C.B., Chapleo, M., Myers, P.L., Myers, J.F., Saville, A.C.B., Smith, M.R., Stilling, I.F., Tulloch, D.S., Walter, A.P., Welbourne, Substituted 1,3,4-thiadiazoles with anticonvulsant activity. 1. Hydrazines. J. Med. Chem, 1986; 29: 2273-2280.
29. C.B. Chapleo, P.L. Myers, A.C. Smith, M.R. Stilling, I.F. Tulloch, D.S. Walter, Substituted 1,3,4-thiadiazoles with anticonvulsant activity. 4. Amidines. J. Med. Chem, 1988; 31: 7-11.
30. D. Cressier, C. Prouillac, P. Hernandez, C. Amourette, M. Diserbo, C. Lion, G., Rima, Synthesis, antioxidant properties and radio protective effects of new benzothiazoles and thiadiazoles. Biol. Med. Chem, 2009; 17: 5275-5284.
31. J.Y., Chou, S.Y., Lai, S.L., Pan, G.M., Jow, J.W., Chern, J.H., Guh, Investigation of anticancer mechanism of thiadiazole-based compound in

human non small cell lung cancer A549 cells. Biochem. Pharmacol, 2003; 66: 115-124.
32. S.N. Swamy, Basappa, B.S. Priya, B. Prabhuswamy, B.H. Doreswamy, J.S. Prasad, K.S. Rangappa, Synthesis of pharmaceutically important condensed heterocyclic 4,6-disubstituted-1,2,4- triazolo-1,3,4-triadiazole derivatives as antimicrobials. Eur. J. Med. Chem, 2006; 41: 531-538.
33. P. Choppara, M.S. Bethu, Y.Vara Prasad, J.Venkateswara Rao, T.J.Uday Ranjan, G.V. Siva Prasad, R. Doradla, Y.L.N. Murthy, Synthesis, characterization and cytotoxic investigations of novel bis (indole) analogues besides antimicrobial study, Arabian Journal of Chemistry (2015) https://doi.org/10.1016/j.arabjc.2015.05.015
34. V. Ugale, H. Patel, B. Patel, S. Bari, Benzofurano-isatins: Search for antimicrobial Agents, Arabian Journal of Chemistry, 2017; 10: S389-S396.
35. J. S. Biradar, S. B. Somappa, Synthesis of novel Indolyl benzo[b][1,4]diazepins as a potent antimicrobial and antioxidant agents, Arabian Journal of Chemistry, 2016; 9: S1063-S1068.
36. M. Kumar, B. Narasimhan, K. Ramasamy, V. Mani, R. K. Mishra, A. B. A. Majeed, Synthesis, antimicrobial and cytotoxic evaluation of 4-(1-aryl-5-halo-2-oxo-1,2-dihydro-indol-3- ylideneamino)-N-substituted benzene sulfonamides. Arabian Journal of Chemistry, 2017; 10: S2845-S2852.
37. A. R. Saundane, Y. Manjunatha, Synthesis, antimicrobial and antioxidant activities of 2-oxo-6-phenyl-2-yl-4-(20-phenyl-50-substituted 1H-indol-30-yl)-1,2-dihydro pyridin-3-carbonitriles and their derivatives, Arabian Journal of Chemistry, 2016; 9: S501-S509.
38. S. S. Swathy, R. Selwin Joseyphus, V.P. Nisha, N. Subhadrambika, K. Mohanan, Synthesis, spectroscopic investigation and antimicrobial activities of some transition metal complexes of a [(2-hydroxyacetophenone)- 3-isatin]-bishydrazone. Arabian Journal of Chemistry, 2016; 9: S1847–S1857.
39. K. Uday, K. Amandeep, An Overview on Some Benzimidazole and Sulfonamide Derivatives with Anti-Microbial Activity. Research Journal of Pharmaceutical, Biological and Chemical Sciences, 2011; 2(4): 1116-1135.
40. B. Masereel, S. Rolin, F. Abbate, A. Scozzafava, C. T. Supuran, Carbonic anhydrase inhibitors: anticonvulsant sulfonamides incorporating valproyl and other lipophilic moieties. J. Med. Chem, 2002; 45(2): 312-320.
41. I. A. Barrios al., Pharmacophoric pattern of anti-epileptic sulfonamides and sulfamates-Theoretical study of the associated requirements. Journal of Molecular Structure (Theochem), 2002; 580: 243-250.
42. Y. Hai, B. S. Richard, New substrates and inhibitors of c-aminobutyric acid aminotransferase containing bioisosteres of the carboxylic acid group: Design, synthesis, and biological activity. Bioorganic & Medicinal Chemistry, 2006; 14: 1331-1338.
