Asian Pac. J. Health Sci., 2019; 6(2):1-20 e-ISSN: 2349-0659, p-ISSN: 2350-0964

Document heading doi: 10.21276/apjhs.2019.6.2.1 Research Article

Triazinone Derivatives as Antibacterial and Antimalarial Agents

Tarawanti Verma[1], Manish Sinha[2], Nitin Bansal[*]

[*]Department of Pharmacology, ASBASJSM College of Pharmacy, BELA, Ropar, Punjab, India

[1]PhD Research scholar, I.K. Gujral Punjab Technical University (IKGPTU), Jalandhar, Punjab, India

[2] Laureate Institute of Pharmacy, Himachal Pradesh, India

Received: 28-04-2019 / Revised: 27-05-2019 / Accepted: 30-06-2019

Abstract

A series of 2,5-disubstituted-3-phenyl-1,2-dihydro-1,2,4-triazin-6(5*H*)-one derivatives (13(a-g), 18(a-g), 21(a_1-a_5), 21b) were synthesized using appropriate synthetic route and characterized by spectral data. Synthesized compounds were evaluated for their antimalarial and antimicrobial activities. *In vitro* antimalarial activity was evaluated against chloroquine-sensitive (3D-7) strains of *Plasmodium falciparum* by using chloroquine and quinine as standard drung. For antimicrobial activity compounds were tested against four bacteria (*Escherichia coli*,*Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Streptococcus pyogenes)* and three fungi*(Candida albicans*, *Aspergillus niger*, *Aspergillus clavatus)*using gentamicin, ampicillin, chloramphenicol, ciprofloxacin, norfloxacin and nystatin, griseofulvin as standard drugs, respectively.

Keywords: Triazinone; pyrazole; antibacterial; antifungal; antimalarial; oxazolone; hydrazides.

Introduction

Microbial infections have increased dramatically in recent years. Microbes have been the cause of some of the most lethal diseases and widespread pandemic in human civilization [1]. Control of deadly infectious diseases is seriously threatened by multidrug emergence and dissemination of resistant pathogenic microbes. The issue is of serious consideration in the developing countries. Malaria is a mosquito born serious endemic disease caused by protozoa that growing over 100 countries. Multidrug resistant *Plasmodium falciparum* is the most common parasite and a serious health concern to health care specifically in tropical and sub-tropical areas. Therefore, it is an ongoing effort to synthesize new antimicrobial and antimalarial agents. In chemotherapeutic point of view, the search for a molecule having manifold targetswith variety of heterocyclic nucleus has always been a very attractive approach for researchersas an antimicrobial and antimalarial agent[2-5].

*Correspondence
Prof.(Dr.) Nitin Bansal
Department of Pharmacology, ASBASJSM College of Pharmacy, BELA, Ropar, Punjab, India

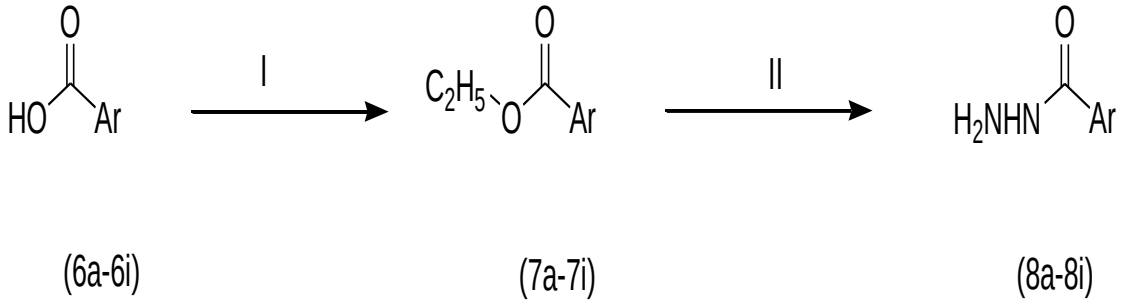
Furthermore, a wide range of chemotherapeutic activities have been ascribed to triazine derivatives including antibacterial, antifungal[6-17], antitumor [18,19], antiproliferative [20],anticancer [21-50], neuro-protective [51], antidepressant [52], anticonvulsant [53-60], neuroleptic [61, 62], nootropic [63], anti-HIV [64-68], anti-inflammatory [25, 69-74], analgesic [75], antihypertensive [76-78], cardiotonic [79], antihistaminergic [80], tuberculostatic [81], antiviral [82], estrogen receptor modulators [83], cyclin-dependent kinase inhibitors [84-86], antimalarial [87-98], and antiparasitic activities [99]potential of triazine-pyrazole derivatives [100] and triazine-furan derivatives [101-102]with hydrazides. Motivated by these facts, we were interested to synthesize and investigate the *in vitro* antimicrobial and antimalarial activities of some novel substituted fused heterocyclic ring systems namely; 2,5-disubstituted-3-phenyl-1,2-dihydro-1,2,4-triazin-6(5*H*)-one derivatives. Such targeted compounds were designed to hybridize the triazine ring with the pyrazole/furan and hydrazide moieties hoping to obtain synergistic antimicrobial activities.As part of our ongoing program directed towards the synthesis and evaluation of novel compounds of biological interest containing the pyrazole/ furan and the triazinone moieties, we have reported the synthesis of triazinones which are flexible

key intermediates for the synthesis of biologically active compounds. In our present work, we highlight the synthesis of 2,5-disubstituted-3-phenyl-1,2-dihydro-1,2,4-triazin-6(5*H*)-one derivatives with their antibacterial, antifungal and antimalarial activities. The structures of the newly synthesized compounds were confirmed by FT-IR, ^{1}H-NMR, ^{13}C-NMR and Mass spectroscopy.Biological screenings of thesynthesized heterocyclic system contain the 1,2,4-triazine moietygave quite interesting results, especially, due to their core structures. All the synthesized compounds were screened for their antimicrobial activity against four bacteria (*Escherichia coli*,*Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Streptococcus pyogenes)* and three fungi*(Candida albicans*, *Aspergillus niger*, *Aspergillus clavatus)* using gentamicin, ampicillin, chloramphenicol, ciprofloxacin, norfloxacin and nystatin, griseofulvin as standard drugs, respectively. Antimalarial activity of synthesized compounds was screened against chloroquine-sensitive (3D-7) strains of*Plasmodium falciparum*by using chloroquine and quinine as standard drug.

Chemistry

2,5-disubstituted-3-phenyl-1,2-dihydro-1,2,4-triazin-6(5*H*)-one derivatives (13(a-g), 18(a-g), 21(a_1-21a_5)& 21b) were synthesized as presented in Scheme 2, 3, 4 by refluxing substituted-2-phenyloxazol-5(4*H*)-one and hydrazine derivatives, which in turn were synthesized from the acid *via* its esterification followed by its nucleophilic substitution reaction *i.e*. hydrazinolysis with hydrazine hydrate. Substituted-2-phenyloxazol-5(4*H*)-one derivatives were synthesized from the hippuric acid & substituted aromatic aldehyde by Erlenmeyer Plochl azalactone synthesis while hippuric acid was synthesized from glycine by Schottene-Baumann benzoylation reaction. The compounds were recrystallized from ethanol. Thin layer chromatography (TLC) was run throughout the reactions to optimize the reactions for purity and completion. Spectral data IR, ^{1}H-NMR, of all the synthesized compounds and ^{13}C-NMR, and HRMS spectra of selected compounds were recorded and found in full agreement with the proposed structures. The physicochemical data for the newly synthesized compounds are presented in Table 1.

Scheme 1



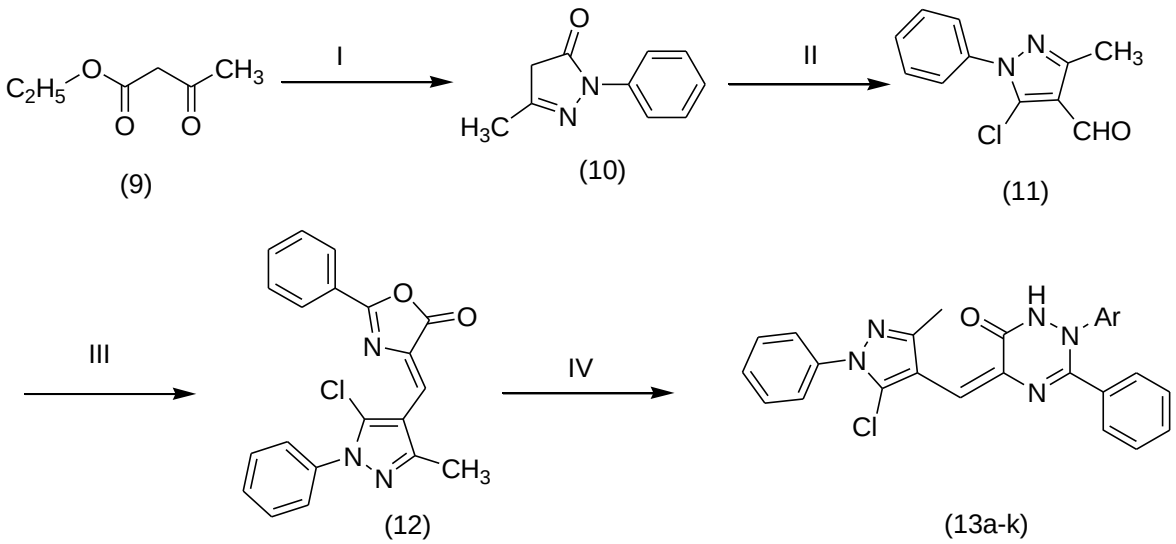
(6a-6i) (7a-7i) (8a-8i)

Reagents and conditions: I:Absoluteethanol, conc. H_2SO_4, refluxfor 10-12 h; II: Absolute ethanol, hydrazine hydrate, refluxfor10-12 h.

Table 1:Substituted acid hydrazide synthesized by Scheme 1 (8a-8e)

Compound No.	Ar
6a, 7a, 8a	*p*-NO_2-phenyl
6b, 7b, 8b	*p*-OH-phenyl
6c, 7c, 8c	*3,5*-dinitrophenyl
6d, 7d, 8d	Phenyl
6e, 7e, 8e	Naphthyl
6f, 7f, 8f	*p*-CH_3-phenyl
6g, 7g, 8g	*p*-Cl-phenyl
6h, 7h, 8h	2-pyridyl
6i, 7i, 8i	*p*-OCH_3-phenyl

Scheme 2

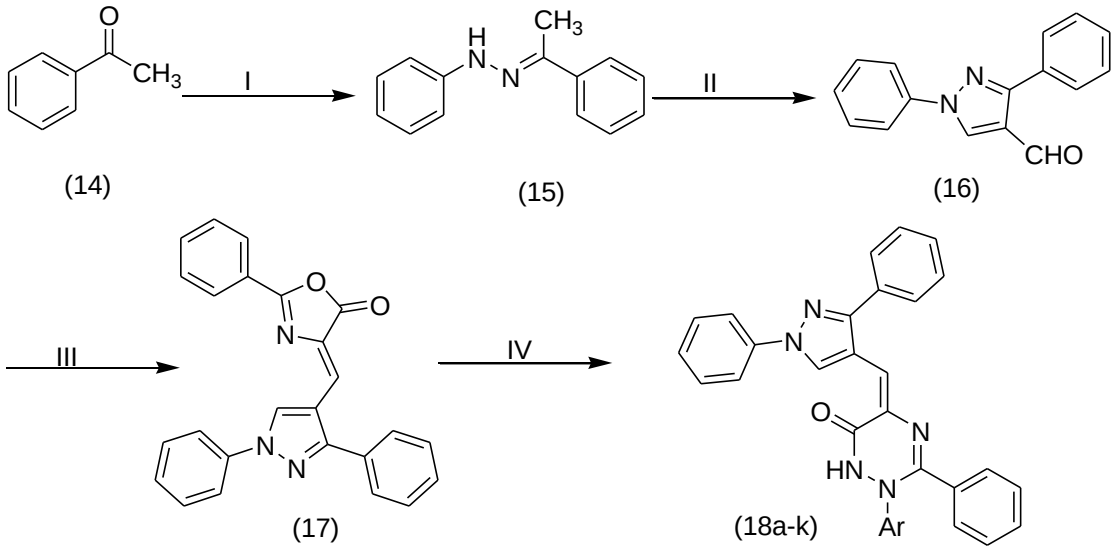


Reagents and conditions: I: Phenyl hydrazine, reflux at 110-120 ˚C for 12 h; II: DMF, $POCl_3$, reflux at 50 ˚C for 10-15 h; III: hippuric acid, acetic anhydride, anhydrous CH_3COONa, melt, heat for 2 h on water bath; IV: substituted acid hydrazide (8a-8e)/phenyl hydrazine/hydrazine hydrate,anhydrous CH_3COONa, glacial acetic acid, reflux for 8-10 h.

Table 2: 2,5-Disubstituted-3-phenyl-1,2-dihydro-1,2,4-triazin-6(5*H*)-one derivatives synthesized by Scheme 2 (13a-13g)

S. No.	Compound No.	Hydrazide used	Ar	R
1.	13a	8a		*p*-NO_2-phenyl
2.	13b	8b		*p*-OH-phenyl
3.	13c	8c		*3,5*-dinitro-phenyl
4.	13d	8d		Phenyl
5.	13e	8e		Naphthyl
6.	13f	8f		*p*-CH_3-phenyl
7.	13g	8g		*p*-Cl-phenyl
8.	13h	8h		2-pyridyl
9.	13i	8i		*p*-OCH_3-phenyl
10.	13j	Phenyl hydrazine	phenyl	-
11.	13k	Hydrazine hydrate	-H	-

Scheme 3

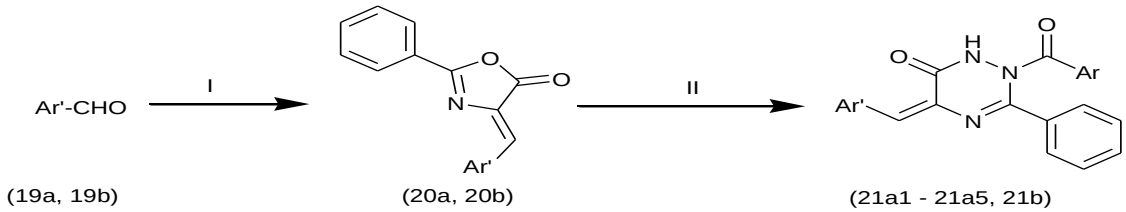


Reagents and conditions: (I) Phenyl hydrazine, ethanol, glacial acetic acid, reflux; (II) DMF, $POCl_3$, reflux at 50 ˚C for 10-15 h; (III) hippuric acid, acetic anhydride, anhydrous CH_3COONa, melt, heat for 2 h on water bath; (IV): substituted acid hydrazide (8a-8e)/phenyl hydrazine/hydrazine hydrate, anhydrous CH_3COONa, glacial acetic acid, reflux, for 8-10 h.

