Section: Research Paper

OVERVIEW OF THIAZOLE AND THEIR DERIVATIVES HAVING ANTIMICROBIAL ACTIVITY

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ABSTRACT

Heterocyclic compounds are those compounds which contain at least one different element, such as oxygen, nitrogen, sulfur, etc. other than a carbon in a ring. Thizaoleis an aromatic heterocyclic compound which means it contains a different element such as nitrogen, sulfur, etc. other than carbon in a ring. Thiazole structure made up of three carbon atoms, with one nitrogen atom and with one sulfur atom which is arranged in the form of a ring.Thiazole comes under the family of azoles which also include oxazoles and imidazoles. Sometimes thiazoles also considered as a functional group. Thiazole is also called 1, 3-thiazole having molecular formula C_3H_3NS. It is clear or pale yellow in color with a pyridine like anodour.Thiazole is a very important part of vitamin B1, which is also called thiamine. It is also used in flavoring agent and in manufacturing of tobacco related products. Thiazoles are also mainly used in dyes and non-steroidal anti-inflammatory drug. Thiazoledyes are mainly used for dyeing cotton. When thiazole fused with benzene ring it becomesbenzothiazole which has various medical importances such as anticancer, antimicrobial, antitubercular, etc. Naturally thiazole found in naturally occurring peptides and these peptides are used in the development of new peptidomimetics.It is generally prepared by the reaction between haloketones and thioamides.Robinson-Gabriel synthesis and Cook-Heilbron synthesis also used for the preparation of thiazoles it includes a reaction between 2-acyclamino-ketones and phosphorus pentasulfide and reaction between α-aminonitrile and carbon disulfide. So keeping in mind we have prepared a review of thiazole and their derivatives having antimicrobial activity.

Keywords: Thiazole, antimicrobial activity, anti-cancer, benzothiazole

1. Review

Reza Mohammad *et al.*,synthesized5-amino-2-oxo-7-aryl-3,7-dihydro-2H-pyrano[2,3-d]thiazole-6-carbonitriles derivatives by adopting an ultrasound irradiation method with environmentally convenient procedure and without using any catalyst or additives. Their derivatives were obtained in a very short period of time with good yield. They also evaluated these derivatives for antimicrobial activity against *Staphylococcus aureus, Escherichia coli, Bacilliussubtilis* and *Pseudomonas aeruginosa* using ofloxacin andnorfloxacin as a standard drug through cup plate agar diffusion method.

Material and methods: In this author take a mixture of monochloroacetic acid, 4-nitrobenzaldehyde, thiourea and malononitrile in TFE and stirred this mixture of different temperature by using the ultrasonic apparatus and elevation of temperature were controlled by adding cold water. The reaction progresses were monitored by TLC and the derivatives were filtered, washed and recrystallized from ethanol.

Result: The result revealed that compounds 5-Amino-2-oxo-7-phenyl-3,7-dihydro-2H-pyrano[2,3-d]thiazole-6-carbonitrile and 5-Amino-7-(naphthalen-2-yl)-2-oxo-3,7-dihydro-2H-pyrano[2,3-d]thiazole-6-carbonitrile showed excellent growth inhibition against *Bacillus subtilis* whereas compound 5-Amino-7-(2-hydroxynaphthalen-1-yl)-2-oxo-3,7-dihydro-2H-pyrano[2,3-d]thiazole-6-carbonitrile showed more potent actions against gram negative bacteria than the ofloxacin.

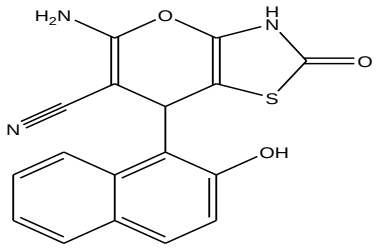

fig. 2.1 5-Amino-7-(2-hydroxynaphthalen-1-yl)-2-oxo-3,7-dihydro-2H-pyrano[2,3-d]thiazole-6-carbonitrile

2.1 Mahmoud Huda *et al.,* synthesized various bis-1,3,4-thiadiazoles and bis-thiazoles from the reaction of bis(hydrazonoyl) chloride with different carbodithioate and thiosemicarbazone derivatives and in last they evaluated antimicrobial activity against two positive bacterial strains (*Bacillus subtilis* and *Staphylococcus aureus*), two fungal strains (*Candida albicans* and *Aspergillusflavus*) and two Gram negative bacterial strains (*Proteus vulgaris* and *Escherichia coli*) by using the diffusion agar method.

Material and methods: In this author firstly prepare bis(hydrazonoyl) chloride by taking 1,3-bis(2-aminophenoxy)propane dihydrochloride and 3-chloropentane-2,4-

dione as starting materials and then they react, this bis(hydrazonoyl) chloride with different derivatives of metyhylcarbodithioateand triethylamine in ethanol at 25° C which give bis-1,3,4-thiadiazoles derivatives andbis-thiazole derivatives were prepared by refluxing between thiosemicarbazone and trethylamine in dioxane for 2-4 hours. The product was washed, filtered and recrystallized. The reaction was monitored by TLC and synthesized derivatives were characterized by IR and NMR.

Results: The result revealed that compound 1-[(5E)-4-[2-(3-{2-[(2E)-5-acetyl-2-[(Z)-2-[1-(pyridin-2-yl)ethylidene]hydrazin-1-ylidene]-2,3-dihydro-1,3,4-thiadiazol-3-yl]phenoxy}propoxy)phenyl]-5-[(Z)-2-[1-(pyridin-2-yl)ethylidene]hydrazin-1-ylidene]-4,5-dihydro-1,3,4-thiadiazol-2-yl]ethan-1-oneshowed higher activity against *Aspergillusflavus* but showed equal activity against *Candida albicans* and compound 1-[(5E)-4-[2-(3-{2-[(2E)-5-acetyl-2-[(E)-2-(phenylmethylidene)hydrazin-1-ylidene]-2,3-dihydro-1,3,4-thiadiazol-3-yl]phenoxy}propoxy)phenyl]-5-[(E)-2-(phenylmethylidene)hydrazin-1-ylidene]-4,5-dihydro-1,3,4-thiadiazol-2-yl]ethan-1-one showed moderate activity against all tested strains except *Aspergillusflavus*. While all other derivatives showed no activity against all tested fungi and bacteria strains.

