IJPSR (2019), Volume 10, Issue 9 (Research Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 30 December 2018; received in revised form, 16 April 2019; accepted, 13 August 2019; published 01 September 2019

SYNTHESIS AND ANTIBACTERIAL SCREENING OF FIVE NEW AZOMETHINE DERIVATIVES OF 2-AMINO-2-METHYL-1-PROPANOL

K. Sudhakar Babu [1], P. Malleswara Reddy [*1], V. Krishna Murthy Naik [1] and K. Ramanjaneyulu [2]

Department of Chemistry [1], Sri Krishnadevaraya University, Anantapuramu - 515003, Andhra Pradesh, India.
Government Junior College [2], B. Camp, Kurnool - 518002, Andhra Pradesh, India.

Keywords:

Azomethines, Anti-bacterial activity *Bacillus thuringiensis*, *E. coli*, Beef extract, Disc diffusion method

Correspondence to Author:
P. Malleswara Reddy

Department of Chemistry, Sri Krishnadevaraya University, Anantapuramu - 515003, Andhra Pradesh, India.

E-mail: pmeshvarreddy@gmail.com

ABSTRACT: In this present investigation author reporting the anti-bacterial activity of five new azo methines, namely 2-((1-hydroxy-2-methyl propan-2-ylimino) methyl)-6-methoxyphenol (AZM_1), 4-((1-hydroxy-2- methyl propan-2-ylimino) methyl)-6-methoxyphenol(AZM_2), 4-((1-hydroxy-2-methyl propan-2-ylimino) methyl)-2,6,dimethxy phenol (AZM_3), 2- (3, 4- dimethoxybenzylideneamino)- 2- methylpropan-1-ol (AZM_4) and 2-(3,4,5-trimethoxybenzylideneamino)-2-methylpropan-1-ol (AZM_5) against and *Bacillus thuringiensis*, *E. coli* bacteria. All new five novel Azomethines were synthesized by the condensation of 2-Amino-2-Methyl-1-Propanol with 2- Hydroxy- 3- methoxybenzaladehyde, 4-Hydroxy- 3- Methoxy-Benzaldehyde, 4- Hydroxy- 3, 5- Dimethoxy Benzaldehyde, 3,4-Dimethoxy Benzaldehyde and 3, 4, 5-Trimethoxy Benzaladehyde respectively, in methanol-water (1:1 ratio) at 42 ºC for 8 h. All the azomethines were characterized by UV, IR and thermal elemental analyzer. Anti-bacterial studies were carried out by using Paper disc diffusion method, beef extract is used as bacterial source, chloromphenicol and ketocanazole used as reference standards, five azomethines gave the following order of antibacterial activity and order of zone of inhibition was AZM_5 (12mm) > AZM_4 (7mm) > AZM_3 (10mm) > AZM_1 (9mm) > AZM_2 (8mm) against *E. coli* and AZM_5 (11mm) > AZM_4 (10mm) > AZM_3 (9mm) > AZM_1 (7mm) >AZM_2 (6mm) against *Bacillus thuringiensis*.

INTRODUCTION: The condensation products of carbonyl compounds and primary amines are often named as Schiff bases. They are also known as Azomethines or anils or imines. The condensation of primary amines with carbonyl compounds was first reported by Schiff [1].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.10(9).4396-03

The article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.10(9).4396-03

On perusal of literature, the survey revealed that the azomethines have got extensive applications in Biological, Industrial and Pharmaceutical fields. Complexes with bidentate azomethines (Schiff bases) were reported to possess biocide activity against bacteria and fungi [2].

Sing and his co-workers synthesized some boran complexes with Schiff bases and studied the antifungal and antibacterial activity [3]. Schiff bases derived from the condensed product of methyl cyclopropyl ketone' and di alkyl phosphates showed aphicidal activity [4]. The twenty-six thiazole Schiff base derivatives prepared Synthesized by

Mahapatra showed antifungal activity against curvularia Species [5]. The antifungal property of some nickel-Schiff base complexes was studied and the complexes were more active than the free ligands against all the fungi tested [6]. Fifteen Transition metal with three different Schiff bases have been synthesized and screened against some fungal Pathogens and among these Cu [II] and Co [II] complexes with benzlil-touldine ligand showed high fungi toxic result [7]. Schiff base derived from 5 nitro and 3-chloro salicylaldehyde and their complexes with Mn [II], Fe [III], Co[II]Ni[II] and Cu[II] have been studied for fungicidal activity using the growth method [8, 9]. Fluorination on the aldehyde part of the molecule enhanced the insect caricidal activity when compared to fluorination of amine part [10] Schiff base obtained from tris and glyoxal was studied for its pesticidal activity by Nicolae *et al*. [11] Quinoline exhibits antipyretic activity, although it is too toxic in nature for use in therapy, efforts were made to prepare non-toxic compounds to replace the expensive Quinine. Nevertheless, several quinine Schiff base complexes possessing antipyretic activity have been synthesized but they failed to exhibit antimalarial action which was a characteristic property of quinine although it is too toxic in nature for used therapy.

