SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL SCREENING OF PYRIDINE DERIVATIVES INCORPORATED WITH CHALCONE MOTIF

Chirag H. Rathod,[a]* Aftab Mithani[a] and Anilkumar S. Patel[b]*

Keywords: Pyridine derivatives; chalcone; antimicrobial activity; antifungal activity.

Herein we report synthesis of 3-methyl-2-((2-styrylphenoxy)methyl)-4-(2,2,2-trifluoroethoxy)pyridine derivatives (**9a-j**) from 2-((3-methyl-4-(2,2,2-trifluoroethoxy)pyridin-2-yl)methoxy)benzaldehyde (**7**) and appropriate acetophenone (**8a-f**) afford very good to excellent yield (80-95 %). The structure of newly synthesized compounds have been established on the basis of ^{1}H-NMR, ^{13}C-NMR, ESI-MS and elemental analysis. All compounds (**9a-f**) were screened for their *in vitro* antibacterial activity against Gram-positive bacteria (*Streptococcus pneumoniae* and *Bacillus subtilis*), Gram-negative bacteria (*Escherichia coli* and *Vibrio cholerae*) and antifungal activity against *C. albicans and A. fumigatus* by MIC method.

* Corresponding Authors
E-Mail: chiragrathod2908@gmail.com, patelanil32@gmail.com,
[a] Department of Chemistry, School of Science, RK University, Rajkot-360020, Gujarat, India.
[b] Department of Chemistry, Atmiya University, Kalawad Road, Rajkot-360005, Gujarat, India.

INTRODUCTION

Infectious diseases have been responsible for the cause of human illness or global health in the world population. Currently, decreases the delicacy of antimicrobial agents in current use has been increasing for a diversity of pathogens and the resistance to multiple drugs is common for various microorganisms like Gram-positive and Gram-negative bacteria.[1,2] Although the discovery of antibiotics has been improved against bacterial infection, and the antibacterial effect was decreases due to the arising of bacterial drug resistance.[3,4] Compound 4-(2,2,2-trifluoroethoxy)pyridine is the key pharmacophore for many drugs like molecule.[5,6] It demonstrates a broad range spectrum biological activity such as anti-microbial,[7] anti-cancer,[8] anti-fungal[9], proton pump inhibitors (PPIs)[10], anti-inflammatory.[11] Moreover, 1,3-diaryl-2-propenones belongs to the flavonoid family are natural and synthetic products that known as an ether isostere is present in a variety of biological active compounds,[12] such as anti-inflammatory,[13] anti-bacterial,[14] anti-cancer,[15] anti-platelet,[16] anti-tubercular,[17] enzyme inhibitory properties,[18] anti-oxidant.[19] As shown in Figure 1, all of the active molecules contain pyridin-2-ylmethyl fragments and chalcone. It can be forecast that these fragments play an important role in antimicrobial and antifungal activity.

In view of the above-mentioned findings, and as a continuation of our effort to identify new candidates that may be valuable in designing new, potent, selective, and less toxic antimicrobial agents, we have reported herein the newly synthesized substituted pyridine incorporate with 1,3-diaryl-2-propenones derivatives. All the synthesized compounds (**9a-j**) have been screened for in vitro antimicrobial activity and antifungal activity.

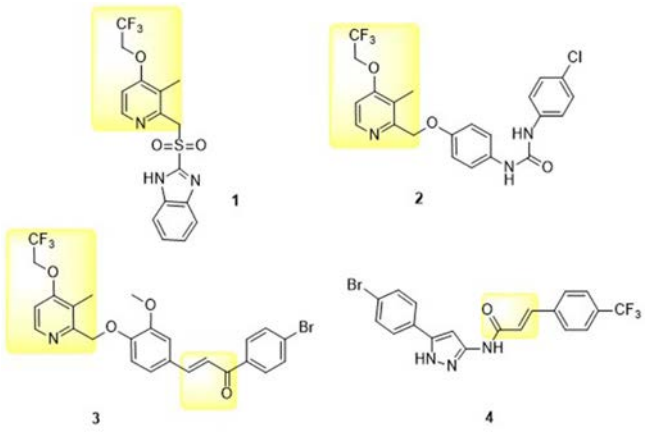


Figure 1. Structure of some 4-(2,2,2-trifluoroethoxy)-pyridine and 1,3-diaryl-2-propenones derivatives.

