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Review Article

Review on the Pharmacological Activities of Hydrazones derivatives

Praveen Kumar[1], Amit Rai[2], Mahendra Singh[2], Durgesh Kumar[2], Anil Kumar Sahdev[2] and Vinit Raj[2]*

[1]Department of Pharmaceutical Chemistry (Pharmacy), SD College of Pharmacy and Vocational Studies, India

[2]Department of Pharmaceutical Sciences, Babasaheb Bhimrao Ambedkar University, Vidya Vihar, India

***Corresponding Author:** Vinit Raj, Department of Pharmaceutical Sciences, Babasaheb Bhimrao Ambedkar University, Vidya Vihar, India. E mail Id: raj.vinit24@gmail.com, Mobile No: +918859383897.

Received: December 23, 2015; **Published:** February 29, 2016

Abstract

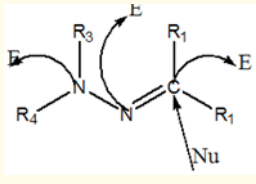
Hydrazones and their derivatives constitute a versatile class of compounds in organic chemistry. The development of novel hydrazones containing compounds possess a wide verities of biological activities like as antioxidant, anti-inflammatory, anticonvulsants, antidepressant and anxiolytic, antihypertensive, anticancer, antimicrobial, anti-tuberculosis, and antifungal activity.

Hydrazones possess –NHN=CH- and more significant for the development of novel drugs. Both nitrogen atoms of the hydrazone group are nucleophilic, although the amino type nitrogen is more reactive. Whereas, the carbon atom of hydrazone group has both electrophilic and nucleophilic. Subsequently, hydrazone derivatives more selective activity and lower side effect continues to be an active area of intensification in medicinal chemistry. This review is compiled which elaborate the medicinal importance and their biological properties.

Keywords: *Hydrazones; Biological activity; Synthesis of hydrazones*

Introduction

Hydrazones and their derivatives constitute a versatile class of compounds in organic chemistry. These compounds have fascinating biological properties, such as anti-inflammatory, analgesic, anticonvulsant, anti-tuberculous, antitumor, anti-HIV and antimicrobial activity. Hydrazones are principle compounds for drug design, as possible ligands for metal complexes, organocatalysis and also for the synthesis of heterocyclic compounds. The ease of preparation, increased hydrolytic stability relative to imines, and tendency toward crystallinity are the desirable characteristics of hydrazones. Due to these positive traits, hydrazones have been under study for a long time, but much of their basic chemistry remains unexplored. Hydrazones contain two connected nitrogen atoms of different nature and a C-N double bond that is conjugated with alone electron pair of the terminal nitrogen atom. These structural fragments are principally responsible for the physical and chemical properties of hydrazones. Both nitrogen atoms of the hydrazone group are nucleophilic, although the amino type nitrogen is more reactive. The carbon atom of hydrazone group has both electrophilic and nucleophilic [1].



E= Electrophilie

Nu= Nucleophile

Figure 1: *Classification of active center.*

Synthesis of Hydrazone

Kumar Arvind., *et al*. in 2009, A series of substituted Hydrazone and Quinoxaline derivatives have been synthesized by appropriate methods. This reaction of diethyl malonate with bromine ultimately yields diethyl-dibromomalonate. The compound diethyl-dibromomalonateon condensation with 4-methyl-o-phenylenediamine in methanol yielded ethyl 2-hydroxy-6-methyl-quinoxaline-3-carboxylate. The compound ethyl 2-hydroxy-6-methyl-quinoxaline-3-carboxylate underwent hydrazinolysis with hydrazine hydrate in methanol yielded 2-hydroxy-6-methyl-quinoxaline-3-carbonylhydrazide. The compound 2-hydroxy-6-methyl-quinoxaline-3-carbonylhydrazide on refluxing with different aromatic aldehydes in ethanol furnished N-(2-hydroxy-6-methyl-3-quinoxalinoyl)-N-(arylidenehydrazine) [31]

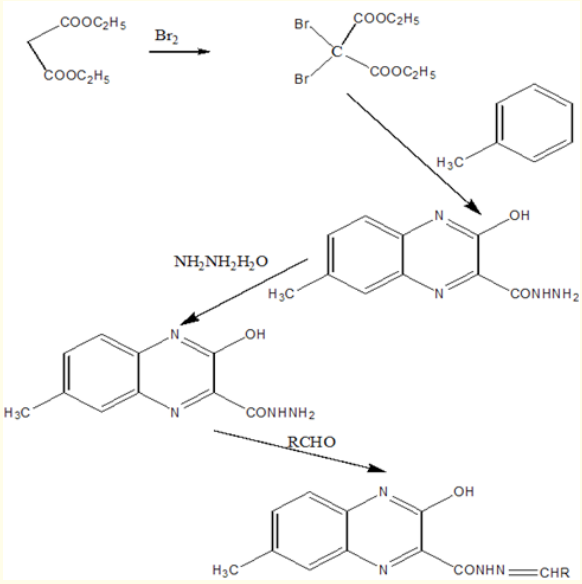


Figure 2: *Synthesis of Hydrazone and Quinoxaline derivatives.*

AP Rajput., *et al*. in 2009, synthesized a series of benzaldehyde substituted phenyl carbonylhydrazones and their formylation has been carried out by using Vilsmeier-Haack reaction. [41]

ZaferAsımKaplancikli., *et al*. in 2012, synthesizedsome hydrazone derivatives via the reaction of 3-cyclohexylpropionic acid hydrazide with various benzaldehydes [32].

AG Yadav et al. in 2012, reported that vilsmeier-Haack reaction provide a route involve formylation of activated aromatic and heteroaromatic systems by ring formation. Recently, pyrazole had been synthesized from various substituted hydrazones using Vilsmeier-Haack reaction. Our interest was in synthesizing pyrazolylbenzothiazole from 2-amino benzothiazole which was refluxed with hydrazine hydrate followed by condensation with substituted acetophenone to form hydrazones derivatives. [33]

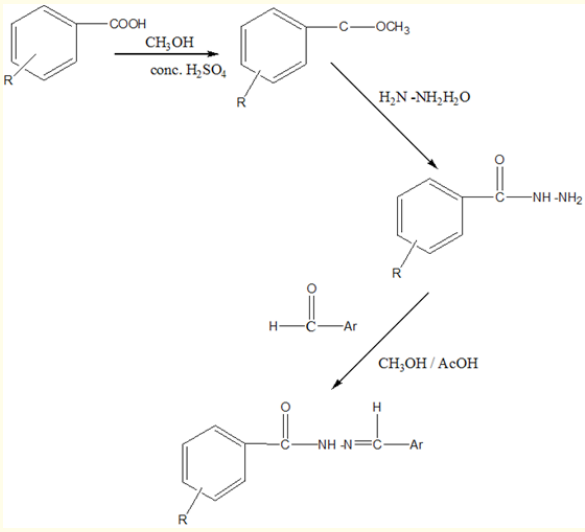


Figure 3: *Scheme for synthesis of benzaldehyde substituted phenyl carbonyl hydrazones.*

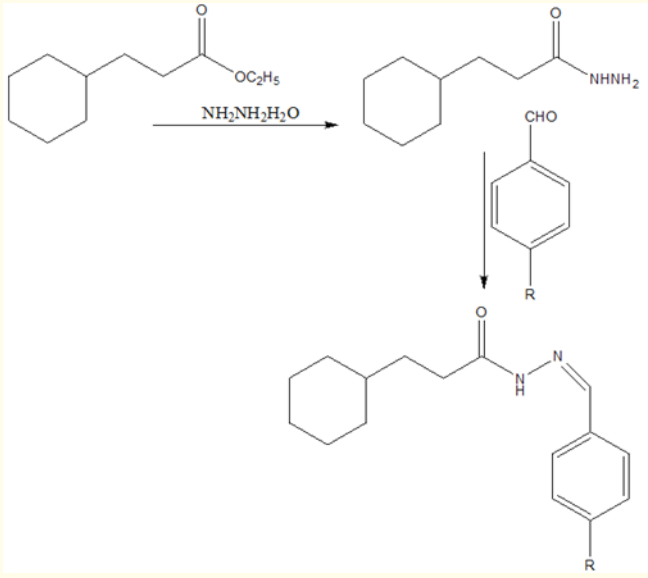


Figure 4: *Scheme for synthesis of hydrazone derivatives via the reaction of 3-cyclohexylpropionic acid hydrazide with various benzaldehydes.*

Activities of Hydrazone

Anticonvulsant activity

Sridhar SK., *et al*. in 2002, had presented the study of anticonvulsant activity of hydrazones, Schiff and Mannich bases of isatin were probed by maximal electroshock method (MES) and metrazol-induced convulsions (MET) at 30, 100 and 300 mg/kg dose levels. Neurotoxicity of the compounds was also assessed at the same dose levels. Eight compounds of the series exhibited significant anticonvulsant activity at 30 mg/kg dose level. 3-(4-chloro-phenylimino)-5-methyl-1,3-dihydro-indol-2-one was found to be the most potent compound

of the series with 87% protection at 100 mg/kg and an ED(50) of 53.61 mg/kg (MET). Although, all the compounds exhibited lesser neurotoxicity compared to phenytoin. All the active compounds showed greater protection than sodium valproate. [2]

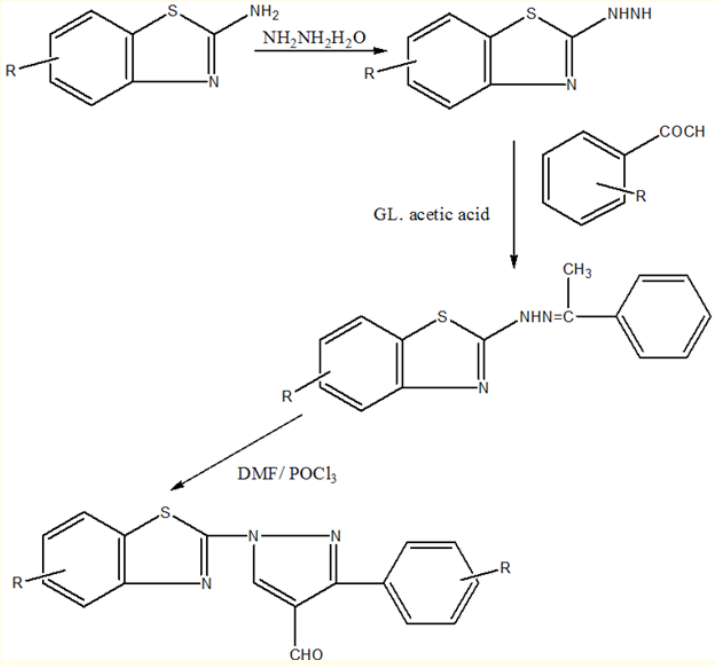


Figure 5: *scheme for synthesis of pyrazolylbenzothiazole from 2-amino benzothiazole with hydrazine hydrate followed by condensation with substituted acetophenone to form hydrazones derivatives.*