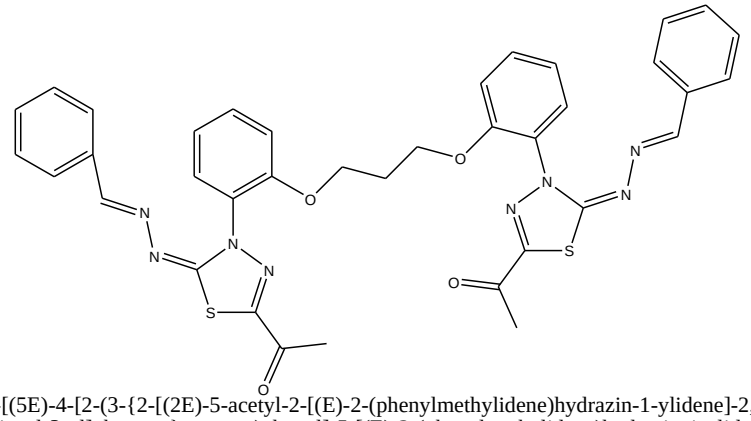

fig. 2.2a 1-[(5E)-4-[2-(3-{2-[(2E)-5-acetyl-2-[(E)-2-(phenylmethylidene)hydrazin-1-ylidene]-2,3-dihydro-1,3,4-thiadiazol-3-yl]phenoxy}propoxy)phenyl]-5-[(E)-2-(phenylmethylidene)hydrazin-1-ylidene]-4,5-dihydro-1,3,4-thiadiazol-2-yl]ethan-1-one

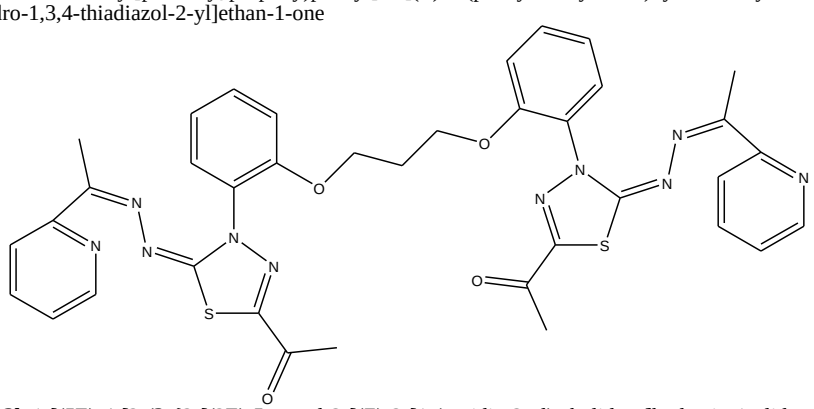

fig. 2.2b 1-[(5E)-4-[2-(3-{2-[(2E)-5-acetyl-2-[(Z)-2-[1-(pyridin-2-yl)ethylidene]hydrazin-1-ylidene]-2,3-dihydro-1,3,4-thiadiazol-3-yl]phenoxy}propoxy)phenyl]-5-[(Z)-2-[1-(pyridin-2-yl)ethylidene]hydrazin-1-ylidene]-4,5-dihydro-1,3,4-thiadiazol-2-yl]ethan-1-one

2.2 Koudad M. *et al.,* synthesized various derivatives of imidathiazole by using aldehyde and different methyl ketones and they were confirmed by NMR, LC-MS and X-ray diffraction. Antimicrobialactivities of these derivatives were evaluated against three bacterial strains (*Pseudomonas aeruginosa*, *Escherichia coli* and *Staphylococcus aureus*) and one fungal strain (*Fusariumoxysporum*) by diffusion method.

Material and method: In this author take carbaldehyde solution in ethanol and added KOH and p-acetophenone solution into it, and then it stirred the mixture for 6-8 hours at 60°C. The mixture was poured into cold water, filtered, washed and recrystallize the product. The reaction was monitored by TLC and synthesized derivatives were characterized by LC-MS, X-ray diffraction and NMR.

Result: The result revealed that compound 6-phenylimidazo[2,1-b]thiazole-5-carbaldehyde and (E)-1-(furan-2-yl)-3-(6-phenylimidazo[2,1-b]thiazol-5-yl)prop-2-en-1-one showed excellent antimicrobial activity and other derivatives showed excellent activity against *F. oxysporum*.

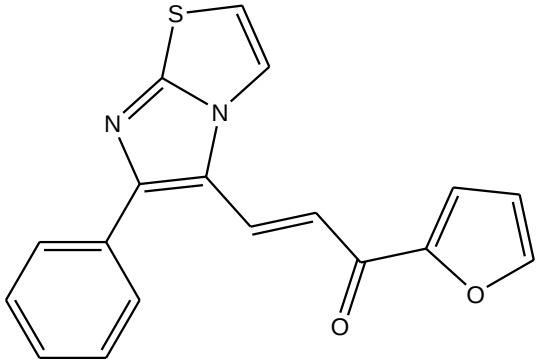

fig. 2.3a (E)-1-(furan-2-yl)-3-(6-phenylimidazo[2,1-b]thiazol-5-yl)prop-2-en-1-one

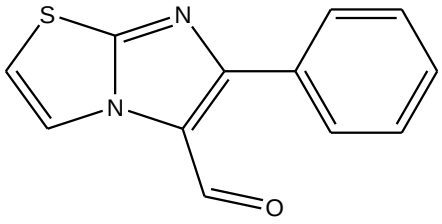

fig. 2.3b 6-phenylimidazo[2,1-*b*]thiazole-5-carbaldehyde

2.3 Althagafi Ismail *et al.,* synthesized various compounds which contain di-, tri- and tetrathiazole moieties. The aim was that to investigate the synthesized compounds for their antimicrobial activity, potency and molecular docking studies against three pathogen proteins.

