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Spectral and Microbial Screening of One-Pot Multicomponent Synthesis of Fused Quinazolinone Derivatives

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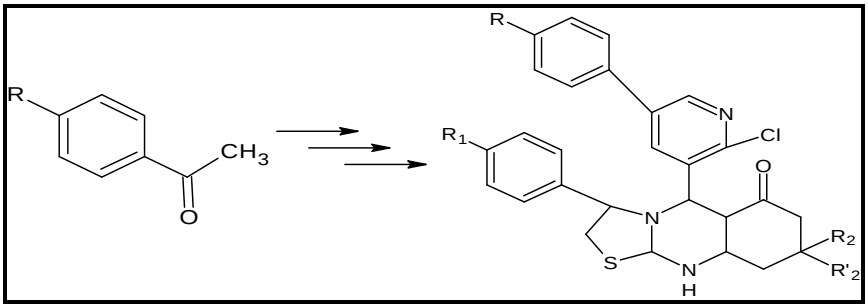
ABSTRACT

Heterocyclic compounds containing)-2-chloro-3-formyl pyridine and 2-amino thiazole quinqzolin-6(7H)-one are reported to possess significant biological activity. Synthesis of 5-(2-chloro-5-(4-substitutedphenyl)pyridin-3-yl)-3-(4-substitutedphenyl)-8,8-disubstituted-8,9-dihydro-5H-thiazolo [2, 3-b] quinazolin-6(7H)-one derivatives have been described. These compounds have been characterized on the basis of UV, IR, ^{1}H NMR, Mass and elemental analysis. Compounds have been evaluated for their antimicrobial activity. Among the series containing some of the compounds showed promising results against standard drugs.

Graphical Abstract



Keywords: Fused Quinazolinone derivatives, Spectral studies, Microbial screening, One-Pot Multicomponent Synthesis.

INTRODUCTION

Recent developments in the chemistry of quinazoline derivatives have given rise to more than ten thousand publication or patents, and yielded more than one thousand derivatives. The quinazolinone moiety is a widely researched and important scaffold in medicinal chemistry because of the variety of pharmacological properties associated with the compounds bearing this heterocycle [**1**]. Although

their importance in cancer chemotherapy is unparalleled [2], these heterocyclic systems also exhibit activities such as kinase inhibition [3], anticancer [4], antimalarial [5, 6], antidiabetes, and antiobesity [7], activities. Quinazoline derivatives are well-known natural alkaloids that are widely distributed in the plant and animal kingdoms [8]. In addition, many fused pyrimidines such as quinazolines and quinazolinones have been reported to exhibit anti-inflammatory [9], antimicrobial [10, 11], anticancer [12], and antimalarial. Activities [13] 3HQuinazoline-4-one is a frequently encountered unit in natural products such as L-vasicinone [14], and chrysogine [15]. Different type of quinazolinone derivative with the aim of interesting pharmaceutical compounds [16-20]. Many biologically active molecules with quinazoline or quinazolinone structures have been reported in the literature [21].