Table: 3: 2,5-Disubstituted-3-phenyl-1,2-dihydro-1,2,4-triazin-6(5*H*)-one derivatives synthesized by Scheme 3 (18a-18g)

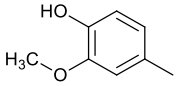
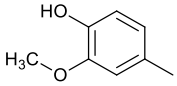
S.No.	Compound No.	Hydrazide used	Ar	R
1.	18a	8a		*p*-NO_2-phenyl
2.	18b	8b		*p*-OH-phenyl
3.	18c	8c		*3,5*-dinitro-phenyl
4.	18d	8d		phenyl
5.	18e	8e		naphthyl
6.	18f	Phenyl hydrazine	phenyl	-
7.	18g	Hydrazine hydrate	-H	-

Scheme 4



Reagents and conditions: (I)Hippuric acid, acetic anhydride, anhydrous CH_3COONa, melt, heat for 2 h on water bath; XII: substituted acid hydrazide (8a-8e), anhydrous CH_3COONa, glacial acetic acid, reflux, for 8-10 h.

Table: 4:2,5-Disubstituted-3-phenyl-1,2-dihydro-1,2,4-triazin-6(5*H*)-one derivatives synthesized by Scheme 4 (21a$_1$-21a$_5$, 21b).

S.No	Compound No.	Hydrazide used	Ar'	Ar
1.	19a, 20a	-		-
2.	19b, 20b	-		-
3.	21a$_1$	8a		*p*-NO_2-phenyl
4.	21a$_2$	8b		*p*-OH-phenyl
5.	21a$_3$	8c		*3,5*-dinitro-phenyl
6.	21a$_4$	8d		Phenyl
7.	21a$_5$	8e		Naphthyl
8	21b	8e		Naphthyl

Biological assay

Antimicrobial susceptibility assay

Broth micro-dilution method: A quantitative assay method is mainly used to determine the minimum inhibitory concentration (MIC) of antimicrobial agents/antibiotics that inhibit or kill the microorganisms.

Minimum Inhibitory Concentration: The minimum concentration of antibiotic that inhibit growth of microorganism after overnight incubation, and minimum bactericidal concentrations (MBCs) as the lowest concentration of antimicrobial that will prevent the growth of an organism after subculture on to antibiotic-free media. A 96 well tissue culture micro plate was used, for the experiment, which is based on serial dilution, first 10 wells of the row were used for serial dilution of chosen compounds, 11th was kept as positive control whereas 12th was left as media control.

- 150µl of liquid media (nutrient/sabouraud dextrose broth) was added in the well of one column then 3µl of antibiotics and constituents to be tested were added from the stock of 100 mg/ml, 20 mg/ml to achieve 1 mg/ml of concentration in first row wells, it was mixed properly and then volume was made to 300µl by addition of 147µl media.
- 150µl of media containing extracts/constituents was added to subsequent wells, same were repeated till 10th well column remained were discarded.
- 10µl of working culture suspension of bacteria/fungi were added to the entire well except media control.
- The plates were incubated at 37ºC overnight for antimicrobial activity whereas for anti- fungal activity it was incubated for 48 h at 28ºC.

Growth was indicated by turbidity and MIC were determined and expressed as µg/ml, absence of turbidity was noted as MIC; viability microbes in

particular well was also confirmed by addition of p-iodonitrotetrazolium violet (INT;0.2 mg/ml)dye.

Chemistry

Present study was undertaken to synthesize some novel 1,2,4-triazine derivatives. All the synthesized compounds were subjected for their antimicrobial and anti-malarial evaluation. The target compounds (13(a-g), 18(a-g), 21(a_1-21a_5), 21b)were synthesized by four step procedure represented inScheme 2,3,4.First step in Scheme 2 involves the formation of compound (10)by the reaction of ethyl acetoacetate with phenyl hydrazineon refluxing. Subsequently, compound (10)on reaction with phosphorus oxychloride ($POCl_3$) reflux in presence of dimethyl formamide (DMF) yieldcompound (11) on refluxing. Compound (11)reacted with hippuric acid and acetic anhydride in presence of sodium acetate anhydrous yield compound (12). Finally, compound (12)reacted withappropriate substituted acid hydrazide by refluxing in glacial acetic acid in presence of sodium acetate anhydrous to form 2,5-disubstituted-3-phenyl-1,2-dihydro-1,2,4-triazin-6 (5*H*) -one derivatives (13(a-g). In Scheme 3, compound (15) formed by reaction of acetophenone and phenyl hydrazine on refluxing. Compound (15) reflux with $POCl_3$ and DMF yields compound (16) which on reaction with hippuric acid and acetic anhydride in presence of sodium acetate anhydrous yield compound (17). Finally, compound (17) reacted with appropriate substituted acid hydrazide by refluxing in glacial acetic acid in presence of sodium acetate anhydrous to form 2,5-disubstituted-3-phenyl-1,2-dihydro-1,2,4-triazin-6 (5*H*) -one derivatives (18(a-g).In Scheme 4, compounds 19a and 19b on reaction with hippuric acid and acetic anhydride in presence of sodium acetate anhydrous yield compounds (20a and 20b), respectively. Compounds (20a and 20b) reacted with appropriate substituted acid hydrazide by refluxing in glacial acetic acid in presence of sodium acetate anhydrous to form 2,5-disubstituted-3-phenyl-1,2-dihydro-1,2,4-triazin-6 (5*H*) -one derivatives 21(a_1-21a_5), 21b), respectively. All the compounds in solid state showed sharp melting points. The compounds were stable and soluble in DMSO, methanol andchloroform. All the synthesized compounds were characterized by IR, ^{1}H NMR, ^{13}C NMR, and Mass spectroscopy. Characteristic IR bands provide significant indication for the formation of compounds (8(a-e), 13(a-g), 18(a-g), 21(a_1-21a_5), 21b). The sharp melting point at 116-120 °C and 106 °C provide strong information about the formation of compound (10 and 15), respectively. The formation of compound (11)was confirmed by the presence of band at/or around 1674 cm^{-1} (C=O), 1593 cm^{-1}(C=N), 1523 cm^{-1} (C=C) and at 763 cm^{-1} (C-Cl). The compound (16) was confirmed by the presence of band at/or around 3121, 3024 (Aromatic C-H stretching), 1666 (C=O), 1613 (C=N), 1593 (C=C). The appearance of characteristic band at/or 1797 cm^{-1}, 1610 cm^{-1},1585 cm^{-1}, 694 cm^{-1}due to Azalactone, C=N, C=C and C-Cl respectively strongly favor the formation of compound (12).The presence of characteristic band at/or 1784 (C=O, Azalactone), 1597 (C=N), 1555 (C=C) and 1789 (C=O, Azalactone), 1596 (C=N), 1555 (C=C) confirms the formation of compounds (20a and 20b), respectively. The disappearance of bands at around 1797 cm^{-1} and appearance of bands at 3310-3229 cm^{-1}, 1723-1704 cm^{-1}, 1693-1638 cm^{-1}, 1597-1611 cm^{-1}, 1537-1580 cm^{-1} due to N-H (stretching),CO and C_6=O, C=N and C=C respectively confirms the formation of compounds (13(a-g), 18(a-g), 21(a_1-21a_5), 21b).The appearance of characteristic band at/or 1789 cm^{-1}, 1597 cm^{-1}, 1556 cm^{-1} due to Azalactone, C=N and C=C respectively strongly favor the formation of compound (17). Further confirmation of all the synthesized compounds was done using ^{1}H NMR spectroscopic data. Appearance of a singlet at9.98 ppm and 2.83 ppm due to C*H*O and CH_3 proton, respectively, provides strong confirmation of the compound (11). Structure of compound (12)was confirmed by the absence of peak at 9.98 ppm due to C*H*O proton and also by the appearance of a singlet at 7.23 ppm due to C*H*=C proton. Structural confirmation of final compounds was achieved by the presence of singlet at 10.58 ppm due to CON*H* proton. The ^{13}C NMR spectra of final compounds showed some prominent signals, such as signals at 170.27 ppm, 164.28 ppm, 157.08 ppm, 151.53 ppm and 150.20 ppm due to presence of *C*=O, C_6, C_3, *C*-NO_2 and *C*-CH_3 respectively and provide strong recommendation for the formation of these compounds (13(a-g), 18(a-g), 21(a_1-21a_5), 21b). Other peaks were also present in the NMR spectra of these compounds at their usual positions described in the experimental section.

Antibacterial activity

All the synthesized compounds (13(a-g), 18(a-g), 21(a_1-21a_5), 21b)were screened for their *in vitro* antimicrobial activity using the Gram-positive, Gram-negativebacteria and fungi. Four different cultures, two each of Gram-negative (*Escherichia coli* and *Pseudomonas aeruginosa*) and Gram-positive (*Staphylococcus aureus*, *Streptococcus pyogenes*)were treated with the synthesized compounds (13(a-g), 18(a-g), 21(a_1-21a_5), 21b)using broth micro dilution method. *In vitro* antimalarial activity of all the compounds was evaluated against chloroquine-sensitive (3D-7) strains

of *Plasmodium falciparum*by using chloroquine and quinine as standard drung.

Table: 5: *In vitro*Antibacterial activity (MIC, µg/mL) of compounds (13(a-g), 18(a-g), 21(a_1-21a_5), 21b)

S. No.	Code No.	Gram Positive		Gram Negative	
		***S. Aureus* MTCC 96**	***S. Pyogenes* MTCC 443**	***E. Coli* MTCC 442**	***P. Aeruginosa* MTCC 441**
1.	13a	250	200	125	125
2.	13b	**100**	250	200	125
3.	13c	**100**	125	250	250
4.	13d	200	200	250	200
5.	13e	**100**	250	125	250
6.	13f	200	250	250	200
7.	13g	**100**	250	**100**	**100**
8.	18a	**100**	**100**	**62.5**	200
9.	18b	**125**	250	**100**	250
10.	18c	**62.5**	**62.5**	**100**	**100**
11.	18d	**62.5**	250	250	250
12.	18e	200	500	200	200
13.	18f	250	200	125	**100**
14.	18g	200	250	**100**	125
15.	21a1	**62.5**	250	250	250
16.	21a2	200	125	125	**100**
17.	21a3	250	**100**	200	**100**
18.	21a4	**100**	125	200	200
19.	21a5	200	125	**100**	**62.5**
20.	21b	500	500	**62.5**	125
	Gentamycin	0.25	0.5	0.05	1
	Ampicillin	250	100	100	-
	Chloramphenicol	50	50	50	50
	Ciprofloxacin	50	50	25	25
	Norfloxacin	10	10	10	10

Table: 6: *In vitro* Antifungal activity (MIC, µg/mL) of compounds (13(a-g), 18(a-g), 21(a_1-21a_5), 21b)

S. No.	Code No.	Fungi		
		C. albicans MTCC 227	***A. niger MTCC 282***	***A. clavatus* MTCC 1323**
1.	13a	1000	1000	1000
2.	13b	**500**	>1000	>1000
3.	13c	>1000	250	500
4.	13d	>1000	500	500
5.	13e	**250**	>1000	>1000
6.	13f	**500**	>1000	>1000
7.	13g	1000	>1000	>1000
8.	18a	1000	500	500
9.	18b	>1000	>1000	>1000
10.	18c	1000	500	500
11.	18d	1000	500	1000
12.	18e	>1000	1000	1000
13.	18f	**500**	500	1000
14.	18g	1000	500	500
15.	21a1	**500**	1000	>1000
16.	21a2	**500**	>1000	>1000

17.	21a3	**250**	1000	1000
18.	21a4	**250**	**250**	500
19.	21a5	**250**	500	500
20.	21b	1000	500	500
	Nystatin	100	100	100
	Greseofulvin	500	100	100

Table: 7: *In vitro*Antimalarial activity of compounds ((13(a-g), 18(a-g), 21(a_1-21a_5), 21b)) against Plasmodium falciparum (3D-7)

S. No.	Code No.	IC_{50} (µg/mL) ***Plasmodium falciparum* (3D-7)**
1.	13a	**0.98**
2.	13b	1.13
3.	13c	1.20
4.	13d	**0.88**
5.	13e	**0.93**
6.	13f	**0.97**
7.	13g	1.13
8.	18a	**0.98**
9.	18b	**0.96**
10.	18c	**0.91**
11.	18d	**0.90**
12.	18e	**0.95**
13.	18f	**0.92**
14.	18g	**0.91**
15.	21a1	1.07
16.	21a2	1.16
17.	21a3	1.00
18.	21a4	**0.85**
19.	21a5	**0.90**
20.	21b	**0.95**
	Chloroquine	0.02
	Quinine	0.27

Results and discussions

The twenty 1,2,4-triazin-6(5*H*)-one derivatives (13(a-g), 18(a-g), 21(a1-21a5), 21b) were synthesized in good yield. The structures of these compounds were confirmed by IR, 1H-NMR, 13C-NMR and mass analysis. The synthesized compounds were evaluated for their antimicrobial and antimalarial activity. Out of the synthesized compounds thirteen analogues have shown MIC in the range of 100–200 µg/mL. Compounds 18c, 18d and 21a1 exhibited excellent activity and 13b, 13c, 13e, 13g, 18a and 21a4 compounds exhibited good activity against *S. Aureus* as compared to Ampicillin (MIC= 250 µg/mL). Compound 18c exhibited excellent activity at 62.5 µg/mL and 18a and 21a3 exhibited good activity at 100 µg/mL against S. Pyogenesas compared to Ampicillin (MIC= 100 µg/mL). Compounds 18a and 21b showed excellent activity at 62.5 µg/mL and 13g, 18b, 18c, 18g and 21a5 exhibited good activity at 100 µg/mLagainst *E. Coli* as compared to Ampicillin (MIC= 100 µg/mL). Compounds 13g, 18c, 18g, 21a2, 21a3 and 21a5 exhibited good activity at 62.5-100µg/mL against *P. Aeruginosa* as compared to Chloramphenicol (MIC= 50 µg/mL). Most of the compounds showed very good antifungal activity against *Candida albicans*, their MIC values were in the range between (250-500 µg/mL). Compounds 13e, 21a3, 21a4 and 21a5 showed excellent activity at 250 µg/mL and compounds 13b, 13f, 18f, 21a1 and 21a2 showed average activity at 500 µg/mL against *C. albicans* as compared to Griseofulvin (MIC= 500 µg/mL). Whereas 13c compound showed good activity against *Aspergillus Niger* as compared to Griseofulvin and Nystatin (MIC= 100 µg/mL). Some compounds showed good antimalarial activity at 0.88-0.98 µg/mL against *Plasmodium falciparum* as compared to quinine. Thus, the existence of aromaticity

and lipophilicity found to have strong significance to the antimicrobial and antimalarial activity.