Material and methods: In this author synthesized 2-bromo-1-(4-methyl-2-(methylamino)thiazol5-yl)ethan-1-one by using bromine, 5-acetyl-4-methyl-2-

(methylamino)thiazole and acid. Then they react 2-bromo-1-(4-methyl-2-(methylamino)thiazol5-yl)ethan-1-one with 2-amino thiazole in ethanol and the derivatives were prepared by using ethanol under reflux. The product was washed, filtered and recrystallized. The reaction was monitored by TLC and spectral analyses were performed such as IR and MS to confirm the structure.

Result: The result revealed that the derivatives having di- and trithiazole showed antimicrobial activity against gram positive and gram negative bacterial and fungal strains. But, the most interesting thing was that none of the derivatives showed activity against Gram-negative *Pseudomonas aeruginosa* and Gram-positive *Streptococcus pyogenes*. The most potent as well as active derivative was 3-(4-Methyl-2-(methylamino)thiazol-5-yl)-7-phenyl-5H-thiazolo[3,2-a]pyrimidin-5-one.

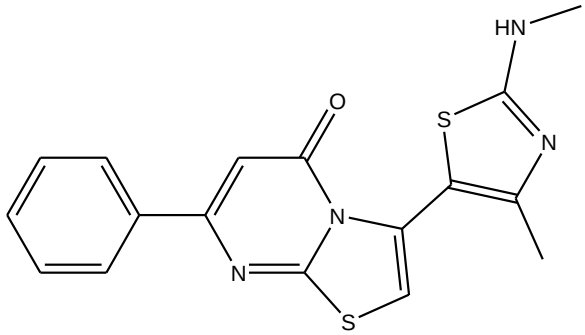

fig. 2.4 3-(4-Methyl-2-(methylamino)thiazol-5-yl)-7-phenyl-5H-thiazolo[3,2-a]pyrimidin-5-one .

2.4 GrybaitėBirutė*et al.,* synthesized various derivatives of substituted thiazole containing different functional groups such as carboxyethylamino, chloromethyl, carboxyl, ethoxyoxoethyl, ethoxycarbonyl, etc. and the synthesized products were tested for antimicrobial activity against *Escherichia coli*, *Staphylococcus aureus*, and Mycobacterium luteum bacterial strains, and *Candida tenuis* and *Aspergillusniger* fungi by serial dilution and diffusion agar method.

Material and methods: In this author take 3-(1-(naphthalen-1-yl)thioureido)propanoic acid and 3-(1-(p-tolyl)thioureido)propanoic acid and react tese with various α-halocarbonyl compounds and dimethyl acetylenedicarboxylate which give thiazoles having different functional groups as a product. The reaction was monitored through TLC and spectral data was confirmed by NMR.

Result: The result revealed that those derivatives which, contain p-tolyl moiety showed high activity against all microbial strains such as compound 3-((4-(2-methoxy-2-oxoethyl)thiazol-2-yl)(p-tolyl)amino)propanoic acid, 3-((4-(hydroxymethyl)thiazol-2-yl)(p-tolyl)amino)propanoic acid, 3-((4-((phenylamino)methyl)thiazol-2-yl)(p-tolyl)amino)propanoic acid and 3-((4-(chloromethyl)thiazol-2-yl)(p-tolyl)amino)propanoic acid.

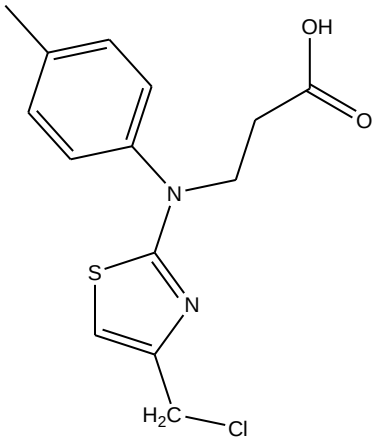

fig. 2.5a 3-((4-(chloromethyl)thiazol-2-yl)(*p*-tolyl)amino)propanoic acid

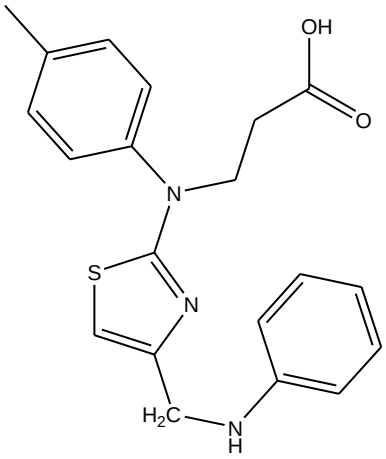

fig. 2.5b 3-((4-((phenylamino)methyl)thiazol-2-yl)(*p*-tolyl)amino)propanoic acid

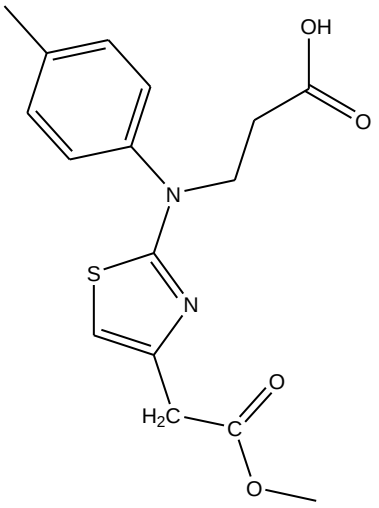

fig. 2.5c 3-((4-(2-methoxy-2-oxoethyl)thiazol-2-yl)(*p*-tolyl)amino)propanoic acid

