SCIENCE PARK
INTERNATIONAL RESEARCH JOURNAL

SYNTHESIS, CHARACTERIZATION AND ANTIBACTERIAL SCREENING OF SOME NOVEL CHALCONE DERIVATIVES CONTAINING IMIDAZO [1,2-A]-PYRIDINE MOIETY

Vikas Dashrath Sonawane[1]
[1] Department of Chemistry, Smt. Kusumtai Rajarambapu Patil Kanya Mahavidyalaya, Islampur, Sangli, Maharashtra, India.
[1]Organic Chemistry Research Laboratory, School of Chemical Sciences, Solapur University, Solapur , Maharashtra, India.

ABSTRACT

A series of condensed Novel Imidazo [1,2-A] Pyridine Chalcones have been prepared by Claisen–Schmidt condensation reaction. Novel Imidazo [1,2-A] Pyridine based chalcones were synthesized using various substituted teralones and 3-formyl-2-phenyl-imidazo [1,2-a] pyridine in PEG-400 as green recyclable solvent. Chalcone synthesis is carried out by forming 3-formyl-2-phenyl-imidazo [1,2-a] pyridine and then its reaction with different substituted tetralones. The structures of these compounds were confirmed on the basis of spectral data. All the title compounds were screened for their antimicrobial activities. The screening data indicated that tested compounds showed good antimicrobial activity against B.coccus, S.aureus, Pseudomona, E.coli,and antibiotics such as A.niger,Ampicillin, Amoxicillin, Norfloxacin. Their minimum inhibitory concentrations (MIC) were determined and the compounds 5a,5b,5c and 5e shows good results of antibacterial activity against standard B.coccus, S.aureus, Pseudomona and E.coli bacteria.

KEYWORDS: *Antibacterial activity, PEG-400, Imidazo[1,2-A]-Pyridines Chalcones, 3-formyl-2-phenyl-imidazo[1,2-a]pyridine.*

INTRODUCTION:

Everyday in our life heterocyclic compounds are of very much recurrence enthusiasm though it brings an extensive variety for requisition to pharmaceuticals and agrochemicals.[1-2] as a basic part in the digestion system. As heterocyclic mixes have varieties of applications found in the field of pharmaceuticals and agrochemicals areas, they play an crucial spirit in the metabolism of all existing bioactive cells. They also found advantages as sentizers, developers, antioxidants, anti-inflammatory, analgesics, or as corrosion inhibitors, as copolymers, dyestuff. Frequently five-membered nitrogen heterocycles subsidiaries gives support in large number of bioactive atoms. Major of organic compounds isolated from nature are comprised of nitrogen heterocycles. Out of all these heterocycles, one of the major biologically active of nitrogen subsidiaries are Imidazo [1,2-a] pyridine. There are several reports are available on the synthesis of Imidazo [1,2-a] pyridine.[3-4] Our intention is that to have such moiety to be present in synthesized chalcones . Hence Imidazo [1,2-a] Pyridines moieties have been added innovatively in the main chain of chalcone backbone by the reaction with 3-formyl-2-phenyl-imidazo [1,2-a] pyridine which plays an important role as powerful pharamacophore units . So that we have selected to synthesize first 3-formyl-2-phenyl-imidazo [1,2-a] pyridine.[5]

Imidazo[1,2-a]-Pyridines are well-known heterocyclic composite and it has wide extent in the synthesize of huge number of innovative pharmaceutical and chemotherapeutical agents and these are used

in remedying new compounds which are constructive in making scientific medicines. Intensively a great idea has been developed behind the synthesis and biological activities of the condensed Imidazo [1,2-A] pyridines have been reported. This molecular scaffold has been used as antifungal, antibacterial, anti-inflammatories, antimicrobial, antitumor, analgesic and antitubeculosis.[6-9]

Kostanecki and Tambor (1899) gave the name "Chalcone". Chalcones are characterized by their possession of a structure in which two aromatic ring are linked by an aliphatic three carbon chain. There are two aromatic rings are in unsaturation coupled together by a three-carbon α, β-unsaturated carbonyl system. Chalcones are potential biocides, some naturally occurring antibiotics and nitrogen containing chalcones probably own their biological activity to the presence of *α, β* - unsaturated carbonyl group. Chalcone derivatives are associated with diverse biological activity. (Structure, Figure 1).

