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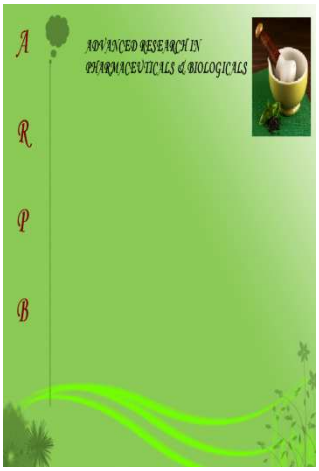

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Corresponding author

P. R. Logesh Kumar,
Department of
Pharmaceutical Chemistry,
Sri Krishna Chaithanya
College of Pharmacy,
Nimmanapalli Road,
Madanapalle,
Chittor(Dt),
A. P.-India.
Email:
loghipharma@gmail.com.

SYNTHESIS AND BIOLOGICAL EVALUATION OF 1-(4-P-TOLUIDINO)-6-(NAPTHYLAMINO)-1,3,5-TRIAZINE 2-YL- 3-METHYL -2,6-DIPHENYL PIPERIDINE-4-ONE

*P. R. Logesh Kumar[1], C.Velmurugan[1], T. Bharathi[1], T.Thiyagarajan[1] and P.Valentina[2]

[1]Department of Pharmaceutical Chemistry, Sri Krishna Chaithanya College of Pharmacy, Madanapalle, Chittor (Dt), Andhra Pradesh-India.

[2]Department of Pharmaceutical Chemistry, SRM University, Kattangluthur, Kanchipuram (Dt), Tamilnadu, India.

ABSTRACT:

Triazine is the chemical species of six-membered heterocyclic ring compound with three nitrogens replacing carbon-hydrogen units in the benzene ring structure. The names of the three isomers indicate which of the carbon-hydrogen units in the benzene ring position of the molecules have been replaced by nitrogens called 1,2,3-triazines. The triazine derivative of 1-(4-p-toludino)-6-(napthylamino)-1,3,5-triazine-2-yl)-3-methyl-2,6-diphenylpiperidine-4-one was synthesized by condensation method by using various amines. The final synthesized compound structure elucidated by spectral analysis and screened for antibacterial and antifungal activity using different strains of bacteria and fungi by turbidometric method at different concentration. Result showed marked anti-bacterial and anti-fungal activity with increasing the concentration and 250 µg revealed equal to standard drug ciprofloxacin in antibacterial activity.

Keywords: Triazine, Napthalamine, Spectral analysis, Antimicrobial, and Antifungal.

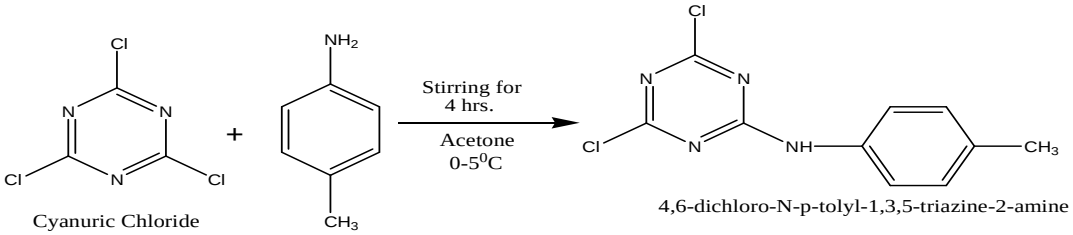
INTRODUCTION

Triazine is the chemical species of six-membered heterocyclic ring compound with three nitrogens replacing carbon-hydrogen units in the benzene ring structure. The names of the three isomers indicate which of the carbon-hydrogen units in the benzene ring position of the molecules have been replaced by nitrogens called 1,2,3-triazines.1,2,4-triazines and 1,3,5-triazine respectively.

