IJBPAS, July, 2023, 12(7): 3143-3161

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

A REVIEW ON *S*-TRIAZINE DERIVATIVES & ITS BIOLOGICAL ACTIVITIES

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Received 10th July 2022; Revised 15th Sept 2022; Accepted 19th Oct. 2022; Available online 1st July 2023

https://doi.org/10.31032/IJBPAS/2023/12.7.7250

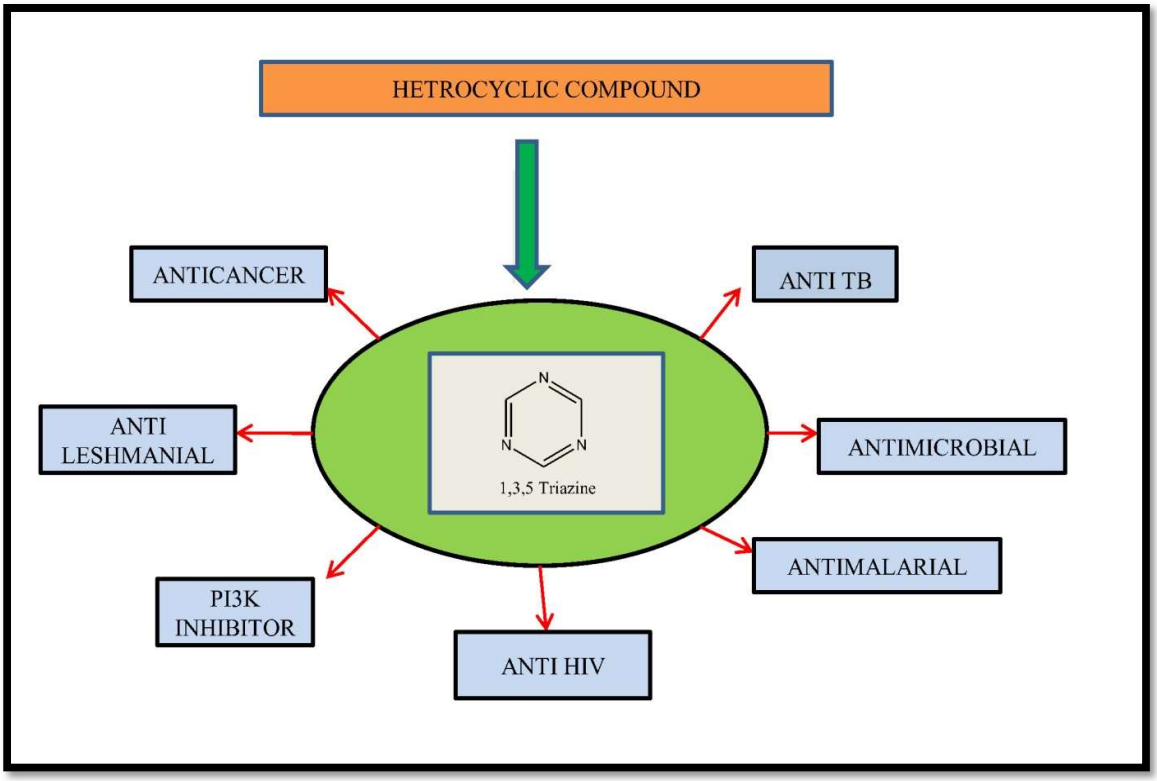
ABSTRACT

Heterocyclic compounds portray as a major part in medicinal chemistry. Distinct derivatives of heterocyclic compounds are effectives for the numerous medicinal activity. S-triazine is the earliest known heterocyclic compounds. They are available in cheap price and have distinct biological activity. Because of this researchers get attracted toward this heterocyclic compound for the synthesis of newly derivatives. They are weak base and utilize to make a potent drug, & have a different pharmacological actions.

Triazine compounds are six membered hetrocyclic compound bearing triple nitrogen atoms. Based on the position of a nitrogen atoms there are 3 different triazines compound called as 1,2,3 triazine, 1,2,4 triazine, & s- triazine respectively. Triazines are the significant core structure with bioactive characteristics. Number of triazines derivative are synthesize and assess for it abundant biological activities. Several derivative of triazine are better and have higher pharmacological action when compared to the standard drugs. The triazine reveals broad biological actions comprising antimicrobial, PI3K inhibitors, Antileshmanial, Anticancer, Anti HIV, Anti Plasmodial, Anti TB. Thus the triazines are believed to be the lead molecule for drug design and for drug discovery.