EXPERIMENTAL

All chemicals, solvents and reagents were purchased from Spectrochem, TCI chemicals, Sigma-Aldrich. Reaction progress was monitored by thin-layer chromatography on 0.2 mm precoated aluminum sheet Silica Gel Merck 60 (F254). Melting points of the synthesized compounds were determined by open glass capillary tubes and are uncorrected. Proton ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker model 400 MHz and 100 MHz respectively, DMSO-d_6 solvents using tetramethylsilane (TMS) as the internal standard. Chemical shift values are given in δ (ppm) scale and the signals are described as s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet), whereas coupling constants (*J*) are expressed in Hz. Mass spectra (ESI-MS) were recorded on SHIMADZU mass spectrometer.

2-((3-Methyl-4-(2,2,2-trifluoroethoxy)pyridin-2-yl)-methoxy)-benzaldehyde (7)

To a solution 2-(chloromethyl)-3-methyl-4-(2,2,2-trifluoro-ethoxy)pyridine (1 g, 4.1 mmol) in Dimethyl formamide (8.0 mL) was added salicylic aldehyde (0.56 g, 4.6 mmol) followed by K_2CO_3 (1.44 g, 10.4 mmol). Reaction mixture was stirred at 70 °C for 1 h. After completion of reaction on TLC (Ethyl acetate: Hexane; 3:7), the reaction mass was poured into cursed ice. Stirred reaction mass for few-minute to obtained solid grey compound. The obtained precipitate was filtered and dried to gate analytical pure compound. Yield 81 %; m.p. 136-138 ^oC; ^1H NMR (DMSO-d_6, 400 MHz, δ ppm): 2.42 (s, 3H, CH_3), 4.69-4.72 (q, 2H, OCH_2CF_3), 5.30 (s, 2H, OCH_2), 7.10 (t, 1H, *J* = 7.8 Hz, ArH), 7.28 (d, 1H, *J* = 8.2 Hz, ArH), 7.32-7.36 (m, 2H, ArH), 7.92 (d, 1H, *J* = 7.2 Hz, ArH), 8.49 (d, 1H, *J* = 6.8 Hz, ArH), 9.82 (s, 1H, CHO); ^{13}C NMR (DMSO-d_6, 100 MHz, δ ppm): 10.22, 76.10, 79.82, 105.01, 111.8, 114.41, 121.63, 122.99, 125.30, 130.8, 134.5, 145.19, 151.3, 159.10, 163.56, 190.50; MS m/z (ES+) 325.1 (M+); Analytical calculation for $C_{16}H_{14}F_3NO_3$: C=59.08 %, H=4.34 %, N=4.31 %, Found: C=59.18 %, H=4.24 %, N=4.34 %.

Synthesis of 1-(substitutedphenyl)-3-(2-((3-methyl-4-(2,2,2-trifluoro-ethoxy)pyridin-2-yl)methoxy)phenyl)prop-2-en-1-ones (9a-j)

To a solution of 2-((3-methyl-4-(2,2,2-trifluoroethoxy)-pyridin-2-yl)methoxy)benzaldehyde **7** (0.62 mmol) in methanol (5 mL) was appropriate acetophenone **8a-j** (0.68 mmol) followed by catalytic amount of piperidine, and the reaction mass was stirred for 12-16 hrs at rt. After completion reaction on TLC (Ethyl acetate: Hexane; 3:7), reaction mixture was filtered and washed with chilled methanol to afford desired product. The physical property and spectral characterization data of desired compounds as follow:

1-(4-Methoxyphenyl)-3-(2-((3-methyl-4-(2,2,2-trifluroethoxy)-pyridine- 2-yl)methoxy)phenyl)prop-2-en-1-one (9a)

Yield 86 %; m.p. 250-252 ^oC; ^1H NMR (DMSO-d_6, 400 MHz, δ ppm): 2.32 (s, 3H, CH_3), 2.57 (s, 3H, OCH_3), 4.80 (s, 2H, CH_2), 5.30 (s, 2H, CH_2), 7.08 (d, 2H, Ar), 7.31 (d, 1H, CH=CH), 7.48 (d, 1H, Ar), 8.00 (m, 3H, Ar), 8.33 (d, 1H, CH=CH), 8.36 (d, 2H, Ar), 8.68 (d, 2H, Ar); ^{13}C NMR (DMSO-d_6, 100 MHz, δ ppm): 10.41, 55.80 (C of –OCH_3), 65.26, 70.15, 108.58, 113.48, 122.53, 123.92, 129.22, 130.42, 132.32, 133.55, 139.57, 142.82, 145.58, 146.53, 148.38, 155.10, 155.26, 157.92, 182.03; MS m/z (ES+) 457.20 (M+); Analytical calculation for $C_{25}H_{22}F_3NO_4$: C=65.64 %, H=4.85 %, N=3.06 %; Found: C=65.70 %, H=4.80 %, N=3.08 %.