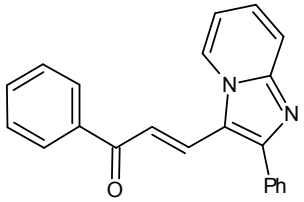


Fig.1- General structural of Imidazo Pyridine chalcone

As poly ethylene glycol (PEG-400) has been is well-known, green, secure, recyclable, non-hazardous, reasonable, simply available, reusable reaction medium and cost-effective solvent to the various catalytic reaction, capable to recycle both solvent and catalyst easily.[10-16] So far we have decided to prepare all the Imidazo [1,2-A] Pyridine Chalcones in PEG-400 as green reaction medium as follows.

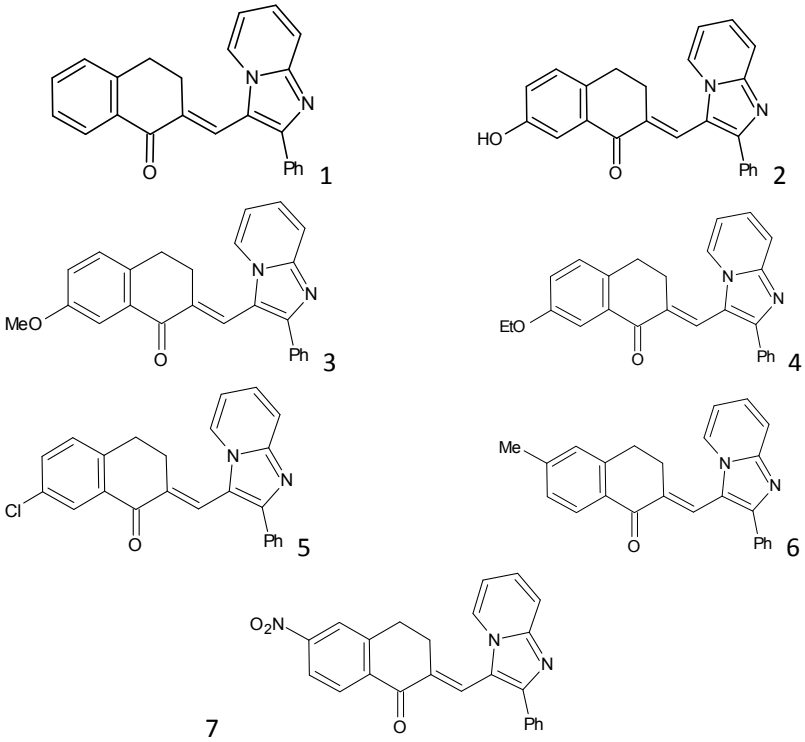
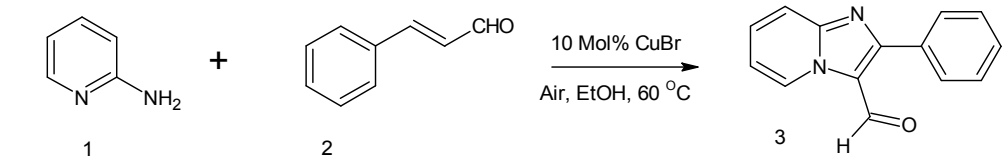


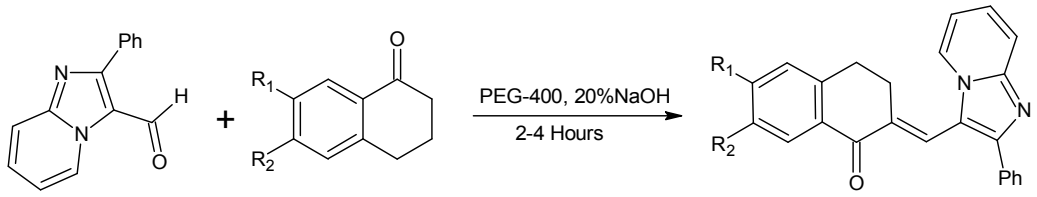
Figure-2 : Synthesized the Imidazo [1,2-A] Pyridine chalcones (5a-g)

