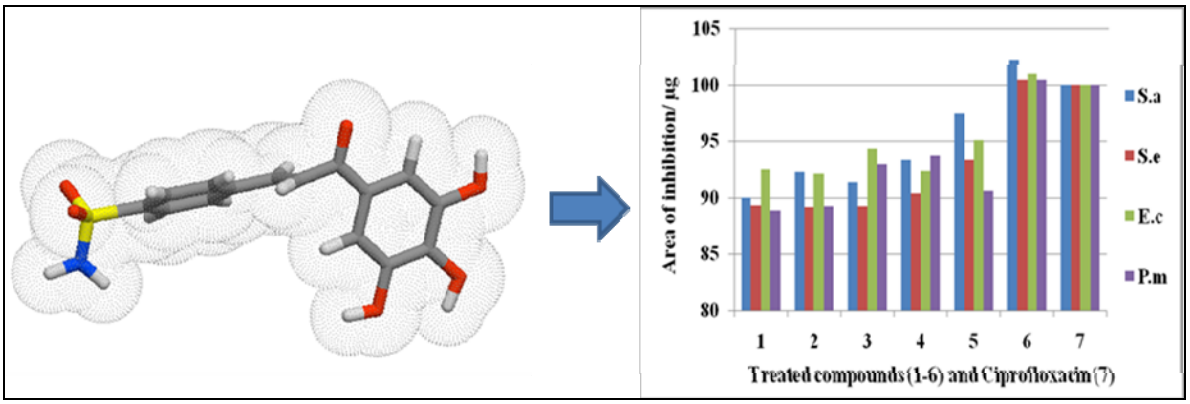
4-[(1*E*)-3-(Substituted-phenyl)-3-oxoprop-1-en-1-yl]benzenesulfonamide: Design, computational, synthesis, characterization and antibacterial assessment

Mohammad Arshad[1*]
Department of Basic Sciences, College of Medicine Al-Dawadmi
Shaqra University, Kingdom of Saudi Arabia
Email: m.arshad@su.edu.sa,Mohdarshad1985@gmail.com

Abstract: The present study is dealing with the designing, computational screening, synthesis and antibacterial assessment of 4-[(1*E*)-3-(Substituted-phenyl)-3-oxoprop-1-en-1-yl] benzenesulfonamide (1-6). The findings revealed that the designed compounds possess the good bioactivity score and follow the Lipinski's Rule of Five. The anti bacterial therapeutic effect of the prepared compounds was testes against S. aureus, S. epidermidis, E. Coli and P. mirabilis and reported to exhibit the significant activity.



Keywords: Chalcones, drug likeness, physicochemical properties, Synthesis, Antibacterial activity

1. Introduction:

Microbial infections in human remain life threatening due to the development of resistant by bacteria and fungi against the antimicrobial agents available in the market [1]. To get rid off with this problem there is always a demand to find out some new antimicrobial agents (Synthetic, semi-synthetic or natural). The synthesis of chalcones and there derivatives have been broadly studied and found to exhibit potential therapeutic effects such as Antibacterial [2], Anticancer [3-6], Anticonvulsant [7], Antiviral [8] Antidiabetic [9], Antitubercular [10], Carbonic anhydrase inhibitor [11-12], P53-MDM2 [13]. The synthetically obtained chalcones especially with hydroxy, alkoxy groups in different position have been reported to possess anti-bacterial [14], antifungal [15], antiulcer [16], antimalarial [17], antioxidant [18], antileshmanial [19] vasodilatory [20], antimitotic [21], and inhibition of chemical mediators release [22], inhibition of leukotriene B412 [22], inhibition of tyrosinase [23-24] and inhibition of aldose reductase [25] activities. On the other hand the Sulfonamide analogs exhibited the broad spectrum of biological potential like anti-microbial [26-29], anti-convulsant [30-33], carbonic anhydrase inhibitors [34-35], aromatase inhibitors [36], anti-cancer [37], anti-diabetic [38-39], anti-plasmodial activity [40], anti-cancer and radiosensitizing [41], anti-malaria [42], Agonist of oxytocin Receptor [43], anti-proliferative activity [44], Inhibitors of cycloxygenase-2 [45]. It was believed that the properties of chalcone individually and with specific substitutions or in combinations with sulfonamide functional groups enhances the probability of possessing the significant antibacterial therapeutic effects of the final compound.

2. Experimental:

2.1. Computational screening:

The structures of the designed compounds were drawn by Chem Draw Ultra 8.0 and the smile files were prepared. The software can be reached at (www.molinspiration.com) for calculating the physicochemical and bioactivity level score, the complete procedure and the detail of properties calculated are reported in the literature [46-52].