3-(2-((3-Methyl-4-(2,2,2-trifluroethoxy)pyridine-2-yl)-methoxy)phenyl)-1-(*p*-tolyl)prop-2-en-1-one (9b)

Yield 80 %; m.p. 280-283 ^oC; ^1H NMR (DMSO-d_6, 400 MHz, δ ppm): 2.22 (s, 3H, CH_3), 2.26 (s, 3H, CH_3), 4.81 (s, 2H, CH_2), 5.37 (s, 2H, CH_2), 7.06 (d, 2H, Ar), 7.30 (d, 1H, CH=CH), 7.46 (d, 1H, Ar), 8.05 (d, 1H, CH=CH), 8.10 (d, 2H, Ar), 8.23 (d, 2H, Ar), 8.58 (m, 3H, Ar); ^{13}C NMR (DMSO-d_6, 100 MHz, δ ppm): 10.09, 21.30, 65.61, 70.76, 108.57, 112.40, 121.52, 122.56, 129.27, 130.01, 132.22, 133.56, 140.92, 142.05, 144.99, 146.58, 148.83, 155.12, 155.32, 156.99, 181.04; MS m/z (ES+) 441.02 (M+); Analytical calculation for $C_{25}H_{22}F_3NO_3$: C=68.02 %, H=5.02 %, N=3.17 %; Found: C=68.06 %, H=5.04 %, N=3.14 %.

1-(4-Chlorophenyl)-3-(2-((3-methyl-4-(2,2,2-trifluro-ethoxy)-pyridine-2-yl)methoxy)phenyl)prop-2-en-1-one (9c)

Yield 91 %; m.p. 252-255 ^oC; ^1H NMR (DMSO-d_6, 400 MHz, δ ppm): 2.32 (s, 3H, CH_3), 4.78 (s, 2H, CH_2), 5.29 (s, 2H, CH_2), 7.09 (d, 2H, Ar), 7.35 (d, 1H, CH=CH), 7.65 (d, 1H, Ar), 8.02 (m, 3H, Ar), 8.31 (d, 1H, CH=CH), 8.59 (d, 2H, Ar), 8.72 (d, 2H, Ar); ^{13}C NMR (DMSO-d_6, 100 MHz, δ ppm): 10.23, 65.30, 76.0, 104.07, 111.08, 120.09, 121.13, 129.33, 130.32, 135.22, 135.99, 141.0, 142.70, 147.22, 147.68, 149.82, 154.12, 157.52, 158.53, 189.80; MS m/z (ES+) 461.10 (M+); Analytical calculation for $C_{24}H_{19}ClF_3NO_3$: C=62.41 %, H=4.15 %, N=3.03 %; Found: C=62.50 %, H=4.18 %, N=2.95 %.

3-(2-((3-Methyl-4-(2,2,2-trifluroethoxy)pyridine-2-yl)-methoxy)phenyl)-1-(4-nitrophenyl)prop-2-en-1-one (9d)

Yield 84 %; m.p. 274-276 ^oC; ^1H NMR (DMSO-d_6, 400 MHz, δ ppm): 2.20 (s, 3H, CH_3), 4.85 (s, 2H, CH_2), 5.32 (s, 2H, CH_2), 7.16 (d, 2H, Ar), 7.49 (d, 1H, CH=CH), 7.58 (d, 1H, Ar), 8.17 (m, 3H, Ar), 8.36 (d, 1H, CH=CH), 8.65 (d, 2H, Ar), 8.79 (d, 2H, Ar); ^{13}C NMR (DMSO-d_6, 100 MHz, δ ppm): 10.41, 64.92, 69.99, 109.01, 113.48, 121.96, 122.53, 129.32, 130.47, 132.82, 135.81, 138.81, 145.72, 145.99, 146.87, 148.93, 155.15, 157.92, 161.99, 182.31; MS m/z (ES+) 427.01 (M+); Analytical calculation for $C_{24}H_{19}F_3N_2O_5$: C=61.02 %, H=4.05 %, N=5.93 %; Found: C=61.03 %, H=4.10 %, N=5.92 %.

