Content available at: https://www.ipinnovative.com/open-access-journals

Current Trends in Pharmacy and Pharmaceutical Chemistry

Journal homepage: https://www.ctppc.org/

Original Research Article

Synthesis, insilico characterization and antibacterial activity of 1,2,4-Triazine derivatives

M. Jerubin Welsingh[1]*, S. Indira[1]

[1]Dept. Pharmaceutical Chemistry, S.A. Raja Pharmacy College, Tirunelveli, Tamil Nadu, India.

Abstract

Triazines are heterocyclic compounds having three hetero atoms. Triazines are of three isomeric types. They being 1,2,3-triazine , 1,2,4-triazine , and 1,3,5-triazine. The 1,3,5-triazine is also called as s-triazine (symmetrical triazine). They have significant interest due to their diverse biological activity, especially antibacterial properties.

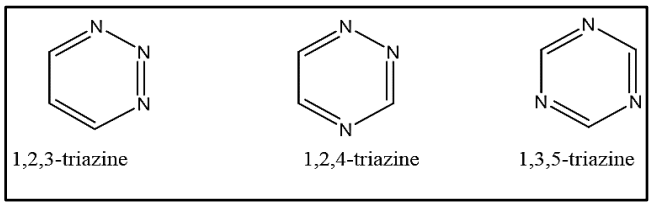
This work focuses on the synthesis of 1,2,4-triazines using chemical methods, analysing their physical properties like Infrared Spectra, partition coefficient, Topical polar surface area, Hydrogen bond donors and acceptors, and process capability index. The antibacterial activity of these compounds against gram +ive and -ive bacteria using disc diffusion technique in Nutrient agar media is also studied.

Keywords: Klebsiella spp, Clostridium spp, 1,2,4-triazines

Received: 15-07-2025; **Accepted:** 10-09-2025; **Available Online**: 17-09-2025

1. Introduction

Heterocyclic compounds play an important role in medicinal chemistry due to their wide range of biological activity like antibacterial antifungal, anticancer antioxidant etc. This triazine is of three isomeric form.



This 1,2,4-triazine is also called as Asymmetrical triazine or isotriazine. They are found in antiviral azaribine, anticancer drug tirapazamine and Lamotrigine antiepileptic drug. Herbicides like atrazine, simazine and propazine inhibits photosynthesis. Hence they are used as weedicide. They block the Electron transport chain at the plastoquinone-binding region of the D1 protein subunit of PSII.

This 1,2,4-triazines is found in various pharmaceuticals and Agrochemicals also.

This study aims to synthesize novel 1,2,4-triazine derivatives using chemical methods and to access their antibacterial activity against Gram + ive and Gram -ive Bacterial organisms. The various physical properties of the synthesized compounds were also studied. The Infrared spectral data of the synthesized compounds were also checked for the presence of various functional groups.

2. Materials and Methods

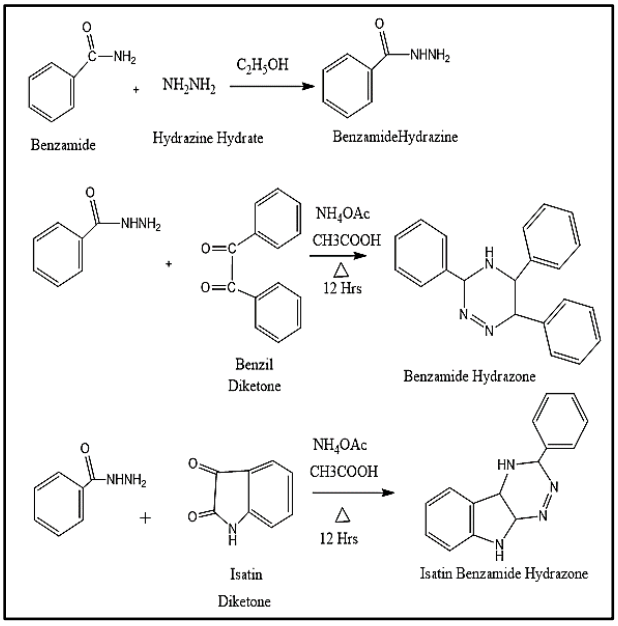
Equimolar quantities of 1,2-Diketone on refluxing at 80℃ for 12 hrs with Acyl Hydrazine in the presence of ammonium acetate and using Glacial Acetic acid as solvent yields 1,2,4-Triazine.Here the diketone used being Benzil and Isatin. The Acyl Hydrazine was prepared by reacting an Amide with hydrazine Hydrate using Glacial Acetic acid as solvent. The component mixture on acidification using Conc HCl, yields more than 75 % of the calculated theoretical yield value. The Compound is filtered, dried, and recrystallized from hot