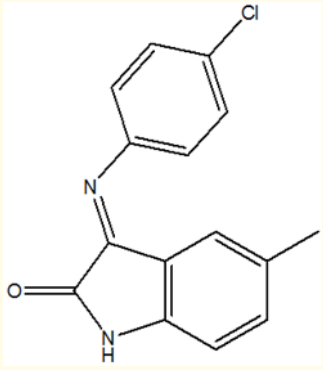


Figure 6: *3-(4-chloro-phenylimino)-5-methyl-1,3-dihydro-indol-2-one.*

Kumar Suresh., *et al*. in 2010, Probed in-vivo anticonvulsant activity profile for differently substituted 2-chloro-quinolinyl hydrazones against electrical and chemical model of convulsions, provides a preliminary SAR, which may be summarized as follows. Among the compounds tested, those with electron with drawing group (Cl, F) in the benzoyl ring 3d 4-Chloro-Ní-[(2-chloroquinolin-3-yl) methyli-dene]benzohydrazide, 2,4-Dichloro-Ní-[(2 chloroquinolin-3-yl)methyli-dene]benzohydrazide) exhibited good anticonvulsant activity.[3]

Jadon gunjan., *et al*. in 2011, got following hydrazones derivatives namely N'- (4-Chlorobenzylidene)-2-phenylacetohydrazide, N'- (2-Chlorobenzylidene) – 2 phenylacetohydrazide, N - (3,4,5-thimethoxybenzylidene) – 2 - phenylacetohydrazide, N-(furan-2-yl-methoxybenzlidene) – 2 — phenylacetohydrazide, N - (3,4,5-thimethoxybenzylidene) – 2 -phenylacetohyrazide and N – 1 - (4-hydroxy-henyl) ethylidine – 2 - phenylacetohydrazide, which makes a remarkable interest in process of development of novel compounds having anticonvulsant activities. All these compounds have been probed for their biological activities and reported with significant action. [4]

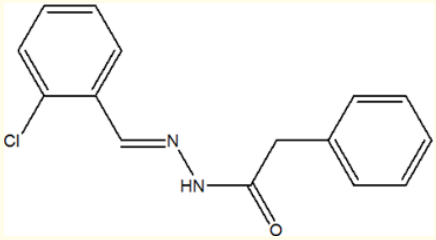


Figure 7: *N'-(2-Chlorobenzylidene) – 2 – phenylaetohydrazide.*

Pandeya SN., *et al*. in 2012, synthesized a series of pyrimidine containing hydrazones. The compound 3c is found to be one of the best of all the tested compound as it resists the death of the mice, i.e. the mice survives. The recovery occurs and also reveals the fact that "Citral" is proved to be a potent and efficient substituent for CNS depressant action and offers the synthesis of newer and potent anticonvulsant having pyrimidine hydrazone along with Citral substituent as Schiff bases. [36]

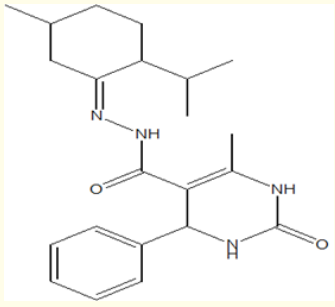


Figure 8: *(3C) 6-Methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydro-pyrimidine-5-carboxylic acid (2-isopropyl-5-methyl-cyclohexylidene)-hydrazide.*

Sharma C S., *et al*. in 2012. Attempt to synthesize Schiff bases of phenyl acetic acid were successfully carried out as per the scheme mentioned. All compounds reported mild to moderate anti-inflammatory and anticonvulsant activity.

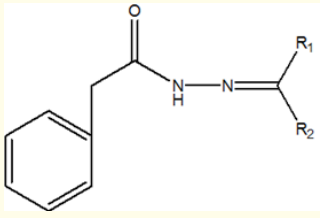


Figure 9: *2-phenylacetohydrazide (3a- 3j).*

Antimicrobial activity

Rauf Abdul., *et al.* in 2008, has derived fatty acids containing hetero atoms as potential antimicrobial agents. Thus, eight different hydrazones were synthesized from four fatty acid hydrazides namely undecanoic hydrazide, octadecanoic hydrazide, 12-hydroxyoctadecanoic hydrazide and 9-hydroxyoctadecanoic hydrazide by condensing them with car-bonyl group of methyl acetoacetate and acetylacetone These compounds were also screened for their microbial activity against Escherichia coli, Staphylococcus aureus and Staphylococcus albus by cup-plate method at 100 µg/ml of DMF using chloromycetin as a standard drug. Results obtained from the antibacterial activity show that some of the synthesized hydrazones, especially C-11 derivatives, i.e. hydrazones Methyl 3-(2'-undecanoylhydrazono) butanoate and (N´-(4-Oxopentane-2-ylidene) undecanohydrazide), may be considered promising for development of new antibacterial agents after performing the significant toxicity tests. [2]

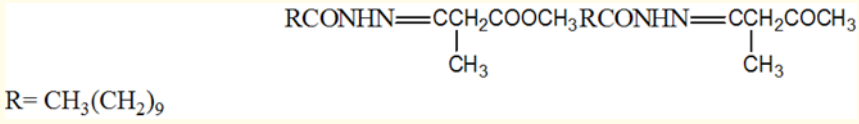


Figure 10: *Methyl-3-(2-undecanoylhydrazono) butanoate & (N´-(4-Oxopentane-2ylidene) undecanohydrazide.*

Jayalakshmi n., *et al*. in 2008, got several 2, 6-diphenyl 4–piperidone derivatives by Mannich reaction (condensation) of ethyl – methyl ketone, substituted aldehydes and ammonium acetate. The synthesized compounds were probed for antibacterial, antifungal, acute toxicity and local anaesthetic activity at various concentrations. It was observed that when the 4-keto functionality was condensed to form selenadiazole [compound 5,7–diphenyl-4- piperidone[3,4-d]- 1,2,3 - selenadiazole and 3-methyl-5,7–diphenyl-4-piperidone[3,4-d]-1,2,3–selenadiazole] and hydrazone derivatives [compound N-(benzimidazol- 2-yl methyl) -3 - methyl -2,6 - diphenyl piperidin4- hydrazone and N-(benzimidazol-2-yl methyl) -2,6 - diphenyl piperidin- 4- hydrazone], the resulting compounds exhibits good antibacterial activity. It was observed that the compounds 5,7–diphenyl-4- piperidone[3,4-d]- 1,2,3 – selenadiazole and (6)show more activity than compounds N-(benzimidazol- 2-yl methyl) -3 - methyl -2,6 - diphenyl piperidin4- hydrazone and (N-(benzimidazol-2-yl methyl) -2,6 - diphenyl piperidin- 4- hydrazone) against all dermatophytes. [3]

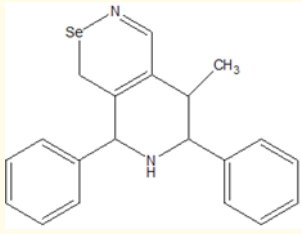


Figure 11: *methyl-5,7–diphenyl-4-piperidone[3,4-d]-1,2,3 selenadiazole.*

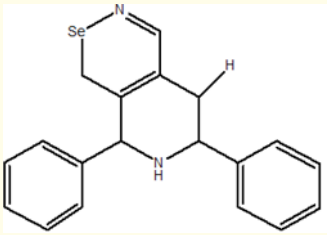
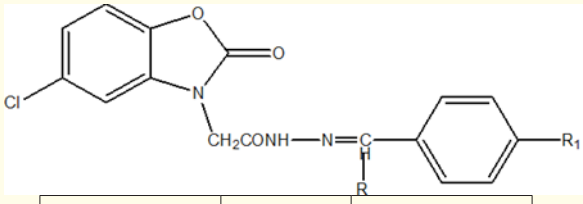


Figure 12: *3-5,7–diphenyl-4-piperidone[3,4d]-1,2,3selenadiazole*

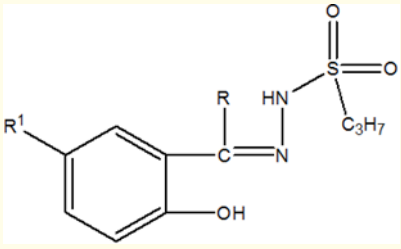
Tijen onkol., *et al*. in 2008, synthesized the seven 5-chloro-2(3H)-benzoxazolinone-3-acetyl-2-(p-substituted benzal-hydrazone derivatives and four 5-chloro-2(3H)-benzoxazolinone-3-acetyl-2-(p-substituted acetophenone) hydrazone derivatives. Compounds IVb, IVc, IVd, Vb, Vc and Vd, are effective against Staphylococcus aureus as standard compound ampicillin. The rest of the IV and V derivatives showed moderate activity towards Gram-positive and Gram-negative bacteria when compared to ampicillin. Entire derivatives of IVb, IVc, IVd, Vb, Vc and Vd have pronounced antifungal activity and exceeded that of fluconazole, which was used as the reference compound. The rest of the IV and V derivatives exhibited equal antifungal activity against Candida parapsilosis with fluconazole. Also IVb, IVc, IVd, Vb, Vc and Vd derivatives have been found two fold active than fluconazole against Candida albicans. [4]



Compounds	R	R1
IV b	H	Br
IV c	H	Cl
IV d	H	F
V b	CH_3	Br
V c	CH_3	Cl
V d	CH_3	OH

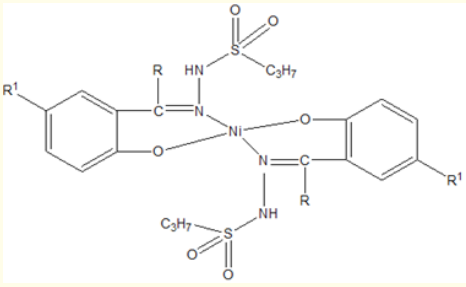
Figure 13: *5-chloro-2(3H)-benzoxazolinone-3-acetyl-2-(p-substituted benzal-hydrazone derivatives.*

U mmuhan O zdemir O zmen., *et al*. in 2008,synthesizedProphane sulfonic acid hydrazide derivatives as salicylaldehydeprophanesulfonylhydrazone (salpsh), 5-methylsalicylaldehydeprophanesulfonylhydrazone (5-msalpsh), 2 hydroxyacetophenoneprophanesulfonylhydrazone, 5-methyl-2 hydroxyacetophenoneprophanesulfonylhydrazone and their Ni (II) complexes have been synthesized The complexes were found to have general compositions [NiL2]. But the decrease of the electron densities by the coordination through the donor atoms causes the lower activities of complexes than ligands. Ligands have the most activity against S. aureus in all bacteria, in which splash have the lowest MIC's (145 g/mL). Complexes have the most activity against *E. coli* in all bacteria, in which Nisalpsh have the lowest MIC's (162 g/mL). [5]



$R=R^1=H$	Salpsh
$R=H, R^1=CH_3$	5Msalpash
$R=CH_3, R^1=H$	Afpsh
$R=CH_3, R^1=CH_3$	5Mafpsh

Figure 14: *Prophane sulfonic acid hydrazide derivatives.*



Nisalpah	$R=R^1=H$
Ni-5msalpash	$R=H, R^1=CH_3$
Niafpsh	$R=CH_3, R^1=H$
Ni-5mafpsh	$R=CH_3, R^1=CH_3$

