Heterocyclic Letters
Vol. 8| No.3|671-678|May-July|2018
ISSN : (print) 2231–3087 / (online) 2230-9632
CODEN: HLEEAI
http://heteroletters.org

DESIGN, FACILE SYNTHESIS AND PHARMACOLOGICAL EVALUATION OF HYBRID 1,3,4-THIADIAZOLE LINKED CHALCONE CONFINED VIA SULPHUR BRIDGE

Vinuta Kamat[a*], Suresh P. Nayak[a], Ganesh Adiga[a], Aminath Rajeena C. H[a]., Saptami U Kanekar[b] and Rekha P. D[b].

[a] Department of Post-Graduate Studies & Research in Chemistry, Mangalore University, Mangalagangothri-574199 (DK), Karnataka, India. Tel.: +91-824-2287262(O); fax: +91-824-2287367/2287424
[b]Yenepoya (Deemed to be University), Mangalore-575018(DK), Karnataka, India.
**e-mail: vinutakamat24@gmail.com*

ABSTRACT
To synthesize the modern lead scaffold with effective pharmocophore activity, a set of 1,3,4-thiadiazole linked chalcones have been aimed by applying the molecular hybridisation approach. These compounds were further examined for their antimicrobial activity versus selected Gram-positive and Gram-negative bacteria. The compounds showed fair to moderate antimicrobial activity on tested organisms.

KEYWORDS: 1,3,4-Thiadiazole, Chalcone, Claisen-Schmidt reaction, Antimicrobial activity.

1. INTRODUCTION
The classical approach of the drug discovery provokes us to combine substrates to construct new pharmacophore that should be coexistent therapeutically fetching target with diminished toxic levels[i]. According to the previous report, nitrogen containing heterocycles connected with sulphur encouraging us to design[ii-iv] more scaffolds. Linking more than one pharmacophores affect their bioactivities or which leads to some other property which is not shown by parent scaffold individually[v,vi]. Modification in the substituent and sulphur containing scaffold may cause deviation in the bio-activity. **Figure 1** shows the strategy behind the work.

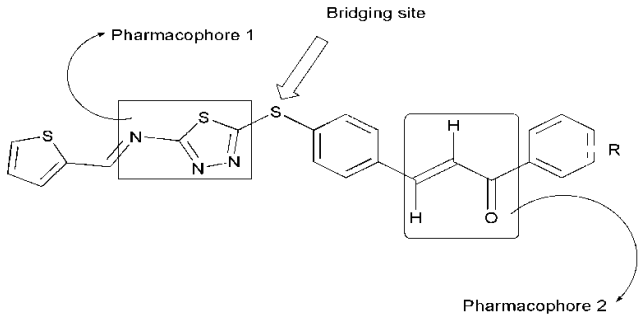


Figure 1: Tactic behind the designing the hybrid scaffolds

Chalcone linked thiadiazole displays various biological activities. Chalcones are the building blocks for various beneficial scaffolds, which have remarkable class of biological activities and their wide range of activities, attract the researchers to explore it more and more[vii]. These possess broad range bioactivities such as anti-bacterial, anti-fungal, anti-oxidant and anti-cancer[viii]. On the other hand, 1,3,4-thiadiazoles are most important scaffolds in medicinal chemistry because of its high therapeutic values[ix]. These were acts as antibacterial[x], antimicrobial, antidepressant, antioxidant and anticancer[xi] .

Our progressive research on productive and diminished toxic levels of antimicrobial pharmacophore, we were focusing on constructing the hybrid molecular frame work containing distinct pharmacophores[xii-xviii]. In this study, we synthesized hybrid 1,3,4-thiadiazole linked chalcones via sulphur bridge. This study focuses on the practical impact of substituent in terms of antimicrobial potency with the modification of previous report[xix]. The synthetic path of the target scaffold was illustrated in the **Scheme 1** via linking two distinct pharmacophores to get new lead scaffold with enhancing the biological potency.

2. EXPERIMENTAL APPROACHES

2.1 Materials and methods

All the reagents for the present study were obtained from commercial dealers of Sigma-Aldrich and Spectrochem. Melting points were acquired in an open capillary tube and were uncorrected. Thin layer chromatography (Merck silica gel 60 F254 coated aluminium plates) confirmed the purity of the products. Synthesized moieties were characterized by ^{1}H-NMR, ^{13}C-NMR, FT-IR, and Elemental analysis. FT-IR spectrum was recorded on Shimadzu-FT-IR Infrared spectrometer (γ_{max} in cm^{-1}). ^{1}H-NMR (400 MHz) and ^{13}C-NMR spectrum, was recorded on a Bruker Advance II 400 spectrometer, with 5mm PABBO BB-1H Tubes, using DMSO-d_6/$CDCl_3$ as a solvent, using TMS as internal standard (Chemical shift in δ ppm). Elemental analysis was carried out by using VARIOEL-III (Elemental analyse system GmBH).

