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Review Article

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Schiff's bases and amides of selected five membered heterocyclic compounds: A review

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ABSTRACT

Among the diazole derivatives, thiazoles, imidazoles and pyrazoles are common scaffolds in highly significant biomolecules. These moieties and their derivatives have long been used as precursors for the synthesis of biologically active molecules since they possess wide spectrum of activity. This review highlights vast number of potential structures and potential therapeutic uses of only on those moieties containing five-membered heterocyclic such as imidazoles, thiazoles and Pyrazoles and their substitutes.

Keywords: Schiff's base, Amides, Thiazole, anti-inflammatory activity, Antimicrobial activity.

INTRODUCTION

Schiff bases and amides derived from various heterocyclic compounds displayed broad range of biological activitiessuch as anticancer, antiviral, antimicrobial, anticonvulsant, antidepressant, angiotension-II receptor antagonist, anti-inflammatory and anti-glycation activity. So far, modifications of the Schiff bases have proven highly effective with improved potency and lesser toxicity.

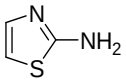
Five-member nitrogen-containing heterocyclic occurs in a diversity of natural products and drugs and is of great importance in a wide variety of applications. Aromatic nitrogen containing five-member heterocycles include pyrroles, pyrazoles, imidazoles etc. Additionally, aromatic nitrogen and sulphur heterocycles may contain another heteroatom, such as the sulfur in isothiazoles and thiazoles.

Thiazole as therapeutic Potential:
Thiazole, or 1, 3-thiazole, is a heterocyclic compound that contains both sulfur and nitrogen; the term 'thiazole' also refers to a large family of derivatives. Thiazole itself is a pale yellow liquid with a pyridine-like odor and the molecular formula C_3H_3NS [1]. The thiazole ring is notable as a component of the vitamin thiamine (B_1).

2-Aminothiazole is a heterocyclic amine with odor similar to pyridine, soluble in water, alcohol and ether. It is a beginning point for synthesis of many compounds including sulfur drugs, biocides, fungicides, dyes and chemical reaction accelerators. 2-Aminothiazole can be used as a thyroid inhibitor in the treatment of hyperthyroidism and it has antibacterial activity. Also used as the acid tartrate. Recent studies using prion-infected neuroblastoma cell lines have suggested that aminothiazole may be used as a therapeutic drug for prion diseases [2]. Thiazole derivatives have also been found to possess many pharmacological properties and are widely implicated in biochemical processes. Members of this class of thiazoles are known to possess antibacterial activity against both gram-positive and gram-negative bacteria. E.g. Cefdinir, a semi-synthetic third generation cephalosporin shows excellent activity against *Staphylococcus* species [3]. The HIV-1 protease inhibitor ritonavir (Norvir) consists of two differently

substituted thiazole rings, which are introduced at the later stages in the synthesis of this peptidomimetic antiviral compound [4]. The dopamine D2-agonist pramipexole (Mirapex) consists of a fused bicyclic tetrahydro-benzothiazole motif [5]. Famotidine (Pepcidine) is an H2-receptor antagonist similar to cimetidine which inhibits many isoenzymes of the hepatic CYP450 system [6].

Thiazole



2-Amino-thiazole

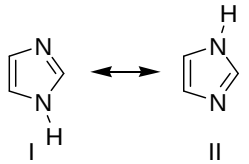
Pyrazole as therapeutic Potential:

Pyrazole refers to the class of simple aromatic ring organic compounds of the heterocyclic series characterized by a 5-membered ring structure composed of three carbon atoms and two nitrogen atoms in adjacent positions. Being so composed and having pharmacological effects on humans, they are classified as alkaloids, although they are rare in nature. In 1959, the first natural pyrazole, 1-pyrazolyl alanine, was isolated from seeds of watermelons. Pyrazole derivatives have a long history of application in agro- chemicals and pharmaceutical industry as herbicides and active pharmaceuticals and pharmacological activities like antimicrobial, anticancer, ACE inhibitory, antiviral as well as anti-inflammatory activities [7].

Pyrazole

Imidazoles as therapeutic Potential:

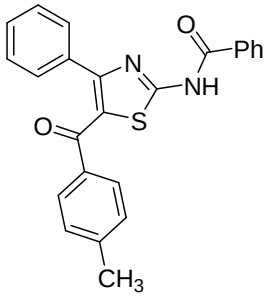
Among the diazole derivatives, imidazoles are common scaffolds in highly significant biomolecules, including biotin, the essential amino acid histidine, histamine, purines, the pilocarpine alkaloids [8,9]and other alkaloids, which have been shown to exhibit interesting biological activity such as antimicrobial, anticryptococcal, inhibition of nitric oxide synthase, and cytotoxic activity [10]. Members of this class of diazoles are known to possess NO synthase inhibition [11], antibiotic [12], antifungal [13], and antiulcerative activities [14] and include compounds, which are inhibitors of 5-lipoxygenase [15] and substances with CB1 receptor [16], VEGF receptor I and II [17], and neuropeptide Y antagonistic activities [18]. Cerreto, et al [19] reported, the imidazole-containing analogue was used some time ago for its inhibition effect on Candida growth.



Resonance structures of Imidazole

Amides of Selected Five membered heterocyclic compounds:

Several studies have been reported on the amides containing five membered heterocyclic compounds such as thiazole and pyrazole. Scheiff, A. B. *et al,* have reported a series of 18, 2-amino-5-benzoyl-4-phenyl-1,3-thiazole derivatives and pharmacologically evaluated at the AdoR subtypes A1, A2A, A2B and A3.The most potent and selective AdoA1R antagonist identified in this study was 2-benzoylamino- 5-p-methylbenzoyl-4-phenylthiazole. This compound may serve as a new lead structure for the development of second-generation, non-xanthine-based AdoA1R antagonists, which are structurally unrelated to adenine [20].



