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A NEW SERIES OF CHALCONES INCORPORATED WITH PYRIDINE MOIETY AS POTENTIAL ANTI-BACTERIAL AGENTS

D. Vimala, P. Subashini and S. Syed Shafi *

Department of Chemistry, Thiruvalluvar University, Serkkadu, Vellore - 632115, Tamil Nadu, India.

Keywords:

Chalcones, Pyridine moiety, Claisen-Schmidt condensation, Anti-bacterial Activity

Correspondence to Author:
Dr. S. Syed Shafi

Registrar,
Department of Chemistry,
Thiruvalluvar University, Serkkadu,
Vellore - 632115, Tamil Nadu, India.

E-mail: vimalarose1@gmail.com

ABSTRACT: A new series of chalcones have been designed and synthesized, which are incorporated with pyridine moiety chalcones possess heterocyclic rings like pyridine, pyrazole, indole, *etc*. These heterocycles are cyclic compounds in which one or more atoms of the ring are hetero atoms: O, N, S, P, *etc*. These are important components in many of the pharmaceuticals and therapeutic drugs. These are present in so many biologically relevant molecules like amino acids, nucleic acids and hormones. In my work, I have used a pyridine compound to synthesis the chalcones. Pyridine is a basic heterocyclic organic compound with chemical formula C_5H_5N. It is structurally related to benzene, with one methine group (=CH-) replaced by a nitrogen atom. The pyridine ring occurs in many important compounds, including agrochemicals, pharmaceuticals and vitamins. Historically, pyridine was produced from coal tar. It has an unpleasant fish-like smell. Nowadays, pyridine is produced on a scale of about 20,000 tonnes per year worldwide. A reaction involving Claisen-Schmidt condensation of 1- (pyridin-2-yl) ethanone with different aryl aldehydes in the presence of base catalyst have been attempted in this work. The product chalcones and their derivatives were compared with standard drugs and were confirmed by FT- IR and ^{1}H-NMR and were also subjected to anti-bacterial analysis.

INTRODUCTION: Chalcones, which are also called as α, β-unsaturated carbonyl based compounds are considered to be the reactive substructures of natural products or synthetic molecules. Chalcones continue to attract a lot of interest in both academia and industry. The α,β-unsaturated ketone moiety is the key pharmacophoric feature, as its full or partial removal leads to a loss of bioactivity [1-5].

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The majority of the naturally occurring chalcones contain benzene rings with hydroxyl methoxy and alkenyl groups, as their aryl substituents. Traditionally, chalcones are synthesized by Claisen-Schmidt condensation of aryl aldehydes and acetophenones. In this work, we have synthesized chalcones using 1-(pyridin-2-yl) ethanone with aryl aldehydes. These reactions are generally base-catalyzed, but acid-catalyzed, solid, and microwave assisted reactions were also known. Herein, we have reported the antibacterial activity of chalcone derivatives (1CX, 1CY) by synthesizing a series of molecules (1A, 1B, 1C), whose structures are determined by IR and NMR spectra [2-14].

MATERIALS AND METHODS: Chemicals were from analytical grade (from Sigma Aldrich

and other commercial suppliers) and used without any purification. All the chemicals were from analytical grade (from sigma Aldrich) and used without any purification. Ethanol solvents were supplied by spectrochem, India. Colum chromatography was performed using silica gel 60-120 mesh (Merck, Hyderabad, India). All the compounds were routinely checked for their purity of synthesized compounds on silica gel 60 F254 TLC plates. The spots formed by the compounds were visualized by exposing them to UV lamps on iodine vapors. Melting points were determined by deep vision instruments. The melting was done in open capillary tubes and was uncorrected. The IR spectra were recorded in the solid-state, as KBr dispersion by means of PerkinElmer Spectrometer IR Version 10.6.0. The ^{1}H NMR spectra were recorded on the BRUKER Advanced 400MHz spectrometer, using approximately 0.03M solutions in $CDCl_3$ as a solvent and TMS as an internal reference.

General Procedure for Chalcone Synthesis: A mixture of aryl adehydes (0.01 mol) and 1-(pyridin-2-yl) ethanone (0.01 mol) were stirred in 30 ml ethanol. Then, an aqueous solution of NaOH (10%), (25 ml) was added slowly and the mixture was continuously stirred for 4-h. Then, it was poured into 400 ml of cold water (distilled water) with constant stirring for 1 h and left overnight in refrigerator. The precipitate obtained was filtered and recrystallized from ethanol.

(2E)-3-(1,3-Benzodioxal-5-yl)-1-(2-pyridinyl)-2-propen-1-one: Pale-yellow powder, yield 95%, m.pt 126-128 °C, TLC (hexane: ethylacetate, 5:5); IR (KBr, cm^{-1}) 3428 cm^{-1} (N-H), 3002 cm^{-1} (Aromatic C-H stretch), 1663 cm^{-1} (NH-C=O), 1594 cm^{-1} (CH=CH of carbonyl conjugated double bond), 1261 cm^{-1} (C-N stretch); ^{1}H NMR (400 MHz,$CDCl_3$) δ/ppm: 6.02 (S, 1H, C-H), 6.83 (d, 1H, Aliphatic C-H), 7.20 (d, 1H, Aromatic C-H), 7.84 (d, 1H, Aromatic C-H), 7.86 (d, 1H, Aromatic C-H).

(2E)-3-(2-Furyl)-1-(3-pyridinyl)-2-propen-1-one: Brown powder, yield 90%, m.pt 110-112 °C, TLC (hexane: ethylacetate, 5:5); IR (KBr, cm^{-1}) 3436 cm^{-1} (N-H), 3006 cm^{-1} (Aromatic C-H stretch), 1692 cm^{-1} (NH-C=O), 1584 cm^{-1} (CH=CH of carbonyl conjugated double bond), 1223cm^{-1} (C-N stretch); ^{1}H NMR (400 MHz,$CDCl_3$) δ/ppm: 6.78 (t,1H, Aromatic C-H), 7.18 (d, 1H, CH=CH), 7.21 (d, 1H, CH=CH), 7.26 (d, 1H, Aromatic C-H), 7.57-7.60 (m,4H, Aromatic C-H), 8.19 (d, 1H, Aromatic C-H),

(2E)- 3- (4- Methoxyphenyl)- 1- (2-pyridinyl)-2-propen-1-one: Yellow powder, yield 92%, m.pt 139-141°C, TLC (hexane: ethylacetate, 5:5); IR (KBr, cm^{-1}) 3411 cm^{-1} (N-H), 3002 cm^{-1} (Aromatic C-H stretch), 1692 cm^{-1} (NH-C=O), 1611 cm^{-1} (C=N stretch), 1583 cm^{-1} (CH=CH of carbonyl conjugated double bond), 1249 cm^{-1} (C-N stretch); ^{1}H NMR (400 MHz, $CDCl_3$) δ/ppm: 3.85 (S, 3H, CH_3), 6.54 (d, 1H, -CO-CH=), 7.51 (d, 1H, Aliphatic C-H), 7.87 (d, 2H, Aromatic C-H), 8.47 (d, 1H, Aromatic C-H).

