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SYNTHESIS AND PHARMACOLOGICAL EVALUATION OF NOVEL HETEROCYCLIC COMPOUND

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ABSRACT

4-(4-chloro-6-(piperazin-1-yl)-1,3,5-triazin-2-yl) morpholine **[2a]** and 4-(4-chloro-6-(piperidin-1-yl)-1,3,5-triazin-2-yl) morpholine **[2b]** were synthesized and studied for their biological activity. These compounds were prepared by the condensation of Piperazine and Piperidine 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.

KEYWORDS: 2,4,6-trichloro-1,3,5-triazine derivative, 4-(4,6-dichloro-1,3,5-triazin-2-yl) morpholine, Morpholine, Anitimicrobial activity.

INTRODUCTION

The Antioxidants are very important and essential for all living things in our world. It's the important component that preserve our body cells from the deactivate due to unstable free radicals molecule. The free radicals make some damage, decompose and cancer cells. The Antioxidant is present in all natural materials like vegetables, fruits and all types of meats. Some time the natural Antioxidant is not sufficient for human body and we need some synthetic materials also. In that way s-triazine compounds has been studied effectively in verity of reviews best for Antioxidant nature. 2,4,6-trichloro-1,3,5-triazine derivative exhibit a wide range of biological activities.[1,2,3,4,5] 2,4,6-trichloro-1,3,5-triazine derivative exhibits such as anti bacterial, anti fungal[6-15], anti oxidant [16,17,18] activities. In the study, the anti microbial activities of novel synthesized s-triazine derivatives have been discussed.

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 point of the compounds were determined. ^{1}H 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.

SYNTHETIC PROCEDURES

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^{o}C) of morpholine (1ml, 0.01mol) in acetone (10mL) and the $_{P}$H 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^{o}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^{o}C).[2]

Scheme: 2

Preparation of 4-(4-chloro-6-(piperazin-1-yl)-1,3,5-triazin-2-yl)morpholine:[2a]

Piprazine (0.18g, 0.002mol) in methanol (10ml) was added 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 at 65^{o}C and the stirring was continued up to 18 hrs. After completion of reaction the white colour precipitate was found. The crude sample was washed and recrystallized by using chloroform and the melting point was noted (251-253^{o}C).

