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SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL SCREENING OF NEW BI-HETEROCYCLIC AZO DERIVATIVE OF QUINAZOLINE COMPOUND

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Abstract:
Quinazoline is the fused benzene ring pyrimidine used in the synthesis of different derivatives for biological and pharmaceutical purposes. 3-aminopyridine also an active constituent for creation of azo-imine group (-N=N-C=N-).Our research group outlines for the synthesis of new 3-pyridylazoquinazoline compound and studies their biological activities. We are deeply affected towards versatile activity of N-heterocycle ring containing such molecules. The invitro antimicrobial screening of the synthesized compound 2-**[(**3′-pyridyl)azo]quinazoline was performed by agar well diffusion technique against Gram positive bacteria (*Bacillus megaterium*, *Bacillus subtilis* and *Streptococcus aureus*) and Gram negative bacteria (*Schigellaflexneri*, *Enterobacteraerogenes* and *Pseudomonas fluorescens*).The synthesized compound showed highest to moderate antibacterial activity against gram positive bacteria and gram negative bacteria. Elemental analysis and spectral studies, like-IR, UV-Vis, and ^{1}HNMR make use of molecular structure determination of the synthesized compound.

Key Words: Quinazoline, 3-aminopyridine, Azo-imine group, Antimicrobial screening.

Introduction:

N-heterocyclic ring compounds are the most valuable and integral component that used ubiquitously in variety of synthetic drugs, bioactive natural products, pharmaceuticals and agrochemicals. Owing to their widespread applications, such heterocyclic skeletons have long been used to the development of synthetic strategies which can lead to the discovery of new biological active compound in medicinal chemistry. Pyridine and quinazoline rings are the building block used for the synthesis of biologically active different compounds among the N-heterocyclic compound. Researcher finding out, pyridine derivatives possess so many activities in biologically related different fields[I]. Quinazoline is the unique N-heterocyclic molecule in different quinazoline derivatives which performed widespread biological activity in different fields, like- antimicrobial[II], anti-malarial[III],analgesic[IV],antifungal[V], anti-

inflammatory[VI], antiulcer[VII], anticonvulsant[VIII], antihypertensive[IX], antidepressant[X], antihelmintic[XI],antihistamine[XII], insecticidal[XIII], fiber reactivedyes[XIV], anticancer drug[XV] etc. Azo-imine(-N=N-C=N-) is a typical electron carrier which can regulate the whole chemical activity of the compounds. Unsymmetrical Bi-heterocyclic compounds are very much meager in literature (**Figure-1**). Searching results exposed that the quinazoline is an important unit to create different derivatives which is used for applying as a potent drug in medicinal fields. We have scrutinized that when biologically active quinazoline unit connect with another biological active pyridine molecule through –N=N- group then the resulted compound will increased their biological potentiality. We are hereby inspired for synthesis of such unsymmetrical bi-heterocyclic azo compounds.