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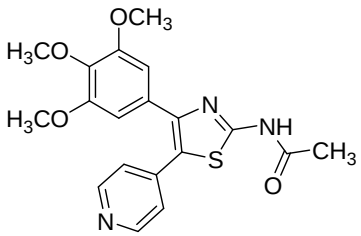
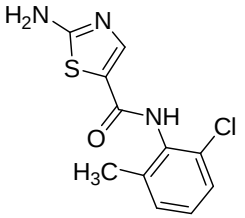


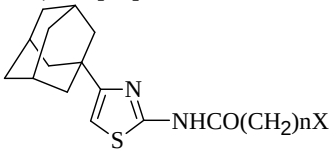
(2)

Bang-Chi, Chen *et al,* have reporteda new and efficient method for the synthesis of 2-aminothiazole-5-carboxamide. The new method involved a chemoselective α-bromination of β-ethoxyacrylamides followed by a one-pot treatment with thiourea to give the desired 2-Aminothiazole-5-carboxylamide in an excellent yield [21].



(**3**)

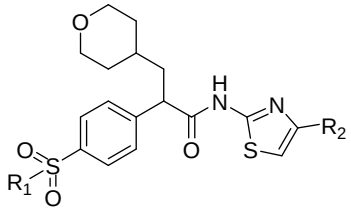
Kouatly, O. *et al*. have synthesized a series of adamantane derivatives of thiazolyl-N-substituted amides in a three-step reaction and tested for anti-inflammatory activity as well as lipoxygenase and cycloxygenase inhibitory actions. Theoretical calculation of their lipophilicity, as C log P was performed. The effect of the synthesized compounds on inflammation, using the carrageenin-induced mouse paw oedema model was studied and compared to indomethacin. Comparison of the in vivo and in vitro results leads to the conclusion that most compounds of this series may be involved in other mechanisms of inflammation, too [22].



(**4**)

Where n = 1, 2. X= N (CH3)2, Pyrrolidinyl, Piperidinyl, Morpholinyl, Ph-piperazinyl, Me-piperazinyl.

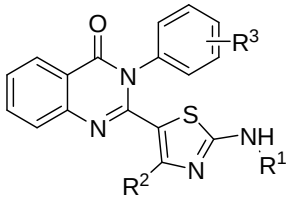
Fuying Li *et al*, have designed a series of N-thiazole substituted arylacetamides on the basis of metabolic mechanism of the aminothiazole fragment as glucokinase (GK) activators for the treatment of type 2 diabetes. Instead of introducing a substituent to block the metabolic sensitive C-5 position on the thiazole cores directly, a wide variety of C-4 or both C-4 and C-5 substitutions were explored. Compound R-9k bearing an iso-propyl group as the C-4 substituent was found possessing the highest GK activation potency with an EC50 of 0.026 lM. This compound significantly increased both glucose uptake and glycogen synthesis in rat primary cultured hepatocytes. Moreover, single oral administration of compound R-9k exerted significant reduction of blood glucose levels in both ICR and ob/ob mice. These promising results indicated that compound R-9k is a potent orally active GK activator and is warranted for further investigation as a new antidiabetic treatment [23].



(**5**)

Where R_1= Me, R_2= H, Et, iPr, iBu, tBu,

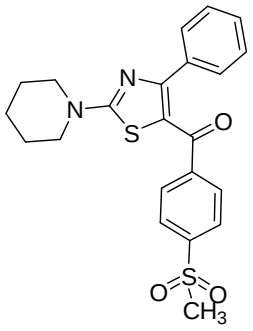
Giri, R. S. *et al*, designed and synthesized a series of 2-(2, 4-disubstituted-thiazole-5-yl)-3-aryl-3H quinazoline-4-one derivatives. Synthesized molecules were further evaluated for their inhibitory activity towards transcription factors NF-kB and AP-1 mediated transcriptional activation in a cell line based in vitro assay as well as for their anti-inflammatory activity in in-vivo model of acute inflammation. This series provides us with selective and dual inhibitors of NF-kB and AP-1 mediated transcriptional activation which also exhibit significant efficacy in in vivo model of inflammation. Two of the compounds 9m and 9o turned out to be the most promising dual inhibitors of NF-kB and AP-1 mediated transcriptional activation with an IC50 of 3.3 mM for both. 9n (IC50¼ 5.5 mM) and 9p (IC50 ¼ 5.5 mM) emerged as selective inhibitors of NF-kB mediated transcriptional activation and 9c (IC50¼ 5.5 mM) and 9d (IC50¼ 5.5 mM) were found to be more selective inhibitor of AP-1 mediated transcriptional activity. Though the relationship between the activities shown by these compounds in in-vivo and in-vitro model is still to be established, these results suggest the suitability of the designed molecular framework as a potential anti-inflammatory molecular framework which also exhibits the inhibitory activity towards NF-kB and AP-1 mediated transcriptional activation [24].