*Corresponding author: M. Jerubin Welsingh
Email: mjerubinwelsingh@gmail.com

https://doi.org/10.18231/j.ctppc.v.7.i.3.4

ethanol. It is stored in sterile containers. The melting point of the final product is also recorded.[1]

3. Synthesis Methodology



3.1. Interpretation

Benzil Benzamide Hydrazone IR Interpretation

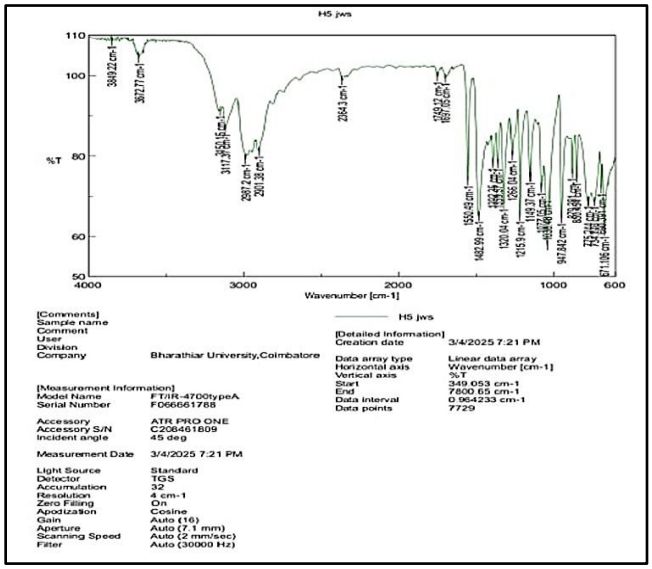


Table 1:

S. No	Peak Wave Number	Functional group
1	3672 cm-1	N-H stretching of Amines
2	1550 cm-1	C=C stretching in aromatic ring
3	2987 cm-1	C-C Stretching
4	1482 cm-1	N=N stretching

3.2. Isatin benzamide hydrazone ir interpretation

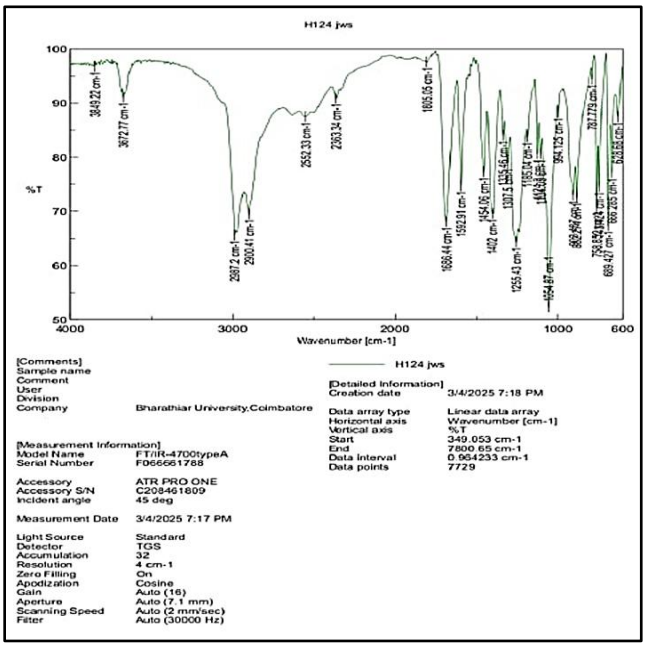


Table 2:

