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## Synthesis and biological evaluation of 1,3,5-triazine based chalcones and their derivatives

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### ABSTRACT

Chalcones, 2,4-bis-(4'-chlorophenylamino)-6-[4'-{3''-(substituted phenyl/2'''-thienyl/2'''-furyl/cinnamyl)-2''-propenon-1''-yl}phenyl amino]-s-triazines (**6a-d**) have been prepared from ketone (**5**) based on s-triazine nucleus. These chalcones (**6a-d**) on cyclisation with guanidine nitrate in presence of alkali, malononitrile in presence of ammonium acetate and hydrazine hydrate in presence of glacial acetic acid give the corresponding aminopyrimidines (**7a-d**), cyanopyridines (**8a-d**) and acetylpyrazolines (**9a-d**) respectively. The structures of newly synthesized compounds have been confirmed on the basis of elemental analysis, IR and <sup>1</sup>H NMR spectral data. They are also tested for their antibacterial activity.

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### KEYWORDS

Aminopyrimidines;  
 Cyanopyridines;  
 Acetylpyrazolines;  
 Antibacterial activity.

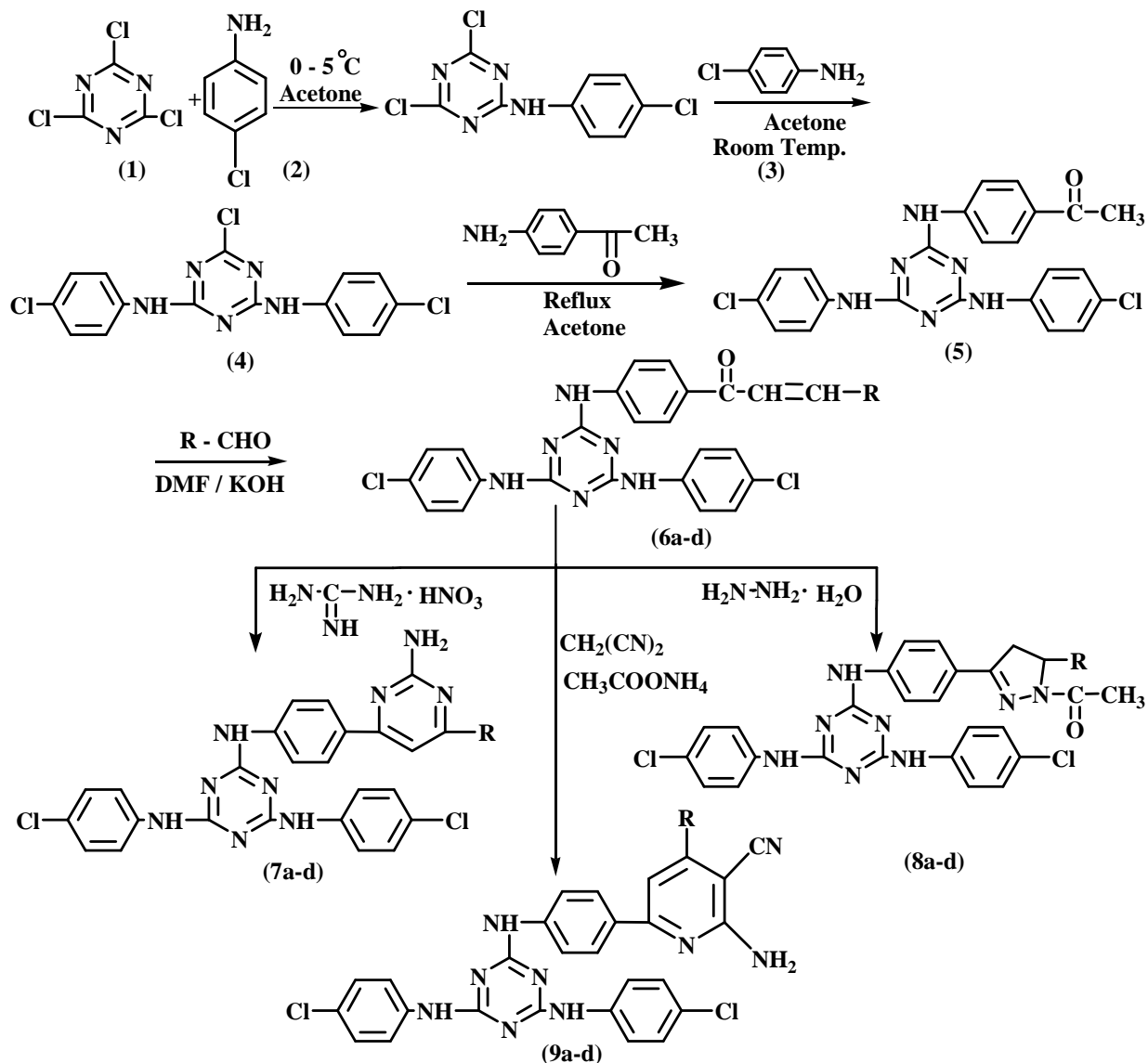
### INTRODUCTION

The synthesis of  $\alpha,\beta$ -unsaturated carbonyl compounds is one of the main structural component in various naturally occurring and biologically essential substances<sup>[1]</sup>. Moreover,  $\alpha,\beta$ -unsaturated ketones are important intermediates in many addition reactions due to carbonyl group at the  $\beta$ -position<sup>[2]</sup>. Several strategies for the synthesis of these systems based on the formation of carbon-carbon bond have been reported and among them the direct Aldol condensation and Claisen-Schmidt condensation still occupy prominent position<sup>[3]</sup>. It is well known that most natural or synthetic chalcones are highly active with extensive pharmaceutical and medicinal application<sup>[4]</sup>. Recently, chalcones have been used as anti-AIDS<sup>[5]</sup>, antimalarial<sup>[6]</sup>, anti-inflammatory<sup>[7]</sup>, antibacterial<sup>[8]</sup> and antitumor<sup>[9]</sup> agents.

Pyrimidine derivatives have been reported to pos-