2.2. Chemistry:

2.2.1. General procedure for the synthesis of compounds 1-6:

A mixture of 4-acetylbenzenesulfonamide and the substituted aldehyde in equimolar ratio were dissolved in ethanol (50 mL). Drop wise addition with stirring was followed for the addition of NaOH (20 %) and to find out the state of reaction TLC plates were employed. After completion of the reaction the mixture was then added to ice cooled water for precipitation and recrystallized from methanol.

4-[(1*E*)-3-(4-methoxyphenyl)-3-oxoprop-1-en-1-yl]benzenesulfonamide (1):

Yield: 90 %; M.p. 118–112 ^{o}C; FT-IR (cm^{-1}): 1040 (SO_2-Sym), 1560 (SO_2-Asym), 1580 (C=C), 1702 (C=O), 2970 (CH-Ar), 3288 (NH_2); ^{1}H NMR ($CDCl_3$) (ppm): 3.788 (s, 3H, OCH_3), 6.940-6.995 (d, 2H, CH-Ar), 7.298-7.320 (d, 2H, CH-Ar), 7.453 (s, 1H, HC=CH), 7.632 (s, 2H, -SO_2NH_2), 7.738-7.774 (d, 2H, CH-Ar), 7.810-7.852 (d, 2H, CH-Ar), 7.882 (s, 1H, HC=CH).

4-[(1*E*)-3-(3,4-dimethoxyphenyl)-3-oxoprop-1-en-1-yl]benzenesulfonamide (2):

Yield: 83 %; M.p. 122–124 ^{o}C; FT-IR (cm^{-1}): 1047 (SO_2-Sym), 1558 (SO_2-Asym), 1589 (C=C), 1721 (C=O), 2982 (CH-Ar), 3308 (NH_2); ^{1}H NMR ($CDCl_3$) (ppm): 3.794 (s, 3H, OCH_3), 3.823 (s, 3H, OCH_3), 7.010-7.047 (d, 2H, CH-Ar), 7.138 (s, 1H, CH-Ar), 7.512 (s, 1H, HC=CH), 7.644 (s, 2H, -SO_2NH_2), 7.758-7.793 (d, 2H, CH-Ar), 7.827-7.863 (d, 2H, CH-Ar), 7.898 (s, 1H, HC=CH).

4-[(1*E*)-3-oxo-3-(3,4,5-trimethoxyphenyl)prop-1-en-1-yl]benzenesulfonamide (3):

Yield: 84 %; M.p. 126-128 ^{o}C; FT-IR (cm^{-1}): 1050 (SO_2-Sym), 1571 (SO_2-Asym), 1592 (C=C), 1718 (C=O), 2983 (CH-Ar), 3256 (NH_2); ^{1}H NMR ($CDCl_3$) (ppm): 3.773 (s, 3H, OCH_3), 3.831 (s, 3H, OCH_3), 3.886 (s, 3H, OCH_3), 7.121 (s, 1H, CH-Ar), 7.209 (s, 1H, CH-Ar), 7.457 (s, 1H, HC=CH), 7.690 (s, 2H, -SO_2NH_2), 7.767-7.803 (d, 2H, CH-Ar), 7.851-7.883 (d, 2H, CH-Ar), 7.914 (s, 1H, HC=CH).

4-[(1*E*)-3-(4-hydroxyphenyl)-3-oxoprop-1-en-1-yl]benzenesulfonamide (4):

Yield: 87 %; M.p. 121–123 ^{o}C; FT-IR (cm^{-1}): 1052 (SO^2-Sym), 1555 (SO^2-Asym), 1588 (C=C), 1737 (C=O), 2977 (CH-Ar), 3293 (NH_2), 3414 (OH); ^{1}H NMR ($CDCl_3$) (ppm): 5.413 (s, 1H, OH), 6.928-6.963 (d, 2H, CH-Ar), 7.238-7.270 (d, 2H, CH-Ar), 7.460 (s, 1H, HC=CH), 7.588 (s, 2H, -SO_2NH_2), 7.714-7.746 (d, 2H, CH-Ar), 7.808-7.839 (d, 2H, CH-Ar), 7.901 (s, 1H, HC=CH),

4-[(1*E*)-3-(3,4-dihydroxyphenyl)-3-oxoprop-1-en-1-yl]benzenesulfonamide (5):

Yield: 89 %; M.p. 126-128 ^{o}C; FT-IR (cm^{-1}): 1044 (SO_2-Sym), 1563 (SO_2-Asym), 1583 (C=C), 1736 (C=O), 2987 (CH-Ar), 3258 (NH_2), 3734 (OH), 3890 (OH); ^{1}H NMR ($CDCl_3$) (ppm): 5.345 (s, 1H, OH), 5.420 (s, 1H, OH), 7.125-7.163 (d, 2H, CH-Ar), 7.240 (s, 1H, CH-Ar), 7.508 (s, 1H, HC=CH), 7.652 (s, 2H, -SO_2NH_2), 7.762-7.799 (d, 2H, CH-Ar), 7.831-7.874 (d, 2H, CH-Ar), 7.888 (s, 1H, HC=CH).