MATERIALS AND METHODS

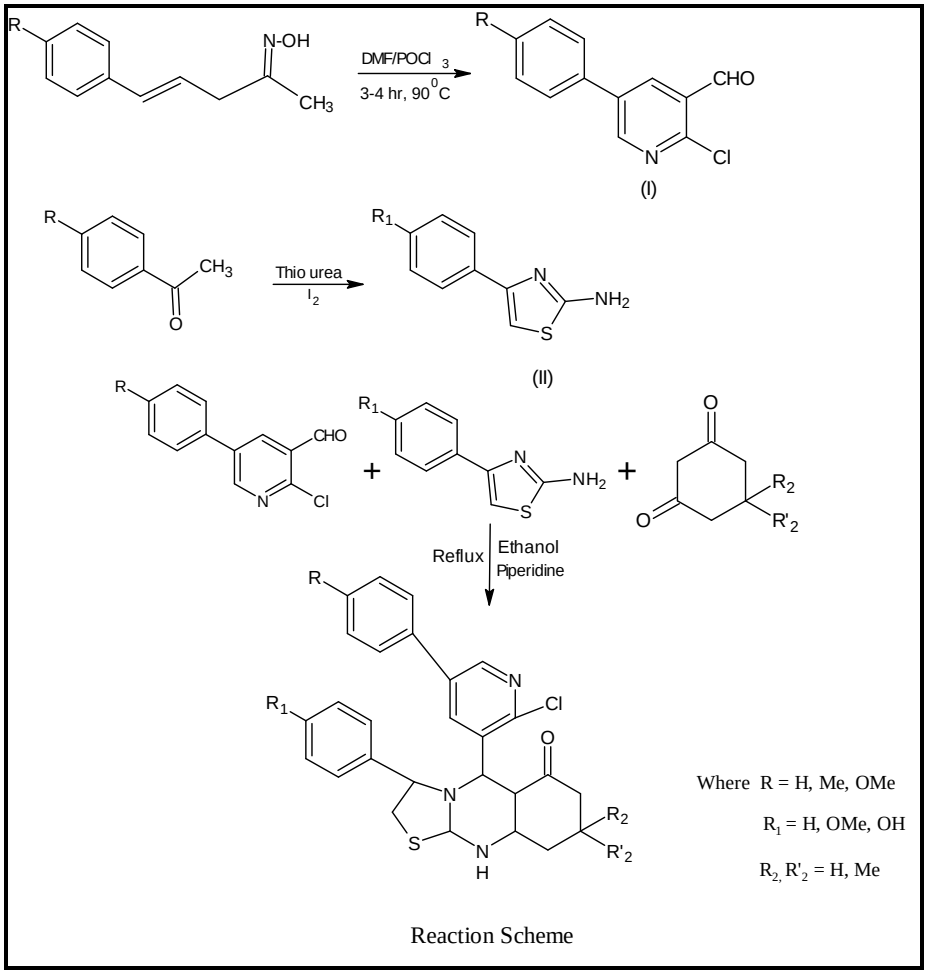
General procedure: All the melting points were determined in PMP-DM scientific melting point apparatus and are uncorrected. The purity of compound was checked routinely by TLC (0.5 mm thickness) using silica gel-G coated Al plates (Merck) and spots were visualized by exposing the dry plates in iodine vapours. The IR spectra (V_{max} in cm^{-1}) were recorded on a Shimadzu FT-IR 8300 spectrophotometer using KBr or Nujol technique, UV spectra (λ_{max} in nm) were recorded at Shimadzu UV -160 A (200-400 nm) using DMF as solvent, ^{1}H NMR spectra on a Bruker WM 400FT MHz NMR instrument using DMSO-d_6 as solvent and TMS as internal reference (chemical shift in δ, ppm; ^{13}C NMR were recorded on Varian AMX 400 (100 MHz) spectrometer as solutions in DMSO-d_6 and mass spectra were recorded on a Jeol JMS D-300 spectrometer. The elemental Analysis (C, H and S) of compounds was performed on Carlo Erba-1108 elemental Analyser.

Synthesis of 5-(4-substitutedphenyl)-2-chloro-3-formyl pyridine [I]: Charged Dimethylformamide (9.66 mL, 60 mmoles) and N-(2-arylethenyl) acetamide (5 mmoles) in a three-necked round-bottomed flask equipped with a thermometer pocket, reflux condenser, guard tube and mechanical stirrer. Reaction mixture cooled to 0°C. To it phosphorous oxychloride (40 mmoles) was added drop wise with stirring over a period of 30-40 min at 0-5°C. Stirred the reaction mixture for 1 hour at room temperature and then stirred at 90°C for 4 h.

After the completion of the reaction the reaction mass cooled to room temperature and poured in crushed ice and neutralized with sodium acetate. The crude solid was filtered and washed with water, mother liquid extracted with chloroform and evaporated to dryness. The resulting crude solid was crystallized from Diethyl ether to give a compound.

Synthesis of substituted 2-amino thiazole [II]: A mixture of 4-substituted acetophenone (0.1 moles), thiourea (0.2 moles) and iodine (0.1 moles) in a three-necked round-bottomed flask equipped with a thermometer pocket, reflux condenser and mechanical stirrer. Reaction mixture was heated on a water bath for 4 h. Cooled the reaction mass to room temperature and the crude hydro iodide, thus separated was filtered, washed with ether and dried. Dissolved the crude product in minimum quantity of hot water, filtered while hot and the clear solution was neutralized with liq. ammonia. The solid separated was filtered, washed with water and dried.