2.2 Synthesis of 5-amino-1,3,4-thiadiazole-2-thiol (2):

Thiosemicarbazide (0.25 mol), anhydrous sodium carbonate (0.125 mol) were dissolved in absolute ethanol (20 mL) and the reaction mixture was refluxed at 80 ^{0}C. Ethanolic carbon disulfide (0.25 mol) was added slowly into the above reaction mass and further refluxed for 4 hrs. The reaction progress was monitored by thin layer chromatography. After completion of the reaction, mass was allowed to attain ambient temperature. The reaction mixture was poured into ice cold water (100 mL) and acidified by concentrated hydrochloric acid to get white precipitate. Yield: 80%, mp: 230 ^{0}C.

2.3 Synthesis of 5-[(thiophen-2-ylmethylidene) amino]-1,3,4-thiadiazole-2-thiol (3):

Compound **2** (5 mmol) was dissolved in absolute ethanol (20 mL), to this added thiophene-2-aldehyde followed catalytic amount of acetic acid. It was refluxed for about 4 hrs and checked for the reaction completion by thin layer chromatography. After completion of the reaction, mass brought to room temperature and quenched with ice cold water (100 mL). The obtained precipitate was filtered, dried and recrystalized with ethanol to afford pure compound. Yield: 82%, mp: 184 ^{0}C.

2.4 Synthesis of 4-({5-[(thiophen-2-ylmethylidene) amino]-1,3,4-thiadiazol-2-yl}sulfanyl)benzaldehyde (4):

Ethanolic solution of compound **3** (5 mmol), 4-fluoro benzaldehyde (5 mmol) and K_2CO_3 (5 mmol) was refluxed for 4 hrs and the reaction completion was examined through thin layer chromatography. After the completion, it was cooled and quenched with crushed ice (100 ml) for the precipitation. Solids were filtered, dried and recrystalized to get pure compound. Yield: 79%; mp: 108 - 110 ^{0}C IR: (KBr cm^{-1}) ν_{max}: 1630 (CH=N) 1630 (CH=N) ^{1}H-NMR (400 MHz, DMSO-d_6): 7.5 (d, 4H *J* = 8.4 Hz Ar-H), 7.8- 7.9 (m, 4H, *J* = 6 Hz Thienyl proton), 9.9 (s, 1H, -CHO).

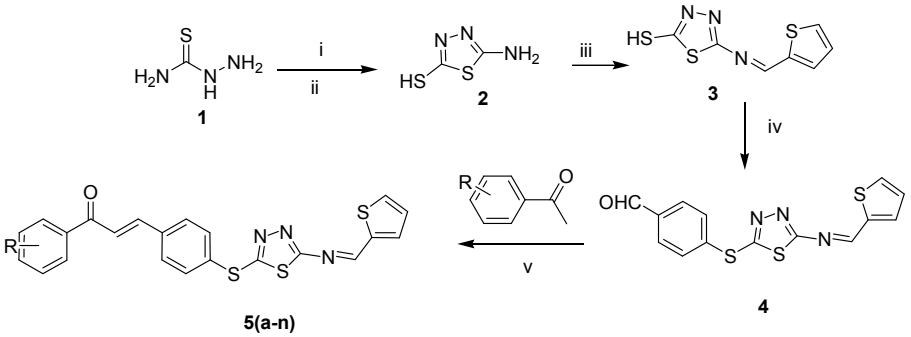
2.5 Synthesis of 1-phenyl-3-[4-({5-[thiophen-2-ylmethylidene)amino]-1,3,4-thiadiazol-2-yl}sulfanyl)phenyl]prop-2-en-1-one (5a-n):

Target compounds were synthesized by treating compound **4** (5 mmol) with substituted acetophenone (5 mmol) in ethanol (20 mL). KOH (alcoholic) was added slowly and stirring continued till the reaction had to complete. Once the reaction was completed, mass was quenched in ice cold water (100 mL) and the precipitate was filtered. The solids were recrystalized in ethanol to get pure compound. The physico-chemical data of newly synthesized scaffolds were tabulated in the **Table 1**.