1-(4-Bromophenyl)-3-(2-((3-methyl-4-(2,2,2-trifluro-ethoxy)-pyridine-2-yl)methoxy)phenyl)prop-2-en-1-one (9e)

Yield 94 %; m.p. 260-262 ^oC; ^1H NMR (DMSO-d_6, 400 MHz, δ ppm): 2.40 (s, 3H, CH_3), 4.50 (s, 2H, CH_2), 5.55 (s, 2H, CH_2), 7.02 (d, 2H, Ar), 7.23 (d, 1H, CH=CH), 7.33 (d, 1H, Ar), 7.98 (m, 3H, Ar), 8.07 (d, 1H, CH=CH), 8.15 (d, 2H, Ar), 8.45 (d, 2H, Ar); ^{13}C NMR (DMSO-d_6, 100 MHz, δ ppm): 10.51, 79.01, 82.80, 104.70, 114.04, 122.10, 122.60, 130.32, 131.18, 133.82, 135.81, 139.52, 156.58, 158.91, 162.17, 189.07; MS m/z (ES+) 505.10 (M+); Analytical calculation for $C_{24}H_{19}BrF_3NO_3$: C=58.93 %, H=3.78 %, N=2.27 %; Found: C=59.10 %, H=3.79 %, N=2.31 %

1-(2,4-Chlorophenyl)-3-(2-((3-methyl-4-(2,2,2-trifluro-ethoxy)-pyridine-2-yl)methoxy)phenyl)prop-2-en-1-one (9f)

Yield 87 %; m.p. 265-258 ^oC; ^1H NMR (DMSO-d_6, 400 MHz, δ ppm): 2.39 (s, 3H, CH_3), 4.46 (s, 2H, CH_2), 5.60 (s, 2H, CH_2), 7.13 (d, 2H, Ar), 7.28 (d, 1H, CH=CH), 7.35 (d, 1H, Ar), 7.96 (m, 3H, Ar), 8.26 (d, 1H, CH=CH), 8.37 (d, 2H, Ar), 8.49 (d, 2H, Ar); ^{13}C NMR (DMSO-d_6, 100 MHz, δ ppm): 11.01, 66.10, 71.82, 110.01, 114.41, 122.63, 122.99,

127.40, 129.51, 131.9, 133.11, 133.99, 140.01, 141.19, 143.30, 145.10, 146.21, 146.58, 149.10, 157.10, 157.56, 190.50; MS m/z (ES+) 495.1 (M+); Analytical calculation for $C_{24}H_{18}Cl_2F_3NO_3$: C=58.08 %, H=3.66 %, N=2.82 %; Found: C=58.10 %, H=3.69 %, N=2.83 %.

3-(2-((3-Methyl-4-(2,2,2-trifluroethoxy)pyridine-2-yl)-methoxy)phenyl)prop-2-en-1-one (9g)

Yield 86 %; m.p. 275-278 °C; ^{1}H NMR (DMSO-d_6, 400 MHz, δ ppm): 2.34 (s, 3H, CH_3), 4.39 (s, 2H, CH_2), 5.58 (s, 2H, CH_2), 7.13 (d, 2H, Ar), 7.26 (d, 1H, CH=CH), 7.37 (d, 1H, Ar), 7.99 (m, 3H, Ar), 8.01 (t, 1H, Ar), 8.30 (d, 1H, CH=CH), 8.46 (d, 2H, Ar), 8.89 (d, 2H, Ar); ^{13}C NMR (DMSO-d_6, 100 MHz, δ ppm): 10.98, 74.20, 81.08, 105.70, 110.35, 121.27, 121.63, 125.70, 128.90, 129.02, 130.15, 136.80, 137.90, 141.0, 147.22, 151.08, 157.60, 165.10, 168.40, 192.10; MS m/z (ES+) 427.01 (M+); Analytical calculation for $C_{24}H_{20}F_3NO_3$: C=67.44 %, H=4.72 %, N=3.28 %; Found: C=67.56 %, H=4.74 %, N=3.26 %.

1-(4-Flurophenyl)-3-(2-((3-methyl-4-(2,2,2-trifluroethoxy)-pyridine-2-yl)methoxy)phenyl)prop-2-en-1-one (9h)

Yield 94 %; m.p. 285-287 °C; ^{1}H NMR (DMSO-d_6, 400 MHz, δ ppm): 2.51 (s, 3H, CH_3), 4.62 (s, 2H, CH_2), 5.76 (s, 2H, CH_2), 7.13 (d, 2H, Ar), 7.43 (d, 1H, CH=CH), 7.51 (d, 1H, Ar), 8.0 (m, 3H, Ar), 8.20 (d, 1H, CH=CH), 8.32 (d, 2H, Ar), 8.61 (d, 2H, Ar); ^{13}C NMR (DMSO-d^6, 100 MHz, δ ppm): 10.01, 72.12, 81.80, 106.66, 115.02, 122.89, 122.99, 130.98, 132.01, 133.87, 136.01, 140.10, 145.98, 147.52, 148.18, 149.66, 157.10, 157.25, 166.23, 187.50 ; MS m/z (ES+) 445.01 (M+); Analytical calculation for $C_{24}H_{19}F_4NO_3$: C=67.72 %, H=4.30 %, N=3.14 %; Found: C=67.73 %, H=4.27 %, N=3.10 %.