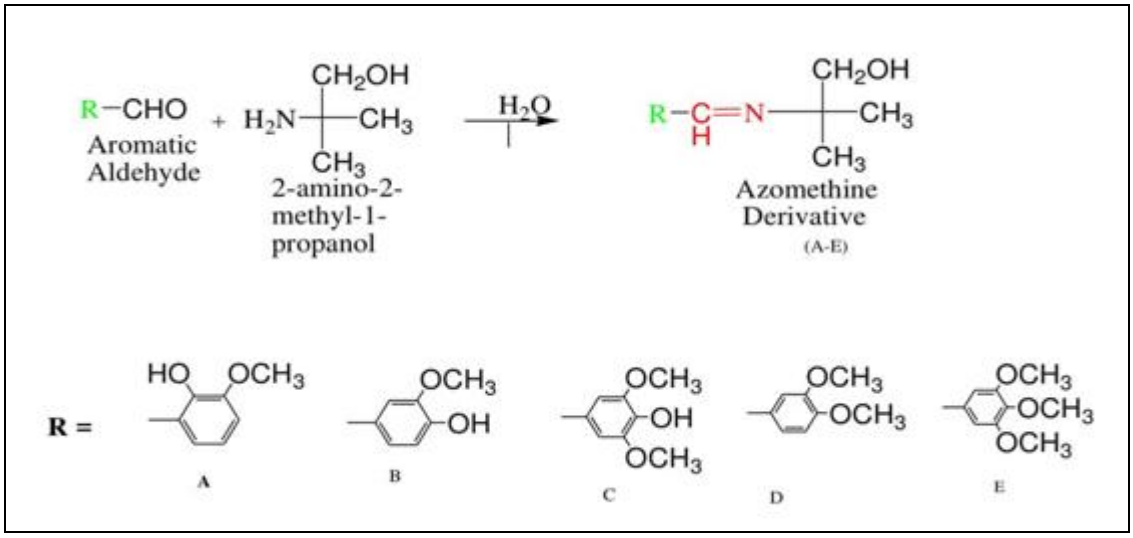

FIG. 1: SYNTHESIS OF NEW AZOMETHINE DERIVATIVES

2-amino-2-methyl-1-propanol: Alkanolamines are chemical compounds that contain both hydroxyl (-OH) and amino (-NH_2, -NHR, and -NR_2) functional groups on an alkane backbone [12]. Literature Survey revealed that not much work has been carried out in establishing the complexing ability of AMP towards metal ions. Metal-AMP complexes were found to wide range applications in biological fields. Metal complexes prepared by the reaction of tetrachloroaurate with AMP in aqueous media were recommended as anti-tumor agents [13] Werner coordination complexes [14] synthesized by reacting benzotrizoles with a mono epoxide afforded mixture of 1-and2-hydroxy alky benzotrizoles and etherifying the mixture with an alkaline succinic anhydride to form a monoester and its salts were prepared with metals selected form IB, IIB, IVB. And VII of the periodic table and complexing these salts with AMP form chelate complexes and they found to exhibit moderate antifungal activity. The NI [II] complexes with AMP and other alkanolamines have been synthesized and screened for antifungal activity [15]. The zinc [II] and Copper [II] complexes of AMP were synthesized and found to exhibit good antifungal activity [16, 17].

EXPERIMENTAL METHODS:

Synthesis of Azomethines: All the chemicals used were analytical grade, bought from Raju chemicals in Ananthapur. India. Aromatic aldehyde (2-hydroxy- 3- methoxybenzaldehyde, 4- hydroxy-methoxybenzaldehyde, 4-hydroxy 3, 5 dimethoxy-benzaldehyde, 3, 4 dimethoxybenzaldehyde, 3, 4, 5- Trimethoxy –benzaldehyde) was added to a mixture of 50 ml of methanol and 2-Amino-2-methyl-1-propanol(AMP) (5 ml; 0.05 mole) and 50 ml of distilled water. The reaction mixture was taken in a clean 250 ml round bottom flask and stirred well with a magnetic stirrer. Then it was refluxed for 8 h.

A Bright yellow [AZM_1] and [AZM_2] buff [AZM_3], colorless [AZM_4], yellow [AZM_5] colored products were formed. These were separated by filtration and washed several times with hot water and methanol and dried in vacuum. The compounds were recrystallized from methanol.

All five new azomethines were characterized by UV spectroscopy, dimethylformamide used as solvent and thermal elemental analyzer in the department of chemistry. S.K. University. Ananthapuram. Thermo Nicolet nexus 670 IR spectrometer with DTGC detector in IICT-HYD.