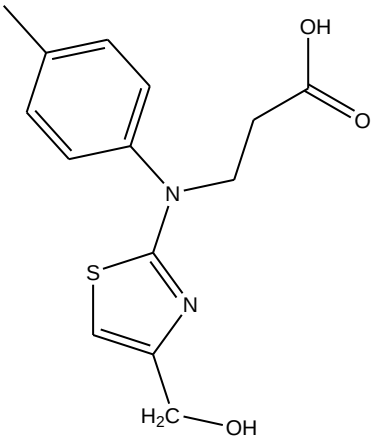

fig. 2.5d 3-((4-(hydroxymethyl)thiazol-2-yl)(*p*-tolyl)amino)propanoic acid

2.5 Farghaly, Thoraya A *et al.*, synthesized derivatives of thiochromanes containing thiazole moiety via rection of different hydrazonoyl chlorides using triethylamine as basic catalyst. The synthesized derivatives were tested for invitroantimicrobial activity against two gram negative bacteria (*Pseudomonas aeruginosa* and *Escherichiacoli*), two gram positive bacteria (*Streptococcus pneumonia* and Bacillus subtilis) and four fungi (*Aspergillusfumigatus*, *Syncephalastrumracemosum*, *Geotricumcandidum*, and *Candida albicans*).

Material and methods: In this author take thiochroman-4-thiocarbohydrazone as a starting material and react this it with N-aryl 2-oxopropane-hydrazonoyl chlorides in

dioxane in the presence of triethylamine. The reaction was monitored through TLC and the structures of all the derivativeswere confirmed by spectral analysis.

Result: The result revealed that the compounds (2E,2Z)-5-((Z)-phenyldiazenyl)-2-(2-(2,3-dihydrothiochromen-4-ylidene)hydrazono)-4-methylthiazol-3(2H)-amineand (2E,2Z,NZ)-5-((Z)-phenyldiazenyl)-N-(3,4-dihydronaphthalen-2(1H)-ylidene)-2-(2-(2,3-dihydrothiochromen-4-ylidene)hydrazono)-4-methylthiazol-3(2H)-amine were the most potent against all the microorganisms than the applied standard drug and also they were the top scorers in the molecular docking study with the affinity of -28.50 and -25.93 kcal/mol respectively.

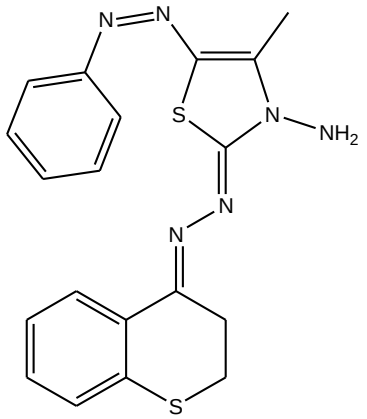

fig. 2.6a (2*E*,2*Z*)-5-((*Z*)-phenyldiazenyl)-2-(2-(2,3-dihydrothiochromen-4-ylidene)hydrazono)-4-methylthiazol-3(2*H*)-amine

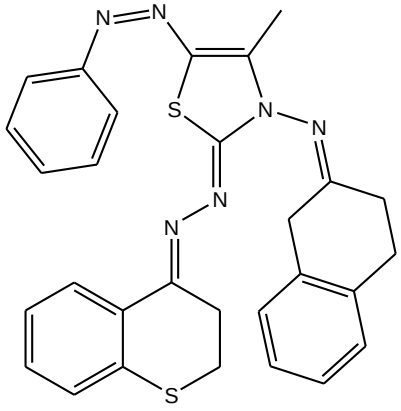

fig. 2.6b (2*E*,2*Z*,*NZ*)-5-((*Z*)-phenyldiazenyl)-*N*-(3,4-dihydronaphthalen-2(1*H*)-ylidene)-2-(2-(2,3-dihydrothiochromen-4-ylidene)hydrazono)-4-methylthiazol-3(2*H*)-amine

2.6 Saleh, Fatma M *et al.*,synthesized different thiazole and thiadiazoles derivatives using ethyl pyruvate as a precursor. Then, they had tested these newly synthesized products for their antimicrobial activity against gram negative bacteria *Escherichia coli* and *Pseudomonas aeruginosa*, gram-positive bacteria *Staphylococcus aureus*and*Bacillus subtilis* and fungus against *Aspergillusflavus* and *Candida albicans.*

Material and methods: In this author refluxed the ethyl pyruvate with methyl hydrazncarbodithioate by using propanol which gave ethyl 2-(2-((methylthio)carbonothioyl)hydrazono)propanoate as a product. On stirring this product with different hydrazonoyl halides by using catalyst triethylamine give thiazole derivatives. The product was washed, filtered and recrystallized.The structures of all the derivatives were confirmed by spectral analysis and the reaction was monitored through TLC.

Result: The result revealed that the compound Ethyl 2-(2-(4-phenylthiazol-2-yl)hydrazono)propanoate was the most potent compound while compounds Ethyl 2-(2-(4-(4-chlorophenyl)-5-(phenyldiazenyl)thiazol-2-yl)hydrazono)propanoate, Ethyl

2-(2-(4-(4-bromophenyl)-5-(phenyldiazenyl)thiazol-2-yl)hydrazono)propanoate, Ethyl 2-(2-(4-(p-tolyl)thiazol-2-yl)hydrazono)propanoate, Ethyl 2-(2-(4-(4-methoxyphenyl)thiazol-2-yl)hydrazono)propanoate and Ethyl 2-((4-oxo-5-(2-phenylhydrazono)thiazolidin-2- ylidene)hydrazono)-propanoate showed some antimicrobial activity and the rest of the compounds showed no anti-bacterial and anti-fungal activities.