Synthesis of 5-(2-chloro-5-(4-substitutedphenyl) pyridin-3yl)-3-(4-substitutedphenyl)-8, 8-disubstituted-8, 9-dihydro5H-thiazolo [2, 3-b] quinazolin-6(7H)-one derivatives (III): A mixture of 5-(4-substitutedphenyl)-2-chloro-3-formyl pyridine (0.01 mole), 2-amino thiazole (0.01 mole), 5,5-disubtituted-1,3-cyclohexandione (0.01 mole), ethanol and 2-3 drops of piperidine in a three-necked round-bottomed flask equipped with a thermometer pocket, reflux condenser and mechanical stirrer. Reaction mixture was heated on a water bath for 2 h. Cooled the reaction mass to room temperature and the separated solid mass was filtered, washed with small amount of ethanol, dried it and recrystallized using dimethyl formamide and methanol (Scheme 1).



Scheme 1. Synthesis of 5-(2-chloro-5-(4-substitutedphenyl) pyridin-3yl)-3-(4-substitutedphenyl) -8, 8-disubstituted-8, 9-dihydro5H-thiazolo [2, 3-b] quinazolin-6(7H)-one derivatives (III).

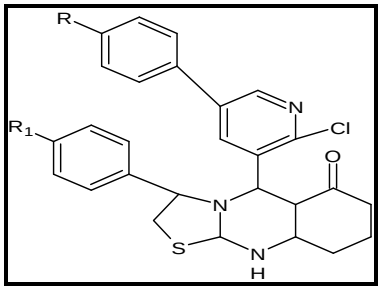
RESULTS AND DISCUSSION

Spectroscopy analysis and analytical data of synthesis of 5-(2-chloro-5-(4-substituted phenyl) pyridin-3yl)-3-(4-substituted phenyl)-8, 8-disubstituted-8, 9-dihydro5H-thiazolo [2, 3-b] quinazolin-6(7H)-one derivatives of structure A.

A-1: M.P. 228-231°C, Yield 59%, **IR cm^{-1}** 700 (C-Clstre.), 1705(C=O stre.), 1320 (C-Nstret.), ^{1}**H NMR δHppm** 6.75-7.81 (13H, m, Ar-H), 2.13-2.56 (6H, m CH2), 5.52 (1H, s,CH).**Mol. For**. $C_{27}H_{20}ClN_3OS$, **Mol.Wt**. 469, **Anal.data**. (Cal/Found) C%69.00/68.77, H% 4.29/3.90, N% 8.94/9.32. (where R, R_1, = -H, -H).

A-3:M.P. 215-218°C, Yield 71%, **IR cm^{-1}** 733 (C-Clstre.), 1728 (C=O stre.), 1322 (C-N stret.), 3615 (C-OH stret.), ^{1}**H NMR δHppm** 6.59-7.92 (12H, m, Ar-H), 8.71 (1H, s, OH), 2.11-2.54 (6H, m CH2), 5.50 (1H, s, CH).**Mol. For**. $C_{27}H_{20}ClN_3O_2S$, **Mol.Wt**.485, **Anal.data**. (Cal/Found) C% 66.73/65.43, H% 4.15/4.06, N% 8.65/9.04. (where R, R_1, = -H, -OH).

A-5: M.P. 251-256°C, Yield 59%, **IR cm^{-1}** 786 (C-Clstre.), 1707 (C=O stre.), 1316 (C-N stret.), ^{1}**H NMR δHppm** 6.60-7.84 (12H, m, Ar-H), 3.94 (3H, s, OCH3), 2.10-2.49 (6H, m, CH2), 5.44 (1H, s, CH). **Mol. For**. $C_{28}H_{22}ClN_3O_2S$, **Mol.Wt**. 500, **Anal.data**. (Cal/Found) C% 67.26/66.69, H% 4.43/4.33, N% 8.40/8.72 (where R, R_1, = -H, -OMe).



Where R = H, Me, OMe, R_1 = H, OH, OMe

Structure A. Substituted 5-(2-chloro-5-phenyl pyridin-3-yl)-3-phenyloctahydro-2H-thiazolo[2,3-b]quinazolin-6(3H)-one.

A-7: M.P. 223-227°C, Yield 62%, **IR cm^{-1}** 824 (C-Clstre.), 1710 (C=O stre.), 1360 (C-N stret.), ^{1}**H NMR δHppm** 6.60-7.81 (12H, m, Ar-H), 2.32 (3H, s, CH3), 2.12-2.43 (6H, m CH2), 5.52 (1H, s, CH).**Mol. For**. $C_{28}H_{22}ClN_3OS$, **Mol.Wt**.484, **Anal.data**. (Cal/Found) C% 69.48/68.32, H% 4.58/4.54, N% 8.68/9.30 (where R, R_1, = -Me).