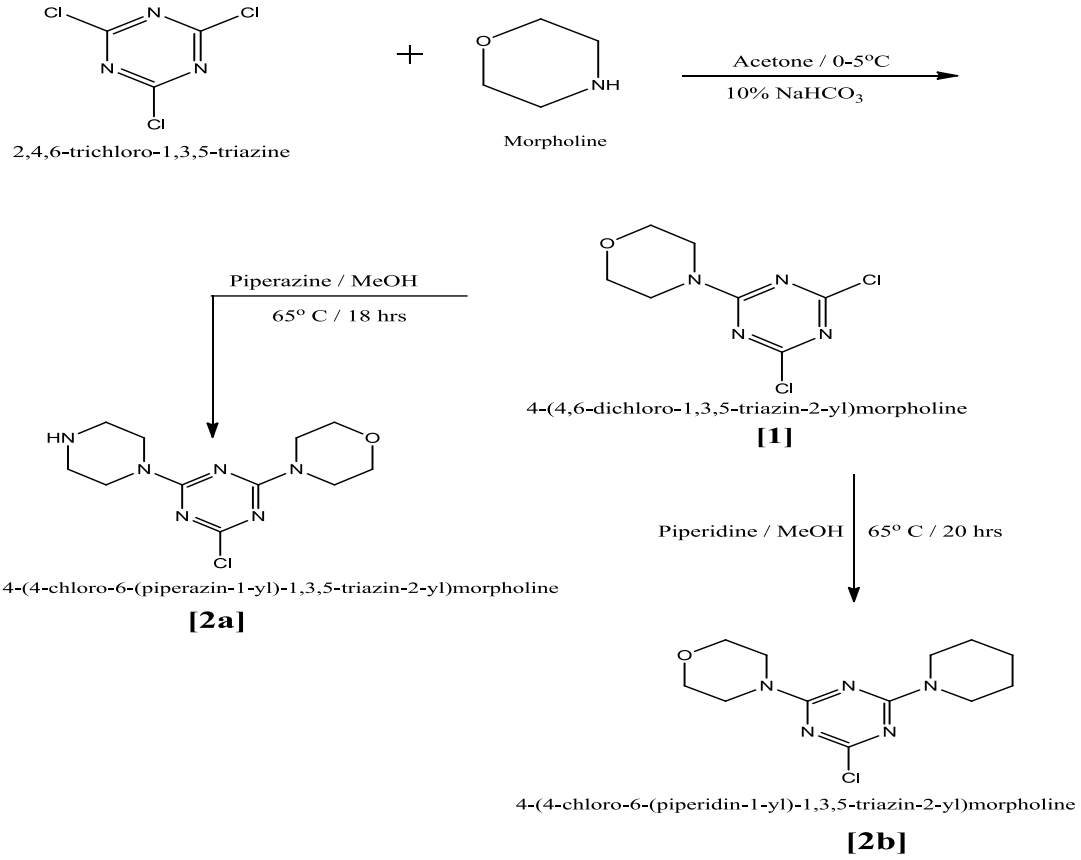
Scheme: 3

Preparation of 4-(4-chloro-6-(piperidin-1-yl)-1,3,5-triazin-2-yl)morpholine:[2b]

To a stirred solution of Piperidine (0.17mL, 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 have water circulation maintaining the temperature at 65^{o}C and the stirring was continued up to 20 hrs.

After completion of reaction the white colour precipitate was found. The crude sample was washed and recrystallized by using chloroform and the melting point was noted (265-268^{o}C).

MECHANISM



SPECTRAL DATA

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

Yield 80%; mp: 138^{o}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-CH$_2$). ^{1}H NMR [500MHz, δ, ppm, CDCl$_3$]: 3.61(4H,s,-OCH$_2$), 3.76(4H,S-NCH$_2$): MS: m/z. 234.34 with 70% relative intensity[M+].

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

Yield 70%; mp: 138^{o}C; FT-IR [v, cm^{-1},KBr]: 1630.0(-C=N),1111.00(-C-N),540(-C-Cl), 794(-CH),1165.0(C-O-C),1581(C-C),2854.65(-C-CH$_2$),3417.86(-NH). ^{1}H NMR [500MHz, δ, ppm, MeOD]: 3.68 (4H,s,-OCH2), 3.76(4H,S,-NCH$_2$), 1.98(1H,S,-NH), 2.70(4H,S,-NHCH$_2$), 3.12(4H,S,-NCH$_2$): MS m/z. 284.12 with 70% relative intensity[M+].

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

Yield 65%; mp: 138^{o}C; FT-IR[v, cm^{-1},KBr]: 1766.80(-C=N),1072.42(-C-N),624.94(-C-Cl), 794.67(-CH),1165.00(C-O-C),1566.20(C-C),2854.65(-C-CH$_2$). ^{1}H NMR[500MHz, δ, ppm, MeOD]: 3.61 (4H,s,-OCH2), 3.70(4H,S,-NCH$_2$), 3.76(4H,S,-NCH$_2$), 1.55(4H,S,-CCH$_2$), 1.58(2H,S,-CH$_2$): MS: m/z. 283.12 with 75% relative intensity[M+].