Keywords: Lead molecule, Triazine, PI3K inhibitors, Anticancer, Antileshmanial, Drug design

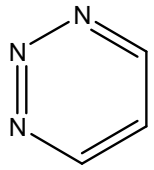
Graphical abstract:



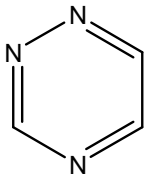
1- INTRODUCTION

1,3,5 triazine derivatives came to be well acknowledged for aprolong period of time. They have observe extensive utilization in the pharma industry, fabric industry, polymer industry and also for manufacturing of rubbers and they are also employed as insecticide ,dye stuffs, optical brightner & surfactants. All over the substituted triazines derivatives that are widely used are 2,4,6 mono, 2,4,6 di or 2,4,6 trisubstituted compound having distinct derivatives. The most valuable reactant for derive these compound is 2,4,6 trichloro 1,3,5 triazine. They are easily obtainable and mostly economical reactant. In a reactant cyanuric chloride displacement of chlorine atoms occurs by nucleophilic substitution reaction in the existence of a HCl acceptor (commonly $NaHCO_3$ or sodium carbonate make this reactant convenient for the formation of mono substituted triazine, di-substituted triazine and trisubstituted 1,3,5 triazine **[1]**. It willl be utilize to achieve an effective compound for the production of biologically effective drugs. However immense research work to be done on the catalytic physicochemical properties of 2,4,6 trichloro 1,3,5 triazine **[2]**. Displacement of chlorine atoms in 2,4,6

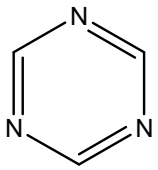
trichloro 1,3,5 triazine give various derivatives of s-triazines was found as pharmacologically effective compounds. These active synthesized compound reveals antiplasmodial, antibacterial, anticancer, & antiviral activity **[3]**. Triazine are consist of 3 nitrogen atoms and they are six membered ring compounds on the basis of location of the 3 nitrogen atoms in the triazine compound, named as 1,2,3 triazine, 1,2,4 triazine, 1,3,5 triazine **[4]**.



1,2,3 Triazine



1,2,4 Triazine



1,3,5 Triazine

1,2,3 Triazine are synthesized from 2-azidocyclopropane, Synthesis of 1,2,4 Triazine were carried out by condensation reaction of 1,2 dicarbonyl organic compound with amidrazone Whereas 2,4,6 trichloro 1,3,5 triazine is utilize for the synthesis of 1,3,5 triazine **[5]**. Out of all the 3 different triazines 1,3,5 triazines were found to be excellent activity and minimum toxic compound **[6]**. It has fascinating pharmacological activities as well as Antimicrobial, Anti HIV agents, Antimalarial, Anticancer agent, PI3K Inhibitors, Antileshmanial,Anti TB Agents,and so on **[7]**.

1.1 Physicochemical properties of triazines

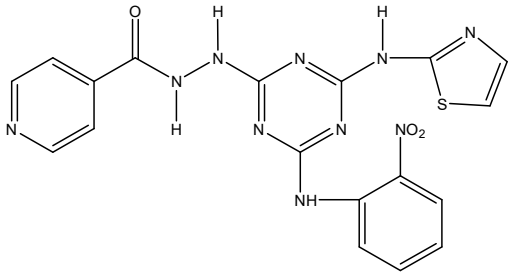
Molecular formula	**$C_3H_3N_3$**
Molecular weight	**81.08**
Boiling point	**144°C**
Melting point	**85-86°C**
Description	**Volatile in nature and Hygroscopic, Whitish crystalline solid.**
Solubility	**Soluble in organic solvents.**

2. PHARMACOLOGICAL ACTIVITIES OF *S*-TRIAZINE

2.1 Antimicrobial activity

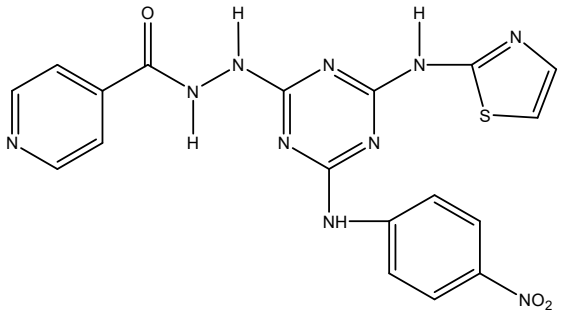
Gavade and colleagues prepared 18 derivatives out of which seven derivative reveals dominant activity against *Bacillus Subtilis & Staphylococus aureus & Escherichia coli, Pseudomonas aeriginosa* with minimum inhibitory concentration range of 6.25-12.5µg/ml **[8]**. Solankee *et al* synthesized the chalcone based novel substituted triazine derivatives as a exceptional antimicrobial agents. Where it can be viable micrococcus flavus is the most delicative bacterial amid bacteria like S.a, B.c in Agar diffusion technique. Entire derivatives evaluated & they exhibit action against entire used bacterial strain while