A-9:M.P. 248-251°C, Yield 67%, **IR cm^{-1}** 820 (C-Clstre.), 1711 (C=O stre.), 1333 (C-N stret.), 3622 (C-OH stret.), ^{1}**H NMR δHppm** 6.66-7.80 (11H, m, Ar-H), 2.30 (3H, s, CH3), 2.11-2.41 (6H, m CH2), 5.52 (1H, s, CH), 8.77 (1H, s, OH). **Mol. For**. $C_{28}H_{22}ClN_3O_2S$, **Mol.Wt**. 500, **Anal.data**. (Cal/Found) C% 67.26/67.77, H% 4.43/4.40, N% 8.40/8.72 (where R, R_1, = -Me, -OH).

A-11: M.P. 202-206°C, Yield 60%, **IR cm^{-1}** 780 (C-Clstre.), 1709 (C=O stre.), 1326 (C-N stret.), ^{1}**H NMR δHppm** 6.62-7.74 (11H, m, Ar-H), 3.90 (3H, s, OCH3), 2.11-2.51 (6H, m, CH2), 5.44 (1H, s, CH), 2.36 (3H, s, CH3). **Mol. For**. $C_{29}H_{24}ClN_3O_2S$, **Mol.Wt**. 514, **Anal.data**. (Cal/Found) C% 67.76/68.33, H% 4.71/4.42, N% 8.17/7.54 (where R, R_1, = -Me, -OMe).
A-13: M.P. 189-191°C, Yield 66%, **IR cm^{-1}** 788 (C-Clstre.), 1707 (C=O stre.), 1310 (C-N stret.), ^{1}**H NMR δHppm** 6.60-7.76 (12H, m, Ar-H), 3.92 (3H, s, OCH3), 2.10-2.50 (6H, m, CH2), 5.54 (1H, s, CH).**Mol. For**. $C_{28}H_{22}ClN_3O_2S$, **Mol.Wt**. 500, **Anal.data**. (Cal/Found) C% 67.26/66.99, H% 4.43/4.13, N% 8.40/8.98 (where R, R_1, = -OMe, -H).

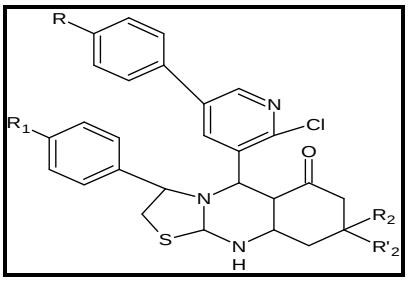
A-15: M.P. 228-232°C, Yield 67%,**IR cm^{-1}** 780 (C-Clstre.), 1701 (C=O stre.), 1325 (C-N stret.), 3605 (C-OH stret.),^{1}**H NMR δHppm** 6.62-7.86 (11H, m, Ar-H), 3.90 (3H, s, OCH3), 2.10-2.45 (6H, m, CH2), 5.59 (1H, s, CH), 8.74 (1H, s, OH). **Mol. For**. $C_{28}H_{22}ClN_3O_3S$, **Mol.Wt**. 516, **Anal.data**. (Cal/Found) C% 65.17/66.12, H% 4.30/4.24, N% 8.14/8.70 (where R, R_1, = -OMe, -OH).

A-17: M.P. 228-232°C, Yield 67%, **IR cm^{-1}** 801 (C-Clstre.), 1715 (C=O stre.), 1355 (C-N stret.), 3618 (C-OH stret.), ^{1}**H NMR δHppm** 6.60-7.76 (11H, m, Ar-H), 3.90-3.95 (6H, s, OCH3), 2.112.40 (6H, m, CH2), 5.52 (1H, s, CH). **Mol. For**. $C_{29}H_{24}ClN_3O_3S$, **Mol.Wt**. 530, **Anal.data**. (Cal/Found) C% 65.71/65.81, H% 4.82/4.76, N% 7.72/7.25 (where R, R_1,=-OMe, -OMe).

Spectroscopy analysis and analytical data of synthesis of 5-(2-chloro-5-(4-substitutedphenyl) pyridin-3yl)-3-(4-substituted phenyl)-8, 8-disubstituted-8, 9-dihydro5H-thiazolo [2, 3-b] quinazolin-6(7H)-one derivatives of structure B.

