A REVIEW ON THE REPORTED ANTIBACTERIAL ACTIVITY OF 1,3,5-TRIAZINE

Abstract: Antibiotics are the class of drugs used for bacterial, viral & fungal infection. Antibiotic resistance is the ability of microorganism to withstand themselves against the effects of a drug. Every year antibiotic resistance causes more than 38000 deaths in Thailand, 23000 deaths in USA. In South Asia one new born child dies every 5 minutes from blood stream infection because antibiotics given are ineffective due to bacterial resistance. Now antibiotic resistance is a threat to global health. In this paper, triazene derivatives are kept in concern. Triazines are six-membered, nitrogen-containing heterocyclic scaffold with a wide range of pharmaceutical properties such as antibacterial, antifungal, anticancer, antioxidants, antitubercular, antimalarial and anti-inflammatory. Due to lack of new antibiotics as well older antibiotic are rapidly proving ineffective, derivatives of triazine would be of great significance in future prospective.

Keywords: Triazine, antibacterial, antifungal

1) INTRODUCTION:

Triazine is one of the most important lead molecules which are widely used in the field of pharmaceuticals. Triazine is the species of six membered heterocyclic structures having the empirical formula $C_3H_3N_3$ [1].Triazine structure is similar to the structure of benzene ring in which three nitrogen atoms replace three carbon atoms present in it. The different position of nitrogen atoms in the ring distinguish the three isomer of triazine and the isomers are referred as 1, 2, 3-triazine, 1, 2, 4-triazine and 1, 3, 5-triazine [2].

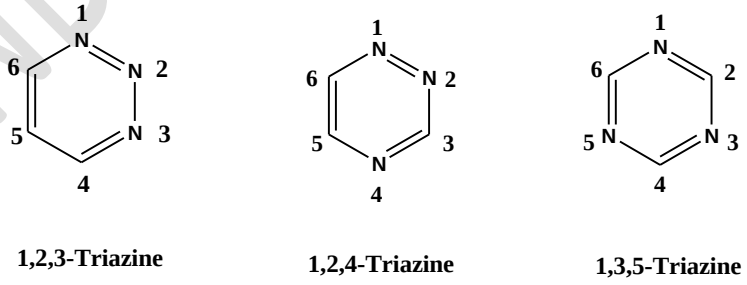


Fig.1.1: Various isomers of triazine.

Among all the isomers of triazine, 1, 3, 5-triazine isomer is the oldest known organic compound. 1, 3, 5-triazine sometimes also called as s-triazine because of the symmetry of three nitrogen atom in the ring [3]. Because of its broad applications in various fields like

pharmaceuticals, textiles, rubbers and plastic industries, 1.3.5-triazine considered as one of the well-known compound from long time. Substituted [1,3,5]-triazine derivatives have become an attractive targets in medicinal chemistry because of their significant biological activities such as antibacterial [4], antifungal [5]**,** antimalarial [6]**,** antitumoranti-inflammatory [7], antileishmanial[8]

Now a days, several studies have been carried out on the antibacterial activity of 1, 3, 5-triazines [9]. All 1, 3, 5-triazine derivatives that have a very wide practical applications consist of 2, 4, 6-mono, di ortri-substituted, symmetrical and non-symmetrical compounds having various kinds of substituent. The most important reagent among all of them for obtaining these synthetic molecule transformations is cyanuric chloride due to the reactivity of the chlorine atoms towards nucleophiles [10].

2) TRIAZINE AND ITS ANTIBACTERIAL ACTIVITY

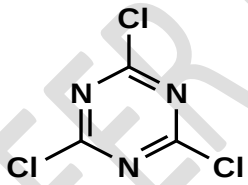


Fig.2.1: 2,4,6 thichloro 1,3,5- triazine (cyanuric chloride).

2.1) Antibacterial activity:

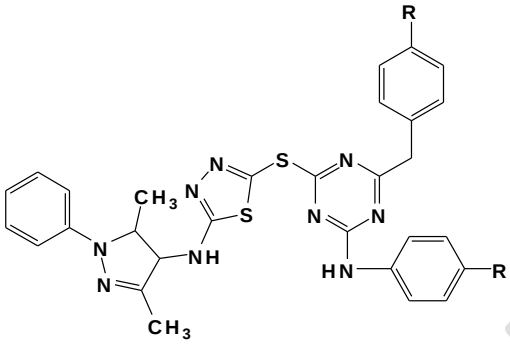
In this review we are going to discuss the antibacterial activity of 1,3,5-triazine derivatives that have been carried out by various researchers. Although a number of work has already been done on this particular, but here some of the important research work on 1,3,5-triazine derivatives have been discussed in brief.

A comprehensive literature survey has been done to search out the current trends in the field of antibacterial. This survey was desigined to find out the different types of molecular structures containing either 1,3,5 triazine. Several publications have focused on derivatives of 1,3,5 triazine with a wide array of substituent.

2.2. Review of the synthetic work

In this part, important research articles has been incorporated which highlights the various synthetic procedures adopted for synthesizing triazine and quinoline derivatives

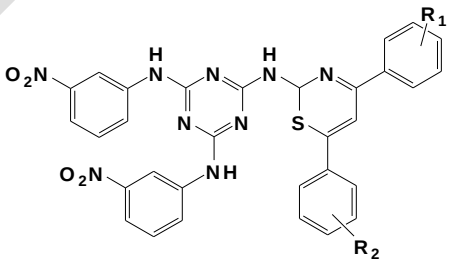
Dubey et al. (2012): Synthesized some hybrid derivatives of 1,3,4-thiadiazole-1,3,5-triazine which was tethered via a –S– bridge and was characterised by different spectroscopic and elemental analysis. The antibacterial activity of those hybrids were evaluated against selected Gram-positive and Gram-negative bacteria. The antibacterial evaluation of the compound suggest that the compounds possessed excellent to moderate antibacterial activity. [11]



R= Cl, Br, F, CH_3, OCH_3,NO_2

Fig 2.2.: hybrid derivatives of 1,3,4-thiadiazole-1,3,5-triazine

Singh et al. (2012) In this research synthesised some novel hybrid 1,3-thiazine-1,3,5-triazine derivatives and the antibacterial potency of those synthesised hybrid were evaluated. Out of those synthesised compounds compound 8c and 8f were found to show antibacterial activity against gram positive and gram negative bacteria. The synthesised compounds were analysed with various spectral analysis and molecular docking study was also carried out on eubacterial ribosomal decoding A site (Escherichia coli 16S rRNA A site) to rationalize the probable mode of action, binding affinity, and orientation of the molecules at the active site of receptor [12].