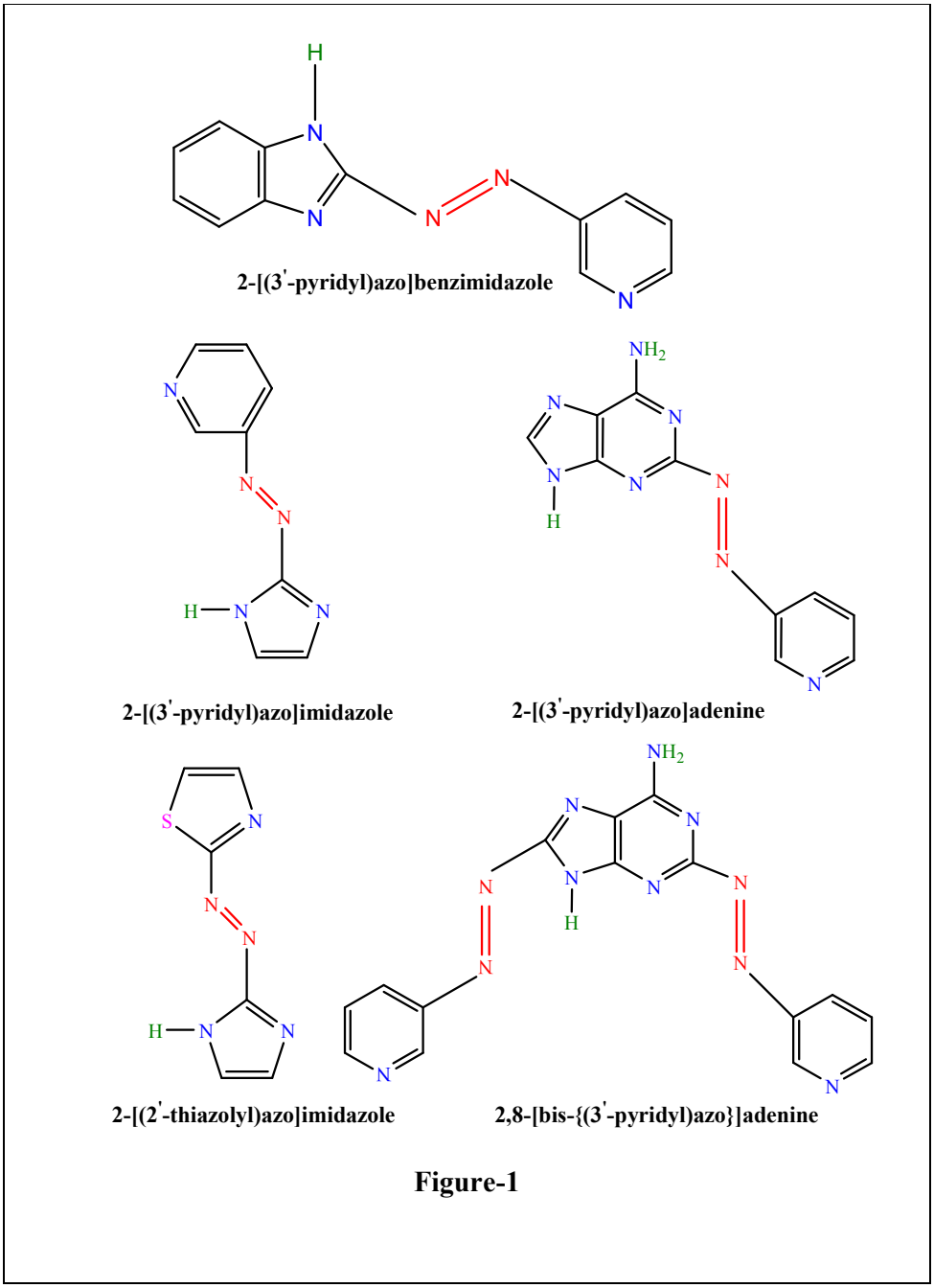


Figure-1

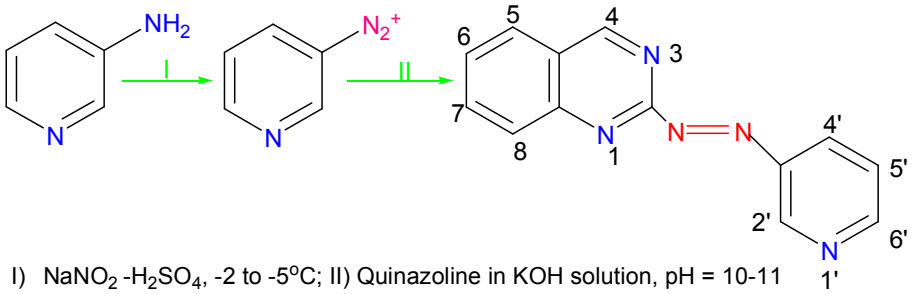
2. Experimental:

2.1. Material and Methods:

All chemical ingredients were analytical grade and purchased from Sigma Aldrich Private Ltd. The other laboratory chemicals were used without further refinement. Infrared spectral data of the synthesized compound was obtained from Shimadzu, FTIR Prestige-21 spectrophotometer in KBr pellets at Department of Chemistry, Burdwan University, Burdwan. UV-Visible Spectra were examined on a UV-1800 Shimadzu spectrophotometer in MeOH solvent. ^{1}HNMR Spectral data were collected from 400MHZ NMR spectrophotometer by used DMSO-d_6 solvent and relative to TMS as internal standard. Elemental Analysis was recorded on an EL-cube elemental analyzer. Both ^{1}HNMR and elemental analysis were examined at SAIF, Cochin University, Kerala, India. The bacteria was obtained from Microbial Type Culture Collection (MTCC) Pune, having accession number *Bacillus megaterium* (MTCC-2412), *Bacillus subtilis* (MTCC-1789), *Streptococcus aureus*(MTCC-9542), *Schigellaflexneri*(MTCC-1457), *Enterobacteraerogenes*(MTCC-111), *Pseudomonas fluorescens*(MTCC-424).

2.2. Synthesis of 2-[(3′-Pyridyl)azo)]quinazoline compound:

3-aminopyridine(400mg;4.26mmol) was diazotized in reaction with $NaNO_2$ (307mg; 4.45mmol) and Con.H_2SO_4(0.40cc/4cc; V/V) at -2^{0}C to -5^{0}C. The orange colour solution of diazonium salt was slowly added into KOH solution (1154mg; 20.1mmol) of Quinazoline(527mg; 4.05mmol) with constant stirring until a reddish-brown precipitate appeared (**Scheme-1**). The precipitate have been filtered and washed with little amount of cold water and then kept into desiccator. The synthesized crude compound was dissolved into methanol and then performed TLC. Pure products are isolated from crude synthesized compound by column chromatographic method. Different pure compounds have been eluted by using benzene, acetonitrile and methanol solvent. The benzene and acetonitrile solvent containing orange colour part was very little amount and did not consideration for the present work. Finally, MeOH solvent eluted shining reddish-brown product was isolated after the evaporating of solvent.



I) $NaNO_2$ -H_2SO_4, -2 to -5^{o}C; II) Quinazoline in KOH solution, pH = 10-11

Scheme-1

2.3. Experimental data of 2-[(3′-Pyridyl)azo)]quinazoline:

Yield: (0.75g) 75%; shinning reddish-brown solid; M.P.:166^{o}C; IR Spectrum,υ,cm^{-1}:1585(-C=N-), 1438(-N=N-);UV-Vis (MeOH), λmax, nm:220(n-π*),288 & 351 (π -π*), 475(-N=N-); ^{1}HNMR Spectrum (400MHz,DMSO-d_6),δ, ppm (J,Hz): 8.69(1H,d,J=1.08, C_4-H-Quinazoline ring), 8.39-8.40(1H,d,J=1.07, C'_6H-Pyridine ring), 8.30(1H,d,C'_2-H-Pyridine ring), 8.12-8.25(1H,dd, C'_5-H-Pyridine ring), 7.88-7.90(2H,d,J=1.00, $C_{5,8}$-H-quinazoline ring),7.43-7.46(1H,q,J=1.06, $C_{6,7}$-H-quinazoline ring); Elemental Analysis: Found, %; C-57.63, H-4.11,N-28.70; Calculated, %; C-57.56, H-4.79, N-27.83.

2.4. Assay of Antibacterial Activity:

Antibacterial activity of the newly synthesized compound**,** 2-**[(**3′-pyridyl)azo]quinazoline was studied in vitro in laboratory condition against Gram positive bacteria (*Bacillus megaterium*, *Bacillus subtilis* and *Streptococcus aureus*) and Gram negative bacteria (*Schigellaflexneri*, *Enterobacteraerogenes* and *Pseudomonas fluorescens*). Broth cultures of the above mentioned bacteria were prepared by inoculating the bacterial isolates on separate sterilized Nutrient Broth(NB) media. On the next day 20µL of the bacterial suspension was spread on separate sterilized Nutrient Agar(NA) plates and wells of 6mm in diameter were made with the help of cork borer. Then 50µL of the newly synthesized compound 2-**[(**3′-pyridyl)azo] quinazoline was added on each well. The plates were incubated at 37±2^{0}C for 24 hours at B.O.D incubator.

