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SYNTHESIS OF DERIVATIVE OF PYRIDINE-3-CARBONITRILE AND EVALUATE THEIR ANTIBACTERIAL ACTIVITY

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ABSTRACT
Pyridine the simplest and perhaps is the best-known heterocyclic compound. Pyridine ring system is highly distributed in nature as pyridine derivatives and in many important alkaloids. The pyridine nucleolus was found in a large number of commonly used drugs, which have diverse pharmacological activities. Interest in the synthesis of pyridine containing compounds has been synthesis namely Synthesis of 2-amino-4-(2-Chlorophenyl)-6-{4-[3-chloro-2-(4 hydroxyphyenyl)-4-oxoazetidin-1-yl] phenyl} pyridine-3-carbonitrile and evaluate their antibacterial activity against *Escherichia coli*, *P.Aeruginosa*, *S. aureus* and *S. pyogenes* microorganism. The result revealed the derivative of Pyridine-3-carbonitrile has been shown good activity against these bacteria. Pyridine is the parent compound of the series of compounds that is important in pharmaceutical, agriculture and industrial chemistry.

KEY WORD- heterocyclic, pyridine-3-carbonitrile, Pyridine derivative etc.

INTRODUCTION
The general structure of heterocycles is similar to that of cyclic organic compounds, which have only carbon atom in their structure, but the substitute of one or more carbon atoms by heteroatoms gives heterocycles physico-chemical properties that are distinct from those of all carbon ring analogs. Heterocycles involve a wide range of uses, including agrochemical, medicinal, and veterinary. Such compounds are also used in sanitizers, antioxidants, copolymers, corrosion inhibitors, dyestuff, *etc*. Heterocycles are currently employed in the production of a wide range of organic chemical substances. Several compounds, mostly of natural origin, such as alkaloids, morphine, vinblastine, and reserpine, and a variety of antibiotics, such as cephalosporin, penicillin, and others, include heterocyclic components.

Most of these derivatives are prepared by manipulation of pyridine and its simple homologues in a manner similar to chemistry of the benzenoid chemistry. However the simple pyridine compounds are prepared by the Cyclization of aliphatic raw materials.

Pyridine with different functional groups, Although many substituted pyridine compounds like other heterocyclic compounds are synthesized with their functional group present in cyclic compounds. The availability of 3- cyanopyridines, nicotinamide and nicotinic acid make possible their use as synthetic intermediates. The extensive use of cyanopyridine derivatives have been established in medicine due to its antihypertensive, anticholestemic, antidiabetic, antifungal and antibacterial properties. Streightoff (1) and Seydel (2) have studied the bacterio static effect of some substituted 3-cyanopyridines. J. A. Van Allan et al. (3) have prepared fused heterocyclic 3-cyanopyridine.

Barton et al. (4) have reported fungicidal and insecticidal properties of cyanopyridines. J.J.Baldwin (5-7) has prepared cyanopyridines exhibiting antihypertensive activity. V. Scott and E. Joseph (8-9) have prepared 2-amino-3- cyanopyridine derivatives which were found to be useful as antipsoriasis. Miertus et al. (10) ynthesized 2-formyl 3-cyanopyridine thiosemicarbazones as a

carcinostatic agent. S. S. Verma et al. (11) and M. D. Ankhiwala (12) have synthesized 2-amino-3-cyano-2, 6- disubstituted pyridines and studied their biological activities. F. Manna et. al. (13) has prepared 3-cyanopyridine derivatives. Gadaginamath and co-workers (14) have synthesized various cyanopyridine derivatives and documented their biological activities.

The insecticidal activities of cyanopyridines have been screened by Y. Sasaki (15) and co workers. Pankaj Patel & co-workers (16) have synthesized cyanopyridines and evaluated their biological activity. Umed Ten et al. (17) have prepared cyanopyridines as agro fungicides.

The oxide activator bleaching activity of cyanopyridine has been proved by Rees W. M. (18) Oshida M. (19) prepared cyanopyridine derivatives, which inhibited cerebral edema and delayed neuron death. Hence, they are useful as cerebral edema inhibitors or cerebrovascular disorder remedies. S. Guru et al. (20) have synthesized various cyanopyridine derivatives and documented their multiple biological activities.

Some other new cyanopyridine derivatives are reported for their cholinesterase inhibitors, (21) antihistaminic and adrenergic, (22) herbicidal, (23) anti-inflammatory (24) & insecticidal (25) activities.