8c (R_1=4-OH, R_2= 2-NO_2)

8f (R_1=4- NO_2, R_2= 4-NO_2)

Fig 2.3.: hybrid 1,3-thiazine-1,3,5-triazine derivatives

Bhat *et al.* (2013) synthesized a series of novel 4-aminoquinoline 1,3,5-triazine derivatives and the synthesized were evaluated for their antibacterial activity using ciprofloxacin as

reference standard drug, against three Gram-positive bacteria, namely *Bacillus subtilis*, *Bacillus cereus* and *Staphylococcus aureus*and four Gram-negative bacteria, namely *Proteus vulgaris*, *Proteus mirabilis*, *Escherichia coli*, and *Pseudomonas aeruginosa*, by broth dilution method. Compound **5** (**Fig 2.4**) and **6** (**Fig 2.4**) showed potent antibacterial activity against all bacterial strains except *Bacillus cereus.* Compound **5** bearing P-aminophenol substitution on 1, 3, 5-triazine nucleus showedmore potent antibacterial activity than the **7** (**Fig 2.4**) derivative bearing 1, 3-diaminopropane groups [13].

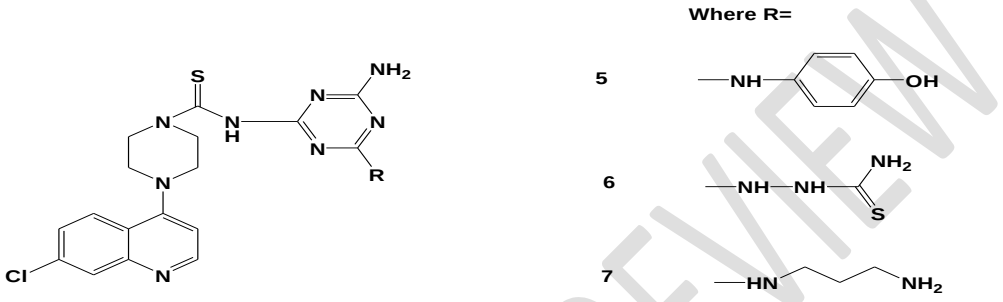
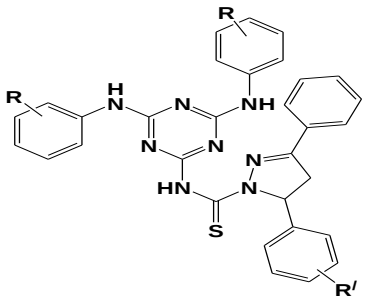


Fig 2.4.: 4-aminoquinoline 1,3,5-triazine derivatives (5,6,7)

Singh *et al.* (2014) synthesized various hybrid of 1,3,5-triazine-pyrazole conjugates with 1,3-thiazine,piperazine, 1,3,4-thiadiazole,4-aminoquiolineand thiazolidin-4-one. The synthesized compounds were evaluated for their antibacterial activity using cefixime as reference standard drug, against Gram-positive bacteria, namely *Bacillus subtilis*, *Bacillus cereus* and *Staphylococcus aureus* and Gram-negative bacteria, namely *Proteus vulgaris*, *Escherichia coli*, and *Pseudomonas aeruginosa*, by broth microdilution method. Due to the presence of unsubstituted phenyl ring on pyrazole, compound **8 (Fig 2.5)** showed significant activity against all the tested micro-organisms except moderate activity against*E. coli* and *P. aeruginosa*. But the introduction of 2-NO_2 (compound **9(Fig 2.5)**) in the substituted phenyl ofpyrazole, led to a decline in activity. The insertion of 2-Cl (compound **10(Fig 2.5))** in the substituted phenyl ring of pyrazoleshowed a marked activity against all tested micro-organisms except *P. Vulgaris*[14].



Where	R	R′
8	4-Cl	H
9	4-Cl	2-NO_2
10	4-Cl	2-Cl

Fig 2.5. hybrid of 1,3,5-triazine-pyrazole conjugates with 1,3-thiazine,piperazine, 1,3,4-thiadiazole,4-aminoquiolineand thiazolidin-4-one.

Kishor *et al.* (2014) reported novel *s*-triazine based aryl/heteroaryl entities by substituting the intermediate 4-((4-chloro-6-methoxy-1,3,5-triazin-2-yl)amino)benzonitrile with various thiophenol, phenol, aniline and piperazine/piperidine/morpholine moieties to get the targeted compounds. The synthesized compounds were characterised by different spectroscopic technique and screened for their antibacterial activity against bacteria (*S.aureus*, *B. cereus*, *E. coli*and *P.aeruginosa*). Methyl group containing compound **15** (**Fig 2.6.)** showed superior activity against *E. coli* whereas compound **16 (Fig 2.6.)** and compound **17 (Fig 2.6.)** showed excellent activity against *P.aeruginosa*and *S.aureus*due to the presence of fluoro group. Similarly compound **18 (Fig 2.6.)** having fluoro group exhibited the high potency against bacteria strain *P. aeruginosa* whereas compound **19 (Fig 2.6.)** and **20 (Fig 2.6.)** exhibited potent inhibitory activity against *S.aureus*and *B. cereus*. Compound **21(Fig 2.6.)** having the N-acetyl group showed high potency against the bacterial strain S. aureus and compound **22** (**Fig 2.6.)** having N-phenyl piperazinyl molecule showed superior to other with respect to inhibiting the growth of *P. aeruginosa* [15].