MATERIAL AND METHODS :

SCHEME- 1 Synthesis of the Imidazo [1,2-A] Pyridine Chalcones (5a-g)



1 2 3



3 4a-f 5a-f

5a	R_1= H	R_2 = H
5b	R_1= H	R_2 = OH
5c	R_1= H	R_2 = OMe
5d	R_1= H	R_2 = OEt
5e	R_1= H	R_2 = Cl
5f	R_1= Me	R_2 = H
5g	R_1= NO_2	R_2 = H

GENERAL

INSTRUMENTATION :

IR spectra were recorded on FT-IR spectrometer (Perkin Elmer, Maharashtra, India) using KBr disk method. 1HNMR spectra were recorded on 1HNMR (Varian-NMR-mercury 300 MHz) spectrometer in $CDCl_3$ as solvent. All chemical shifts (δ) are quoted in parts per million downfield from TMS and coupling constants (J) are given in hertz. Abbreviations used in the splitting pattern were as follows: s = singlet, d = doublet, t = triplet, q = quintet and m = multiplet. All the reagents and solvents were used of analytical grade and used as supplied unless otherwise stated. Thin layer chromatography was performed on silica gel coated plates for monitoring the reactions. The spots could be visualized easily under UV light.

General procedure for synthesis of imidazo[1,2-A] pyridine carbaldehydes (3) :

To the mixture of 2-aminopyridine (1.0 equiv.) and cinnamaldehyde (1.2 equiv.) in ethanol was added 10 mol% CuBr and the reaction mixture was stirred at 60 °C for 8 h. After completion of the reaction (monitored by TLC), the reaction mixture was filtered using Whatman paper. The filtrate was dried on a rota vapor and was then extracted with water and ethyl acetate. The EtOAc layer was dried over anhydrous sodium sulphate and evaporated on a vacuo rotavapor to get the crude product. The crude product was purified by silica gel (#100–200) column chromatography using n-hexane and EtOAc as eluents to obtain pure products [5] in 70–90% yield.

2-Phenyl-imidazo[1,2-a]pyridine-3-carbaldehyde (3) [5] :

Yellow solid; m.p. 122–123 °C; 1H NMR (CDCl3, 300 MHz): δ 10.07 (s,1H), 9.68 (d, J = 8.0 Hz, 1H), 7.85–7.81 (m, 3H), 7.61–7.53 (m,4H), 7.14 (t, J = 8.0 Hz, 1H); 13C NMR (CDCl3, 100 MHz): δ 179.7, 158.4, 147.8, 132.3, 130.5, 129.9, 129.8, 128.9, 128.8, 120.8, 117.5, 115.4; IR ($CHCl_3$): vmax 2924, 1646, 1634, 1494,1407, 1326, 1248 cm^{-1};

Synthesis of Imidazo[1,2-a]pyridine Chalcones (5a-f):

A mixture of various heterocyclic ketones having moieties like different substituted tetralones (4a-f) and 2- Phenyl-imidazo[1,2-a]pyridine-3-carbaldehyde 3 (1 mmol) was dissolved in 15 ml PEG-400.[10-16] To this mixture, sodium hydroxide (20%, 1ml) was added and the reaction mixture was stirred at 40-50 ^{0}C temperature for 1 hr. The reaction mixture was then poured into 100 ml ice cold water. The product was separated out, it was filtered and processed out. The obtained products were recrystallised (5a-f) from ethanol to afford pure compounds .

The spectral data of synthesized compounds(5a-f) :

5a : (2*E*)-2-[(2-phenylimidazo[1,2-*a*]pyridin-3-yl)methylidene]-3,4-dihydronaphthalen-1(2*H*)-one

1H NMR (CDCl3, 300 MHz) : Imidazole ring :
δ 7.51 (d, 1H) aromatic C_3, δ 7.03 (d, 1H) aromatic C_4, δ 6.65 (d,1H) aromatic C_5, δ 8.09 (d, 1H) aromatic C_6.
Benzene attached to imidazole ring :
δ 7.48 (d, 1H) aromatic J=7.0 Hz ortho coupling, δ 7.32 (d, 1H) aromatic J=7.0 Hz ortho coupling , δ 7.22 (d,1H) aromatic, δ 7.48 (d, 1H) aromatic , Trans δ7.60 (s,1H) unsaturated C=C bond.