Anti Bacterial Screening: Disc diffusion method of antimicrobial screening of newly synthesized azo methines AZM_1, AZM_2, AZM_3, AZM_4, AZM_5 were studied against bacteria by following procedures employed by Gananamanickam [18] *et al*.

Material Required: Peptone, beef extract, NaCl. Agar, Petri plates, Hot air oven, Autoclave (fazal engineering works), Sterilized pipettes and filter paper.

Medium: The medium used for testing was a nutrient agar medium. The medium was prepared by dissolving peptone-5g, Beef extract-3g, NaCI-5gm, agar-15gm in 1 liter of distilled water. The contents were mixed thoroughly. The pH was adjusted to 7.4-7.6. The medium was sterilized in the autoclave at 15 lbs. per Sq. inch pressure for 15 min.

Inoculums Preparation: The inoculums were prepared by picking up five to ten colonies bacilli and *E. coli* with a loop. The colonies were suspended in a nutrient broth and incubated at 37 ºC for 3 to 4 h.

Disc Preparations: What man filter paper No.1 was taken and discs of 6 mm in diameter were punched with a puncher. The filter paper discs were sterilized in a hot air oven. The sterilized paper discs are soaked in 5 ml of methanol containing known concentration (150 ug/ml) of the samples AZM_1, AZM_2, AZM_3, AZM_4, AZM_5 for 2-3 min. The discs were of allowed to dry for solvent and they get evaporated from the paper discs.

Maintenance and Sterility: All the required apparatus were sterilized before use and every reasonable Precaution was observed to avoid contamination throughout the operation.

Procedure of Testing: Sterilized nutrient agar medium 15-20 ml was poured into sterile Petri plates of the same size in aseptic conditions. The medium was allowed to solidify the bacterial Culture was spread uniformly on the surface of nutrient agar medium with sterile cotton swabs.

The Paper discs soaked with a solution of known concentration of the desired Schiff base metal complex and they were placed under aseptic conditions at a particular distance in each per plates, containing known bacterial suspension. The Petri dishes were labeled with the compound and then incubated at 37 ºC for 24 h of incubation. The latch Petri plate was observed for bacterial growth and the zone of inhibition of bacterial growth in each Petri plate was measured. The discs Soaked with the respective solvents of test solutions were used as controls. The zone of inhibition of bacterial growth in the Petri plates under examination was measured. The minimum inhibitory concentration (MIC) was measured by taking 150 ug/ml of the test sample for antibacterial studies.

RESULTS AND DISCUSSION: Electronic spectra of the AZM1 in UV region show an intense band at 285 nm and weaker band at 288 nm which were assigned to the $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ Transitions respectively. Electronic spectra of the AZM2 in UV region show an intense band at 275 nm and weaker band at 280 nm which are assigned to the $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ Transitions respectively. Electronic spectra of the AZM3 Schiff base in UV region show an intense band at 270 nm and weaker band at 290 nm which are assigned to the $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ Transitions respectively. Electronic spectra of the AZM_4 Schiff base in UV region show an intense band at 328 nm and weaker band at 332 nm which are assigned to the $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ Transitions respectively. Electronic spectra of the AZM_5 Schiff base in UV region show an intense band at 275 nm and weaker band at 323 nm which are assigned to the $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ Transitions respectively.

Fig. 2, 3, 4, 5, 6 shows the electronic spectral data of other newly synthesized azomethine.