3. Results and Discussion:

The destination of azo compound is produced from mixed N-heterocyclic compound, by the reaction between3-diazoniumpyridine salt with alkaline solution of quinazoline compound. Pure crystalline reddish-brown compound is obtained after the chromatographic separation of crude product. Finally, the compound is characterized by the experimental supporting spectral data such as IR, UV-Vis, ^{1}HNMR and also Elemental analysis data. Antimicrobial activity of the newly synthesized compound was also done on both Gram positive, Gram negative bacteria.

3.1. Spectroscopic recitation of 2-[(3′-Pyridyl)azo)]quinazoline:

All the spectral values of2-**[(**3′-pyridyl)azo]quinazoline is taken for determination of structural characterization after comparison with the spectral values of pure quinazoline and 3-amino-pyridine compounds. The FTIR spectral data reveals the distinct absorption bands at 1438cm^{-1}and 1585cm^{-1}indicate the stretching vibration of –N=N- group and –C=N- group.

Investigation of UV-Visible spectra in methanol solution of the synthesized compound produce three absorptions bands at four different wavelengths. Sharp intense absorption band at 220nm indicate the n-π* transition. Another moderately broad band seem at the region 255nm- 288nm which express the π-π*transition into quinazoline. A little peak with low absorption band is invented at the 332nm-359nm region, it implies the π-π*transition in pyridine ring. Lastly, a broad and low intense absorption band appear at 445nm-490nm wavelength which indicates for the presence of –N=N- group.

The ^{1}HNMR spectra of the 2-**[(**3′-pyridyl)azo]quinazoline gives comparatively strong sharp peak at the chemical shift position 8.69ppm which imply the C_4-H proton in the quinazoline moiety. Multiple peaks at the region 8.0-8.3ppm indicate the $C_{2,4,5,6}$-H's of pyridine ring. We could not search out any peak at the chemical shift position 9.41ppm indicate the absence of C_2-H in the quinazoline moiety. Presence of fused benzene ring with pyrimidine ring is identified by the presence of multiple peak at the chemical shift position 7.4ppm-8.05ppm($C_{6,7}$-H doublet of doublet; $C_{5,8}$-H doublet). Linkage betweenC_2 of quinazoline and C_3 of pyridine through azo(–N=N-) group leads to overall blue-shift of the synthesized compound compared to the chemical shift value of the pure quinazoline and pyridine molecules[XVI].

3.2. Investigation of antibacterial activities on 2-[(3′-Pyridyl)azo)]quinazoline:

After 24hrs. incubation, the inhibition zone of the synthesized compound against tested bacteria was measured by an antibiotic zone scale. The Zone Diameter Inhibition (ZDI) values [Mean(±S.D)] of the synthesized compound 2-**[(**3′-pyridyl)azo]quinazoline against gram positive bacteria *Bacillus megaterium* and *Bacillus subtilis* were[20.7(±1.24)] and [17(±0.81)] respectively. Bacterium *Streptococcus aureus* was found to be resistant against the tested compound. Whereas ZDI values of gram negative bacteria as *Pseudomonas*

fluorescence, *Enterobacteraerogens* and *Schigellaflexner* were [18(±0.81)], [15(±0.81)] and [13.3(±1.24)] respectively (**Table-1**). The ZDI values of the tested bacteria against synthesized compound2-**[(**3′-pyridyl)azo]quinazoline at 500µg/ml concentration were compared with ZDI values of the tested bacteria against standard antibiotic Kanamycin at a concentration of 30µg/disc and represented in **figure-2**.