(6)

Where R^1 = -CH_3, -Ph, p-Cl-Ph, R^2 =-CH_3, -Ph, R^3 = H, -CH3, -OCH_3, -Cl, -$COCH_3$

Franklin, P.X.*et al*, synthesized and screened Substituted thiazoles with different structural features for their anti-inflammatory activity in acute carrageenin induced rat paw edema model and chronic formalin induced rat paw edema model. The compounds showed 83, 30, 63, 69 and 73% protection, respectively, in acute carrageenin induced rat paw edema model. In 5-day chronic formalin induced rat paw edema model on the fifth day 1 and 5 gave 66 and 41% protection. Both studies were carried out at a dose of 100 mg/kg body weight. The activity was compared with that of Ibuprofen, Rofecoxib, and Dexamethasone both in acute and chronic anti-inflammatory models. Compound without COX-1 and COX-2 inhibitory activity showed good activity profile almost mimicking the gold standard Dexamethasone in terms of efficacy. A 7-day study in rats at dose of 100 mg/kg showed that this compound does not have any ulcerogenic activity and toxicity. 2, 4-Diaminothiazoles with an aliphatic oxime esters attached via a ketone bridge to the 5th position of thiazole was identified as a novel scaffold for designing anti-inflammatory agents [25].



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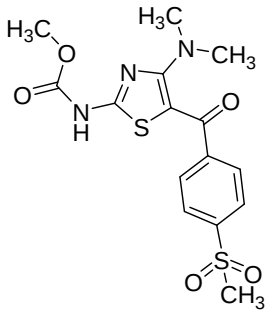

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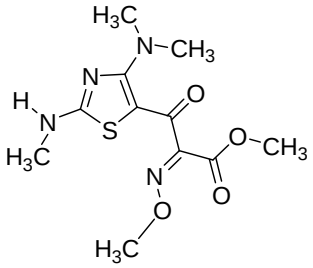

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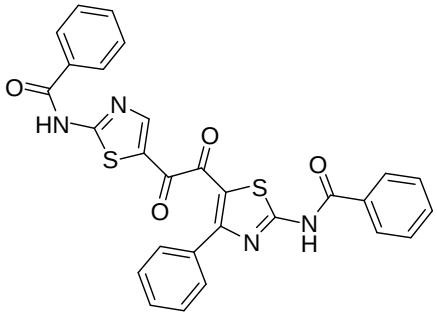

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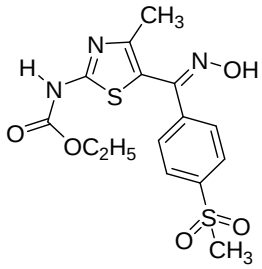
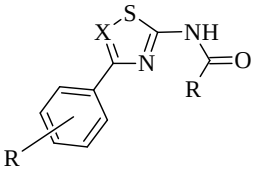


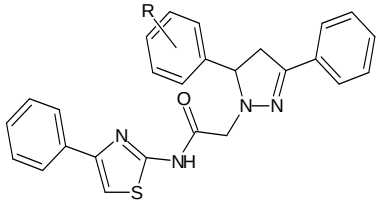
(11)

Kwan-Young Jung *et al*. have synthesized and evaluated 4-(4-Methoxyphenyl)-2-aminothiazole and 3-(4-methoxyphenyl)-5-aminothiadiazole derivatives as selective antagonists for human adenosine A3 receptors. A methoxy group in the 4-position of the phenyl ring and N-acetyl or propionyl substitutions of the aminothiazole and aminothiadiazole templates displayed great increases of binding affinity and selectivity for human adenosine A3 receptors. The most potent A3 antagonist of the present series, N-[3-(4-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-acetamide exhibiting a Ki value of 0.79 nMat human adenosine A3 receptors, showed antagonistic property in a functional assay of cAMP biosynthesis involved in one of the signal transduction pathways of adenosine A3 receptors. Molecular modeling study of conformation search and receptor docking experiments to investigate the dramatic differences of binding affinities between two regioisomers of thiadiazole analogues, suggested possible binding mechanisms in the binding pockets of adenosine receptors [26].



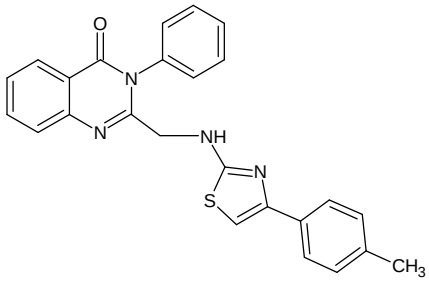
(**12**)

Saravanan, G. *et al*, synthesizednovel thiazoles by incorporation of pyrazole moiety at 2nd position of 2-hydrazinyl-N-(4-phenylthiazol-2-yl) acetamide by treating with chalcones. These compounds were screened for anti-bacterial and anti-fungal activities by paper disc diffusion technique [27].



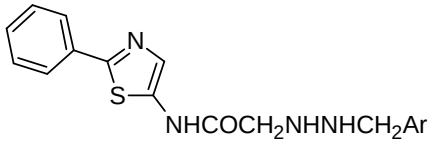
(13)

Pattanaik, J. M. *et al*, have been synthesized a series of 3-aryl-2-(4'-aryl thiazole-2'-yl-amino- methyl) quinazol-4(3H)-ones have been prepared by condensing 3-aryl-2-chloro-methylquinazol-4(3H)-ones with 2-amino-4-substituted phenyl thiazoles and antifungal activity was determined [28].



(14)

Sonawane, S.*et al*, synthesized several new 2-(2'-substituted-arylidene-hydrazino acetyl amino)-4-phenyl-1,3-thiazoles and 2-[2'-{4"-substituted –aryl-3"-chloro-2"-oxo-azetidine}-acetyl-amino]-4-phenyl-1,3-thiazoles, from 2-(2'-hydrazino-acetyl)-amino-4-phenyl-1,3-thiazole using 2-amino-4-phenyl thiazole as the starting material and evaluated for the anti fungal activity [29].