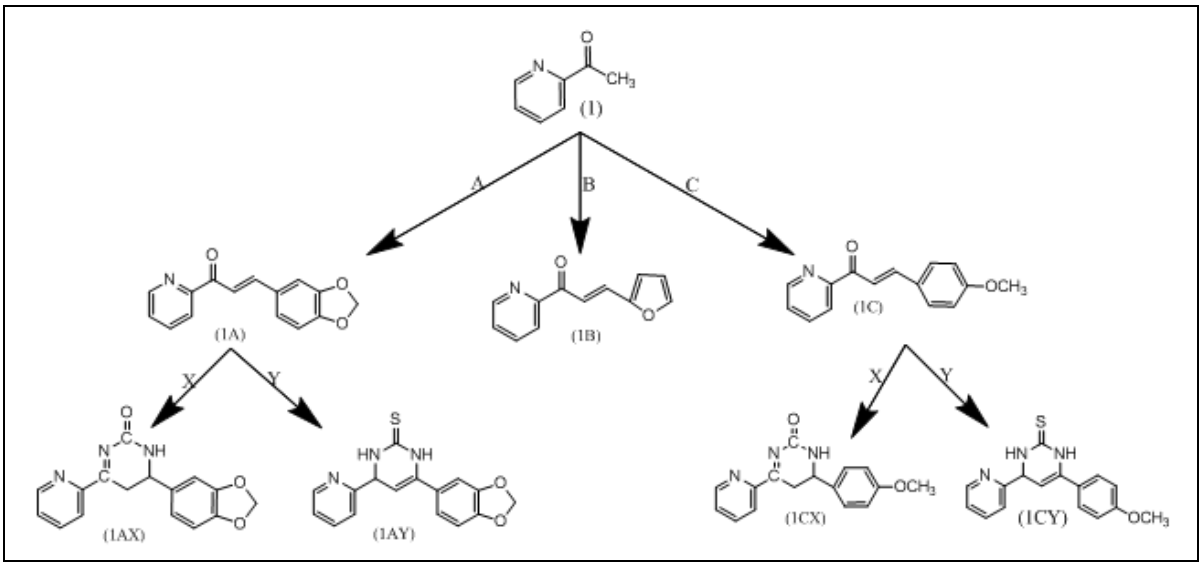
6- (4- Methoxyphenyl)- 4- (pyridin-2-l)-5,6-dihydropyrimidin-2(1H)-one: Pale powder, yield 65%, m.pt 140-142 °C, TLC (hexane: ethylacetate, 5:5); IR (KBr, cm^{-1}) 3429 cm^{-1} (N-H), 3002 cm^{-1} (Aromatic C-H stretch), 1692 cm^{-1} (NH-C=O), 1611 cm^{-1} (C=N stretch), 1583 cm^{-1} (CH=CH of carbonyl conjugated double bond), 1249 cm^{-1} (C-N stretch); ^{1}H NMR (400MHz,$CDCl_3$) δ/ppm: 3.72 (S, 3H, CH_3), 5.48 (d, 1H, Aliphatic C-H), 6.54 (d, 2H, Aromatic CH), 7.62 (d, 1H, Aromatic C-H), 8.14 (S, 1H, N-H).

6- (4- Methoxyphenyl)- 4- (pyridin- 2- yl)- 3, 4-dihydropyrimidine-2(1H)-thione: Creamy white powder, yield 58%, m.p 153-155 °C, TLC (hexane: ethyl acetate, 5:5); IR (KBr, cm^{-1}) 3372 cm^{-1} (N-H), 3002 cm^{-1} (Aromatic C-H stretch), 1693 cm^{-1} (NH-C=O), 1611 cm^{-1} (C=N stretch), 1583 cm^{-1} (CH=CH of carbonyl conjugated double bond), 1512 cm^{-1} (-OCH_3), 1249 cm^{-1} (C-N stretch); ^{1}H NMR (400 MHz,$CDCl_3$) δ/ppm: 3.72 (s, 3H, CH_3), 5.48 (d,1H, Aliphatic C-H), 6.54 (d, 1H, -CO-CH=), 7.62 (d, 1H, Aromatic C-H), 8.13 (s, 1H, NH).

6-(Benzo[d][1,3]dioxol-5-yl)-4-(pyridin-2-yl)-5,6-dihydropyrimidin-2(1H)-one: Pale mustard powder, yield 67%, m.pt 130-132 °C, TLC (hexane: ethylacetate, 5:5); IR (KBr, cm^{-1}) 3404 cm^{-1} (N-H), 3008 cm^{-1} (Aromatic C-H stretch), 1685 cm^{-1} (NH-C=O), 1583 cm^{-1} (CH=CH of carbonyl conjugated double bond), 1252 cm^{-1} (C-N stretch); ^{1}H NMR (400 MHz, $CDCl_3$) δ/ppm: 8.19 - 8.23 (m, 4H, Aromatic C-H), 7.68 (d, 1H, Aromatic

C-H), 7.26 (s, 1H, Aromatic CH), 7.16 (d, 1H, Aromatic C-H), 6.87 (s, 1H, Aromatic C-H), 5.53 (s, 2H, O-CH_2-O).

6-(Benzo[d][1,3]dioxol-5-yl)-4-(pyridin-2-yl)-3,4-dihydropyrimidine- 2(1H)- thione: Creamy mustard powder, yield 77%, m.pt 146-148 °C, TLC (hexane: ethylacetate, 5:5); IR (KBr, cm^{-1}) 3384 cm^{-1} (N-H), 3056 cm^{-1} (Aromatic C-H stretch), 1687 cm^{-1} (NH-C=O), 1583 cm^{-1} (CH=CH of carbonyl conjugated double bond), 1240 cm^{1} (C-N stretch); ^{1}H NMR (400 MHz,$CDCl_3$) δ/ppm:7.17-7.71 (m, 6H, Aromatic CH) 6.47 (s, 6H, Aromatic C-H), 5.46 (s, 2H, O-CH_2-O).