S. No	Peak Wave Number	Functional group
1	3672 cm-1	N-H stretching of Amines
2	1686 cm-1	C=C stretching in aromatic ring
3	2987 cm-1	C-C Stretching
4	1592 cm-1	N=N stretching

4. Interpretation of Physical Properties

Table 3:

	Isatin Benzamide hydrazone	Benzil Benzamide hydrazone
logP	2.63	4.56
TPSA	48.78	36.76
natoms	19	24
mw	250.31	313.40
nON	4	3
nOHNH	2	1
nViolations	0	0
nrotb	1	3
Volume	228.16	293.01

LogP is a prediction of the logP of a molecule. LogP values are used in drug discovery to predict how well a drug will be absorbed and permeated by the body.

4.1. LogP interpretation

1. A negative logP value means the molecule is more hydrophilic.
2. A positive logP value means the molecule is more lipophilic.

3. A logP value of 0 means the molecule is equally partitioned between water and octanol.

According to Lipinski's rule of 5, an oral drug should have a LogP value <5, ideally between 1.35-1.8 for good oral and intestinal absorption. It is observed that these compounds obey Lipinski rule of 5.

5. TPSA is Topical Polar Surface Area

It refers to the total surface area occupied by polar atoms and their attached hydrogen atoms. It indicated the molecule's polarity and potential for hydrogen bonding. It shows the oral absorption and permeability across cell membranes. Normal range is 60-140. Higher TPSA above 140 may have poor intestinal absorption due to high polarity. Lower value below 60 might suggest poor membrane permeability to reach the target site. Hence these drugs will be modified with other polar groups for effective membrane permeability.

A drug with topological polar surface area value below 140-150 A^o2 and nRotB less than or equal to 10 has acceptable bioavailability. nRotB is number of rotatable bonds which should be less than 10 nON is the number of hydrogen bond acceptors within a molecule. The oxygen atoms that have an electronegative atom with a lone pair of electron nOHNH refers to the number of hydrogen bond donors in a molecule, which is calculated as the sum of hydroxyl (OH) and amine (NH) groups Violation is the number of the Lipinski rule violation or fails to meet. nViolation less than 0 or =1 means the compound easily bind to receptor.[2]

Volume refers to the 3D space occupied by a molecule, calculated using group contribution.

6. Antibacterial Activity

Antimicrobial studies was conducted against gram positive and gram-negative organism. The Clostridium spp. is the Gram-positive bacteria and Klebsiella spp. is the Gram-negative bacteria using nutrient agar media via disc diffusion methods.[3]

In this disc diffusion method, the halo zone is measured and the zone of inhibition was compared against the standard amoxycillin using DMSO 1:10 solution as control.

1. Standard- Amoxicillin 10mcg from HiMedia (susceptibility test disc).
2. Control- DMSO 1:10 solution in sterile disc
3. Incubation time is 48 hrs and the temperature is maintained at 37ºC.
4. MIC (Minimum inhibitory concentration) is calculated with the zone of inhibition via the disc diffusion method.
5. Test drug of conc 1000µg,750 µg,500 µg.