Table-1: Antimicrobial Activity of 2-[(3′-Pyridyl)azo)]quinazoline

Name of Bacteria		**Zone of inhibition (mm) (Mean±SD)**	
		Kanamycin (30µg/disc)	**2-[(3′-pyridyl)azo]quinazoline (500µg/mL)**
Gram positive	*Bacillus megaterium*	15.3(±0.47)	20.7(±1.24)
	Bacillus subtilis	-	17(±0.81)
	Streptococcus aureus	12.7(±1.24)	-
Gram negative	*Pseudomonas fluorescens*	18(±0.81)	18(±0.81)
	Enterobacteraerogenes	13.7(±1.24)	15(±0.81)
	Schigellaflexneri	17(±0.81)	13.3(±1.24)

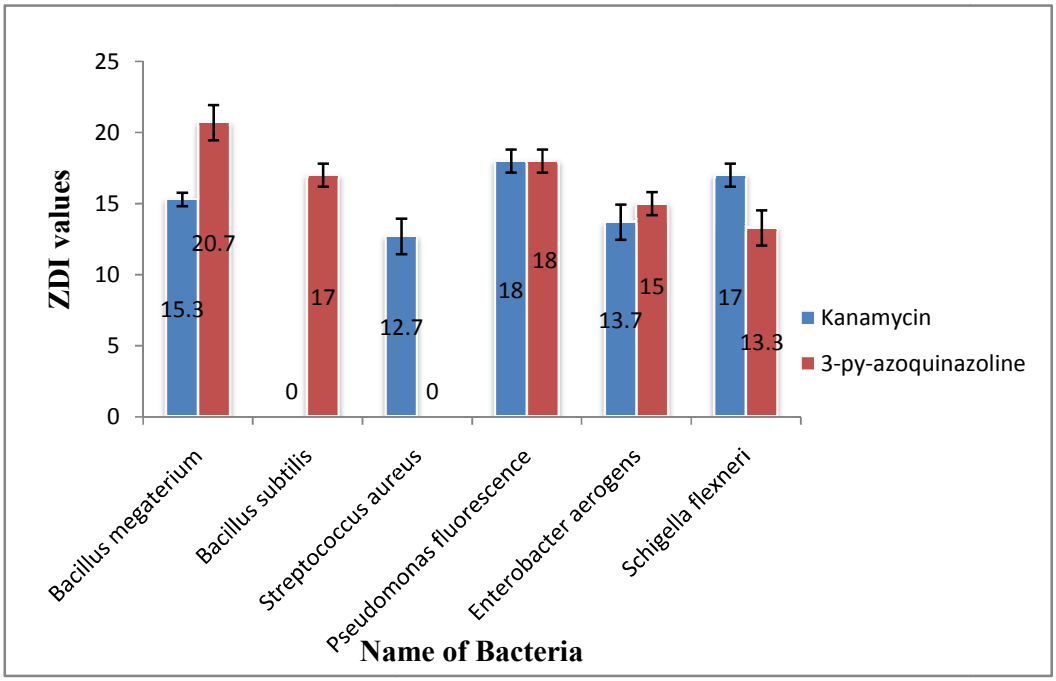


Figure-2: ZDI values of Kanamycin and 2-[(3′-Pyridyl)azo)]quinazoline against tested bacteria.

4. Conclusion:

Investigation and searching motivated for synthesized a new powerful biological active unsymmetrical bi-heterocyclic 2-**[(**3′-pyridyl)azo]quinazoline compound. Here also important distinguishing features come out positive movement in the study of antimicrobial activities on both the gram positive and gram negative bacterial strain. Such activities of the synthesized compound can inspire further studied for application in medicinal purposes.

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References:

I. Mathur, T.;Seal,M.;Chatterjee,S.N.; Saha,N.C.Heterocyclic Letters.**2017,**7, 1121.

II. a)Devi,K. A.;Sriram,M.S.International journal of Drug development and Research.**2012,**4, 324. b)Amar, M.A.; Alaa, A. M.; Abdel, A.; Taghreed Z. S.; Rezak R. A.;Al-abaid,A. M.; Mohamed, H. M.; Alagami, A. R.; Maarouf, A.;El-Azab,S.Journal of enzyme inhibition and medicinal chemistry.**2015,**31,721.c) Patel, D. J.; Patel,A. K. M.; Pandya, K. S.Der Chemica Sinica.**2014,**5, 37.