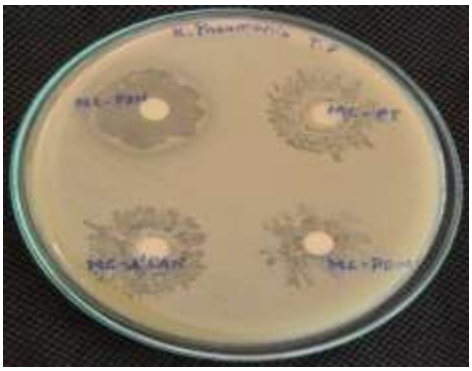
ANTI MICROBIAL STUDY

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

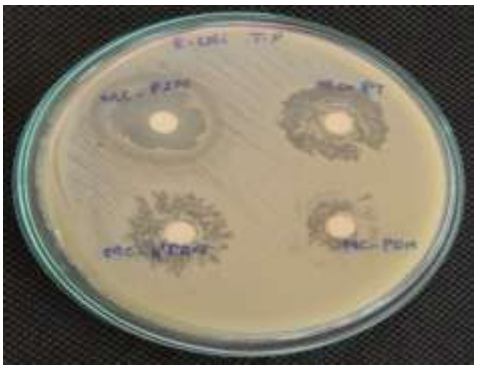
Table-1: Anti bacterial study (concentration 40µl).

S.NO	NAME OF ORGANISM	CONTROL	PDN [2b]	PZN [2a]	MC [1]
1	*S.aureus*	18	26	26	12
2	*P.aeruginosa*	17	22	27	8
3	*K.pneumoniae*	17	24	23	7
4	*E.coli*	18	16	21	8
5	*B.substilis*	15	17	23	9

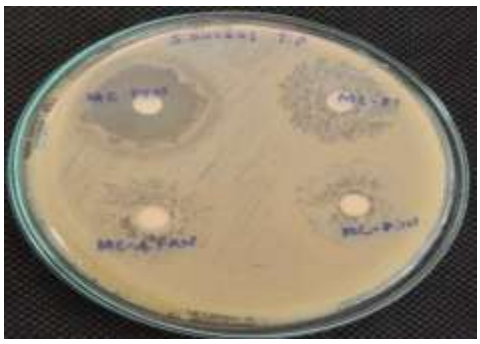
***MC PZN & MC PDN = Compound [2a] & [2b]**



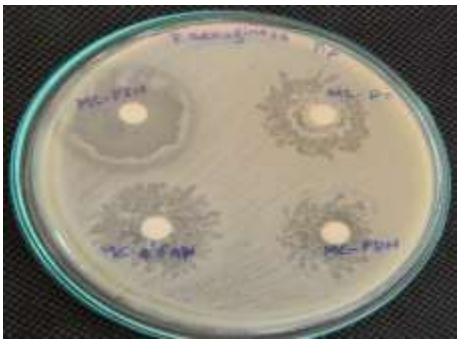
(*K.pneumoniae)*



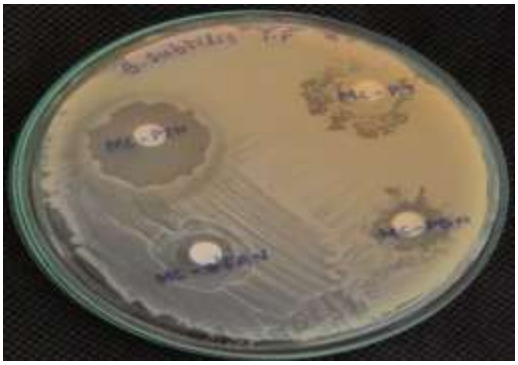
(*E.coli)*



(*S.aureus)*



(*P.aeruginosa)*



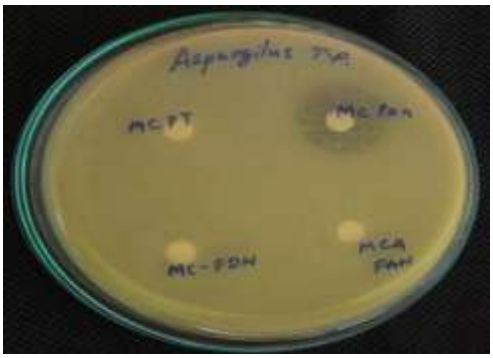
(*B.substilis)*

Fig: 1 Photocopy Evidence for Bacterial Activity of compound [2a & 2b = MC PZN & MC PDN].