Figure 15: *Prophane sulfonic acid hydrazide derivatives.*

Ioana MC., *et al*. in 2008, probed the antimicrobial activity of some novel compounds from this class (esters, hydrazides, hydrazones), against bacterial and fungical strains using the disc-diffusion method under standard conditions. The microbiological evaluation results reported that the substitution of the aniline in an aromatic ring from salicylanilide, with 2-CF_3, provides compounds having more biological activity than the unsubstituted ones. The 3-CF_3 substitution of the aniline in an aromatic ring gives compounds with more activity against Bacillus cereus, *Escherichia coli, Staphylococcus aureus*, the rest of the microorganisms were easily inhibited by the unsubstituted salicylanilide. The 5-chloro-2- hydroxy-N-phenyl-benzamide derivatives possess higher biological effect than salicylanilide, only *Sacharomyces cerevisiae* and *Candida albicans* species were easier inhibited by the salicylanilideitself. [6]

Suroor A Khan., et al. in 2009, synthesized aquinoxalinone derivatives by the condensation of 1,2-diaminobenzenewith α-ketoglutaric acid to yield 3-(3-oxo-3,4-dihydroquinoxalin-2-yl) propionic acid and then treated with hydrazine hydrate to yield its hydrazones . This was further reacted with substituted aromatic aldehydes to produce final compounds (4a-r). All the synthesized compounds were probed for their antimicrobial and antiinflammatory activity. The results obtained designates that a majority of these compounds show

only moderate activity, however, few of them like 4a, 4d, 4k,and 4n show comparatively good activity against both types of microorganisms. All synthesized compounds were probed for anti-inflammatory activity, and among them only compounds having the methoxy group at the para position, i.e. 4f and 4p, showed comparatively good percentage of inhibition of edema than the other synthesized compounds. [7]

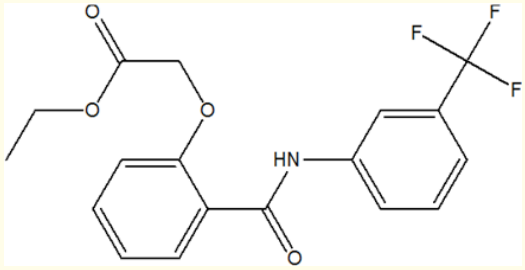
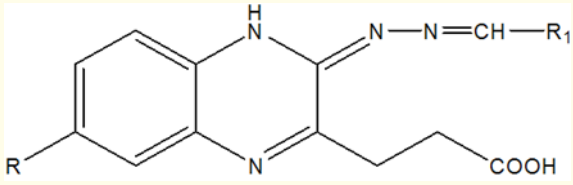


Figure 16: *(3-trifluoromethyl-phenylcarbamoyl phenoxy)-acetic acid ethyl ester.*



Compounds	R	R
4a	H	4F-C_6H_4
4d	H	4Cl-C_6H_4
4k	H	4F-C_6H_4
4f	CH_3	4-OCH_3-C6H_4
4n	H	4-Cl-C_6H_4
4p	CH_3	4-F-C_6H_4

Figure 17: *Qquinoxalinone derivatives.*

AP Rajput., *et al*. in 2009, synthesized a series of benzaldehyde substituted phenyl carbonyl hydrazones and their formylation has been carried out by using Vilsmeier-Haack reaction. All the hydrazones and their formyl derivatives were screened for antibacterial activity. The compounds 4a, 4c, 4d, 4-methoxybenzaldehyde -2-chlorophenyl-1-carbonyl hydrazone, benzaldehyde -2-chlorophenyl-1-carbonylhydrazone, 4-methoxybenzaldehyde phenyl-1-carbonyl hydrazone, 4-hydroxybenzaldehyde phenyl-1-carbonylhydrazone, 2-nitrobenzaldehydephenyl-1-carbonylhydrazone were found to be active against P vulgaris.Other compounds were found inactive against *P. vulgaris, S.aureus*, and S. *typhimurium*. Compounds 4-methoxybenzaldehyde -4-chlorophenyl-1-carbonyl hydrazone, 4-hydroxybenzaldehyde -4-chlorophenyl-1-carbonylhydrazone, 1-(3-4-methoxybenzaldehyde-N-formyl-1-carbonyl) 4 chlorobenzene hydrazone, 1-(3-benzaldehyde-N-formyl-1-carbonyl)4- chlorobenzene hydrazone and 1-(3-2-nitrobenzaldehyde-C-formyl-1-carbonyl)4-chlorobenzene hydrazone showed remarkable activity against *S. aureus* where as -4-chlorophenyl-1-carbonylhydrazone, 1-(3-4-hydroxybenzaldehyde-N-formyl-1-carbonyl) 4-chlorobenzene hydrazone, 9b1-(3-4-methoxybenzaldehyde-N-formyl-1-carbonyl) 4-chlorobenzene hydrazoneand 9d1-(3-2-nitrobenzaldehyde-C-formyl-1-carbonyl)4-chlorobenzene hydrazone were found active against *E. coli* [8].

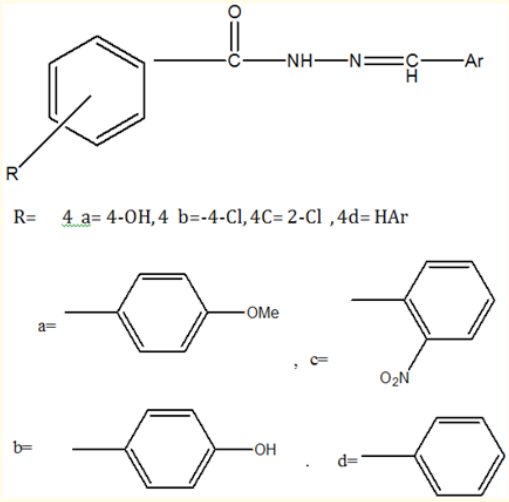


Figure 18: *benzaldehyde substituted phenyl carbonyl hydrazones.*

Toliwal SD., *et al*. in 2009, Reported hydrazones with an azometine -NHN=CH- proton constitutes an important class of compounds for new drug development. Certain hydrazones exhibited remarkable antibacterial and antifungal activities when compared with standards. Neem oil hydrazone and karanja oil hydrazone can be used as antibacterial agent against *Bacillus subtilis* due to sustained antibacterial activity relative to Streptomycin. Karanja oil hydrazone and rice bran oil hydrazone can be utilized as antifungal agent against *Aspergillus niger.* [9]

Arvind Kumar., *et al*. in 2009, synthesized a series of substituted Hydrazone and Quinoxaline derivatives by appropriate methods. All the compounds have been screened for their antibacterial activity against staphylococcus aureus and *Escherichia coli*. We have reported the synthesis of ten new Hydrazones and Quinoxaline. The activity of these compounds (3-hydroxy-7-methyl-N'-(3-nitrobenzylidene) quinoxaline-2-carbohydrazide, N'-(2-chlorobenzylidene)-3-hydroxy-7-methylquinoxaline-2-carbohydrazide, & 3-hydroxy-7-methyl-N'-(4-nitrobenzylidene) quinoxaline-2-carbohydrazide) was comparable with that of indomethacin. All compounds were probed for their antibacterial activity against *E. coli,* and *S. Aureus* by using cup plate technique. The compounds 3-hydroxy-7-methyl-N'-(4-nitrobenzylidene) quinoxaline-2-carbohydrazide shows maximum activity against *E. coli.* [10].

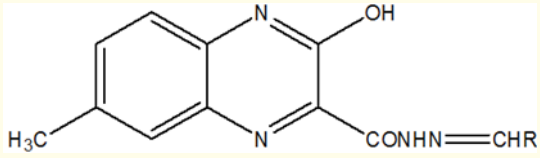


Figure 19: *N'-benzylidene-3-hydroxy-7-methylquinoxaline-2-*

MosselhiAbdelnabiMosselhi., et al. synthesizedpoly-O-acetyl derivatives 12-16. Attempted dehydrogenative cyclization of the products 7-11 and 12-16 using various conditions did not afford the corresponding acycloC-nucleosides (R=sugar or R`= acetylated sugar) 18. Nevertheless, the reaction of 7-11 or 12-16 with brominein acetic acid and sodium acetate afforded 8-bromo-7-ethyltheophylline 17. The compounds 9 and 12-16 were tested for their antimicrobial activities using four fungal species and Compound 9 reports the highest degree of inhibition against AF, PI and SA and weak inhibition against SR. [11]

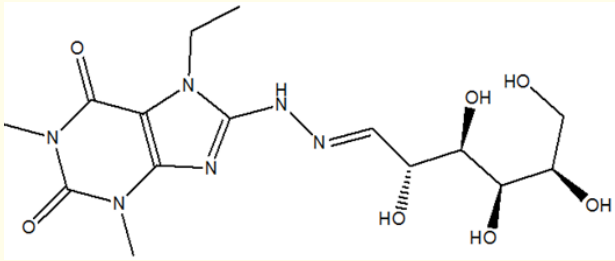


Figure 20: *(9) D-Mannose-7-ethyl-8-theophylinylhydrajone.*

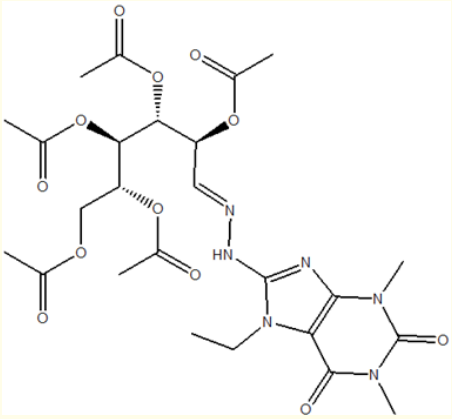


Figure 21: *2,3,4,5,6-Penta-O-acetyl-D-glucose-7-ethyl-8-theophyllinyl-hydrazone (12).*

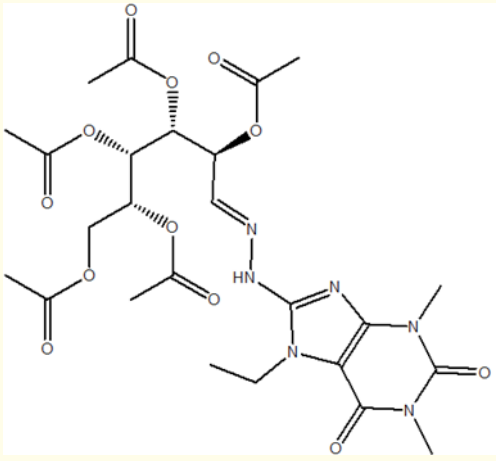


Figure 22: *2,3,4,5,6-Penta-O-acetyl-O-galactose-7-ethyl-8-theophyllinyl-hydrazone.*

Srivsatava Ritu., *et al*. in 2010, Synthesized twelve aryl acetic acid hydrazones and examined for the first time their antimicrobial activity. Some of the target compounds RSP 7, RSP 5 ,RSP 10 show moderate activity against H 37 RV strain of Mycobacterium tuberculosis at a concentration of 10μM. [12]