Conclusion

In this article, we have report a series of 1,2,4-triazin-6(5*H*)-one derivatives showing better activity. All the synthesized compounds have been established by IR, ^{1}H NMR and ^{13}C-NMR and mass spectral data. In conclusion, the potency and selectivity of synthesized compounds against standard drugs make them effective leads for new research in future that possess better activity antimicrobial and antimalarial chemotherapy. These new molecules are very useful for more optimization effort in microbial and protozoal chemotherapy.

Experimental

Chemistry

All the chemicals used were laboratory grade and procured from E. Merck (Germany), S.D. Fine Chemicals, Rankem and Spectrochem Pvt. Ltd. (India). Melting points were determined by open glass capillary tube and are uncorrected. Thin layer chromatography (TLC) plates were used to confirm the purity of commercial reagents used, compounds synthesized and to monitor the reactions as well. Two different solvent systems; toluene: ethyl acetate: formic acid (5:4:1) and ethyl acetate: hexane (0.5:9.5), were used to run the TLC. The spots were located under iodine vapors/UV light. IR spectra were obtainedin the region 4000-400 cm^{-1} range using potassium bromide (KBr) discs on Nicolet 380 FT-IR. The proton nuclear magnetic resonance ^{1}H-NMR, ^{13}C-NMR and mass spectra of a few compounds were recorded on Bruker Avance II 400 NMR spectrometer & Bruker model DRX-300 NMR spectrometer-using TMS as internal standard in DMSO-d_6/$CDCl_3$. The ESI-MS spectrums were recorded on a Waters Micromass Q-TOF Micro Mass Spectrometer.

Synthesis of 3-methyl-1-phenyl-2-pyrazolin-5-one (*10*) [103-106]:A mixture of (0.1mol) ethyl acetoacetate (***4***) and (0.1mol) phenylhydrazine was refluxed in RBF at 110-120 ˚C for 12 h. After cooling the reaction mixture, diethyl ether was added with stirring to obtain the solid product. Washed the crude product with diethyl ether and further with water. After drying, it was recrystallized with ethanol to obtain pure crystals as a pale yellow crystalline compound. Yield: 73%; m.p.:116-120 ˚C; R_f:0.58 (Toluene: Ethyl acetate: Formic acid (5:4:1)).

Synthesis of acetophenone phenylhydrazone (*15*) [107,108]:Reflux a mixture of (0.1 mol) acetophenone (***9***) and (0.1 mol) phenylhydrazine with 60 mL of ethanol and a few drops of glacial acetic acid. The crude product so obtained on cooling was recrystallised from ethanol to obtain a pure acetophenone phenylhydrazone as a white solid. Yield: 76%; m.p.: 106 ˚C; R_f:0.76 (Ethyl acetate: Hexane (0.5:9.5)).

Procedure for synthesis of 5-chloro-3-methyl-1-phenyl-1*H*-pyrazole-4-carboxaldehyde (*11*) [109]:Phosphorous oxy chloride was added dropwise with stirring in dry di-methyl formamide placed at 0 ˚C. The solution was stirred at the same temperature. After two hours 3-methyl-1-phenyl-2-pyrazolin-5-one was added in the solution and again stirred for one hour at 50 ˚C. Then the solution was refluxed for 10-15 h. Poured the solution in to the crushed ice with stirring and neutralized with saturated solution of sodium bicarbonate. The crude product so obtained was filtered and washed with water. It was further recrystallized from ethanol and desired compound obtained as brown needles. Yield: 62.5%; m.p.: 140-144 ˚C; R_f:0.71 (Toluene: Ethyl acetate: Formic acid (5: 4: 1)). IR ν_{max} (cm^{-1}): 3053 (Aromatic C-H stretching), 2921 (Aliphatic C-H stretching), 1674 (C=O), 1593 (C=N), 1523 (C=C), 763 (C-Cl). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) 9.98 (s, 1H, C*H*O), 7.56-7.47 (m, 5H, Ar-*H*) 2.83 (s, 3H, CH_3).

Procedure for synthesis of 1,3-diphenyl-1*H*-pyrazole-4-carbaldehyde (*16*) [110]:Phosphorous oxy chloride was added dropwise with stirring in dry di-methyl formamide placed at 0 ˚C. The solution was stirred at the same temperature. After two hours acetophenone phenylhydrazone was added in the solution and again stirred for one hour at 50 ˚C. Then the solution was refluxed for 10-15 h. Poured the solution in to the crushed ice with stirring and neutralized with saturated solution of sodium bicarbonate. The crude product so obtained was filtered and washed with water. It was further recrystallized from ethanol and desired compound obtained as brown needles. Yield: 70%; m.p.: 138-140 ˚C; R_f: 0.39 (Toluene: Ethyl acetate: Formic acid (5:4:1)). IR ν_{max} (cm^{-1}): 3121, 3024 (Aromatic C-H stretching), 1666 (C=O), 1613 (C=N), 1593 (C=C). ^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm) 10.05 (1s, 1H, C*H*O), 8.54 (1s, 1H, C_5-*H*), 7.83-7.77 (m, 4H, Ar-*H*), 7.53-7.41 (m, 5H, Ar-*H*), 7.41-7.38 (t, 1H, Ar-*H*).

Procedure for the synthesis of 4-((5-chloro-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)methylene)-2-phenyloxazol-5(4*H*)-one (*12*) [111]:A mixture of 5-chloro-3-methyl-1-phenyl-1*H*-pyrazole-4-carboxaldehyde (0.25 mol), hippuric acid (0.25 mol),

acetic anhydride (0.75 mol) and anhydrous sodium acetate was taken in a 500 mL conical flask and heated on an electric hot plate with constant shaking. As soon as the mixture liquefied completely, transferred the flask to a water bath and heated for 2 h. Then added 100 mL of ethanol slowly to the contents of the flask and allowed the mixture to stand overnight. Filtered the crystalline product with suction and first washed with two 25 mL portions of ice-cold alcohol and then washed with two 25 mL portions of boiling water & dried at 100 ˚C. Yellow solid; Yield: 60%; m.p.: 184-186 ˚C; R_f: 0.82 (Toluene: Ethyl acetate: Hexane (5:4:1)). IRν_{max} (cm^{-1}): 3053 (Aromatic C-H stretching), 2929 (Aliphatic C-H stretching), 1797 (C=O, Azalactone), 1610 (C=N), 1585 (C=C), 694 (C-Cl). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) 8.13-8.10 (d, 2H, Ar-*H*), 7.63-7.43 (m, 8H, Ar-*H*), 7.23 (s, 1H. C*H*=C), 2.79 (s, 3H, CH_3).^{13}C-NMR (75 MHz, $CDCl_3$): δ (ppm) 167.60 (*C*=O), 161.96 (C_2, Azalactone), 151.03 (C_3, pyrazole), 137.57 (N_1-*C*), 133.11, 131.48, 131.02, 129.23, 129.01, 128.84, 128.04, 125.70, 124.91, 121.91, 114.04, 16.42 (*C*H_3).

Procedure for the synthesis of 4-[(1,3-diphenyl-1*H*-pyrazol-4-yl)methylidene]-2-phenyl-1,3-oxazol-5(4*H*)-one (*17*):A mixture of 1,3-diphenyl-1*H*-pyrazole-4-carbaldehyde (0.25 mol), hippuric acid (0.25 mol), acetic anhydride (0.75 mol) and anhydrous sodium acetate was taken in a 500 mL conical flask and heated on an electric hot plate with constant shaking. As soon as the mixture liquefied completely, transferred the flask to a water bath and heated for 2 h. Then added 100 mL of ethanol slowly to the contents of the flask and allowed the mixture to stand overnight. Filtered the crystalline product with suction and first washed with two 25 mL portions of ice-cold alcohol and then washed with two 25 mL portions of boiling water & dried at 100 ˚C. Orange solid; Yield: 70%; m.p.: 110-116 ˚C; R_f: 0.81 (Toluene: Ethyl acetate: Formic acid (5:4:1)). IR ν_{max} (cm^{-1}): 3056 (Aromatic C-H stretching), 2917 (Aliphatic C-H stretching), 1789 (C=O, Azalactone), 1597 (C=N), 1556 (C=C). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) 9.23 (s, 1H, C_5-*H*), 8.19-8.17 (d, 2H, Ar-*H*), 7.91-7.88 (d, 2H, Ar-*H*), 7.73-7.71 (d, 2H, Ar-*H*), 7.65-7.49 (m, 8H, Ar-*H*), 7.42-7.38 (m, 2H, Ar-*H*, C*H*=C). ^{13}C-NMR (75 MHz, $CDCl_3$): δ (ppm) 167.03 (*C*=O), 162.19 (C_2), 155.25 (C_3, pyrazole), 139.40 (N_1-C_1), 137.84 (C_4), 133.18, 131.69, 131.62, 131.42, 129.65, 129.47, 128.98, 128.18, 127.63, 125.70, 123.59, 119.80, 116.13.

Procedure for the synthesis of 4-(furan-2-ylmethylene)-2-phenyloxazol-5(4*H*)-one (*20a*):A mixture of furfuraldehyde (0.25 mol), hippuric acid (0.25 mol), acetic anhydride (0.75 mol) and anhydrous sodium acetate was taken in a 500 mL conical flask and heated on an electric hot plate with constant shaking. As soon as the mixture liquefied completely, transferred the flask to a water bath and heated for 2 h. Then added 100 mL of ethanol slowly to the contents of the flask and allowed the mixture to stand overnight. Filtered the crystalline product with suction and first washed with two 25 mL portions of ice-cold alcohol and then washed with two 25 mL portions of boiling water & dried at 100 ˚C.Orange solid; Yield: 80%; m.p.: 202-203 ˚C; R_f: 0.80 (Toluene: Ethyl acetate: Formic acid (5:4:1)). IRν_{max} (cm^{-1}): 3107 (Aromatic C-H stretching), 2845 (Aliphatic C-H stretching), 1784 (C=O, Azalactone), 1597 (C=N), 1555 (C=C). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) 8.17-8.14 (d, 2H, 2-furan, Ar-*H*), 7.68 (s, 1H, C*H*=C), 7.63-7.49 (m, 5H, 4-furan, Ar-*H*), 7.17 (s, 1H, 3-furan).

Procedure for the synthesis of 4-(4-hydroxy-3-methoxybenzylidene)-2-phenyloxazol-5(4*H*)-one (*20b*):A mixture of vanillin (0.25 mol), hippuric acid (0.25 mol), acetic anhydride (0.75 mol) and anhydrous sodium acetate was taken in a 500mL conical flask and heated on an electric hot plate with constant shaking. As soon as the mixture liquefied completely, transferred the flask to a water bath and heated for 2 h. Then added 100 mL of ethanol slowly to the contents of the flask and allowed the mixture to stand overnight. Filtered the crystalline product with suction and first washed with two 25 mL portions of ice-cold alcohol and then washed with two 25 mL portions of boiling water & dried at 100 ˚C. Yellow solid; Yield: 79%; m.p.: 240-242 ˚C; R_f: 0.81 (Toluene: Ethyl acetate: Formic acid (5:4:1)). IRν_{max} (cm^{-1}): 3100 (Aromatic C-H stretching), 2845 (Aliphatic C-H stretching), 1789 (C=O, Azalactone), 1596 (C=N), 1555 (C=C). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) 8.14-8.12 (d, 3H, Ar-*H*), 7.64-7.59 (m, 3H, Ar-*H*, C*H*=C), 7.55-7.50 (m, 2H, Ar-*H*), 7.20 (s, 1H, O*H*), 7.14- 7.11 (d, 1H, Ar-*H*), 3.94 (s, 3H, CH_3).

General procedure for the synthesis of acid hydrazide (*8a-e*)[107, 112]:Aromatic acids were first converted to its ester by esterification procedure using conc. sulphuric acid as a catalyst in absolute ethanol. The mixture of acid, absolute ethanol and conc. sulphuric acid were refluxed for 10-12 h, distilled off about half of the alcohol on a water bath after this, diluted the residue with sufficient quantity of water and removed the upper layer of the crude ester and extracted the aqueous layer with ether. Later on, combined ethereal extract and crude ester were washed with water, then with saturated sodium hydrogen carbonate solution until effervescence ceased, and finally with water. Dried with anhydrous sodium sulphate & removed the ether on a water bath. To an alcoholic solution of aromatic ester, hydrazine hydrate

was added. The resulting reaction mixture was refluxed for10-12 h. The excess of alcohol was distilled off and cooled. Filtered off, the crystals of acid hydrazide and recrytallised from ethanol. The physicochemical data of the substituted hydrazine derivatives is given below:

***p*-Nitrobenzohydrazide (8a)**: White solid; Yield: 76%; m.p.: 144-146 ˚C; R_f: 0.15 (Toluene: Ethyl acetate: Formic acid (5:4:1)). IRν_{max} (cm^{-1}): 3337 (N-H, stretching), 3109 (Aromatic C-H stretching), 3060(Aliphatic C-H stretching), 1650 (C=O), 1597 (C=N), 1503 (C=C).

***p*-Hydroxybenzohydrazide (8b)**: Off white solid; Yield: 70%; m.p.: 258-260 ˚C; R_f: 0.21 (Toluene: Ethyl acetate: Formic acid (5:4:1)). IRν_{max} (cm^{-1}): 3313 (N-H, stretching), 3198 (Aromatic C-H stretching), 2802(Aliphatic C-H stretching), 1613 (C=O), 1535 (C=N), 1503 (C=C).

***3,5*-Dinitrobenzohydrazide (8c):** White solid; Yield: 83%; m.p.: 155-157˚C; R_f: 0.35 (Toluene: Ethyl acetate: Formic acid (5:4:1)). IRν_{max} (cm^{-1}): 3298 (N-H, stretching), 3123 (Aromatic C-H stretching), 3046(Aliphatic C-H stretching), 1637 (C=O), 1524 (C=N), 1424 (C=C).