SCHEME 1: SYNTHESIS OF NEW CHALCONES AND THEIR DERIVATIVES
A–Piperonal; B–2-Furfualdehyde; C–Anisaldehyde; X–Urea; Y–Thiourea

TABLE 1: PHYSICAL PROPERTIES OF SYNTHESIZED CHALCONES

S. no.	Compound	Mol. formula	Mol. weight	M.P (°C)	R_f	Yield (%)
1	1A	$C_{15}H_{11}NO_3$	253.26	126 – 128	0.68	95
2	1B	$C_{12}H_9NO_2$	199.21	110 – 112	0.76	90
3	1C	$C_{15}H_{13}NO_2$	239.27	139 – 141	0.75	92
4	1CX	$C_{17}H_{18}N_3O_2$	296.35	140 – 142	0.62	65
5	1CY	$C_{17}H_{20}SN_3O$	314.43	153 – 155	0.81	58
6	1AX	$C_{16}H_{13}N_3O_3$	295.30	130 – 132	0.58	67
7	1AY	$C_{16}H_{15}SN_3O_2$	313.37	148 – 146	0.60	77

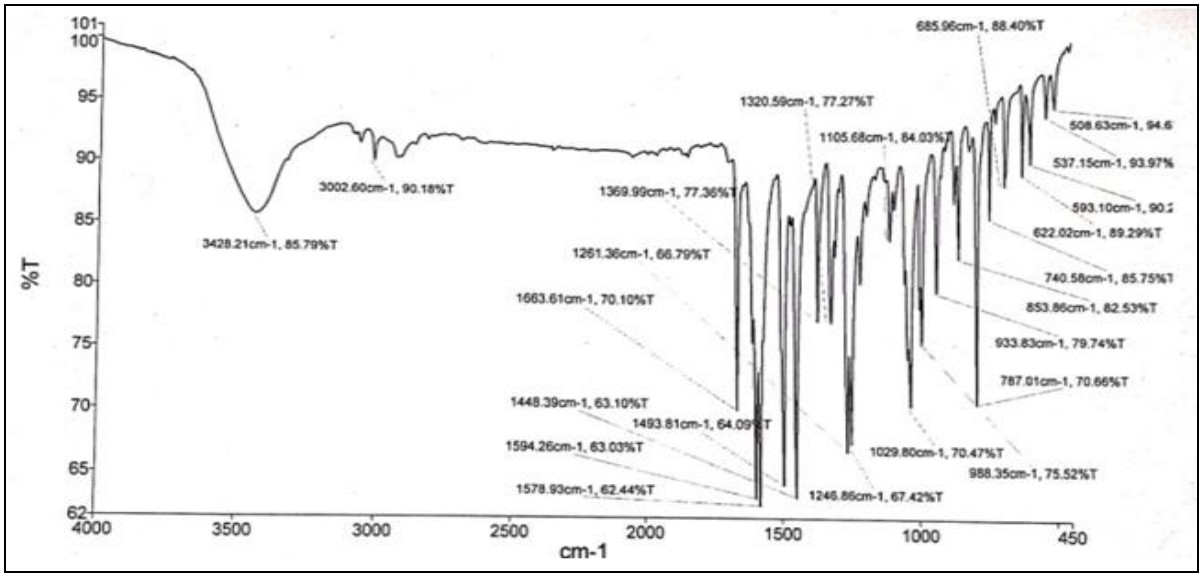