1-(4-Hydroxyphenyl)-3-(2-((3-methyl-4-(2,2,2-trifluroethoxy)-pyridine-2-yl)methoxy)phenyl)prop-2-en-1-one (9i)

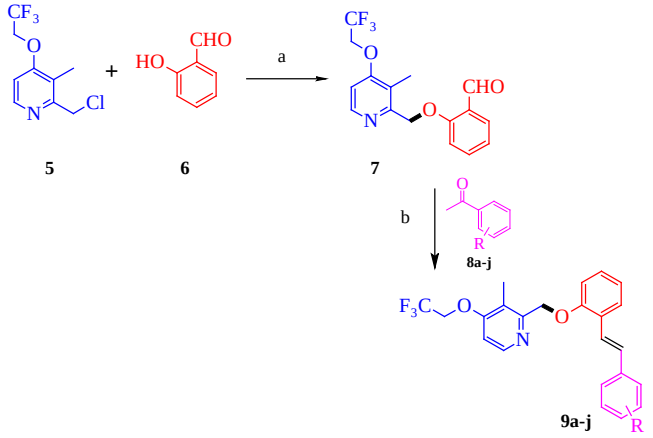
Yield 95 %; m.p. 248-250 °C; ^{1}H NMR (DMSO-d_6, 400 MHz, δ ppm): 2.69 (s, 3H, CH_3), 4.81 (s, 2H, CH_2), 4.94 (s, 1H, OH), 6.01 (s, 2H, CH_2), 7.22 (d, 2H, Ar), 7.39 (d, 1H, CH=CH), 7.69 (d, 1H, Ar), 8.22 (m, 3H, Ar), 8.29 (d, 1H, CH=CH), 8.32 (d, 2H, Ar), 8.41 (d, 2H, Ar); ^{13}C NMR (DMSO-d^6, 100 MHz, δ ppm): 9.98, 71.10, 80.0, 105.13, 116.09, 122.73, 123.01, 131.11, 132.27, 134.22, 135.99, 131.37, 146.47, 148.06, 148.23, 148.99, 159.15, 159.87, 167.44, 192.04; MS m/z (ES+) 443.01 (M+); Analytical calculation for $C_{24}H_{20}F_3NO_4$: C=65.01 %, H=4.55 %, N=3.16 %; Found: C=62.09 %, H=4.52 %, N=3.13 %.

4-(3-(2-((3-Methyl-4-(2,2,2-trifluroethoxy)pyridine-2-yl)-methoxy)phenyl)acryloyl)benzonitrile (9j)

Yield 87 %; m.p. 256-258 °C; ^{1}H NMR (DMSO-d^6, 400 MHz, δ ppm): 2.72 (s, 3H, CH_3), 5.01 (s, 2H, CH_2), 6.22 (s, 2H, CH_2), 7.31 (d, 2H, Ar), 7.42 (d, 1H, CH=CH), 7.60 (d, 1H, Ar), 8.15 (m, 3H, Ar), 8.23 (d, 1H, CH=CH), 8.69 (d, 2H, Ar), 8.73 (d, 2H, Ar); ^{13}C NMR (DMSO-d_6, 100 MHz, δ ppm): 11.12, 73.33, 81.10, 106.05, 116.55, 118.60 (CN), 122.82, 124.15, 132.12, 132.27, 135.55, 136.92, 142.66, 147.16, 148.55, 148.59, 149.71, 159.74, 159.89, 168.15, 193.09; MS m/z (ES+) 452.1 (M+); Analytical calculation for $C_{25}H_{19}F_3N_2O_3$: C=66.37 %, H=4.23 %, N=6.19 %; Found: C=66.39 %, H=4.19 %, N=6.22 %.

RESULTS AND DISCUSSION

The entire synthesis of targeted compounds is depicted in Scheme 1. Initially, 2-((3-methyl-4-(2,2,2-trifluoroethoxy)-pyridin-2-l)methoxy)benzaldehyde (**7**) was prepared by the reaction of 4-(2,2,2-trifluoroethoxy)pyridine (**5**) and 2-hydroxybenzaldehyde (**6**) in the presence of anhydrous K_2CO_3 as a base catalyst and DMF as a solvent. Claisen-Schmidt condensation of compound 2-((3-methyl-4-(2,2,2-trifluoroethoxy)pyridin-2-yl)methoxy)benzaldehyde (**7**) with substituted acetophenones (**8a-j**) in the presence of base piperidine in methanol to afford the targeted 1-(substituted)-3-(2-((3-methyl-4-(2,2,2-trifluoroethoxy)pyridin-2-yl)meth-oxy)phenyl)prop-2-en-1-one derivatives (**9a-j**) in very good to excellent yields. The targeted compound was confirmed by ^{1}H NMR were methylene protons at 4.80 δ ppm while alkene double bond appears at 7.30-8.40 δ ppm.