4-[(1*E*)-3-oxo-3-(3,4,5-trihydroxyphenyl)prop-1-en-1-yl]benzenesulfonamide (6):

Yield: 85 %; M.p. 130-132^{o}C; FT-IR (cm^{-1}): 1061 (SO_2-Sym), 1580 (SO_2-Asym), 1599 (C=C), 1743 (C=O), 2970 (CH-Ar), 3319 (NH_2), 3354 (OH), 3768 (OH), 3980 (OH);

^{1}H NMR ($CDCl_3$) (ppm): 5.349 (s, 1H, OH), 5.428 (s, 1H, OH), 5.556 (s, 1H, OH), 7.188 (s, 1H, CH-Ar), 7.237 (s, 1H, CH-Ar), 7.478 (s, 1H, HC=CH), 7.712 (s, 2H, -SO_2NH_2), 7.788-7.819 (d, 2H, CH-Ar), 7.912-7.957 (d, 2H, CH-Ar), 7.998 (s, 1H, HC=CH).

2.3. Antimicrobial screening:

The Disc Diffusion methodwith some modification was utilized to evaluate the antimicrobial therapeutic effects of 4-[(1*E*)-3-(Substituted-phenyl)-3-oxoprop-1-en-1-yl] benzenesulfonamide (1-6) against the gram (positive and negative) pathogens like S. aureus, S. epidermidis, E. Coli and P. mirabilis. To assess the inhibitory zone and MIC of the chalcone derivatives (1-6) and the ciprofloxacin (7) was performed by the protocol mentioned in [53-70].

3. Results and Discussion:

The structures of the target derivatives 4-[(1*E*)-3-(Substituted-phenyl)-3-oxoprop-1-en-1-yl] benzenesulfonamide (1-6), were prepared with the help of Chem Draw Ultra 8.0 and ChemSketch. The physicochemical properties and the bioactivity score were calculated with the help of online available software. The derivative responses were positive to the Lipinski Rule's of Five and significant bioactive score for the active drugs as an enzyme inhibitor, Table-1. After computational screening the derivatives (1-6) were synthesized by the protocol as discussed in Figure-1, by a very simple one step procedure in Which the Aromatic adehyde and aromatic ketone in equimolar ratios and 10 % NaOH solution, undergoes Claisen-Schmidt condensation reaction to yield the corresponding Chaconne. Many spectroscopic techniques were utilized to confirm the structures of the prepared compounds like FTIR, NMR, Mass Spectro-photometry. The representations of the bands in the range 1702-1743, 1580-1599 cm^{-1} due to the presence of characteristic groups like C=O and HC=CH confirmed the formation of the derivatives. Besides this the availability of other bands in the range 1040-1061, 1555-1580 and 3248-3319 cm^{-1} due to the presence of SO_2-sym, SO_2-Asym and NH_2 recommended the formation of compounds.

Besides this the presence of singlet in NMR spectra in the range 7.453-7.512 and 7.882-7.998 ppm due to the presence of HC=CH that confirms the α-β un-saturation and strongly supported the formation of the compounds. Additional singlet was also observed in the range 7.588-7.712 ppm due to the SO_2-NH_2 protons present in the structure. Other singlets in the range 5.200-5.600 ppm and 3.700-3.900 ppm for OH and OCH_3 were also observed in the spectra due to the presence of substitution accordingly. The compounds (1-6) and the standard drug ciprofloxacin were then subjected for the antibacterial assessment against the gram positive and negative pathogens like S. aureus, S. epidermidis, E. Coli and P. mirabilis employing disc Diffusion method. The results declared that the compound one and two were found to have less significant zone against all pathogens. While the significant zone of inhibition were observed in case of compounds 3-6 against all the pathogens, Table-2, Figure-2. The minimum inhibitory concentration of all the compounds was found similar to the level of ciprofloxacin, Table-2, Figure-2. The results strongly supported the findings of computational screening and can be lead to the in vivo studies.

Table-1: Representing the detailed physicochemical properties and bioactivity score of the designed compounds (1-6) and Ciprofloxacin (7).