FIG. 2: IR OF 1A

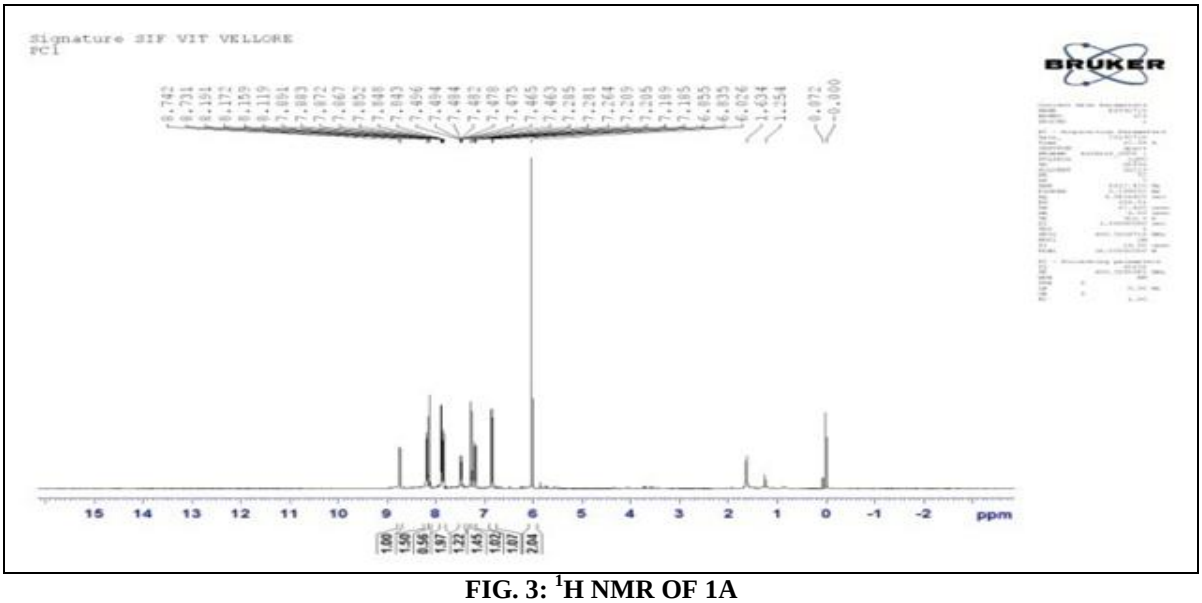


FIG. 3: ^{1}H NMR OF 1A

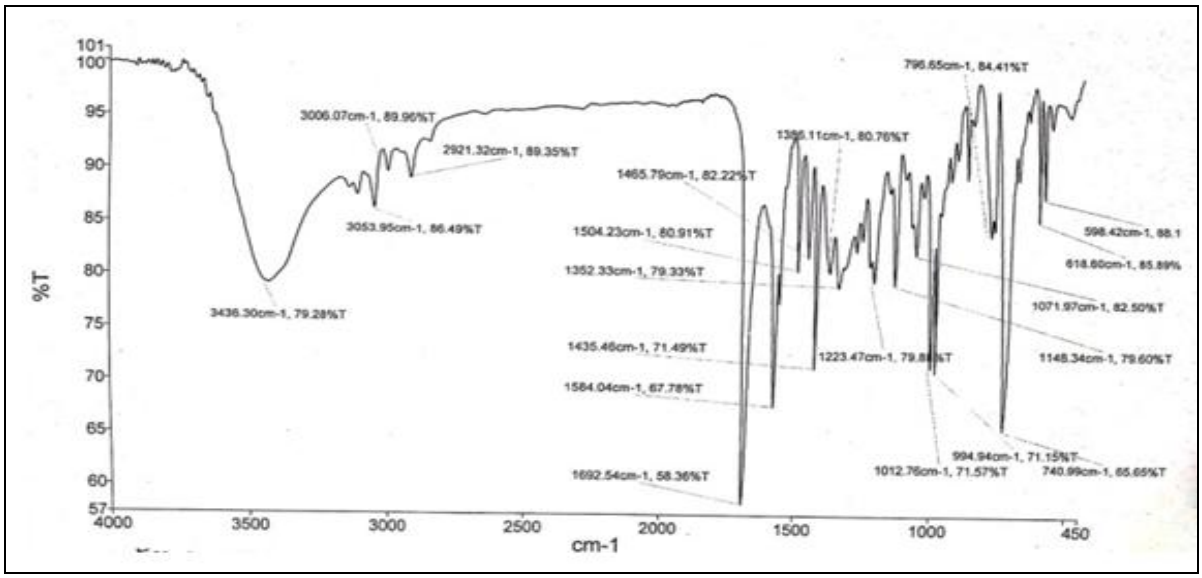


FIG. 4: IR OF 1B

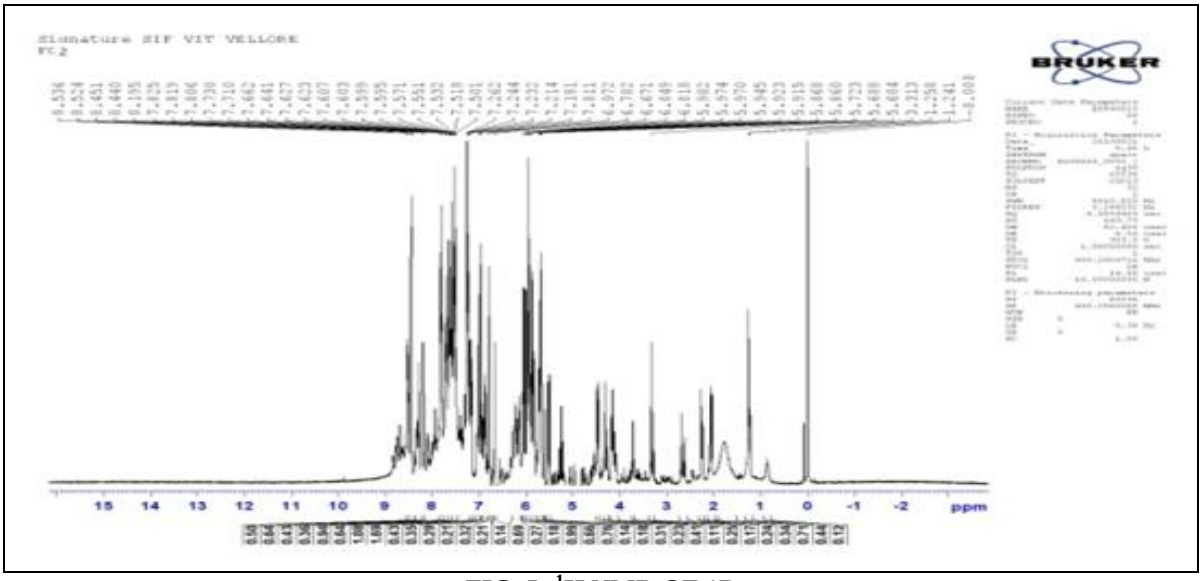


FIG. 5: ^{1}H NMR OF 1B

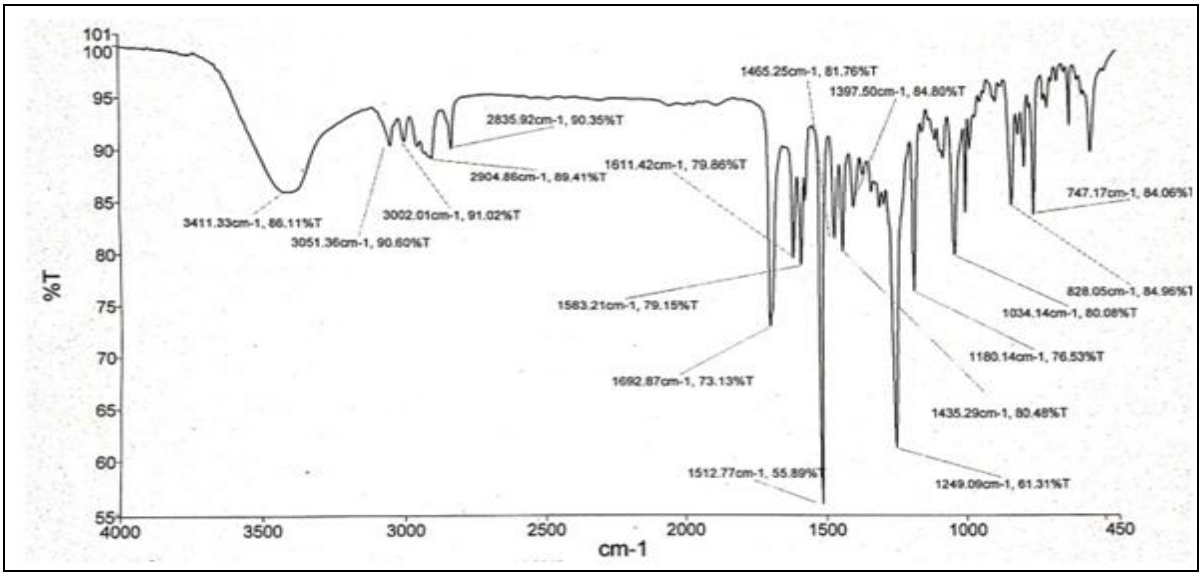


FIG. 6: IR OF 1C

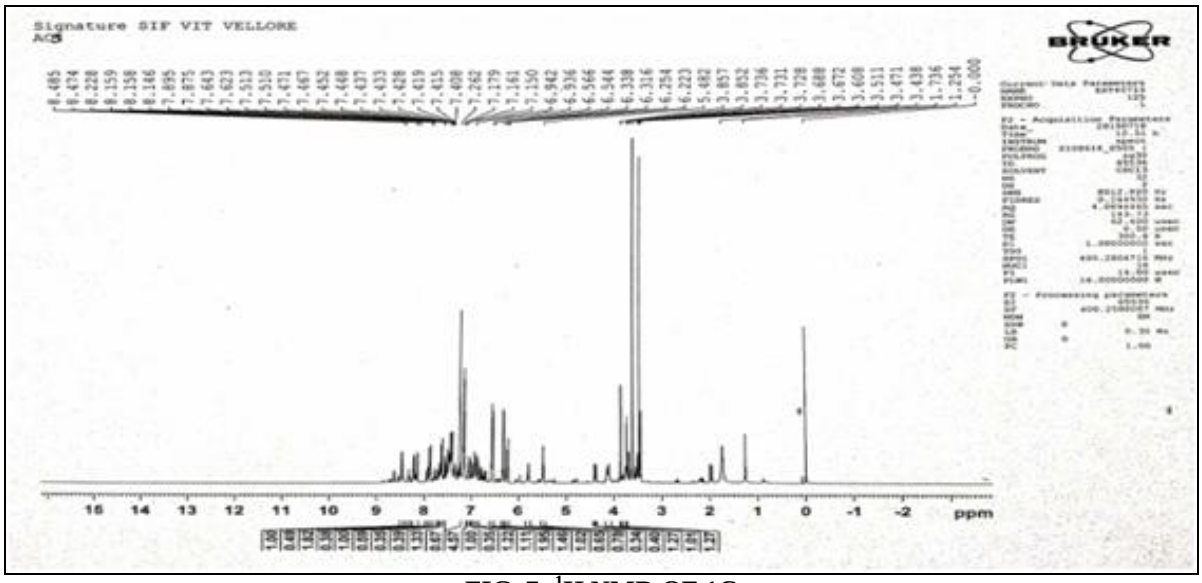


FIG. 7: ^{1}H NMR OF 1C

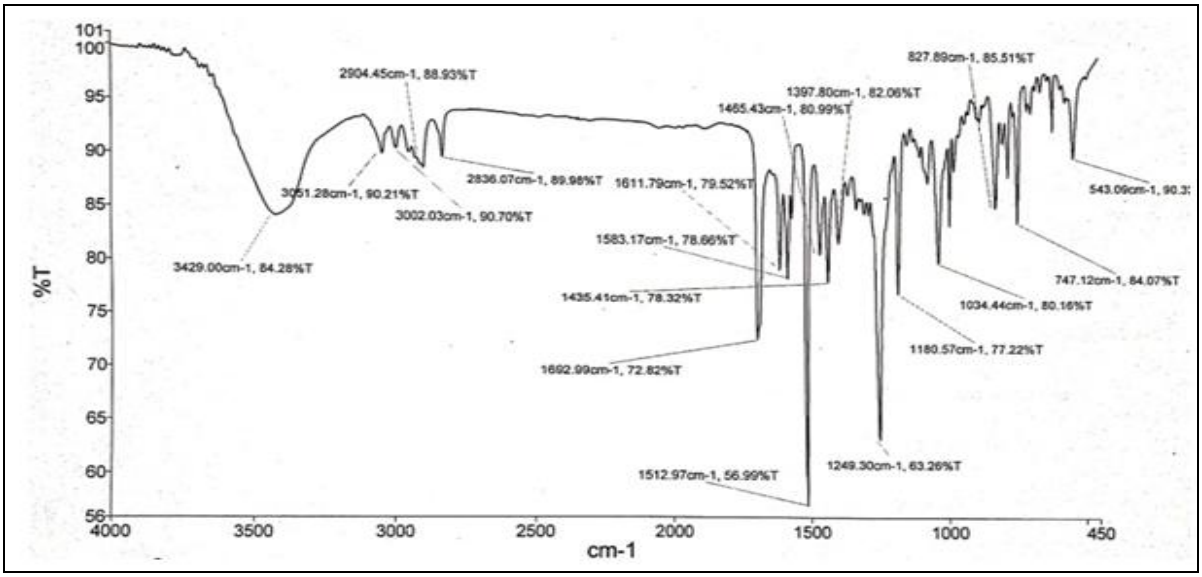


FIG. 8: IR OF 1CX

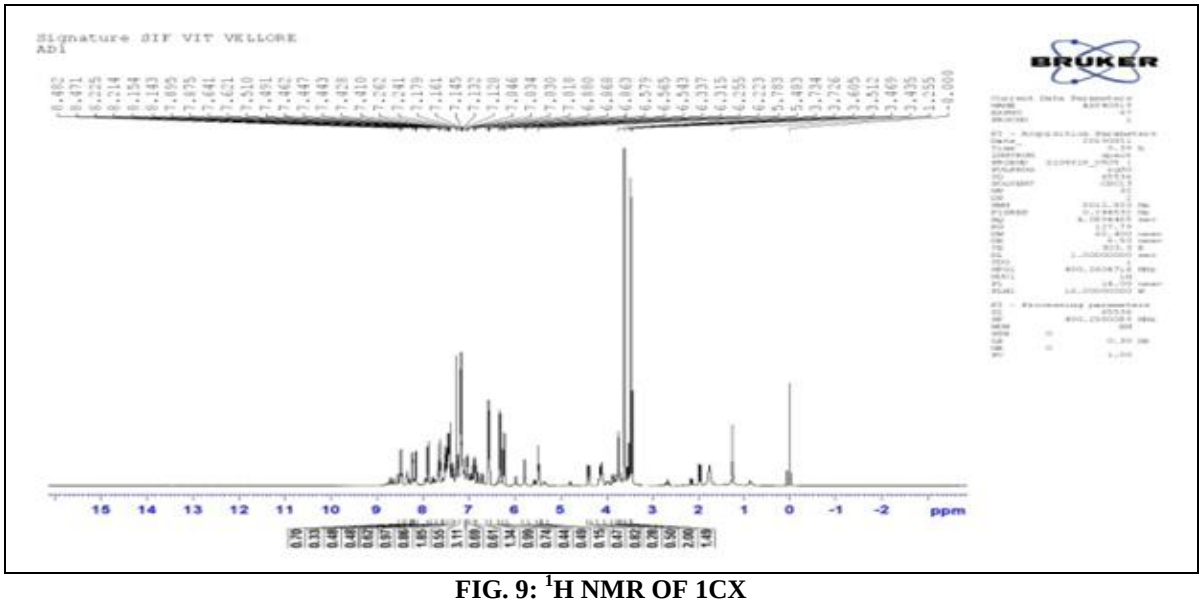


FIG. 9: ^{1}H NMR OF 1CX

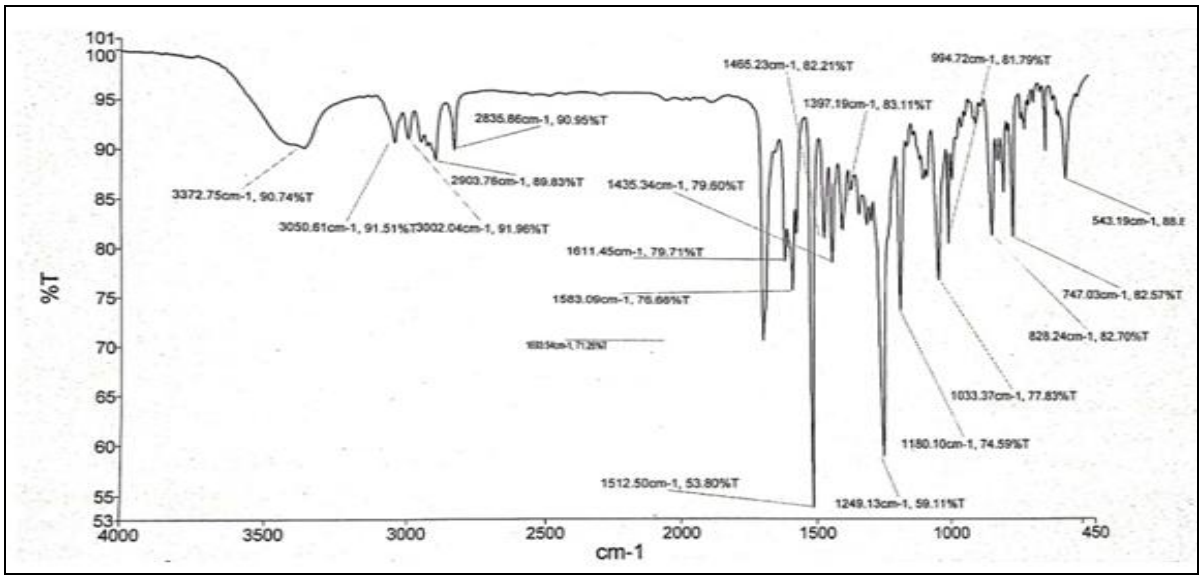


FIG. 10: IR OF 1CY

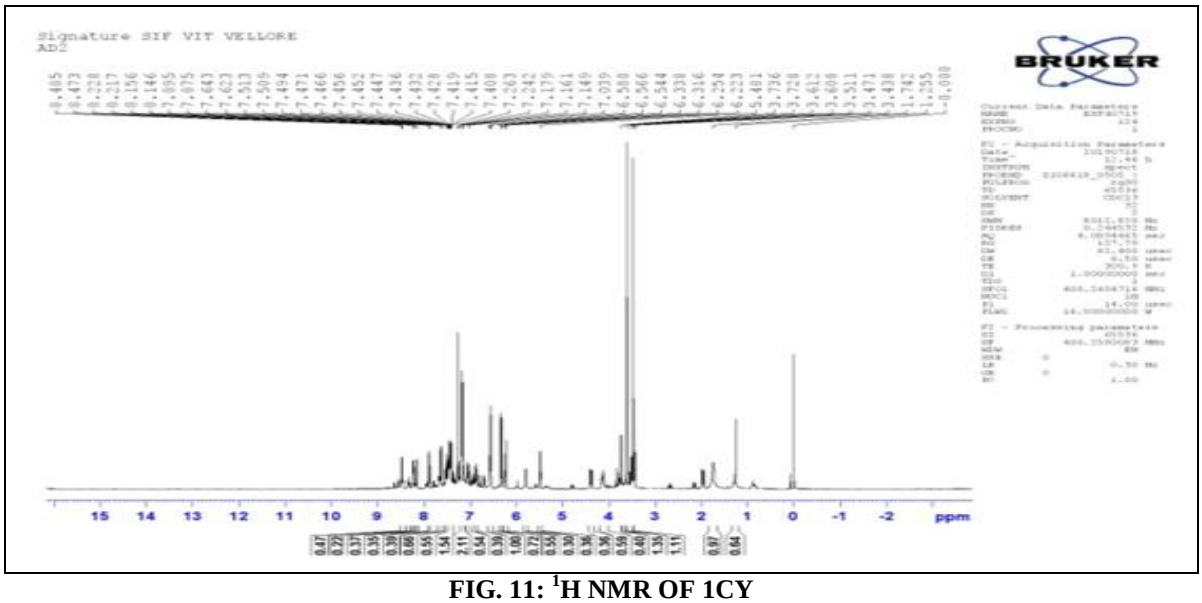


FIG. 11: ^{1}H NMR OF 1CY