sess a variety of biological activity such as analgesic<sup>[10]</sup>, antihypertensive<sup>[11]</sup>, antipyretic<sup>[12]</sup>, antiviral<sup>[13]</sup> and anti-inflammatory<sup>[14]</sup>. Many of the pyrimidine derivatives are reported to possess potential CNS depressant properties<sup>[15]</sup>. The chemistry of pyridines and their derivatives has gained increasing attention because pyridine ring substituted with amino and cyano groups may be having good biologically active properties such as antibacterial<sup>[16]</sup>, antifungal<sup>[17]</sup>, antitubercular<sup>[18]</sup> and analgesic<sup>[19]</sup> activities. Pyrazoline derivatives have been found to be anticancer<sup>[20]</sup>, antitubercular<sup>[21]</sup> and antibacterial<sup>[22]</sup> activities. It has been reported that introduction of acetyl group at 1<sup>st</sup>-position enhances the molluscicidal<sup>[23]</sup> activity as well as increases the stability of pyrazolines.

In continuation of our work on chalcones and their derivatives<sup>[24-26]</sup>, we have synthesized 2,4-bis-(4'-chlorophenylamino)-6-[4'-{3''-(substituted phenyl/2'''-thienyl/2'''-furyl/cinnamyl)-2''-propenon-1''-



SCHEME 1

yl}phenyl amino]-s-triazines (**6a-d**) according to Claisen-Schmidt condensation by using ketone (**5**) with different aromatic aldehydes. Further these chalcones (**6a-d**) on cyclisation with guanidine nitrate in presence of alkali, malononitrile in presence of ammonium acetate and hydrazine hydrate in presence of glacial acetic acid give the corresponding aminopyrimidines (**7a-d**), cyanopyridines (**8a-d**) and acetylpyrazolines (**9a-d**) respectively. The IR spectra of compound (**6a**) revealed the presence of ( $-\text{C}=\text{O}$ ) group by exhibiting a strong absorption at  $1652\text{cm}^{-1}$ . The IR spectrum of compounds (**7a**) and (**8a**) showed the absorption at  $3409\text{cm}^{-1}$  and  $3413\text{cm}^{-1}$  which indicate the presence of

( $-\text{NH}_2$ ) group. A strong absorption at  $1568\text{cm}^{-1}$  due to the presence of ( $-\text{C}=\text{N}$ ) group in compounds (**9a**). The  $^1\text{H NMR}$  spectrum of (**6a**) displayed doublet at  $\delta$  6.90 due to ( $-\text{CO}-\text{CH}=\text{CH}-$ ) proton. A singlet appeared at  $\delta$  5.18 and  $\delta$  5.25 due to the ( $-\text{NH}_2$ ) protons presence in (**7a**) and (**8a**) respectively. The  $^1\text{H NMR}$  spectrum of (**9a**) showed a sharp singlet at  $\delta$  2.45 due to ( $-\text{COCH}_3$ ) protons.

