



## BIOLOGICAL ACTIVITIES OF SOME SUBSTITUTED N-HETEROCYCLIC MOLECULES

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### ABSTRACT

*The antifungal activity of some substituted N-heterocyclic molecules have been observed and discussed. The antifungal activity of 2-benzylamino-4-methylpyridine, 2-chloro-6-methoxypyridine and 4-amino-3,5-dichloro-2,6-difluoropyridine have been evaluated at different concentrations against Aspergillusflavus, Aspergillusniger,Aspergillusfumigatus and Rizopus by Growth method. This study become more relevant in view of that such acitivites have an important role in the field of toxicology.*

**Keyword:** *4-Amino-3, 5-Dichloro-2,6-Difluoropyridine, Antifungal Activity, 2-Benzylamino-4-Methylpyridine, 2-Chloro-6-Methoxypyridine, Toxicology.*

### I. INTRODUCTION

Fungi may cause many infections in plants , e.g. blights , midlews, leaf spots, galls, rusts, smuts etc. in contrast, they have rare infections on animals and human beings. Fungal toxins[1] are widely distributed in nature causing a wide range of effects on living beings, some of these are very harmful. A variety of both inorganic [2] and organic [3,4] compounds have been reported to possess antifungal property. Various organic compounds containing nitrogen, oxygen and sulphur are known to possess antifungal activity[5,6,7]. Organic compounds having sulphur, chlorine and fluorine are good fungicides [8]. Various heterocyclic compounds such as imidazoline, thiozoline, condensed oxazoles and a few 2-aminothiozoles have been found to possess good fungicidal activity [9,10,11].

### II. EXPERIMENTAL

The antifungal activitiy of 2-benzylamino-4-methylpyridine, 2-chloro-6-methoxypyridine, 4-amino-3,5-dichloro-2,6-difluoropyridine have been evaluated at different concentrations against Aspergillusflavus, Aspergillusniger ,Aspergillusfumigatus and Rizopus by Growth method [12] Which consist of following steps :



## 2.1 Preparation of Czapek'sDox Agar medium

Czapek'sDox Agar medium [13] was prepared by dissolving the following compounds in the quantity mentioned against each in one litre double distilled water in a beaker.

Compound	quantity(gms)
Sodium nitrate	2.00
Potassium dihydrogen phosphate	1.0
Magnesium sulphate	0.50
Potassium chlorite	0.50
Ferrous sulphate	0.01
Sucrose	30.0
Agar-Agar	150

The beaker was autoclaved at 10-15 lbs pressure for about half an hour. The hot medium was filtered. The test solutions of 2-benzylamino-4-methylpyridine, 2-chloro-6-methoxypyridine and 4-amino-3,5-dichloro-2,6-difluoropyridine were prepared by dissolving appropriate amount in double distilled water.

### 1.1 Measurement of fungal growth

Czapek'sDox Agar medium was divided into ten equal parts of 100 ml each and poured into 500 ml conical flasks. Now the solution of different concentrations of the compounds were added into nine flasks, while one flask serves as the control set containing zero concentration of the test compound.

All the ten flask were tightly closed with sterilized cotton and autoclaved at 15 lbs pressure for about 15 minutes. Their content were poured into 50×70 mm sterilized petridishes (borosil) keeping three replicates of each treatment. Thus, three petridishes were required for the contents of one flask. So, in all, 30 petridishes were needed at a time for one fungus for one compound. When the contents of the dishes solidify, they were inoculated with the respective fungus for about 168 hours at  $27 \pm 1^\circ\text{C}$ .

The growth of test fungi have been measured in terms of colony diameter from each petridishes. The diameter of 20 colonies have been measured. The values from the three replicates give the average colony diameter at the given concentration. The percentage inhibition has been then calculated as follows:

$$\% \text{ inhibition} = [(C-T)/C] \times 100$$

Where C and T are average diameter (in ml) of fungus colony in check set and treated set, respectively.

## III. RESULTS AND DISCUSSION

Most fungi are completely resistant to the action of antimicrobial drugs. Only a few substances have been discovered which exerts an inhibitory effect on the fungi pathogenic for man and most of these are relatively toxic. Consequently, spurred by the need of new antifungal agents and the fact that many effective antimicrobial drugs possess heterocyclic systems in their structure. We observed the antifungal data of the compounds 2-benzylamino-4-methylpyridine, 2-chloro-6-methoxypyridine and 4-amino-3,5-dichloro-2,6-difluoropyridine are given in tables-1,2,3 respectively. The growth of fungi are given in figure- 1,2,3 at different concentrations for the said compounds.