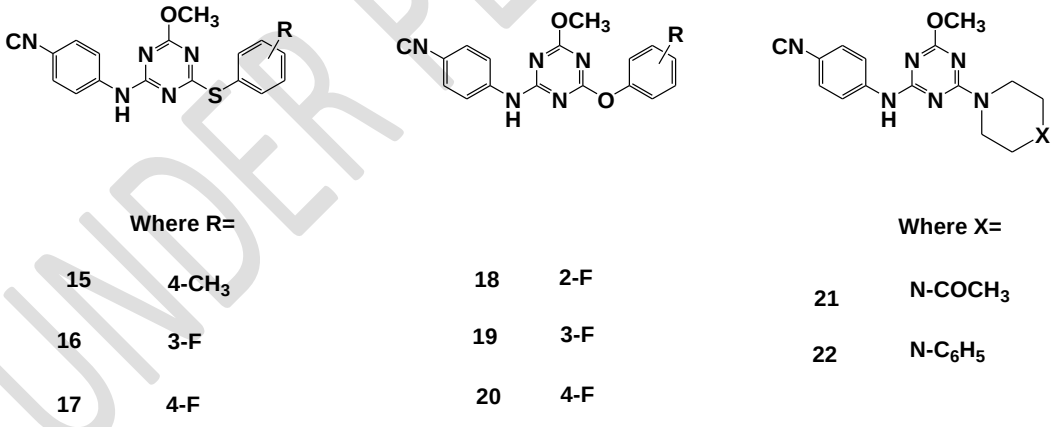
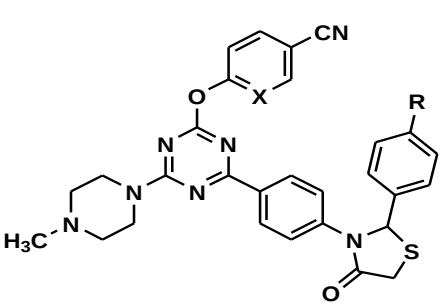


Fig 2.6. triazine based aryl/heteroaryl entities

Kumari *et al.* (2014) reported 4/6-(4-(4-methylpiperazin-1-yl)-6-(4-(4-oxo-2-phenylthiazolidin-3-yl)phenyl)-1,3,5-triazin-2-yloxy)benzonitriles/nicotinonitriles derivatives, which were characterised by several spectroscopic and elemental analysis and tested for *in-vitro* antimycobacterial activity against *Mycobacterium tuberculosis*. Benzonitrile based compound **36** and nicotinotrile based compounds **37(Fig 2.7.)**, **38** (**Fig**

2.7.) and **39 (Fig 2.7.)** exhibited highest inhibitions at concentration level 6.25 µg/ml. Compound **38** (**Fig 2.7.**) with hydroxyl group to thiazolidin-4-one showed inhibition against *Mycobacterium tuberculosis* at 3.12 µg/ml of MIC and compound **37** (**Fig 2.7.**) with fluoro group and compound **39** (**Fig 2.6.**) with methoxy group substituent to thiazoliduine-4-one showed inhibition at 6.25 µg/ml of MIC [16].



Where

	R	X
36	OH	CH
37	F	N
38	OH	N
39	OCH_3	N

Fig 2.7. 4/6-(4-(4-methylpiperazin-1-yl)-6-(4-(4-oxo-2-phenylthiazolidin-3-yl)phenyl)-1,3,5-triazin-2-yloxy)benzonitriles/nicotinonitriles derivatives

Kishor *et al.* (2014) reported some new quinolone condensed *s*-triazine derivatives (**Fig 2.8.**) endowed with different heterocycles and 4-aminobenzonitrile moiety and evaluated for their antibacterial activity against eight bacteria, namely *Staphylococcus aureus*, *Bacillus cereus*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, *Salmonella typhi*, *Proteus vulgaris* and *Shigella flexineri*. Compounds with halogen substituents, **40(-Cl), 41 (-Br)** and **42 (-F)** showed significant inhibition against both Gram-positive and Gram-negative bacteria at MIC of 6.25-12.5 µg/ml and MIC of 25 µg/ml respectively. However the compound **42** having fluoro substituent was found more active than the other halogen substituent. Compound **43** (thiazole), **44** (benzothiazole) and **45** (nitro heterocycles) exhibited diminished antibacterial efficacies against *Klebsiella pneumonia*at MIC of 50 µg/ml. Compound **46** and **47** having quinoline moiety on *s*-triazine showed excellent activity against *Salmonella typhi* at MIC of 12.5 µg/ml [17].

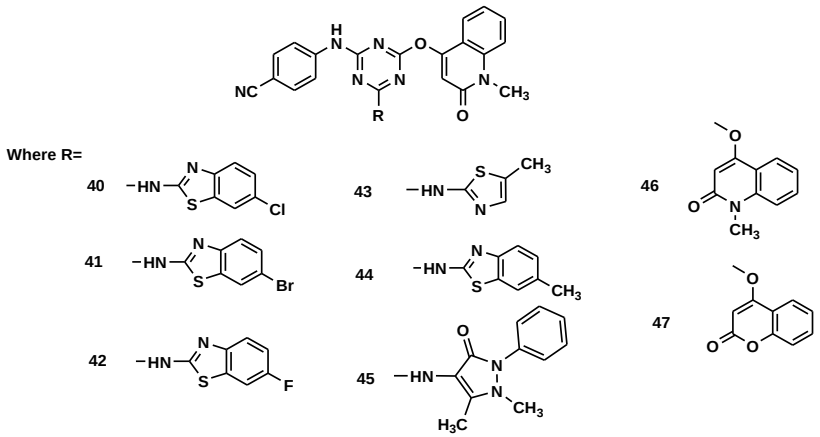
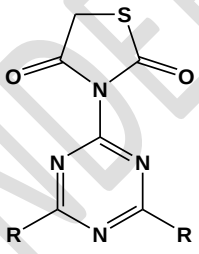


Fig 2.8. quinolone condensed *s*-triazine derivatives

Singh *et al.* (2015) Synthesized a novel series of 1, 3, 5 triazine-thiazolidine-2, 4-diones and characterised by various analytical and spectroscopic techniques. The synthesized compound (**Fig 2.9.**) **11** showed potent activity against all the microorganisms except *Proteus vulgaris*and *Pseudomonas aeruginosa.* Compound **12** showed moderate to zero activity against the tested microorganisms. Compound **13** showed equipotent activity in comparison to standard against *E. coli* where compound **14** showed improved activity in comparison to standard against *E. coli, B. subtilis* and *S. aureus* [18].