Reagents and conditions: (a) K_2CO_3, DMF, 70 °C, 1 h; (b) Piperidine, methanol, RT, 12-16 h

Scheme 1. Synthesis of 1-(substituted phenyl)-3-(2-((3-methyl-4-(2,2,2-trifluoro-ethoxy)pyridin-2-yl)methoxy)phenyl)prop-2-en-1-ones (**9a-j**).

***In vitro* antimicrobial activity**

The antimicrobial activity of the newly synthesized pyridine based chalcone derivatives at the minimal inhibitory concentration (MIC) in µg mL^{-1} was carried out by broth microdilution method[20]. The antibacterial activity was screened against Gram-positive bacteria (*Streptococcus pneumoniae* MTCC 1936 and *Bacillus subtilis* MTCC 441) and Gram-negative bacterium (*Escherichia coli* MTCC 443, and *Vibrio cholerae* MTCC 3906) bacteria using Ampiciline and Kanamycin as the standard antibacterial drugs. Antifungal activity was screened against fungal species (*Aspergillus fumigatus* MTCC 3008 and *Candida albicans* MTCC 227) and Chloramphenicol was used as the standard antifungal drugs. The strain was employed for the assay were produced from the Institute of Microbial Technology, Chandigarh (MTCC-Micro Type Culture Collection). Mueller Hinton broth was used as a nutrient medium to grow and dilute drug suspension for the experiment. DMSO was used as a diluent to the rich desired concentration.

Table 1. *In vitro* antimicrobial activity (MIC, µg mL^{-1}) of compound **9a-j**

Entry	R	Gram-Positive bacteria		Gram-negative bacteria		Fungi	
		SP, MTCC 1936	BS, MTCC 441	EC, MTCC 443	VC, MTCC 3906	CA, MTCC 227	AF, MTCC 3008
9a	4-OCH_3	20	25	40	25	55	50
9b	4-CH_3	40	45	50	45	60	65
9c	4-Cl	20	35	30	30	50	80
9d	4-NO_2	55	65	60	70	95	75
9e	4-Br	25	30	45	35	55	65
9f	2,4-Cl	35	55	50	45	85	70
9g	H	40	65	60	55	55	95
9h	4-F	20	30	40	30	60	55
9i	4-OH	30	25	50	25	50	60
9j	4-CN	40	75	65	30	55	85
A	-	30	20	55	30	n.t.	n.t.
B	-	25	35	40	35	n.t.	n.t.
C	-	n.t.	n.t.	n.t.	n.t.	55	60

SP: *Streptococcus pneumonia*, BS: *Bacillus subtilis*, EC: *Escherichia coli*, VC: *Vibrio cholera*, CA: *Candida albicans*, AF: *Aspergillus fumigatus*, MTCC: Microbial Type Culture Collection.

Investigation of antimicrobial activity data (table 1), it was revealed that synthesized pyridine based chalcone were possessed moderate to high potency. Compounds **9a, 9c, 9e,** and **9h** shows good potency against Gram-positive bacteria *Streptococcus pneumonia* and *Bacillus subtilis* as compared to standard drugs Kanamycin and Ampicillin. While compounds **9c, 9h** and **9i** were possessed good potency against Gram-negative bacteria *Escherichia coli* and *Vibrio cholera* as comparable with standard drug Kanamycin and Ampicillin. Compound **9c** and **9i** remarkably inhibit the growth of fungal stain *Candida albicans*. In comparison, compounds **9a** and **9h** show good potency against fungal stain *Aspergillus fumigatus* compared with Chloramphenicol.