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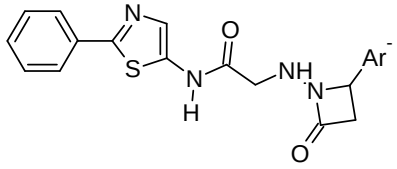
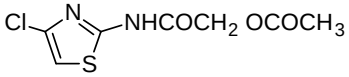


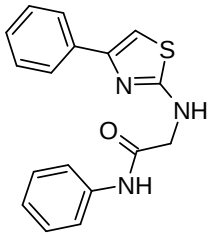
(16)

Pattan, S. R.*et al*, synthesized substituted amino thiazoles and tested for their anti-bacterial activity against two micro-organisms viz. E.coli, S. aureus by disc diffusion method using Mullar-Hinton agar [30].



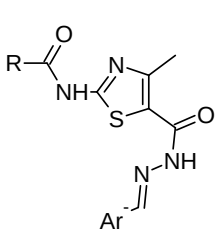
(17)

Pattan*et al*, have synthesized and evaluated some of the new substituted phenyl thiazole derivatives for anti-tubercular activities where 2-amino-4-phenyl thiazole reacts with different substituted acetanilides and chloro-acetylations of it or their substituted derivatives [31].



(18)

Dighe, R. D. *et al*, reported the synthesis of thiazole derivatives, starting from ethyl acetoacetate, by microwave organic reaction enhancement method (MORE) and results of investigations of their antimycobacterial and antimicrobial activities. Many compounds have shown promising activity while others were inactive [32].



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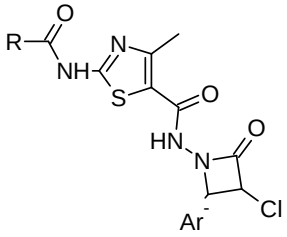

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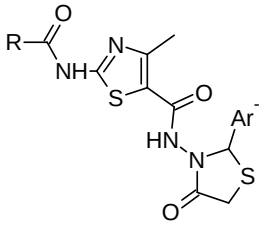
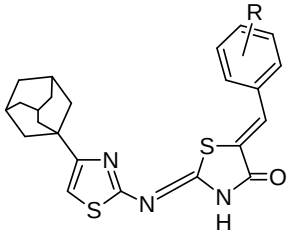


(21)

Ar = -C_6H_5, -4-F -C_6H_4, -3, 4, 5-CH_3O -C_6H_2, -4-$(CH_3)_2N$-C_6H_4, -2-F -C_6H_4, -4-Cl -C_6H_4, -3-NO_2 -C_6H_4, -4-OH -C_6H_4-2-Cl -C_6H_4, -2-NO_2-C_6H_4,
R = $NHCOCH_3$, -$NHCOC_6H_5$

Schiff's Bases of selected Heterocyclic Compounds:

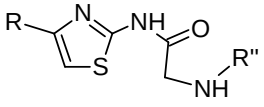
Schiff bases derived from thiazoles and pyrazoles heterocyclic compounds displayed broad range of biological activities. Kouatli O. *et al*, have reported synthesis of structurally novel 4-thiazolidinone derivatives incorporating three known bioactive nuclei such as thiazole, thiazolidinone and adamantine by the multi-step reaction protocol. Evaluation of antibacterial and antifungal activity showed that almost all compounds exhibited better results than reference drugs thus they could be promising candidates for novel drugs [33].



(22)

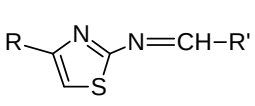
Where R= -Cl, -NO_2, -OH, -OCH_3

Pattan, S. R. *et al*. synthesized some substituted thiazoles. These compounds were evaluated for various biological activities like antibacterial and antifungal activity [34].



(23)

Where, R- OCH_3, -Cl



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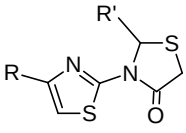
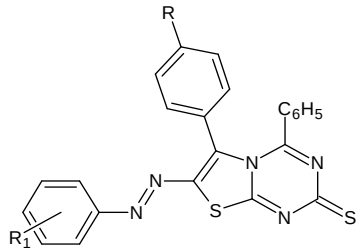


(25)

R' and R''- C_6H_5

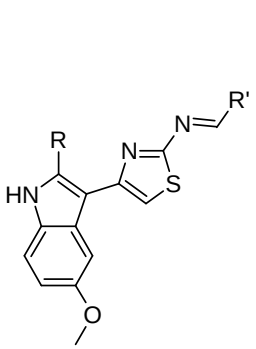
Pande, A. *et al*, have been synthesized some new 6-aryl-7-arylazo-4-phenyl-2H-thiazolo-[3, 2-α]-1,2,5-triazine-2-thiones and studied for their antiviral activity against Ranikhet disease virus [35].



(26)

R_1 = 2-NO_2, R = -OCH_3

Sharma, S. *et al*, Synthesized Some heterocyclic schiff's bases by the condensation of 5-methoxy-2-phenyl/ methyl-3-(2′-amino-1′,3′-thiazol-4′-yl) indoles with different aromatic aldehydes. Then, these compounds were converted into novel azetidinones and thiazolidinones congeners. Compounds were evaluated for antibacterial and antifungal activities against various strains of bacterium and fungus, and substantial results were obtained [36].