### Antibacterial activity

All the synthesized compounds were screened for their antibacterial activity by using agar diffusion method<sup>[27]</sup> against *S.aureus*(MTCC 96), *B.subtilis*

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(MTCC 441) Gram positive and *E.coli*(MTCC 443), *S.paratyphi-B*(MTCC 733) Gram negative bacteria in nutrient agar medium. The sterilized agar media [2.4 % (w/v) agar-agar, 5% (w/v) NaCl, 3% (w/v) peptone, pH(6.8 to 7.0)] was poured into petridishes and allowed to solidify. On the surface of the media microbial suspension was spread over the agar plates to solidify. A stainless steel cylinder (pre-sterilized) was used to bore the cavities. All the synthesized compounds (100µg/ml) in DMF were placed serially in the cavities, with the help of micropipette. It is then allowed to diffuse for 10 minutes in refrigerator. The plates were incubated at 37°C for 24 hours. After incubation the diameter of zone of inhibition was measured in mm. Under similar conditions controlled experiment was carried out by using Ciprofloxacin as standard drug for comparison.

### EXPERIMENTAL

All the melting points were determined in an open capillary and are uncorrected. The IR spectra were recorded on Perkin-Elmer 237 spectrophotometer. <sup>1</sup>H NMR spectra on a Bruker Avance DPX 300 MHz spectrometer with CDCl<sub>3</sub> as a solvent and TMS as internal reference. Purity of the compounds were checked on TLC using silica gel-G.

#### Preparation of 2-(4'-chlorophenylamino)-4,6-dichloro-*s*-triazine (3)

4-Chloroaniline (**2**) (0.01 mole) was added slowly to cyanuric chloride (**1**) (0.01 mole) in acetone (30 ml) with constant stirring for 4 hours at 0-5°C. Sodium carbonate solution was added to neutralize HCl evolved during the reaction. Finally the content was poured into crushed ice. The solid separated out was filtered, washed with water and recrystallised from alcohol to give (**3**).

Yield 94%; m.p. 238°C.

#### Preparation of 2,4-bis-(4'-chlorophenylamino)-6-chloro-*s*-triazine (4)

4-Chloroaniline (0.01 mole) was added slowly to 2-(4'-chlorophenylamino)-4,6-dichloro-*s*-triazine (**3**) (0.01 mole) in acetone (35ml) with constant stirring for 6-hours at room temperature. Sodium carbonate solution was added to neutralize HCl evolved during the

reaction. Finally the content was poured into crushed ice. The solid separated out was filtered, washed with water and recrystallised from alcohol to give (**4**).

Yield 87%; m.p. 212°C; IR (KBr, cm<sup>-1</sup>): 813 (C-N, *s*-triazine), 770 (C-Cl); <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ7.00 to 7.75(m, 8 Ar-H and 2 NH). Anal. Calcd. for C<sub>15</sub>H<sub>10</sub>N<sub>5</sub>Cl<sub>3</sub>: C,49.11; H,2.73; N,19.10. Found: C,49.13; H,2.70; N,19.12.

#### Preparation of 2,4-bis-(4'-chlorophenylamino)-6-(4'-acetylphenylamino)-*s*-triazine (5)

4-Aminoacetophenone (0.01 mole) and 2,4-bis-(4'-chlorophenylamino)-6-chloro-*s*-triazine (**4**) (0.01 mole) were dissolved in acetone(40ml). The reaction mixture was refluxed for 6 hours. Periodically sodium carbonate solution was added to neutralize HCl evolved during the reaction. Finally the reaction mixture was cooled and the content was poured into crushed ice. The solid separated out was filtered, washed with water and recrystallised from alcohol to give (**5**).

