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## Pharmacological activities of hybrid derivatives of -S-triazine: A review

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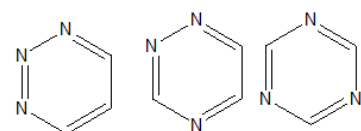
### Abstract

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 heterocyclic 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

### Introduction

1, 3, 5 triazine derivatives came to be well acknowledged for a prolong 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<sub>3</sub> or sodium carbonate make this reactant convenient for the formation of mono substituted triazine, di-substituted triazine and trisubstituted 1, 3, 5 triazine (Gregorz Blotny 2006) <sup>[14]</sup>. It will 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 (Gholap & Gunjal 2017) <sup>[11]</sup>. 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 (Khadijah *et al.*, 2017) <sup>[2]</sup>. 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 (Vishwanatha *et al.* 2011) <sup>[49]</sup>.



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 (Quirke J.M.E 1984). Out of all the 3 different triazines 1, 3, 5 triazines were found to be excellent activity and minimum toxic compound (Giacomelli *et al.* 2004) [12]. It has fascinating pharmacological activities as well as Antimicrobial, Anti HIV agents, Antimalarial, Anticancer agent, PI3K Inhibitors, Antileishmanial, Anti TB Agents, and so on (V.M Mounisammy & B Priya 2020) [47]

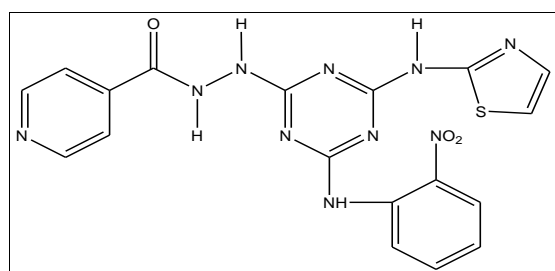
### Physicochemical properties of triazines

Molecular formula	C <sub>3</sub> H <sub>3</sub> N <sub>3</sub>
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.

### Pharmacological activities of s-triazine

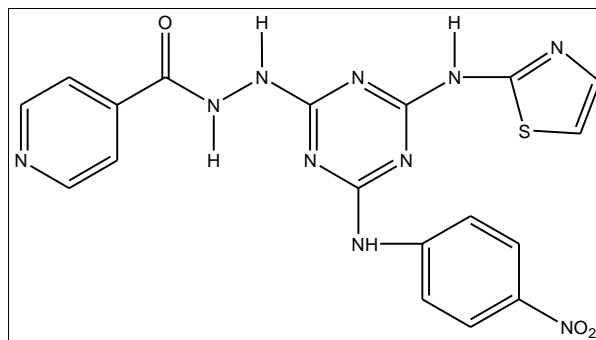
#### Antimicrobial activity

Gavade and colleagues prepared 18 derivatives out of which seven derivative reveals dominant activity against bacillus subtilis & staphylococcus aureus & Escherichia coli, Pseudomonas aeruginosa with minimum inhibitory concentration range of 6.25-12.5 µg/ml (Gavade N Sandip *et al.* 2012) [10]. 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 delicate 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 (Solankee A *et al.* 2009) [40]. 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 (Staphylococcus. 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 (Desai NC *et al.* 2012) [7]