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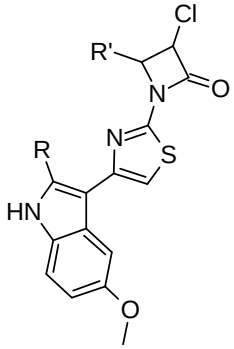

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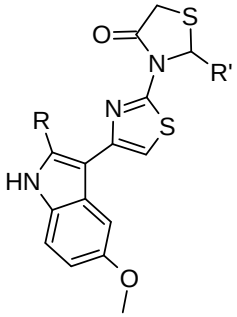
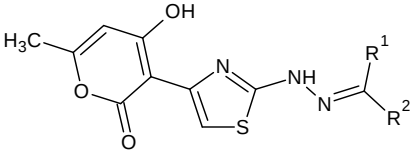
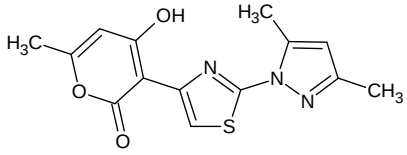


(29)

Vedula, R. R. and Penta, S. synthesized Thiazoles and thiazolyl-pyrazole derivatives, under neat reaction conditions in excellent yields. Condensation of 3-(2-bromo- acetyl)-4-hydroxy-6-methyl-2H-pyran-2-one, thiosemicarbazide and various carbonyl compounds gave corresponding thiazole and thiazolyl pyrazole derivatives in excellent yields by using Hantzsch-thiazole synthesis [37].

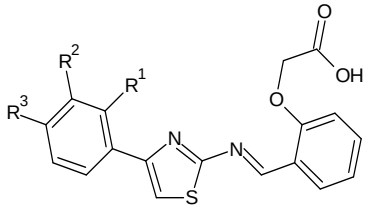


(30)



(31)

Siddiqui, H. L.*et al*, have prepared five novel Schiff's bases from *o*-formyl-phenoxy-acetic acid and a series of amino-thiazoles to form a number of potentially biologically active compounds. The structures of these Schiff bases have been characterized using IR and 1H NMR and 13C-NMR spectroscopy [38].

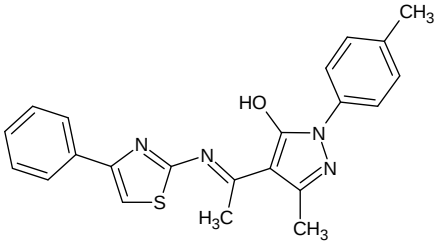


(32)

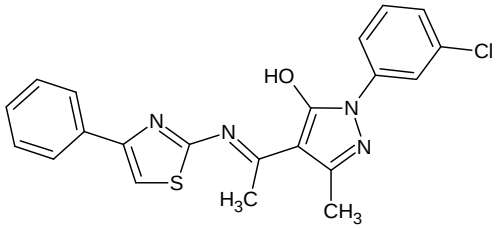
R^1, R^2, R^3 = H,Br,F

Thakar, A. S. *et al*, synthesized Novel Schiff bases and their metal complexes from some heterocyclic β-diketones with 4-phenyl-2-aminothiazole. All the synthesized compounds were confirmed their structure by Elemental analysis, FT-IR, 1H NMR, 13C NMR, Mass spectra, TGA analysis and UV spectra. All the compounds were tested for their antibacterial activity. Spectroscopic measurements suggest that all Schiff base metal complexes are of type

ML2.(H_2O)2 (M=Mn, Fe, Co, Ni, and Cu) and all the metal complexes shows moderate antibacterial activity in the agar cup assay method [39].

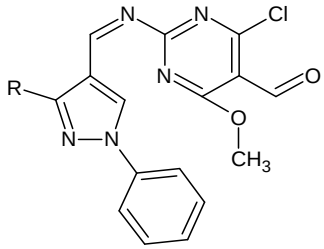


(33)



(34)

Patel, A. R. et al, reported Schiff's base derivatives prepared by the condensation of aldehyde group of 4-formyl-pyrazole and amine group of substituted pyrimidine and these compounds were tested for antimicrobial activities [40].

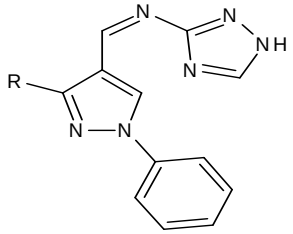


(35)

R=Aryl halide

R= -C_6H_5,-Cl-C_6H_4 , -OH-C_6H_4 ,-NO2-C_6H_4 ,-Br-C_6H_4 ,-CH3SO2-C_6H_4 ,-OCH_3-C_6H_4 ,-CH_3-C_6H_4

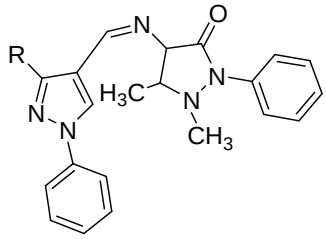
Patel, A. R. *et al*, synthesized Schiff base derivatives by the condensation of aldehyde group of 4-formyl-pyrazole and amino group of triazole and these compounds were characterized by chemical and instrumental methods. Their Antimicrobial activities have been investigated [41].



(36)

R = Aryl

Patel, A. R. *et al*, have taken 2-amino-antipyrine and 4-formyl-pyrazole as starting material for the synthesis of Schiff base derivatives and these compounds were characterized by chemical and instrumental methods. Their Antimicrobial activities have been investigated [42].

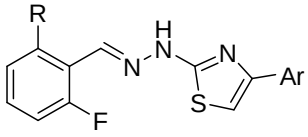


(37)

R=Aryl

Boja Poojary, *et al*, synthesized novel 2, 4-disubstituted-[1, 3]-thiazole derivatives by the reaction of 2-chloro-6-fluoro/2-fluorobenzaldehyde thiosemicarbazone with phenacyl bromide. New compounds were screened for their antimicrobial study and cytotoxic study. The cytotoxicity study was performed by the MTT assay. The MTT [3-(4, 5-dimethylthiazol-2-yl)-2,5-diphenyl-tetra- zollium bromide] assay was performed on HeLa cells (human epithelial cervical cancer). For antibacterial studies micro-organisms employed were *Staphylococcus aureus*, *Escherichia coli*,

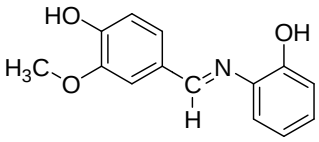
Pseudomonas aeruginosa and *Bacillus cereus.* For antifungal screening, *Candida albicans* strain was used. Both microbial studies were assessed by Minimum Inhibitory Concentration (MIC) by serial dilution method [43].