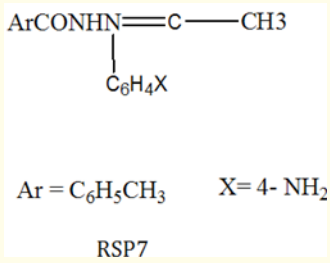


Figure 23: *Aryl acetic acid hydrazones.*

Vijay V Dabholkar., *et al*. in 2010, synthesized 2, 4-disubstituted Oxazolesfrom Hippuric acid/acetyl glycine, substituted aromatic aldehydes, acetic anhydride and sodium acetate as a catalyst. Further reacting with hydrazine hydrate yielded corresponding hydrazones, which on condensation reaction with different aldehydes revealed final Schiff base. The Schiff base of 2-methyl / phenyl -4-benzylidene -5-hydrazino -1, 3-Oxazole were obtained by condensation of 2-methyl / phenyl-4-benzylidene-5-Oxo-1, 3-Oxazole with hydrazine hydrate followed by different aromatic aldehydes with desirable yield. Besides, the representative compounds were screened for their antimicrobial activity against gram negative as well as gram positive bacteria, which shows convincing activity. [13]

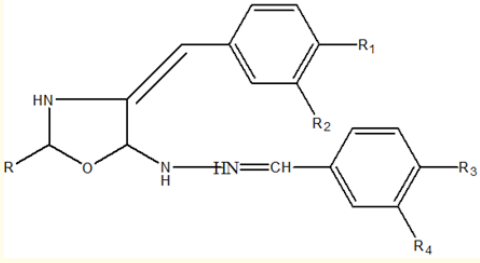


Figure 24: *2-methyl / phenyl -4-benzylidene -5-hydrazino -1, 3-Oxazole.*

Ahmet Özdemir,. *et al*. in 2010, synthesized new hydrazone derivatives and probed for anti-tuberculosis activity. The reaction of (5,6,7,8-tetrahydronaphthalen-1-yl) acetic acid hydrazide with various benzaldehydes gave 5,6,7,8-tetrahydronaphtalen acetic acid benzylidene hydrazide derivatives. The compounds were Probed for anti-tuberculosis activity against Mycobacterium tuberculosis H37Rv (ATCC 27294) using the BACTEC 460 radiometric system and BACTEC 12B medium. The preliminary results designates that all of the tested compounds showed low activity against the test organism. The compound A10 showed high anti-tuberculosis activity (IC50: 3.072 μg/mL and IC90: 3.358 μg/mL) and low cytotoxicity (CC50: >40 μg/mL). [14]

OW Salawu., *et al*. in 2011, synthesized Salicylaldehyde benzoyl acid hydrazone and Acetylaldehyde benzoyl acid hydrazone and their complexes with Metal [II] sulphates salts of Co, Ni, Cu, Pb, and Zn. The complexes were proposed to have the formulae [ML 1 L 2] SO 2-4. nH 2 O (where M= Ni(II), Co(II) , Zn(II) , Cu(II) , Pb(II) and L 1 = salicyladehyde benzoyl acid hydrazone and L 2 = acetylaldehyde benzoyl acid hydrazone , n = 2,6,7). Both the ligands and complexes show no significant activities with the microorganisms tested with probably due to few nitrogen atoms attached with the compounds. [15]

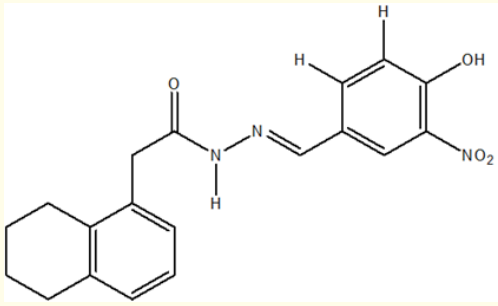


Figure 25: *(A10) 5,6,7,8-tetrahydronaphtalen acetic acid benzylidene hydrazide derivatives.*

Thiyagarajan Govindasami., *et al*. in 2011, reported hydrazone derivatives of vanillin are found to possess anti-bacterial activities. Based on higher bio-activity of hydrazones, new hydrazone derivatives were synthesized from Piperdine-4-carboxylicacid methyl ester. The compounds 1-pyrimidine-2-yl piperidine-4-carboxylicacid (4-hydroxy-3-methoxy benzylidine)-hydrazide, 1-pyrimidine-2-yl piperidine-4-carboxylicacid (3,4-dimethoxy benzylidine) hydrazide, 1-pyrimidine-2-yl piperidine-4-carboxylicacid (4-butoxy-3 -methoxy benzylidine)-hydrazide, 1-pyrimi- dine-2-yl piperidine-4-carboxylicacid (3-methoxy-4 (2-methoxy ethoxy) benzylidine)-hydrazide were synthesized. The synthesized hydrazone derivatives were further probed for anti-bacterial activities by paper disc diffusion method against *Pseudomonas aeruginosa* and *Staphylococcus aureus* bacterial strains. The anti-bacterial results showed that some of the compounds were active against both Gram-positive *S. aureus* and Gram-negative *P. aeruginosa bacteria*. The compounds 1-pyrimidine-2-yl piperidine-4-carboxylicacid (4-butoxy-3-methoxy benzylidine)-hydrazide and 1-pyrimi- dine-2-yl piperidine-4-carboxylicacid (3-methoxy-4 (2-methoxy ethoxy) benzylidine)-hydrazide showed good antibacterial activity against the test organ- isms and 1-pyrimidine-2-yl piperidine-4-carboxylicacid (3,4-dimethoxy benzylidine) hydrazide had moderate effective against *S. aureus* and less effective against *P. aeruginosa*.[16]

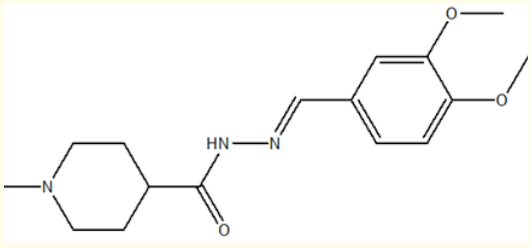


Figure 26: *1-Pyrimidin-2-yl-piperidine-4-carboxylic acid (4-butoxy-3-methoxy - benzylidene)- hydrazide.*

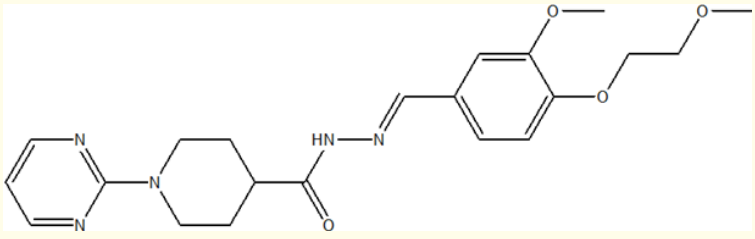


Figure 27: *1-Pyrimidin-2-yl-piperidine-4-carboxylic acid [3-methoxy-4-(2-methoxy-ethoxy)-benzylidene] hydrazide.*

Mahmoud MM Ramiz., *et al*. in 2011, synthesized number of new 2,5-disubstituted 1,3,4-thiadiazole and their S- or N-substituted derivatives as well as the corresponding sugar hydrazone derivatives and tested for their antimicrobial activity against *Bacillus subtilis* (Gram-positive), *Pseudomonas aeruginosa* (Gram-negative), and Streptomyces species (Actinomycetes). Where as fig 2.27 were the most active among the series of tested compounds against *Streptomyces* species with MIC values of 75 µg/Ml. [17]

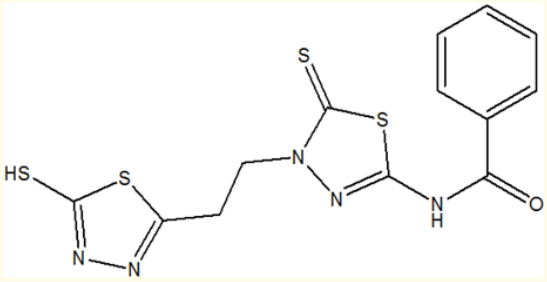


Figure 28: *N- (4-(2-(5-Mercapto-1,34-thiadiazol-2-yl)ethyl) -4,5-dihydro-1,3,4-thiadiazol-2-yl)benzamide.*

SAM Shedid., *et al*. in 2011, synthesized a new series of 3-chloro-6-methylbenzo [b]-thiophene-2-carbonylamino acid methyl ester, hydrazide and their corresponding hydrazone derivatives as potential antibacterial agents. The results were compared with the activity of that was found to be biologically inactive against all the tested bacteria. This study revealed that incorporation of 3-chloro-6- methylbenzo [b]-thiophene-2-carbonyl chloride with amino acid methyl ester and their corresponding hydrazide, dipeptide and hydrazone derivatives decreased or completely abolished the antibacterial activity of the synthesized derivatives. [18]

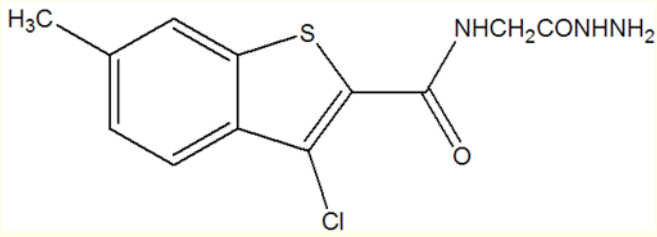


Figure 29: *(v) 3-chloro-6-methylbenzo[b]-thiophene-2-carbonylamino acid methylester, hydrazide*

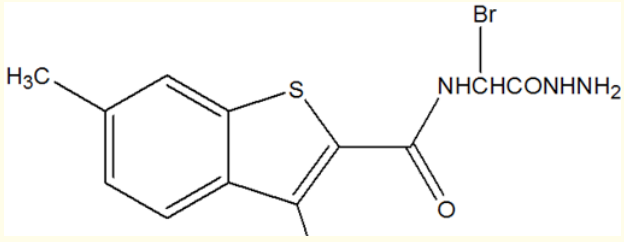


Figure 30: *(VIII) 3-chloro-6-methylbenzo-thiophene-2-carbonylamino acid methyl ester, hydrazide*

DC Dash., *et al*. in 2012, synthesized a series of complexes of the type [M2L2Cl2], where L= 2-(salicylidene acetone- 2'-imino) aminobenzoimidazole (HSAIAB) and 2-(salicylideneacetophenone- 2'- imino) amino benzimidazole (HSAPIAB), M= Cu(II), Co(II), Ni(II) and Zn(II). The results are in consistent with tridentate chelation of ligand with azomethine nitrogen, ring nitrogen and oxygen atom. The fungi toxicity of the ligands & their complexes against some fungal pathogen has been studied. [19]

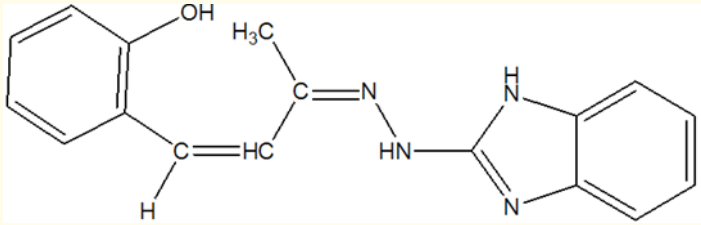


Figure 31: *2-(salicylideneacetophenone- 2'- imino) amino benzimidazole.*

Gadhawala zm., *et al*. in 2012, synthesized various oximes, phenyl hydrazones and 2, 4 dinitrophenyl hydrazones by reaction with different ketonic compounds. The structures of these compounds have been confirmed on the basis of spectral data. The antimicrobial activity of the prepared compounds was discussed and some of them are found to be active. Among these compound KIJ3 showed significant inhibiton. Compounds KIJ1 and KIJ 2 showed moderate activity. While the remaining compounds showed no activity against *E. coli* and *S. aureus* bacteria. [20]

