

Synthesis and Pharmacological Evaluation of Novel Heterocyclic Compound

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Abstract— 2-[(4-bromo anilino)]-4-chloro-6-morpholino-1,3,5-triazine[2a] and 4-chloro-N-(4-fluorophenyl)-6-morpholino-1,3,5-triazin-2-amine [2b] were synthesized and studied for their biological activity. These compounds were prepared by the condensation of 4-bromoaniline and 4-fluoroaniline with 4-(4,6-dichloro-1,3,5-triazin-2-yl)morpholine [1] which is prepared by the reaction between 2,4,6-trichloro-1,3,5-triazine and morpholine. All the compounds were characterized by elemental analysis and spectral studies.

Key words: 2, 4, 6-trichloro-1, 3, 5-triazine derivative, 4-(4, 6-dichloro-1, 3, 5-triazin-2-yl)morpholine, morpholine, Antimicrobial activity

I. INTRODUCTION

Now a day's so many health hazards due to infectious problem by polluted environment have a wide range of microbes. The variety of microorganism makes different types of disease in the world. From this bacteria and fungi are in the special position in microbial list. Basically all synthetic drugs have some potential against the growth of microbes and that was reported at many articles in previous research. 2, 4, 6-trichloro-1, 3, 5-triazine derivatives exhibit a wide range of biological activities [1-15]. So the substituted triazine derivatives have a potential for against the microbes because of it contain more than one hetero atoms(O,N) and halogen atoms(F,Cl,Br) [16-18].

II. MATERIALS AND METHOD

All the chemicals were purchased from Alfa Aesar, A Johnson malthey company, shore road, Heysham, England. The purity of the derivatives was checked routinely by TLC (0.5 mm thickness) using silica gel and spots were visualized by exposing the dry plates in iodine. The melting points of the compounds were determined. ¹H NMR spectral data was done in PROBHD 5mm PABBO BB-PULPROG 500.12 FT MHZ using TMS as internal standard. IR spectra was recorded on FT-IR Bruker with KBr disc.

III. SYNTHETIC PROCEDURES

A. SYNTHETIC PROCEDURES

1) *Scheme:1* Preparation of 4-(4,6-dichloro-1,3,5-triazin-2-yl)morpholine:[1]

A solution of cyanuric chloride (1.844g, 0.01mol) in 100 mL of acetone was added with stirring to a cold solution (0-5°C) of morpholine(1mL,0.01mol) in acetone(10mL) and the pH is being maintained neutral by the addition of 10% sodium bicarbonate(0.85 g, 0.001mol)in 10 ml of distilled water in a three necked round bottom flask(250mL) equipped with a mechanical stirrer. The mixture was stirred for 3h at 0-5°C. The white precipitate was found in

solutions and it is filtered. The clear solution containing the product was get from slow solvent evaporation technique. The crude product was recrystallized using chloroform and the melting point was noted (135-138°C)[2].

2) *Scheme:2* Preparation of 2-[(4-bromoanilino)]-4-chloro-6-morpholino-1,3,5-triazine[2a]

4-bromo aniline(0.344g, 0.002mol) in methanol (10mL) was added to the solution of 4-(4,6-dichloro-1,3,5-triazin-2-yl)morpholine (0.469g, 0.002 mol) in methanol(10 mL) in hot condition in round bottom flask(100mL) fitted with reflux condenser and maintaining the temperature 70 °C and the stirring was continued up to 30 hrs. After completion of reaction the white precipitate was found. The crude sample was washed and recrystallized by using methanol and the melting point was noted (284-287 °C).

3) *Scheme:3* Preparation of 4-chloro-N-(4-fluorophenyl)-6-morpholino-1,3,5-triazin-2-amine[2b]

To a stirred solution of 4-fluoro aniline(0.23mL, 0.002mol) in methanol (10mL) was added to the solution of 4-(4,6-dichloro-1,3,5-triazin-2-yl)morpholine (0.469g, 0.002 mol) in methanol(10 mL) in hot condition in round bottom flask(100mL) with reflux condenser with water circulation maintaining the temperature at 70 °C and the stirring was continued up to 19 hrs. After completion of reaction the white precipitate was found. The crude sample was washed and recrystallized by using methanol and the melting point was noted (261-263 °C).