Physicochemical property score	**Components**						
	1	**2**	**3**	**4**	**5**	**6**	**STANDARD (7)**
miLogP	2.56	2.15	2.14	2.03	1.54	1.25	-0.071
TPSA	86.47	95.70	104.94	97.46	117.69	137.92	74.569
Natoms	22	24	26	21	22	23	24.0
MW	317.37	347.39	377.42	303.34	319.34	335.34	331.347
nON	5	6	7	5	6	7	6
nOHNH	2	2	2	3	4	5	2
Nviolations	0	0	0	0	0	0	0
Nrotb	5	6	7	4	4	4	3
Volume	270.12	295.66	321.21	252.59	260.61	268.63	285.460
Bioactivity score	**Components**						
	1	**2**	**3**	**4**	**5**	**6**	**STANDARD (7)**
GPCR ligand	-0.24	-0.22	-0.21	-0.18	-0.16	-0.15	0.12
Ion channel modulator	-0.32	-0.31	-0.29	-0.19	-0.20	-0.19	-0.04
Kinase inhibitor	-0.31	-0.27	-0.25	-0.26	-0.25	-0.20	-0.07
Nuclear receptor ligand	-0.39	-0.36	-0.40	-0.25	-0.25	-0.25	-0.19
Protease inhibitor	-0.06	-0.05	-0.05	-0.01	-0.00	0.03	-0.21
Enzyme inhibitor	0.08	0.07	0.06	0.21	0.19	0.22	**0.28**

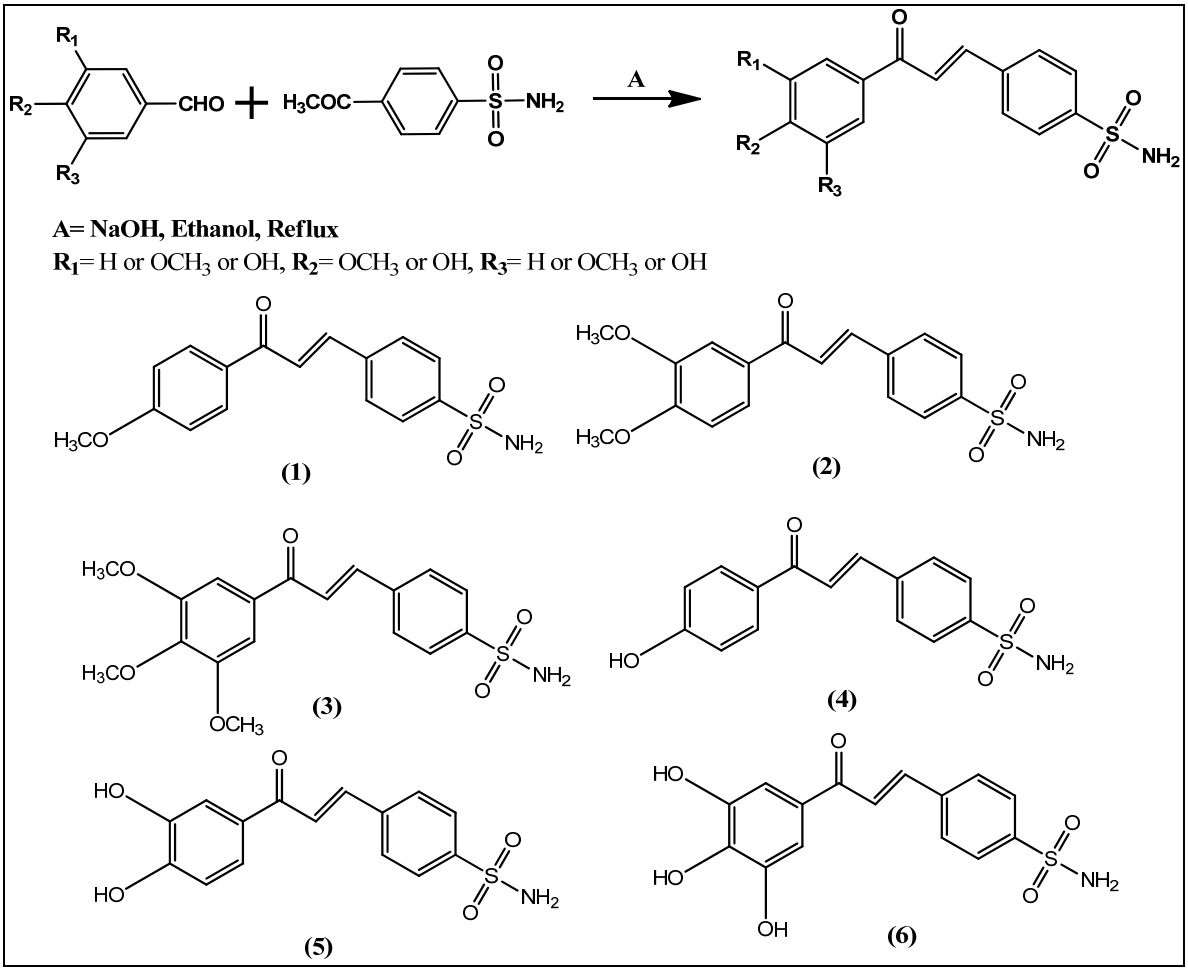


Figure-1: Representing the route adopted for the synthesis of Chalcone derivatives (1-6), and their corresponding structures.