B-2: M.P.223-227°C, Yield 70%, **IR cm^{-1}** 745(C-Clstre.), 1715(C=O stre.), 1325(C-N stret.), ^{1}**H NMR δHppm** 6.76-7.88 (13H, m, Ar-H), 2.13-2.51(4H, m CH2), 5.58 (1H, s, CH), 0.91-1.09(6H, s, CH3). **Mol. For**. $C_{29}H_{24}ClN_3OS$, **Mol.Wt**. 498, **Anal.data**. (Cal/Found) C% 69.94/70.22, H% 4.86/4.85, N% 8.44/7.92. (where R, R_1, R_2, R'_2= -H, -H, Me).

B-4: M.P.230-234°C, Yield 73%, **IR cm^{-1}**769 (C-Clstre.), 1708 (C=O stre.), 1330 (C-N stret.), 3618 (C-OH stret.), ^{1}**H NMR δHppm** 6.62-7.82 (12H, m, Ar-H), 8.77 (1H, s, OH), 2.10-2.50 (4H, m CH2), 5.50 (1H, s, CH), 0.90-1.08(6H, s, CH3).**Mol. For**. $C_{29}H_{24}ClN_3O_2S$, **Mol.Wt**. 514, **Anal.data**. (Cal/Found) C% 67.76/68.28, H% 4.71/4.95, N% 8.17/8.55. (where R, R_1, R_2, R'_2= -H, -OH, Me).



Where R = H, Me, OMe, R_1 = H, OH, OMe,
R_2, R'_2 = H, Me

Structure B.

B-6: M.P.208-211°C, Yield 71%, **IR cm^{-1}** 835 (C-Clstre.), 1714 (C=O stre.), 1342 (C-N stret.). ^{1}**H NMR δHppm** 6.51-7.72 (12H, m, Ar-H), 2.32 (3H, s, CH3), 2.13-2.44 (4H, m CH2), 5.44 (1H, s, CH), 0.90-1.07 (6H, s, CH3). **Mol. For**. $C_{30}H_{26}ClN_3O_2S$, **Mol.Wt**. 528, **Anal.data**. (Cal/Found) C% 68.23/69.48, H% 4.96/4.72, N% 7.96/8.48. (where R, R_1, R_2, R'_2= -H, -OMe, Me).

B-8: M.P 242-244°C, Yield 59%, **IR cm^{-1}** 806 (C-Clstre.), 1712 (C=O stre.), 1355 (C-N stret.). ^{1}**H NMR δHppm** 6.61-7.82 (12H, m, Ar-H), 3.90 (3H, s, OCH3), 2.14-2.43 (4H, m CH2), 5.40 (1H, s, CH), 0.91-1.09 (6H, s, CH3). **Mol. For**. $C_{30}H_{26}ClN_3OS$, **Mol.Wt**. 512, **Anal.data**. (Cal/Found) C% 70.37/69.35, H% 5.12/5.46, N% 8.21/8.05. (where R, R_1, R_2, R'_2= -Me, -H, Me).

B-10: M.P.213-217°C, Yield 65%, **IR cm^{-1}** 830 (C-Clstre.), 1713 (C=O stre.), 1340 (C-N stret.), 3620 (C-OH stret.). ^{1}**H NMR δHppm** 6.61-7.82 (11H, m, Ar-H), 2.30 (3H, s, CH3), 2.10-2.44 (4H, m CH2), 5.54 (1H, s, CH), 0.91-1.09 (6H, s, CH3), 8.76 (1H, s, OH). **Mol. For**. $C_{30}H_{26}ClN_3O_2S$, **Mol.Wt**. 528, **Anal.data**. (Cal/Found) C% 68.23/67.85, H% 4.96/4.75, N% 7.96/8.19 (where R, R_1, R_2, R'_2= -Me, -OH, -Me).

B-12: M.P.211-214°C, Yield 65%, **IR cm^{-1}** 810 (C-Clstre.), 1718 (C=O stre.), 1345 (C-N stret.). ^{1}**H NMR δHppm** 6.51-7.72 (11H, m, Ar-H), 3.91 (3H, s, OCH3), 2.10-2.42 (4H, m CH2), 5.41 (1H, s, CH), 0.92-1.08 (6H, s, CH3), 2.33 (3H,s, CH3). **Mol. For**. $C_{31}H_{28}ClN_3O_2S$, **Mol.Wt**. 469, **Anal.data**. (Cal/Found) C% 68.68/67.63, H% 5.21/5.63, N% 7.75/7.25. (where R, R_1, R_2, R'_2= -Me, -OMe, -Me).