III. a)All-Gamal-Al-Kal-Anas, A. A. M.; Hammed, A.; Azeddine, I.; Abdul-Malik, A. Research in Pharmacy and Health Sciences.**2016,**2, 227.b) Bule,M. H.;Ahmed, I.; Maqbool, F. and Zia, M. A. International journal of pharmacology.**2017,**13, 818.

IV. a)Osaru, -M.W.Continental. J. Applied Sciences.**2017,**12, 29. b) Sheorey, R V.; Thangathiruppathy, A.; Alagarsamy, V. Trop.Journal Pharm.Res.; **2013**,12, 583-89.

V. a)Maner, A. El-H.; Manal, M. E.; Eman, A. R.; Sanaa, N.Synthetic communication. **2015,**45,2240.b) Arora, S.; Nagori, B. P.International Research journal of pharmacy. **2014,** 5, 476.

VI. a) EL-Feky, S.A.;Mohd, I.; Naycem, N. Oriental journal of Chemistry.**2017,**33, 707. b) Abuelizz, HA.; A.;Hassane, AE.; Marzouk, M.; Ezzeldin, E.; Ali, AA.; Al- Salahi R. Future Medicinal Chemistry.**2017,**9, 17.

VII. Patil, A.; Ganguly, S.; Surana, S. J.Chem.Sci.**2010,**122, 443.

VIII. Georgey,H.;Abdel- Gowad, N.; Abbas, S. molecules.**2008,**13, 2557.

IX. a) Pathak,S. R.; Malhotra,V.; Nath,R.;Shanker, K.Central Nervous system agents in medicinal Chemistry.**2014,** 14, 34.b)Rahman,MU.; Rathore,A.; Siddiqui,A. A.; Parveen, G.; Shahar, Yar M.BioMed Research International; **2014,** 2014, 739056.

X. a) Srivastav,M. K.; Shamshuddin,Md.; Shantakumar, S.M.American journal of Chemistry; **2013,** 3, 14.b) Alam, Md.J.; Alam, O.;Alam M. P.International journal of Advance research; **2015,**3, 1656.

XI. a) Rakesh, K.R.; Darshini, N.; Shubhavathi, T.; Mallesha, N. Organic and medicinal Chemistry; 2017, 2, 1. b) Selvam, T. P.; Kumar, P. V. Drug discovery and Therapeutics. **2010**, 4, 392.

XII. a)Alagarsamy, M. G. V.Journal of Saudi Chemical Society. **2015,**19, 282. b) Alagarsamy, V.; Giridhar, R.; Yadav, M. R. Journal of Pharmacy and Pharmacology. **2010,**58, 1249.

XIII. a) Venugopala, K. N.; Nayak, S. K.; Gleiser, R. M.; Sanchez-Borzone, M. E.; Garcia, D. A.; Odhar, B. Chemical Biology and Drug Design. 2016, 88, 88. b) Wu, J.; bai, S.;

Yue, M.; Luo, Li-. J.; Shi, Q. C.; Ma, J.; Du, Xi. Li.; Kang, S. H.; Hu, D.; Yung, S. Chemical Papers. **2014**, 68, 969.

XIV. a) Otutu, J.O.; Efurhievwe, E. M. Journal of Applied Sciences. **2013**, 13, 924. b) El-Hashash, M. A.; Darwish, K.M.; Rizk, S. K.; El-Bassiouny, F. A. Organic Chemistry International. **2011**, 2011, 205491.

XV. a) Sumathy, A.;Palamsamy, S. Global Journal of Pharmacy & Pharmaceutical Science. **2017**, 3, 1. b) Abuelizz, H. A. Marzouk, M.; Ghabbour, H.; Al-Salahi, R. Saudi Pharmaceutical Journal. 2017, 25, 1047.

XVI. Huang,C.; Fu,Y.; Fu,H.; Jiang, Y.; Zhao, Y. Chemical Communication.**2008,**47, 6333.

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