Tetralone ring : : δ 2.29 (t, 2H), δ 2.59 (t, 2H), δ 7.14 (d,1H) aromatic , δ 6.96 (d, 1H), for two neighbouring aromatic protons, δ 7.23 (d, 1H) aromatic.

5b : (2*E*)-7-hydroxy-2-[(2-phenylimidazo[1,2-*a*]pyridin-3-yl)methylidene]-3,4- dihydronaphthalen-1(2*H*)-one :

1H NMR (CDCl3, 300 MHz) : Imidazole ring :
δ 7.51 (d, 1H) aromatic C_3, δ 7.03 (d, 1H) aromatic C_4, δ 6.65 (d,1H) aromatic C_5, δ 8.09 (d, 1H) aromatic C_6.

Benzene attached to imidazole ring :
δ 7.48 (d, 1H) aromatic J=7.0 Hz ortho coupling, δ 7.32 (d, 1H) aromatic J=7.0 Hz ortho coupling , δ 7.22 (d,1H) aromatic, δ 7.48 (d, 1H) aromatic , Trans δ7.60 (s,1H) unsaturated C=C bond.

Tetralone ring : : δ 2.29 (t, 2H), δ 2.59 (t, 2H), δ 7.14 (d,1H) aromatic , δ 6.96 (d, 1H) aromatic, δ 5.0 (s, 1H) due to alcoholic -OH, δ 7.23 (d, 1H) aromatic.

5c : (2*E*)-7-methoxy-2-[(2-phenylimidazo[1,2-*a*]pyridin-3-yl)methylidene]-3,4- dihydronaphthalen-1(2*H*)-one :

1H NMR (CDCl3, 300 MHz) : Imidazole ring :
δ 7.51 (d, 1H) aromatic C_3, δ 7.03 (d, 1H) aromatic C_4, δ 6.65 (d,1H) aromatic C_5, δ 8.09 (d, 1H) aromatic C_6.

Benzene attached to imidazole ring :
δ 7.48 (d, 1H) aromatic J=7.0 Hz ortho coupling, δ 7.32 (d, 1H) aromatic J=7.0 Hz ortho coupling , δ 7.22 (d,1H) aromatic, δ 7.48 (d, 1H) aromatic , Trans δ7.60 (s,1H) unsaturated C=C bond.
Tetralone ring : : δ 2.29 (t, 2H), δ 2.59 (t, 2H), δ 7.14 (d,1H) aromatic , δ 7.0 (d, 1H) aromatic, δ 3.73 (s, 3H) due to methoxy, δ 7.27 (d, 1H) aromatic.

5d : (2*E*)-7-ethoxy-2-[(2-phenylimidazo[1,2-*a*]pyridin-3-yl)methylidene]-3,4-dihydronaphthalen-1(2*H*)-one :
1H NMR (CDCl3, 300 MHz) : Imidazole ring :
δ 7.51 (d, 1H) aromatic C_3, δ 7.03 (d, 1H) aromatic C_4, δ 6.65 (d,1H) aromatic C_5, δ 8.09 (d, 1H) aromatic C_6.
Benzene attached to imidazole ring :
δ 7.48 (d, 1H) aromatic J=7.0 Hz ortho coupling, δ 7.32 (d, 1H) aromatic J=7.0 Hz ortho coupling , δ 7.22 (d,1H) aromatic, δ 7.48 (d, 1H) aromatic , Trans δ7.60 (s,1H) unsaturated C=C bond.
Tetralone ring : : δ 2.29 (t, 2H), δ 2.59 (t, 2H), δ 7.14 (d,1H) aromatic , δ 7.0 (d, 1H) aromatic, δ 3.98 (q, 2H) & , δ 1.33(t,3H) due to ethoxy, δ 7.27 (d, 1H) aromatic.

5e : (2*E*)-7-chloro-2-[(2-phenylimidazo[1,2-*a*]pyridin-3-yl)methylidene]-3,4-dihydronaphthalen-1(2*H*)-one :

1H NMR (CDCl3, 300 MHz) : Imidazole ring :
δ 7.51 (d, 1H) aromatic C_3, δ 7.03 (d, 1H) aromatic C_4, δ 6.65 (d,1H) aromatic C_5, δ 8.09 (d, 1H) aromatic C_6.