Yield 82%; m.p. 195°C; IR(KBr, cm<sup>-1</sup>): 1662(C=O), 818(C-N, *s*-triazine), 773 (C-Cl); <sup>1</sup>H NMR(CDCl<sub>3</sub>): δ2.54(s, 3H, -COCH<sub>3</sub>), δ7.26 to 8.41(m, 12 Ar-H and 3 NH). Anal. Calcd. for C<sub>23</sub>H<sub>18</sub>N<sub>6</sub>Cl<sub>2</sub>: C,59.35; H,3.87; N,18.06. Found: C,59.36; H,3.85; N,18.09.

#### Preparation of 2,4-bis-(4'-chlorophenylamino)-6-[4'-{3''-(3''',4''',5''')-trimethoxyphenyl}-2''-propenon-1''-yl]-phenylamino]-*s*-triazine (6a)

2,4-Bis-(4'-chlorophenylamino)-6-(4'-acetylphenylamino)-*s*-triazine (**5**)(0.01 mole) was dissolved in DMF(30ml) and 40% KOH in distilled water was added to it. Then 3,4,5-trimethoxy benzaldehyde (0.01mole) was added with constant stirring at room temperature. After 24 hours the reaction mixture was poured into crushed ice and neutralize with HCl. The product separated out was filtered, washed with water and recrystallised from alcohol to give (**6a**).

Yield 78%; m.p. 153°C; IR (KBr, cm<sup>-1</sup>):1652 (C=O), 1026 (C-O-C), 815 (C-N, *s*-triazine), 757(C-Cl); <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ3.74(s, 6H, m-OCH<sub>3</sub>), δ3.84(s, 3H, p-OCH<sub>3</sub>), δ7.30(d, 1H, -CO-CH=), δ7.10 to 7.81(m, 14 Ar-H and 3 NH), δ8.05 (d, 1H, Ar-CH=). Anal. Calcd. for C<sub>33</sub>H<sub>28</sub>N<sub>6</sub>O<sub>4</sub>Cl<sub>2</sub>: C,61.59; H,4.35; N,13.06. Found: C,61.62; H,4.33; N,13.08.

#### Preparation of 2,4-bis-(4'-chlorophenylamino)-6-

TABLE 1 : Physical and analytical data of compounds (6a-d), (7a-d), (8a-d) and (9a-d)

No.	R	M.P. °C	Yield (%)	M.F.	Found (calcd)%		
					C	H	N
6a	3,4,5-Trimethoxyphenyl	153	78	C <sub>33</sub> H <sub>28</sub> N <sub>6</sub> O <sub>4</sub> Cl <sub>2</sub>	61.62(61.59)	4.33(4.35)	13.08(13.06)
6b	2-Furanyl	137	72	C <sub>28</sub> H <sub>20</sub> N <sub>6</sub> O <sub>2</sub> Cl <sub>2</sub>	61.90(61.88)	3.70(3.68)	15.49(15.47)
6c	2-Thienyl	148	73	C <sub>28</sub> H <sub>20</sub> N <sub>6</sub> O <sub>2</sub> Cl <sub>2</sub>	60.13(60.11)	3.55(3.58)	15.06(15.03)
6d	Cinnamyl	174	70	C <sub>32</sub> H <sub>24</sub> N <sub>6</sub> OCl <sub>2</sub>	66.30(66.32)	4.18(4.15)	14.54(14.51)
7a	3,4,5-Trimethoxyphenyl	160	72	C <sub>34</sub> H <sub>29</sub> N <sub>9</sub> O <sub>3</sub> Cl <sub>2</sub>	59.84(59.82)	4.27(4.25)	18.49(18.48)
7b	2-Furanyl	170	66	C <sub>29</sub> H <sub>21</sub> N <sub>9</sub> OCl <sub>2</sub>	59.78(59.79)	3.58(3.61)	21.67(21.65)
7c	2-Thienyl	165	68	C <sub>29</sub> H <sub>21</sub> N <sub>9</sub> SCl <sub>2</sub>	58.21(58.19)	3.54(3.51)	21.09(21.07)
7d	Cinnamyl	159	63	C <sub>33</sub> H <sub>25</sub> N <sub>9</sub> Cl <sub>2</sub>	64.06(64.08)	4.06(4.05)	20.36(20.39)
8a	3,4,5-Trimethoxyphenyl	170	71	C <sub>36</sub> H <sub>29</sub> N <sub>9</sub> O <sub>3</sub> Cl <sub>2</sub>	61.21(61.19)	4.13(4.11)	17.82(17.85)
8b	2-Furanyl	183	67	C <sub>31</sub> H <sub>21</sub> N <sub>9</sub> OCl <sub>2</sub>	61.36(61.39)	3.49(3.47)	20.76(20.79)
8c	2-Thienyl	123	68	C <sub>31</sub> H <sub>21</sub> N <sub>9</sub> SCl <sub>2</sub>	59.84(59.81)	3.36(3.38)	20.24(20.26)
8d	Cinnamyl	187	62	C <sub>35</sub> H <sub>25</sub> N <sub>9</sub> Cl <sub>2</sub>	65.45(65.42)	3.90(3.89)	19.66(19.63)
9a	3,4,5-Trimethoxyphenyl	157	70	C <sub>35</sub> H <sub>32</sub> N <sub>8</sub> O <sub>4</sub> Cl <sub>2</sub>	60.06(60.09)	4.60(4.58)	16.00(16.02)
9b	2-Furanyl	176	69	C <sub>30</sub> H <sub>24</sub> N <sub>8</sub> O <sub>2</sub> Cl <sub>2</sub>	60.13(60.10)	4.03(4.01)	18.72(18.70)
9c	2-Thienyl	238	68	C <sub>30</sub> H <sub>24</sub> N <sub>8</sub> O <sub>2</sub> Cl <sub>2</sub>	58.57(58.54)	3.93(3.90)	18.24(18.21)
9d	Cinnamyl	143	67	C <sub>34</sub> H <sub>28</sub> N <sub>8</sub> OCl <sub>2</sub>	64.27(64.25)	4.39(4.41)	17.66(17.64)