ampicillin don't showed the activity in the outcome of TLC- bioautographic method. According to acquired outcomes it reveals that pyridine fused compound exhibit the best pharmacological action against entire utilized bacteria with low minimum inhibitory concentration and minimum bactericidal concentration values. When contrast with standard drug & 1.5 fold lesser than streptomycin **[9]**. N.C. Desai *et al* synthesize the thiazole derivatives of 1,3,5 triazine as antimicrobic compounds. All the novel prepared compounds were analyse for their bactericidal action against strains of (*Staphylococus. aureus, Streptococcus. pyogens*) and (*Escherichia coli, Pseudomonas aeruginosa*). The novel synthesize 1,3,5 triazine reveals a greater antimicrobial potency. **Derivative I 2-nitrophenyl 1,3,5 triazine** and **Derivative II 4-nitrophenyl 1,3,5 triazine** exhibit outstanding inhibitory activity at minimum inhibitory concentration at 25 & 12.5 microgram/ml against *P. Aeruginosa* [**10]**



Derivative I

N(4-(2-nitrophenylamino)-6-(thiazol-2-ylamino)-1,3,5-triazine-2y-l)isonicotino hydrazide



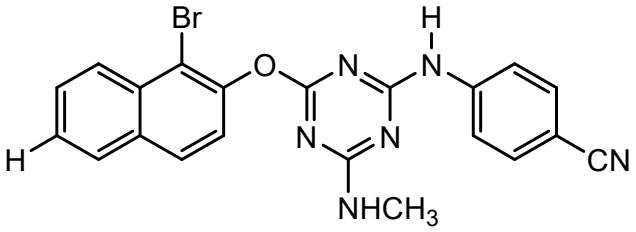
Derivative II

N(4-(4-nitrophenylamino)-6-(thiazol-2-ylamino)-1,3,5-triazine-2y-l)isonicotino hydrazide

2.2 Anti –HIV agents

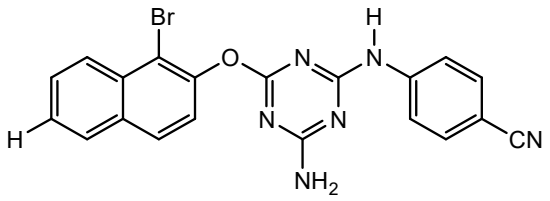
A newly synthesized list of substituted Diaryl triazine (DATA) compounds were estimate for their anti-retroviral activity in MT4-cell (In vitro) by Yuan-xiong and colleagues. The outcomes reveals that mostly compounds inhibited replication of Human immuno deficiency virus-1 at nm concentration. Amid of total 25 newly synthesized compounds, the compound

with N methyl **Derivative (III)** & the compound with amine **Derivative IV** substituents reveals to be excellent effect in inhibit replication with IC 50 = 0.0093µm, SI = 15,385 & IC_{50}= 0.0094 µm, SI= 14,094 individually and it also exhibit 15 times increased potency than nevirapine (Standard drug) **[11]**. Xiong & his colleagues also synthesized newly Diaryl triazine with a fluorinated phenyl group & evaluated their potential to block HIV-1 replica. Mostly prepared compounds bearing fluorinated phenyl group exhibit anti Hiv action in MT4 cells **[12]**. Due to discovery of DATA analogs Lie *et al* synthesized novel triazine derivatives as newly HIV-1 (NNRTIs). The chief compound exhibit outstanding activity counter to viral strains. Additionally, in vivo pharmacokinetic study in rats reveals that prepared compound (16) is good along with lower Ec50 **[13]** Lozano *et al*, prepared triazines compounds and functionalized through aroma amino acids to allow dimers, monomers and trimers. Although monomers were inactive against HIV replication and dimers, trimers exhibit outstanding activity with EC_{50}=16µm, CC_{50}=250µm. Additionally SPR research studies exhibit that proto type trimers were efficacious binders of CXCR4 & CCR5 HIV-1 (glycoprotein 120) at the extent of 1.6-2.8 µm **[14]**. Venkatraj and his co-workers described the prepared newly antiviral agents as a triazine dimers. These newly antiviral agents were acquired via divalent ligand path & paired triazine constituent are covalently attached with convenient linkage. Some derivative reveals submicromolar action in opposition to HIV-1 in TZM-bl cells & mild action toward isolated mutant genetic variant **[15]**. Norikazu sakakibara and his co-workers were synthesized the novel triazines compounds. The anti retroviral activity of these derivatives predicted when they inhibit virus induced in cytopathic in MT4 cells. Several prepared compounds exhibit excellent to mild activities against HIV-1 with (EC_{50}) in submicromolar range. Dihydro-1-(4-amino benzyl) triazine derivative exhibit excellent anti HIV-1 activity with an EC_{50} of 0.110µm & SI of 909 **[16]**.