Benzene attached to imidazole ring :
δ 7.48 (d, 1H) aromatic J=7.0 Hz ortho coupling, δ 7.32 (d, 1H) aromatic J=7.0 Hz ortho coupling , δ 7.22 (d,1H) aromatic, δ 7.48 (d, 1H) aromatic , Trans δ7.60 (s,1H) unsaturated C=C bond.

Tetralone ring : : δ 2.29 (t, 2H), δ 2.59 (t, 2H), δ 7.14 (d,1H) aromatic , δ 7.50 (d, 1H) aromatic, δ 7.77 (d, 1H) aromatic due to electronegative 6- Chloro group.

5f : (2*E*)-6-methyl-2-[(2-phenylimidazo[1,2-*a*]pyridin-3-yl)methylidene]-3,4-dihydronaphthalen-1(2*H*)-one

1H NMR (CDCl3, 300 MHz) : Imidazole ring :
δ 7.51 (d, 1H) aromatic C_3, δ 7.03 (d, 1H) aromatic C_4, δ 6.65 (d,1H) aromatic C_5, δ 8.09 (d, 1H) aromatic C_6.
Benzene attached to imidazole ring :
δ 7.48 (d, 1H) aromatic J=7.0 Hz ortho coupling, δ 7.32 (d, 1H) aromatic J=7.0 Hz ortho coupling , δ 7.22 (d,1H) aromatic, δ 7.48 (d, 1H) aromatic , Trans δ 7.60 (s,1H) unsaturated C=C bond.
Tetralone ring : : δ 2.29 (t, 2H), δ 2.59 (t, 2H), δ 7.14 (d,1H) aromatic , δ 7.11 (d, 1H) aromatic, δ 2.35 (s, 3H) for 7- methyl protons δ 7.07 (d, 1H) aromatic , δ 7.64 (d, 1H) aromatic

5g : (2*E*)-6-nitro-2-[(2-phenylimidazo[1,2-*a*]pyridin-3-yl)methylidene]-3,4-dihydronaphthalen-1(2*H*)-one :

1H NMR (CDCl3, 300 MHz) : Imidazole ring :
δ 7.51 (d, 1H) aromatic C_3, δ 7.03 (d, 1H) aromatic C_4, δ 6.65 (d,1H) aromatic C_5, δ 8.09 (d, 1H) aromatic C_6.
Benzene attached to imidazole ring :
δ 7.48 (d, 1H) aromatic J=7.0 Hz ortho coupling, δ 7.32 (d, 1H) aromatic J=7.0 Hz ortho coupling , δ 7.22 (d,1H) aromatic, δ 7.48 (d, 1H) aromatic , Trans δ7.60 (s,1H) unsaturated C=C bond.

Tetralone ring : : δ 2.29 (t, 2H), δ 2.59 (t, 2H), δ 7.14 (d,1H) aromatic , δ 8.24 (d, 1H) aromatic, Increase in value due to 7- NO_2 group, 8.20 (d, 1H) aromatic , δ 8.02 (d, 1H) aromatic.

BIOLOGICAL EVALUATION :

All the compounds have been evaluated for antimicrobial activity using Cup plate agar diffusion method at a concentration of 40µg using DMF as a solvent against different strains of bacteria and fungi. The

antimicrobial activity was compare with standard drug *viz* ciprofloxacin, Amoxicillin, Benzyl-penicillin and antifungal activity was compared with *viz* greseofulvin. The zone of inhibition were measured in mm.

ANTIBACTERIAL ACTIVITY :

The purified products were screened for their antimicrobial activity. The nutrient agar broth prepared by the usual method, was inoculated aseptically with 0.5 ml of 24 hrs. old subcultures of ***B.cocus, S.aureus, Pseudomonas*** and ***E.coli*** in separate conical flask at 40-50°C and mixed well by gentle sacking. About 25ml content of the flask were poured and evenly spreaded in a petridish (13mm in diameter) and allowed to set for 2 hrs. The cups (10mm in diameter) were formed by the help of borar in agar medium and filled with 0.04 ml (40mg) solution of sample in DMF. The plates were incubated at 37°C for 24.0 hrs. and the control was also maintained with 0.04 mole of DMF in a similar manner and the zones of inhibition of bacterial growth were measured in millimeter.[6]

Table-1: In vitro antibacterial activity of Imidazo [1,2 A] Pyridine chalcones.