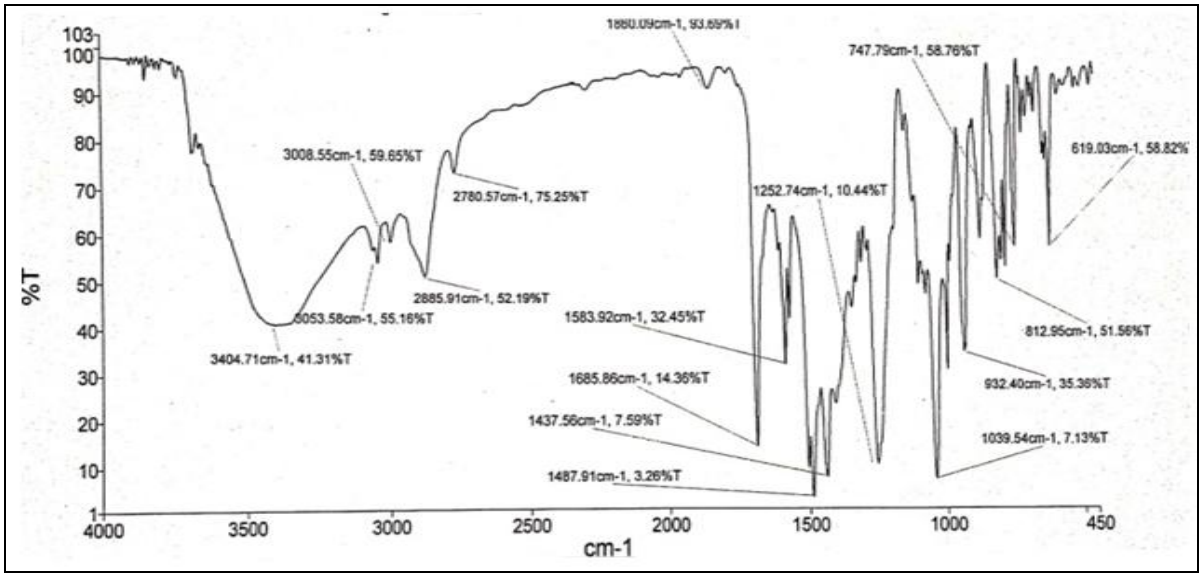


FIG. 12: IR OF 1AX

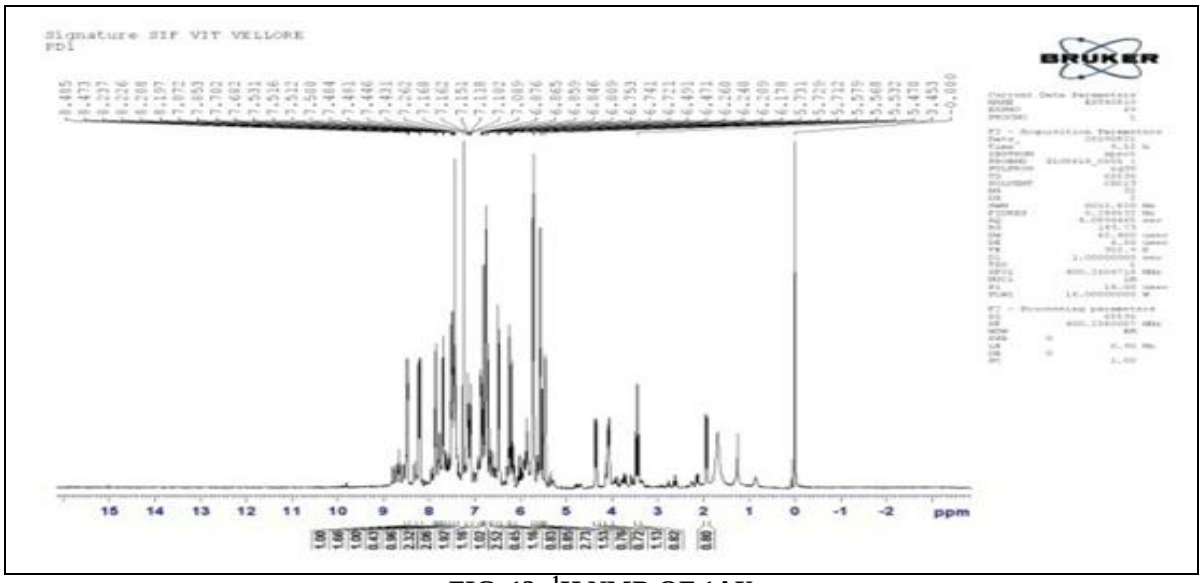


FIG. 13: ^{1}H NMR OF 1AX

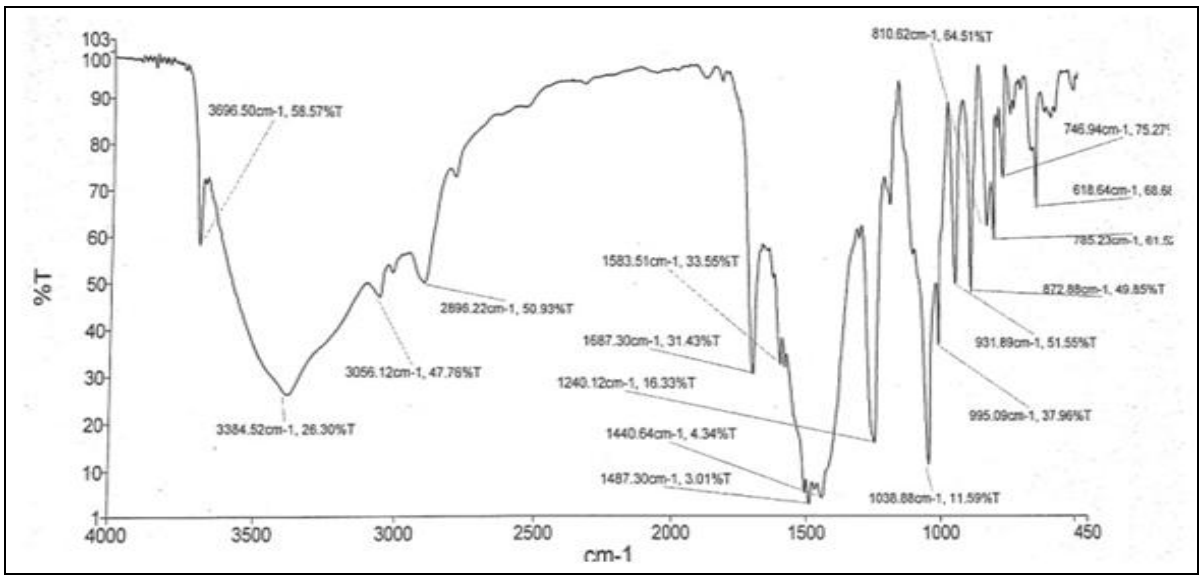


FIG. 14: IR OF 1AY

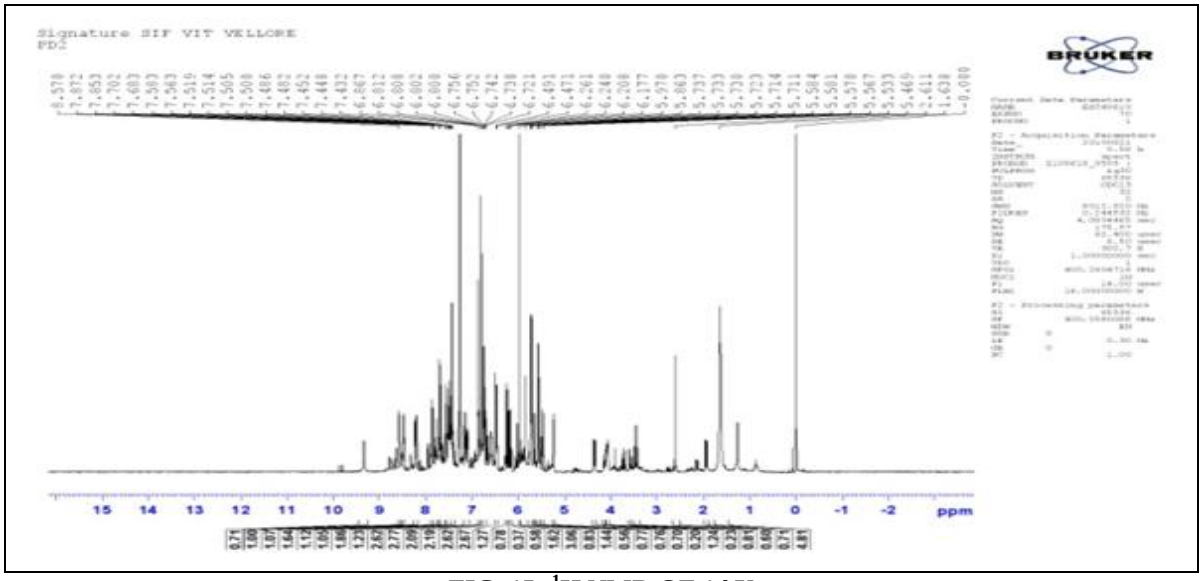


FIG. 15: ^{1}H NMR OF 1AY

RESULTS AND DISCUSSION: In this reaction synthesis of chalcones and its derivatives, 1-(pyridin-2-yl) ethanone and different aryl aldehydes with 10% NaOH in Abs. ethanol reacted through Claisen-Schmidt condensation, and their products were purified by recrystallized from suitable solvents. The synthesized products have been totally characterized by IR and ^{1}H-NMR