Table 1. physico-chemical data of newly synthesized scaffolds.

Compound	R	Molecular formula	Molecular weight	Yield (%)	Melting point (^{0}C)	Elemental Analysis Calculated (Found)		
						C	H	N
5a	4-Br	$C_{22}H_{14}BrN_3OS_3$	510.95	62	220-222	51.56(51.55)	2.75(2.74)	8.20(8.18)
5b	4-Me	$C_{23}H_{17}N_3OS_3$	447.05	45	162-164	61.00(61.03)	3.83(3.80)	9.39(9.40)
5c	4-F	$C_{22}H_{14}FN_3OS_3$	451.03	91	186-188	58.52(58.51)	3.12(3.10)	9.31(9.30)
5d	4-NH_2	$C_{22}H_{16}N_4OS_3$	448.05	69	170-172	58.90(58.89)	3.60(3.62)	12.49(12.50)
5e	4-H	$C_{22}H_{15}N_3OS_3$	433.03	55	148-150	60.94(60.96)	3.49(3.50)	9.69(9.67)
5f	4-OH	$C_{22}H_{15}N_3O_2S_3$	449.03	33	92-94	58.78(58.75)	3.36(3.40)	9.35(9.38)
5g	4-NO_2	$C_{22}H_{14}N_4OS_3$	478.02	51	102-104	55.21(55.24)	2.95(2.98)	11.71(11.70)
5h	4-Cl	$C_{22}H_{14}ClN_3OS_3$	467.00	85	192-194	56.46(56.45)	3.02(3.00)	8.98(8.95)
5i	4-OMe	$C_{23}H_{17}N_3O_2S_3$	463.05	94	126-128	59.59(59.60)	3.70(3.72)	9.06(9.05)
5j	3- NO_2	$C_{22}H_{14}N_4O_3S_3$	478.02	43	120-122	55.21(55.23)	2.95(2.92)	11.71(11.75)

5k	2-Cl	$C_{22}H_{14}ClN_3OS_3$	467.00	31	90-92	56.46(56.45)	3.02(3.03)	8.98(8.99)
5l	2,4-dihydroxy	$C_{22}H_{15}N_3O_3S_3$	465.03	39	96-98	56.76(56.75)	3.25(3.21)	9.03(9.05)
5m	2,4-dichloro	$C_{22}H_{13}Cl_2N_3OS_3$	501.96	40	78-80	52.59(52.61)	2.61(2.63)	8.36(8.35)
5n	3- NH_2	$C_{22}H_{16}N_4OS_3$	448.05	30	108-110	58.90(58.92)	3.60(3.62)	12.49(12.50)



Scheme1: Synthetic pathway for the preparation of 1,3,4-thiadiazole linked chalcone. Reagents and condition: i) Na_2CO_3, EtOH ii) CS_2, reflux for 4 hrs. iii) Thiophene 2-aldehyde, EtOH reflux for 4hrs. iv) 4-Fluoro benzaldehyde, K_2CO_3, EtOH v) Alc. KOH

2.6 Spectral characterisation of synthesized compounds (5a-5n)

1-(4-bromophenyl)-3-[4-({5-(thiophen-2-ylmethylidene)amino]-1,3,4-thiadiazol-2-yl}sulfanyl)phenyl]prop-2-en-1-one (5a)
IR: (KBr cm^{-1}) ν_{max}: 1630 (CH=N) ^{1}H-NMR (400 MHz, DMSO-d_6) δ: 7.4 (d, 3H, *J* = 8 Hz, Ar-H), 7.5 (d, 5H, *J* = 8.4 Hz Ar-H, *J* = 15.6 Hz olefinic H), 7.6 (d, 3H, *J* = 8 Hz Ar-H) 7.9 (d, 3H, *J* = 6.4 Hz Thienyl proton) ^{13}C-NMR (DMSO-d_6, 100 MHz) δ: 123.64, 129.07, 129.29, 129.80, 129.92, 130.44, 130.77, 130.82, 131.29, 132.21, 132.50, 134.51, 134.77, 136.49, 142.82, 143.05, 144.16, 144.23, 152.31, 163.29, 189.00, 192.61.