Entry	Acetyl ketones R	In vitro activity - Zone of Inhibition in mm. Antibacterial			
		B.Coccus	S.aureus	pseudomonas	E.Coli
5a	Tetralone	**18**	17	14	12
5b	6-OH Tetralone	**19**	17	**19**	**19**
5c	6- OMe-Tetralone	**18**	16	16	**18**
5d	6- OEt-Tetralone	17	15	16	15
5e	6- ChloroTetralone	**19**	**19**	16	16
5f	7- Me-Tetralone	17	16	14	13
5g	7- NO_2-Tetralone	14	13	14	15
Standard	**Amoxicilin**	**23**	**22**	**21**	**22**
---	**Ampicilin**	**21**	**20**	**22**	**23**
---	**Norfloxacin**	**24**	**23**	**22**	**23**
----	**Ciprofloxacin**	**25**	**24**	**23**	**22**

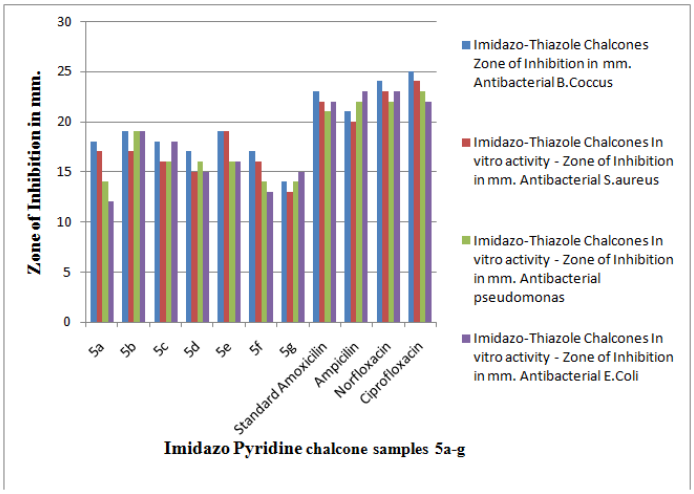


Figure- 3: In vitro activity - Zone of Inhibition in mm. Antibacterial

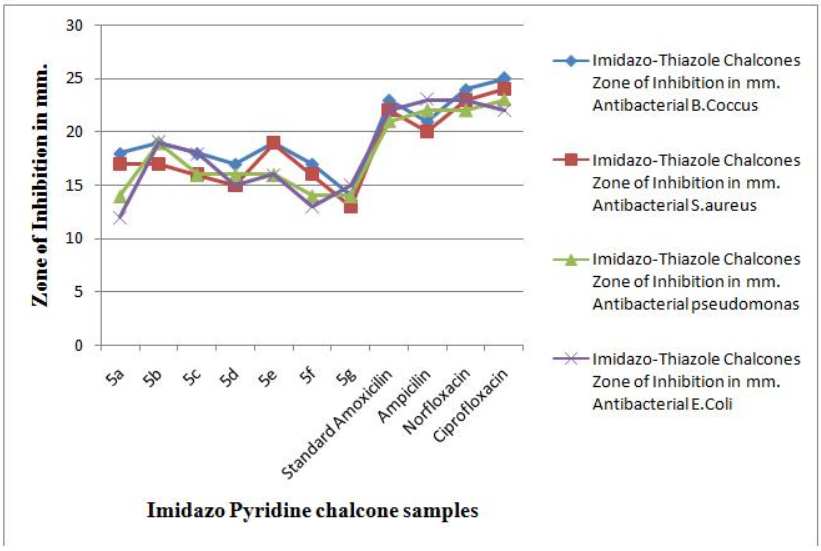


Figure- 4: Comparative In vitro activity - Zone of Inhibition in mm. Antibacterial

RESULT AND DISCUSSION :