spectral studies. The IR spectrum of the new series of synthesized chalcones and their derivatives was recorded, and they give absorption bands near 1700 - 1650 cm^{-1} representing the presence of -C=O group. The absorption bands at 1650-1580 cm^{-1} confirm the aromatic –C=C- group. Also, the ^{1}H NMR of synthesized chalcones gives ^{1}H NMR (400 MHz, $CDCl_3$) δ/ppm: 6.70-6.38 (d, 1H, -CO-CH=), 7.99-7.97 (d, 1H, =CH-Ar) confirms the formation of chalcones.

Pharmacological Results- Anti-bacterial Activity: The *in-vitro* Anti-bacterial screening of the compounds (1CX) and (1CY) were evaluated against Gram-positive organisms *Staphylococcus aureus* and Gram-negative organism *Escherichia coli* by cup and plate method. Nutrient Agar (NA) plates were seeded with 8 h broth culture of different bacteria. Sterile paper disc (6 mm in diameter) impregnated with 50 µl of different concentrations of samples were allowed to dry before being placed on to the seeded top layer of the agar plates. Each of the discs was gently placed at equidistance on top of the agar layer to give better contact with agar. The plates were then incubated at 37 °C for 24 h. Ciprofloxacin (100 ml) was used as positive controls and DMSO/ chloroform as a negative control.