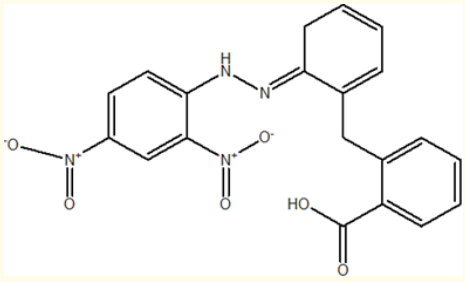


Figure 32 A: *(KIJ 3) 2, 4 dinitrophenyl hydrazones.*

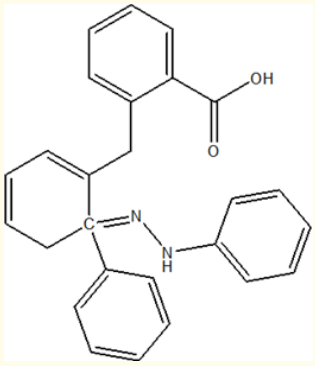


Figure 32 B: *(KIJ 3) oximes, phenyl hydrazones.*

Jian Wu., *et al*. in 2012, reported that Ralstoniasolanacearum, one of the most important bacterial diseases of plants, is a devastating, soilborne plant pathogen with a global distribution and an unusually wide host range. In order to discover new bioactive molecules and pesticides acting on tobacco bacterial wilt, we sought to combine the active structure of hydrazone and pyridine together to design and synthesize a series of novel hydrazone derivatives containing a pyridine moiety. This study suggests that the hydrazone derivatives containing a substituted pyridine ring could inhibit the growth of Ralstoniasolanacearum. [21] Maliki Reddy Dastagiri Reddy., *et al*. in 2013, synthesized, characterized and probed the antimicrobial activity of certain novel 3-methyl-5-oxo-4-(phenyl hydrazono)-4,5-dihydro-pyrazol-1-yl]-acetic acid N|-(4-substituted thiazol-2-yl)-hydrazides. The synthesized compounds were characterized by elemental analysis and IR, NMR and mass spectral data. The antimicrobial activity of novel compounds was probed by broth dilution method. These Compound XVe, XVf and XVg have shown better antibacterial activity than other compounds of the series. XVa, XVc, XVd and XVe have shown better antifungal activity than the other compounds of the series. All compounds were found to exhibit fair degree of antimicrobial activity. [22]

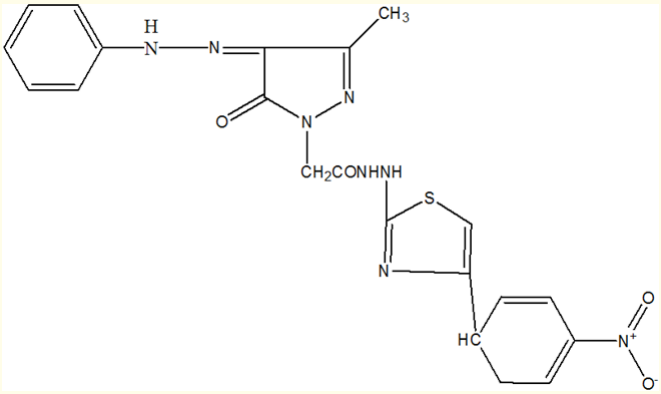


Figure 33: *(XVe)3-methyl-5-oxo-4-(phenyl hydrazono)-4,5-dihydro-pyrazol-1-yl]-acetic acid N|-(4-substituted thiazol-2-yl)-hydrazides.*

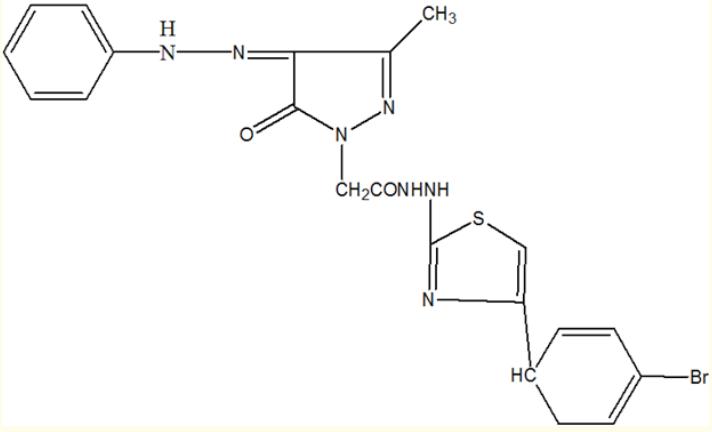


Figure 34: *(XVg) 3-methyl-5-oxo-4-(phenyl hydrazono)-4,5-dihydro-pyrazol-1-yl]-acetic acid N|-(4-substituted thiazol-2-yl)-hydrazides.*

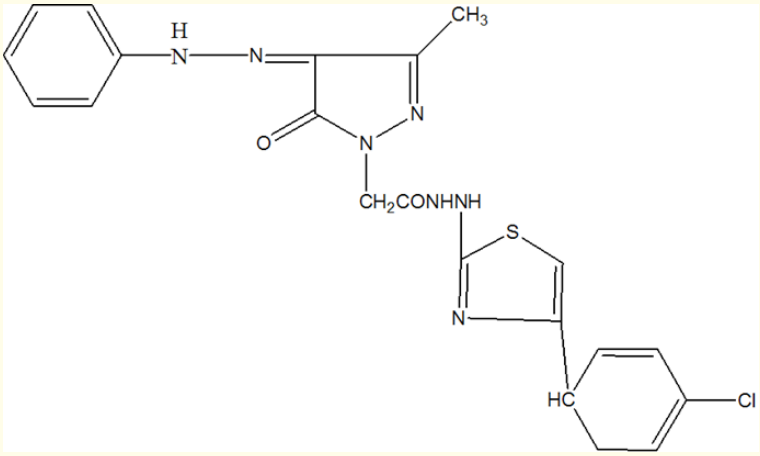


Figure 35: *(XVF) 3-methyl-5-oxo-4-(phenyl hydrazono)-4,5-dihydro-pyrazol-1-yl]-acetic acid N|-(4-substituted thiazol-2-yl)-hydrazides.*

RaminHajikhani., *et al*. In 2013, All Rapid and efficient solvent-free one-pot synthesis of dialkylamino alkyl -1- (4-bromobenzylidene) phosphonohydrazone derivatives by the condensation reaction of N, N-dialkylamino alkyl-phosphoro-hydrazides with pbromo-benzaldehyde using silica under microwave irradiation is described. The newly synthesized compounds are screened for results showed that some of these compounds were showed activity against all the tested bacteria. The synthesized compounds probed, compound 2c was found to exhibit excellent activity against all the tested bacteria. Biological evaluation of these derivatives may furnish some other important applications that could be useful for the searching of new antimicrobial molecules from synthesis methods. [23]

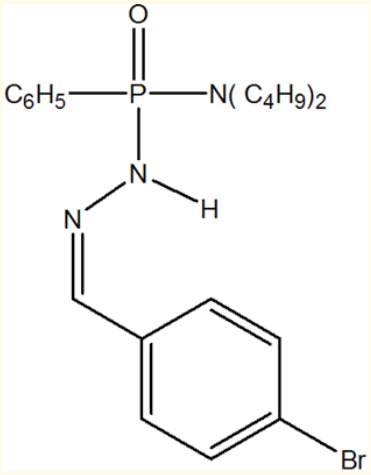


Figure 36: *(2c) dialkylamino alkyl-1-(4-bromobenzylidene) Phosphonohydrazone derivatives.*

IlknurBabahan., *et al*. in 2013, synthesized three novel hetero aromatic hydrazone derivatives having vic-dioxime groups (L^1H_2: 5-methyl-2-furfural hydrazoneglyoxime, L^2H_2: 3-acetylpyridine hydrazoneglyoxime and L^3H_2: 4-acetylpyridine hydrazoneglyoxime) and their Ni(II), Cu(II) and Co(II) complexes. The antimicrobial activities of compounds L_1H_2, L_2H_2, L_3H_2 and their Ni(II), Cu(II) and Co(II) complexes were probed using the disc diffusion method against 13 bacteria and 5 yeasts. The minimal inhibitory concentrations (MICs) against 3 bacteria and 3 yeasts were also determined. Among the test compounds attempted, L_1H_2,$[Co(L_1H)_2(H_2O)_2]$,

$[Ni(L_2H)_2]$, $[Cu(L_2H)_2]$, L_3H_2, $[Ni(L_3H)_2$ and $[Co(L_3H)_2(H_2O)_2]$ showed some activities against certain Gram-positive bacteria and some of the yeasts tested. [24]

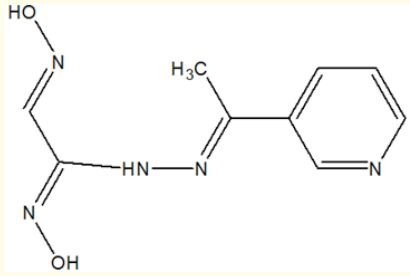


Figure 37 A: *(L^2H_2) 3-acetylpyridine hydrazoneglyoxime.*

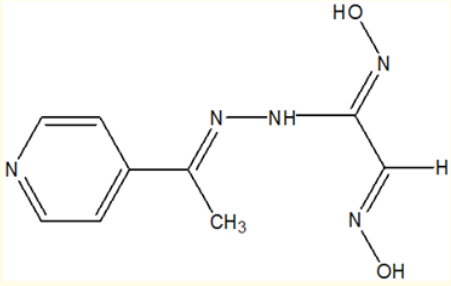


Figure 37 B: *(L^3H_2) 4-acetylpyridine hydrazoneglyoxime.*

Anti-inflammatory activity

Todeschini AR., *et al*. in 1998, reported the most important anti-inflammatory derivative 2-(2-formylfuryl) pyridylhydrazone presented a 79 % inhibition of pleurisy at a dose of 80.1 µmol/kg. Compound -(2-formylfuryl) pyridylhydrazone was able to complex Ca^{2+} in *in-vitro* experiments at 100 µM concentration indicating that these series of compounds can act as Ca^{2+} scavenger depending on the nature of the aryl moiety present at the imine subunit. [25]

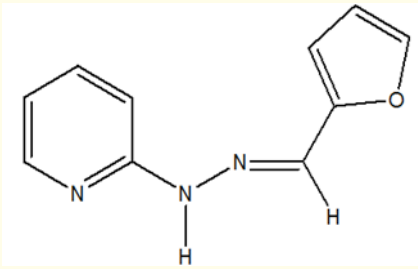


Figure 39: *2-(2-formylfuryl) pyridylhydrazone derivative.*

Lima PC., *et al*. in 2000, synthesized a new series of antinociceptive compounds that belong to the N-acylarylhydrazone class of natural safrole. [(4′-N,N Dimethylaminobenzylidene-3-(3′,4′-methylenedioxyphenyl) propionylhydrazine] was more potent than dipyrone and indomethacine, are used as standard antiinflammatory/antinociceptive drugs. [26]