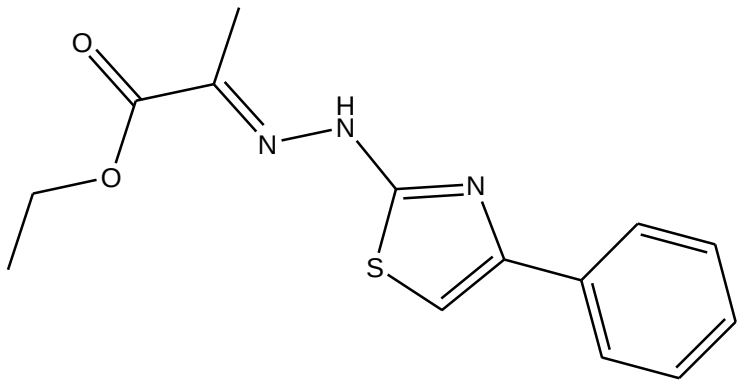

fig. 2.7a Ethyl 2-(2-(4-phenylthiazol-2-yl)hydrazono)propanoate

2.7 Imran Mohd*et al.,* synthesized different napthalenylthiazole derivatives based on quinolone-pyrazoline and then evaluated these derivatives for antimicrobial activity against gram positive bacteria, gram negative bacteria and fungi species.

Material and methods: In this author react 5-(2-chloroquinolin-3-yl)-3-substitutedphenyl-4-dihydro-1H-pyrazole-1-carbothiamides with 2-bromo-(2-naphthyl)ethanone and 2-bromo-(1-naphthyl)ethanone using ethanol as solvent. Reaction was monitored through TLC and for elucidation and confirmation of the derivatives IR, NMR, elementalanalysis and mass spectrometry were performed.

Results: The result revealed that all the derivatives had some antimicrobialactivity, but the compounds 2-chloro-3-(3-(2-chlorophenyl)-1-(4-(naphthalen-2-yl)thiazol-2-yl)-4,5-dihydro-1H-pyrazol-5-yl)quinolone, 2-chloro-3-(3-(2-fluorophenyl)-1-(4-(naphthalen-2-yl)thiazol-2-yl)-4,5-dihydro-1H-pyrazol-5-yl)quinolone and 2-chloro-3-(3-(3-fluorophenyl)-1-(4-(naphthalen-2-yl)thiazol-2-yl)-4,5-dihydro-1H-pyrazol-5-yl)quinoline showed goodantimicrobial action.

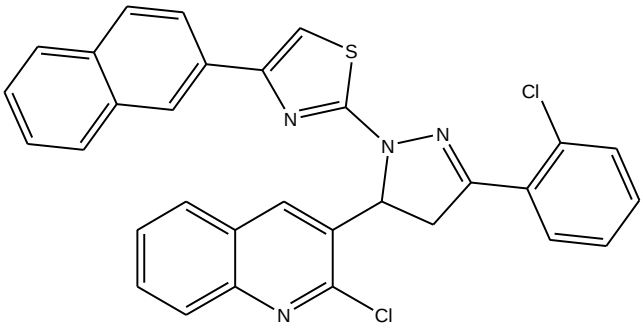

fig. 2.8a 2-chloro-3-(3-(2-chlorophenyl)-1-(4-(naphthalen-yl)thiazol-2-yl)-4,5-dihydro-1*H*-pyrazol-5-yl)quinoline

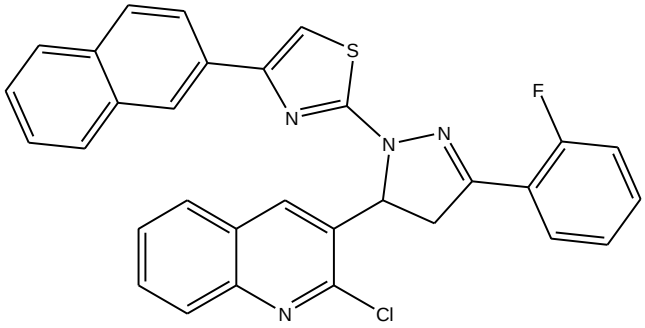

fig. 2.8b 2-chloro-3-(3-(2-fluorophenyl)-1-(4-(naphthalen-2-yl)thiazol-2-yl)-4,5-dihydro-1*H*-pyrazol-5-yl)quinoline

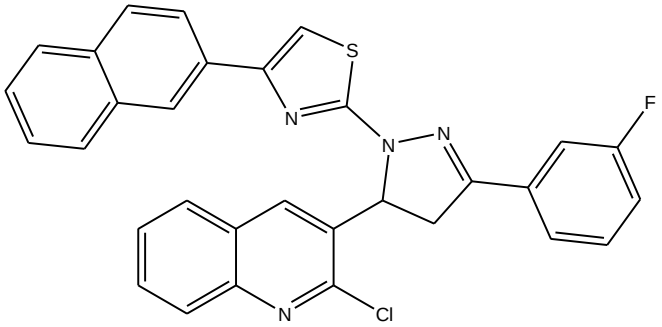

fig. 2.8c 2-chloro-3-(3-(3-fluorophenyl)-1-(4-(naphthalen-2-yl)thiazol-2-yl)-4,5-dihydro-1*H*-pyrazol-5-yl)quinoline

2.8 Turan-ZitouniGülhan*et al.,* synthesized different 2-[(benzazole-2-yl)thioacetylamino-thiazole derivatives and evaluated for toxicity and antimicrobial activity. Antimicrobial activity tested against *Staphylococcus aureus*, *Escherichia coli*, *Bacillus subtilis*, *Streptococcus faecium*, *Staphylococcus epidermidis*and *C. albicans*.
Material and methods: In this author synthesized 2-[(benzazole-2-yl)thioacetylamino-thiazole derivatives by reacting different derivatives of 4-methyl-2-(chloroacetylamino)thiazole and benzazol-2-thiole in the presence of K_2CO_3 and by using solvent acetone. The reaction was monitored through TLC and the structures of all the derivatives were confirmed by spectral analysis.

Result: The result revealed that compound N-(4-methylthiazol-2-yl)-2-(5-nitro-2,3-dihydrobenzo[d]oxazol-2-ylthio)acetamide was the most active as well as non-toxic and this compound showed antimicrobial activity against all strains.