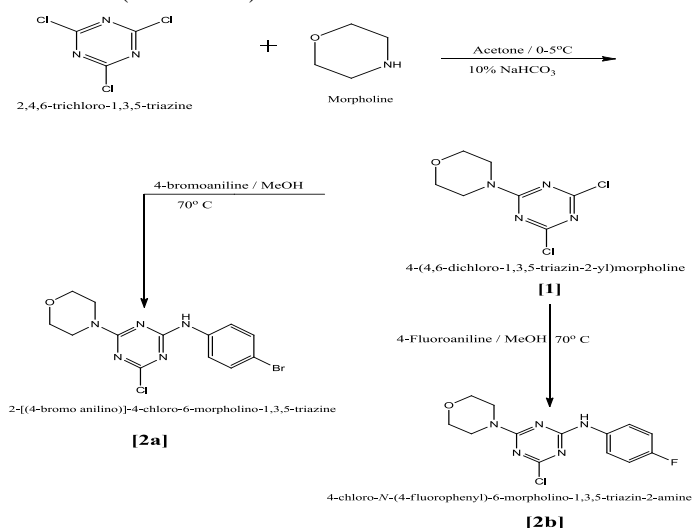


Fig.1: Mechanism

B. SPECTRAL DATA

1) 4-(4,6-dichloro-1,3,5-triazin-2-yl)morpholine:[1]

Yield 80%; mp: 138 °C; FT-IR[v, cm⁻¹, KBr]: 1615(-C=N), 1072(-C-N), 632(-C-Cl), 786(-CH), 1234(C-O-C), 1581(C-C), 2862(-C-CH₂).

¹H NMR[500MHz, δ, ppm,

CDCl₃]: 3.61(4H,s,-OCH₂), 3.76(4H,S-NCH₂): MS: m/z. 234.34 with70% relative intensity[M+].

2) 2-[(4-bromoanilino)]-4-chloro-6-morpholino-1,3,5-triazine[2a]

Yield 70%; mp: 138 °C;FT-IR[v, cm⁻¹,KBr]: 1615(-C=N),1072(-C-N),501(-C-Br),540(-C-Cl),770(-CH),1200(C-O-C),1543(C-C),2854(-C-CH₂),3309(-NH). ¹H NMR[500MHz, δ, ppm, MeOD]:3.67 (4H,s,-OCH₂), 3.78(4H,S,-NCH₂), 4.02(1H,S-NH), 7.06(4H,S,-CCH₂), 7.38(4H,S,-BrCH₂): MS m/z. 367.67 with70% relative intensity[M+].

3) 4-chloro-N-(4-fluorophenyl)-6-morpholino-1,3,5-triazin-2-amine[2b]

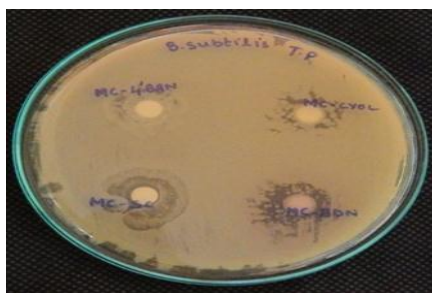
Yield 65%; mp: 138 °C;FT-IR[v, cm⁻¹,KBr]: 1627(-C=N),1064(-C-N),547(-C-Cl),1026(-C-F),771(-CH),1219(C-O-C),1535(C-C),2816(-C-CH₂). ¹H NMR[500MHz, δ, ppm, MeOD]: 3.68 (4H,s,-OCH₂), 3.76(4H,S,-NCH₂), 4.04(1H,S-NH), 7.09(4H,S,-CCH₂), 7.31(4H,S,-BrCH₂): MS : m/z. 310.01 with75% relative intensity[M+].

C. Anti-Microbial Study

The synthesized compounds were also tested for their antibacterial, antifungal and anti-oxidant activity in table 1, table 2 ,table 3, figure1, figure 2, figure 3 and figure 4.

S.N O	NAME OF ORGANISM	CONTRO L	MC-4BA N [2a]	MC-4FA N [2b]	M C [1]
1	S.aureus	18	21	25	12
2	P.aeruginosa	17	18	27	8
3	K.pneumonia e	17	20	23	7
4	E.coli	18	22	23	8
5	B.substilis	15	21	17	9

Table 1: Anti-Bacterial Study: (Concentration 40µl)
MC 4BAN & MC 4FAN = Compound[2a] & [2b]



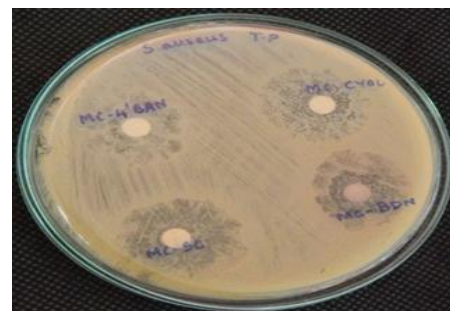
(B.substilis)



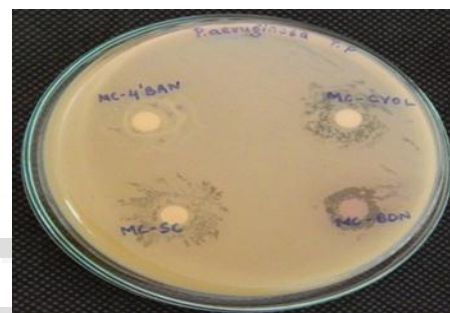
(K.pneumoniae)