(Derivative III)

4-(4-(1-bromonaphthalen-2-yloxy)-6-(methylamino)-1,3,5-triazin-2-ylamino)benzonitrile



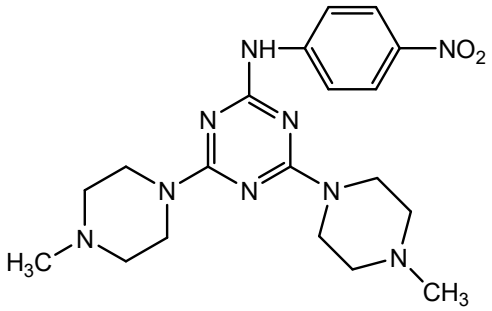
(Derivative IV)

4-(4-(1-bromonaphthalen-2-yloxy)-6-amino-1,3,5-triazin-2-ylamino)benzonitrile

2.3 Anti-Malarial

Katiyar *et al* prepared 2-(3,5 substituted pyrazol-1-yl) -4,6 trisubstituted triazine. A chain of 22 derivative is prepared and evaluation against *P. falciparum* NF 54 a genetic variant several derivative exhibit outstanding activity with minimum inhibitory concentration in the extent of 1&2 µg/ml. These derivatives are 32 times higher potent when compared to the standard drug (cycloguanil) **[17]**. Kumar *et al* synthesize a novel series of 22 compounds of acridine triazines as hybrid antiplasmodial agents. In vitro activity against 3D7 genetic variant of *P.falciparum* as well as cytotoxicity were evaluated on vitro cell line. The inhibitory concentration of derivative 17 is 4.2 nm & the inhibitory concentration of derivative 22 is 4.27nm exhibit 2 fold higher potency than CQ (IC_{50}- 8.15 nm). Additionally compound 13 & 29 exhibit > 96.59% & 98.73% suppression individually , several compounds become capable lead against N-67 strain of plasmodium yoelii in mice at oral administration of 100 mg/kg until four days **[18]**. Gahtori *et al.,* describe docking study of phenyl thiazolyl – s-triazine to the estimation of a effective tool for antifolates in antiplasmodial treatment. Mercapto (-S-) attached with 1,3,5 core derivative exhibit outstanding antiplasmodial action with % dead (ring &schizonots) = 12.0 at 50µg/ml dose [**19]**. Chellan *et al* synthesize substituted triazine pyridyl aromatic ethers. Entire prepared compounds showed mild to higher antimalarial activity on the chloroquinine sensitive genetic variant NF54 of Plasmodium .falciparum **[20]**. Pinku Gogoi *et al* snthesize a newly derivative dimethoxy s- triazine compounds, 7e,7g, & 7h evaluated and the outcome reveals IC_{50} value ranges from 53.85 to 10µg/ml against CQ. Delicate genetic variant 3D7 of P.falciparum **[21]**. Agarwal *et al* prepared a set of 19 derivatives & assess in vitro antiplasmodium activity against NF 54 genetic variant of plasmodium falciparum. From the series of 19 compound synthesize eight derivative show MIC in the extent of 1-2 µg/ml. N-methyl piperzine exhibited a MIC of 1µg/ml. The **Derivative 5** having methyl substituent reveals a minimum inhibition concentration of 1µg/ml. Substituted of methyl with benzyl it

reveals a minimum inhibitory concentration of 2µg/ml & when it substituted with phenyl it reveals a minimum inhibitory concentration of 10µg/ml. While subsitution of morpholine group with imidazole it reveals increase in activity with MIC of 1µg/ml. These outcomes highlights the greater activity of imidazole when compare to morpholine in the antiplasmodial activity **[22]**.



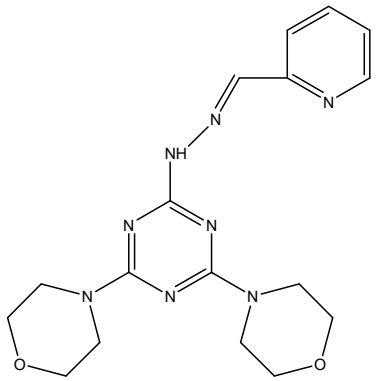
(Derivative 5)
4,6-bis(4-methylpiperazin-1-yl)-N-(4-nitrophenyl)-1,3,5-triazin-2-amine