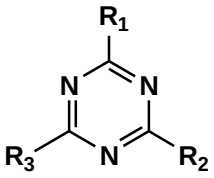


	Where R=
11	NHC_6H_5 2-NO_2
12	$NHNH_2$
13	NHC_6H_5
14	NHC_6H_5 2-NH_2

Fig 2.9.: 1, 3, 5 triazine-thiazolidine-2, 4-diones

Shafi *et al*. (2015) reported a series of s-triazine derivatives by treating 4,7-dichloroquinoline with ethylene diamine afforded 4-substituted 7-chloroquine, which further reacted with 1,5-disubstituted cyanuric chloride. All the synthesized compounds (**Fig 2.10.**) were characterized by different spectroscopic techniques and evaluated for their antibacterial activity against some Gram positive and Gram negative bacteria. Compound **29**, **30** and **31**

exhibited good inhibition against all the tested bacteria, whereas compound **32**, **33** and **34** exhibited moderate to low activity against all strains [19].



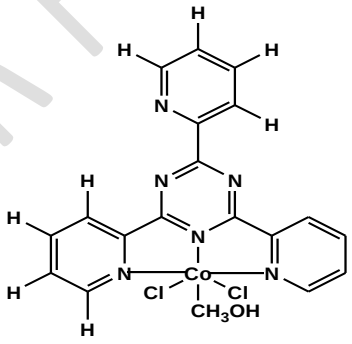
Where

R_1, R_2=P-Nitroaniline and R_3=N^1-7(Chloroquinoline-4-yl)ethane-1,2-Diamine for compound 29, 30 and 31.

R_1=P-Nitroaniline, R_2= Aniline and R_3=N^1-7(Chloroquinoline-4-yl)ethane-1,2-Diamine for compound 32, 33 and 34.

Fig 2.10. s-triazine derivatives

Farzaneh *et al.* (2015) prepared a cobalt complex from $CoCl_2$.6H2O and 2,4,6-tris(2 pyridyl)-1,3,5-triazine**(tptz)** and characterised by several spectroscopic techniques and TGA analysis. The complex (**Fig 2.11.**) was screened for antibacterial activity against Gram positive bacteria, namely *Bacillus subtilis*and *Staphylococcus aureus* and Gram-negative bacteria, namely *Escherichia coli*, and *Pseudomonas aeruginosa* using Nalidixic acid and Vancomycin as reference standard. Tptz exhibited moderate activity against *B. subtilis* and *S. aureus* and *P. aeruginosa* including no activity against *E. coli*. When compared to parent ligand, all the complexes (compound **35**) exhibited more inhibition than parent ligand [20].

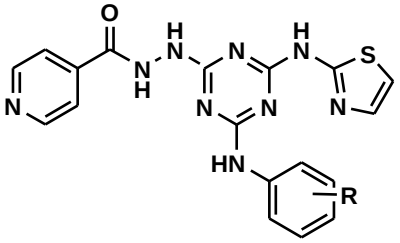


35 cobalt complex

Fig 2.11. cobalt complex

Desai *et al.* (2016) reported a series of novel compounds N/-(4-(arylamino)-6-(thiazol-2-ylamino)-1,3,5-triazin-2-yl)isonicotinohydrazides by a series of multistep reactions and the compounds (**Fig 2.12**) were characterised by different spectroscopic techniques. Antimicrobial screening of title compounds was evaluated against Gram-positive bacteria (*Staphylococcus aureus, Streptococcus pyogenes*), Gram-negative bacteria (*Escherichia coli,*

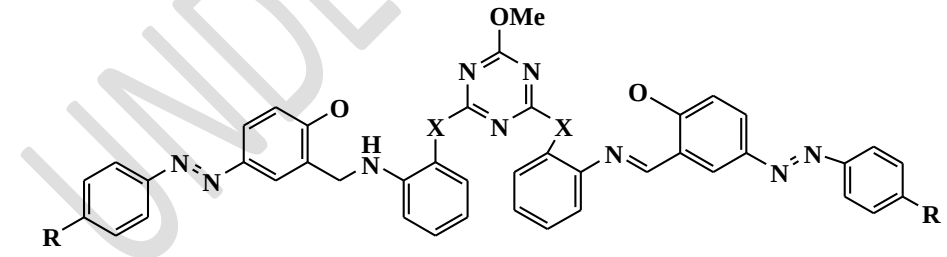
Pseudomonas aeruginosa) by using serial broth dilution method. Compound **23** (2-NO_2) and compound **24** (4-NO_2) showed highest inhibition at MIC 12.5 and 25 µg/ml while compound **25** (2,5-$(Cl)_2$) and compound **26** (4-F) displayed a significant activity at MIC 50 µg/ml against *E. coli*. Compound **27** showed a very good activity at MIC 50 µg/ml against *P. aeruginosa* compound **28** displayed pronounced activity at MIC 50 µg/ml against *S. aureus* [21].



Where R=			
23	2-NO_2	26	4-F
24	4-NO_2	27	4-Br
25	2,5-$(Cl)_2$	28	4-F

Fig 2.12. N/-(4-(arylamino)-6-(thiazol-2-ylamino)-1,3,5-triazin-2-yl)isonicotinohydrazides

Ali *et al.* (2016) synthesized 2,2'-(((6-methoxy- 1,3,5-triazine-2,4 diyl)bis(sulfanediyl)bis(2,1-phenylene))bis(azanylylidene)bis (methanylylidene))bis(4-(phenyldiazenyl)phenol and its derivatives (**Fig 2.13**), were characterised by elemental analysis and spectroscopic techniques and screened for their antibacterial activity against some Gram positive and Gram negative bacteria by disc diffusion method. In the disc diffusion antimicrobial sensitivity testing, none of the compounds showed inhibitory effects against all the tested pathogens [22].