Table-2: The zone of inhibition and the minimum inhibitory concentration of the compounds (1-6) and Ciprofloxacin (7).

S. No.	Effect of compounds on microorganism			
	Gram positive		Gram negative	
	S. aureus	*S. epidermidis*	*E. coli*	*P. mirabilis*
1	19.24±0.14	20.42±0.25	21.92±0.12	19.85±0.22
2	19.74±0.32	20.38±0.32	21.82±0.24	19.94±0.16
3	19.54±0.22	20.40±0.42	22.34±0.22	20.76±0.24
4	19.96±0.30	20.66±0.18	21.88±0.26	20.94±0.30
5	20.84±0.16	21.34±0.21	22.52±0.30	20.24±0.24
6	21.88±0.18	22.96±0.24	23.92±0.26	22.44±0.35
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
6	6.25	3.125	6.25	12.5
Ciprofloxacin	6.25	3.125	6.25	12.5

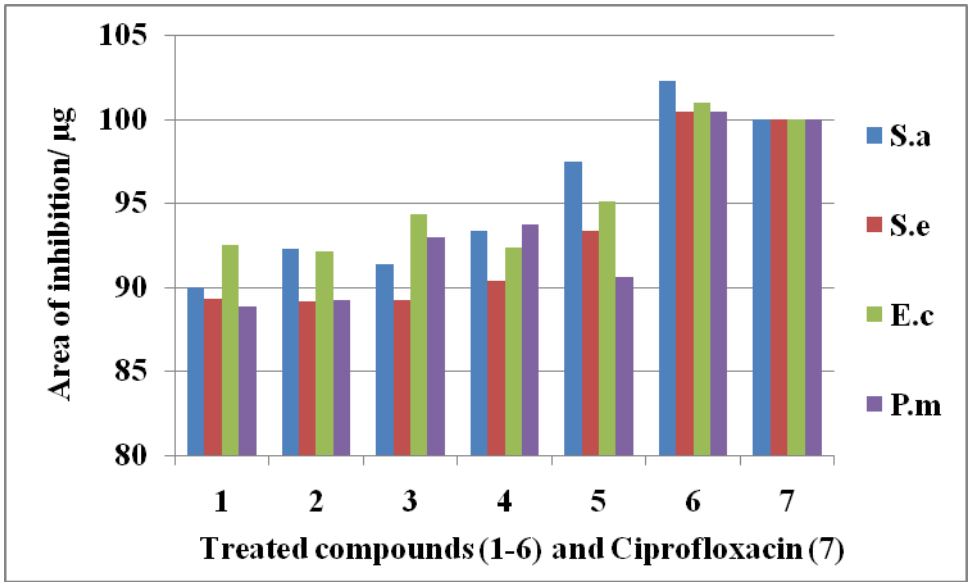


Figure-2: Showing the area of inhibition permicrogram of the compounds

4. Conclusion:

In recent study the series of 4-[(1*E*)-3-(Substituted-phenyl)-3-oxoprop-1-en-1-yl] benzenesulfonamide (1-6) was designed and subjected for calculation of bioactivity and physicochemical score computationally by the software available online. Computational screening exhibited that all the compounds follow the Lipinski Rule's of Five, and bioactive. Computational findings exhibited that all compounds are bioactive in nature. After computational screening the compounds were synthesized, characterized and subjected for antibacterial assessment. On comparing in between the computational and experimental findings it was observed that the similar findings obtained.