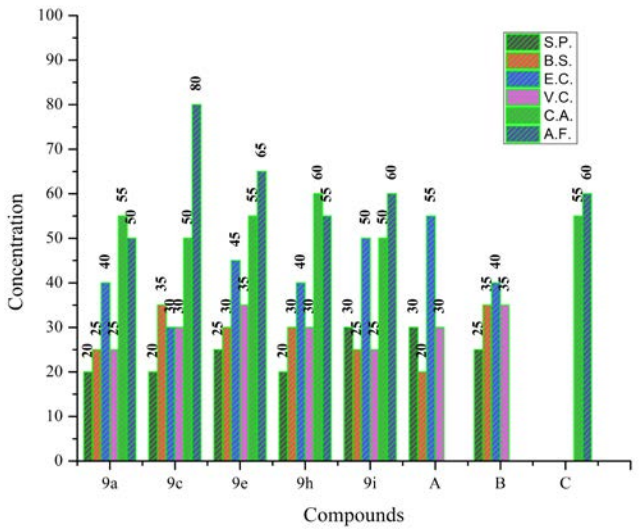


Figure 2. *In Vitro* antimicrobial activity of **9a-j**.

CONCLUSION

In summary, we have demonstrated the synthesis of 4-(2,2,2-trifluoroethoxy)pyridine based chalcone derivatives (**9a-j**). All newly synthesized compounds were confirmed by spectroscopic techniques (^{1}H NMR, ^{13}C NMR and ESI-MS) and elemental analyzer. The pharmacological efficacy of newly synthesized compounds has been determined against various bacterial and fungi stains. Compounds 9a, 9c and 9h were found excellent potency against antibacterial and antifungal microorganisms as comparable with standard drugs. Consequently, 4-(2,2,2-trifluoroethoxy)pyridine based chalcones may be a lead compound for further investigation to finding a potent microbial agent.

REFERENCES

[1]Juna, S., Wen, H., Han-yu, L., Jie, Q., Chun-Lin, Y., Design, synthesis and molecular docking of 1,4-benzodioxane thiazolidinedione piperazine derivatives as FabH inhibitors, *Bioorg. Chem.*, **2019**, *88*, 102958. https://doi.org/10.1016/j.bioorg.2019.102958

[2]Varshney, V., Mishra, N., Sukla, P., Sahu, D., Synthesis of nitroimidazole derived oxazolidinones as antibacterial agents, *Eur. J. Med. Chem.*, **2010,** *45*, 661-666. https://doi.org/10.1016/j.ejmwch.2009.11.009

[3]Chohan, Z., Youssoufi, M., Jarrahpour, Y., Hadda, T., Identification of antibacterial and antifungal pharmacophore sites for potent bacterial and fungi inhibition: Indolenyl sulphonamide derivatives, *Eur. J. Med. Chem.*,**2010**, *45*, 1189-1199. https://doi.org/10.1016/j.ejmech.2009.11.029

[4]Ibrahim, M., Panda, S., Oliferenko, A., Oliferenko, P., Girgis, A., Elgawany, M., Kucubay, Z., Panda, C., Pillai, G., Ahemd, S., Tamm, K., Hall, D., Katrizky, A., Macrocyclic peptidomimetics with antimicrobial

activity: synthesis, bioassay, and molecular modelling studies, *Org. Biomol. Chem.*, **2015**, *13(36)*, 9492-9503. https://doi.org/10.1039/C50B01400J

[5]Lugini, L., Federici, C., Borgis, M., Azzarito, T., Marino, M., Cesolini, A., Spugnini, E., Fais, S., Proton pump inhibitor while belonging to the same family of generic drugs shows different anti-tumour effect, *J. Enzyme Inhib. Med. Chem.*, **2016**, *31(4)*, 538-545. https://doi.org/10.3109/14756366.2015.1046062

[6]Pandya, M., Kapadiya, K., Pandit, C., Purohit, D., Synthesis of Halogenated Chalcones, Pyrazolines and Microbial Evaluation of Derived Scaffolds, *J. Sci. Ind. Res. India* **2016**, *79*, 173-178. https://nopr.niscair.res.in/handle/123456789/40646

[7]Pathare, P., Tekale, S., Damale, M., Sangshetti, J., Shaikh, R., Kotai, L., Pawar, R., Pyridine and benzoisothiazole based pyrazolines: synthesis, characterization, biological activity, molecular docking and admet study, *Eur. Chem. Bull.*, **2020**, *9(1)*, 10-21. https://dx.doi.org/10.17628/ecb.2020.9.6-9

[8]Mohammad, H., Alzweiri, M., Khanfar, M., Al-Hiari, Y., 6-Substituted nicotinic acid analogues, potent, inhibitors of CAIII, used as therapeutic candidates in hyperlipidaemia and cancer, *Med. Chem. Res.*, **2017**, *26*, 1397-1404. https://doi.org/10.1007/s00044-1825-x