A novel series of Imidazo [1,2-A] Pyridine chalcones (5a-g) were synthesized by reacting a variety of substituted tetralones with 3- formyl imidazo [1,2-A] pyridine carbaldehyde in the presence of alkali NaOH in PEG-400 as green and recyclable solvent as shown in scheme-1. Synthesized all Imidazo [1,2-A] pyridine chalcones derivatives were obtained in good yield. The structures of newly synthesized Imidazo [1,2-A] thiazole pyridine chalcones (5a-g) compounds was characterized by IR, ^{1}H –NMR spectroscopic methods.. The presence of a band around 1580 cm-1 due to C=C stretch band at 1685 cm-1 is due to carbonyl C=O stretch and band at 650 cm-1 due to Chloro C- Cl stretching. In ^{1}H NMR spectrum of δ 7.48, (d, 1H), δ 7.32 (d, 1H) aromatic J =7.0 Hz Ortho coupling, δ 7.22 (d,1H), δ 7.48 (d,1H), Trans δ7.60 (s,1H) unsaturated C=C bond. δ 2.29 (t, 2H), δ 2.59 (t, 2H), δ 7.14 (d,1H) aromatic , δ 8.24 (d, 1H) aromatic, Increase in chemical shift δ value due to - NO_2 group, δ 8.20 (d, 1H) aromatic δ 8.02 (d, 1H) aromatic shows presence of tetralone ring system. chalcones doublet at δ 7.51 (d, 1H) aromatic C_3, δ 7.03 (d, 1H) aromatic C_4, δ 6.65 (d,1H) aromatic C_5, δ 8.09 (d, 1H) aromatic shows presence of Imidazole-pyridine ring system.

Synthesized compounds were evaluated for their antibacterial screening against B. coccus, S. aureus, P. aeruginosa and Aerogenes. Compound 5a and 5b shows moderate activity against B.coccus and pseudomonas. Compound 5c and 5e showed maximum zone of inhibition against B. Coccus and bacteria S. aureus but less than standard used for screening.

Amoxicillin differs from ampicillin only in the presence of hydroxyl group in the *para* position of the benzene side chain. Its in vitro activity is identical to that of Ampicillin.

Amoxicillin, and ampicillin analogoues is a penicillin-derived, broad spectrum, bactericidal, semisynthetic beta-lactam antibiotic, with superior absorption high bioavailability, and very low toxicity. It acts through the inhibition of cell wall biosynthesis during bacterial multiplication that leads to the bacterial death. All the synthesized Imidazo (1,2-a) pyridine chalcones shows active results against derived antibiotics Ampicillin, Amoxicillin and A.niger.

CONCLUSION :

In the present study we have the synthesized of a series of (2*E*)-2-[(2-phenylimidazo[1,2-*a*]pyridin-3-yl)methylidene]-3,4-dihydronaphthalen-1(2*H*)-one. All the synthesized chalcones were characterized by IR, and PMR spectra and screened for their in vitro antibacterial activity against B.coccus, S.aureus, Pseudomona, E.coli, Ampicillin, Amoxicillin and Norfloxacin, Their minimum inhibitory concentrations (MIC)

were determined. The results of antibacterial activity showed that 5a, 5b, 5c and 5e good response to the *B. coccus, S. aureus, P. aeruginosa* and *Aerogenes* , Ampicillin, Amoxicillin and Norfloxacin as standard drug. Further bioevaluation, bioassay, optimization and structure-activity relationship of the title synthesized compounds are under inspection.

ACKNOWLEDGEMENT:

The authors thankful to the Dr. R. B. Bhosale, Director School of chemical sciences, Solapur university, Solapur for providing research facility. Dr K.D. Sonawane HOD of Microbiology department for their help in biological evaluation. And also thankful to the Principle, Smt. Kusumtai Rajarambapu Patil kanya Mahavidyalaya, Islampur for their immence help throught the experiment.

CONFLICT OF INTEREST:

The authors confirm that this article content has no conflict of interest.