2.4 Anticancer

Brzozowski *et al* reveals diamino – s-triazine derivatives as a antitumor agent. Synthesized derivative 11 reveals the highly effective with the values of $\log_{10}$ GI50, $\log_{10}$ TGI 50 & $\log_{10}$ LC50 of all test uniform to -5.26,-4.81, & -4.37 individually **[23]**. Brozozowski & Saczewski synthesize and evaluate the newly 1,3,5 pyrazolino triazines derivatives. Entire prepared derivative are assess in vitro antitumor activity against a series of 60 tumor cell lines at the NCI. Out of all the synthesized derivative which contain nitro moiety reveals outstanding activity to all tumor cells & reveal excellent activity against bloodcancer, CNS tumor (SF-539), cancer of breast (T-47D) **[24]**. Menicagli *et al.,* Reported the potential 2 alkyl-4,6- dihetro (N,O) alkyl-1,3,5 triazines & evaluated against cancer cell lines. It exhibit excellent activity against HL 60, L1210, C6 cell lines **[25]**. Additionally Saczewski *et al* newly synthesized & evaluated substituted 2,4,6 s-triazine acetonitrile against tumor of bladder 5637 (cell line), exocrine tumor, MCF-7 cell line & lung carcinoma. Derivative bearing (4-phenyl piperazine-1-yl) substituted at triazine ring at the locus 6 exhibited excellent action against skin cancer with GI 50 = 3.3×10^{-8}M **[26]**. Rahul V. Patel and coworkers prepared 21 derivative of newly s-triazine & these derivative were studied against prostatic carcinoma. Out of the derivatives, compound with piperazine moiety was reveals to be highly potent with the GI 50 value of 14.1µg/ml **[27].** G.Jagadeesh

kumar *et al*., prepared di and trisubstituted triazine derivatives & evaluated in vitro for anticarcinoma & assess against the carcinoma cell lines PA-1(ovarian carcinoma), AS49 (lung carcinoma), MCF-7 cell line & HT-29 (rectal cancer). It was fascinating to know that anticancer activity of trisubstituted s-triazines is more potent as contrast to disubstituted s- triazine derivatives **[28]**. Weixin Yan & coworkers study on 1,3,5 triazine derivative (EGFR-TK). The outcomes indicate that s-triazine analogs showed excellent drugs & reveals activity as a potential anticancer agent. Derivative 1d showed to be the excellent activity with an inhibitor constant (ki) 0.44nM against (EGFR-TK). Compound 1d also evaluated against 3 breast carcinoma cell lines, MDAMB231, BT474, & MCF 7 cell which results showed the derivative 1d may show the anticarcinoma effect by inhibiting catenin β signalling transduction path **[29]**. The sequence of newly compound prepared from 2,4-diamino- s-triazine & 2- iminocoumarin evaluated against the pancrease tumor cell line DAN-G, Human A427 lung carcinoma , LCLC-103H cervical carcinoma (SIS0), & bladder carcinoma RT-4 respectively. In the first series the excellent activity exhibited by compound 6 and 7 with IC_{50} in the range of 5.67-9.21µm & 8.16-15.02µm, individually. In the second series the excellent activity with less cytotoxic activity exhibited by compound 11 when compared to cisplastin **[30]**. Hessa H. Al Rasheed *et al.,* prepared a panel of 11 compounds of 1,3,5 hydrazone derivatives. Entire prepared compound was screened against MCF-7 (breast carcinoma) & HCT – 116 (Colon cancer) by utilizing MTT assay. The chief reactant for acquire these compound is cyanuric chloride or cyanuryl chloride. They reported synthesis and analysis of a few s-triazine hydrazone derivatives. The derivative (I) exhibit selective inhibitor of Mtor. The outcomes reveals that the methoxy derivative exhibit decrease effect whereas the phenolic hydroxyl group reveals greater effect. Other sequence of derivatives of 1,3,5 triazine hydrazone was detailed with individually inhibitor to (EGFR TKS). Out of all these analog the derivative of fluoro**(II)** exhibit the excellent potency against (EGFR). In addition it also shows anticancer activity against cell lines like AS49, A431, & NCI H1975. The subsituent on the 1,3,5 triazine ring mainly piperidine and CH_3O group reveals greater activity for hepatic carcinomacell line (HepG2). Although the existence of the piperidine ring and morpholine shows excellent selectivity for lung carcinoma (AS49)(III). They also study further series of s-triazine & 2 hydroxy benzylidene derivative, 4 hydroxy benzylidene derivatives (IV & V) with their anticancer activity which shows the

excellent actionagainst the MCF-7 (breast carcinoma cell) & HCT-116 (rectal carcinoma). **Derivative 6** bearing with 2 morpholine rings on the 1,3,5 triazine core exhibited excellent anti proliferative activity **[31]**.