**3.1 Antifungal activity**

Antifungal data of the compounds 2-benzylamino-4-methylpyridine, 2-chloro-6-methoxypyridine and 4-amino-3,5-dichloro-2,6-difluoropyridine have been observed (tables1,2,3) against *Aspergillusflavus*, *Aspergillusniger*, *Aspergillusfumigatus* and *Rizopus* at varying concentrations (0.005% to 0.050%).

The observations show, that in case of of 2-benzylamino-4-methylpyridine, 2-chloro-6-methoxypyridine and 4-amino-3,5-dichloro-2,6-difluoropyridine molecules, the antifungal growth were effected with the addition of the compounds. The percentage inhibition is directly proportional to the concentration of the compound upto a optimum value (MIC) i.e. the compound has minimum toxic effect at low concentration while maximum at high concentration.

It is evident from the present findings, that all the three compounds are antifungal agents. The compound 4-amino-3,5-dichloro-2,6-difluoropyridine has maximum antifungal effect on *Aspergillusflavus*, *Aspergillusniger*, *Aspergillusfumigatus* and *Rizopus*.

**Table 1 fungicidal data of 2-benzylamino-4-methylpyridine**

Name of Fungi		Concentration of Compounds(%)											
		0	0.005	0.01	0.015	0.02	0.025	0.03	0.035	0.04	0.045	0.05	MIC
Af	D	4.72	4.28	3.86	3.5	3.16	2.82	2.48	2.14	1.8	1.45	1.1	0.654
	I	0	9.32	18.22	25.85	33.05	40.25	47.46	54.66	61.86	69.28	76.69	
An	D	4.82	4.5	4.25	3.9	3.6	3.35	3	2.75	2.4	2.15	1.85	0.08
	I	0	6.63	11.82	19.08	25.31	30.49	37.75	42.94	50.2	55.39	61.61	
As	D	0.62	0.58	0.56	0.53	0.5	0.47	0.45	0.42	0.39	0.37	0.34	0.1
	I	0	6.45	0.67	14.51	19.35	24.19	27.41	32.25	37.09	40.32	45.16	
Rz	D	4.6	4.26	3.92	3.56	3.2	2.9	2.55	2.2	1.86	1.54	1.2	0.67
	I	0	7.39	14.78	22.61	30.43	36.96	44.57	52.17	59.57	66.52	73.91	

- Where,
- D == Diameter of fungi colony
  - I == % Inhibition
  - Af == *Aspergillusflavus*
  - An == *Aspergillusnigar*
  - As == *Aspergillusfumigatus*
  - Rz == *Rizopus*

**Table 2 fungicidal data of 2-chloro-6-methoxypyridine**

Name of Fungi		Concentration of compounds(%)											
		0.000	0.005	0.010	0.015	0.020	0.025	0.030	0.035	0.040	0.045	0.050	MIC
Af	D	4.72	2.83	2.62	2.45	2.21	2	1.73	1.47	1.1	0.89	0.65	0.062
	I	0	40.04	44.49	48.09	53.17	57.62	63.34	68.85	76.69	81.14	86.23	
An	D	4.82	3.6	3.39	3.17	2.93	2.72	2.49	2.21	1.95	1.67	1.44	0.079
	I	0	24.48	29.66	35.47	39.27	43.56	48.34	54.14	59.54	65.35	70.12	
As	D	0.62	0.51	0.49	0.47	0.45	0.44	0.43	0.4	0.38	0.36	0.34	0.13
	I	0	17.74	20.97	24.19	27.42	29.03	30.65	35.48	38.71	41.93	45.16	
Rz	D	4.6	3.55	3.3	3.05	2.68	2.55	2.27	2	1.77	1.53	1.28	0.081
	I	0	22.83	28.26	33.7	41.74	44.57	50.65	56.52	61.52	66.74	72.17	