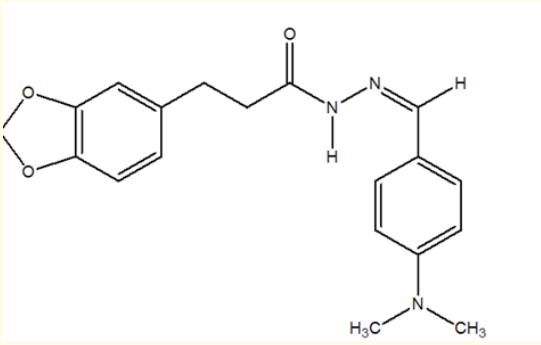


Figure 40: *(8) N-acylarylhydrazone.*

GokhanKelekçi., *et al*. in 2007, synthesized hydrazones containing 5-methyl-2-benzoxazoline. The analgesic effects of 2-[2-(5-methyl-2-benzoxazoline-3-yl)acetyl]-4-chloro- / 4-methyl benzylidene hydrazine 11c and 11d were exaggregated than those of morphine and aspirin. In addition, 2-[2-(5-methyl-2-benzoxazoline-3-yl)acetyl]-4- methoxy benzylidene hydrazine 11e at 200 mg/kg dose possessed the most antiinflammatory activity. [27]

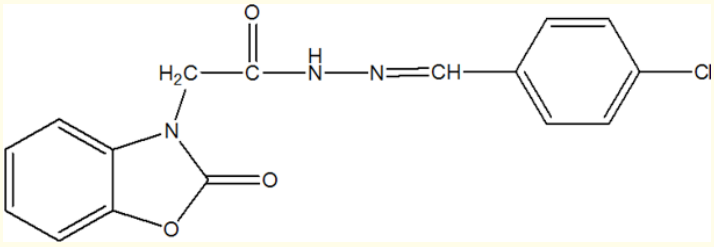


Figure 41: *(11c)2-[2-(5-methyl-2-benzoxazoline-3-yl)acetyl]-4-chloro-/4-methyl benzylidene hydrazine*

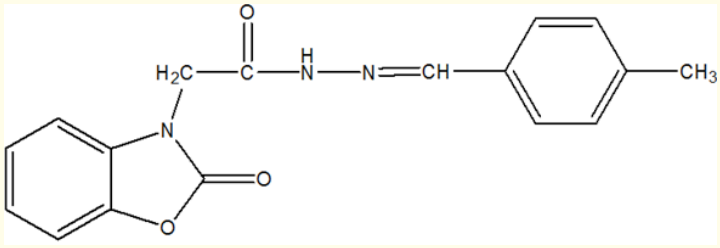


Figure 42: *(11d) 2-[2-(5-methyl-2-benzoxazoline-3-yl)acetyl]-4-chloro-/ 4-methyl benzylidene hydrazine.*

Duarte., *et al*. in 2007, described N′-(3,5-Di-tert-butyl-4-hydroxybenzylidene)-6-nitro-1,3-benzodioxole-5-carbohydrazine as a novel antiinflammatory compound. [28]

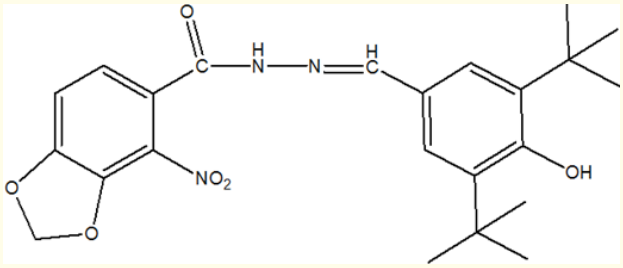


Figure 43: *N'-(3,5-Di-tert-butyl-4-hydroxybenzylidene)-6-nitro-1,3-benzodioxole-5- carbohydrazine.*

Arvind Kumar., *et al*. in 2009, synthesized a series of substituted Hydrazone and Quinoxaline derivatives have been synthesized by appropriate methods. All the compounds have been screened for Anti-inflammatory activity. We have reported the synthesis of ten new Hydrazones and Quinoxaline. It has been observed that the test compounds exhibited interesting anti-inflammatory activity, however with a degree of variation. Compound N'-(4-fluorobenzylidene)-3-hydroxy-7-methylquinoxaline-2-carbohydrazide, N'-(2-chlorobenzylidene)-3-hydroxy-7-methylquinoxaline-2-carbohydrazide, and 3-hydroxy-7-methyl-N'-(4-nitrobenzylidene)quinoxaline-2-carbohydrazide exhibited highly remarkable anti-inflammatory activity. [29]

WalfridoBispoJúnior., *et al*. in 2011, salicylaldehyde 2-chlorobenzoyl hydrazine, salicylaldehyde4-chlorobenzoyl hydrazone and their complexes $[Zn(LASSBio\text{-}466)H_2O]_2$ (1) and $[Zn(HLASSBio\text{-}1064)\ Cl]_2$ were probed in animal models of peripheral and central nociception, and acute inflammation. All studied compounds significantly inhibited acetic acid-induced writhing response. Upon coordination the antinociceptive activity was favored in the complex 1. H2LASSBio-466 inhibited only the first phase of the formalin test, while 1 was active in the second phase, like indomethacin, indicating its ability to inhibit nociception associated with the inflammatory response. Hence coordination to zinc (II) altered the pharmacological profile of H2LASSBio-466. H2LASSBio-1064 inhibited both phases but this effect was not improved by coordination. All compounds showed levels of inhibition of zymosan-induced peritonitis comparable or superior to indomethacin, indicating an expressive anti-inflammatory profile. [30]

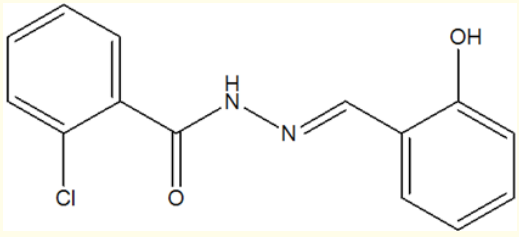


Figure 44: *Salicylaldehyde 2-chlorobenzoyl hydrazone.*

ZaferAsımKaplancikli., *et al*. in 2012, synthesized some hydrazone derivatives via the reaction of 3-cyclohexylpropionic acid hydrazide with various benzaldehydes..All synthesized compounds were probed for their anti-inflammatory effects and cytotoxicity in mammalian cells. Anti-inflammatory activity was determined by monitoring the effects of these compounds on cellular targets for inflammation. The appreciable inhibition of NF-κB activity in SW1353 cells was observed for compounds 2a, 2c and 2h with IC50 values of 6.9, 7.7 and 6.4 g/mL, respectively. This outcome confirms that methyl and chloro groups have an appreciable influence on the inhibition of NF-κB mediated transcription. Other compounds (2d, 2e, 2g, 2i) inhibited the NF-κB activity to a much lesser extent, and their IC50 values were in the range 10-14 g/mL. [31]

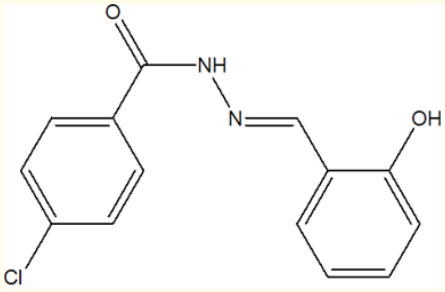


Figure 45: *Salicylaldehyde 4-chlorobenzoyl hydrazone.*

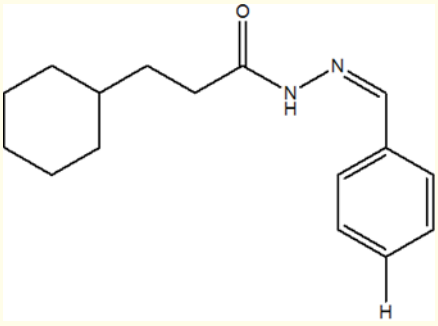


Figure 46 A: *(2a) hydrazone derivatives.*

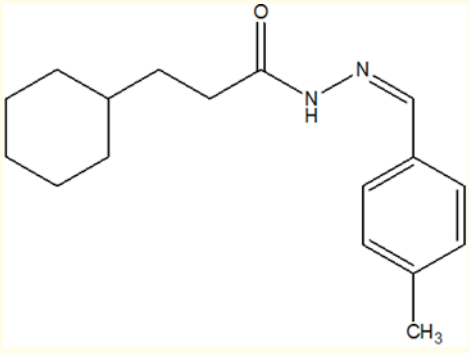


Figure 46 B: *(2c) hydrazone derivatives.*

Antimalarial activity

Walcourt A., *et al*. in 2004, reported aroylhydrazone chelator 2-hydroxy-1-naphthylaldehyde isonicotinoylhydrazone13 showed greater antimalarial agent activity than desferrioxamine against chloroquine-resistant and –sensitive parasites. [32]

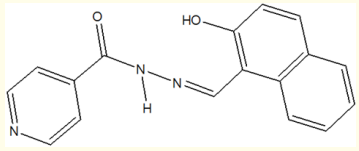


Figure 47: *(13) 2-hydroxy-1-naphthylaldehyde isonicotinoylhydrazone.*

Gemma S., *et al*. in 2006, synthesized a series of N1-arylidene-N2-quinolyl- 14 and N2-acrydinylhydrazones- 15 and tested for their antimalarial properties. The new synthesized compounds, including 14d-g and 15a-c showed an antiplasmodial activity against the chloroquine-sensitive D10 strain in the same range of chloroquine (CQ). Similarly, 14f and 14g displayed the same activity as CQ against chloroquinesensitive 3D-7 strain, while compound 15b was 10 times more potent than CQ. Two analogues 15b and 15c, were more active against W2 CQ-resistant than D10 CQ-sensitive strains. [34]

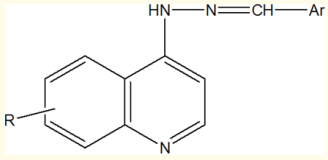


Figure 49: *N1-arylidene-N2-quinolyl- 14 and N2-acrydinylhydrazones.*

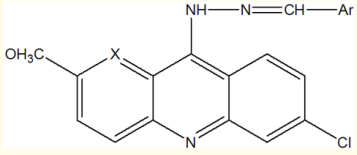


Figure 50: *(15a-c) N1-arylidene-N2-quinolyl- 14 and N2-acrydinylhydrazones.*

Bernardino A., *et al.* synthesized1-Substituted phenyl-N′-[(substitutedphenyl)methylene]-1H-pyrazole-4-carbohydrazides 16 and their leishmanicidal and cytotoxic effects were compared to the prototype drugs (ketoconazole, benznidazole, allopurinol and pentamidine) *in- vitro*. The 1H-pyrazole-4-carbohydrazide derivatives with X = Br, Y = NO2 and X = NO2, Y = Cl manifested the highest activity and they were more effective on promastigotes forms of *L. amazonensis* than on *L. chagasi* and *L. braziliensisspecies.* [35]

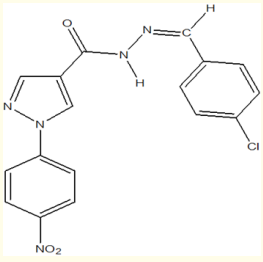


Figure 51: *(16) 1-Substituted phenyl-N′-[(substitutedphenyl)methylene]-1 H-pyrazole-4-carbohydrazides.*