(2*E*)-1-(4-methylphenyl)-3-[4-({5-[(*E*)-(thiophen-2-ylmethylidene)amino]-1,3,4-thiadiazol-2-yl}sulfanyl)phenyl]prop-2-en-1-one (5b)
IR: (KBr cm^{-1}) ν_{max}: 1630 (CH=N) ^{1}H-NMR (400 Hz, DMSO-d_6) δ: 2.5 (s, 3H, CH_3), 7.4 (d, 3H, *J* = 8.4 Hz Ar-H), 7.5 (d, 2H, *J* = 8.4 Hz Ar-H), 7.6 (d, 2H, *J* = 8.4 Hz Ar-H) 7.9 (d, 4H, *J* = 8.4 Hz Ar-H, *J* = 15.6 Hz olefinic H) 8.0 (d, 3H, *J* =8.4Hz Thienyl proton) ^{13}C-NMR (DMSO-d_6,100 MHz) δ: 21.68, 123.02, 123.44, 129.01, 129.17, 129.21, 129.68, 129.75, 129.86, 130.43, 130.67, 130.87, 131.29, 133.48, 134.51, 134.77, 135.49, 142.82, 143.05, 144.16, 144.23, 189.00, 192.61.

(2*E*)-1-(4-fluorophenyl)-3-[4-({5-[(*E*)-(thiophen-2-ylmethylidene)amino]-1,3,4-thiadiazol-2-yl}sulfanyl)phenyl]prop-2-en-1-one (5c)
IR: (KBr cm^{-1}) ν_{max}: 1630 (CH=N) ^{1}H-NMR (400 MHz, DMSO-d_6) δ: 7.4 (d, 3H, *J* = 8 Hz, Ar-H), 7.5 (d, 5H, *J* = 8.4 Hz Ar-H, *J* = 15.6 Hz olefinic H), 7.6 (d, 3H, *J* = 8Hz Ar-H) 7.9 (d, 3H, *J* = 6.4 Hz Thienyl proton) ^{13}C-NMR (DMSO-d_6, 100 MHz) δ: 110.32, 110.44, 123.64, 129.07, 129.29, 129.80, 129.92, 130.44, 130.82, 132.21, 132.50, 134.51, 134.77, 136.49, 142.82, 143.05, 144.16, 144.23, 150.89, 152.35, 189.00, 192.61.

(2*E*)-1-(4-aminophenyl)-3-[4-({5-[(*E*)-(thiophen-2-ylmethylidene)amino]-1,3,4-thiadiazol-2-yl}sulfanyl)phenyl]prop-2-en-1-one (5d)
IR: (KBr cm^{-1}) ν_{max}: 1630(CH=N) ^{1}H-NMR (400 Hz, DMSO-d_6) δ: 3.5 (s, 2H, NH), 7.0 (d, 2H, *J* = 8Hz, Ar-H), 7.4 (d, 6H, *J* = 8.4 Ar-H, *J* = 15.6 Hz olefinic H) 7.6 (d, 3H, *J* = 8 Hz Ar-H), 7.9 (d, 3H, *J* = 6.4 Hz Thienyl proton) ^{13}C-NMR (DMSO-d_6, 100 MHz) δ: 110.32, 110.44, 123.46, 129.07, 129.29, 129.80, 129.92, 130.44, 131.59, 132.21, 132.50, 134.51, 134.77, 136.49, 142.82, 143.05, 144.16, 150.23, 152.30, 154.75, 189.00, 192.61.

(2*E*)-1-phenyl-3-[4-({5-[(*E*)-(thiophen-2-ylmethylidene)amino]-1,3,4-thiadiazol-2-yl}sulfanyl)phenyl]prop-2-en-1-one (5e)
IR: (KBr cm^{-1}) ν_{max}: 1630 (CH=N) ^{1}H-NMR (400 Hz, DMSO-d_6) δ: 7.4 (d, 3H, *J* = 8.4 Hz Ar-H), 7.5 (d, 3H, *J* = 8.4 Hz Ar-H), 7.6 (d, 2H, *J* = 8.4 Hz Ar-H) 7.9 (d, 4H, *J* = 8.4 Hz Ar-H *J* = 15.6Hz olefinic H) 8.0 (d, 3H, *J* = 8.4 Hz Thienyl proton) ^{13}C-NMR (DMSO-d_6,100 MHz) δ: 121.34, 128.46, 129.05, 129.15, 129.22, 129.68, 129.74, 129.86, 130.29, 130.52, 130.92, 131.12, 133.32, 134.25, 134.69, 135.29, 142.62, 143.12, 144.16, 144.89, 189.55, 190.00.