Where, D == Diameter of fungi colony

I == % Inhibition

Af == Aspergillusflavus

An == Aspergillusnigar

As == Aspergillusfumigatus

Rizopus

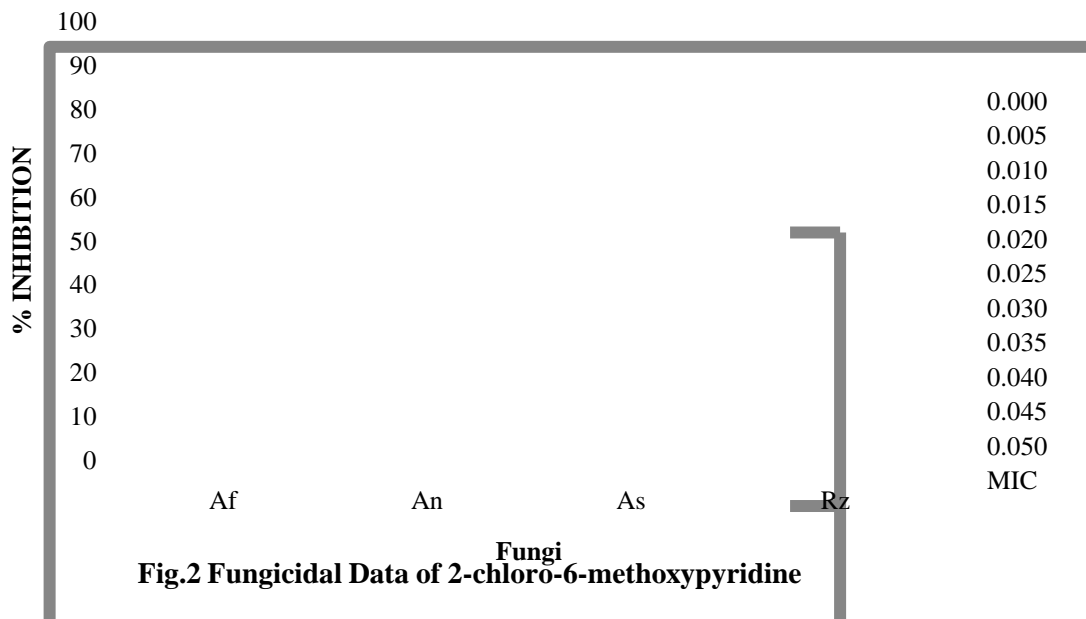
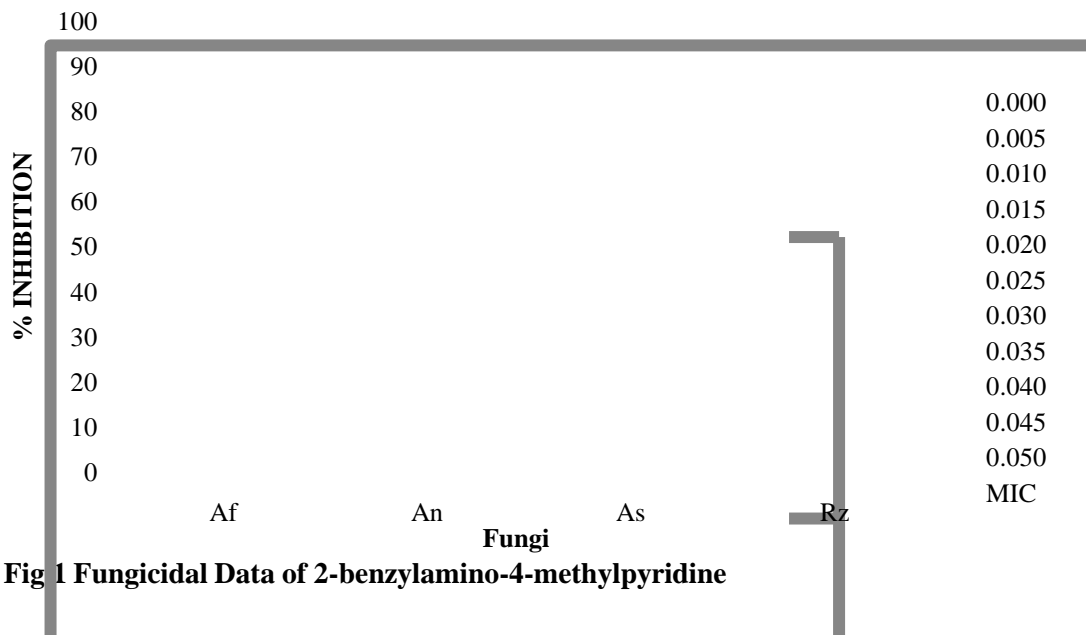
Rz ==