B-14: M.P.237-240°C, Yield 63%, **IR cm^{-1}** 800 (C-Clstre.), 1722 (C=O stre.), 1345 (C-N stret.). ^{1}**H NMR δHppm** 6.50-7.70 (11H, m, Ar-H), 3.95 (3H, s, OCH3), 2.11-2.42 (4H, m CH2), 5.51 (1H, s, CH), 0.90-1.08 (6H, s, CH3). **Mol. For**. $C_{30}H_{26}ClN_3O_2S$, **Mol.Wt**. 528, **Anal.data**. (Cal/Found) C% 68.23/67.18, H% 4.96/5.22, N% 7.96/7.58. (where R, R_1, R_2, R'_2= -OMe, -H, -Me).

B-16: M.P.255-259°C, Yield 69%, **IR cm^{-1}** 844 (C-Clstre.), 1712 (C=O stre.), 1340 (C-N stret.), 3607 (C-OH stret.). ^{1}**H NMR δH** 6.52-7.77 (11H, m, Ar-H), 3.90 (3H, s, OCH3), 2.10-2.40 (4H, m CH2), 5.52 (1H, s,CH), 0.90-1.06 (6H, s, CH3), 8.76 (1H, s, OH). **Mol. For**. $C_{27}H_{20}ClN_3OS$, **Mol.Wt**. 544, **Anal.data**. (Cal/Found) C% 66.23/65.81, H% 4.82/4.76, N% 7.72/7.25. (where R, R_1, R_2, R'_2= -OMe, -H, -Me).

B-18: M.P.226-230°C, Yield 59%, **IR cm^{-1}** 840 (C-Clstre.), 1715 (C=O stre.), 1344 (C-N stret.). ^{1}**H NMR δH** 6.52-7.70 (11H, m, Ar-H), 3.91-3.95 (6H, s, OCH3), 2.112.40 (4H, m CH2), 5.51 (1H, s,

CH), 0.91-1.07 (6H, s, CH3), **Mol. For**. $C_{31}H_{28}ClN_3O_3S$, **Mol.Wt**. 558, **Anal.data**. (Cal/Found) C% 66.72/67.08, H% 5.06/4.80, N% 7.53/7.18. (where R, R_1, R_2, R'_2= -OMe, -OMe, -Me).

APPLICATION

Antimicrobial Activity: All the synthesized compounds A-B 1 to 18 were tested against micro-organism species at 1000 ppm concentration. The observed results of antibacterial screening reported in table 1 indicate that compounds B-4, A-5, and A-7 shows good activity against the bacterial species used. The results indicate that *B. substilis* shows good results compared to other two species used. Compounds B-2, B-16 and A-17 show poor activity against the bacterial species used. From the antifungal assay it has been also observed that compounds having methoxy substituents on quinoline ring show the highest activity against *A. parasiticus* and *S. rolfsii*. Rest of the compounds show significant activity but it could not reach the effectiveness of the conventional fungicidal griseofulvine.

Table 1. Antimicrobial activity of Synthesis of 5-(2-chloro-5-(4-substitutedphenyl) pyridin-3yl)-3-(4-substitutedphenyl)-8, 8-disubstituted-8, 9-dihydro5H-thiazolo [2, 3-b] quinazolin-6(7H)-one derivatives

Compound Name	Inhibition Zone (in mm)against			Growth diameter in mm (% inhibitation)	
	E. coli	*B. subtilis*	*B. cereus*	*A. parasiticus*	*S. rolfsii*
A-1	09	09	15	20.3 (71.08)	19.4 (69.40)
B-2	07	10	10	18.1 (74.21)	17.2 (72.87)
A-3	09	10	11	17.4 (75.21)	16.3 (74.29)
B-4	11	17	12	16.2 (76.92)	15.2 (76.02)
A-5	11	18	10	13.1 (81.33)	14.4 (77.28)
B-6	10	11	10	17.2 (75.49)	17.8 (71.92)
A-7	12	14	11	18.8 (73.21)	18.3 (71.13)
B-8	10	15	10	19.4 (72.36)	19.1 (69.87)
A-9	11	10	09	13.7 (80.48)	14.2 (77.60)
B-10	10	14	11	13.2 (81.19)	13.7 (78.39)
A-11	10	12	09	12.1 (82.76)	12.8 (79.81)
B-12	09	13	09	11.4 (83.76)	10.2 (83.91)
A-13	09	12	09	16.5 (76.49)	15.4 (75.70)
B-14	11	11	11	13.2 (81.19)	12.5 (80.28)
A-15	11	10	12	12.4 (82.33)	12.7 (79.96)
B-16	10	10	12	10.1 (85.61)	10.3 (83.75)
A-17	10	09	10	11.3 (83.90)	11.5 (81.86)
B-18	10	09	11	9.4 (86.60)	10.3 (83.75)
Ciprofloxacine	30	33	17	-	-
Ampicilline	13	21	13	-	-
Griseofulvin	-	-	-	00 (100)	00 (100)