MATERIALS AND METHODS

Scheme of the work:

Step 1: Synthesis of 4,6-dichloro-N-p-tolyl-1,3,5-triazine-2-amine[1]

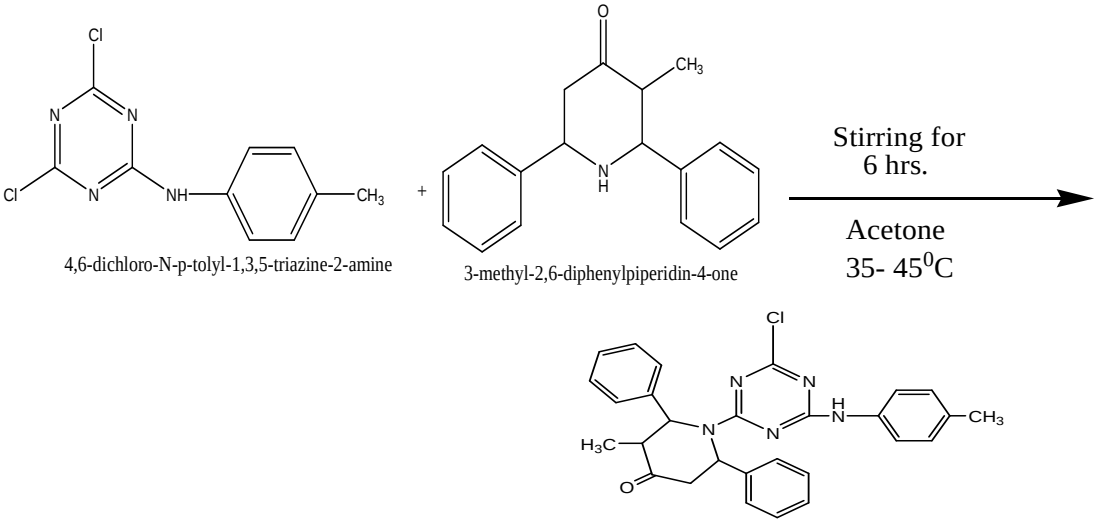


Cyanuric Chloride p-methyl aniline

4,6-dichloro-N-p-tolyl-1,3,5-triazine-2-amine

The Chlorine atom of 2, 4, 6-trichloro-1, 3, 5-triazine was replaced by nucleophillic reagent e g. P-methylaniline. 4,6-dichloro-N-p-tolyl-1,3,5-triazine-2-amine has been prepared by treating 2,4,6-trichloro-1,3,5-triazine in acetone with p-methylaniline at 0-5°c and stirring for 4 hr.

Step 2: Synthesis of 1-(4-(p-toluidino)-6-chloro-1,3,5-triazine-2-yl)-3-methyl-2,6-diphenylpiperidine-4-one[2]



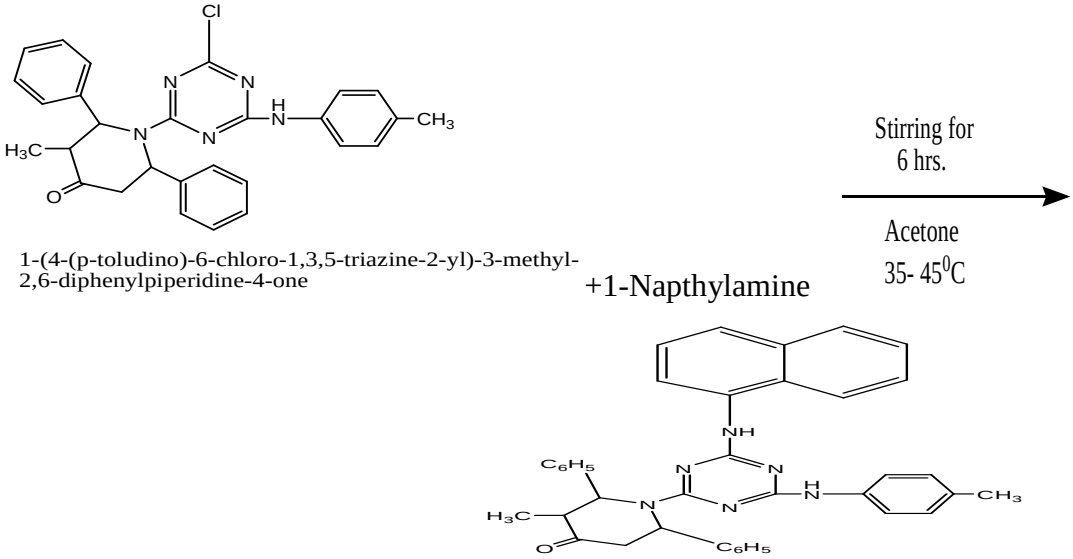
4,6-dichloro-N-p-tolyl-1,3,5-triazine-2-amine