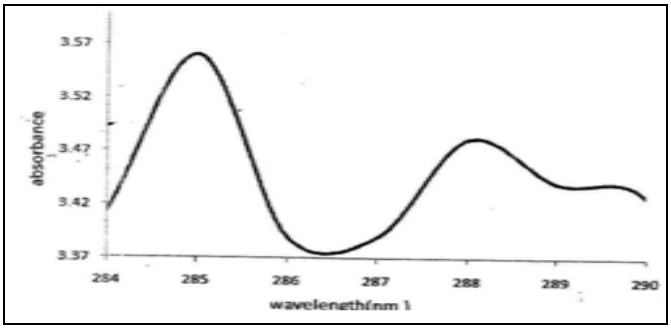

FIG. 2: ELECTRONIC SPECTRA OF AZM_1

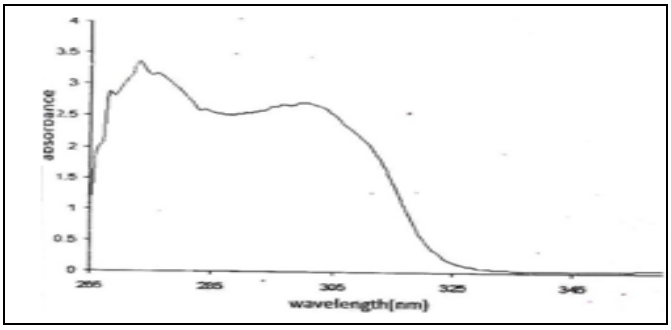

FIG. 3: ELECTRONIC SPECTRA OF AZM_2

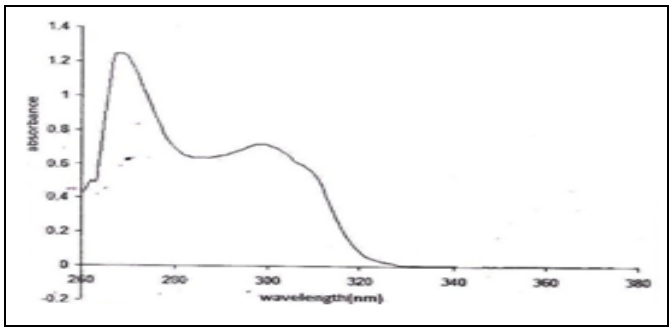

FIG. 4: ELECTRONIC SPECTRA OF AZM_3

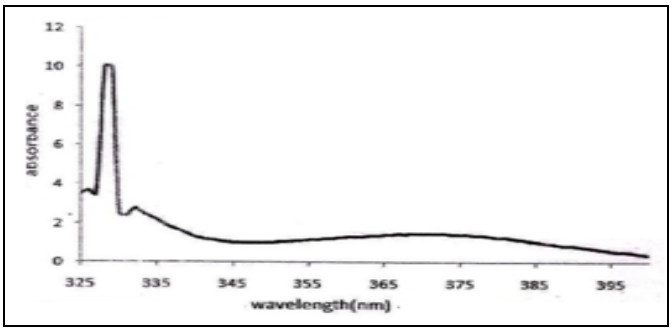

FIG. 5: ELECTRONIC SPECTRA OF AZM_4

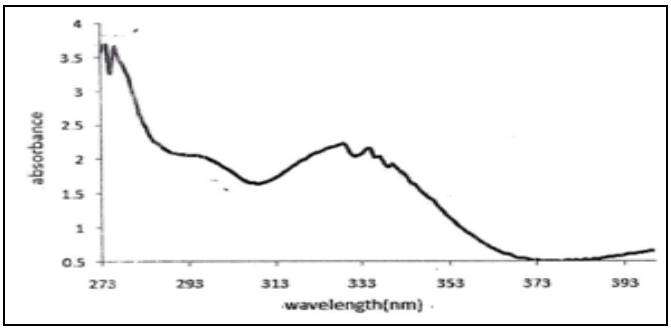

FIG. 6: ELECTRONIC SPECTRA OF AZM_5

Interpretation of IR data of Newly Synthesized Schiff Bases: The IR spectra of newly synthesized azomethines were recorded in KBr Palette in the IR range of 4000-400 cm^{-1} and IR data establishes the Molecular structure of AZM1. 3446 cm^{-1} (intra molecular H- bonding), 3036 cm^{-1} (Ar-H, stretching), 2846 cm^{-1} (Aliphatic C-H stretching), 1686 cm^{-1} (>C=N stretching), 1235 cm^{-1} (C-O stretching vibrations of Alcohol / Phenol. The IR spectra was shown in **Fig. 7**. The IR data of other Novel azomethines, AZM_2, AZM_3, AZM_4, AZM_5 was depicted in **Table 2**. IR spectra were detected in **Fig. 8, 9, 10, 11**.