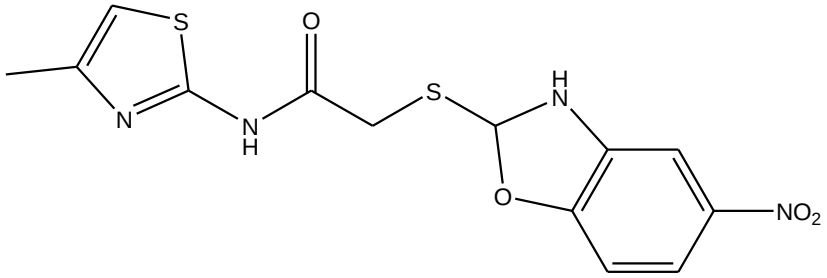

fig. 2.9 *N*-(4-methylthiazol-2-yl)-2-(5-nitro-2,3-dihydrobenzo[*d*]oxazol-2-ylthio)acetamide

2.9 Singh Narendra*et al.,* synthesized different derivatives of 2-amino thiazole and then these derivatives were evaluated for antimicrobial activity against *Bacillus subtilus*, *E.coli*, *Candida albicans*, *Aspergillusniger* by Cup-plate agar diffusion method.

Material and methods: In this author firstly synthesized compound 2-Chloro-N-(thiazol-2yl) acetamide (intermediate) by reacting 2-amino thiazole, potassium carbonate and chloro acetyl chloride in chloroform. Then on reaction of different amines and potassium carbonate with this intermediate was given 2- Substituted - N-(thiazol-2-yl) acetamide. The product was washed, filtered and recrystallized. The reaction was monitored through TLC and the structures of all the derivatives were confirmed by spectral analysis and sharp melting point.

Result: The result revealed that all compounds have mild to good anti-bacterial and an anti-fungal activity. From all these compounds only 2-(4-Methylpiperazin-1-yl)-N-(thiazol-2-yl) acetamide compound showed great anti-bacterial activity and 2-(2-Methyl-1H-imidazol-1-yl)-N-(thiazol-2-yl) acetamide showed great anti-fungal activity.

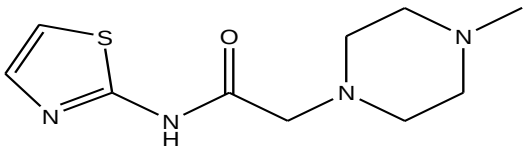

fig. 2.10a 2-(4-Methylpiperazin-1-yl)-N-(thiazol-2-yl) acetamide

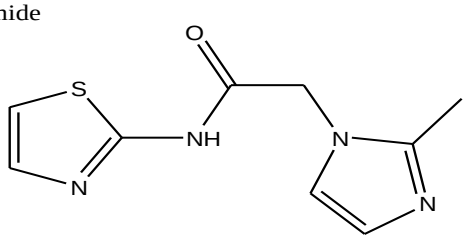

fig. 2.10b 2-(2-Methyl-1H-imidazol-1-yl)-N-(thiazol-2-yl) acetamide

2.10 Karegoudar Prakash *et al.,* synthesized different derivatives of 4-aryl/chloroalkyl-2-(2,3,5-trichlorophenyl)-1,3-thiazoles and then evaluated these derivatives for antimicrobial activity against *E. coli* , *S. aureus*, *P. aeruginosa* and *B. subtilis* by using the serial plate dilution method.

Material and methods: In this author synthesized different derivatives of 4-aryl/chloroalkyl-2-(2,3,5-trichlorophenyl)-1,3-thiazoles by reaction between 2,3,5-trichlorobenzenecarbothioamide and phenacyl bromide or dichloroacetone. On treating 2,3,5-Trichlorobenzaldehyde thiosemicarbazone with phenacyl bromide give 4-aryl-2-(2,3,5-trichlorophenylidenehydrazino)-1,3-thiazoles. The reaction was monitored through TLC and the structures of all the derivatives were confirmed by spectral analysis.

Result: The result revealed that the compounds 4-[4-(Methylthio)phenyl]-2-(2,3,5-trichlorophenyl)-1,3-thiazole, 4-[4-(Methylthio)phenyl]-2-[(E)-(2,3,5-trichlorobenzyl)-diazenyl]-1,3-thiazole, 2-[Amino(hydroxy)methyl]-4-[2-(2,3,5-trichlorophenyl)-1,3-thiazol-4-yl]phenol, 2-[Amino(hydroxy)methyl]-4-{2-[(E)-(2,3,5-trichlorobenzyl)diazenyl]-1,3-thiazol-4-yl}phenol, 1-Methyl-4-{[2-(2,3,5-trichlorophenyl)-1,3-thiazol-4-yl]-methyl}piperazine and 1-{[2-(2,3,5-Trichlorophenyl)-1,3-thiazol-4-yl] methyl}piperidine were greateranti-bacterial activity whereas compound 4-(1,10-Biphenyl-4-yl)-2-(2,3,5-trichlorophenyl)-1,3-thiazole was showed greater anti-fungal activity.

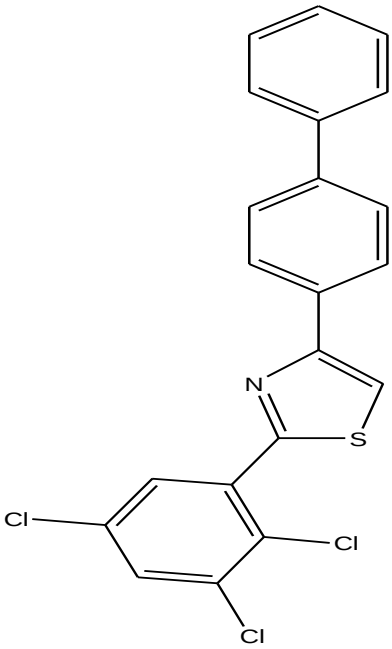

fig. 2.11 4-(1,10-Biphenyl-4-yl)-2-(2,3,5-trichlorophenyl)-1,3-thiazole

2.11 Bondock Samir *et al.*, synthesized different derivatives of 2-(3- pyridyl)-4,5-disubstituted thiazoles and then evaluated these derivatives for in vitro antimicrobial activity against ten bacterial strains (*Staphylococcus aureus*, *Staphylococcusepidermidis*, *Streptococcus pyogenes*, *Bacillissubtilis*, *Enterococcus faecalis,Neisseriagonorrhoeae*, *Proteous vulgaris*, *Klebsiella pneumonia*, *Shigellaflexneri* and *Pseudomonas aeruginosa*) and five fungal human pathogenic strains (*Aspergillusfumigates*, *Aspergillusclavatus*, *Candida albicans*, *Geotricumcandidum*, and *Penicilliummarneffei*) using the agar diffusion method.