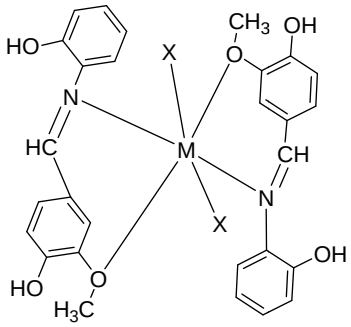
(38)

R= Cl, H

M. B. Fugu, *et al*, have synthesized some new transition metal complexes of Mn(II), Co(II), Ni(II), Cu(II) and Zn(II) with Schiff base ligand (HL) derived from condensation of vanillin with 2-amino- phenol in alcoholic medium. The in vitro antibacterial activities of the complexes were tested using number of bacteria species such as Escherichia coli, Salmonella typhi, Klebsiella pneummiae, Pseudomonas aeruginosa, Staphylococcus aureus, Streptocuccus pyogenes, corynebacterium specie, and Basillus subtilis [44].



(39)

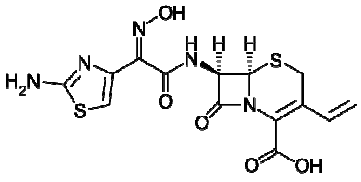
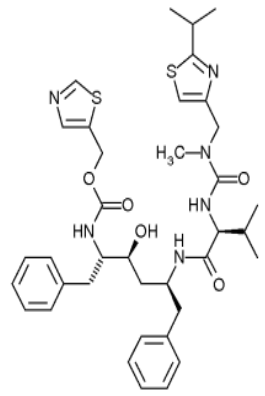
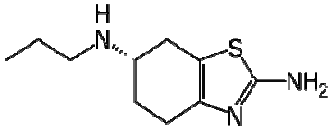


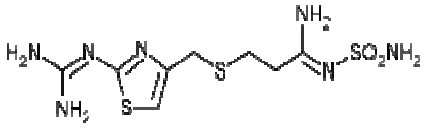
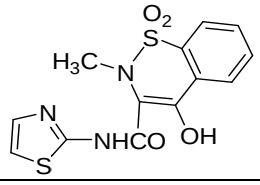
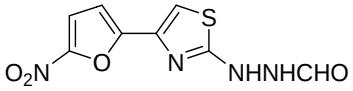
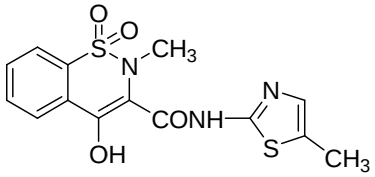
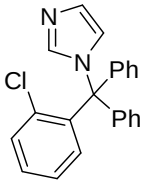
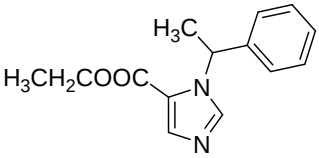
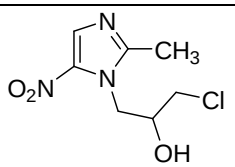
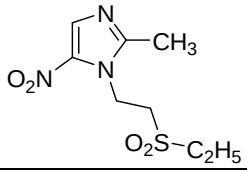
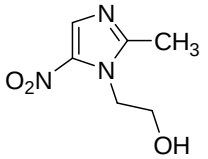
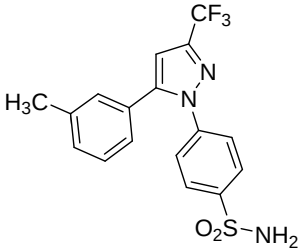
(40)

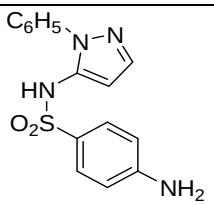
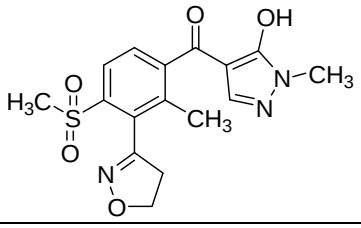
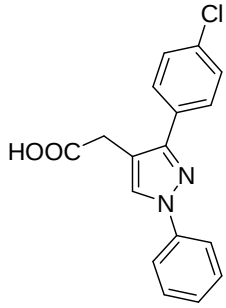
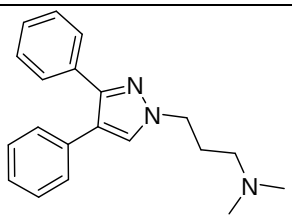
M= Mn, Co, Ni, Cu, Zn

Valuable insight has been emphasized above on the reported synthesis of the structures containing Thiazole, imidazole, pyrazole and their amides & Schiff base derivatives. Moreover very significant clinically approved drugs are also available containing thiazole, imidazole, pyrazole derivatives as pharmacophore in these drugs which has been represented in the following **Table-I**