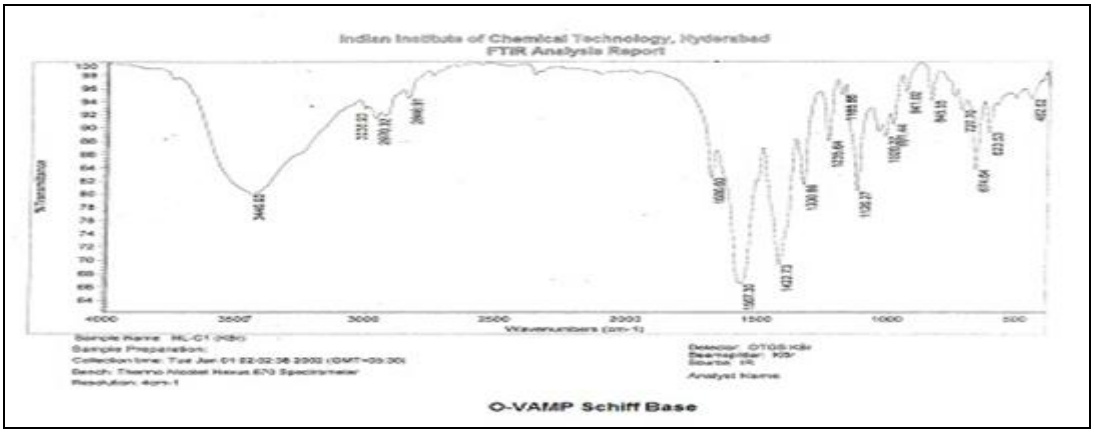

FIG. 7: VIBRATIONAL SPECTRA OF AZM_1

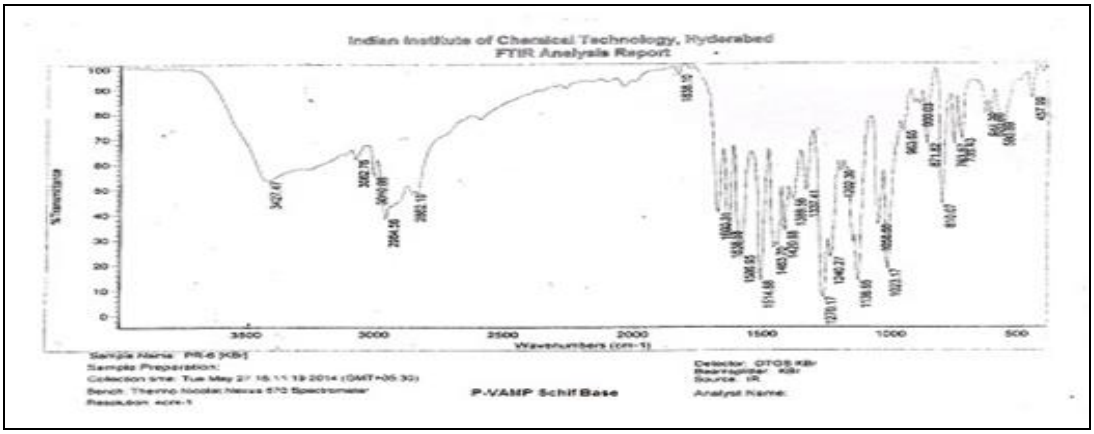

FIG. 8: VIBRATIONAL SPECTRA OF AZM_2

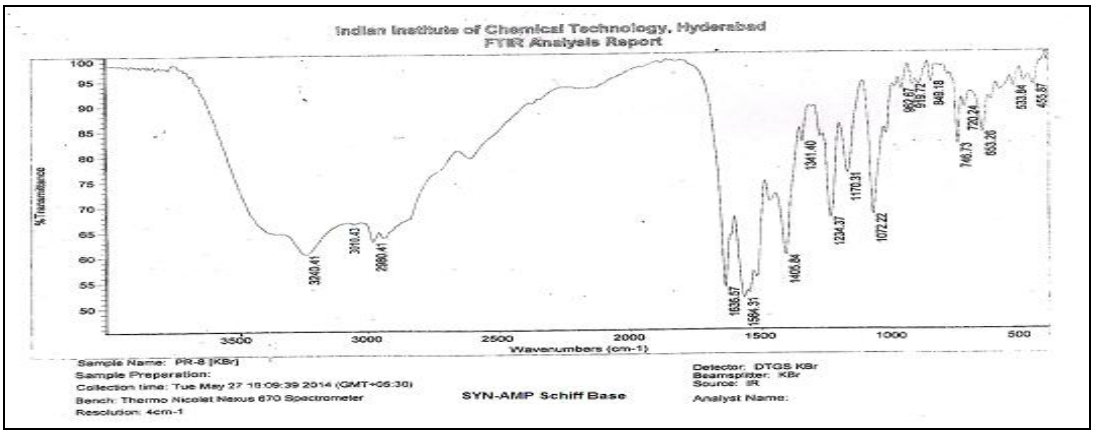

FIG. 9: VIBRATIONAL SPECTRA OF AZM_3

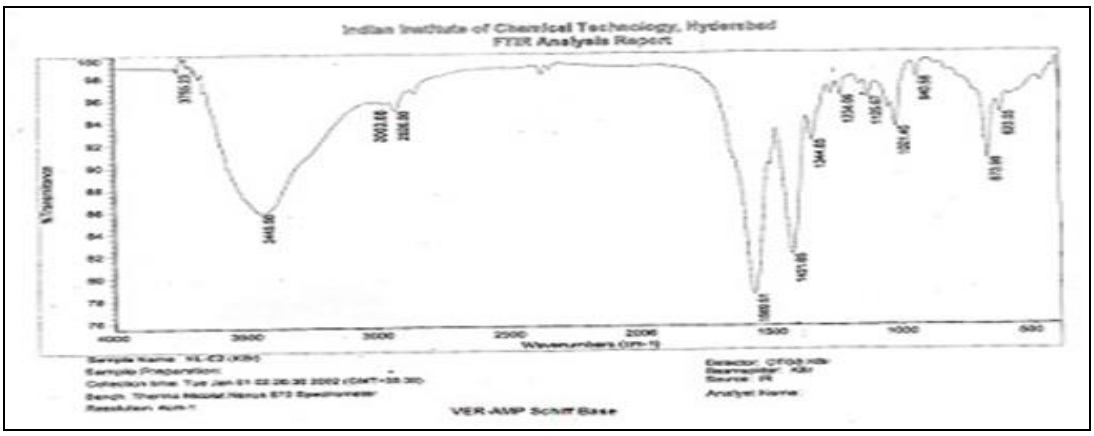

FIG. 10: VIBRATIONAL SPECTRA OF AZM_4

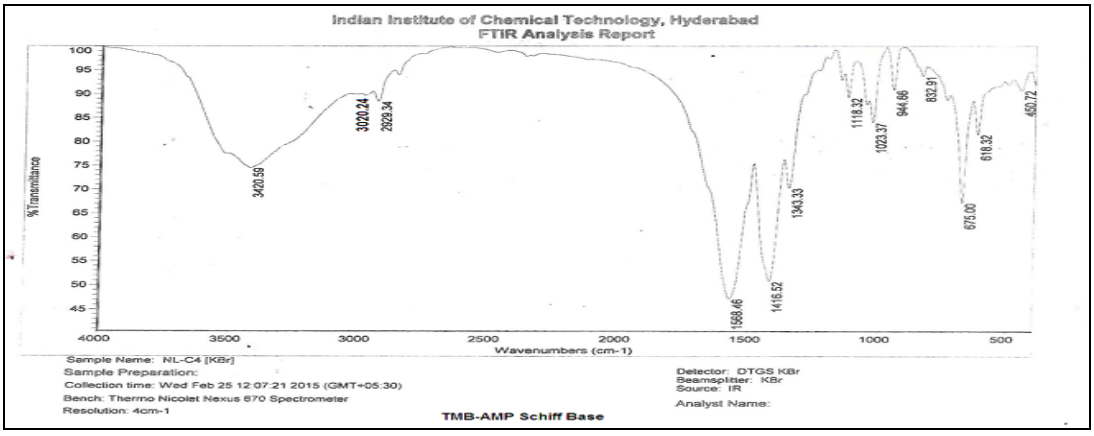

FIG. 11: VIBRATIONAL SPECTRA OF AZM_5

TABLE 1: IR SPECTRAL DATA OF AZO METHINES

AZOMETHINES	V⁻, cm^{-1}			
	-OH (cm^{-1})	Ar-H (cm^{-1})	Aliphatic C-H (cm^{-1})	>C=N (cm^{-1})
AZM_1	3446	3036	2846	1686
AZM_2	3427	3082	2964	1680
AZM_3	3240	3010	2980	1636
AZM_4	3446	3003	2926	1569
AZM_5	3420	3020	2929	1568

TABLE 2: ANALYTICAL DATA OF FIVE NEW AZOMETHINES

Schiff Base	Molecular Formula	M. Wt	Colour	M.P °C	Elemental Analysis						Yield
					Carbon %		Hydrogen %		Nitrogen %		
					Found	calc	Found	calc	Found	calc	
AZM_1	$C_{12}H_{17}NO_3$	223	Yellow	160-162	64.44	64.49	7.58	7.61	6.23	6.27	80%
AZM_2	$C_{12}H_{17}NO_3$	223	Bright Yellow	194-197	64.44	64.49	7.58	7.61	6.23	6.27	75%
AZM_3	$C_{13}H_{19}NO_4$	253	Buff	80-84	61.61	61.66	7.47	7.4	5.49	5.53	65%
AZM_4	$C_{13}H_{19}NO_3$	237	Colorless	102-104	65.77	65.82	7.98	8.01	5.05	5.09	70%
AZM_5	$C_{14}H_{21}NO_4$	267	Light Yellow	82-84	62.85	62.9	7.83	7.86	5.21	5.24	65%