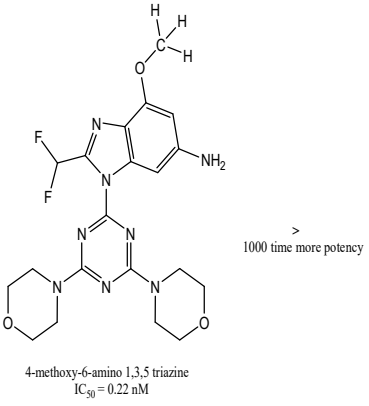


(*E*)-1-(4,6-dimorpholino-1,3,5-triazin-2-yl)-2-((pyridin-2-yl)methylene)hydrazine

(Derivative 6)

2.5 PI3K inhibitors

Richard & co-workers incorporate (R)-3-methyl morpholine straight associate to 1,3,5 triazines as newly excellent inhibitor of (Mtor). Triazine associated with methylmorpholine substituent and a ureidophenyl substitutent exhibit 400-time excellent activity through associated lipid kinase PI3K alpha **[32]**. Rewcastle *et al.,* prepared a scheme to substitute 4&6 position of ZSTK474. Out of all prepared **(Derivative7)**, 6 amino-4-methoxy analogue exhibit 1000 time more potent activity (IC_{50}= 1290nm) against the 3 enzymes (p110α, p110β, p110δ) & also shows remarkable activity against dual mutant. (H1047R & E545K). In vivo evaluation were also done of this compound against a U87MG which reveals excellent inhibiton of growth of cancer upto 81% **[33]**.

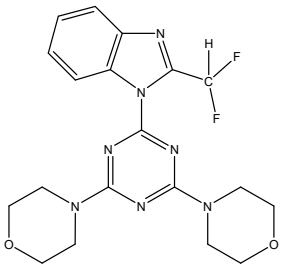


4-methoxy-6-amino 1,3,5 triazine
IC_{50} = 0.22 nM

4-methoxy-6-aza 1,3,5 triazine
IC_{50} = 1290 nM

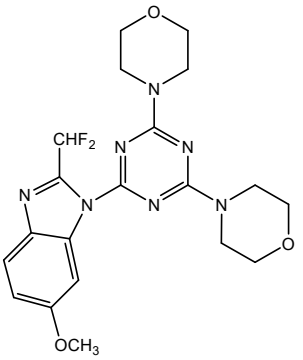
(Derivative 7)

Poulsen *et al.,* accomplish a virtual screening of a number of triazine that find to be inhibitors of mTOR along with little selectivity over PI3Kα . Finally the compound was prepared and it reveals mTOR inhibitor including an IC_{50} of 0.35µm. It exhibit **(ZSTK474)** to be a excellent PI3K inhibitor **[34]**.



ZSTK-474
mTOR IC_{50} 0.35µm
2-(difluoromethyl)-1-(4,6-dimorpholino-1,3,5-triazin-2-yl)-1H-benzo[d]imidazole

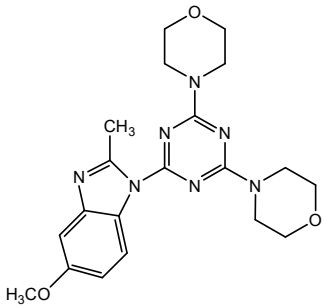
Karunakar Tanneeru & co-workers carried out 3D-QSAR, study 40 triazine analog of ATP-Competitive mTOR inhibitors via molecular field analysis study along G/PLS. Developing QSAR model via utilizing a 33 compounds. After analyzing 3D QSAR we come to the conclusion that steric and electric charges which is not in motion have a major act in approving appropriate inhibitor on the effective area of mTOR kinase [**35]**. Rew castle synthesized a analog of difluromethylmorpholinyl-s-triazine. Out of all prepared solubilized derivatives 4 amino alkoxy substituent showed the potent PI3K inhibitors as well as excellent aqueous soluble. This derivative evaluated in U-87MG Mouse model however reveals less potency than ZSTK474 **[36]**. Zask & co-workers synthesized 2-ureidophenyltriazines incorporating 2,6 & 3,5 ethylene bridge morpholine. Compound incorporating with morpholine triazine moiety exhibit potent inhibitor as compare to another morpholine analog. Analog 16 show selective mTOR suppressor each in vitro& in vivo in MDA361 & mouse carrying U-87MG tumor as well as show excellent inhibition of tumor growth **[37]**. Adrial L. Smith *et al* prepared a compounds to enhance the potency a structure base approach was utilized. The outcomes reveals compound S4 as a potent inhibitors with exceptional selectivity over m-TOR. They also exhibit inhibition of mTOR pathway along with carcinoma evolution in U87MG model **[38].** Michelle S.Miller *et al*., report an effective procedure for synthesis of derivative of s triazine 5 & 6 benzimidazolemethoxy s-triazine in which study reveals that **(Derivative 8)** 6- methoxy benzimidazole was constantly exhibited excellent potency by inhibiting PI3K when compared with **(Derivative 9)** 5 substituted benzimidazole methoxy **[39]**.