Benzohydrazide (8d): White solid; Yield: 65%; m.p.: 120-122˚C; R_f: 0.29 (Toluene: Ethyl acetate: Formic acid (5:4:1)). IRν_{max} (cm^{-1}): 3310 (N-H, stretching), 3190 (Aromatic C-H stretching), 2911(Aliphatic C-H stretching), 1650 (C=O), 1550 (C=N), 1510 (C=C).

***2*-Naphthohydrazide (8e):** Yellow solid; Yield: 85%; m.p.: 160-163˚C; R_f: 0.20 (Toluene: Ethyl acetate: Formic acid (5:4:1)). IRν_{max} (cm^{-1}): 3329 (N-H, stretching), 3243 (Aromatic C-H stretching), 2847(Aliphatic C-H stretching), 1680 (C=O), 1550 (C=N), 1510 (C=C).

Synthesis of 5-((5-chloro-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)methylene)-2-(4-nitrobenzoyl)-3-phenyl-1,2-dihydro-1,2,4-triazin-6(5*H*)-one (*13a*) [113]: An equimolar quantity of (0.01 mol) 4-((5-chloro-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)methylene)-2-phenyloxazol-5(4*H*)-one, (0.01 mol) *p*-nitrobenzohydrazide and (0.2 g) anhydrous sodium acetate in 15 mL glacial acetic acid was refluxed for 8-10 h. The reaction mixture was poured into crushed ice and stirred. The crystals so obtained were filtered, washed with water, dried and recrystallized from ethanol. Yellow solid; Yield: 36.8 %; m.p.: 242-244 ºC; R_f: 0.75 (Toluene: Ethyl acetate: Formic acid (5:4:1)). IR (KBr) ν_{max} (cm^{-1}): 3273 (N-H stretching), 3052 (Aromatic C-H stretching), 2933 (Aliphatic C-H stretching), 1719 (CONH), 1665 (C_6=O), 1609 (C=N, imine), 1576 (C=C stretching), 697 (C-Cl).**^{1}H-NMR (CDCl$_3$): δ (ppm)** 10.58 (s, 1H, CON*H*), 8.17-8.15 (d, 2H, Ar-*H*), 7.99-7.92 (m, 4H, Ar-*H*), 7.60-7.44 (m, 8H, Ar-*H*), 7.37 (s, 1H, C*H*=C), 2.82 (s, 3H, -CH_3). **^{13}C-NMR (CDCl$_3$): δ (ppm)** 170.27 (*C*=O, benzoyl), 164.28 (C_6), 157.08 (C_3), 151.53(*C*-NO_2), 150.20(*C*-CH_3), 133.78, 132.11, 131.59, 129.24, 129.01, 128.87, 128.15, 127.51, 124.98, 123.82, 122.75, 114.11, 16.65 (C-*C*H_3). **ESI-MS: *m/z*=** 527.2 (M^+, 100%), 529.2 (M^++2, 38%), 530.29 (M^++3, 11.5%).

Synthesis of 5-((5-chloro-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)methylene)-2-(4-hydroxybenzoyl)-3-phenyl-1,2-dihydro-1,2,4-triazin-6(5*H*)-one (*13b*): An equimolar quantity of (0.01 mol) 4-((5-chloro-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)methylene)-2-phenyloxazol-5(4*H*)-one (*12*), (0.01 mol) *p*-hydroxybenzohydrazide and (0.2 g) anhydrous sodium acetate in 15 mL glacial acetic acid was refluxed for 8-10 h. The reaction mixture was poured into crushed ice and stirred. The crystals so obtained were filtered, washed with water, dried and recrystallized from ethanol. Orange solid; Yield: 36.8%; m.p.: 226-230 ºC; R_f: 0.71 (Toluene: Ethyl acetate: Formic acid (5:4:1)). IR (KBr) ν_{max} (cm^{-1}): 3229 (N-H, stretching), 3027 (Aromatic C-H stretching), 2929 (Aliphatic C-H stretching), 1716 (C=O), 1641 (C_6=O), 1609 (C=N), 1580 (C=C), 689 (C-Cl). **^{1}H-NMR (CDCl$_3$) (δ, ppm)** 11.03 (s, 1H, CON*H*, D_2O exchangeable), 8.06-8.04 (d, 2H, Ar-*H*), 7.87-7.84 (d, 2H, Ar-*H*), 7.60-7.58 (d, 2H, Ar-*H*), 7.54-7.40 (m, 6H, Ar-*H*), 7.21 (s, 1H, C*H*=C), 6.91-6.88 (d, 2H, Ar-*H*), 2.78 (s, 3H, CH_3), 2.34 (s, 1H, O*H*, D_2O exchangeable). **^{13}C-NMR (CDCl$_3$): δ (ppm)** 168.97 (*C*=O), 162.97 (*C*=O), 159.11 (C_3), 151.60 (C_3 pyrazole), 137.90 (C_5), 136.14 (N_1-C_1), 133.44, 131.80, 130.47, 124.32, 117.92, 117.68, 116.38, 116.03, 109.16, 108.88, 106.48.

Synthesis of 5-((5-chloro-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)methylene)-2-(3,5-dinitrobenzoyl)-3-phenyl-1,2-dihydro-1,2,4-triazin-6(5*H*)-one (*13c*): An equimolar quantity of (0.01 mol) 4-((5-chloro-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)methylene)-2-phenyloxazol-5(4*H*)-one, (0.01 mol) *3,5*-dinitrobenzohydrazide and (0.2 g) anhydrous sodium acetate in 15 mL glacial acetic acid was refluxed for 8-10 h. The reaction mixture was poured into crushed ice and stirred. The crystals so obtained were filtered, washed with water, dried and recrystallized from ethanol. Yellow solid; Yield: 52 %; m.p.: 190-194 ºC; R_f: 0.71 (Toluene: Ethyl acetate: Formic acid (5:4:1)). IR (KBr) ν_{max} (cm^{-1}): 3210 (N-H, stretching), 3020 (Aromatic C-H stretching), 2900 (Aliphatic C-H stretching), 1697 (C_6=O), 1640 (C=N), 1515 (C=C), 690 (C-Cl).

^{1}H-NMR (CDCl$_3$): δ (ppm) 8.05-8.03 (d, 2H, CON*H*, Ar-*H*), 7.92-7.80 (m, 4H, Ar-*H*, C*H*=C), 7.78-7.48 (m, 4H, Ar-*H*), 7.36-7.33 (d, 5H, Ar-*H*), 2.78 (s, 3H, CH_3). **^{13}C-NMR (CDCl$_3$): δ (ppm)** 171.10 (*C*=O), 166.52 (*C*=O), 158.25 (C_3), 152.20 (C_3 pyrazole), 147.72 (C_5),

139.82 (N_1-C_1), 136.33, 131.59, 124.79, 121.58, 117.81, 117.77, 116.39, 116.01, 109.24, 108.75, 106.19.

Synthesis of 2-benzoyl-5-((5-chloro-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)methylene)-3-phenyl-1,2-dihydro-1,2,4-triazin-6(5*H*)-one (*13d*). Mol. formula: An equimolar quantity of (0.01 mol) 4-((5-chloro-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)methylene)-2-phenyloxazol-5(4*H*)-one, (0.01 mol) benzohydrazide and (0.2 g) anhydrous sodium acetate in 15 mL glacial acetic acid was refluxed for 8-10 h. The reaction mixture was poured into crushed ice and stirred. The crystals so obtained were filtered, washed with water, dried and recrystallized from ethanol. Orange solid; Yield: 50 %; m.p.: 235-237 ºC; R_f: 0.70 (Toluene: Ethyl acetate: Formic acid (5:4:1)). IR (KBr) ν_{max} (cm^{-1}): 3200 (N-H, stretching), 3010 (Aromatic C-H stretching), 2890 (Aliphatic C-H stretching), 1699 (C_6=O), 1637 (C=N), 1523 (C=C), 690 (C-Cl). **^{1}H-NMR ($CDCl_3$): δ (ppm)** 8.03-8.01 (d, 2H, CON*H*, Ar-*H*), 7.86-7.74 (m, 4H, Ar-*H*, C*H*=C), 7.60-7.38 (m, 6H, Ar-*H*), 7.34-7.31 (d, 5H, Ar-*H*), 2.79 (s, 3H, CH_3). **^{13}C-NMR ($CDCl_3$): δ (ppm)** 169.01 (*C*=O), 163.08 (*C*=O), 159.25 (C_3), 151.02 (C_3 pyrazole), 147.82 (C_5), 139.92 (N_1-C_1), 136.43, 130.59, 124.89, 121.58, 117.91, 117.67, 116.39, 116.11, 109.14, 108.85, 106.39.

Synthesis of 2-(2-naphthoyl)-5-((5-chloro-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)methylene)-3-phenyl-1,2-dihydro-1,2,4-triazin-6(5*H*)-one (*13e*). An equimolar quantity of (0.01 mol) 4-((5-chloro-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)methylene)-2-phenyloxazol-5(4*H*)-one, (0.01 mol) *2*-naphthohydrazide and (0.2 g) anhydrous sodium acetate in 15 mL glacial acetic acid was refluxed for 8-10 h. The reaction mixture was poured into crushed ice and stirred. The crystals so obtained were filtered, washed with water, dried and recrystallized from ethanol. Off Green solid; Yield: 60 %; m.p.: 172-175 ºC; R_f: 0.61 (Toluene: Ethyl acetate: Formic acid (5:4:1)). IR (KBr) ν_{max} (cm^{-1}): 3210 (N-H, stretching), 3182 (Aromatic C-H stretching), 2999 (Aliphatic C-H stretching), 1692 (C_6=O), 1610 (C=N), 1570 (C=C), 695 (C-Cl). **^{1}H-NMR ($CDCl_3$): δ (ppm)** 7.98-7.85 (m, 4H, CON*H*, Ar-*H*), 7.78 (s, 1H, C*H*=C), 7.60-7.42 (m, 10H, Ar-*H*), 7.21 -7.12 (m, 3H, Ar-*H*), 4.20 (s, 1H, Ar-*H*), 2.76 (s, 3H, CH_3).**^{13}C-NMR ($CDCl_3$): δ (ppm)** 169.08 (*C*=O), 162.96 (*C*=O), 159.09 (C_3), 152.20 (C_3 pyrazole), 144.69 (C_5), 138.47 (N_1-C_1), 137.90, 131.92, 131.80, 130.46, 124.32, 121.93, 116.36, 116.03, 115.48, 106.50, 106.41.

Synthesis of 5-((5-chloro-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)methylene)-2,3-diphenyl-1,2-dihydro-1,2,4-triazin-6(5*H*)-one (*13f*): An equimolar quantity of (0.01 mol) 4-((5-chloro-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)methylene)-2-phenyloxazol-5(4*H*)-one, (0.01 mol) phenyl hydrazine and (0.2 g) anhydrous sodium acetate in 15 mL glacial acetic acid was refluxed for 8-10 h. The reaction mixture was poured into crushed ice and stirred. The crystals so obtained were filtered, washed with water, dried and recrystallized from ethanol. Dark orange solid; Yield: 55 %; m.p.: 222-224 ºC; R_f: 0.78 (Toluene: Ethyl acetate: Formic acid (5:4:1)). IR (KBr) ν_{max} (cm^{-1}): 3267 (N-H, stretching), 3057 (Aromatic C-H stretching), 2938 (Aliphatic C-H stretching), 1716 (C=O), 1645 (C_6=O), 1600 (C=N), 1537 (C=C), 689 (C-Cl). **^{1}H-NMR ($CDCl_3$) (δ, ppm)** 11.06 (s, 1H, CON*H*), 8.28-8.25 (d, 2H, Ar-*H*), 7.58-7.45 (m, 9H, Ar-*H*), 7.31 (s, 1H, C*H*=C), 7.01-6.95 (t, 2H, Ar-*H*), 6.85-6.83 (d, 2H, Ar-*H*), 2.83 (s, 3H, CH_3).**^{13}C-NMR ($CDCl_3$): δ (ppm)** 171.89 (*C*=O), 167.40 (*C*=O), 160.67 (C_3), 150.00 (C_3 pyrazole), 149.69 (C_5), 145.08 (N_1-C_1), 143.91, 138.04, 131.33, 127.94, 123.76, 12.16, 123.79, 116.11, 115.01, 113.72, 112.59, 111.27.

Synthesis of 5-((5-chloro-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)methylene)-3-phenyl-1,2-dihydro-1,2,4-triazin-6(5*H*)-one (13g): An equimolar quantity of (0.01 mol) 4-((5-chloro-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)methylene)-2-phenyloxazol-5(4*H*)-one, (0.01 mol) hydrazine hydrate and (0.2 g) anhydrous sodium acetate in 15 mL glacial acetic acid was refluxed for 8-10 h. The reaction mixture was poured into crushed ice and stirred. The crystals so obtained were filtered, washed with water, dried and recrystallized from ethanol. Orange solid; Yield: 40 %; m.p.: 230-232 ºC; R_f: 0.73 (Toluene: Ethyl acetate: Formic acid (5:4:1)). IR (KBr) ν_{max} (cm^{-1}): 3230 (N-H, stretching), 3045 (Aromatic C-H stretching), 2930 (Aliphatic C-H stretching), 1660 (C_6=O), 1607 (C=N), 1567 (C=C), 691 (C-Cl). **^{1}H-NMR ($CDCl_3$) (δ, ppm)** 11.11 (bs, 1H, CON*H*, *D_2O* exchangeable), 8.62 (bs, 1H, N*H*, *D_2O* exchangeable), 8.10-8.07 (d, 2H, Ar-*H*), 7.58-7.56 (d, 2H, Ar-*H*), 7.50-7.36 (m, 7H, Ar-*H*, C*H*=C), 2.35 (s, 3H, CH_3). **^{13}C-NMR ($CDCl_3$): δ (ppm)** 172.99 (*C*=O), 168.66 (*C*=O), 162.98 (C_3), 159.15 (C_3 pyrazole), 147.07 (C_5), 139.09 (N_1-C_1), 137.89, 131.82, 130.49, 129.14, 127.60, 124.33, 123.89, 119.95, 116.38, 116.04, 106.48.