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] N. Ahmed, N. Kumar Konduru, M. Owais. Design, synthesis and antimicrobial activities of novel ferrocenyl and organic chalcone based sulfones and bis-sulfones. Arabian Journal of Chemistry. 2015, https://doi.org/10.1016/j.arabjc.2014.12.008.
[2] Salman A. Khan, Abdullah M. Asiri, Green synthesis, characterization and biological evaluation of novel chalcones as anti bacterial agents, Arabian Journal of Chemistry. 2017, 10: s2890-s2895.
[3] S. Madhavi, R. Sreenivasulu, J. Pragathi Yazala, et al., Synthesis of chalcone incorporated quinazoline derivatives as anticancer agents, Saudi Pharmaceutical Journal, 2017, 25 (2): 275-279.
[4] S. Park, E. Hye Kim, J. Kim, et al., Biological evaluation of indolizine-chalcone hybrids as new anticancer agents. European Journal of Medicinal Chemistry. 2018, 144: 435-443.
[5] B. Zengin Kurt, N. Ozten Kandas, A. Dag, Fatih Sonmez, et al., Synthesis and biological evaluation of novel coumarin-chalcone derivatives containing urea moiety as potential anticancer agents. Arabian Journal of Chemistry, 2017, https://doi.org/10.1016/j.arabjc.2017.10.001.
[6] U. Sankappa Rai, A.M. Isloor, P. Shetty, et al., Synthesis and in vitro biological evaluation of new pyrazole chalcones and heterocyclic diamides as potential anticancer agents, Arabian Journal of Chemistry. 2015, 8, (3): 317-321.
[7] N. Beyhan, B. Kocyigit-Kaymakcioglu, S. Gümrü, et al., Synthesis and anticonvulsant activity of some 2-pyrazolines derived from chalcones, Arabian Journal of Chemistry. 2017, 10: s2073-s2081.
[8] Z. Chen, P. Li, D. Hu, et al., Synthesis, antiviral activity, and 3D-QSAR study of novel chalcone derivatives containing malonate and pyridine moieties, Arabian Journal of Chemistry. 2015, https://doi.org/10.1016/j.arabjc.2015.05.003
[9] C-Y. Cai, L. Rao, Y. Rao, et al., Analogues of xanthones-Chalcones and bis-chalcones as α-glucosidase inhibitors and anti-diabetes candidates, European Journal of Medicinal Chemistry, Volume 130, 21 April 2017, Pages 51-59.
[10] M. N. Gomes, R. C. Braga, E. M. Grzelak, et al., QSAR-driven design, synthesis and discovery of potent chalcone derivatives with antitubercular activity, European Journal of Medicinal Chemistry, 2017, 137: 126-138.
[11] T. Arslan, G. Çelik, H. Çelik et al., Synthesis and biological evaluation of novel bischalcone derivatives as carbonic anhydrase inhibitors. Arch. Pharm. Chem. Life Sci., 2016, 349 :741-748.
[12] T. Arslan, E.A. S. Tu¨ rkog˘ lu, M. entu¨ rk., Synthesis and carbonic anhydrase inhibitory properties of novel chalcone substituted benzenesulfonamides. Bioorg. Med. Chem. Lett. 2016, 26: 5867-5870.
[13] D. Pereira, R. T. Lima, A. Palmeira, et al., Design and synthesis of new inhibitors of p53-MDM2 interaction with a chalcone scaffold, Arabian Journal of Chemistry, 2016, https://doi.org/10.1016/j.arabjc.2016.04.015
[14] L. XL,. X. YJ, G. ML. Functionalized chalcones with basic functionalities have antibacterial activity against drug sensitive, Staphylococcus aureus. European Journal of Medicinal Chemistry. 2008, 43: 681-1687.
[15] KL Lahtchev, DI. Batovska, SP. Parushev, et al., Antifungal activity of chalcones: A mechanistic study using various yeast strains. European Journal of Medicinal Chemistry. 2008, 43: 2220-2228.
[16] JA. Jeffrey, EO. Pamela, LR. Jared, et al., Synthesis and biological evaluation of flavonoids and related compounds as gastro-protective agents. Bioorganic & Medicinal Chemistry Letters. 1996, 6 (8): 995-998.