X=S **X=O**

a R=H, b R=Me, c R=Cl, d R=NO_2 **e R=H, f R=Me, g R=Cl, h R=NO_2**

Fig 2.13. 2,2'-(((6-methoxy- 1,3,5-triazine-2,4 diyl)bis(sulfanediyl)bis(2,1-phenylene))bis(azanylylidene)bis (methanylylidene))bis(4-(phenyldiazenyl)phenol

Zhang et al. (2017): Synthesised a series of 1,4-dihydro-1,3,5-triazine derivatives and the antibacterial activity of those compounds were evaluated against some selected gram positive and gram negative bacteria. the evaluation of antibacterial study suggest that the compounds showed potent inhibition of several Gram-positive bacterial strains and Gramnegative bacterial strains, in which the MIC was within the range of 2.1– 181.2mmol/L. Out of all the synthesised compounds 7a was found to be most potentwith MIC of 2.1 mmol/L against four multidrug-resistant, Gram-positive bacterial strains[23].

7a[R_1= 2,4 $(Cl)_2$]

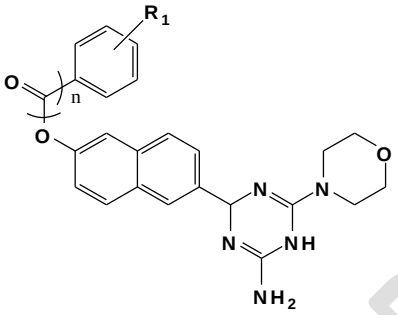


Fig 2.14: 1,4-dihydro-1,3,5-triazine derivatives

Zhang X. *et al*. (2017) synthesized two covalent organic frameworks, namely COFs-Trif-Benz and COF-SDU1 by facile solvo thermal reaction between tri-(4-formacylphenoxy)-1,3,5-triazine (trif) and benzidine or *p*-phenylenediamine and the structures were confirmed by FTIR, NMR, PXRD and BET analyses. The two material was the evaluated for antibacterial activity against Gram positive (*S. aureus*) and Gram negative (*E. coli*) bacteria [24].

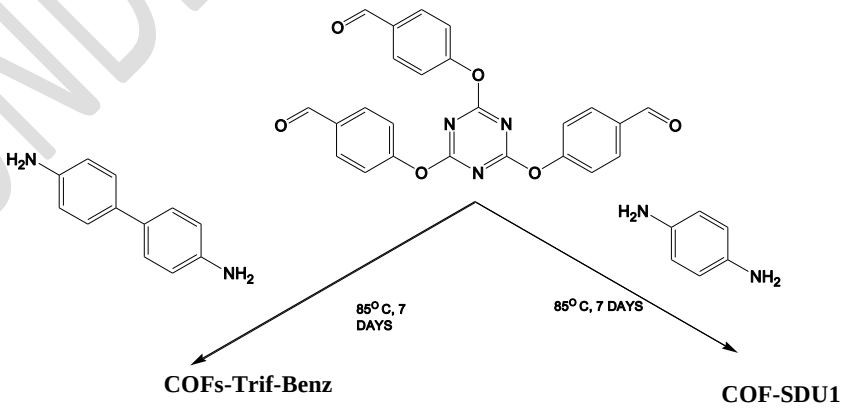


Fig 2.15.: synthetic scheme of two covalent organic frameworks, namely COFs-Trif-Benz and COF-SDU1 by facile solvo thermal reaction

Schiroky et al (2017): In this study prepared a formulation of an experimental adhesive resin with the addition of 1,3,5-triacryloylhexahydro-1,3,5-triazine at different concentration and the antibacterial activity was evaluated. Different groups of resins were prepared based on the different concentration of triazine compound along with it one group with no triazine compound was also prepared which was considered to be the control group. The study suggest that along with improvement in the other physical characteristics the formulated triazine added resins showed potent antibacterial activity against Streptococcus mutans (p0.05) [25].

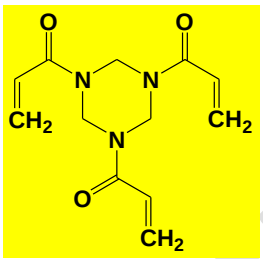


Fig 2.16: 1.3.5-triacryloylhexahydro-1.3.5- triazine.

Martin *et al.*, (2019) synthesized 2,4,6-tris(thiomorpholine)-1,3,5-triazine, 2,4,6-tris(piperazine)-1,3,5-triazine and their new Sb(III) and Bi(III) complexes. The synthesized compounds were than characterised by different spectroscopic technique and screened for their antibacterial activity against bacterial species *Staphylococcus aureus.* The antibavterial evaluation of those synthesised complexes shopwed that Sb(III) complexes exhibited quite moderate activities against the tested strains of bacteria with minimum inhibitory concentration (MIC) in range of 512-1024 mg/mL [26].

I **II**

Fig 2.17: 1,3,5 triazine derivative ligands where,

I- 2,4,6-tris(thiomorpholine)-1,3,5-triazine.

II- 2,4,6-tris(piperazine)-1,3,5-triazine.

Masih *et al.*, (2020) synthesized a series of dihydydropyrimidine-1,3,5-triazines. The synthesized compounds were than subjected to molecular docking and antibacterial activity evaluation of of three Gram-positive, *viz. Staphylococcus aureus*, *Bacillus subtilis*, *Bacillus cereus* and three Gram-negative bacterial strains *viz. Pseudomonas aeruginosa*, *Escherichia coli*, and *Proteus vulgaris*. The antibacterial activity evaluation showed significant to moderate antibacterial activity. The compound also exhibited a very distinct antibiofilm activity against *S. aureus* and *B. subtilis.* The 11th and the 12th compound proved to be most potent as it was found to be bacteriostatic in time-kill assay using numerous H-bonds via inhibition of DNA gyrase enzyme and interacting with Glu58, Val130, Ile175 and Ile186 [27].