The anti-bacterial activity of 2-((1-hydroxy-2-methylpropan-2-ylimino)methyl)-6-methoxyphenol (AZM1), 4-((1-hydroxy-2- methyl propan-2-ylimino) methyl)-6-methoxyphenol (AZM2), 4-((1-hydroxy-2-methyl propan-2-ylimino) methyl)-2,6, dimethxy phenol (AZM3), 2-(3,4-dimethoxy-benzylideneamino)-2-methylpropan-1-ol (AZM4) and 2- (3, 4, 5- trimethoxybenzylideneamino)-2-methylpropan-1-ol (AZM5) were studied against Bacilli (gram positive) and *E. coli* (gram negative) bacteria.

The antibacterial studies were carried out using the chloramphenicol and ketocanazole as reference standards. The results pertaining to the antibacterial activity of azomethines against gram-positive and gram-negative bacteria was presented in the **Table 3** and the zone of inhibition of azomethines was demonstrated in **Plate 1** and **Plate 2**.

The experimental results on antibacterial studies revealed that all azo azmethines under present investigations exhibit good antibacterial activity. The order of azoethines activity was AZM_5 (12mm) > AZM_4 (7mm) > AZM_3 (10mm) > AZM_1 (9mm) > AZM_2 (8mm) against *E. coli* and AZM_5 (11mm) >AZM_4 (10mm) > AZM_3 (9mm) > AZM1 (7mm) >AZM_2 (6mm) against bacilli, from this data it was cleared that as the methoxy content on benzene ring increases the antimicrobial activity also increases.