[9]Kapadiya, S., Jadeja, Y., Purohit, D., Synthesis and biological screening of 3-aryl-5-{[(3'-difluoro-methoxy)-5'-(3"-methyl)-4"-(2"',2"',2"'-trifluroeth-oxy)pyridine-2"-yl]methoxyphenyl}-3,4-dihydropyra-zoles, *Heterocycl. Lett.*, **2018**, *8(3)*, 2230-9632. https://doi.org/10.1.1.848.9008

[10]Feng, J., Li, T., Liang, S., Zhang, C., Tan, X., Ding, N., Wang, X., Liu, X., Hu, C., Synthesis and biological evaluation of a new series of 1-aryl-3-[4-(pyridine-2-ylmethoxy)phenyl]urea derivatives as new anticancer agents, *Med. Chem. Res.*, **2020**, *29*, 1413-1423. https://doi.org/10.1007/s00044-020-02554-z

[11] Zhang, C., Tan, X., Feng, J., Ding, N., Li, Y., Jin, Z., Meng, Q., Liu, X., Hu, C., Design, Synthesis and Biological Evaluation of a New Series of 1-Aryl-3-{4-[(pyridin-2- ylmethyl)thio]phenyl}urea Derivatives as Antiproliferative Agents , *Molecules*, **2019**, *24*, 2108**.** https://doi.org/10.3390/molecules24112108

[12]Zhuang, C., Zhang, W., Sheng, C., Zhang, W., Xing, C., Miao, Z., Chalcone: A privileged structure in Medicinal Chemistry, *Chem. Rev.*, **2017**, *117(12)*, 7762-7810. https://doi.org/10.1021/acs.chemrev.7b00020

[13]Li, J., LI, D., Xu, Y., Guo, Z., Xu, L., Hua, Y., Wang, L., Wu, L., Design, synthesis, biological evaluation, and molecular docking of chalcone derivatives as anti-inflammatory agents, *Bioorg. Med. Chem. Lett.*, **2016,** *27(3)*, 602-606. https://dx.doi.org/10.1016/j.bmcl.2016.12.008

[14]Patel, A. P., Bhadani, V. N., Bhatt, P. V., Purohit, D. M., Synthesis and biological evaluation of novel chalcone and pyridine derivatives bearing substituted vanillin nucleus, *J. Heterocyclic Chem.*, **2014**, *52(4)*, 1119-1125. https://doi.org/10.1002/jhet.2215

[15]Chen, J., Yan, J., Hu, J., Pang, Y., Huang, L., Li, X., Synthesis, Biological, Evaluation and Mechanism Study of Chalcone Analogues as Novel Anti-cancer Agents, *RSC Adv.*, **2015**, *5(83)*, 68128-68135. https://doi.org/10.1039/C5RA14888J

[16]Zhao, L., Jin, H., Sun, L., Piao, H., Quan, Z., Synthesis and evaluation of antiplatelet activity of trihydroxychalcone derivatives, *Bioorg. Med. Chem. Lett.*, **2005**, *15*, 5027-5029. https://doi.org/10.1016/j.bmcl.2005.08.039

[17]Wang, S., Yin, Y., Zhang, Y., Mi, S., Zhao, M., Lv, P., Wang, B., Zhu, H., Synthesis, biological evaluation and 3D-QSAR studies of novel 5-phenyl-1*H*-pyrazol cinnamamide derivatives as novel antitubulin agents, *Eur. J. Med. Chem.*, **2015**, *93*, 291-299. https://doi.org/10.1016/j.ejmech.2015.02.018

[18]Won, S., Liu, C., Tsao, L., Weng, J., Ko, H., Wang, J., Lin, C., Synthetic, chalcones as potential anti-inflammatory and cancer chemopreventive agents, *Eur. J. Med. Chem.*, **2005**, *40*, 103-112. https://doi.org/10.1016/j.ejmech.2004.09.006

[19]Džambić, A., Muratović, S., Veljović, E., Softić, A., Dautović, E., Husejnović, M., Horozić, E., Smajlović, A., Evaluation of antioxidantative, antimicrobial and cytotoxic activity of the synthesized arylmethylenbis(3-hydroxy-5,5-dimethyl-2-cyclohexan-1-one) derivatives, *Eur. Chem. Bull.*, **2020**, *9(9)*, 285-290. https://dx.doi.org/10.17628/ecb.2020.9.285-290

[20]Kalaia, P. N., Makawana, J.A., Satasia, S. P., Raval, D. K., Zhu, H-L, Design, synthesis and molecular docking of novel bipyrazolylthiazolone scaffold as a new class of antibacterial agents, *Med. Chem. Commun.*, 2014, *5(10)*, 1555-1562. https://doi.org/10.1039/C4MD00238E

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