#### [4'-(2''-amino-6''-(3''',4''',5'''-trimethoxy phenyl)-pyrimidine-4''-yl)-phenylamino]-s-triazine (7a)

A mixture of 2,4-bis-(4'-chlorophenylamino)-6-[4'-(3''-(3''',4''',5'''-trimethoxy phenyl)-2''-propanon-1''-yl)-phenylamino]-s-triazine(6a) (0.01mole) in 25ml dioxane, guanidine nitrate (0.01mole) and 40% KOH in distilled water (2ml) was refluxed for 10 hours. Then the reaction mixture was cooled and poured into crushed ice. The product separated out was filtered, washed with water and recrystallised from alcohol to give (7a).

Yield 72%; m.p. 160°C; IR (KBr, cm<sup>-1</sup>): 3380 (-NH<sub>2</sub>), 1613(C=N, pyrimidine moiety), 1021(C-O-C), 819(C-N, s-triazine), 770(C-Cl); <sup>1</sup>H NMR(CDCl<sub>3</sub>): δ 3.74 (s, 6H, m-OCH<sub>3</sub>), δ 3.84(s, 3H, p-OCH<sub>3</sub>), δ 5.18(s, 2H, -NH<sub>2</sub>), δ 7.0 to 8.12(m, 15 Ar-H and 3 NH). Anal. Calcd. for C<sub>34</sub>H<sub>29</sub>N<sub>9</sub>O<sub>3</sub>Cl<sub>2</sub>: C,59.82; H,4.25; N,18.48. Found: C,59.84; H,4.27; N,18.49.

#### Preparation of 2,4-bis-(4'-chlorophenylamino)-6-[4'-(2''-amino-3''-cyano-4''-(3''',4''',5'''-trimethoxyphenyl)-pyridine-6''-yl)-phenylamino]-s-triazine (8a)

A mixture of 2,4-bis-(4'-chlorophenylamino)-6-[4'-(3''-(3''',4''',5'''-trimethoxy phenyl)-2''-propanon-1''-yl)-phenylamino]-s-triazine (6a) (0.01mole) in 50ml alcohol, malononitrile (0.01mole) and ammonium acetate (0.02mole) was refluxed for 10 hours. Then the

reaction mixture was cooled and poured into crushed ice. The product separated out was filtered, washed with water and recrystallised from alcohol to give (8a). Yield 71%; m.p. 170°C; IR(KBr, cm<sup>-1</sup>): 3383(-NH<sub>2</sub>), 2213(C=N, pyridine moiety), 1027 (C-O-C), 815(C-N, s-triazine), 774(C-Cl); <sup>1</sup>H NMR(CDCl<sub>3</sub>): δ 3.72 (s, 6H, m-OCH<sub>3</sub>), δ 3.83 (s, 3H, p-OCH<sub>3</sub>), δ 5.25 (s, 2H, -NH<sub>2</sub>), δ 7.0 to 8.0 (m, 15 Ar-H and 3 NH). Anal. Calcd. for C<sub>36</sub>H<sub>29</sub>N<sub>9</sub>O<sub>3</sub>Cl<sub>2</sub>: C,61.19; H,4.11; N,17.85. Found: C,61.21; H,4.13; N,17.82.