3-methyl-2,6-diphenylpiperidin-4-one

1-(4-(p-toludino)-6-chloro-1,3,5-triazine-2-yl)-3-methyl-2,6-diphenylpiperidine-4-one

1-(4-(p-toludino)-6-chloro-1,3,5-triazine-2-yl)-3-methyl-2,6-diphenylpiperidine-4-one has been prepared by treating 4,6-dichloro-N-p-tolyl-1,3,5-triazine-2-amine in acetone with 3-methyl-2,6-diphenylpiperidine-4-one.

Step 3: Synthesis of 1-(4-p-toluidino)-6-(arylamino)-1,3,5-triazine-2-yl)-3-methyl-2,6-diphenylpiperidine-4-one[3]



1-(4-(p-toludino)-6-chloro-1,3,5-triazine-2-yl)-3-methyl-2,6-diphenylpiperidine-4-one

1-(4-(*p*-toluidino)-6-(napthylamino)-1,3,5-triazin-2-yl)-3-methyl-2,6-diphenylpiperidin-4-one

Compound -2 (0.01 mole) was dissolved in acetone (50 ml) then it was added to 1-Napthylamine (0.01 mole) in acetone (50 ml) and contents are to be stirred for 3 hours at 85-90°C poured in to ice water and neutralized with sodium carbonate solution to get the product. Then it was filtered, washed, dried, and recrystallized from ethanol.

Physical characterization:

- ✓ Molecular formula : $C_{38}H_{34}N_6O$
- ✓ Molecular weight (gm) : 590.72
- ✓ Soluble in Methanol, Ethanol, DMSO and DMF.
- ✓ Melting points were determined using Veego Digital melting point apparatus.
- ✓ Melting point -210ºC
- ✓ The purity of synthesis compound was monitored on TLC.
- ✓ Absorbent used: Precoated Silica gel-G plate
- ✓ Mobile Phase: Chloroform: methanol (3:7)
- ✓ R_f value: 0.76.

Biological Screening

Antibacterial Activity: The synthesized compounds were screened for *invitro* antimicrobial activity by Turbidimetric method. This method was used for

determining the selective effectiveness of the antibacterial activity. The standard antibiotic selected for study of the antibacterial activity was ciprofloxacin. The activity was compared with standard ciprofloxacin drug.

Material Used: Nutrient broth, Sterile borosil boiling test tube, Sterile test tube, Sterile pipettes and Sterile cotton swabs.

Bacteria: In the present study the following bacteria were used.

A. *Escherichia coli* (Gram – ve)

B. *Bacillus subtillus* (Gram + ve)

C. *Staphylococcus aureus* (Gram + ve)

Antifungal activity

Turbidimetric method by using sabouraund dextrose broth: The synthesized compounds were screened for *invitro* antimicrobial activity by Turbidimetric method. This method was used for determining the selective effectiveness of the antifungal activity.

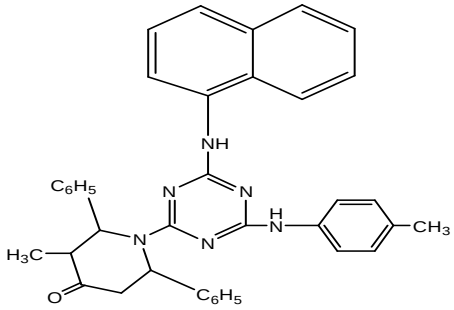
The standard antibiotic selected for study of the antifungal activity was ketoconazole. The activity was compared with standard ciprofloxacin drug.

Material Used: Sabouraud dextrose broth, sterile borosil boiling test tube, Sterile test tube, Sterile pipettes and Sterile cotton swabs.

Fungal: In the percent study the following fungi were used.