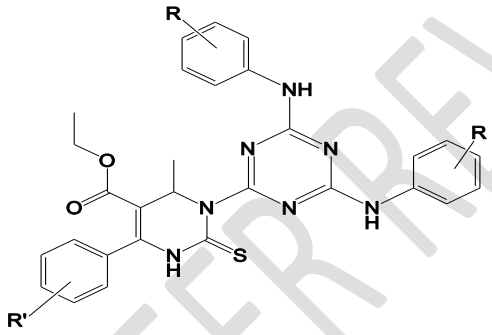


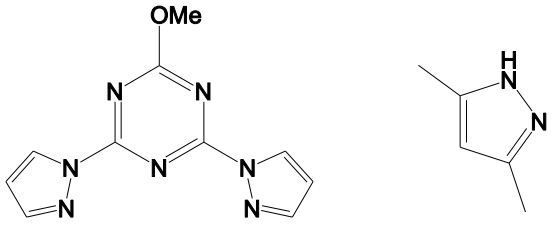
Fig 2.18: dihydydropyrimidine-1,3,5-triazine derivatives, where

11th compound:- R=3-F R'=4-F

12th compound:- R= 3-Cl R'=4-F

Soliman *et al.*, (2020): synthesized [Zn(BPT)(NO3)2] (2), and [Zn(BPT)(H2O)Cl]ClO4 (3) complexes, respectively upon reacting 2,4-bis(3,5-dimethyl-1H-pyrazol-1-yl)-6-methoxy-1,3,5-triazine (BPT) pincer ligand with Zn(NO3)2 and Zn(ClO4)2·6H2O/HCl. On the other hand [Zn(DMP)2Cl2] (1) complex (DMP = 3,5-dimethylpyrazole) was obtained upon reacting zinc(II) chloride with BPT which involved C-N rupture. The synthesised complexes were characterised by different spectroscopic technique and screened for their antibacterial activity against *E. Coli, B. subtilis, B. cereus, P. aeruginosa, St. aureus.* The antibacterial activity evaluation was done by determining the MICs values of the studied Zn(II) complexes and compared with Amoxicillin antibiotic (which was used as standard). The result obtained after completion of the process showed that the complexes [Zn(BPT)(NO3)2] (2), and

[Zn(BPT)(H2O)Cl]ClO4 (3) are more potent antimicrobial agents against the studied microbes in comparison with complex [Zn(DMP)2Cl2] (1) [28].



BPT **DMP**

Fig 2.19: Structure of the s-triazine based ligand (BPT) and 3,5-dimethylpyrazole (DMP).

Patil. *et al.*, (2020) synthesized a series of 1,3,5-triazine derivatives (3a-o)were characterised by different spectroscopic technique and screened for their antibacterial activity against against five bacterial strains, *Staphylococcus aureus (S. aureus), Escherichia coli (E. coli), Klebsiella pneumonia (K. pneumonia), Acinetobacter baumannii (A. baumannii) and Pseudomonas aeruginosa (P. Aeruginosa.* The result obtained after the antibacterial evaluation showed that the synthesized compounds were moderate to vey potent against the bacterial growth. The compound 6-(thiazol-4-yl)-1,3,5-triazine-2,4-diamine (**3o**) was found to be very active against the strains of *E. coli, K. pneumoniae, A. Baumannii.* The molecular docking study of those compounds also showed a very prominent result when performed on X-ray crystal structure of E. coli 24 kDa domain in complex with clorobiocin (PDB code: 1KZN; resolution 2.30 Å) using Surflex-Dock program of Sybyl-X software [29].

Fig 2.20: 1,3,5-triazine derivatives

Bhat et al. (2020) Synthesised a series of 4-aminoquinoline 1,3,5-triazine derivatives and were subjected to spectral and elemental analysis. The antibacterial activity of the synthesised compounds were evaluated against Bacillus subtilis, Bacillus cereus, Staphylococcus aureus, Proteus vulgaris, Escherichia coli, Pseudomonas aeruginosa using cefixime as standard.After the antibacterial evaluation it was found that the compound 7c proved to be the most potent and have shown significant activity against S. aureus, P. aeruginosa, and P. vulgaris [30].

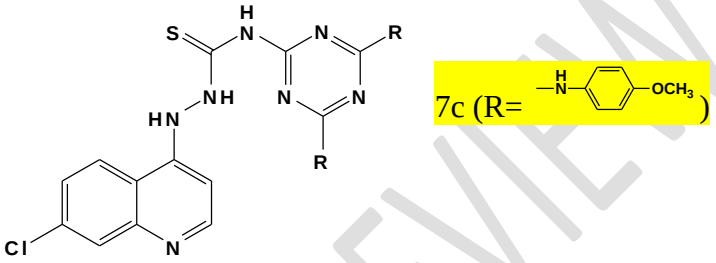


Fig 2.21: 4-aminoquinoline 1,3,5-triazine derivatives

Bodige et al. (2020) Synthesised a series of novel N-{2-fl uoro-6-[(4,6-dimethoxy-1,3,5-triazin-2-yl)methyl]phenyl} carboxamide derivatives and were subjected to spectral analysis for confirmation of the structures. The docking study of the compounds were also carried out into MTB enoyl reductase (PDB code: 4U0J) to explore their binding interactions at the active sites. The synthesised compounds were subjected to antibacterial activity evaluation using the Agar well diffusion method against Escherichia coli (gramnegative) and Staphylococcus aureus (gram-positive) strains. which suggest that the compound 7b and 7c were the most potent in comparison with the standard drug Chloramphenicol [31].

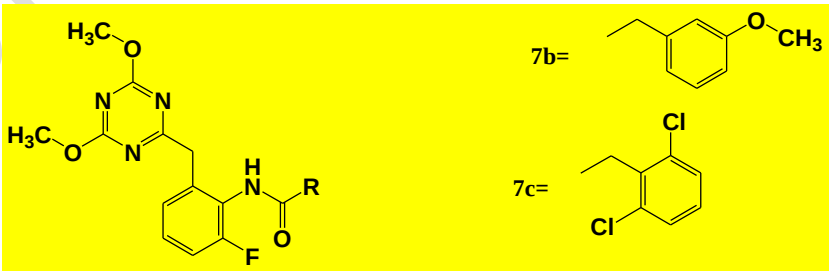


Fig 2.22.: N-{2-fl uoro-6-[(4,6-dimethoxy-1,3,5-triazin-2-yl)methyl]phenyl} carboxamide.