CONCLUSION

In concluded a new series of derivatives A-B 1 to 18 were synthesized. Examinations of the IR-spectra of these compounds reveal the expected frequencies. Some of the important frequencies are indicated as: 1730-1700 cm^{-1} (C=O stretching of quinolinoqionazolinone), 1630-1590 cm^{-1} (Aromatic C=C stretching), 850-700 (C-Cl stretching). The characteristic IR band of these compounds appears at 850-700 cm-1 (C-Cl stretching) and at 1730-1700 cm-1 (C=O stretching) confirmed the structure. ^{1}H-NMR spectra also showed the peak at 2.11-2.40 (4H, m CH_2), 5.51 (1H, s, CH), 0.91-1.07 (6H, s, CH_3) δ value. The other protons of the compound were resonated at expected frequencies and biological study. The investigation of antimicrobial activities data revealed that some of the derivatives displayed excellent activity and the showed moderate activity against standard drugs.

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REFERENCES

[1]. G. F. Xu, B.A. Song, P.S. Bhadury, S. Yang, P.Q. Zhang, L.H. Jin, W. Xue, D. Y. Hu, P. Lu, 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, *Bioorg. Med. Chem*, **2007**, 15, 3768–3774.

[2]. N. Sirisoma, S. Kasibhatla, A. Pervin, H. Zhang, S. Jiang, J. Willardsen, M. B. Anderson, V. Baichwal, G. Mather, K. Jessing, R. Hussain, K. Hoang, C. M. Pleiman, B. Tseng, J. Drewe, S. X. Cai, Discovery of 2-chloro-N-(4-methoxyphenyl)-N-methylquinazolin-4-amine (EP128265, MPI-0441138) as a potent inducer of apoptosis with high in vivo activity, *J. Med. Chem.*, **2008**, 51, 4771–4779.

[3]. K. W. Fowler, D. Huang, E. A. Kesicki, H. C. Ooi, A. R. Oliver, F. Ruan, J. Treiberg, (Icos Corporation, USA). Patents WO2005113556 **2005**, US16778 **2005**, *Chem. Abstr.*, 144, **2006**, 22759.

[4]. J. B. Jiang, D. P. Hesson, B. A. Dusak, D. L. Dexter, G. J. Kang, E. Hamel, Synthesis and biological evaluation of 2-styrylquinazolin-4(3H)-ones, a new class of antimitotic anticancer agents which inhibit tubulin polymerization, *J. Med. Chem.*, **1990**, 33, 1721–1728.

[5]. Y. Takaya, H. Tasaka, T. Chiba, K. Uwai, M. A. Tanitsu, H. S. Kim, Y. Wataya, M. Miura, M. Takeshita, Y. Oshima, New type of febrifugine analogues, bearing a quinolizidine moiety, show potent antimalarial activity against Plasmodium malaria parasite**,** *J. Med. Chem.*, **1999**, 42, 3163–3166.

[6]. Y. Takeuchi, M. Koike, K. Azuma, H. Nishioka, H. Abe, H. S. Kim, Y. Wataya, T. Harayama, Synthesis and antimalarial activity of febrifugine derivatives, *J. Med. Chem. Pharm.*, **2001**, 49, 721–725.

[7]. J. Rudolph, W. P. Esler,S. O'Connor, P. D. Coish, P. L. Wickens, M. Brands, D. E. Bierer, B. T. Bloomquist, G. Bondar, L. Chen, C. Y. Chuang, T. H. Claus, Z. Fathi, W. Fu, U. R. Khire, J. A. Kristie, X. G. Liu,D. B. Lowe, A. C. McClure, M. Michels, A. A. Ortiz, P. D. Ramsden, R. W. Schoenleber, T. E. Shelekhin, A. Vakalopoulos, W. Tang, L. Wang, L. Yi, S. J. Gardell, J. N. Livingston, L. J. Sweet, W. H. Bullock, Quinazolinone derivatives as orally available ghrelin receptor antagonists for the treatment of diabetes and obesity, *J. Medicinal. Chemistry*, **2007**, 50, 5202–5216.

[8]. A. Witt, J. Bergman, Recent Developments in the Field of Quinazoline Chemistry**,** *Curr. Org. Chem.*, **2003**, 7, 659–677.