(2*E*)-1-(4-hydroxyphenyl)-3-[4-({5-[(*E*)-(thiophen-2-ylmethylidene)amino]-1,3,4-thiadiazol-2-yl}sulfanyl)phenyl]prop-2-en-1-one (5f)
IR: (KBr cm^{-1}) ν_{max}: 1630 (CH=N) ^{1}H-NMR (400 Hz, DMSO-d_6) δ: 5.4 (s, 1H, OH) 7.4 (d, 3H, *J* = 8.4 Hz Ar-H), 7.5 (d, 2H, *J* = 8.4 Hz Ar-H), 7.6 (d, 2H, *J* = 8.4 Hz Ar-H) 7.9 (d, 4H, *J* = 8.4 Hz Ar-H, *J* = 15.6 Hz olefinic H) 8.0 (d, 3H, *J* = 8.4 Hz Thienyl proton) ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 115.23, 115.84, 12,3.19, 123.55, 129.48, 129.55, 129.78, 129.99, 130.52, 130.99, 131.82, 133.29, 134.15, 134.69, 135.78, 142.21, 143.25, 144.02, 144.59, 165.20, 188.86, 191.59.

(2*E*)-1-(4-nitrophenyl)-3-[4-({5-[(*E*)-(thiophen-2-ylmethylidene)amino]-1,3,4-thiadiazol-2-yl}sulfanyl)phenyl]prop-2-en-1-one (5g)
IR: (KBr cm^{-1}) ν_{max}: 1630 (CH=N) ^{1}H-NMR (400 Hz, DMSO-d_6) δ: 7.5 (d, 3H, *J* = 8.4 Hz Ar-H), 7.6 (d, 2H, *J* = 8.4 Hz Ar-H), 7.9 (d, 2H, *J* = 15.6 Hz olefinic H) 8.0 (d, 4H, *J* = 8.4 Hz Ar-H) 8.1 (d, 3H, *J* = 8.4 Hz Thienyl proton) ^{13}C-NMR (DMSO-d_6, 100 MHz) δ: 113.33, 114.24, 12,3.19, 124.25, 128.56, 129.72, 129.95, 130.19, 130.59, 130.89, 131.23, 133.56, 134.72, 134.99, 136.78, 141.11, 142.05, 143.90, 144.12, 160.00, 180.86, 190.09.

(2*E*)-1-(4-chlorophenyl)-3-[4-({5-[(*E*)-(thiophen-2-ylmethylidene)amino]-1,3,4-thiadiazol-2-yl}sulfanyl)phenyl]prop-2-en-1-one (5h)
IR: (KBr cm^{-1}) ν_{max}: 1630 (CH=N) ^{1}H-NMR (400 Hz, DMSO-d_6) δ: 7.4 (d, 3H, *J* = 8 Hz, Ar-H), 7.5 (d, 5H, *J* = 8.4 Hz Ar-H, *J* = 15.6 Hz olefinic H), 7.6 (d, 3H, *J* = 8Hz Ar-H) 7.9 (d, 3H, *J* = 8.4 Hz Thienyl proton) ^{13}C-NMR (DMSO-d_6, 100 MHz) δ: 121.75, 125.21, 129.02, 129.30, 129.50, 129.90, 130.22, 130.45, 131.43, 131.55, 131.78, 132.46, 132.98, 133.80, 136.41, 138.39, 139.38, 141.29, 144.16, 151.11, 167.28, 188.94

(2*E*)-1-(4-methoxyphenyl)-3-[4-({5-[(*E*)-(thiophen-2-ylmethylidene)amino]-1,3,4-thiadiazol-2-yl}sulfanyl)phenyl]prop-2-en-1-one (5i)
IR: (KBr cm^{-1}) ν_{max}: 1630 (CH=N) ^{1}H-NMR (400 Hz, DMSO-d_6) δ: 3.9 (s, 3H, OCH_3) 7.2 (d, 3H, *J* = 8.4 Hz Ar-H), 7.5 (d, 2H, *J* = 8.4 Hz Ar-H), 7.6 (d, 2H, *J* = 8.4 Hz Ar-H) 7.9 (d, 4H, *J* = 8.4 Hz Ar-H, *J* = 15.6 Hz olefinic H) 8.0 (d, 3H, *J* = 8.4 Hz Thienyl proton) ^{13}C-NMR (DMSO-d_6, 100MHz) δ: 56.20, 114.32, 116.24, 123.72, 123.98, 128.48, 129.05, 129.56,

129.95, 131.31, 131.99, 132.26, 133.45, 134.54, 134.69, 136.78, 141.21, 143.14, 144.22, 144.59, 162.00, 180.86, 190.86.