#### Preparation of 2,4-bis-(4'-chlorophenylamino)-6-[4'-(1''-acetyl-5''-(3''',4''',5'''-trimethoxy phenyl)-2''-pyrazoline-3''-yl)phenylamino]-s-triazine (9a)

A mixture of 2,4-bis-(4'-chlorophenylamino)-6-[4'-(3''-(3''',4''',5'''-trimethoxy phenyl)-2''-propanon-1''-yl)-phenylamino]-s-triazine (6a) (0.01mole) in 20ml glacial acetic acid, hydrazine hydrate (0.01mole) was refluxed for 8 hours. Then the reaction mixture was cooled and poured into crushed ice. The product separated out was filtered, washed with water and recrystallised from alcohol to give (9a).

Yield 70%; m.p. 157°C; IR (KBr, cm<sup>-1</sup>): 1568 (C=N, pyrazoline moiety), 1030 (C-O-C), 813(C-N, s-triazine), 764(C-Cl); <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 2.45 (s, 3H, -COCH<sub>3</sub>), δ 3.04 (dd, 1H, -CH<sub>A</sub>), δ 3.45(dd, 1H, -CH<sub>B</sub>), δ 3.72(s, 6H, m-OCH<sub>3</sub>), δ 3.83(s, 3H, p-OCH<sub>3</sub>), 5.62(dd, 1H, -CH), 6.90 to 7.70 (m, 14 Ar-

TABLE 2: Antimicrobial activity of compounds (6a-d), (7a-d), (8a-d) and (9a-d)

No.	R	Zone of inhibition (mm)			
		<i>S.aureus</i>	<i>B.subtilis</i>	<i>E.coli</i>	<i>S.paratyphi-B</i>
6a	3,4,5-Trimethoxyphenyl	10	17	15	19
6b	2-Furanyl	12	16	-	20
6c	2-Thienyl	10	-	16	16
6d	Cinnamyl	12	18	-	18
7a	3,4,5-Trimethoxyphenyl	10	14	19	21
7b	2-Furanyl	14	16	16	18
7c	2-Thienyl	13	-	18	20
7d	Cinnamyl	-	15	18	20
8a	3,4,5-Trimethoxyphenyl	22	13	-	-
8b	2-Furanyl	12	16	18	20
8c	2-Thienyl	10	15	18	21
8d	Cinnamyl	11	16	19	20
9a	3,4,5-Trimethoxyphenyl	-	17	16	16
9b	2-Furanyl	12	16	-	21
9c	2-Thienyl	-	17	-	18
9d	Cinnamyl	10	15	12	20
Standard drug	Ciprofloxacin	22	20	20	18

H and 3 NH). Anal. Calcd. for  $C_{35}H_{32}N_8O_4Cl_2$ : C,60.09; H,4.58; N,16.02. Found: C,60.06; H,4.60; N,16.00.

## CONCLUSION

By visualizing activity data, it is observed that compound (8a) exhibit significant activity against *S.aureus*. Compound (6d) showed moderately active against *B. subtilis*. In case of *E.coli* (7a), (7c), (7d), (8b), (8c) and (8d) showed good activity. compounds (6a), (6b), (6d), (7a), (7b), (7c), (7d), (8b), (8c), (8d), (9b), (9c) and (9d) showed remarkable activity against *s.paratyphi-B*. All the antibacterial data are represented in TABLE 2.

From the above data, it can be concluded that most of the compounds showed promising activity against Gram negative bacteria in comparison of Gram positive bacteria.

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## REFERENCES

[1] G.Forkmann, W.Heller; 'Comprehensive Natural

Products Chemistry', D.Barton, K.Nakanishi, O.Meth-Cohn (Eds.); Elsevier Science, Amsterdam, 713-748 (1999).