Synthesis of 5-((1,3-diphenyl-1*H*-pyrazol-4-yl)methylene)-2-(4-nitrobenzoyl)-3-phenyl-1,2-dihydro-1,2,4-triazin-6(5*H*)-one (*18a*): An equimolar quantity of (0.01 mol**)** 4-[(1,3-diphenyl-1*H*-pyrazol-4-yl)methylidene]-2-phenyl-1,3-oxazol-5(4*H*)-one, (0.01 mol) *p*-nitrobenzohydrazideand (0.2 g) anhydrous sodium acetate in 15 mL glacial acetic acid was refluxed for 8-10 h. The reaction mixture was poured into crushed ice and stirred. The crystals so obtained were filtered, washed with water, dried and recrystallized from ethanol. Color: Yellow solid; Yield:

52 %; m.p.: 268-270 ºC; R_f: 0.69 (Toluene: Ethyl acetate: Formic acid (5:4:1)). IR (KBr) ν_{max} (cm^{-1}): 3276 (N-H, stretching), 3015 (Aromatic C-H stretching), 2929 (Aliphatic C-H stretching), 1711 (C=O), 1642 (C_6=O), 1608 (C=N), 1564 (C=C). **^{1}H-NMR ($CDCl_3$) (δ, ppm)** 9.37 (s, 1H, CON*H*), 9.27 (s, 1H, C_5-*H*), 8.21-8.18 (d, 2H, Ar-*H*), 7.99-7.95 (d, 2H, Ar-*H*), 7.86-7.84 (d, 2H, Ar-*H*), 7.73-7.71 (d, 2H, Ar-*H*), 7.55-7.38 (m, 8H, Ar-*H*, C*H*=C), 7.36-7.29 (m, 4H, Ar-*H*). **^{13}C-NMR ($CDCl_3$): δ (ppm)** 167.40 (*C*=O), 160.67 (*C*=O), 150.00 (C_3), 149.69 (C_3 pyrazole), 145.08 (C_5), 143.91 (N_1-C_1), 138.04, 131.33, 127.94, 123.76, 123.16, 116.11, 115.01, 113.72, 112.59, 111.27, 106.25.

Synthesis of 5-((1,3-diphenyl-1*H*-pyrazol-4-yl)methylene)-2-(4-hydroxybenzoyl)-3-phenyl-1,2-dihydro-1,2,4-triazin-6(5*H*)-one (*18b*): An equimolar quantity of (0.01 mol) 4-[(1,3-diphenyl-1*H*-pyrazol-4-yl)methylidene]-2-phenyl-1,3-oxazol-5(4*H*)-one, (0.01 mol) *p*-hydroxybenzohydrazide and (0.2 g) anhydrous sodium acetate in 15 mL glacial acetic acid was refluxed for 8-10 h. The reaction mixture was poured into crushed ice and stirred. The crystals so obtained were filtered, washed with water, dried and recrystallized from ethanol. Orange solid; Yield: 80 %; m.p.: 250-252 ºC; R_f: 0.70 (Toluene: Ethyl acetate: Formic acid (5:4:1)). IR (KBr) ν_{max} (cm^{-1}): 3292 (N-H, stretching), 3030 (Aromatic C-H stretching), 2920 (Aliphatic C-H stretching), 1707 (C=O), 1638 (C_6=O), 1601 (C=N), 1560 (C=C). **^{1}H-NMR ($CDCl_3$) (δ, ppm)** 9.43 (bs, 1H, CON*H*, D_2O exchangeable), 9.28 (s, 1H, C_5-*H*), 8.27-8.25 (d, 2H, Ar-*H*), 7.90-7.87 (d, 2H, Ar-*H*), 7.74-7.71 (d, 2H, Ar-*H*), 7.60-7.36 (m, 11H, Ar-*H*), 6.99-6.95 (t, 1H, Ar-*H*), 6.83-6.81 (d, 2H, Ar-*H*), 6.58 (s, 1H, O*H*, D_2O exchangeable). **^{13}C-NMR ($CDCl_3$): δ (ppm)** 169.70 (*C*=O), 168.32 (*C*=O), 149.81 (C_3), 144.50 (C_3 pyrazole), 142.98 (C_5), 134.89 (N_1-C_1), 132.19, 131.03, 128.97, 128.21, 127.58, 122.88, 117.54, 113.90, 111.16.

Synthesis of 2-(3,5-dinitrobenzoyl)-5-((1,3-diphenyl-1H-pyrazol-4-yl)methylene)-3-phenyl-1,2-dihydro-1,2,4-triazin-6(5H)-one (*18c*): An equimolar quantity of (0.01 mol**)** 4-[(1,3-diphenyl-1*H*-pyrazol-4-yl)methylidene]-2-phenyl-1,3-oxazol-5(4*H*)-one, (0.01 mol) *3,5*-dinitrobenzohydrazideand (0.2 g) anhydrous sodium acetate in 15 mL glacial acetic acid was refluxed for 8-10 h. The reaction mixture was poured into crushed ice and stirred. The crystals so obtained were filtered, washed with water, dried and recrystallized from ethanol. Color: Yellow solid; Yield: 52 %; m.p.: 273-274ºC; R_f: 0.68 (Toluene: Ethyl acetate: Formic acid (5:4:1)). IR (KBr) ν_{max} (cm^{-1}): 3270 (N-H, stretching), 3005 (Aromatic C-H stretching), 2919 (Aliphatic C-H stretching), 1710 (C=O), 1640 (C_6=O), 1600 (C=N), 1560 (C=C). **^{1}H-NMR ($CDCl_3$) (δ, ppm)** 9.36 (s, 1H, CON*H*), 9.25 (s, 1H, C_5-*H*), 8.19-8.16 (d, 2H, Ar-*H*), 7.97-7.92 (d, 2H, Ar-*H*), 7.81-7.82 (d, 2H, Ar-*H*), 7.72-7.71 (d, 2H, Ar-*H*), 7.52-7.37 (m, 7H, Ar-*H*, C*H*=C), 7.32-7.27 (m, 4H, Ar-*H*). **^{13}C-NMR ($CDCl_3$): δ (ppm)**167.38 (*C*=O), 160.65 (*C*=O), 150.01 (C_3), 149.67 (C_3 pyrazole), 145.07 (C_5), 143.89 (N_1-C_1), 138.08, 131.29, 127.90, 123.74, 123.14, 116.09, 115.00, 113.69, 112.57, 111.25, 106.15.

Synthesis of 2-benzoyl-5-((1,3-diphenyl-1*H*-pyrazol-4-yl)methylene)-3-phenyl-1,2-dihydro-1,2,4-triazin-6(5*H*)-one (*18d*): An equimolar quantity of (0.01 mol) 4-[(1,3-diphenyl-1*H*-pyrazol-4-yl)methylidene]-2-phenyl-1,3-oxazol-5(4*H*)-one, (0.01 mol) benzohydrazide and (0.2 g) anhydrous sodium acetate in 15 mL glacial acetic acid was refluxed for 8-10 h. The reaction mixture was poured into crushed ice and stirred. The crystals so obtained were filtered, washed with water, dried and recrystallized from ethanol. Orange solid; Yield: 35 %; m.p.: 270-274 ºC; R_f: 0.69 (Toluene: Ethyl acetate: Formic acid (5:4:1)). IR (KBr) ν_{max} (cm^{-1}): 3258 (N-H, stretching), 2918 (Aromatic C-H stretching), 2851 (Aliphatic C-H stretching), 1726 (C=O), 1670 (C_6=O), 1624 (C=N), 1575 (C=C).^{1}H-NMR ($CDCl_3$): δ (ppm) 9.26 (s, 1H, CON*H*), 9.12 (s, 1H, C*H*-N), 8.01-7.99 (d, 2H, Ar-*H*), 7.85-7.78 (m, 4H, Ar-*H*, C*H*=C), 7.74-7.71 (d, 2H, Ar-*H*), 7.53-7.48 (m, 10H, Ar-*H*), 7.40-7.36 (t, 3H, Ar-*H*). **^{13}C-NMR ($CDCl_3$): δ (ppm)** 171.68 (*C*=O), 164.62 (*C*=O), 158.77 (C_3), 155.00 (C_3pyrazole), 139.89 (C_5), 139.77 (N_1-C_1), 135.66, 133.14, 132.23, 130.76, 129.52, 128.89, 128.81, 128.72, 128.60, 128.10, 127.77, 127.29, 123.11, 119.81, 116.21.

Synthesis of 2-(2-naphthoyl)-5-((1,3-diphenyl-1*H*-pyrazol-4-yl)methylene)-3-phenyl-1,2-dihydro-1,2,4-triazin-6(5*H*)-one (*18e*): An equimolar quantity of (0.01 mol) 4-[(1,3-diphenyl-1*H*-pyrazol-4-yl)methylidene]-2-phenyl-1,3-oxazol-5(4*H*)-one (*17*), (0.01 mol) *2*-naphthohydrazide and (0.2 g) anhydrous sodium acetate in 15 mL glacial acetic acid was refluxed for 8-10 h. The reaction mixture was poured into crushed ice and stirred. The crystals so obtained were filtered, washed with water, dried and recrystallized from ethanol. Orange solid; Yield: 40 %; m.p.: 250-252 ºC; R_f: 0.67 (Toluene: Ethyl acetate: Formic acid (5:4:1)). IR (KBr) ν_{max} (cm^{-1}): 3300 (N-H, stretching), 2980 (Aromatic C-H stretching), 2905 (Aliphatic C-H stretching), 1723 (C=O), 1663 (C_6=O), 1600 (C=N), 1504 (C=C). **^{1}H-NMR ($CDCl_3$): δ (ppm)** 9.21 (s, 1H, CON*H*), 7.94-7.83 (m, 5H, Ar-*H*, C*H*-N), 7.75-7.58 (m, 6H, Ar-*H*, C*H*=C), 7.55-7.37 (m, 7H, Ar-*H*), 7.26-7.17 (m, 4H, Ar-*H*), 4.20 (s, 2H, Ar-*H*).

^{13}C-NMR ($CDCl_3$): δ (ppm) 184.98 (*C*=O), 179.90 (*C*=O), 159.34 (C_3), 142.31 (C_3 pyrazole), 139.03 (C_5), 134.97 (N_1-C_1), 134.71, 134.12, 131.95, 131.29, 130.72, 126.57, 126.03, 124.06, 120.62, 111.44.

Synthesis of 5-((1,3-diphenyl-1*H*-pyrazzol-4-yl)methylene)-2,3-diphenyl-1,2-dihydro-1,2,4-triazin-6(5*H*)-one (*18f*): An equimolar quantity of (0.01 mol) 4-[(1,3-diphenyl-1*H*-pyrazol-4-yl)methylidene]-2-phenyl-1,3-oxazol-5(4*H*)-one, (0.01 mol) phenyl hydrazine and (0.2 g) anhydrous sodium acetate in 15 mL glacial acetic acid was refluxed for 8-10 h. The reaction mixture was poured into crushed ice and stirred. The crystals so obtained were filtered, washed with water, dried and recrystallized from ethanol. Orange solid; Yield: 45 %; m.p.: 140 ºC; R_f: 0.72 (Toluene: Ethyl acetate: Formic acid (5:4:1)). IR (KBr) ν_{max} (cm^{-1}): 3152 (N-H, stretching), 3055 (Aromatic C-H stretching), 2855 (Aliphatic C-H stretching), 1642 (CONH), 1597 (C=N), 1556 (C=C). **^{1}H-NMR ($CDCl_3$) (δ, ppm)** 9.48 (s, 1H, CON*H*), 9.32 (s, 1H, C_5-*H*), 8.27-8.25 (d, 2H, Ar-*H*), 7.89-7.87 (d, 2H, Ar-*H*), 7.74-7.71 (d, 2H, Ar-*H*), 7.66-7.36 (m, 11H, 10 Ar-*H*, 1 C*H*=C), 7.28-7.20 (m, 1H, Ar-*H*), 6.98-6.93(t, 1H, Ar-*H*), 6.82-6.76 (m, 2H, Ar-*H*). **^{13}C-NMR ($CDCl_3$): δ (ppm)** 172.50 (*C*=O), 159.10 (C_3), 156.65 (C_3 pyrazole), 140.43 (C_5), 140.27 (N_1-C_1), 136.48, 134.34, 133.83, 131.56, 130.20, 129.99, 129.96, 128.97, 128.70, 128.51, 127.57, 127.24, 123.55, 119.58, 116.64.

Synthesis of 5-((1,3-diphenyl-1*H*-pyrazol-4-yl)methylene)-3-phenyl-1,2-dihydro-1,2,4-triazin-6(5*H*)-one (*18g*): An equimolar quantity of (0.01 mol) 4-[(1,3-diphenyl-1*H*-pyrazol-4-yl)methylidene]-2-phenyl-1,3-oxazol-5(4*H*)-one, (0.01 mol) hydrazine hydrate and (0.2 g) anhydrous sodium acetate in 15 mL glacial acetic acid was refluxed for 8-10 h. The reaction mixture was poured into crushed ice and stirred. The crystals so obtained were filtered, washed with water, dried and recrystallized from ethanol. Buff yellow solid; Yield: 41 %; m.p.: 244-246 ºC; R_f: 0.74 (Toluene: Ethyl acetate: Formic acid (5:4:1)). IR (KBr) ν_{max} (cm^{-1}): 3258 (N-H, stretching), 3037 (Aromatic C-H stretching), 2920 (Aliphatic C-H stretching), 1648 (C_6=O), 1601 (C=N), 1556 (C=C). **^{1}H-NMR ($CDCl_3$) (δ, ppm)** 9.43 (s, 1H, CON*H*), 9.23 (s, 1H, C_5-*H*), 8.32 (s, 1H, N*H*), 8.02-7.98 (d, 2H, Ar-*H*), 7.85-7.71 (m, 6H, Ar-*H*), 7.63-7.38 (m, 8H, Ar-*H*, C*H*=C). **^{13}C-NMR ($CDCl_3$): δ (ppm)** 169.88 (*C*=O), 158.88 (C_3), 157.05 (C_3 pyrazole), 139.99 (C_5), 139.54 (N_1-C_1), 135.11, 133.98, 131.99, 130.66, 129.32, 128.54, 128.49, 128.16, 127.91, 127.77, 127.54, 119.26, 116.32.