Derivative I

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



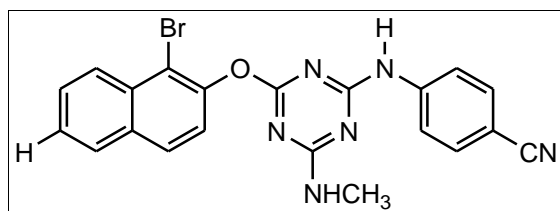
#### Derivative II

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

#### Anti-HIV agents

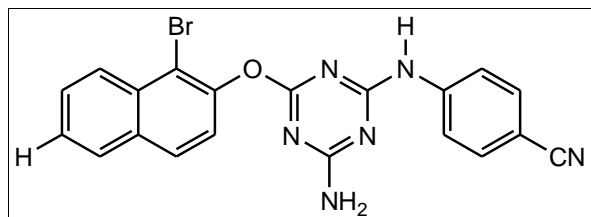
A newly synthesized list of substituted Diaryl triazine (DATA) compounds were estimate for their anti-retroviral activity in MT4-cell (*In vitro*) by Yuan-xiong and colleagues. The outcomes reveals that mostly compounds inhibited replication of Human immuno deficiency virus-1 at nm concentration. Amid 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<sub>50</sub> = 0.0093 µm, SI = 15,385 & IC<sub>50</sub> = 0.0094 µm, SI= 14,094 individually and it also exhibit 15 times increased potency than nevirapine (Standard drug) (Xiong Y-Z *et al.* 2007) [52]. 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 (Xiong Y-Z *et al.* 2009) [50]. 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 Ec<sub>50</sub> (Liu Bin *et al.* 2010) [20]. 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<sub>50</sub>=16 µm, CC<sub>50</sub>=250 µm. 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 (Lozan V *et al.* 2011) [21]. 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 (Venkatraj M *et al.* 2012) [48]. 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<sub>50</sub>) in submicromolar range. Dihydro-1-(4-amino benzyl)

triazine derivative exhibit excellent anti HIV-1 activity with an  $EC_{50}$  of 0.110 $\mu$ m & SI of 909 (Sakakibara Norikazu *et al.* 2015) [37].



#### (Derivative III)

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



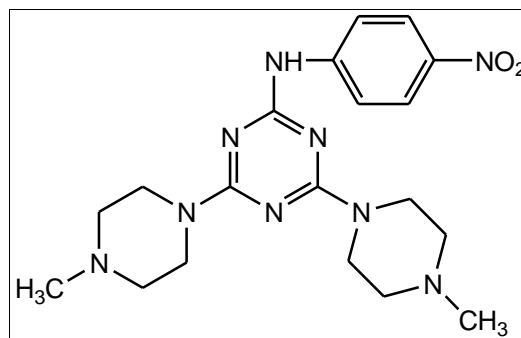
#### (Derivative IV)

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

#### 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  $\mu$ g/ml. These derivatives are 32 times higher potent when compared to the standard drug (cycloguanil) (Katiyar Sb *et al.* 2005) [42]. 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 (Kumar A, Srivastava K *et al.*). Gahtori *et al.* [9] 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 &schizonts) = 12.0 at 50 $\mu$ g/ml dose (Gahtori P *et al.* 2012) [9] Chellan et al. synthesize substituted triazine pyridyl aromatic ethers. Entire prepared compounds showed mild to higher antimalarial activity on the chloroquine sensitive genetic variant NF54 of Plasmodium falciparum (Chellan P *et al.* 2013) [6] Pinku Gogoi *et al.* synthesize a newly derivative dimethoxy s-triazine compounds, 7e,7g, & 7h evaluated and the outcome reveals  $IC_{50}$  value ranges from 53.85 to 10 $\mu$ g/ml against CQ. Delicate genetic variant 3D7 of P.falciparum (Gogoi Pinku *et al.* 2021) [13] 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  $\mu$ g/ml. N-methyl piperazine exhibited a MIC of 1 $\mu$ g/ml. The Derivative 5 having methyl substituent reveals a minimum inhibition concentration of 1 $\mu$ g/ml. Substituted of methyl with benzyl it reveals a minimum inhibitory concentration of 2 $\mu$ g/ml & when it substituted with phenyl it reveals a minimum inhibitory concentration of 10 $\mu$ g/ml. While substitution of morpholine group with imidazole it reveals increase in activity with MIC of 1 $\mu$ g/ml. These outcomes highlights the greater activity of imidazole when compare to morpholine in the antiplasmodial activity (Agarwal Anu *et al.* 2005) [1].