(2*E*)-1-(3-nitrophenyl)-3-[4-({5-[(*E*)-(thiophen-2-ylmethylidene)amino]-1,3,4-thiadiazol-2-yl}sulfanyl)phenyl]prop-2-en-1-one (5j)
IR: (KBr cm^{-1}) ν_{max}: 1630 (CH=N) ^{1}H-NMR (400 Hz, DMSO-d_6) δ: 7.5 (d, 2H, *J* = 8.4 Hz Ar-H), 7.6 (d, 2H, *J* = 8.4 Hz Ar-H), 7.9 (d, 2H, *J* = 15.6 Hz olefinic H) 8.0 (d, 3H, *J* = 8.4 Hz Ar-H) 8.1 (d, 3H, *J* = 8.4 Hz Thienyl proton) 8.3 (d, 2H, *J* = 8.4 Hz Ar-H) ^{13}C-NMR (DMSO-d_6, 100 MHz) δ: 119.33, 119.98, 124.09, 124.55, 127.56, 128.72, 129.90, 130.19, 130.42, 130.89, 131.72, 133.26, 134.72, 134.98, 136.78, 140.11, 140.29, 145.21, 148.12, 159.80, 160.86, 189.29.

(2*E*)-1-(2-chlorophenyl)-3-[4-({5-[(*E*)-(thiophen-2-ylmethylidene)amino]-1,3,4-thiadiazol-2-yl}sulfanyl)phenyl]prop-2-en-1-one (5k)
IR: (KBr cm^{-1}) ν_{max}: 1630 (CH=N) ^{1}H-NMR (400 Hz, DMSO-d_6) δ: 7.4 (d, 2H, *J* = 8 Hz, Ar-H), 7.5 (d, 5H, *J* = 8.4 Hz Ar-H, *J* = 15.6 Hz olefinic H), 7.6 (d, 4H, *J* = 8 Hz Ar-H) 7.9 (d, 3H, *J* = 8.4 Hz Thienyl proton) ^{13}CNMR (DMSO-d_6, 100 MHz) δ: 120.23, 124.11, 128.12, 129.25, 129.66, 129.89, 130.12, 130.85, 131.40, 131.58, 131.99, 132.46, 132.89, 134.20, 135.21, 136.24, 140.38, 140.75, 143.72, 150.21, 165.72, 180.02.

(2*E*)-1-(2,4-dihydroxyphenyl)-3-[4-({5-[(*E*)-(thiophen-2-ylmethylidene)amino]-1,3,4-thiadiazol-2-yl}sulfanyl)phenyl]prop-2-en-1-one (5l)
IR: (KBr cm^{-1}) ν_{max}: 1630 (CH=N) ^{1}H-NMR (400 Hz, DMSO-d_6) δ: 5.4 (s, 2H, OH) 6.8 (d, 2H, *J* = 8.4 Hz Ar-H), 7.0 (d, 2H, *J* = 8.4 Hz Ar-H), 7.6 (d, 2H, *J* = 8.4 Hz Ar-H) 7.9 (d, 4H, *J* = 8.4 Hz Ar-H, *J* = 15.2 Hz olefinic H) 8.0 (d, 3H, *J* = 8.4 Hz Thienyl proton) ^{13}C-NMR (DMSO-d_6, 100 MHz) δ: 114.11, 115.58, 122.22, 123.45, 128.48, 129.05, 129.54, 129.79, 130.22, 130.98, 131.44, 132.29, 134.50, 134.75, 136.72, 142.74, 143.51, 144.09, 145.21, 160.22, 185.24, 190.27.

(2*E*)-1-(2,4-dichlorophenyl)-3-[4-({5-[(*E*)-(thiophen-2-ylmethylidene)amino]-1,3,4-thiadiazol-2-yl}sulfanyl)phenyl]prop-2-en-1-one (5m)
IR: (KBr cm^{-1}) ν_{max}: 1630 (CH=N) ^{1}H-NMR (400 Hz, DMSO-d_6) δ: 7.4 (d, 2H, *J* = 8.4 Hz Ar-H), 7.5 (d, 4H, *J* = 8.4 Hz Ar-H) 7.6 (d, 2H, *J* = 8.4 Hz, Ar-H), 7.9 (d, 2H, *J* = 15.2 Hz olefinic H) 8.0 (d, 3H, *J* = 8.4 Hz Thienyl proton) ^{13}C-NMR (DMSO-d_6, 100 MHz) δ: 108.16, 111.29, 111.54, 120.21, 121.10, 123.23, 125.78, 126.41, 128.75, 129.43, 130.07, 130.50, 131.00, 131.26, 133.52, 138.74, 140.45, 142.78, 145.18, 152.45, 161.92, 189.02.