Table-I: Clinically approved Thiazole, imidazole and pyrazole containing Drugs

Name Category	Structure	Chemical name
Cefdinir (Antibiotics)		(6R,7R)-7-[[2-(2-amino-1,3-thiazol-4-yl)-2-hydroxyiminoacetyl]amino]-3-ethenyl-8-oxo-5-thia-1-azabicyclo [4.2.0]oct-2-ene-2-carboxylic acid
Ritonavir (Antibiotics)		(5S,8S,10S,11S)-10-hydroxy-2-methyl-5-(1-methylethyl)-1-[2-(1-methylethyl)-4-thiazolyl]-3,6-dioxo-8,11-bis (phenylmethyl)-2,4,7,12-Etra-aza-tri-decan-13-oic acid 5 - thiazolyl methyl ester
Pramipexole (Parkinsons disease)		(S)-2-Amino-4,5,6,7-tetrahydro-6-(propylamino) benzothiazole

Famotidine (Antihistamine)		N^2-(Aminosulphonyl)-3-[[[2-[diaminomethylene) amino]thiazol-4-yl]methyl]-thio]propanamidine
Sudoxicam (Antiinflammatory)		4- Hydroxy-2-methyl-N-2-thiazolyl-2H-1, 2-benzo thiazine -3-carbox- amide 1,1- Dioxide
Nifurthiazole (Antimicrobial)		N-(4-(5-nitrofuran-2-yl) thiazol-2-yl) formohydrazide
Meloxicam (Antiinflammatory, Analgesic, Antipyretic)		4-hydroxy-2-methyl-N-(5-methyl-2-thiazolyl)-2H-1,2-benzothiazine-3-carboxamide-1,1-dioxide
Clotrimazole (Antifungal)		1-((2-chlorophenyl) diphenylmethyl)-1H-imidazole
Etomidate (Anaesthetic and sedative)		Ethyl 1-(1-phenylethyl)-1H- imidazole-5-carboxylate
Ornidazole (Antiprotozoal)		1-chloro-3-(2-methyl-5-nitro-1H-imidazol-1-yl)propan-2-ol
Tinidazole (Ani-parasitic) (Antiprotozoal)		1-(2-(ethylsulfonyl)ethyl)-2-methyl-5-nitro-1H-imidazole
Metronidazole (Antiprotozoal)		2-(2-methyl-5-nitro-1H-imidazole-1-yl) ethanol
Celecoxib (Nonsteroidal anti-inflammatory)		4-[5-(4-methylphenyl)-3-(trifluoro- methyl) pyrazol-1-yl] benzene-sulfonamide

Sulphaphenazole (Antimicrobial)		N^1- (1-phenylpyrazol-5-yl) sulphanilamide
Topramezone (Herbicide and pesticide)		[3-(4,5-dihydro-3-isoxazolyl)-2-methyl-4-(methylsulfonyl) phenyl](5-hydroxy-1-methyl-1H-pyrazol-4-yl)methanone
Lonazolac (Non-steroidal anti-inflammatory)		[3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl]acetic acid
Fezolamine (Antidepressant)		3-(3,4-diphenyl- 1H-pyrazol- 1-yl)- N,N-dimethylpropan- 1-amine

DISCUSSION AND CONCLUSION

This review highlights vast number of potential structures and potential therapeutic uses five-membered heterocyclic such as imidazoles, thiazoles and pyrazoles and their substitutes. Schiff bases and amides derived from imidazoles, thiazoles and pyrazoles heterocyclic compounds displayed broad range of biological activities such as anticancer, antiviral, antimicrobial, antimycobacterial, anticonvulsant, antidepressant, angiotensin-II receptor antagonist, anti-inflammatory, antidiabetic and anti-glycation activity. So far, modifications of the Schiff bases have proven highly effective with improved potency and lesser toxicity.

Acknowledgement
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REFERENCES

[1] E Theophil; H Siegfried.The Chemistry of Heterocycles: Structure, Reactions, Syntheses and Applications. ISBN: 3-527-30720-6.
[2] A Gallardo-Godoy; J Gever; KL Fife; BM Silber; SB Prusiner; AR Renslo. *J Med Chem*., **2011**, 54(4), 1010–21.
[3] DR Guay. *P. Clin. Ther*., **2002**, 24, 473–489. Doi: 10.1016/S0149-2918(02) 85125-6.
[4] DJ Kempf; KC Marsh; JF Denissen; E McDonald; S Vasavanonda; CA Flentge; BE Green; L Fino; CH Park; XP Kong. *Proc. Natl. Acad. Sci. U. S. A*., **1995**, 92, 2484–2488.
[5] C Schneider; G Griss; R Hurnaus; W Kobinger; L Pichler; R Bauer; J Mierau; D Hinzen; G Schingnitz. Eur. Patent., 1,860, 87B1, 1986.
[6] DU Miodragović; GA Bogdanović; ZM Miodragović; MĐ Radulović; SB Novaković; GN Kaluđerović; H Kozłowski. *J. Inorg. Biochem*., **2006**, 100, 1568–1574.
[7] A Chauhan; PK Sharma; NiranjanKaushik. *International Journal of ChemTech Research*., **2011**, 3(1), 11-17.
[8] MR Grimmett; AR Katritsky; EFScriven. In Comprehensive Heterocyclic Chemistry II, 5thEdn, Ed.; Pergamon: Oxford; Vol. 3, **1996**; 77–220.