Material and methods: In this author synthesized 2-(3- pyridyl)-4,5-disubstituted thiazoles by using a hot solution of thionicotinamide. In the hot solution of thionicotinamidetriethylamine was added and in this mixture p-chloroacetylacetanilide, 3- bromoacetylcoumarin, chloroacetone and 3-chloroacetylacetonewere added and the reaction mixture was put it on reflux for 8 hours. The reaction was monitored through TLC and the structures of all the derivatives were confirmed by spectral analysis.

Result: The result revealed that the compound 2-(3-pyridyl)thiazoles has excellent antimicrobial activity and the greatest antimicrobial activity was shown by 5-acetyl4-methyl-2-(3-pyridyl)thiazole than the 4-methyl-2-(3- pyridyl)thiazol which revealed that with increasing the size of substitutions bythiazole nucleus decreased the antimicrobial activity.

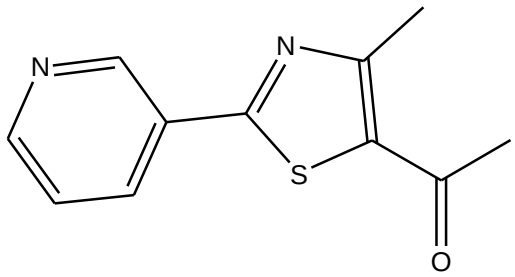

fig. 2.12 5-acetyl4-methyl-2-(3-pyridyl)thiazole

2.12 Sharshira E. M. *et al.*, synthesized different derivatives 2-HydrazinylN-[4-(p-substituted phenyl)-thiazol-2-yl]-acetamides and then evaluated these derivatives for in-vitro antimicrobial activity against *Staphylococcus aureus*, *Pseudomonasaeruginosa,Escherichia coli* and *Candida albicans* by using the agar well-diffusion method.

Material and methods: In this author synthesized 2-HydrazinylN-[4-(p-substituted phenyl)-thiazol-2-yl]-acetamides by reacting pyridine and chloroacetyl chloride. This reaction mixture was stirred cooled and the product was washed, recrystallized and dried. Make a solution of the above product in ethanol and hydrazine hydrate was added. Above mixture was heated for about 6 hours, then add cold water. The product

was washed, filtered and recrystallized. The reaction was monitored through TLC and the structures of all the derivatives wereconfirmedby spectral analysis.

Result: The result revealed that the compounds 2-[3-cyclopropyl-5-(p-substitutedphenyl)-4,5-dihydropyrazol-1-yl]-N-[4-(p-substitutedphenyl)-thiazol-2-yl]-acetamides showed excellent antimicrobial activity against all strains.

2.13 Bharti S. K.*et al.,* synthesized different derivatives of arylidene-2-(4-(4-methoxy/bromophenyl) thiazol-2-yl) hydrazines and 1-(4-(4-methoxy/bromophenyl)thiazol-2-yl)-2-cyclohexylidene/cyclopentylidene hydrazines and then evaluated for in-vitro antimicrobial activity against bacterial strains (*Escherichia coli*, *Staphylococcus aureus*, *Salmonella typhi*, *Pseudomonas aeruginosa*, *Klebsiellapneumoniae*and *Vibrio cholera*) and fungal strains (*Candida albicans*, *Cryptococcus neoformans*, *Aspergillusflavus*and *Chrysosporiumtropicum*) by the agar disc diffusion method.

Material and methods: In this author synthesized arylidene-2-(4-(4-methoxy/bromophenyl) thiazol-2-yl) hydrazines and 1-(4-(4-methoxy/bromophenyl)thiazol-2-yl)-2-cyclohexylidene/cyclopentylidene hydrazinesvia cyclization of thosemicarbazone with different phenacyl bromide. Firstly, the author prepared Schiff base of thiosemicarbaone by using different aldehyde or ketone, thiosemicarbazone, ethanol and glacial acetic acid. Then, they react the above product with different phenacyl bromide. The product was washed, filtered and recrystallized. The reaction was monitored through TLC and the structures of all the derivatives wereconfirmedby spectral analysis.

Result: The result revealed that the compound 2-(2-(4-(4-Bromophenyl)thiazol-2-yl)hydrazono)-1,2-diphenylethanol which contains imino-1,2-diphenylethanol substituent showed excellent anti-bacterial activity and the compounds 1-Benzylidene-2-(4-(4-bromophenyl)thiazol-2-yl)hydrazine, 2-(2-(4-(4-Bromophenyl)thiazol-2-yl)hydrazono)-1,2-diphenylethanol, 1-Cyclohexylidene-2-(4-(4-methoxyphenyl) thiazol-2-yl) hydrazine and 1-(4-(4-Bromophenyl) thiazol-2-yl)-2-cyclohexylidenehydrazine were showed magnificent anti-fungal action against all the strains.