Synthesis of 5-(furan-3-ylmethylene)-2-(4-nitrobenzoyl)-3-phenyl-1,2-dihydro-1,2,4-triazin-6(5*H*)-one (*21a$_1$*): An equimolar quantity of (0.01 mol) 4-(furan-2-ylmethylene)-2-phenyloxazol-5(4*H*)-one, (0.01 mol) *p*-nitrobenzohydrazide and (0.2 g) anhydrous sodium acetate in 15 mL glacial acetic acid was refluxed for 8-10 h. The reaction mixture was poured into crushed ice and stirred. The crystals so obtained were filtered, washed with water, dried and recrystallized from ethanol. Buff solid; Yield: 60.5 %; m.p.: 168-170 ºC; R_f: 0.61 (Toluene: Ethyl acetate: Formic acid (5:4:1)). IR (KBr) ν_{max} (cm^{-1}): 3168 (N-H, stretching), 3010 (Aromatic C-H stretching), 2860 (Aliphatic C-H stretching), 1634 (CONH), 1593 (C=N), 1520 (C=C). ^{1}H-NMR ($CDCl_3$): δ (ppm) 8.27-8.25 (d, 2H, Ar-*H*), 7.99-7.96 (d, 4H, Ar-H), 7.69 (s, 1H, CON*H*), 7.62-7.61 (d, 1H, Ar-*H*), 7.57-7.42 (m, 4H, Ar-*H*), 7.18 (s, 1H, C*H*=C), 6.66 (s, 1H, 3-furan). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 153.85 (*C*=O, benzoyl), 147.41 (C_6), 147.17 (C_3), 145.34 (2'-Furan), 142.08 (C_5-furan), 129.06, 128.61, 126.07, 121.90.

Synthesis of 5-(furan-3-ylmethylene)-2-(4-hydroxybenzoyl)-3-phenyl-1,2-dihydro-1,2,4-triazin-6(5*H*)-one (*21a$_2$*). An equimolar quantity of (0.01 mol) 4-(furan-2-ylmethylene)-2-phenyloxazol-5(4*H*)-one, (0.01 mol) *p*-hydroxybenzohydrazide and (0.2 g) anhydrous sodium acetate in 15 mL glacial acetic acid was refluxed for 8-10 h. The reaction mixture was poured into crushed ice and stirred. The crystals so obtained were filtered, washed with water, dried and recrystallized from ethanol. Green solid; Yield: 51.5 %; m.p.: 178-180 ºC; R_f: 0.69 (Toluene: Ethyl acetate: Formic acid (5:4:1)). IR (KBr) ν_{max} (cm^{-1}): 3145 (N-H, stretching), 3085 (Aromatic C-H stretching), 2855 (Aliphatic C-H stretching), 1633 (CONH), 1540 (C=N), 1520 (C=C). ^{1}H-NMR ($CDCl_3$): δ (ppm) 8.97 (s, 3H, Ar-*H*), 7.729-7.696 (d, 3H, CON*H*, Ar-*H*), 7.50-7.30 (m, 7H, Ar-*H*), 6.38 (s, 1H, C*H*=C), 6.19 (s, 1H, 3- furan). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 153.65 (*C*=O, benzoyl), 148.26 (C_6), 148.06 (C_3), 136.26 (2'-Furan), 134.08 (C_5-furan) 131.34, 129.12, 128.70, 128.51, 125.23, 120.11.

Synthesis of 2-(3,5-dinitrobenzoyl)-5-(furan-3-ylmethylene)-3-phenyl-1,2-dihydro-1,2,4-triazin-6(5*H*)-one (*21a$_3$*): An equimolar quantity of (0.01 mol) 4-(furan-2-ylmethylene)-2-phenyloxazol-5(4*H*)-one, (0.01 mol) *3,5*-dinitrobenzohydrazide and (0.2 g) anhydrous sodium acetate in 15 mL glacial acetic acid was refluxed for 8-10 h. The reaction mixture was poured into crushed ice and stirred. The crystals so obtained were filtered, washed with water, dried and recrystallized from ethanol. Yellowish green solid; Yield: 50.6 %; m.p.: 170-172 ºC; R_f: 0.65 (Toluene: Ethyl acetate: Formic acid (5:4:1)). IR (KBr) ν_{max} (cm^{-1}): 3155 (N-H, stretching), 3093 (Aromatic C-H stretching), 2852 (Aliphatic C-H stretching), 1630 (CONH), 1536 (C=N), 1516 (C=C). ^{1}H-NMR ($CDCl_3$):

δ (ppm) 8.97 (s, 3H, Ar-*H*), 7.729-7.696 (d, 3H, CON*H*, Ar-*H*), 7.50-7.36 (m, 5H, Ar-*H*), 6.38 (s, 1H, C*H*=C), 6.19 (s, 1H, 3- furan). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 166.90 (*C*=O, benzoyl), 156.48 (C_6), 153.98 (C_3), 151.42 (2'-Furan), 147.97 (C_5-furan) 145.25, 139.94, 131.57, 130.72, 123.77, 123.13, 120.32, 118.79, 110.84.

Synthesis of 2-benzoyl-5-(furan-3-ylmethylene)-3-phenyl-1,2-dihydro-1,2,4-triazin-6(5H)-one(*21a*$_4$): An equimolar quantity of (0.01 mol) 4-(furan-2-ylmethylene)-2-phenyloxazol-5(4*H*)-one, (0.01 mol) benzohydrazide and (0.2 g) anhydrous sodium acetate in 15 mL glacial acetic acid was refluxed for 8-10 h. The reaction mixture was poured into crushed ice and stirred. The crystals so obtained were filtered, washed with water, dried and recrystallized from ethanol. Buff solid; Yield: 60 %; m.p.: 165-166 ºC; R_f: 0.60 (Toluene: Ethyl acetate: Formic acid (5:4:1)). IR (KBr) ν_{max} (cm^{-1}): 3165 (N-H, stretching), 3005 (Aromatic C-H stretching), 2855 (Aliphatic C-H stretching), 1630 (CONH), 1590 (C=N), 1518 (C=C). ^{1}H-NMR ($CDCl_3$): δ (ppm) 8.24-8.21 (d, 2H, Ar-*H*), 8.10-7.99 (m, 6H, Ar-H), 7.68 (s, 1H, CON*H*), 7.61-7.60 (d, 1H, Ar-*H*), 7.55-7.40 (m, 4H, Ar-*H*), 7.15 (s, 1H, C*H*=C), 6.64 (s, 1H, 3-furan). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 153.83 (*C*=O, benzoyl), 147.31 (C_6), 147.18 (C_3), 144.33 (2'-Furan), 141.08 (C_5-furan), 128.06, 127.61, 127.07, 122.90.

Synthesis of 2-(2-naphthoyl)-5-(furan-3-ylmethylene)-3-phenyl-1,2-dihydro-1,2,4-triazin-6(5*H*)-one (*21a*$_5$): An equimolar quantity of (0.01 mol) 4-(furan-2-ylmethylene)-2-phenyloxazol-5(4*H*)-one, (0.01 mol) *2*-naphthohydrazide and (0.2 g) anhydrous sodium acetate in 15 mL glacial acetic acid was refluxed for 8-10 h. The reaction mixture was poured into crushed ice and stirred. The crystals so obtained were filtered, washed with water, dried and recrystallized from ethanol. Brownish black; Yield: 80 %; m.p.: 172–175 °C; R_f: 0.76 (Toluene: Ethyl acetate: Formic acid (5:4:1)). IR cm^{-1}: 3176 (N-H), 3009 (aromatic C-H), 2933 (aliphatic C-H), 1724 (CONH), 1640 (C=O), 1580 (C=N, imine), 1525 (C=C). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) 10.29 (s, 1H, CONH, D_2O exchangeable), 8.01–7.98 (d, 1H, J= 8.7 Hz, Ar-H), 7.78–7.69 (m, 3H, Ar-*H*), 7.55 (s, 1H, CH=C), 7.44–7.3 (m, 4H, Ar-H), 7.32–7.28 (m, 3H, Ar-H), 7.16-7.05 (m, 4H, Ar-H), 6.52 (s, 1H, Ar-H), 4.02 (s, 1H, CH=C). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 153.5 (*C*=O, benzoyl), 148.1 (C_6), 135.3 (C_3), 134.8 (2'-Furan), 134.6 (C_5-furan) 134.0, 131.9, 130.0, 129.3, 128.6, 128.4, 128.2, 128.0, 127.8, 126.8, 126.5, 124.9, 108.4. ESI-MS: *m*/*z* = 407.1264(M^+), 408.1342(M^+ + 2); found: 407.13(M^+), 408.13(M^+ + 2).

Synthesis of 2-(2-naphthoyl)-5-(4-hydroxy-3-methoxybenzylidene)-3-phenyl-1,2-dihydro-1,2,4-triazin-6(5*H*)-one (*21b*): An equimolar quantity of (0.01 mol) 4-(4-hydroxy-3-methoxybenzylidene)-2-phenyloxazol-5(4*H*)-one, (0.01 mol) *2*-naphthohydrazideand (0.2 g) anhydrous sodium acetate in 15 mL glacial acetic acid was refluxed for 8-10 h. The reaction mixture was poured into crushed ice and stirred. The crystals so obtained were filtered, washed with water, dried and recrystallized from ethanol. Buff solid; Yield: 50 %; m.p.: 194-195 ºC; R_f: 0.70 (Toluene: Ethyl acetate: Formic acid (5:4:1)). IR (KBr) ν_{max} (cm^{-1}): 3140 (N-H, stretching), 3010 (Aromatic C-H stretching), 2844 (Aliphatic C-H stretching), 1624 (CONH), 1590 (C=N), 1537 (C=C). ^{1}H-NMR ($CDCl_3$): δ (ppm) 8.18 (s, 1H, CON*H*), 7.98-7.74 (m, 6H, Ar-*H*), 7.62-7.59 (d, 2H, Ar-*H*), 7.54-7.43 (m, 7H, Ar-*H*, C*H*=C), 7.18-7.08 (m, 1H, Ar-*H*), 4.17 (s, 1H, Ar-*H*), 4.088 (s, 1H, O*H*), 3.95 (s, 3H, CH_3). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 168.32 (*C*=O, benzoyl), 149.81 (C_6), 144.50 (C_3), 142.98 (2'-Furan), 134.89 (C_5-furan) 132.19, 131.03, 128.97, 128.21, 127.58, 122.88, 117.54, 113.90, 111.16.

Acknowledgement

We express our thanks to IIT, Delhi for carrying out ^{1}HNMR, ^{13}CNMR and Mass spectroscopy of samples.

References

1. K. Srinivas, U. Srinivas, K. Bhanuprakash, K. Harakishore, U.S. Murty, V.J. Rao, Synthesis and antibacterial activity of various substituted *s*-triazines, Eur. J. Med. Chem. 41 (2006) 1240-1246.
2. P. Gahtori, B.K. Singh,A. Das, Synthesis of phenyl-1,3-thiazole substituted amino *s*-triazines as antibacterial agents, J. Pharm. Sci. 7(2008) 107-111.
3. G. Blotny, Recent applications of 2,4,6-trichloro-1,3,5-triazine and its derivatives in organic synthesis, Tetrahedron, 62 (2006) 9507-9522.
4. Zhou Y, Sun Z, Froelich JM, Hermann T, Wall D, Structure-activity relationships of novel antibacterial translation inhibitors; 3,5-Diaminopiperidinyl triazines, Bioorg. Med. Chem. Lett. 16 (2006) 5451-5456.
5. S. Nishigaki, U.H. Yoneda, H. Tsumoto, A.I. Jiorinaga, Synthetic Antibacterials. I. Nitrofurylvinyl-*s*-triazine derivatives, J. Am. Chem. Soc. 12 (1969) 39-42.
6. M. Saleh, S. Abbott, V. Perron, C. Lauzon, C. Penney, B. Zacharie, Synthesis and antimicrobial activity of 2-fluorophenyl-4,6-disubstituted[1,3,5]triazines, Bioorg. Med. Chem. Lett. 20 (2010) 945-949.

7. J. Saravanan, S. Mohan, J.J. Roy, Synthesis of some 3-substituted amino-4,5-tetramethylene thieno[2,3-*d*][1,2,3]-triazin-4(3*H*)-ones as potential antimicrobial agents, Eur. J. Med. Chem. 45 (2010) 4365-4369.

8. M. Kidwai, Y. Goel, R. Kumar, Microwave assisted synthesis and antifungal activity of 1, 2, 4-triazine, 1, 2, 4-triazole, tetrazole and pyrazole derivatives, Indian J. Chem. 37B(1998)174-179.

9. B.B. Baldaniya, P.K. Patel, Synthesis, antibacterial and antifungal activities of *s*-triazine derivatives, e-J Chem. 6(2009)673-680.

10. S.Y. Hassan, Synthesis, antibacterial and antifungal activity of some new pyrazoline and pyrazole derivatives,Molecules,18 (2013) 2683-2711. doi:10.3390/molecules18032683.

11. M. Hala, H.M. Refat, A.A. Fadda, Synthesis and antimicrobial activity of some novel hydrazide, pyrazole, triazine, isoxazole, and pyrimidine derivatives, J. Heterocyclic Chem. Doi: 10.1002/jhet.

12. N.C. Desai, A.H. Makwana, K.M. Rajpara, Synthesis and study of 1,3,5-triazine based thiazole derivatives as antimicrobial agents, J. Saudi. Chem. Soc. http://dx.doi.org/10.1016/j.jscs.2012.12.004.

13. S.N. Gavade, V.L. Markad, K.M. Kodam, M.S. Shingare, D.V. Mane, Synthesis and biological evaluation of novel 2,4,6-triazine derivatives as antimicrobial agents, Bioorg. Med. Chem. Lett. 22 (2012) 5075-5077.

14. D.H. Patel, K.H. Chikhalia, N.K. Shah, D.P. Patel, P.B. Kaswala, V.M. Buha, Synthesis and antimicrobial studies of *s*-triazine based heterocycles, J. Enzyme Inhib. Med. Chem.25 (2010) 121-125.

15. S. Jain, A. Sharma, M. Agrawal, S. Sharma, J. Dwivedi, D. Kishore, Synthesis and antimicrobial evaluation of some novel trisubstituted s-triazine derivatives based on isatinimino, sulphonamido, and azacarbazole, J. Chem. http://dx.doi.org/10.1155/2013/925439.

16. S. Katugampala, I.C. Perera, C. Nanayakkara, T. Perera, Synthesis, characterization, and antimicrobial activity of novel sulfonated copper-triazine complexes, Bioinorg. Chem. Appl. https://doi.org/10.1155/2018/2530851.

17. Z.A. Kaplancikli, G. Turan-Zitouni, A. Ozdemir, M.D. Altintop, Y. Tunali, Synthesis of some thienyl-triazine derivatives and antimicrobial activity, Asian J. Chem. 22 (2010) 6701-6707.