Güven el al. (2021): Prepared a new Zn(II) complex of 2,4,6-tri(2- pyridyl)-1,3,5-triazine. The synthesised complex was than subjected to spectral and elemental analysis and the molecular structure of the complex was investigated by X-Ray single crystal technique. The prepared [Zn(tptz)(Cl)2] was subjected to antibacterial activity evaluation against some specific strains of Gram-positive, Gram-negative and yeast by using minimal inhibitory concentration method (MIC), which suggest that the prepared complex showed significant antibacterial activity [32].

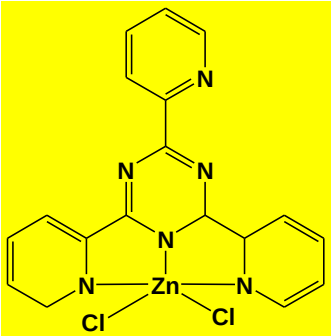


Fig 2.23.: Zn(II) complex of 2,4,6-tri(2- pyridyl)-1,3,5-triazine

3. CONCLUSION:

The resistance problem demands that a scientific effort be made to seek antibacterial agents effective against pathogenic bacteria resistant to current antibiotics. One of the possible strategies towards this objective is rational localization of bioactive photochemical. Thus making an approach for newer antibiotics is of outmost need. One of this approach is to develop newrer derivaties of 1,3,5 triazine, as triazine derivaties have found an extensive use in treating bacterial infection. In this paper we have made an extensive literature survey which compiles the effectiveness of various 1,3,5- triazine derivaties proved by various research works. From this paper, it can be concluded that the compounds various types substitutions on cyanuric chloride are potential key approach to design newer antibacterial agents. On the basis of the study carried out in this paper we can put these investigated molecules not only as lead for further synthetic and biological evaluation pursuit to discover novel class of antibacterial agents but it can also show a better path for future researchers to make an approach for developing newer antibacterial 1,3,5-triazine derivatives.

4. REFERENCES:

1) D.R. Shah, R.P. Modh, K.H. Chikhalia, Privileged s-triazines: structure and pharmacological applications, Future Med. Chem.,2014, 6, 463-477.
2) Liu, H., Long, S., Rakesh, K. P., & Zha, G.-F. " Structure-activity relationships (SAR) of triazine derivatives: Promising antimicrobial agents". European Journal of Medicinal Chemistry, 2019, 111804.
3) G. Blotny, Recent applications of 2,4,6-trichloro-1,3,5-triazine and its derivatives in organic synthesis, Tetrahedron 2006, 62, 9507-9522.
4) Gunasekaran P., Fan M., Kim E. Y., Shin J. H., Lee J. E., Son E. Bang J. K. "Amphiphilic Triazine Polymer Derivatives as Antibacterial And Anti-atopic Agents in Mice Model". Scientific Reports, 2019, 9(1).
5) Sharma A., Singh S., Utreja D., "Recent Advances in Synthesis and Antifungal Activity of 1,3,5-triazines". Current Organic Synthesis, 2016, 13(4), 484-503.
6) Adhikari, N., Kashyap, A., Shakya, A., Ghosh, S. K., Bhattacharyya, D. R., Bhat, H. R., & Singh, U. P. "Microwave assisted synthesis, docking and antimalarial evaluation of hybrid PABA-substituted 1,3,5-triazine derivatives". Journal of Heterocyclic Chemistry. 2020, 1-11.
7) Zacharie, B., Abbott, S. D., Duceppe, J.-S., Gagnon, L., Grouix, B., Geerts, L., Laurin, P. "Design and Synthesis of New 1,3,5-Trisubstituted Triazines for the Treatment of Cancer and Inflammation'. Chemistry Open,2018, 7(9), 737–749.
8) Baréa, P., Barbosa, V. A., Bidóia, D. L., de Paula, J. C., Stefanello, T. F., da Costa, W. F., Sarragiotto, M. H. " Synthesis, antileishmanial activity and mechanism of action studies of novel β -carboline-1,3,5-triazine hybrids". European Journal of Medicinal Chemistry, 2018, 150, 579–590
9) Basedia D. K., Dubey B. K., Shrivastava B.," A review on synthesis and biological activity of heterocyclic compounds bearing 1, 3, 5-triazine lead moiety". Am. J. Pharmtech Res. 2011, 1, 174–193.
10) D. R. Shah, R. P. Modh, K. H. Chikhalia, "Privileged s-triazines: structure and pharmacological applications"*Future Med. Chem* , **2014,** 6(4), 463-77.
11) Dubey V, Pathak M, Bhat HR, Singh UP. Design, Facile Synthesis, and Antibacterial Activity of Hybrid 1, 3, 4-thiadiazole-1, 3, 5-triazine Derivatives Tethered via–S–Bridge. Chemical biology & drug design. 2012,80(4):598-604.
12) Singh UP, Pathak M, Dubey V, Bhat HR, Gahtori P, Singh RK. Design, synthesis, antibacterial activity, and molecular docking studies of novel hybrid 1, 3-thiazine-1, 3,

5-triazine derivatives as potential bacterial translation inhibitor. Chemical biology & drug design. 2012;80(4):572-83.

13) Bhat H. R, Pandey P. K, Ghosh S. K, Singh U. P, "Development of 4-aminoquinoline-1,3,5-triazine conjugates as potent antibacterial agent through facile synthetic route", Medicinal Chemistry Research, 2013, 22(10), 5056-5065.

14) Singh U. P., Singh B., Bhat H. R., and Kumawat M. K., Structure-guided discovery of 1,3,5-triazine–pyrazole conjugates as antibacterial and antibiofilm agent against pathogens causing human diseases with favorable metabolic fate, Bioorganic & Medicinal Chemistry Letters, 2014, 24, 3321–3325.