(E.coli)



(S.aureus)



(P.aeruginosa)

Fig. 2: Photocopy Evidence for Bacterial Activity of compound [2b = MC 4FAN]

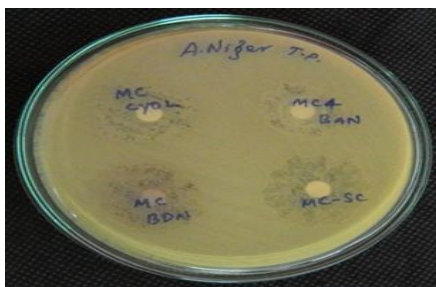
S.N O	NAME OF ORGANIS M	CONTRO L	MC-4BA N [2a]	MC-4FA N [2b]	M C [1]
1	A.niger	18	25	22	7
2	Aspergillus	18	18	25	7
3	C.albicans	18	22	25	8
4	C.lunata	20	17	21	7
5	T.simii	19	18	28	7

Table 2: Anti-fungal Study: (concentration 40µl)

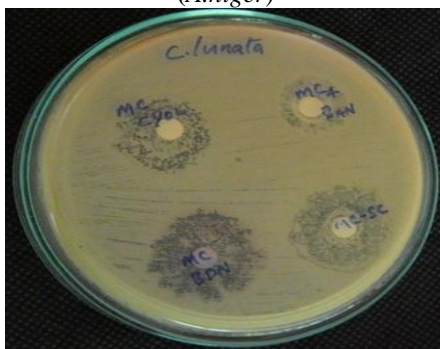
*MC 4BAN & MC 4FAN = Compound[2a] & [2b]



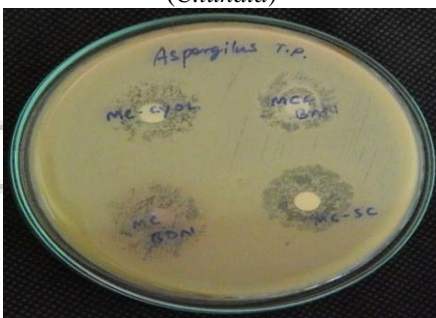
(C.albicans)



(*A.niger*)



(*C.lunata*)



(*Aspergillus*)

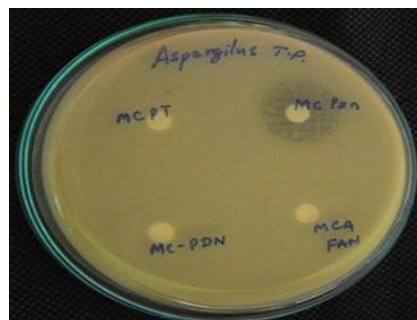


(*T.simii*)

Fig. 3: Photocopy Evidence for Fungal Activity of compound [2a = MC 4BAN]:



(*C.lunata*)



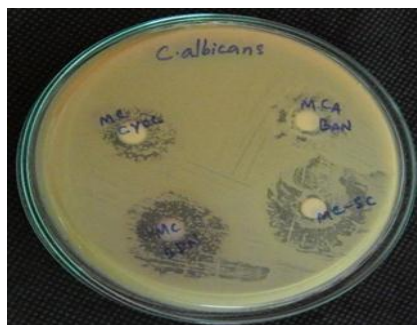
(*Aspergillus*)



(*T.simii*)



(*A.niger*)



(*C.albicans*)

Fig. 4: Photocopy Evidence for Fungal Activity of compound [2b = MC 4FAN]

The percentage of Inhibition has been shown in table 3
The percentage of inhibition at different concentration.

S.No	Conc	% Inhibition
1	31.25	48.35
2	125	57.61
3	500	69.05
4	1000	78.43

Sample code: MC

S.No	Conc	% Inhibition
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1	31.25	40.12
2	125	48.25
3	500	58.37
4	1000	67.01

Sample code: MC 4BAN

S.No	Conc	% Inhibition
1	31.25	39.27
2	125	49.13
3	500	58.96
4	1000	68.75

Sample code: MC 4FAN

Table-3: Anti-Oxidant study

IV. CONCLUSION

The anti-bacterial, anti-fungal and anti-oxidant activity of 4-(4,6-dichloro-1,3,5-triazin-2-yl)morpholine, 2-[(4-bromoanilino)]-4-chloro-6-morpholino-1,3,5-triazine[2a] and 4-chloro-N-(4-fluorophenyl)-6-morpholino-1,3,5-triazin-2-amine[2b] were studied. The results showed that the synthesized compounds have high antimicrobial and antioxidant activity because of the presence of halogen (Cl, Br and F) groups in phenyl ring system.

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