Anti tumor activity

Rafat M Mohareb., *et al*. in 2010, reported that reaction of cyanoacetyl hydrazine (1) with the N-haloketones2a-2c in 1,4-dioxane afforded the hydrazidehydrazone derivatives 3a-3c. The latter products were used in a series of heterocyclization to give 1,3,4-oxadiazine, 1,2,4-triazine and pyrazole derivatives. Some of the synthesized products exhibted high inhibitory effect towards the three cell lines. All the tested compounds were able to inhibit the growth of the human tumor cell lines in a dose-dependent manner. The 1,3,4-oxadiazine derivative 4c, the 1,2,4-triazine derivative 11a and the pyrazole derivative 15c exhibited the highest inhibitory effect of the tested compounds, exhibiting an equivalent potency in all the three tumor cell lines. [36]

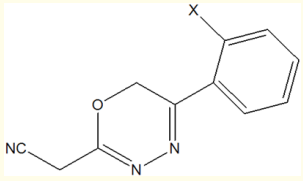


Figure 52: *(4C) hydrazide hydrazone derivatives.*

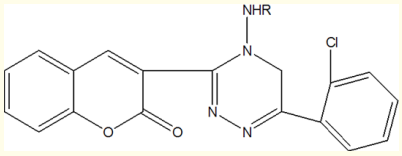


Figure 53: *(11 a) hydrazide hydrazone derivatives.*

NipawanPongprom., *et al*. in 2012, synthesizedazanaphthoquinoneannelatedpyrrolo-hydrazone derivatives as cytostatic compounds. The synthetic pathway was started from the commercially available 5-hydroxyisoquinoline by 3-steps reaction to obtain 1H-pyrrolo[3,2-g]isoquinoline-4,9-dione. N-Alkylation of nitrogen atom in pyrrole ring was carried out under basic conditions with different side chains to obtain mono-substituted azaphthoquinoneannelated pyrroles with 2 to 4-carbon side chains in moderate to good yields. The results suggests that the mono-substituted products with 2-carbon side chain (5b) exhibited a very good activity with IC50 value of 0.008 μM. The hydrazone6a manifested higher inhibitory activity with IC50 value of 0.282 μM compared to the mono-substituted derivative 5a. The side chains with cyclic amine are of interest for the further studies. [37]

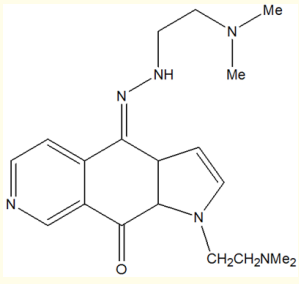


Figure 54: *(6a) aza naphthoquinone annelated pyrrolo hydrazone derivatives.*

Wagnatwahbawardakhan., *et al*. in 2013, reported that reaction of cyclopentanone with cyanoacetylhydrazine gave 2-cyano-2-cyclopentylideneacetohydrazide(1). Treatment of compound with elemental sulphur in the presence of triethylamine afforded 2-amino-5,6 dihydro--4H-cyclopenta[b]thiophene-3-carbohydrazide, which in-turn formed the corresponding intermediate diazonium salt. The latter was coupled with either ethyl cyanoacetateor ethyl acetoacetate to form 2-cyano-2-(3-(hydrazinecarbonyl)-5,6-dihydro-4H-cyclopenta[b]thiophen-2-yl)hydrazono) acetate and ethyl 2-(2-(3-(hydrazinecarbonyl)-5,6-dihydro-4H-cyclopenta[b]thiophen-2-yl) hydrazono)-3-oxobutanoate, respectively. On the other hand, the reaction ofcompound1 with either benzaldehyde or acetophenone afforded N'-benzylidene-2-cyano-2-cyclopentylideneacetohydrazide and 2-cyano-2-(2-cyclopentylidene)phenylacetohydrazide, respectively. Moreover, compound 1 was used to synthesize 2-cyano-2-cyclopentylidene- N'-(arylthiazol-2(3H)-ylidene) aceto-hydrazides (6a,b), 2-(2-benzylidenecyclopentylidene)-2-cyanoacetohydrazide, 2-amino-N'-benzylidene-5,6-dihydro-4H- -cyclopenta[b] thiophene-3-carbohydrazide, 2-cyano- -2-(2-(2-phenylhydrazono)cyclopentylidene) acetohydrazide, N'-(1-chloropropan-2-ylidene)-2-cyano-2-cyclopentylideneacetohydrazide, and 2-cyclopentylidene-3- -(3,5-disubstituted-1H-pyrazol-1-yl)-3-oxopropanenitriles through its reaction with the respective reagents. The most potent compoundswere 2-cyano-2-cyclophentylideneacetohydrazido-N-(4-cyano-3-phenyl-4-phenyl-thiazol--2-ylideno) hydrazone (6b)and 2-cyano-2-(2-phenylhydrazono)-cyclopentylideneacetohydrazide with inhibitory effects higher than that of the reference doxorubicin. [38]

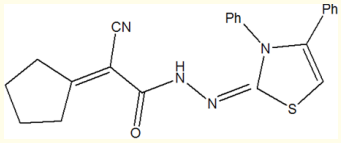


Figure 55: *2-cyano-2-cyclophentylideneacetohydrazido-N- (4-cyano-3-phenyl-4-phenyl-thiazol--2-ylideno) hydrazone.*

Kh M Abu-Zied., *et al*. in 2013, reported that 2-Methylene (aryl) hydrazinobenzimidazole derivatives 2a-e were obtained when compound 1 refluxed with each of p-methoxybenzadehyde (Badr., et al. 1988), p-fluorobenzaldehyde, pnitrobenzaldehyde1, acetaldehyde and formaldehyde in presence of ethanol and catalytic amount ofpiperidine. Also, the triazole derivatives 3a–e were obtained by stirring compounds 2a-e with mixture ofbromine, glacial acetic acid and anhydrous sodium acetate. The most effective compound was found to be compound 6b having the aldopentose xylose linked to the 2- position of benzimidazole nucleus through hydrazine nitrogen. Compounds 2a, 2d, 2e, 3d, 5, 6a, 6b, 7a, 7b, 8a and 8b have high antitumor activity than starting compound 1. The open structures 2a, 2b, 2c, 2dand 2ehave high anti tumor activity than there closed structure 3a,3b,3c,3d and 3e respectively. Compounds 2d and 2c which have aliphatic chainmoiety also have high antitumor activity than those which have aromatic rings (2a, 2b and 2c) either in open or closed form. Compound4 have acetyl thiophene linked to the 2-position of benzimidazole is less active than the other compounds may be Selement reduced an anti-tumor potency, or S is not working for increased activity. Derivatives which have pentose sugar moiety in its N-nucleoside structure (6b or 7b and 8b) has high antitumor activity than those which have hexose sugar moiety (5, 6a.7a and 8a). [39]

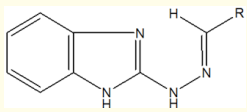


Figure 56 A: *(6b) triazole derivatives.*

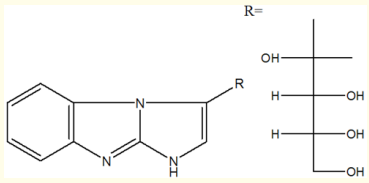


Figure 56 B: *(8b) triazole derivatives.*

Antioxidant

AG Yadav., *et al*. in 2012 reported that vilsmeier –Haack reaction provide a route involve formylation of activated aromatic and hetero-aromatic systems by ring formation. Recently pyrazole have been synthesized from various substituted hydrazones using Vilsmeier- Haack reaction. Our interest in synthesizing pyrazolylbenzothiazole from 2-amino benzothiazole, refluxed with hydrazine hydrate followed by condensation with substituted acetophenone to form hydrazones derivatives. The synthesized compounds were investigated for antioxidant and antimicrobial activities. The antioxidant activities of compounds were tested by measuring their capacity to scavenge DPPH radical. The most active compound was proved to be 9i shows good antioxidant activity. Compounds 1a, 5e, 6f and 9i shows IC50 value 18% µg/mL, 17% µg/mL and 9% µg/mL respectively. Among them 9i was most active compound shows IC50 value 9% µg/mL. The rest of the compounds possess moderate antioxidant activity. [40]

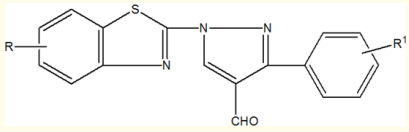


Figure 57: *Formylated Pyrazolyl Benzothiazole.*

Antiplatelet aggregation activity

Kamaleddin Haj., *et al*. in 2013, suggested that the structural features of a group of known potent inhibitors of human platelet aggregation containing hydrazone structural backbone, a series of novel hydrazone derivatives of 2-hydrazinyl-1,3,4- thiadiazole were synthesized using a one-pot process and tested for their inhibitory activity against platelet aggregation induced by arachidonic acid and ADP. Among the derivatives, compounds 3l, 3o and 3p exhibited the highest antiplatelet aggregation activity. The derivatives were also screened for their potential anti-mycobacterial activity and compounds 3g, 3k, 3p and 3q were among the most active compounds. [41]

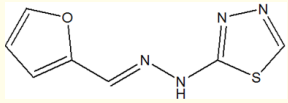


Figure 58: *(3o) hydrazone derivatives of 2-hydrazinyl-1,3,4- thiadiazole.*

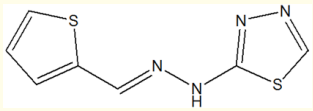


Figure 59: *(3p) hydrazone derivatives of 2-hydrazinyl-1,3,4- thiadiazole.*

Antidepressant activity

RM Mohareb., *et al*. in 2010 reported the reaction of cyanoacetylhydrazine with ω-bromo(4-methoxyacetophenone) yeild the hydrazidehydrazone derivative. Compound hydrazidehydrazone derivative reacted with either potassium cyanide or potassium thiocyanide to give the cyanide or thiocyanide derivatives 4a or 4b respectively. The reaction of compound hydrazidehydrazone derivative with either hydrazine hydrate or phenylhydrazineyeild the hydrazine derivatives. The latter compounds underwent a series of heterocyclization. when reacts with different reagents to give 1,3,4-triazine and pyridine derivatives. The antidepressant, sedative and analgesic activities of the newly synthesized products were probed. Some compounds showed mild non-significant antidepressant activity at high doses and were active, compared with the control group, using saline as negative control. The rest of compounds failed to display antidepressant properties in the swimming test. [42]

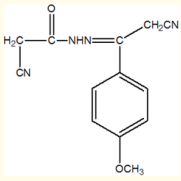


Figure 60: *A (4a) hydrazidehydrazone.*

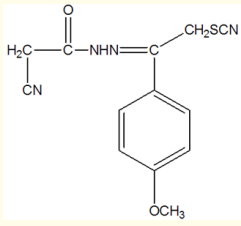


Figure 61: *B (4b) hydrazidehydrazone.*

Conclusion

Hydrazone derivatives exhibit versatile pharmacological activity because its contain essential pharmacophore. This review have been covered all latest update about hydrazone derivative which wide range of derivatives had shown potent biological effects against variety of disease on invivo animal models. The revealed data showed the essential pharmacological active feature for the development of new drug.Some of the synthesized derivatives exhibited high inhibitory effect towards the cell lines, whether most of compounds showed the potent antimicrobial activities. We observed that Hydrazone derivatives containing derivatives had potent new light to medicinal chemist or scientist to discover new drug. Because of its high efficacy and lower side effect, this ring may be useful tool of new light for modern therapy.