15) Nirali S. Mewada, Dhruvin R. Shah, Harshad P. Lakum, Kishor H. Chikhalia, "Synthesis and biological evaluation of novel s-triazine based aryl/heteroaryl entities: Design, rationale and comparative study", Journal of the Association of Arab Universities for Basic and Applied Sciences, 2014, 20(1), 8-18.

16) Patel A. B., Chikhalia K. H., & Kumari P. "Facile synthesis of benzonitrile/nicotinonitrile based s-triazines as new potential antimycobacterial agents". European Journal of Medicinal Chemistry, 2014, 79, 57–65.

17) Patel P. K., Patel R. V., Mahajan D. H., Parikh P. A., Mehta G. N., Pannecouque C., Clercq E. D., Chikhalia K. H. "Different Heterocycles Functionalizeds-Triazine Analogues: Design, Synthesis andIn VitroAntimicrobial, Antituberculosis, and Anti-HIV Assessment". Journal of Heterocyclic Chemistry, 2014, 51(6), 1641–1658.

18) Srivastava J. K., Dubey P., Singh S., Bhat H. R., Kumawat M. K., & Singh U. P."Discovery of novel 1,3,5-triazine-thiazolidine-2,4-diones as dipeptidyl peptidase-4 inhibitors with antibacterial activity targeting the S1 pocket for the treatment of type 2 diabetes". RSC Advances, 2015, 5(19), 14095–14102.

19) Kavithaa N, Arunb A, Shafi S. S, "Synthesis, characterization and antimicrobial activity of some novel s-triazine derivatives incorporating quinoline moiety", Der Pharma Chemica, 2015, 7(10),453-458

20) Maghami M., Farzaneh F., Simpson J., Ghiasi M., Azarkish M. "Synthesis, crystal structure, antibacterial activity and theoretical studies on a novel mononuclear cobalt(II) complex based on 2,4,6-tris(2-pyridyl)-1,3,5-triazine ligand". Journal of Molecular Structure, 2015, 1093, 24–32.

21) Desai N.C., Makwana A. H. and Rajpara K.M., Synthesis and study of 1,3,5-triazine based thiazole derivatives as antimicrobial agents, Journal of Saudi Chemical Society, 2016, 20, S334–S341.

22) Ghasemian M., Kakanejadifard A., Azarbani F., Zabardasti A., Shirali S., Saki Z., & Kakanejadifard S. " The triazine-based azo-azomethine dyes; synthesis, characterization, spectroscopy, solvatochromism and biological properties of 2,2′-(((6-methoxy-1,3,5-triazine-2,4-diyl)bis(sulfanediyl)bis(2,1-phenylene))bis(azanylylidene)bis(methanylylidene))bis(4-(phenyldiazenyl)phenol)". Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, 2016, 138, 643–647.

23). Zhang TY, Li C, Tian YS, Li JJ, Sun LP, Zheng CJ, Piao HR. Synthesis and biological evaluation of dihydrotriazine derivatives as potential antibacterial agents. Chinese Chemical Letters. 2017,1;28(8):1737-42.

24) Liu T., Hu X., Wang Y., Meng, L., Zhou Y., Zhang J., Chen M, Zhang X. " Triazine-based covalent organic frameworks for photodynamic inactivation of bacteria as type-II photosensitizers". Journal of Photochemistry and Photobiology B: Biology, 2017, 175, 156–162.

25) Schiroky PR, Leitune VC, Garcia IM, Ogliari FA, Samuel SM, Collares FM. Triazine compound as copolymerized antibacterial agent in adhesive resins. Brazilian dental journal. 2017, 28:196-200.

26) 26. Martins, E. P. S., Lima, E. O., Martins, F. T., de Almeida Vasconcellos, M. L. A., & Rocha, G. B. " Synthesis, spectroscopic characterization, DFT studies, and preliminary antimicrobial evaluation of new antimony(III) and bismuth(III) complexes derived from 1,3,5-triazine". Journal of Molecular Structure, 2019, 1183 373-383.

27) Masih, A., Shrivastava, J. K., Bhat, H. R., & Singh, U. P. " Potent antibacterial activity of Dihydydropyrimidine-1,3,5-triazines via inhibition of DNA gyrase and antifungal activity with favourable metabolic profile". Chemical Biology & Drug Design, 2020;00:1–9.

28) Soliman, S. M., Elsilk, S. E., & El-Faham, A. " Synthesis, structure and biological activity of zinc(II) pincer complexes with 2,4-bis(3,5-dimethyl-1H-pyrazol-1-yl)-6-methoxy-1,3,5-triazine". Inorganica Chimica Acta, 2020, 119627.

29) Patil, V., Noonikara-Poyil, A., Joshi, S. D., Patil, S. A., Patil, S. A., Lewis, A. M., & Bugarin, A. "Synthesis, molecular docking studies, and in vitro evaluation of 1,3,5-

triazine derivatives as promising antimicrobial agents". Journal of Molecular Structure, 2020, 128687.

30) Güven GB, Çınarlı M, Şaş EB, İdil Ö, Yağcı NK. Synthesis, crystal structure, antibacterial activity and theoretical studies on a novel Zn (II) complex based on 2, 4, 6-tris (2-pyridyl)-1, 3, 5-triazine ligand. Journal of Molecular Structure. 2021, 1234:130187.

31) Bodige S, Ravula P, Gulipalli KC, Endoori S, Cherukumalli PK, Chandra JN, Seelam N. Design, Synthesis, Antitubercular and Antibacterial Activities of 1, 3, 5-Triazinyl Carboxamide Derivatives and In Silico Docking Studies. Russian Journal of General Chemistry. 2020 Jul;90(7):1322-30.

32) Bhat HR, Masih A, Shakya A, Ghosh SK, Singh UP. Design, synthesis, anticancer, antibacterial, and antifungal evaluation of 4-aminoquinoline-1, 3, 5-triazine derivatives. Journal of Heterocyclic Chemistry. 2020,57(1):390-399.