(2*E*)-1-(3-aminophenyl)-3-[4-({5-[(*E*)-(thiophen-2-ylmethylidene)amino]-1,3,4-thiadiazol-2-yl}sulfanyl)phenyl]prop-2-en-1-one (5n)
IR: (KBr cm^{-1}) ν_{max}: 1630 (CH=N) ^{1}H-NMR (400 Hz, DMSO-d_6) δ: 3.5 (s, 2H, NH), 7.0 (d, 2H, *J* = 8 Hz, Ar-H), 7.4 (d, 6H, *J* = 8.4 Ar-H, *J* = 15.6 Hz olefinic H) 7.8 (d, 4H, *J* = 8 Hz Ar-H), 7.9 (d, 3H, *J* = 6.4 Hz Thienyl proton) ^{13}C-NMR (DMSO-d_6, 100 MHz) δ: 122.31, 123.24, 123.59, 123.75, 123.99, 124.75, 124.98, 125.83, 127.15, 127.42, 132.23, 133.21, 133.45, 134.21, 134.98, 136.78, 137.52, 144.21, 152.90, 165.81, 167.32, 189.23.

3. Result and discussion

The synthetic path of the target compound was sketched in the **Scheme 1**. 1,3,4-thiadiazole linked chalcone were synthesized by Claisen-Schmidt condensation reaction with favourable yield as shown in **Table 1**. FT-IR spectrum of the compound showed the absorption band at

1630 cm^{-1} which corresponds to CH=N, sharp band at 2920-3100 cm^{-1} corresponds to aromatic C-H stretching, absorption band at 1660 cm^{-1} characterises C=O and 1650-1670 cm^{-1} characterises C=C stretching frequencies. Absorption at 700 cm^{-1} corresponds to C-S stretching. The 400 MHz ^{1}H-NMR spectrum of all the compounds showed singlet at 7.4-7.5 confirmed the presence of HC=N, doublet at 7.5-7.9 with the coupling constant of 15.6 Hz, showed the presence of trans alkene and 7.9-8.1 with the coupling constant 6.4 Hz confirmed the presence of thienyl protons.

3.1 BIOLOGY

Bacteria and culture conditions

Two Gram-negative bacteria i.e *Pseudomonas aeruginosa (P. aeruginosa)* and *Escherchia coli (E. Coli)* and two Gram-positive bacteria i.e *Staphylococcus aureus (S. Aureus)* and *Bacillus subtilis (B. Subtilis)* maintained at Microbial collection repository of Yenepoya Research Centre, Mangalore were used for the experiments. Muller Hinton broth media was used for growing the cultures.

Broth dilution value for antimicrobial activity

The compounds were tested to determine the Minimal Inhibitory Concentration (MIC) for each bacterial strains. 100 µL of 10^6 cells/mL of each bacterial culture was inoculated in labelled 96 well microtiter plates in triplicates containing Muller Hinton broth. The test compounds at concentration of 500 µg/mL were supplemented into the broth and incubated at 37 ^{0}C for 24 hrs. The MIC of individual sample was gained by estimating the optical density in the spectrophotometer (600 nm).

Table 2 Percentage inhibition of the tested compounds against the four bacterial isolates.

Bacterial isolates	*P.aeruginosa*	*S. aureus*	*E. coli*	*B. subtilis*
5a	32.69	38.80	79.06	91.42
5b	68.49	5.80	60.07	10.11
5c	81.17	50.03	61.37	74.37
5d	53.12	73.05	65.11	88.32
5e	77.80	61.95	56.76	81.71
5f	52.27	78.54	26.40	82.51
5g	85.59	70.99	73.88	82.18
5h	86.18	69.87	65.76	89.56
5i	88.88	71.24	77.19	93.28
5j	74.30	63.38	75.90	77.66
5k	77.30	72.55	65.68	0.88
5l	44.27	71.49	64.82	64.15
5m	80.16	16.59	39.86	8.11
5n	69.92	75.30	57.48	51.08