43. K. Gregory Current Understanding of Delayed Anticonvulsant Hypersensitivity Reactions. Epilepsy Currents, 2006; 6(2): 33-37.
44. S. Nadeem, P. Surendra Nath, A. K. Suroor, P. S. James, R. Arpana, A. Mahfuz, A. Md. Faiz, A. Mashooq, Synthesis and anticonvulsant activity of sulfonamide derivatives-hydrophobic domain. Bioorganic & Medicinal Chemistry Letters, 2007; 17: 255-259.
45. W., Jean-Yves, T., Anne, El C., Khaled, D., Jean-Michel, M., Jean-Louis, V., Daniela S., Andrea, M., Bernard, T., Claudiu, Supuran, Carbonic anhydrase inhibitors. Inhibition of isoforms I, II, IV, VA, VII, IX, and XIV with sulfonamides incorporating fructopyranose–thioureido tails. *Bioorganic &* Medicinal Chemistry Letters, 2007; 17: 2685-2691.
46. R. Gitto, S. Ferro, S. Agnello, L. De Luca, G. De Sarro, E. Russo, D. Vullo, C. T. Supuran, A. Chimirri, Synthesis and evaluation of pharmacological profile of 1-aryl-6,7-dimethoxy-3,4-dihydroisoquinoline-2(1H)-sulfonamides. Bioorganic & Medicinal Chemistry, 2009; 17: 3659-3664.
47. A. I. Marc, M. Bernard, R. Stephanie, S. Andrea, C. Gheorghe, C. Valentin, T. S. Claudiu, Carbonic anhydrase inhibitors: aromatic and heterocyclic sulfonamides incorporating adamantyl moieties with strong anticonvulsant activity. Bioorganic & Medicinal Chemistry, 2004; 12: 2717-2726.
48. A. Kareema, Laxmi, M. Arshad, N. Nishat, Herbo-Mineral based Schiff base ligand and its metal complexes: synthesis, characterization, catalytic potential and its biological applications, Journal of Photochemistry and Photobiology B: Biology, 2016; 160: 163-171.
49. N. Iram, M. S. Khan, R. Jolly, M. Arshad, M. Alam, P. Alam, R. H. Khan, Fa. Firdaus, Interaction mode of polycarbazole-titanium dioxide nanocomposite with DNA: Molecular docking simulation and in-vitro antimicrobial study, Journal of Photochemistry and Photobiology B: Biology, 2015; 153: 20-32.
50. S. A. A. Nami, M. Arshad, M. Shakir, M. S. Khan, M. Alam, D. U. Lee, S. Park, N. Sarikavakli, Morphological, structural, molecular docking and biocidal studies of newly synthesized Ppy-MA/TiO2 nanocomposites, Polymers for advanced technology, 2015; 26: 1627-1638.
51. R. Bushra, M. Shahadat, M. A. Khan, R. Adnan, M. Arshad, M. Rafatullah, M. Naushad, Preperation of Polyaniline based Nanocomposite material and their Environmental Applications, Int. J. Env. Sci. Technol, 2015; 12: 3635-3642.
52. S. A. A. Nami, M. S. Khan, M. Arshad, M. A. Raza, Imran Khan, Spectral, morphological, and antibacterial studies of conducting copolymers, Ppy-MA, and their nanocomposites, Ag@Ppy-MA, Polymers for advanced technology, 2017; 28: 10-19.

53. E. A. Alodeani, M. Arshad, M. A. Izhari, Antimicrobial screening of crude extract of Pluchea arabica: Chemical components, Drug likeness, Physicochemical property and molecular docking assessment, European Journal of Pharmaceutical and Medical Research, 2017; 4: 447-454.
54. E. A. Alodeani, M. Arshad, M. A. Izhari, Drug likeness and physicochemical properties evaluation of the alkaloids found in black pepper: piperine, piperidine, piperettine and piperanine, European Journal of Pharma and medical research, 2015; 2: 296-301.
55. M. Arshad, M. Shadab, Antimicrobial screening of crude extract of Zingber officinalle: Chemical components, Drug likeness, Physicochemical property and molecular docking assessment, European Journal of Pharmaceutical and Medical Research, 2017; 4: 364-368.
56. E. A. Alodeani, M. Arshad, M., A. Izhari, Antiuropathogenic activity, drug likeness, physicochemical and molecular docking assessment of (E-)-N'-(substitutedbenzylidene)-2-(quinolin-8-yloxy) acetohydrazide, Asian Pac J Trop Biomed, 2015; 5: 676-683.