**Table 3 fungicidal data of 4-amino-3,5-dichloro-2,6-difluoropyridine**

Name of Fungi		Concentration of Compounds(%)											
		0	0.005	0.01	0.015	0.02	0.025	0.03	0.035	0.04	0.045	0.05	MIC
Af	D	4.72	1.62	1.46	1.24	1.03	0.83	0.62	0.4	0.2	0	0	0
	I	0	65.68	69.07	73.73	78.18	82.42	86.86	91.52	95.76	100	100	
An	D	4.82	2.47	2.35	2.22	2.1	1.98	1.85	1.73	1.61	1.5	1.39	0.11
	I	0	48.76	51.24	53.94	56.43	58.92	61.62	64.11	66.6	68.88	71.16	
As	D	0.62	0.35	0.31	0.28	0.25	0.22	0.18	0.15	0.1	0.08	0.05	0.06
	I	0	43.54	50	54.84	59.68	64.52	70.97	75.81	83.87	87.1	91.94	
Rz	D	4.6	2.07	1.98	1.87	1.76	1.68	1.57	1.48	1.39	1.22	1.15	0.1
	I	0	55	56.96	59.35	61.74	63.48	65.87	67.83	69.78	73.48	75	



- Where, D == Diameter of fungi colony  
 I == % Inhibition  
 Af == Aspergillusflavus  
 An == Aspergillusnigar  
 As == Aspergillusfumigatus  
 Rz == Rizopus



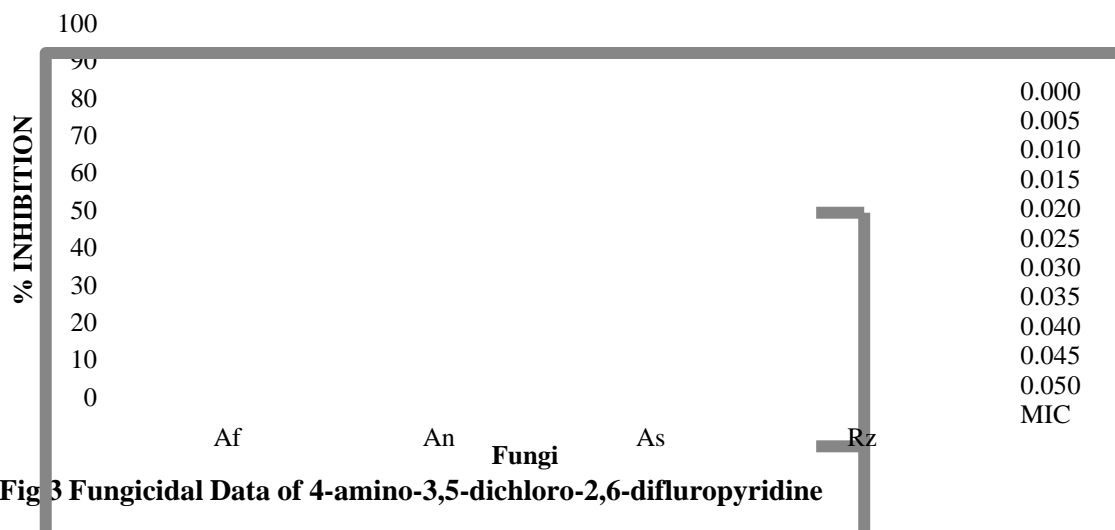


Fig 3 Fungicidal Data of 4-amino-3,5-dichloro-2,6-difluoropyridine

#### IV. CONCLUSION

Thus 2-benzylamino-4-methylpyridine, 2-chloro-6-methoxypyridine and 4-amino-3,5-dichloro-2,6-difluoropyridine compounds can be used as commercial fungicides. Out of these three compounds 4-amino-3,5-dichloro-2,6-difluoropyridine shows 100% antifungal effect on *Aspergillus flavus* and hence can be used as a powerful commercial fungicide.

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