RESULTS

All the tested compounds exhibited effective antibacterial activity against *E. coli*. Further, compound **5i** showed maximum antibacterial activity with 88.8 % of growth inhibition in *P.aeruginosa.* Compounds **5c**, **5d**, **5e**, **5g** and **5j** shows promising activity. **5a**, **5f**, **5l**, **5n** exhibits reasonable activity. These results were recorded in the **Table 2.**

4. Conclusion

This study concentrates on the practical impact of substituent in terms of antimicrobial potency. In this work, we synthesized some 1,3,4-thiadiazole linked chalcone scaffolds. These newly synthesized scaffolds were analysed for their antimicrobial activity against Gram positive and Gram negative bacteria. Few of them showed promising activity, so these can be availed for therapeutic use and can also be employed for designing and exploiting new synthetic routes.

5. Acknowledgement

Authors are thankful to USIC Karnataka University Dharwad for providing FT-IR facility.

REFERENCES

i C.G. Wermuth, *J. Med. Chem.,* **47,** 1303 (2004).
ii D. Kaushik, S.A. Khan, and S. Chawla, *Eur. J. Med. Chem.,* **45,** 3960 (2010).
iii D. Kaushik, S.A. Khan, S. Chawla S and S. Kumar, *Eur. J. Med. Chem.*, **45,** 3943 (2010).
iv S. Kumar, S. Bawa, S. Drabhu, R. Kumar, and L. Machawal, *Acta. Pol . Pharm.,* **67,** 567(2010).
v C.R.M. Araujio, C.A. LeiteFilho, V.L.A. Santos, G.L.A. Maia, and A.D. Gonsalves, *Quím. Nova.,* **38,** 868(2015).
vi R. Raj, K.M. Land, and V. Kumar, *RSC Adv.,* **5,** 82676 (2015).
vii Hiren H. Variya, Vikram Panchal, Falguni G. Bhabhor and G. R. Patel, *International letters of chemistry , Physics and Astronomy.,***61**, 77 (2015).
viii C.K.Thansneem, C.R. Biju and G. Babu, *World J Pharm Pharm Sci.,* **4,** 643 (2015)
ix Zi-Ning Cui, Ya-Sheng Li, De-Kun Hu, Hao Tian, Jia- Zhan Jiang, Yuan Wang and Xiao- Jing Yan, *Sci. Rep.*, **6,** 20204 (2016).
x C.H. Aminath Rajeena, Suresh P. Nayak, and G. Ganesh, J. *Chem.&Cheml. Sci.*, **7,** 1276 (2017)
xi C.H. Aminath Rajeena, Suresh P. Nayak, G. Ganesh, Vinuta Kamat, B. C. Revanasiddappa, and Hemanth Kumar, *Heterocycl. Lett.*, **8,** 49 (2018)
xii U.P. Singh, R.K. Singh, H.R. Bhat, Y.P. Subhaschandra, V. Kumar, M.K. Kumawat, and P. Gahtori, *Med. Chem. Res.,* **20,** 1603 (2011).
xiii H.R. Bhat, U.P. Singh, Y.P. Subshchandra, V. Kumar, P. Gahtori, A. Das, D. Chetia, A. Prakash, and J. Mahanta, *Arabian J. Chem.,*doi:10.1016/j.arabjc.2011.07.001 (2011).
xiv M.K. Kumawat, U.P. Singh, B. Singh, A. Prakash and D. Chetia, *Arabian J. Chem.,*doi:10.116/j.arabjc.2011.07.007 (2011).
xv U.P. Singh, H.R. Bhat, and P. Gahtori, *J. Mycol. Med.,* **22,** 134 (2012).
xvi P. Gahtori, S.K. Ghosh, B. Singh, U.P. Singh, H.R. Bhat, and U. Archana, *Saudi. Pharm. J.,* **20,** 35 (2012).
xvii P. Gahtori, S.K. Ghosh, P. Pratap, A. Prakash, K. Gogoi, and U.P. Singh, *Exp. Parasitol.,* **130,** 292 (2012).
xviii H.R. Bhat, S.K. Ghosh, A. Prakash, K. Gogoi, and U.P. Singh, *Lett. Appl. Microbiol.,* **54,** 483 (2012).
xix V.Dubey, M. Pathak, H.R. Bhat, U.P. Singh, *Chem. Biol. Drud Des.,* doi:10.1111/j.1747-0285.2012.01433.x. (2012).

Received on April 27, 2018.