H. Yoshida et al. (26) have studied the antihistaminic & Antiallergic activity of 3-cyanopyridine derivatives. John A. Tucker et al. (27) have synthesized novel piperazinyl oxazolidinone containing cyanopyridine as an antibacterial agent.

MATERIAL AND METHOD

Synthesis of 2-amino-4-(2-Chlorophenyl)-6-{4-[3-chloro-2-(4 hydroxyphyenyl)-4-oxoazetidin-1-yl] phenyl} pyridine-3-carbonitrile

Chalcone 0.011 Mole dissolved in 37alcohol, then 0.011 Mole of malano nitrile and 0.06 Mole of ammonium acetate 7 h refluxed. Then resulting cooled. filtered, washed by H_2O, dried and recrystallized by ethanol. The % yield and melting point was determined. The compound has been characterized by elemental analysis and IR Spectroscopy.

Antibacterial activity

Disc diffusion method was used for antibacterial activity. A stock solution of extract was prepared by dissolving 0.1 g of extract with 100 mL of their respective solvents (distilled water and absolute ethanol) to produce a final concentration of 100 mg/mL. The stock solution was then diluted to concentrations of 2.5, 5, 10, 20, 50, and 100 mg/mL of extract. 20 µL of each dilution was impregnated into sterile, blank discs 6 mm in diameter. 5 µL of extract was spotted alternately on both sides of the discs and allowed to dry before the next 5 µL was spotted to ensure precise impregnation. Distilled water and ethanol-loaded discs were used as negative controls for aqueous and ethanol extracts, respectively. All discs were fully dried before the application on bacterial lawn. Antibacterial activity was evaluated by measuring the diameter of the inhibition zone (IZ) around the discs. The assay was repeated trice. Antibacterial activity was expressed as the mean zone of inhibition diameters (mm) produced by the synthesized compound. The following bacterial culture used for antibacterial activity namely *Escherichia coli* (MTCC– 443), *P.Aeruginosa* (P.Aeruginosa MTCC-1688), *S. aureus* (MTCC-96) and *S. pyogenes* (MTCC-442).

RESULT AND DISCUSSION

Table -1 Physical Constant of Compound

R	M.F.	M.W.	%	ºC	% C		%N		% H	
					F	Calcd	F	Calcd	F	Calcd

-2-Cl	$C_{27}H_{18}Cl_2N_4O_2$	501.36	68	215	64.63	64.68	11.14	11.17	3.59	3.62

Table -2 IR Interpretation of Compound

Part	>NH-	-OH	=C-H	-C□□	>C=O (Stretch)	>C=N- (Stretch)	>C=C< aromatic	C-N	C-Cl
Frequency (cm^{-1})	3440	3330	3045	2240	1710	1625	1540	1285	655

Molecular Formula = $C_{27}H_{18}Cl_2N_4O_2$
Formula Weight = 501.36
Composition Required = Carbon (64.68%) Hydrogen (3.62%) Nitrogen (11.17%)
Composition Founded = Carbon (64.63%) Hydrogen (3.59%) Nitrogen (11.14%)

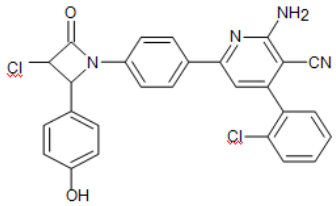

Figure-1 Structure of Synthesized compound

The Percentage of yield was 68% and M.P. of the Product at 215 °C. It is found that the synthesized compounds belonging to Chalcone derivatives show good activity against *E.coli* but are less active or inactive against *S.aureus*. They are also found to give fine activity against S. pyogenes and *S. pyogenes*. Overall evaluation of the synthesized compounds suggests their very good to good/moderate biological activity as compared to the standard Drugs.

Overall analysis of the Results suggests that compounds numbered as compound showed good antibacterial activity than the standard test-Drugs used for bio-assay.

CONCLUSION

On continuation of our interest to synthesis the heterocyclic compounds, the present work is focused on synthesis of some novel heterocyclic derivatives and to evaluate for their various biological activities. The rate at which heterocyclic compounds continue to be invented testifies to the strength and vitality of this area of medicinal chemistry. Keeping this mind the challenges of discovering new heterocyclic systems and study of their properties and also investigate their applications in medical field. Overall analysis of the Results suggests that compounds numbered as compound showed good antibacterial activity than the standard test-Drugs used for bio-assay.

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