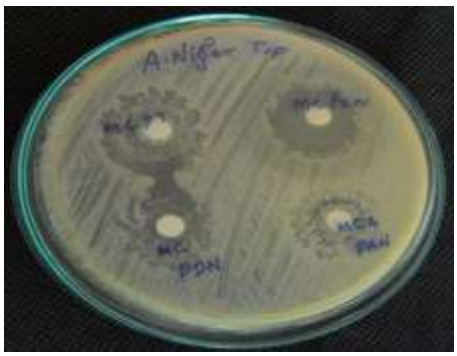
Table-2: Anti fungal Study: (concentration 40µl).

S.NO	NAME OF ORGANISM	CONTROL	PDN [2b]	PZN [2a]	MC [1]
1	*A.niger*	18	23	23	7
2	*Aspergilus*	18	21	21	7
3	*C.albicans*	18	22	31	8
4	*C.lunata*	20	25	22	7
5	*T.simii*	19	25	24	7

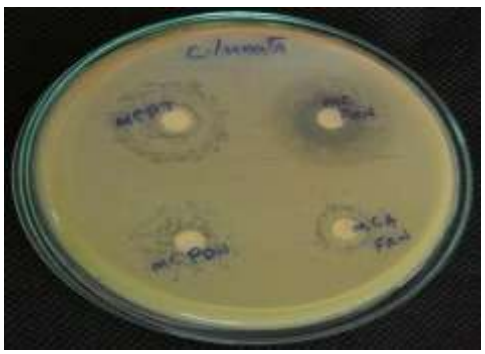
***MC PZN & MC PDN = Compound [2a] & [2b].**



(*Aspergilus)*

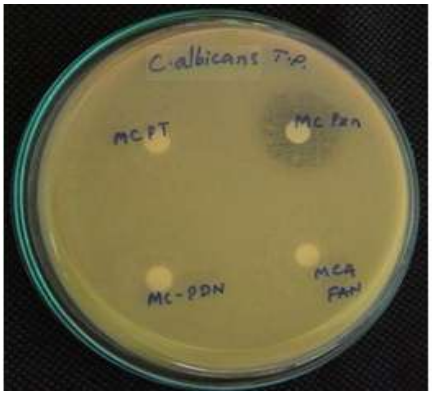


(*A.niger)*



(*C.lunata)*

(*T.simii)*



(*C.albicans)*

Fig: 2 Photocopy Evidence for Fungal Activity of compound [2a & 2b = MC PZN & MC PDN].

The percentage of Inhibition has been shown in table 3

Table-3: Anti-Oxidant study

The percentage of inhibition at different concentration.

Sample code: MC.

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

Sample code: MC PZN [2a].

S.No	Conc	% Inhibition
1	31.25	32.67
2	125	38.09
3	500	46.34
4	1000	59.71

Sample code: MC PDN [2b].

S.No	Conc	% Inhibition
1	31.25	27.15
2	125	36.24
3	500	43.09
4	1000	56.31

CONCLUSION

The anti microbial bacterial, anti fungal and anti oxidant activity of 4-(4,6-dichloro-1,3,5-triazin-2-yl) morpholine**[1]**, 4-(4-chloro-6-(piperazin-1-yl)-1,3,5-triazin-2-yl) morpholine **[2a]** and 4-(4-chloro-6-(piperidin-1-yl)-1,3,5-triazin-2-yl) morpholine **[2b]** were studied. The

results showed that the synthesized compound **[2a]** and **[2b]** have high anti microbial activity because of the presence of hetero atom (N and O) and halogen atom (Cl) groups in phenyl ring system. Compound **[2b]** showed high antioxidant activity when compare to compound **[2a].**

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