2-(difluoromethyl)-6-methoxy-1-(4,6-dimorpholino-1,3,5-triazin-2-yl)-1*H*-benzo[*d*]imidazole

Derivative 8

More potent



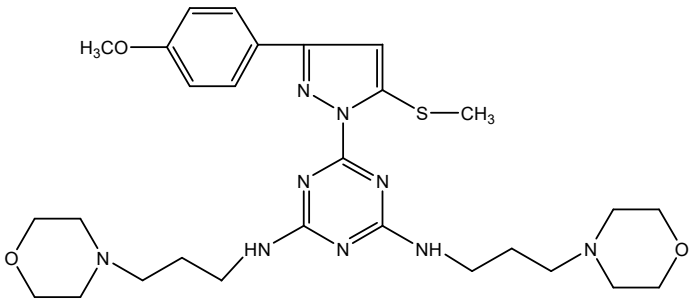
5-methoxy-2-methyl-1-(4,6-dimorpholino-1,3,5-triazin-2-yl)-1*H*-benzo[*d*]imidazole

Derivative 9

Takako Takeda *et al* develop a QSAR model to allow an perception into the mechanism of this dual inhibiton utilizing derivatives consist of morpholine triazines structure. After docking study it reveals the binding approach of MACs, LACs, & PKI-S87. Pharmacophore models is identical for PI3kα & mTOR. As recommended by the Quantitative structure activity relationship& docking study the mechanism of inhibition is identical for PI3Kα & mTOR. It seems to be alike binding approach were seen for PKI-S87 to PI3Kα & mTOR, that may be a chief principle to accomplish both inhibition activity **[40]**. Ronald A. Nelson Jr. *et al.,* synthesize a novel trisubstituted triazine (PI3K) inhibitors by virtue of 3 step. Process using consecutive nucleophilic aromatic substitution. All the novel synthesized triazines estimated as PI3K inhibitors contrast to standard PI3K inhibitors, ZSTK474. Results reveals that the novel triazine exhibited excellent potent activity at 1m(2-4 times) when contrast to the standard inhibitors ZSTK474 **[41]**. Ting-Ting Wu *et al* synthesize a newly substituted triazines containing benzimidazole based on a structure of familiar anticancer drugs named as gedatolisib. Entire novel analog prepared were evaluated & they exhiibited out of all the compound some of them inhibit PI3Kα & mTOR . From all the compounds prepared compound19 f reveals better inhibitory action with IC_{50}2.3nm for PI3Kδ when compared with PI3Kα with IC_{50} of 14.6, PI3Kβ with IC_{50}value 34.0, PI3Kγ with IC_{50} value 849.0 & mTOR with IC_{50} value 15.4 nm. Compound 19f also exhibit excellent inhibitory action toward colon carcinoma. This outcome will come after in vitro cellular metabolic activity was performed for evaluationof cellulr growth &cytostatic effects. Newly synthesize 19i derivative also exhibit 4 times excellent activity than the anticancer drug gedatolisib **[42]**.

2.6 Antileshmanial

Sunduri *et al.,* Prepared a derivative of pyrimidine trisubstituted triazines and evaluated invitro activity against promastigote model. Nine compounds exhibit > 90 % inhibition, 4 compound exhibit 80-90 % of inhibition against promastgotes of L donovani. The **derivative (10)** with N-propylaminomorpholine as R_1 has reveals excellent activity as a inhibitor at 10 µg /ml 100% inhibition will be seen , at 5 µg/ml 88.8% inhibition will be seen & at 2µg/ml 71.2% inhibition will be seen against the promastigotes of L donovani. **[43]** Naresh sunduru & coworkers again prepared a 2,4,6 trisubstituted triazines compounds and assess activity against parasite. Dihydrofolate reductase enzyme is a target of a synthesized derivative in the area of parasitic disease. Piperazine associated derivatives exhibit 100% inhibition, at 10µg/ml against luciferase-promastigote system. Although compound o. 32,33, & 13 found to be potent in vivo inhibition 48.46% 54.10%, & 56.58% at administration of 50 mg / kg for 5 working days in golden hamsters (Mesocricetus auratus) **[44]**. Leena gupta *et al* synthesize a series of thio s-triazine &thio – pyrimidines 1,2,4 triazine were prepared & evaluated which reveals activity in opposition to parasite Leishmania donovani. Out of entire synthesized compound, 8 compound reveals above 90% inhibit capability with IC_{50} in the extent of 4 - 57.7 µm amastigotes & promastigotes individually. As contrast to the drug pentamidine and (SSG) the thio s-triazine derivative exhibit outstanding activitywith minimum toxicity **[45]**. Sharma *et al* prepared novel hybrid derivative of Quinazolinone triazines, from a newly class of Natural product exhibit excellent potency as a antileshmanial agents. They discover 4 newly series of 53 derivatives of quinazolinone. All of the newly synthesized 53 compounds 8a exhibited outstanding inhibitor of parasite 73.15 ± 12.69% & 8g also exhibit excellent in vivo % inhibition 80.93 ± 10 % against mice model individually **[46]**. Paula Barea, *et al* synthesize newly β carboline s-triazine derivative. Among all the prepared compound, four compounds exhibit excellent activity in opposition to promastigote with IC_{50} values 7.6 ± 2.02, 5.1 ± 0.1, 7.5 ± 2.5, 6.2 ± 1.4 respectively. Although 9 e & 16 b also exhibit great activity against amastigote with IC_{50} value 1.1 ± 0.2, 1.2 ± 0.5 respectively **[47]**.