Conflict of interests: The authors declare that they have no conflict of interests.

Acknowledgements

The authors would like to express their gratitude to Babasaheb Bhimrao Ambedkar University (a Central University) Lucknow for providing the research data facilities.

Bibliography

1. Nataliya P., *et al*. "Synthesis and properties of hydrazones bearing amide, thioamide and amidine functions". *ARKIVOC* (2010): 275-332.
2. Sridhar SK., *et al*. "Anticonvulsant activity of hydrazones, Schiff and Mannich bases of isatin derivatives". *European Journal of Pharmaceutical Sciences* 16.3 (2002): 129-132.
3. Suresh kumar., *et al*. "synthesis and in vivo anticonvulsant evaluation of 2-chloroquinolinyl hydrazone derivatives". *ActaPoloniae Pharmaceutica* 67.5 (2010): 567-573.
4. Jodongunjan and diwakerawadh. "syntheses and biological evaluation of some phenyl acetic acidnhydrozonederivativs". *International research journal of pharmacy* 2.11 (2011): 110-112 .
5. SN Pandeya., *et al*. "Sythesis and Anticonvulsant Activity of Pyrimidine Hydrazones". *Journal of Scientific Research in Pharmacy* 1.3 (2012): 92-97.
6. Abdul Rauf., *et al*. "Synthesis, Characterization and Antimicrobial Activity of Long-Chain Hydrazones". *Acta Chimica Slovenica* 55.2 (2008): 448–452.
7. N jayalakshmi and S Nanjundan. "synthesis, characterization and pharmacological studies of selenadiazole and hydrazone derivatives of 2, 6–diphenyl–4–piperidone". *International Journal of Chemical Sciences* 6.3 (2008): 1177-1188.
8. Tijen Onkol., *et al*. "microwave synthesis and antimicrobial evaluation of 5-chloro-2(3h)-benzoxazolinone-3- acetyl-2-(P-substituted benzal) hydrazone and 5- chloro-2(3h)-benzoxazolinone-3-acetyl-2-(P-substituted acetophenone) hydrazone derivatives". *Turk J. Pharm. Sci*. 5.3 (2008): 155-166.
9. SA khan., *et al*. "synthesis of hydrazones derivatives of quinoxalinone prospective antimicrobial and antiinflammatory agents". *ActaPoloniaePharmaceutica* 66.2 (2009): 169-172.
10. Rajput AP and Rajput SS. "Synthesis of benzaldehyde substituted phenyl carbonyl hydrazones and their formylation using Vilsmeier-Haack reaction". *International Journal of Pharm Tech Research* 1.4(2009): 1605-1611.
11. Toliwal SD., *et al*. "Synthesis and Biological Evaluation of Hydrazones from Nontraditional oils". *Journal of Applied Chemical Research* 10 (2009): 64-72.
12. Mosselhi., *et al*. "Synthesis, structure and antimicrobial evaluation of new derivatives of theophylline sugar hydrazones". *ARKIVOC* (2009): 53.
13. SrivsatavaRitu., *et al.* "Synthesis of some new Acid hydrazones and their activity against Mycobacterium". *International Journal of Chemical Research* 2.1 (2010): 18-19.
14. Vijay V Dabholkar and Sagir Ahmed Sabir Ali Syed. "synthesis of novel oxazoles and their hydrazones". *Rasayan journal of chemistry* 3.4 (2010): 761- 765.
15. Ahmet Özdemir., *et al*. "Synthesis of some novel hydrazone derivatives and evaluation of their antituberculosis activity". *Marmara Pharmaceutical Journal* 14.2 (2010): 79-83.
16. OW Salawu., *et al*. "Studies on some metal (II) sulphates salts chelates of salicylaldehyde benzoyl acid hydrazone and acetylaldehyde benzoyl acid hydrazone". *Der ChemicaSinica* 2.2 (2011): 25-34.
17. WalfridoBispoJúnior., *et al*. "Analgesic and Anti-Inflammatory Activities of Salicylaldehyde 2-Chlorobenzoyl Hydrazone (H2LASSBio-466), Salicylaldehyde 4-Chlorobenzoyl Hydrazone (H2LASSBio-1064) and Their Zinc(II) Complexes". *Molecules* 16.8 (2011): 6902-6915.

18. ThiyagarajanGovindasami., *et al*. "Synthesis Characterization and Antibacterial Activity of Biologically Important Vanillin Related Hydrazone Derivatives". *International Journal of Organic Chemistry* 1.3 (2011): 71-77.
19. Mahmoud MM Ramiz and Adel AH Abdel-Rahman. "Antimicrobial Activity of Newly Synthesized 2,5-Disubstituted 1,3,4-Thiadiaozle Derivatives". *Bulletin of the Korean Chemical Society* 32.12 (2011):4227
20. D. C. Dasha, A. Mahapatraa, U. K. Mishraa and R. K. Mohapatrab. 2012. Synthesis and characterization of transition metal complexes with benzimidazolyl-2-hydrazones of salicylidene acetone and salicylideneacetophenone, *Journal of Chemical and Pharmaceutical Research*, 2012, 4(1) pp. 279-285.
21. ZM Gadhawala., *et al*. "Synthesis and Biological evaluation of some new oxime, phenyl hydrazone and 2, 4 dinitro phenyl hydrazone derivatives of ketones". *Ultra Chemistry* 8.2 (2012): 269-272.
22. Jian Wu., *et al*. "Synthesis and antibacterial activity against ralstoniasolanacearum for novel hydrazone derivatives containing a pyridine moiety". *Chemistry Central Journal* 6.28 (2012): 4-5.
23. SAM Shedid., *et al*. "Synthesis and antibacterial activity of some new amino acid derivatives of 3-chloro-6-methylbenzo[b] thiophene-2-carboxylic acid". *Journal of Chemical and Pharmaceutical Research* 3.1(2011): 388-394.
24. Maliki Reddy Dastagiri Reddy., *et al*. "Synthesis, Characterization and Antimicrobial Activity of Certain Novel Aryl Hydrazone Pyrazoline-5-Ones Containing Thiazole Moiety". *Advanced Pharmaceutical Bulletin* 3.1 (2013): 153-159.
25. RaminHajikhani., *et al*. "Microwave Assisted Efficient One-pot Synthesis,Characterization of Organophosphorus Based Hydrazone Derivatives under Solvent-FreeConditions and Their Antimicrobial Activity Middle-East". *Journal of Scientific Research* 13.9 (2013): 1186-1189.
26. Ilknur Babahan., *et al*. "Synthesis, characterisation and antimicrobial activities of vicdioxime derivatives containing heteroaromatichydrazone groups and their metal complexes". *Maejo International Journal of Science and Technology* 7.1 (2013): 26-41.
27. Todeschini AR., *et al*. "Synthesis and evaluation of analgesic, antiinflammatory and antiplatelet properties of new 2-pyridylarylhydrazone derivatives". *European Journal of Medicinal Chemistry* 33.3 (1998): 189-199.
28. Lima PC., *et al*. "Synthesis and analgesic activity of novel N-acylhydrazones and isosters, derived from natural safrole". *European Journal of Medicinal Chemistry* 35.2 (2000): 187-203.
29. SalgınGokşen U., *et al*. "1-Acylthiosemicarbazides, 1,2,4-triazole-5(4H)-thiones, 1,3,4-thiadiazoles andhydrazones containing 5-methyl-2-benzoxazolinones: Synthesis, analgesic-anti-inflammatory and antimicrobial activities". *Bioorganic and Medicinal Chemistry* 15.17 (2007): 5738-5751.
30. Duarte CD., *et al*. "Synthesis, pharmacologicalevaluation and electrochemical studies of novel 6-nitro-3,4-methylenedioxyphenyl Nacylhydrazone derivatives : Discovery of LASSBio-881, a new ligand of cannabinoid receptors". *Bioorganic and Medicinal Chemistry* 15.6 (2007): 2421-2433.
31. Arvind Kumar., *et al*. "Synthesis Antiinflammatory and Antimicrobial Activities of New Hydrazone and Quinoxaline derivatives". *International Journal of ChemTech Research* 1.4 (2009): 1177-1181.
32. ZaferAsımKaplancikli., *et al*. "Synthesis and Biological Evaluation of Some Hydrazone Derivatives as Anti-inflammatory Agents". *Letters in Drug Design & Discovery* 9 (2012): 310-315.
33. Walcourt, A. Loyevsky, M. Lovejoy, D.B. Gordeuk, V.R. Richardson, D.R., 2004. Novel Aroylhydrazone and thiosemicarbazone iron chelators with anti-malarial activity against chloroquine-resistant and -sensitive parasites., *Int. J. Biochem. Cell Biol*. 36, pp. 401-407.
34. Gemma S., et al. "Synthesis of N1-arylidene-N2-quinolyl- and N2-acrydinylhydrazones as potent antimalarial agents active against CQ-resistant P. Falciparum strains". *Bioorganic & Medicinal Chemistry Letters* 16.20 (2006): 5384-5388.
35. Bernardino Am., *et al*. "Synthesis and leishmanicidal activities of 1-(4-X-phenyl)-N′-[(4-Yphenyl)methylene]-1H-pyrazole-4-carbohydrazides". *European Journal of Medicinal Chemistry* 41.1 (2006): 80-87.
36. Rafat M. *et al*. "Hydrazide-Hydrazones in the Synthesis of 1,3,4-Oxadiazine, 1,2,4-Triazine and Pyrazole Derivatives with Antitumor Activities". *The Open Organic Chemistry Journal* 4 (2010): 8-14.
37. NipawanPongprom and PornpanPungpo. Synthesis and Cytotoxic Activities of AzanaphthoquinoneAnnelatedPyrroloHydrazone Derivatives KKU Res. J. 17(2) pp. 195-202.

38. WagnatWahbaWardakhan., *et al*. "Synthesis and anti-tumor evaluation of novel hydrazide and hydrazide-hydrazone derivatives". *Acta Pharmaceutica* 63.1 (2013): 45–57.
39. Kh M Abu-Zied., *et al*. "Synthesis of Novel BenzimidazoleHydrazone Derivatives and Its C-Nucleosides with Antitumor Activity". *Journal of Applied Sciences Research* 9.1 (2013): 852-859.
40. AG Yadav., *et al*. "anti-oxidant and anti-microbial activities of pyrazolyl-benzothiazole derivatives using vilsmeier-haack reaction". *Rasayan journal of chemistry* 5.1 (2012): 117-120.
41. Haj Mohammad Ebrahim Tehrani K., *et al*. "One Pot Synthesis and Biological Activity Evaluation of Novel Schiff Bases Derived from 2-Hydrazinyl-1,3,4-thiadiazole". *Chemical and Pharmaceutical Bulletin* 61.2 (2013): 160–166.
42. RM Mohareb., *et al*. "Synthesis of hydrazidehydrazone derivatives and their evaluation of antidepressant, sedative and analgesic agents". *Journal of Pharmaceutical Sciences and Research* 2.4 (2010): 185-196.

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