18. R.M. Mohareb, R.A. Ibrahim, H.E. Moustafa, Hydrazide-hydrazones in the synthesis of 1,3,4-oxadiazine, 1,2,4-triazine and pyrazole derivatives with antitumor activities, The Open Org. Chem. J.4 (2010) 8-14.

19. K. Sztanke, K. Pasternak, M. Sztanke, M. Kandefer-Szerszen, A.E. Kozioł, I. Dybała Crystal structure, antitumour and antimetastatic activities of disubstituted fused 1,2,4-triazinones, Bioorg. Med. Chem. Lett. 19 (2009) 5095-5100.

20. K. Sztanke, J. Rzymowska, M. Niemczyk, I. Dybała, A.E. Kozioł, Synthesis, crystal structure and anticancer activity of novel derivatives of ethyl 1-(4-oxo-8-aryl-4,6,7,8 tetrahydroimidazo[2,1-*c*][1,2,4]triazin-3-yl)formate, Eur. J. Med. Chem. 41 (2006) 539-547.

21. L. Garuti, M. Roberti, T. Rossi, M. Castelli, M. Malagoli, Synthesis and antiproliferative activity of substituted l*H*-indole [3,2-d&1,2,3-triazin-4 (3*H*)-ones, Eur. J. Med. Chem. 33 (1998) 43-46.

22. R.H Smith, D.A. Scudiero, C.J. Michejda, 1, 3-Dialkyl-3-acyltriazenes, a novel class of antineoplastic alkylating agents, J. Med. Chem. 33 (1990) 2579-2583.

23. R. Sztanke, J. Rzymowska, M. Niemczyk, I. DybałaI, Kozioł AE, Synthesis, crystal structure and anticancer activity of novel derivatives of ethyl 1-(4-oxo-8-aryl-4,6,7,8 tetrahydroimidazo[2,1-*c*][1,2,4]triazin-3-yl)formate, Eur. J. Med. Chem. 41 (2006) 539-547.

24. K. Sztanke, K. Pasternak, M. Sztanke, M. Kandefer-Szerszen, A.E. Koziol, I. Dybała, Crystal structure, antitumour and antimetastatic activities of disubstituted fused 1,2,4-triazinones, Bioorg. Med. Chem. Lett. 19 (2009) 5095-5100.

25. H. Singh, V.K. Kapoor, Medicinal and Pharmaceutical Chemistry, Vallabh Prakashan, Delhi (2007).

26. R.M. Abdel-Rahman, J.M. Morsy, Synthesis of heterobicyclic nitrogen systems bearing the 1,2,4-triazine moiety as anti-HIV and anticancer drugs: Part I. Pharmazie. 54 (1999) 347-351.

27. S.M. Riyadh, Enaminones as building blocks for the synthesis of substituted pyrazoles with antitumor and antimicrobial activities, Molecules16 (2011) 1834-1853.

28. B. Kaur, A. Kaur, Anticancer activity of aminoacid linked novel 4-methylumbelliferone derivatives, Curr. Bioact. Compd. 13 (2017) 000-000. doi:10.2174/1573407213666170210143503.

29. V. Issartel, V. Spehner, P. Coudert, E. Seilles, J. Couquelet, Synthesis of new pyrrolo[1,2-*d*] [1,2,4] triazines and thiazolo[3,4-*d*][1,2,4] triazines as immunostimulating agents, Bioorg. Med. Chem. 6 (1998) 349-354.

30. Z. Brzozowski, F. Saczewski, M. Gdaniec. Synthesis, structural characterization and antitumor activity of novel 2, 4-diamino-1, 3, 5-triazine derivatives, Eur. J. Med. Chem. 35(2000) 1053-1064.

31. Z. Brzozowski, F. Saczewski, Synthesis and antitumor activity of novel 2-amino-4-(3, 5, 5-trimethyl-2-pyrazolino)-1, 3, 5-triazine derivatives, Eur. J. Med. Chem. 37 (2002) 709-720.

32. P. Diana, P. Barraja, A. Lauria, A. Montalbano, A.M. Almerico, G. Dattolo, G. Cirrincione, Pyrrolo[2,1-*c*][1,2,4] triazines from 2-diazopyrroles: Synthesis and antiproliferative activity, Eur. J. Med. Chem. 37 (2002) 267-272.

33. I. Lakomska, B. Golankiewicz, J. Wietrzyk, M. Pelczynska, A. Nasulewicz, A. Opolski, J. Sitkowski, L. Kozerski, E. Szlyk, Synthesis, spectroscopial characterization and the biological activity *in vitro* of new platinum (II) complexes with imidazo[1,5-*a*]-1,3,5-triazine derivatives and dimethylsulfoxide, Inorganica. Chim. Acta. 358 (2005) 1911-1917.

34. H.M. Dalloul, E.H.A.R. Mohamed, H.Z. Shorafa, A.Z. El-Shorafa, Heterocyclic synthesis using nitrilimines. Part 11. Synthesis of 1-aryl-3-phenylaminocarbonyl-4,5-dihydro-1,4,5-triazin-6-ones, Arkivoc. 13 (2008) 207-217.

35. M. Mojzych, Cytotoxic activity of some pyrazolo[4,3-*e*][1,2,4]triazines against human cancer cell lines, J. Chem. Soc. Pak. 33 (2011) 123-128.

36. S. Ünsalan, P. Çıkla, S.G. Küçükgüzel, S. Rollas, F. Şahin, O.F. Bayrak, Synthesis and characterization of triazenes derived from sulfonamides, Marmara Pharm. J. 15(2) (2011) 11-17.

37. W. Abdel-Sayed, I.F. Nassar, A.A.H. Abdel-Rahman, Synthesis and antitumor activity of new 1,2,4-triazine and [1,2,4]triazolo[4,3-*b*][1,2,4]triazine derivatives and their thioglycoside and acyclic *C*-nucleoside analogs, J. Heterocyclic Chem. 48 (2011) 135-143.

38. N.W. Gibson, L.C. Erickson, J.A. Hickman, Effects of the antitumor agent 8-carbamoyl-3-(2-chloroethyl)imidazo[5,1-*d*]-1,2,3,5-tetrazin-4(3*H*)-one on the DMA of Mouse L1210 cells, Cancer Res. 44 (1984) 1767-1771.

39. B.L. Hodous, S.D. Geuns-Meyer, P.E. Hughes, B.K. Albrecht, S. Bellon, J. Bready, S. Caenepeel, V.J. Cee, S.C. Chaffee, A. Coxon, M. Emery, J. Fretland, P. Gallant, Y. Gu, D. Hoffman, R.E. Johnson, R. Kendall, J.L. Kim, A.M. Long, M. Morrison, P.R. Olivieri, V.F. Patel, A. Polverino, P. Rose, P. Tempest, L. Wang, D.A. Whittington, H. Zhao, Evolution of a highly selective and potent 2-(pyridin-2-yl)-1,3,5-triazine tie-2 kinase inhibitor, J. Med. Chem. 50 (2007) 611-626.

40. T. Gucky, I. Frysˇova´, J. Slouka, M. Hajdu´ch, P. D_zuba´k, Cyclocondensation reaction of heterocyclic carbonyl compounds, Part XIII: Synthesis and cytotoxic activity of some 3,7-diaryl-5-(3,4,5-trimethoxyphenyl)pyrazolo[4,3-*e*][1,2,4]triazines, Eur. J. Med. Chem. 44 (2009) 891-900.

41. S. Manohar, S.I. Khan, D.S. Rawat, Synthesis, antimalarial activity and cytotoxicity of 4-aminoquinoline–triazine conjugates, Bioorg. Med. Chem. Lett. 20 (2010) 322-325.

42. R.M. Mohareb, E.M. Samir, The reaction of cyanoacetylhydrazine with chloroacetone: Synthesis of 1,2,4-triazine, 1,3,4-oxadiazine and their fused derivatives with antitumor activities, **Open** J. Med. Chem. 2 (2012) 1-9.

43. A.S. Abd El-All, A.S. Hassan, S.A. Osman, H.A.A. Yosef, W.H. Abdel-Hady, M.A. El-Hashash, S.R. Atta-Allah, M.M. Ali, A.A. El Rashedy, Synthesis, characterization and biological evaluation of new fused triazine derivatives based on 6-methyl-3-thioxo-1,2,4-triazin-5-one, Acta Pol. Pharm. 73 (2016) 79-92.

44. S. Manohar, A. Pepe, C.E.V. Gerena, B. Zayas, S.V. Malhotra, D.S. Rawat, Anticancer activity of 4-aminoquinoline-triazine based molecular hybrids. RSC Adv. 4 (2014) 7062.

45. J.K. Srivastava, G.G. Pillai, H.R. Bhat, A. Verma, U.P. Singh, Design and discovery of novel monastrol-1,3,5-triazines as potent anti-breast cancer agent *via* attenuating epidermal growth factor receptor tyrosine kinase, Sci. Rep. 7 (2017)5851.doi:10.1038/s41598-017-05934-5.

46. A.B. Patel, K.H. Chikhalia, P. Kumari, An efficient synthesis of new thiazolidin-4-one fused *s*-triazines as potential antimicrobial and anticancer agents, J. Saudi Chem. Soc. 18 (2014) 646-656.

47. D.J. Fu, J. Song, Y.H. Hou, R.H. Zhao, J.H. Li, R.W. Mao, J.J. Yang, P. Li, X.L. Zi, Z.H. Li, Q.Q. Zhang, F.Y. Wang, S.Y. Zhang, Y.B. Zhang, H.M. Liu, Discovery of 5,6-diaryl-1,2,4-triazines hybrids as potential apoptosis inducers, Eur. J. Med. Chem.doi: 10.1016/j.ejmech.2017.07.011.

48. M.R.E. Aly, A.A. Gobouri, S.H.A. Hafez, H.A. Saad, Synthesis, reactions, and biological activity of some triazine derivatives containing sulfa drug moieties, Russ. J. Bioorg. Chem. 41 (2015) 437-450.

49. A. Lauria, A. Alfio, R. Bonsignore, C. Gentile, A. Martorana, G. Gennaro, G. Barone, A. Terenzi, A.M. Almerico, Almerico, New benzothieno[3,2-*d*]-1,2,3-triazines with antiproliferative activity: Synthesis, spectroscopic studies, and biology activity, Bioorg. Med. Chem. Lett.

50. H.A. Saad, M.M. Youssef, M.A. Mosselhi, Microwave assisted synthesis of some new fused 1,2,4-triazines bearing thiophene moieties with expected pharmacological activity, Molecules, 16 (2011) 4937-4957.

51. H. Irannejad, M. Amini, F. Khodagholi, N. Ansari, S.K. Tusi, M. Sharifzadeh, A. Shafiee. Synthesis and in vitro evaluation of novel 1,2,4-triazine derivatives as neuroprotective agents, Bioorg. Med. Chem. 18 (2010) 4224-4230.

52. R.M. Mohareb, K.A. El-Sharkawy, M.M. Hussein, H.M. El-Sehrawi, Synthesis of hydrazide-hydrazone derivatives and their evaluation of antidepressant, sedative and analgesic agents, J. Pharm. Sci. & Res. 2 (2010) 185-196.

53. B.P. Mallikarjuna, S.G.V. Kumar, B.S. Sastry, Nagaraj, K.P. Manohara KP, (2007) Synthesis and anticonvulsant activity of some potent 5,6-bis aryl 1,2,4-triazines, J. Zhejiang Univ. Sci. B 8: 526-532.

54. D. Kaushik, S.A. Khan, G. Chawla, Design & synthesis of 2-(substituted aryloxy)-5-(substituted benzylidene)-3-phenyl-2,5-dihydro-1*H*-[1,2,4] triazin-6-one as potential anticonvulsant agents, Eur. J. Med. Chem. 45 (2010) 3960-3969.

55. H. Irannejad, H. Nadri, N. Naderi, S.N. Rezaeian, N. Zafari, A. Foroumadi, M. Amini, M. Khoobi, Anticonvulsant activity of 1,2,4-triazine derivatives with pyridyl side chain: Synthesis, biological and computational study, Med. Chem. Res. doi 10.1007/s00044-014-1315-3.

56. M. Sahu, N. Siddiqui, M.J. Naim, O. Alam, M.S. Yar, V. Sharma, S. Wakode, Design, synthesis, and docking study of pyrimidine-triazine hybrids for GABA estimation in animal epilepsy models, Arch. Pharm. Chem. Life Sci. 350 (2017) e1700146.

57. M. Amir, I. Ali, M.Z. Hassan, N. Mulakayala, Incorporated 1,2,4-triazines as anticonvulsant agents, Arch. Phar. Chem. Life Sci. 347(2014) 958-968.

58. H. Irannejad, N. Naderi, S. Emami, R.Q. Ghadikolaei, A. Foroumadi, T. Zafari, A. Mazar-Atabaki, S. Dadashpour, Microwave-assisted synthesis and anticonvulsant activity of 5,6-bisaryl-1,2,4-triazine-3-thiol derivatives, Med. Chem. Res. 23 (2014) 2503-2514.

59. P. Ahuja, N. Siddiqui Anticonvulsant evaluation of clubbed indole-1,2,4-triazine derivatives: A synthetic approach, Eur. J. Med. Chem. 10.1016/j.ejmech.2014.04.043.

60. A.A. Khan, N. Siddiqui, M.J. Akhtar, Z. Ali, M.S. Yar, Design, synthesis, and biological evaluation of 6-(2-aminosubstituted phenyl)-4-(substituted phenyl)-1,2,4-triazine-3,5(2*H*,4*H*)-dione derivatives as anticonvulsant agents, Arch. Pharm. Chem. Life Sci. 349 (2016) 277-292.

61. A. Tobe, T. Kobayashi, Pharmacological studies on triazine derivatives V. Sedative and neuroleptic actions of 2-amino-4-[4(2-hydroxyethyl)-piperazin-1-yl]-6-trifluoromethyl s-triazine (TR-10), Japan J. Pharmacol. 26 (1976) 559-570.

62. Rao DS, Kumar1 GVP, Pooja B, Harika G, Kumar YA, Rao GS, An extensive review on 1,2,3 and 1,2,4-triazines scaffold-valuable lead molecules with potent and diverse pharmacological activities, Der. Chemica. Sinica. 7(2) (2016) 101-130.

63. W. Froestl, A. Muhs, A. Pfeifer, Cognitive enhancers (nootropics). Part 1: Drugs interacting with receptors, J. Alzheimer's Dis. 32 (2012) 793-887. doi 10.3233/JAD-2012-121186.