- *Aspergillus niger*

Spectral Analysis



IUPAC Name:

1-(4-p-toludino)-6-(napthylamino)-1,3,5-triazine-2-yl)-3-methyl-2,6-diphenylpiperidine-4-one.

IR Interpretation

I.R. Spectral data (KBr discs) (in Cm^{-1})	
N-H str.	3379.94
C=N str.	1590.63
=C-H str.	3181.63
C-N str.	1343.52
C=O str.	1758.83

^{1}HNMR Interpretation

^{1}HNMR Spectral data Absorption position (in PPM)	
6.34 – 7.66	m, 21H, ArH
1.16	d, 3H, CH_3
2.35	s, 3H, CH_3
3.10, 2.85	d, 2H, CH_2
3.14	q, 1H, CH
4.0	s, 2H, NH
4.12	d, 1H, CH
4.13	t, 1H, CH

RESULTS AND DISCUSSION

Synthesis: The present study report the Synthesis of 1, 3, 5-Triazine derivatives. Nucleophilic substitution of Chloro group in Cyanuricchloride was carried out stepwise at different temperature by various amines. The first step involve the substitution of p-methylaniline and the next by 3-methyl-2, 6-diphenyl

piperidine-4-one. The final chloro group in the synthesized compound-2 was replaced by 1-Napthylamine. Since the report regarding this compound suggest a good bioactive moiety.

Physical Characterization: Melting point of the synthesize compound was taken in open capillary tubes and was uncorrected and were found to be in the range of 180-240°C. TLC was performed using precoated silica gel plates of 0.25mm thickness. Eluents used were Chloroform, Methanol (3:7). Spots were visualized in U.V. light.

At room temperature solubility of newly synthesize compound were determined by various organic solvents and it was found that compound were freely soluble in DMSO, DMF, Methanol and Ethanol.

Antibacterial activity: The table shows the 250 µg/ml concentration having good antibacterial activity and equal to ciprofloxacin 100 µg/ml compare to other concentration. The compound most effective against gram^{-ve} microorganism compare to gram^{+ve}.

Table 1: Results of antibacterial activity

Sample	Bacteria	Concentration	% inhibition of growth
Control	Escherichia coli, Bacillus subtillus, Staphylococcus aureus	------	0
1-(4-p-toludino)-6-(napthylamino)-1,3,5-triazine-2-yl)-3-methyl-2,6-diphenylpiperidine-4-one.	Escherichia coli	50 µg/ml 100 µg/ml 150 µg/ml 200 µg/ml 250 µg/ml	34.24 47.39 63.69 69.31 91.36
1-(4-p-toludino)-6-(napthylamino)-1,3,5-triazine-2-yl)-3-methyl-2,6-diphenylpiperidine-4-one.	Bacillus subtillus	50 µg/ml 100 µg/ml 150 µg/ml 200 µg/ml 250 µg/ml	33.28 33.83 46.57 55.61 62.32
1-(4-p-toludino)-6-(napthylamino)-1,3,5-triazine-2-yl)-3-methyl-2,6-diphenylpiperidine-4-one.	Staphylococcus aureus	50 µg/ml 100 µg/ml 150 µg/ml 200 µg/ml 250 µg/ml	24.65 31.25 45.65 56.42 61.24
Ciprofloxacin	Escherichia coli	100 µg/ml	82.35
Ciprofloxacin	Bacillus subtillus	100 µg/ml	65.47
Ciprofloxacin	Staphylococcus aureus	100 µg/ml	68.91

Antifungal activity

The below table revealed that activity increase with concentration

Sample	**Microorganism**	**Concentration**	**% inhibition of growth**
Control	*Aspergillus niger*	------	0
1-(4-p-toludino)-6-(napthylamino)-1,3,5-triazine-2-yl)-3-methyl-2,6-diphenylpiperidine-4-one.	*Aspergillus niger*	50 µg/ml 100 µg/ml 150 µg/ml 200 µg/ml 250 µg/ml	18.13 23.46 32.00 39.72 51.56
Ketaconazole	*Aspergillus niger*	100 µg/ml	82.67

CONCLUSION

In the present study we concluded that the triazine derivative of synthesized compound having significant anti-microbial activity compare to the Standard and most effective against gram^{-ve} bacteria.

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