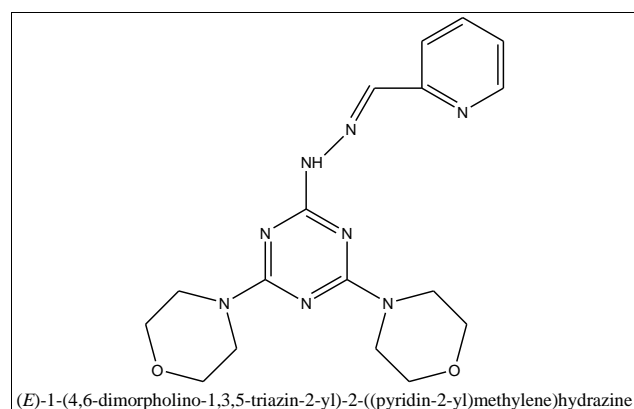
#### (Derivative 5)

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

#### Anticancer

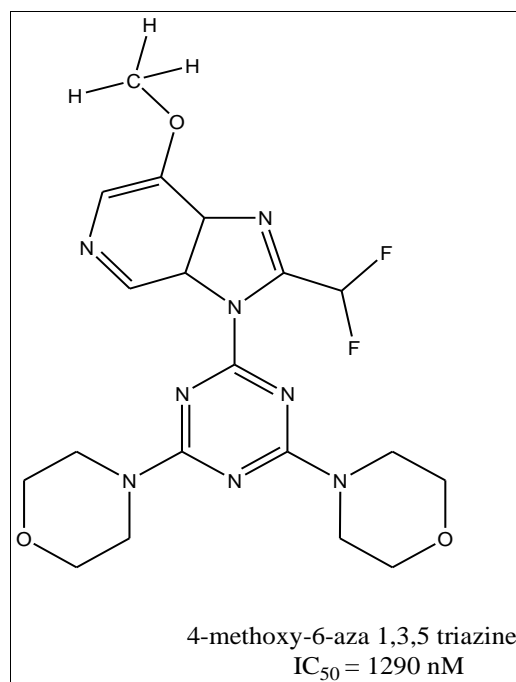
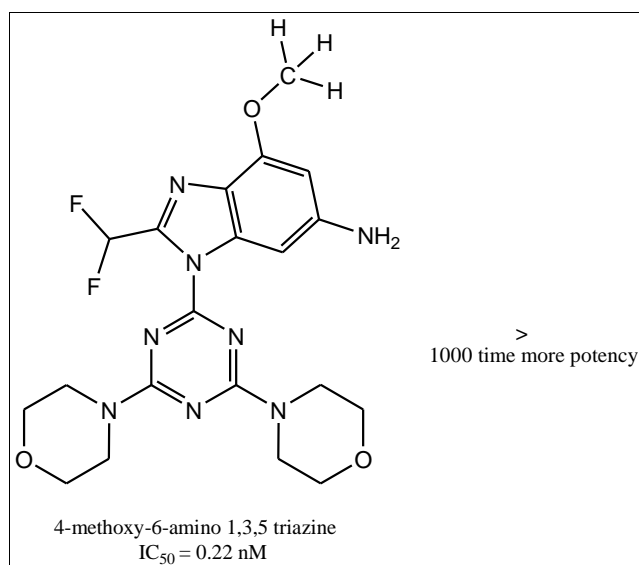
Brozowski *et al.* reveals diamino - s- triazine derivatives as a antitumor agent. Synthesized derivative 11 reveals the highly effective with the values of  $\log_{10}$  GI50,  $\log_{10}$  TGI 50 &  $\log_{10}$  LC50 of all test uniform to -5.26,-4.81, & -4.37 individually (Brozowski *et al.* 2000). Brozowski & 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) (Brozowski Saczewski f. *et al* 2002) [22]. Menicagli *et al.* Reported the potential 2 alkyl-4, 6- dihydro (N, O) alkyl-1, 3, 5 triazines & evaluated against cancer cell lines. It exhibit excellent activity against HL 60, L1210, C6 cell lines (Menicagli R, Samaritani S *et al.* 2004) [23]. Additionally Saczewski *et al.* [22] 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 $\times$ 10<sup>-8</sup>M (Saczewski F *et al.* 2006) [22]. 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 14.1 $\mu$ g/ml (Patel RV *et al.* 2011) [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 (Kumar G.J *et al.* 2013) [26]. 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  $\beta$  signalling transduction path. (Weixin Yan *et al.* 2018) [50]. The sequence of newly compound prepared from 2,4-diamino- s-triazine & 2- iminocoumarin evaluated against the pancreas 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 5.67-9.21 $\mu$ m & 8.16-15.02 $\mu$ m, individually. In the second series the excellent activity with less cytotoxic activity exhibited by compound 11 when compared to cisplatin. (Makowska Anna *et al.* 2018) [22]. 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 substituent 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 (Hessa H.Al Rasheed *et al.* 2020) [16].