64. Chen X, Meng Q, Qiu L, Zhan P, Liu H, lercq ED,Pannecouque C, Liu X, Design, synthesis and anti-HIV evaluation of novel triazine derivatives targeting the entrance channel of the NNRTI binding pocket, Chem. boil. drug des. https://doi.org/10.1111/cbdd.12471.

65. N. Sakakibara, G. Balboni, C. Congiu, V. Onnis, Y. Demizu, T. Misawa, M. Kurihara, Y. Kato, T. Maruyama, M. Toyama, M. Okamoto, M. Baba, Design, synthesis, and anti-HIV-1 activity of 1-substituted 3-(3,5-dimethylbenzyl)triazine derivatives, Antivir. Chem. Chemother. 24 (2015) 62-71. doi: 10.1177/2040206615612208.

66. R.V. Patel, P. Kumari, D.P. Rajani, C. Pannecouque, E.D. Clercq, K.H. Chikhalia, Antimicrobial, anti-TB, anticancer and anti-HIV evaluation of new *s*-triazine-based heterocycles, Future Med. Chem. 4 (2012) 1053-1065.

67. R.P. Modh, E.D. Clercq, C. Pannecouque, K.H. Chikhalia, Design, synthesis, antimicrobial activity and anti-HIV activity evaluation of novel hybrid quinazoline–triazine derivatives, J. Enzyme Inhib. Med. Chem. doi: 10.3109/14756366.2012.755622.

68. D.H. Mahajan, C. Pannecouque, E.D. Clercq, K.H. Chikhalia, Synthesis and studies of new 2-(coumarin-4-yloxy)-4,6-(substituted)-s-triazine derivatives as potential anti-HIV agents, Arch. Pharm. Chem. Life Sci. 342 (2009) 281-290.

69. P. Mullick, S.A. Khan, Synthesis of 1,2,4-triazine derivatives as potential anti-anxiety and anti-inflammatory agents, Acta. Pol. Pharm. Drug Res. 66 (2009) 379-385.

70. Z.K.A. Abdl-Samii, Synthesis and anti-inflammatory activity of some novel 1,3,4-oxadiazole derivatives, J. Chem. Technol. Biotechnol. 53 (1992) 143-146.

71. Apropazone, http://en.wikipedia.org/wiki/ Azapropazone, 2011 accessed 18 April 2011.

72. R.S. Shinde, S.D. Salunke, Synthesis and studies of novel piperidine-substituted triazine derivatives as potential anti-inflammatory and antimicrobial agents, J. Chem. Pharm. Res. 7 (2015) 704-714.

73. T. Rihong, Synthesis and biological activities of 1,2,4-triazine derivatives,Adv. Mat. Res. 1033-1034 (2014) 283-286.

74. M. Khoshneviszadeh, M.H. Ghahremani, A. Foroumadi, R. Miri, O. Firuzi, A. Madadkar-Sobhani, N. Edraki, M. Parsa, A. Shafiee, Design, synthesis and biological evaluation of novel anti-cytokine 1,2,4-triazine derivatives, Bioorg. Med. Chem. 21 (2013) 6708-6717.

75. R.M. Mohareb, K.A. El-Sharkawy, M.M. Hussein, H.M. El-Sehrawi, Synthesis of hydrazide-hydrazone derivatives and their evaluation of antidepressant, sedative and analgesic agents, J. Pharm. Sci. & Res. 2 (2010) 185-196.

76. K. Ho, J.R. Beasley, L. Belanger, D. Black, J. Chan, D. Dunn, B. Hu, A. Klon, S.G. Kultgen, M. Ohlmeyer, S.M. Parlato, P.C. Ray, Q. Pham, Y. Rong, A.L. Roughton, T.L. Walker, J. Wright, K. Xu,

Y. Xu, L. Zhang, M. Webb, Triazine and pyrimidine based ROCK inhibitors with efficacy in spontaneous hypertensive rat model, Bioorg. Med. Chem. Lett. 19 (2009) 6027-6031.

77. W.P. Heilman, R.D. Heilman, J.A. Scozzie, R.J. Wayner, J.M. Gullo, Z.S. Ariyan, Synthesis and antihypertensive activity of novel 3-hydrazino-5-phenyl- 1,2,4-triazines, J. Med. Chem. 22 (1979) 671-677.

78. R. Kumar, A.D. Singh, J. Singh, H. Singh, R.K. Roy, A. Chaudhary, 1,2,3-Triazine scaffold as a potent biologically active moiety: A mini review, Mini-Rev. Med. Chem. 14 (2014)72-83.

79. Y. Nomoto, H. Obase, H. Takai, M. Teranishi, J. Nakamura, K. Kubo, Studies on cardiotonic agents. II. Synthesis of novel phthalazine and 1,2,3-benzotriazine derivatives, Chem. Pharma. Bull. 38 (1990) 2179-2183.

80. G.L. Viswanatha, B.J. Priyadarshini, N. Krishnadas, S. Janardhanan, S. Rangappa, S. Hanumanthappa, Synthesis and antihistaminic activity of 3H-benzo [4,5] thieno [2,3-d][1,2,3] triazin-4-ones, Saudi Pharm. J. 20 (2012) 45-52.

81. E.V. Shchegol'kov, O.G. Khudina, A.E. Ivanova, Y.V. Burgart, E.V. Sadchikova, M.A. Kravchenko, V.I. Saloutin, Synthesis and tuberculostatic activity of some 1,2,4-triazines, Pharma. Chem. J.48 (2014) 383-386. doi 10.1007/s11094-014-1115-6.

82. V.K. Pandey, S. Tusi, Z. Tusi, M. Joshi, S. Bajpai, Synthesis and biological activity of substituted 2,4,6-s-triazines, Acta. Pharm. 54 (2004) 1-12.

83. B.R. Henke, T.G. Consler, A new series of estrogen receptor modulators that display selectivity for estrogen receptor *a*, J. Med. Chem. 45 (2002)5492-5505.

84. G. Kuo, A. DeAngelis, S. Emanuel, A. Wang, Y. Zhang, P.J. Connolly, X. Chen, R.H. Gruninger, C. Rugg, A. Fuentes-Pesquera, S.A. Middleton, L. Jolliffe, W.V. Murray, Synthesis and identification of [1,3,5]triazine-pyridine biheteroaryl as a novel series of potent cyclin-dependent kinase inhibitors, J. Med. Chem.48 (2005)4535-4546.

85. F. Popowycz, G. Fournet, C. Schneider, K. Bettayeb, Y. Ferandin, C. Lamigeon, O.M. Tirado, S. Mateo-Lozano, V. Notario, P. Colas, P. Bernard, L. Meijer, B. Joseph,Pyrazolo[1,5-*a*]-1,3,5-triazine as a purine bioisostere: access to potent CDK inhibitor (*R*)-roscovitine analogue, J. Med. Chem. 52 (2009) 655-663.

86. Wesierska-Godek J, Chamrad I, Krystof V, Novel potent pharmacological cyclin-dependent kinase inhibitors, Future Med. Chem. 1(2009) 9.

87. M. Schunk, T. Jelinek, K. Wetzel, H.D. Nothdurft, Detection of *Giardia lamblia* and *Entamoeba histolytica* in stool samples by two enzyme immunoassays, Eur. J. Clin. Microbiol. Infect. Dis. 20 (2001) 389-391.

88. World Health Organization (1994) Bench aids for the diagnosis of intestinal parasites. Geneva: World Health Organization. http://www.who.int/iris/handle/10665/37323.

89. I. Abdullah, H. Tak, F. Ahmad, N. Gul, S. Nabi, T. A. Sofi, Predominance of gastrointestinal protozoan parasites in children: A brief review, J. Health Educ. Res. Dev. 4(2016) 194. doi: 10.4172/2380-5439.1000194.

90. S. Kondaparla, U. Debnath, A. Soni, V. R. Dola, M. Sinha, K. Srivastava, S. K. Puri, S.B. Katti, Synthesis, biological evaluation and molecular modeling studies of chiral chloroquine analogues as antimalarial agents, Antimicrob. Agents Chemother. doi:10.1128/AAC.02347-17.

91. G. Greif (2009) Triazinone compounds for treating diseases resulting from infestation with parasitic protozoans. US Patent 20090181040 filled October 12, 2007, Issued July 16, 2009.

92. Ponazuril. http://en.wikipedia.org/wiki/Ponazuril, 2011 accessed 7 February 2011

93. M.L. Stock, S.T. Elazab, W.H. Hsu Review of triazine antiprotozoal drugs used in veterinary medicine, J. Vet. Pharmacol. Therap.2017 (2017) 1-11. doi: 10.1111/jvp.12450

94. A. Agarwal, K. Srivastava, S.K. Puri, P.M.S. Chauhan, Synthesis of 2, 4, 6-trisubstituted triazines as antimalarial agents, Bioorg. Med. Chem. Lett. 15 (2005) 531-533.

95. S.B. Katiyar, K. Srivastava, S.K. Puri, P.M.S. Chauhan, Synthesis of 2-[3, 5- substituted pyrazol-1-yl]-4, 6-trisubstituted triazine derivatives as antimalarial agents, Bioorg. Med. Chem. Lett. 15 (2005) 4957-4960.

96. H.R. Bhat, U.P. Singh, P. Gahtori, S.K. Ghosh, K. Gogoi, A. Prakash, R.K. Singh, Synthesis, docking, *in vitro* and *in vivo* antimalarial activity of hybrid 4-aminoquinoline-1,3,5-triazine derivatives against wild and mutant malaria parasites,Chem. Biol. Drug Des. 86 (2015) 265-71.

97. H.R. Bhat, U.P. Singh, A. Thakur, S.K. Ghosh, K. Gogoi, A. Prakash, R.K. Singh, Synthesis, antimalarial activity and molecular docking of hybrid 4-aminoquinoline-1,3,5-triazine derivatives, doi: 10.1016/j.exppara.2015.06.016.

98. H.R. Bhat, U.P. Singh, P.S. Yadav, V. Kumar, P. Gahtori, A. Das, D. Chetia, A. Prakash, J. Mahanta, Synthesis, characterization and antimalarial activity of hybrid 4-aminoquinoline-1,3,5-triazine derivatives, Arab. J. Chem. 9 (2016) S625-S631.

99. Stephen, E. Viayna, E. Jung, Ian, M. Georg, Maria, T. James T, Lars, Henrik, Imidazo[l,2-b][l,2,4]triazine derivatives as antiparasitic agents. World Intellectual Property Organization Patent WO

2016/193111 Al, Filled May 26, 2016, Issued December 8, 2016.

100. K. Karrouchi, S. Radi, Y. Ramli, J. Taoufik, Y.N. Mabkhot, F.A. Al-aizari, M. Ansar, Synthesis and pharmacological activities of pyrazole derivatives: A review, Molecules, 23 (2018) 134. doi:10.3390/molecules23010134.

101. Z.A. Kaplancikli, G. Turan-Zitouni, A. Ozdemir, M.D. Altintop, Y. Tunali, Synthesis of some thienyl-triazine derivatives and antimicrobial activity, Asian J. Chem. 22 (2010) 6701-6707.

102. A. Krutošíková, J.K. Vac, P. Banák, Synthesis and reactions of 3,4-dichIorophenyl-substituted furocondensed derivatives, Chem. Zvesti. 38 (1984) 707-713.

103. C. Sharma, B. Thadhaney, G. Pemawat, G.L. Talesara, Synthesis of some novel ethoxyphthalimide derivatives of pyrazolo[3,4-*c*]pyrazoles, Indian J. Chem. 47B (2008) 1892-1897.

104. B. Datterl, N. Tröstner, D. Kucharski, W. Holzer, Heterocyclic analogues of xanthone and xanthione. 1*H*-pyrano[2,3-*c*:6,5-*c*]dipyrazol-4(7*H*)-ones and thiones: Synthesis and NMR data, Molecules, 15 (2010) 6106-6126.

105. Y. Higashi, D. Jitsuiki, K. Chayama, M. Yoshizumi, Edaravone (3-methyl-1-phenyl-2-pyrazolin-5-one), A novel free radical scavenger, for treatment of cardiovascular diseases, Recent Pat. Cardiovasc. Drug Discov. 1 (2006)85-93.

106. N.B. Ahasan, M.R. Isla, Cytotoxicity study of pyrazole derivatives, Bangladesh J. Pharmacol. 2 (2007) 81-87.

107. R. Pundeer, P. Ranjan, K. Pannu, O. Prakash, One-pot synthesis of some new semicarbazone, thiosemicarbazone and hydrazone derivatives of 1-phenyl-3-arylpyrazole-4-carboxaldehyde from acetophenone phenylhydrazones using Vilsmeier-Haack reagent, Synth. Commun. 39 (2009) 316-324.

108. B.S. Furniss, A.J. Hannaford, P.W.G. Smith, A.R. Tatchell, Vogel's Textbook of Practical Organic Chemistry, Longman Publisher, Singapore (1996).

109. D. Kaushik, S.A. Khan, G. Chawla, S. Kumar,*N*'-[(5-chloro-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)methylene] 2/4-substitutedhydrazides: Synthesis and anticonvulsant activity, Eur. J. Med. Chem. 45 (2010) 3943-3949.

110. O. Prakash, K. Pannu, R. Naithania, H. Kaur, One-pot synthesis of oxime derivatives of 1,3-diphenylpyrazole-4-carboxaldehydes from acetophenone phenylhydrazones using Vilsmeier-Haack reagent, Synth. Commun. 36 (2006) 3479-3485.

111. D. Kaushik, S.A. Khan, G. Chawla, Synthesis of (substituted benzamidostyryl) l*H*-benzimidazoles and their screening for anti-inflammatory activity, Med. Chem. Res. doi 10.1007/s00044-011-9552-1.

112. R. Pundeer, P. Ranjan, K. Pannu, O. Prakash, One-pot synthesis of some new semicarbazone, thiosemicarbazone and hydrazone derivatives of 1-phenyl-3-arylpyrazole-4-carboxaldehyde from acetophenone phenylhydrazones using Vilsmeier-Haack reagent, Synth. Commun. 39 (2009) 316-324.

113. D. Kaushik, S.A. Khan, G. Chawla, Design & synthesis of 2-(substituted aryloxy)-5-(substituted benzylidene)-3-phenyl-2,5-dihydro-1*H*-[1,2,4] triazin-6-one as potential anticonvulsant agents, Eur. J. Med. Chem. 45 (2010) 3960-3969.

Conflict of Interest: None
Source of Support: Nil