- [2] W.J.Ebenezer, P.Wight; 'Comprehensive Organic Functional Group Transformation', edited by A.R.Katritzky, O.Meth-Cohn, C.W.Rees; Pergamon Press, Oxford, 3, 206-276 (1995).
- [3] (a) J.March; Advanced Organic Chemistry, Reactions, Mechanisms and Structure.(John Wiley and Sons, New York) 937-945 (1993).  
(b) U.P.Kreher, A.E.Rosamilia, C.L.Raston, J.L.Scott, C.R.Strauss; Org.Lett., 5, 3107 (2003).
- [4] D.N.Dhar; 'Chemistry of Chalcones and Related Compounds', Wiley, New York, (1981).
- [5] J.H.Wu, X.H.Wang, Y.H.YiK, H.Lee; Bioorg.and Med.Chem.Lett, 13, 1813 (2003).
- [6] X.Wu, P.Wilairat, M.L.Go; Bioorg.and Med.Chem.Lett, 12, 2299 (2002).
- [7] F.Herencia, M.L.Ferrandiz, A.Ubeda, J.N.Dominguez, J.E.Charris, G.M.Lobo, M.J.Alcaraz; Bioorg. and Med.Chem.Lett, 8, 1169 (1998).
- [8] Anjani Solankee, Indrajit Thakor; Indian J.Chem., 45B, 517 (2006).
- [9] Y.Xia, Z.Y.Yang, P.Xia, K.F.Bastow, Y.Nakanishi, K.H.Lee; Bioorg. and Med.Chem.Lett, 10, 699 (2000).
- [10] M.Pemmsin, C.Lnu-Due, F.Hoguet, C.Gaultier, J.Narcisse; Eur.J.Chem., 23, 534 (1986).
- [11] A.Commito, M.Pemmsin, C.Lnu-Due, F.Hoguet, C.Gaultier, J.Narcisse; Eur.J.Chem., 25, 635 (1990).
- [12] P.A.Smith, R.O.Kan; J.Org.Chem., 29, 2261 (1964).

- [13] J.Balzarini, C.Mc Guigan; J.Antimicrob.Chemothr., **50**, 5 (2002).
- [14] S.Nega, J.Aionso, A.Diazj, F.Junquere; J. Heterocycl Chem., **27**, 269 (1990).
- [15] C.J.Shishoo, M.B.Devani, G.V.Ullas, S.Ananhan, V.S.Bhadti; J.Heterocycl Chem., **18**, 43 (1981).
- [16] N.Latif, N.Mishrky, N.S.Girgis; Indian J.Chem., **20B**, 147 (1981).
- [17] Neela J.Datta, C.Khunt, A.R.Parikh; Oriental J. Chem., **18(1)**, 131 (2002).
- [18] VEB Leuna- Werke; 'Water Ulbricht', Edited by W.L.Hoefling, D.Elhafer, G.Reckling; Ger 1.193, 506(1CO7D) May 26 (1965); Chem.Abstr., **63**, 6979 (1965).
- [19] Thiele Kurt, Von Be Benburg, E.Walter, Dentsche Gold, Silber-Scheideantalt Varm Rossler; S.African, **6**, 905, 13 Feb., (1970).
- [20] G.Appendino, E.Bombardeli; Tetrahedron Lett., **37**, 7836 (1996); Chem.Abstr., **126**, 19064r (1997).
- [21] H.M.Kanjariya, T.V.Radhakrishan, K.R.Ramchandran, H.H.Parekh; Indian J.Chem., **43B**, 1569 (2004).
- [22] N.B.Das, A.S.Mittra; Indian J.Chem., **16B**, 638 (1978).
- [23] N.Mishriky, F.M.Asaad, Y.A.Ibrahim, A.S.Giris; Indian J.Chem., **35B**, 935 (1996).
- [24] A.Solankee, K.Kapadia, I.Thakor, J.Patel, S.Lad; Oriental J.Chem., **19(3)**, 637 (2003).
- [25] A.Solankee, K.Kapadia, I.Thakor, J.Patel, S.Lad; Asian J.Chem., **16**, 921 (2004).
- [26] A.Solankee, I.Thakor; Indian J.Chem., **45B**, 517 (2006).
- [27] A.L.Barry; The Antimicrobial susceptibility test Principale and Practice, Illus lea and Febiger, Philadelphia, Pa. U.S.A., 180-93 (1976).