[17] VJ. Ram, A. Saxena, S. Srivastava, et al., Oxygenated chalcones and bischalcones as potential antimalarial agents. Bioorganic & Medicinal Chemistry Letters. 2000, 10: 2159-2161.
[18] A. Detsi, M. Majdalani, AK. Christos, et al., Natural and synthetic 20-hydroxy-chalcones and aurones: Synthesis, characterization and evaluation of the antioxidant and soybean lipoxygenase inhibitory activity. Bioorganic & Medicinal Chemistry. 2009, 17: 8073-8085.
[19] M. Liu, P. Wilairat, SL. Croft, et al., Structure-Activity Relationships of antileishmanial and antimalarial Chalcones. Bioorganic & Medicinal Chemistry. 2003, 11: 2729-2738.
[20] X. Dong, J. Chen, C. Jiang, et al., Design, synthesis, and biological evaluation of prenylated chalcones as vasorelaxant agents. Arch Pharm (Weinheim). 2009, 342(7): 428-32.
[21] YK. Rao, SH. Fang, YM. Tzeng. Synthesis and biological evaluation of 3,4,5-trimethoxychalcone analogues as inhibitors of nitric oxide production and tumor cell proliferation. Bioorganic & Medicinal Chemistry. 2009, 17: 7909-7914.
[22] HK. Horng, TT. Lo, LY. Kun, et al., Structure-activity relationship studies on chalcone derivatives: the potent inhibition of chemical mediators release. Bioorganic & Medicinal Chemistry. 2003, 11: 105-111.
[23] S. Khatib, O. Nerya, R. Musa, et al., Chalcones as potent tyrosinase inhibitors: the importance of a 2,4-substituted resorcinol moiety. Bioorganic & Medicinal Chemistry. 2005, 13: 433-441.
[24] SC. Te An Updated Review of Tyrosinase Inhibitors. Int. J. Mol. Sci, 2009, 10: 2440-2475.
[25] S. Fabio, B. Stefania, C. Luca, Synthesis and activity of a new series of chalcones as aldose reductase inhibitors. European Journal of Medicinal Chemistry, 1998, 33(11): 859-866.
[26] A. R. Bhat, M. Arshad, E. J Lee, et. al., Synthesis, Characterization and Antiamoebic activity of N-(pyrimidine-2-yl)benzenesulfonamide Derivatives, Chemistry & Biodiversity. 2013, 10: 2267-2277.
[27] 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.
[28] K. Ahmed, P. Swapna Rajesh, V.C.R.N.C. Shetti, et al. Synthesis, biological evaluation of new oxazolidino-sulfonamides as potential antimicrobial agents. Eur. J. Med. Chem., 2013, 62: 661-669.
[29] Z. Hui-Zhen, H. Shi-Chao, P. Yan-Jun, et al., Design, synthesis and antimicrobial evaluation of novel benzimidazole-incorporated sulfonamide analogues. Eur J Med Chem. 2017 Aug 18;136:165-183.
[30] B. Masereel, S. Rolin, F. Abbate, et. al., Carbonic anhydrase inhibitors: anticonvulsant sulfonamides incorporating valproyl and other lipophilic moieties. J. Med. Chem., 2002 45 (2): 312-320.
[31] K. Gregory. Current Understanding of Delayed Anticonvulsant Hypersensitivity Reactions. Epilepsy Currents., 2006, 6 (2): 33-37.
[32] S. Nadeem, P. Surendra Nath, A. K. Suroor, et. al., Synthesis and anticonvulsant activity of sulfonamide derivatives-hydrophobic domain. Bioorganic & Medicinal Chemistry Letters., 2007, 17: 255-259.
[33] A. I. Marc, M. Bernard, R. Stephanie, et.al., Carbonic anhydrase inhibitors: aromatic and heterocyclic sulfonamides incorporating adamantyl moieties with strong anticonvulsant activity. Bioorganic & Medicinal Chemistry., 2004, 12: 2717-2726,
[34] W. Jean-Yves, T. Anne, El C. et. al., 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.
[35] F. M. Awadallah, T. A. El-Waei, M. M. Hanna, et. al., Synthesis, carbonic anhydrase inhibition and cytotoxic activity of novel chromone-based sulfonamide derivatives. European Journal of Medicinal Chemistry., 2015, 96: 425-435.
[36] R. Pingaew, P. Mandi, V. Prachayasittikul, et.al., Synthesis, molecular docking, and QSAR study of sulfonamide-based indoles as aromatase inhibitors. Eur. J. Med. Chem., 2018, 143: 1604-1615.
[37] M. G. Mostafa, S. A. Mansour, H. A. Ghada, et. al., Analogue based drug design, synthesis, molecular docking and anticancer evaluation of novel chromene sulfonamide hybrids as aromatase inhibitors and apoptosis enhancers. Eur. J. Med. Chem., 2016, 124: 946-958
[38] R. Sharma, S. S. Soman. Design and synthesis of sulfonamide derivatives of pyrrolidine and piperidine as anti-diabetic agents. Eur. J. Med. Chem., 2015, 90: 342-350
[39] M. Taha, M. Irshad, S. Imran, Synthesis of piperazine sulfonamide analogs as diabetic-II inhibitors and their molecular docking study, Eur. J. Med. Chem., 2017, 141: 530-537.
[40] N. Devender, Sarika Gunjan, Renu Tripathi, et. al., Synthesis and antiplasmodial activity of novel indoleamide derivatives bearing sulfonamide and triazole pharmacophores. Eur. J. Med. Chem., 2017, 131: 171-184
[41] M. G. Mostafa, A. R. Fatma, I. H. Synthesis, anticancer and radiosensitizing evaluation of some novel sulfonamide derivatives, Eur. J. Med. Chem., 2015, 92: 682-692.
[42] R. Pingaew, V. Prachayasittikul, A. Worachartcheewan, et. al., Novel 1,4-naphthoquinone-based sulfonamides: Synthesis, QSAR, anticancer and antimalarial studies, Eur. J. Med. Chem., 2015, 103: 446-459
[43] A. K. Timothy, A. R. Tristan, L. W. Eryn, et.al., Investigation of pyrazolo-sulfonamides as putative small molecule oxytocin receptor agonists. Eur. J. Med. Chem., 2017, 136: 330-333.
[44] M. G. Mahmoud, M. I. El-Gamal, M. S. Abdel-Maksoud, et. al., Synthesis and in vitro antiproliferative activity of new 1,3,4-oxadiazole derivatives possessing sulfonamide moiety. Eur. J. Med. Chem., 2015, 90: 45-52.
[45] L. Basile, S. Álvarez, A. Blanco, et. al., Sulfonilamidothiopyrimidone and thiopyrimidone derivatives as selective COX-2 inhibitors: Synthesis, biological evaluation, and docking studies. Eur. J. Med. Chem., 2012, 57: 149-161.
[46] 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.
[47] 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.
[48] 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.
[49] 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.
[50] M. Arshad. Synthesis, characterization, antimicrobial and computational studies of some sulfonamide derivatives possessing thiadiazole and indole nucleus. European Journal of Pharmaceutical and Medical Research. 2017, 4 (12): 511-517.
[51] E. A. Alodeani, M. Arshad, M. A. Izhari. Antileishmanial screening, physicochemical properties and drug likeness of pyrazole carbaldehyde derivatives. Asian Pac. J. Health Sci. 2015, 2 (2): 41-47.
[52] E. A. Alodeani, M. Arshad, M. A. Izhari. Antileishmanial activity and computational studies of some hydrazone derivatives possessing quinoline nucleus. European Journal of Pharma and medical research. 2015, 2 (7): 324-328.
[53] M. Arshad, A. R. Bhat, K. K. Hoi, et. al., Synthesis, characterization and antibacterial screening of some novel1,2,4-triazine derivatives, Chinese Chemical Letters. 2017, 28: 1559-1565.