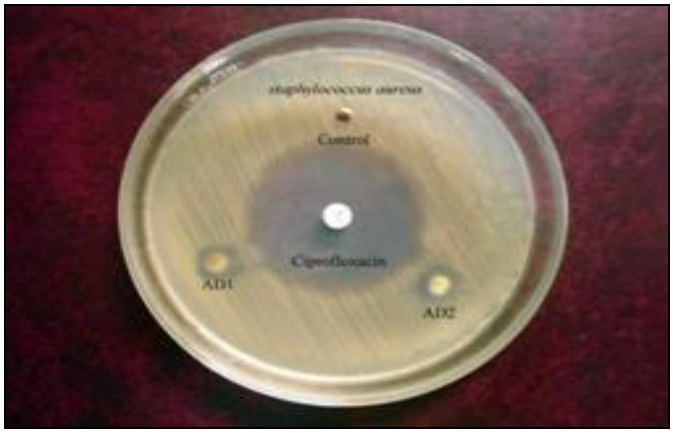


PLATE I: ZONE OF INHIBITION OF COMPOUNDS (1CX) AND (1CY) AGAINST *STAPHYLOCOCCUS AUREUS*. STANDARD – CIPROFLOXACIN; CONTROL – DMSO

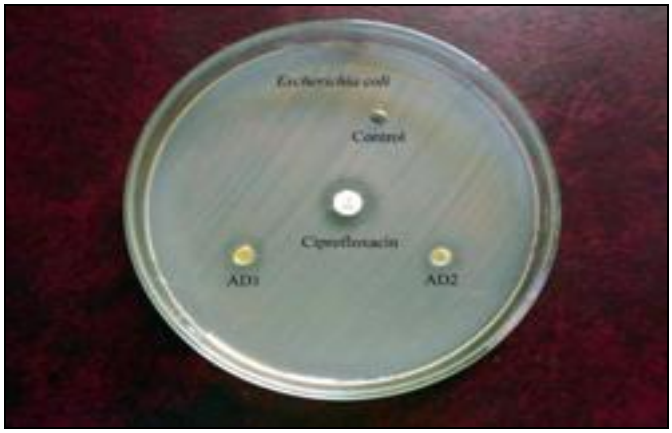


PLATE II: ZONE OF INHIBITION OF COMPOUNDS (1CX) AND (1CY) AGAINST *ESCHERICHIA COLI*. STANDARD – CIPROFLOXACIN; CONTROL – DMSO

TABLE 2: ANTI-BACTERIAL ACTIVITY DATA OF COMPOUNDS

S. no.	Micro-organisms	Control	AD1 (8a)	AD2 (9a)	Ciprofloxacin
1	*Staphylococcus aureus*	DMSO	8mm	7mm	40
2	*Escherichia coli*	DMSO	7mm	5mm	11

Zone of inhibition in mm. Standard – ciprofloxacin; control – DMSO

The antibacterial activity was evaluated by measuring the diameter of the inhibition zone. Solvent and growth controls were kept; the zones of inhibition and minimum inhibitory concentrations (MIC) noted. The results of these studies are compared with the standard minimum inhibitory concentrations (MIC) noted. The results of these studies are compared with the standard.

CONCLUSION: In conclusion, we have successfully synthesised "a new series of chalcones incorporated with pyridine moiety". Among these new series of chalcones synthesised, 6-(4-methoxy-phenyl)-4-(pyridin-2- yl)- 5, 6- dihydropyrimidin-2(1H)- one (8a) and 6- (4- methoxyphenyl)- 4-(pyridin-2-yl)-3,4-dihydropyrimidine-2(1H)-thione (9a) were tested for their bacterial activity.

The anti-bacterial screening suggests that the newly synthesised compounds showed moderated to good activity against the tested organisms.

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CONFLICTS OF INTEREST: Nil

REFERENCES:

1. Mohana D: Design and synthesis of novel chalcone derivatives and their antioxidant activity. IOSR-JPBS 2018; 13(5): 25-28.
2. Burmaoglu S, Algul O, Gobek A, Aktas DA, Ulger M, Erturk BG, Kaplan E, Dogen A and Aslan G: Design of potent fluoro-substituted chalcones as antimicrobial agents. Journal of Enzyme Inhibition and Medicinal Chemistry 2017; 32(1): 490-95.
3. Elavarasan M, Thendral MT and Shafi S: Synthesis, characterization and antimicrobial activity of some new chalcones International Journal of Pharmaceutical Sciences and Research IJPSR., 2018; 9(5): 1969-73.
4. Reddy BN, Reddy SM: Der.M, pharma. Chemical, 2017; 9(9): 102-08.
5. Venkataramireddy V, Shankaraiah V, Rao AT, Kalyani C, Narasu ML, Varala R and Jayashree A: Rasayan Synthesis and anti-cancer activity of novel 3- aryl thiophene-2-carbaldehydes and their aryl/heteroaryl chalcone derivatives Journal of Chemistry 2016; 9(1): 31-39.
6. Ardiansah B: Chalcones bearing N, O, and S-heterocycles: recent notes on their biological significances. J Appl Pharmsci 2019; 9(08): 117-29.
7. Chen G, Wang Z, Zhang X and Fan X: Synthesis of functionalized pyridines *via* Cu(II)-catalyzed one-pot cascade reactions of inactivated saturated ketones with electron-deficient enamines. J Org Chem 2017; 82: 11230-37.
8. Cheng G, Xue L, Weng Y and Cui X: Transition-metal-free cascade approach toward 2-Alkoxy/2-Sulfenylpyridines and Dihydrofuro[2,3-b]pyridines by trapping *in-situ* generated 1,4-Oxazepine. J Org Chem 2017; 82: 9515-24.
9. Abd El-Sattar NEA, Badawy EHK and Abdel-Mottale MSA: Synthesis of some pyrimidine, pyrazole, and pyridine derivatives and their reactivity descriptors. J Chem 2018; 11.
10. Yang L, Wu Y, Yang Y, Wen C and Wan JP: Catalyst-free synthesis of 4-acyl-NH-1,2,3-triazoles by water-mediated cycloaddition reactions of enaminones and tosyl azide. Beilstein J Org Chem 2018; 14: 2348-2353.
11. Wei Y, Weijie C, Fu-Xiaomin L, Yuting Z, Dan W, Zhi Z and Hui G: Rh(III)-Catalyzed and Solvent-Controlled Chemoselective Synthesis of Chalcone and Benzofuran Frameworks via Synergistic Dual Directing Groups Enabled Regioselective C–H Functionalization: A Combined Experimental and Computational Study. ACS Catalysis 2018, 8(10): 9508-19.
12. Manna T, Pal K, Jana K and Misra AK: Anti-cancer potential of novel glycosylated 1,4-substituted triazolylchalcone derivatives. Bioorganic & Medicinal Chemistry Letters 2019, 29(19): 126615.
13. Riaz S, Iqbal M, Ullah R, Zahra R, Chotana GA, Faisal A and Saleem RSZ: Synthesis and evaluation of novel α-substituted chalcones with potent anti-cancer activities and ability to overcome multidrug resistance. Bioorganic Chemistry 2019; 87: 123-35.
14. Duddukuri NK, Thatikonda S, Godugu C, Kumar RA and Doijad N: Synthesis of novel thiophene-chalcone derivatives as anticancer- and apoptosis-inducing agents. Chemistry Select 2018; 3(24): 6859-64.

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