[9]. M. M. Gineinah, M. A. El-Sherbeny, M. N. Nasr, and A. R. Maarouf, Synthesis of Dynamic 2-Ethoxycarbonyl-4H-3, 1-Benzoxazin-4-one and its Behavior Towards Nitrogen Nucleophiles, *Arch. Pharm. Med. Chem.*, **2002**, 4(3), 548-553.
[10]. D. Ramesh, B. Sreenivasulu, Synthesis and biological activity of esters of 2-methyl-1,8-naphthyridine-3-carbamic acid, *Indian J. Chem.*, **2004**, 43B, 897-900.
[11]. M. E. Azab, E. A. Kassab, M. A. El-Hashash, R. S. Ali, Synthesis and Antibacterial Activity of Some New 4(3H)Quinazolin-4-one Derivatives, *Phosphorus, Sulfur and Silicon*, **2009**, 184, 610-625.
[12]. J. V. Partin, I. E. Anglin, N. Kyprianou, Quinazoline-based α1-adrenoceptor antagonists induce prostate cancer cell apoptosis via TGF-β signalling and IκBα induction, *J. Cancer*, **2003**, 88(10), 1615-1621.
[13]. H. Kikuchi, H. Tasaka, S. Hirai, Y. Takaya, Y. Lwabuchi, H. Ooi, S. Hatakeyama, H. S. Kim, Y. Wataya, Y. Oshima, New Type of Febrifugine Analogues, Bearing a Quinolizidine Moiety, Show Potent Antimalarial Activity against *Plasmodium* Malaria Parasite, *J. Medicinal. Chemistry*, **1999**, (16)**,** 3163-3166.
[14]. S. Eguchi, T. Suzuzi, T. Okawa, Y. Matsushita, E. Yashima, and Y. Okamoto, Synthesis of Optically Active Vasicinone Based on Intramolecular Aza-Wittig Reaction and Asymmetric Oxidation(1), *J. Org. Chem.*, **1996**, 61, 7316-7319.
[15]. **J**. Bergman, A. Brynolf**,** Quinoline, quinazoline and acridone alkaloids, *Tetrahedron*, **1990**, 46, 1295-1310.
[16]. M. R. Mahmoud, E. A. El-Bordany, M. E. Azab, and E. A. Soliman, Synthesis and Spectral Characterization of Novel Pyridotriazolo-, Pyridothiazolo-, Pyridotetrazolopyrimidines and Pyridopyrimidotriazepine Derivatives for Potential Pharmacological Activities, *Phosphorus, Sulfur and Silicon*, **2007**, 182, 1275-1289.
[17]. M. E. Azab, G. A. M. El-Hag Ali, and A. F. Abdel-Wahab, synthesis of novel pyrazole, pyridazine and pyrimidine derivatives containing sulfonamido moiety, *Acta Chemica Pharmaceutica*, **2003**, 53, 213-218.
[18]. M. E. Azab, M. E. A. Ibraheem, H. M. F. Madkour, Synthesis and Antibacterial Evaluation of Novel Heterocyclic Compounds Containing a Sulfonamido Moiety, *Phosphorus, Sulfur and Silicon*, **2006**, 181, 1299-1313.
[19]. M. A. I. Salem, E. A. Soliman, M. B. Smith, M. R. Mahmoud, M. E. Azab, Utility of 1-(2, 4-dimethoxyphenyl)-3-aryl-prop-2-ene-1-ones as ring transformer in preparing heterocyclic compounds and their potential biological activities, *Phosphorus, Sulfur and Silicon*, **2004**, 179, 61-66.
[20]. A. S. Hamad, M E. Azab, synthesis of novel pyrazole, pyridazine and pyrimidine derivatives containing sulfonamido moiety, *Phosphorus, Sulfur and Silicon*, **2001**, 18(2),167-178
[21]. Riyaz-ur-Rahaman Khan, Mangalavathi, Mohamed Afzal Pasha, Atomized Sodium Catalyzed, Ultrasound Assisted, One-pot four-component Synthesis of a Series of Polysubstituted-tetrahydroquinolines, *J. Applicable Chem.*, **2019**, 8(1), 154-164.
[22]. Anil Kumar, Punam, Sharwan K. Dewan, One Pot Synthesis and Antimicrobial Activity of 1,3,6-Trisubstituted Pyrimidine-2, 4-diones Catalyzed by TsOH, *J. Applicable Chem.*, **2018**, 7(2), 449-452.