[54] M. Arshad. 1, 3, 4-oxadiazole nucleus with versatile pharmacological applications: a review. International Journal of Pharmaceutical Sciences and Research., 2014; 5(4): 1124-1137.
[55] 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.
[56] 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.
[57] M. Arshad. An insight to the synthetically obtained triazole possessing numerous biological activities. International Journal of Pharmacy and Pharmaceutical Sciences., 2014, 9: 16-24.
[58] 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.
[59] 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.
[60] 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.
[61] N. Iram, M. S. Khan, R. Jolly, et. al., 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.
[62] S. A. A. Nami, M. Arshad, M. Shakir, et. al., Morphological, structural, molecular docking and biocidal studies of newly synthesized Ppy-MA/TiO2 nanocomposites, Polymers for advanced technology. 2015, 26: 1627-1638.
[63] R. Bushra, M. Shahadat, M. A. Khan, et. al., Preperation of Polyaniline based Nanocomposite material and their Environmental Applications. Int. J. Env. Sci. Technol. 2015, 12: 3635-3642.
[64] S. A. A. Nami, M. S. Khan, M. Arshad. Spectral, morphological, and antibacterial studies of conducting copolymers, Ppy-MA, and their nanocomposites, Ag@Ppy-MA. Polymers for advanced technologies. 2017, 28: 10-19.
[65] P. S. Nayab, R. Arif, M. Arshad, et. al., Synthesis, characterization, antibacterial, dna binding and molecular docking studies of novel n-substituted phthalimides. Heterocyclic letters., 2015, 5: 223-239.
[66] 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(6): 150-158.
[67] E. A. Alodeani, M. Arshad, M. A. Izhari. Pharmacological potential and medicinal significance of versatile pyrimidine nucleus. European Journal of Biomedical and Pharmaceutical Sciences. 2014, 1 (3): 504-527.
[68] M. Arshad. 1-(Substituted-phenylsulfonyl)-2H-thieno[2,3-d][1,3]oxazine-2,4(1H)-dione: Drug likeness, physicochemical, Synthesis, Characterization, antibacterial and cytotoxicity assessment. 2014, Accepted in IJPSR.
[69] 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.
[70] Tuhfa, M. Y. Wani, M. Arshad et. al., Chalcone scaffold: Synthesis, modification, characterization, molecular properties and screening against microbes. Journal of Natural Science Biology and Medicine. 2011, 2: 1-156.