TABLE 3: ANTI-BACTERIAL ACTIVITY OF SCHIFF BASES DERIVED FROM AMP

S. no.	Sample	Zone of Inhibition in mm	
		Bacillus	*E. coli*
	DMSO (Center)	00	00
1	AZM_1	08	07
2	AZM_2	07	06
3	AZM_3	10	10
4	AZM_4	09	09
5	AZM_5	12	11

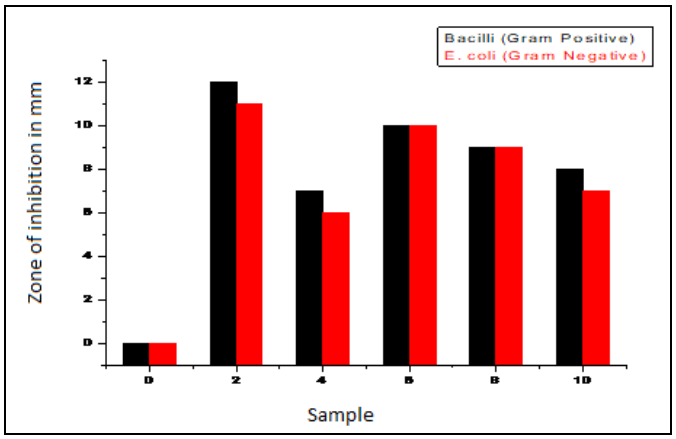

FIG. 12: ANTI-BACTERIAL ACTIVITY OF (0) DMSO (2) AZM_5 (4) AZM_2 (3) AZM_3 (6) AZM_4 (5) AZM_1 AGAINST BACILLUS AND *ESCHERICHIA COLI*

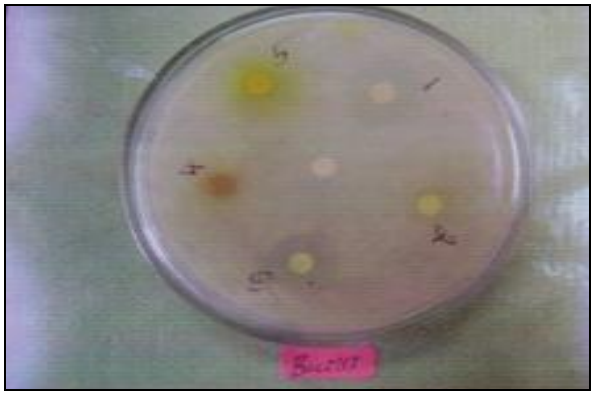

PLATE 1: ANTI-BACTERIAL ACTIVITY OF (1) AZM_1 (2) AZM_2 (3) AZM_3 (4) AZM_4 (5) AZM_5 AGAINST *BACILLUS THURINGIENS*

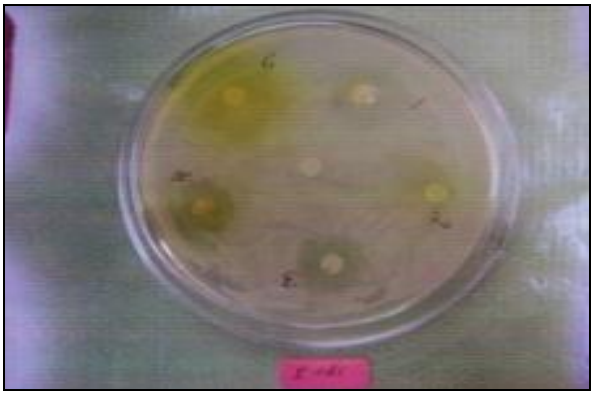

PLATE 2: ANTI-BACTERIAL ACTIVITY OF (1) TMB-AMP (2) P-VAMP (3) VER-AMP (4) SYN-AMP (5) O-VAMP AGAINST *ESCHERICHIA COLI*

CONCLUSION: Five newly synthesized azo azomethines of 2-amino-2-methyl-1- propanol were a new addition to literature, these five azo methines under present investigations exhibit good antibacterial activity. As the methoxy moiety on aromatic ring increases the antibacterial activity was increases.

The order of azomethine activity was AZM_5 (12mm) > AZM_4 (7mm) > AZM_3 (10mm) > AZM_1 (9mm) > AZM_2 (8mm) against *E. coli* and AZM_5 (11mm) > AZM_4 (10mm) > AZM_3 (9mm) > AZM_1 (7mm) > AZM_2 (6mm) against bacilli. We hope that this present investigation is more helpful to the invention of new drugs against bacteria.