### (Derivative 6) PI3K inhibitors

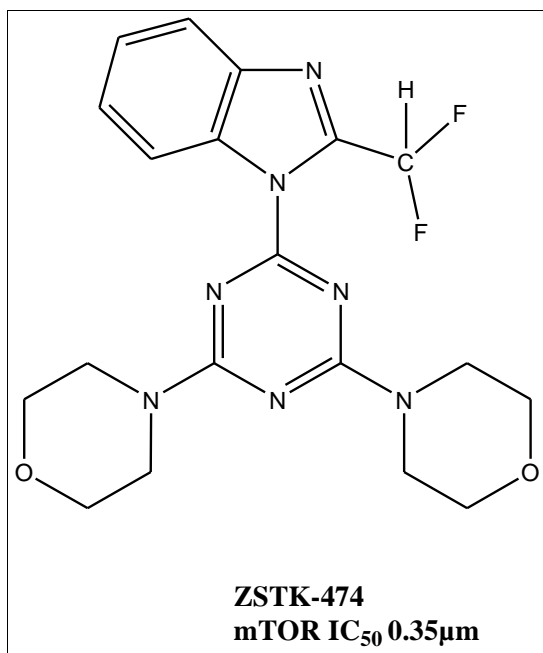
Richard & co-workers incorporate (R)-3- methyl morpholine straight associate to 1, 3, 5 triazines as newly excellent inhibitor of (Mtor). Triazine associated with methylmorpholine substituent and a ureidophenyl substituent exhibit 400-time excellent activity through associated lipid kinase PI3K alpha (Richard DJ *et al.* 2010) [34]. Rewcastle *et al.* prepared a scheme to substitute 4&6 position of ZSTK474. Out of all prepared (Derivative 7), 6 amino-4-methoxy analogue exhibit 1000 time more potent activity ( $IC_{50}$ = 1290nm) against the 3 enzymes (p110 $\alpha$ , p110 $\beta$ , p110 $\delta$ ) & also shows remarkable activity against dual mutant. (H1047R & E545K). *In vivo* evaluation were also done of this compound against a U87MG which reveals excellent inhibition of growth of cancer upto 81% (Rewcastle Gw *et al.* 2011) [32].



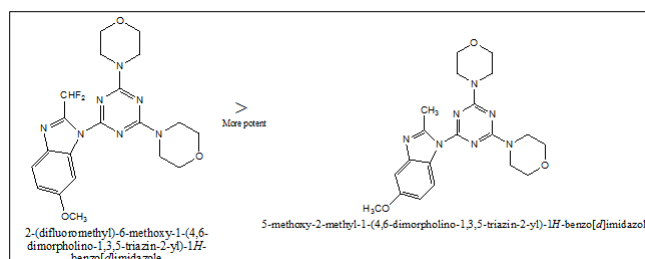
### (Derivative 7)

Poulsen *et al.* accomplish a virtual screening of a number of triazine that find to be inhibitors of mTOR along with little selectivity over PI3K $\alpha$ . Finally the compound was prepared

and it reveals mTOR inhibitor including an  $IC_{50}$  of  $0.35\mu\text{m}$ . It exhibit (ZSTK474) to be a excellent PI3K inhibitor (Poulsen A *et al.* 2012)<sup>[30]</sup>.



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 (Tanneru K *et al.* 2012). Rew castle synthesized a analog of difluoromethylmorpholinyl-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 (Rewcastle Gw *et al.* 2013)<sup>[33]</sup>. 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 (Zask A *et al.* 2010)<sup>[53]</sup> 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 (Smith AL *et al.* 2012)<sup>[39]</sup>. 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 (Miller MS *et al.* 2013)<sup>[24]</sup>.