6-(3-(4-methoxyphenyl)-5-(methylthio)-1*H*-pyrazol-1-yl)-N^2,N^4-bis(3-morpholinopropyl)-1,3,5-triazine-2,4-diamine

Derivative 10

2.7 Anti TB Agents

Sunduru Naresh & coworkers prepared newly anti tuberculosis agents 2,4,6 trisubstituted s-triazines. They prepared 81 compounds and they are assess (invitro) against M. Tuberculosis H37RV, out of 81 prepared compounds 34 compounds exhibit excellent activity. Some derivative are more potent with MIC 1.56µg / ml – 3.12µg /ml they also evaluated cytotoxicity &they are non toxic against vero cells **[48]**. Rahul V. Patel *et al* Synthesize the substituted triazine, with fluoro group. The derivative comprise of a trifluromethyl group exhibit outstanding activity with 3.12 µg/ml MIC as contrast with sole fluorine substituent **[49]**. Avupati *et al* synthesize schiff base conjugate s- triazine and assess for estimation of anti Tb activity against H37RV (M.tuberculosis) utilizing Alamar Blue assay. Compound consist of 3,4,5 trimethoxy phenyl substituent exhibit outstanding actionwith 3.125 µg/ml MIC as contrast with the reference drugs like ethambutol, pyranzinamide, streptomycin **[50]**. Patel *et al* prepare a new derivative of s-triazine through suzuki cross-coupling reaction to evaluate the antitubercular action and antimicrobial action of prepared compounds. From all of the prepared compound some compound exhibit potential good activity against all the M.O at minimum inhibitory concentration 6.25 - 50µg/ml. All the novel derivative exhibit 6.2-25 µg/ml of MIC against bacterial compound 5h,5i, exhibit 12.5 µg/ml against mycobacterial & 25-50 µg/ml fungi (Aspergillus Niger, Aspergillus clavatus, Candida albicans) **[51]**. Mohammed H.Younis *et al* prepared novel thiazolidin-4-one & thiazole [3,2-α] [1,3,5 triazine]. They prepared 17 novel derivatives and they were estimated for their potential activity against Mycobacterium tuberculosis (Mtb) strains. Several compounds exhibit activity against the mycobacterium tuberculosis strain where DS exhibit MIC of 2.49, MDR reveals

MIC of 9.91 & XDR exhibit MIC at 39.2µm individually. Compounds 3 & 7c also reveals increased inhibitor activity against Mycobacterium Tuberculosis with IC_{50} of 3.90 & 2.47µm **[52]**. Subbarayal Reddy Dwarampudi & *et al* synthesize newly series of s-triazine chalcone derivatives & evaluated against H37RV Mycobacterium Tuberculosis. From all the synthesized compound, 4z compound show excellent potent inhibitory activity, with minimum inhibitory concentration value 3.125 µg/ml. Several other synthesized compounds lie 4e, 4p & 4b also exhibit inhibitory activity **[53]**.

CONCLUSION

This review article previewed a diverse pharmacological action of the triazine derivatives. Triazines exhibit various therapeutics activity, involving antimicrobial, antimalarial, PI3k inhibitors, Anticancer etc. This review gives information about the selection of basic moieties. Newly triazines prepared drugs have various biological activity so now a days triazines is utilized as a intensive area of research for the cure of a various diseases.

ACKNOWLEDGEMENT:

The authors would like to thank to Kharvel Subharti College of Pharmacy, Swami Vivekannad Subharti University, Meerut (U.P) for their kind support lab & literature studies.

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