ACKNOWLEDGEMENT: The author expresses sincere thanks to IICT-HYD for providing IR facilities, the author also expressing thanks to the Department of Chemistry, Sri Krishnadeveraya University for supporting to carry out research work. One of the authors is thankful to UGC, New Delhi for providing financial assistance as PDF, UGC Postdoctoral fellowship.

We are also thanks to Department of Chemistry Sri Krishnadeveraya University, Anantha Puram, India for supporting this study.

CONFLICT OF INTEREST: The authors declare no conflict of interest.

REFERENCES:

1. Schiff H: Mittheilungen aus dem Universitätslaboratorium in Pisa: Eine neue Reihe organischer Basen. Justus Liebigs Annalen der Chemie 1864; 131: 118-19.
2. Tandon, Bhal L and S. K. Sinha SK: Biological studies of some organoboron complexes on pathogenic microbes. Current Science 1984; 53(11): 566-69.
3. Khaleel AMN and Jaafar MI: Synthesis and Characterization of Boran and 2-aminophenol Schiff Base Ligands with their Cu(II) and Pt(IV) complexes and Evaluation as antimicrobial agents. Orient J Chem 2017; 33(5).
4. Goszczyńska A, Kwiecień H and Fijałkowski K: Synthesis and antibacterial activity of Schiff bases and amines derived from alkyl 2-(2-formyl-4-nitrophenoxy)alkanoates, Med Chem Res 2015; 24(9): 3561-77.
5. Chandra S, Jain D, Sharma AK and Sharma P: Coordination Modes of a Schiff Base Pentadentate Derivative of 4-Aminoantipyrine with Cobalt(II), Nickel(II) and Copper(II) Metal Ions: Synthesis, Spectroscopic and Antimicrobial Studies. Molecules 2009; 14: 174-90.
6. Sahu KL, Prasad PK, Panda AK, Sahu KL, Prasad PK and Panda AK: Complexes of cobalt(II), nickel(II), copper(II), cadmium(II), and mercury(II) with tetradentate Schiff base ligands Transition Met Chem 1990; 15: 270.
7. Reddy PS and Reddy KH: Transition metal complexes of benzil-α- monoxime (BMO); X-ray structure determination of $Co(BMO)_3$. Polyhedron 2000; 19(14): 1687-92.
8. Goyal, Sudha and Lal K: Study on metal complexs of schiff bases derived from sulphadiazine and sulphadimadine from 5 substituted salisylaldehyde. Asian J Chem 1990; 2(3): 271-74.
9. Ejidike IP and Ajibade PA: Transition metal complexes of symmetrical and asymmetrical Schiff bases as antibacterial, antifungal, antioxidant, and anticancer agents: Progress and prospects. Rev Inorg Chem 2015; 35(4): 191-24.
10. Shakira M, Shahida N, Basamia N, Azama M and Khanb U: Synthesis, spectroscopic characterization and comparative DNA binding studies of Schiff base complexes derived from L-leucine and glyoxal. 82(1): 2011; 31-36.
11. Bardulescu, Nicolae, Moga-gheorghe, Spiridon, Sintamanian, Ana, Bardulescuhown, Emilia, Cuza, Olga, Peteu, Maria and Vasilescu: Virginia Ro. Ro 1984; 85: 084.
12. Smith and Michael B: March, Jerry Advanced Organic Chemistry: Reactions, Mechanisms, and Structure (6^{th} ed.), New York: Wiley-Interscience 2007.
13. John H: N-Substituted-2-amino-2-methyl-1-propanols as potential antitumor agents Billman. Journal of Pharmaceutical Sciences. 58(6): 767-69.
14. Prasad SN, Karthik CS, Mallesha L and Mallu P: A short review on biological activity of triazole containing metal

complexes. Asian Journal of Pharmaceutical Analysis and Medicinal Chemistry 2014; 2(4): 214-29.
15. Majid K, Mushtaq R and Ahmad S: Synthesis, characterization and coordinating behaviour of aminoalcohol complexes with transition metals. E-Journal of Chemistry 2008; 5(S1): S969-79.
16. Ji YF, Wang R, Ding S, Du CFand Liu ZL: Synthesis, crystal structures and fluorescence studies of three new Zn(II) complexes with multidentate Schiff base ligands. 2012; 16: 47-50.
17. Ahmed AJ: Metal complexes of dithiocarbamate derivatives and its biological activity. Asian Journal of Chemistry 2018; 30(12): 2595-02.
18. Gnanamanickam SS and Smith DA: Selective toxicity of isoflavonoid phytoalexins to Gram-positive bacteria. Phytopathology 1980; 70: 894-96.

How to cite this article:
Babu KS, Reddy PM, Naik VKM and Ramanjaneyulu K: Synthesis and antibacterial screening of five new azomethine derivatives of 2-amino-2-methyl-1-propanol. Int J Pharm Sci & Res 2019; 10(9): 4396-03. doi: 10.13040/IJPSR.0975-8232.10(9).4396-03.