[9] PN Preston. *Chemical Reviews*., **1974**, 74(3), 279.
[10] L De Luca. *Curr. Med. Chem*., **2006**, 13, 1–23.
[11] N Sennequier; D Wolan; D Stuehr. *J. Biol. Chem*., **1999**, 274, 930–938.
[12] RN Brogden; RC Heel; TM Speight; GS Avery. *Drugs.*, **1978**, 16, 387–417.
[13] Y Niwano; ASeo; K Kanai; H Hamaguchi; K Uchida; H Yamaguchi. *Antimicrob*. *Agents Chemother*., **1994**, 38, 2204–2206.
[14] RW Brimblecombe; WAM Duncan; GJ Durant; JC Emmett; CR Gannellin; ME Parsons. *J. Int. Med. Res*., **1975**, 3, 86–92.
[15] T Mano; RW Stevens; K Ando; K Nakao; Y Okumura; M Sakakibara; T Okumura; T Tamura; K Miyamoto. *Bioorg. Med. Chem.*, **2003**, 11, 3879–3887.
[16] B Dyck; VS Goodfellow; T Phillips; J Grey; M Haddach; M Rowbottom; G. S Naeve; B Brown; Saunders. J. *Bioorg. Med. Chem. Lett*., **2004**, 14, 1151–1154.
[17] AS Kiselyov; M Semenova; VV Semenov. *Bioorg. Med. Chem. Lett*., **2006**, 16, 1440–1444.
[18] CA Blum; X Zheng; S De Lombaert. *J. Med. Chem*., **2004**, 47, 2318–2325.
[19] F Cerreto; AVilla; A Retico; M Scalzo. *Eur. J. Med. Chem*., **1992**, 27, 701–708.
[20] AB Scheiff;SG Yerande; Ali El-Tayeb; Wenjin Li; GS Inamdar; KK Vasu; V Sudarsanam; EM Christa. *Bioorg. Med. Chem.*, **2010**, 18, 2195–2203.
[21] B Chen; R Zhao; B Wang; R Droghini; J Lajeunesse; P Sirard; M Endo; BBalasubramanian; JC Barrish. *ARKIVOC.*, **2010**, vi, 32-38.
[22] O Kouatly; AGeronikaki; C Kamoutsis; D Hadjipavlou-Litina; P Eleftheriou. *European Journal of Medicinal Chemistry*., **2009**, 44, 1198-1204.
[23] Li Fuying; Zhu Qingzhang; Yi Zhang; Ying Feng; YingLeng; AoZhang. *Bioorg. Med. Chem*., **2010**, 18, 3875–3884.
[24] RS Giri; HM Thaker; T Giordano; J Williams; D Rogers; V Sudersanam; KK Vasu. *European Journal of Medicinal Chemistr*y., **2009**, 44, 2184–2189.
[25] PX Franklin;AD Pillai; PD Rathod; S Yerande; M Nivsarkar; H Padh; KK Vasu; V Sudarsanam. *European Journal of Medicinal Chemistry.*, **2007**, xx, 1-6.
[26] J Kwan-Young; K Soo-Kyung; G Zhan-Guo; AS Gross; M Neli; KA Jacobson; K Yong- Chul. *Bioorg. Med. Chem*., **2004**,12, 613–623.
[27] G Saravanan; V Alagarsamy; TGV Pavitra; GC Kumar; Y Savithri; L Naresh; P Avinash. *International Journal of Pharma And Bio Sciences.*, **2010**, 1(3), 1-8.
[28] J Pattanaik; M Pattanaik; D Bhatta. *Ind. J. Chem.*, **1998**, 37B, 1304-1306.
[29] SK Sonawne; SD Shrivastava; SK Shrivastava. *Ind. J. Chem.*, **2008**, 47B, 633-636.
[30] S Pattan; N Dighe; S Nirmal; A Merekar; R Laware; H Shinde; D Musmade. *Asian J.Research Chem.,* **2009**, 2(2), 196-201.
[31] SR Pattan; AA Bukitagar; KG Bhat; JS Pattan; BS Kittur; AB Khade. *Ind. Drugs.*, **2007**, 44(9), 689-692.
[32] RD Dighe; MR Shiradkar; SS Rohom; PD Dighe; SR Chaudhari. *International Journal of Drug Design and Discovery.*, **2011**, 2(2), 464-473.
[33] O Kouatli; A Geronikaki; P Zoumpoulakis; C Camoutsis; M Sokovic; A Ciric; J Glamoc lija. *Bioorg. Med. Chem*., **2010**, 18, 426–432.
[34] SR Pattan; NS Dighe; SA Nirmal; AN Merekar; RB Laware; HV Shinde; DS Musmade. *Asian J. Research Chem.*, **2009**, 2(2), 196-201.
[35] A Pande; VK Saxena. *Ind. J. Pharm. Sci.*, **1985**, 689-692.
[36] V Kumar; S Singh; S Sharma; A Kumar. *International Journal of Drug Design and Discovery*., **2010**, 1(3), 239-251.
[37] S Penta; RR Vedula. *Org. Commun*., **2012**, 5(3), 143-149.
[38] HL Siddiqui; Amjid Iqbal; Saeed Ahmad; WW George. *Molecules*., **2006**, 11, 206-211.
[39] AS Thakar; KS Pandya; KT Joshi; AM Pancholi. *E-Journal of Chemistry.*, **2011**, 8(4), 1556-1565.
[40] JJ Vora; AR Patel; DR Patel; S Dholakiya. *American Journal of PharmTech Research.*, **2011**, 1(3), 170-178.
[41] JJ Vora; DR Patel; AR Patel; YS Patel. *Der Pharma Chemica.*, **2010**, 2(3), 257-266.
[42] JJ Vora; AR Patel; DR Patel; S Dholakia. *IJPSR.*, **2012**, 3(1), 162-167.
[43] V Sumangala; Boja Poojary; N Chidananda; T Arulmoli; Shalini Shenoy. *J. Chem. Pharm. Res*., **2012**, 4(12), 4979-4987.
[44] MB Fugu; NP Ndahi; BB Paul; AN Mustapha. *J. Chem. Pharm. Res.*, **2013**, 5(4), 22-28.