The lowest concentration at which the drug completely inhibits the organism is called MIC (Minimum inhibitory concentration) Activity index of all the synthesized compounds were calculated against the standard drug Amoxycillin.[5-7]

7. Isatin Benzamide Hydrazone

7.1. Inhibitory effect of compounds on halo zone measurement

Table 4:

S. No	Gram +ive Clostridium Spp	Gram -ive Klebsiella spp
1	3.12 ± 0.1	4.31 ± 0.02
2	7.20 ± 0.04	6.82 ± 0.03
3	6.82 ± 0.03	6.03 ± 0.02
4	6.66 ± 0.02	6.22 ± 0.02
Standard Amoxycillin	8.85 ± 0.02	7.22 ± 0.02

8. Results and Discussion

1,2,4-Triazine derivatives are synthesized[1] using chemical methods. The following parameters are noted.

1. IR spectroscopy[1] of the various derivative is analyzed to find out the functional groups.
2. *Insilico* data about physical properties[5] like molecular weight, Partition Coefficient, Hydrogen bond donors and acceptors to find the ADME properties[5] of the drug.
3. Antibacterial activity of the synthesized drugs with Gram +ive and Gram-ive organism using Nutrient agar media. The standard drug used is Amoxycillin[4] sterile disc is obtained from HIMEDIA. The zone of inhibition is measured from the halo zone.
4. The 1,2,4-Triazine derivative is synthesized and the Yield was more than 75%.
5. The partition Coefficient (LogP), Topical polar surface area of the 3D structure of the compound, Molecule lipophilicity, Process capability index, hydrogen bond donors and acceptors, and the Violations from Lipinski rule of are analysed.[3] Thus the drug may have sufficient Bioavailability.
6. The Antibacterial activity activity[7] of the two derivative is observed and the Benzil Benzamide Hydrazone was found to have sufficient activity when compared with the standard amoxycillin.

9. Conclusion

The 1,2,4-Triazine derivatives were synthesized, their IR Spectroscopy peaks were found to have functional groups. The Insilico activity were observed and found to have good ADME properties. The Antibacterial activity was found to have considerable zone of inhibition against Gram +ive and Gram-ive organism. This parent lead molecule can be modified with some polar groups so that the antibacterial activity can be further increased.

10. Acknowledgement

The Author wishes to thank our Honorable Chairman Dr. Jacob Raja and the Principal of S.A. Raja Pharmacy College.

11. Source of Funding

None.

12. Conflict of Interest

None.

References

1. Arshad M, Bhat AR. Synthesis,Characterization and antibacterial screening of some novel 1,2,4-triazine derivatives by, *J Chinese Chem Lett*. 2017;28(7):1560-6.
2. Chinchilli KK, Angeli A. Design Synthesis and Biological Evaluation of 1,2,3-triazole linked Triazine [5,6-B] Indole-Benzene sulphonamide conjugates as carbonic anhydrase inhibitor, *J Metab*. 2020:10(5):200.
3. Arshad M, Khan TA. 1,2,4-Triazine derivatives Synthesis and Biological applications, *Int J Pharma Sci Res*. 2002:46(4):
4. Mojzych M. Annals of Medicinal Chemistry, Biological Activity Evaluation of Pyrazolo[1,2,4-triazino] sulphonamide, 2019;1(1):1-5.
5. Congreve M, Andrews SP, Doré AS, Hollenstein K, Hurrell E, Langmead CJ. et al. 1,2,4-Triazine Derivatives as Adenosine A2A Antagonists using Structure Based Drug Design. *J Med Chem*. 2012;55(5):1898-903.
6. Katherine M, Lucantoni L. The Novel bis-1,2,4-Triazine potent activity against all blood stages of Malaria. Antimicrobial Agents and Chemotherapy. *Am Soc Microb*. 2021:65(11):e0031121.
7. Mohammed S.I., Makki Reda M. Abdel-Rahman A. 1,2,4-triazinones as potential Anti-HIV and CDK2 Inhibitors. *J Chemi*, 2014;1-14.

Cite this article. M. Jerubin Welsingh S. Indira. Synthesis, insilico characterization and antibacterial activity of 1,2,4-Triazine derivatives. *Curr Trends Pharm Pharm Chem*. 2025;7(3):103-106.