REFERENCES :

1. Arora P, Arora V, Lamba HS, and Wadhwa D (2012). Importance Of Heterocyclic Chemistry: A Review , International Journal of pharmaceutical science and research. 3(9), 2947-2954.
2. Alexandru TB,(2004). Aromaticity as a Cornerstone of Heterocyclic Chemistry. Chem. Rev., 104, 2777−2812.
3. Bagdi AK, S. Santra S, Monira K, and Hajra A (2015). Reviews on the synthesis of imidazo[1,2-a]pyridines. Chem. Commun., 51, 1555–1575.
4. Pericherla K, Kaswan P, Pandey K, and Kumar A (2015). Reviews on the synthesis of imidazo[1,2-a]pyridines. Synthesis, 887–912.
5. Bharate JB, Abbat S, Bharatam PV, Vishwakarma RA, and Bharate SB (2015). CuBr catalyzed aerobic oxidative coupling of 2-aminopyridines with cinnamaldehydes: direct access to 3-formyl-2-phenyl-imidazo[1,2-a]- pyridines. Org. Biomol. Chem., 13, 7790.
6. Rupala RG, Dinesh S, Patel K (2014). Synthesis, Characterization and Biological Evaluation of Some Novel Chalcone Derivatives Containing Imidazo[1,2-a]Pyridine Moiety. Journal of Chemistry, Environmental Sciences and its Applications, 1(1), 23–32.
7. Gaadaoui,SR, Koudad A, Ousaid1 M, Elaatiaoui1 A, Hamal, A, Zarrouk A, and Benchat N (2014). Synthesis, antimicrobial and antifungal screening of novel chalcones containing imidazo[1,2-a] pyridine nucleus. Der Pharma Chemica, 6(4), 147-152.
8. Raut DG, Kadu VD, Sonawane VD, Bhosale RB (2015). Synthesis Of Thiazole Scaffolds By Novel Method And Their In Vitro Anthelmintic Activity Against Indian Adult Earthworm. Europian Journal Of Biomedical And Pharmaceutical Science, 2(4), 922-931.
9. Raut DG, Sonawane KD, Jadhav sY, Sonawane VD, Jadhav DB, and Dhanavade MJ, Bhosale RB (2016). Synthesis And Potential Antibacterial Activities Of 2-Chloro-N-(4- Phenylthiazol-2-Yl) Acetamide Derivatives, Der Pharma Chemica, 8(20), 292-297.
10. Jadhav SY, Shirame SP, Kulkarni SD, Patil SP, Pasale SK, Bhosale RB (2013). PEG mediated synthesis and pharmacological evaluation of some fluoro substituted pyrazoline derivatives as anti-inflammatory and analgesic agents Bioorganic Medicinal Chemistry Letter 23, 2575–2578.
11. Jadhav SY, Bhosale RB, Shirame SP, Patil SB, and Kulkarni SD (2015). PEG Mediated Synthesis and Biological Evaluation of Asymmetrical Pyrazole Curcumin Analogues as Potential Analgesic, Anti-Inflammatory and Antioxidant Agents. Chem Biol Drug Des., 85, 377–384.
12. Sonawane VD, (2013). Design, Synthesis, Characterization And In Vitro Antioxidant Screening Of Novel Chromone Chalcones. Review Of Research, 3, (2), 1-8.
13. Sonawane VD, (2016). Design, Synthesis, Chracterization And Antioxidant valuation Of Novel Asymmetrical Methoxy Curcumin Analogues Containing Chromone Moiety. Review Of Research, 5, (9), 1-17.

14. Jadhav Y,. Bhosale RB, Shirame SP, Sonawane VD, Hublikar M, Sonawane KD, Shaikh R (2013). Synthesis And Biological Evaluation Of Fluoro-Hydroxy Substituted Pyrazole Chalcones as Anti-Inflammatory, Antioxidant And Antibacterial Agents. International Journal of Pharma and Bio Sciences, 4(2): (P) 390 – 397.
15. Chen J, Spear SK, Huddlestn JG, Roggers Rd (2005). Polyethylene glycol and solutions of polyethylene glycol as green reaction. Green chem. 7 , 64-82.
16. Jayapal MR, Sreenivasa PK, and Sreedhar NY, (2010). Synthesis and haracterization of 2,6-Dihydroxy Substituted Chalcones Using PEG-400 as a Recyclable Solvent. J Pharm Sci & Res. 2(8) :450-458.