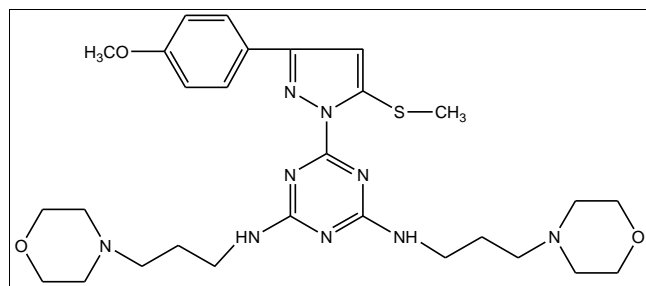
**Derivative 8**      **Derivative 9**

Takako Takeda *et al.* develop a QSAR model to allow an perception into the mechanism of this dual inhibitor 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 PI3K $\alpha$  & mTOR. As recommended by the Quantitative structure activity relationship & docking study the mechanism of inhibition is identical for PI3K $\alpha$  & mTOR. It seems to be alike binding approach were seen for PKI-S87 to PI3K $\alpha$  & mTOR, that may be a chief principle to accomplish both inhibition activity (Takako Takeda *et al.* 2016)<sup>[44]</sup>. 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 (Ronald A *et al.* 2018)<sup>[35]</sup>. 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 exhibited out of all the compound some of them inhibit PI3K $\alpha$  & mTOR. From all the compounds prepared compound 19 f reveals better inhibitory action with  $IC_{50}$  2.3nm for PI3K $\delta$  when compared with PI3K $\alpha$  with  $IC_{50}$  of 14.6, PI3K $\beta$  with  $IC_{50}$  value 34.0, PI3K $\gamma$  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 evaluation of cellular growth & cytostatic effects. Newly synthesize 19i derivative also exhibit 4 times excellent activity than the anticancer drug gedatolisib (Ting – Ting Wu *et al.* 2020).

### 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 promastigotes of L donovani. The derivative (10) with N- propylaminomorpholine as R<sub>1</sub> has reveals excellent activity as a inhibitor at 10  $\mu\text{g/ml}$  100% inhibition will be seen, at 5  $\mu\text{g/ml}$  88.8% inhibition will be seen & at 2 $\mu\text{g/ml}$  71.2% inhibition will be seen against the promastigotes of L donovani. (Sunduru N *et al.* 2006). 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 10 $\mu\text{g/ml}$  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*) (Sunduru N *et al.* 2009) [43]. 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<sub>50</sub> 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 activity with minimum toxicity (Gupta L *et al.* 2010) [15]. Sharma *et al.* prepared novel hybrid derivative of Quinazolinone triazines, from a newly class of Natural product exhibit excellent potency as a antileishmanial 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 (Sharma M *et al.* 2013) [38]. 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<sub>50</sub> 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<sub>50</sub> value 1.1 ± 0.2, 1.2 ± 0.5 respectively. (Paula Barea *et al.* 2018) [29].



6-(3-(4-methoxyphenyl)-5-(methylthio)-1H-pyrazol-1-yl)-N<sup>2</sup>,N<sup>4</sup>-bis(3-morpholinopropyl)-1,3,5-triazine-2,4-diamine

Derivative 10

### 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 1.56 μg / ml – 3.12 μg / ml they also evaluated cytotoxicity & they are non toxic against vero cells. (Sunduru N Gupta *et al.* 2010) [15]. Rahul V. Patel *et al.* Synthesize the substituted triazine, with fluoro group. The derivative comprise of a trifluoromethyl group exhibit outstanding activity with 3.12 μg/ml MIC as contrast with sole fluorine substituent. (Patel RV *et al.* 2011) [27]. 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 action with 3.125 μg/ml MIC as contrast with the reference drugs like ethambutol, pyranzinamide, streptomycin. (Avupati Vr *et al.* 2013) [3]. 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 -50 μg/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*) (Patel Ab *et al.* 2013) [26]. 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 39.2 μm individually. Compounds 3 & 7c also reveals increased inhibitor activity against *Mycobacterium Tuberculosis* with IC<sub>50</sub> of 3.90 & 2.47 μm (Mohammed H Younis *et al.* 2022) [25]. 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. (Dwarampudi Reddy Subbarayal *et al.* 2000) [8].

### 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.

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