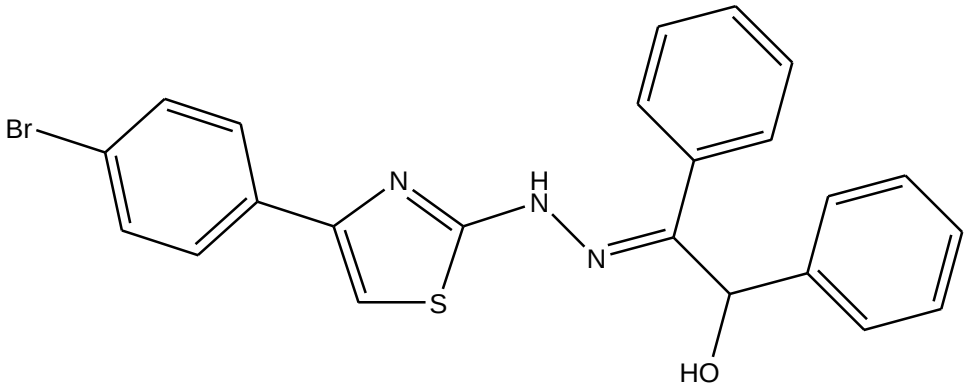

fig. 2.14 2-(2-(4-(4-Bromophenyl)thiazol-2-yl)hydrazono)-1,2-diphenylethanol

2.14 Arora Preeti*et al.*, synthesized different derivatives of N-(4-phenyl-thiazol-2-yl)-benzamide/amide, (3,4-dimethoxy-benzylidene)-(4-phenyl-thiazol-2-yl)-amine and 4-(4-nitro-phenyl)-thiazol-2-ylbenzamide derivatives and then evaluated these derivatives for their antimicrobial activity against *B. subtilis*, *E. coli*, *S. aureus*, *C.albicans* and *A. niger* by the tube dilution method.

Material and methods: In this author synthesized different derivatives of N-(4-phenyl-thiazol-2-yl)-benzamide/amide, (3,4 -dimethoxy-benzylidene)-(4-phenyl-thiazol-2-yl)-amine and 4-(4-nitro-phenyl)-thiazol-2-ylbenzamide by using 2-amino-4-phenylthiazole which was prepared by using acetophenone/p-nitroacetophenone, thiourea, ethanol and bromine. In next step author take 2-amino-4-phenylthiazole with an acid chloride in dry pyridine. Solid precipitates of N-(4-phenyl-thiazol-2-yl)-benzamide/amide derivatives were obtained. Then, these derivatives were reacting with veratraldehyde in the presence of acetic acid. The product was washed, filtered and recrystallized. The reaction was monitored through TLC and the structures of all the derivatives wereconfirmedby spectral analysis.

Result: The result showed that the compounds N-(4-Phenyl-thiazol-2-yl)-benzamide, N-(4-phenyl-thiazol-2-yl)-isonicotinamide, N-[4-(4-Nitro-phenyl)-thiazol-2-yl]-benzamide, 4-Methoxy-N-[4-(4-nitro-phenyl)-thiazol-2-yl]-benzamide and (3,4-Dimethoxy-benzylidene)-(4-phenyl-thiazol-2-yl)-amine have excellent antimicrobial activity and when they replaced $–NH_2$ group with phenyl ring it increased antimicrobial activity. Molecular docking studies result also gave the highest binding score of compounds N-[4-(4-Nitro-phenyl)-thiazol-2-yl]-benzamide and 4-Methoxy-N-[4-(4-nitro-phenyl)-thiazol-2-yl]-benzamide(-9.2 kcal/mol and -9.1 kcal/molindividually).

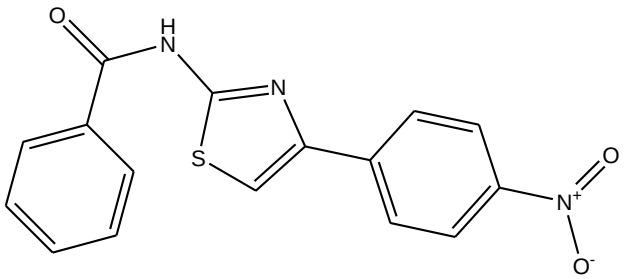

fig. 2.15a N-[4-(4-Nitro-phenyl)-thiazol-2-yl]-benzamide

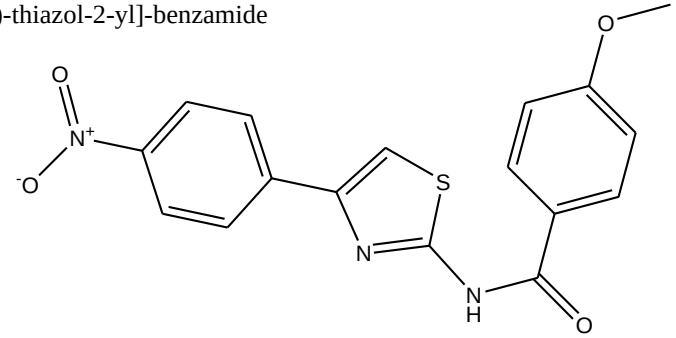

fig. 2.15b 4-Methoxy-N-[4-(4-nitro-phenyl)-thiazol-2-yl]-benzamide

2.15 SadekBassem*et al.,* synthesized different derivatives of 1,3-thiazole and then evaluated for their antimicrobial activity against Gram positive bacteria (*Staphylococcus aureus*), Gram negative bacteria (*Escherichia coli*) and the fungal strain (*Aspergillusniger*) by the cup plate method.

Material and methods: In this author synthesized different derivatives of 1,3-thiazole and benzothiazole by doing cyclocondensation of α-haloketones such as bromo with different thioamide derivatives under basic conditions. Then these derivatives were reactingwith BBr3 in dichloromethane. The reaction was monitored through TLC and the structures of all the derivatives wereconfirmedby spectral analysis.

Result: The result revealed that all the compounds showed moderate antimicrobial activity from which compound 2-(3-Hydroxyphenyl)benzo[d]thiazole showed great anti-bacterial activity.

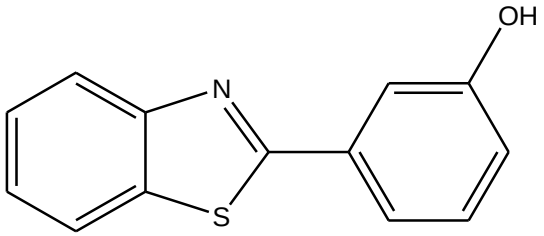

fig. 2.16 2-(3-Hydroxyphenyl)benzo[d]thiazole

2.16 SarojiniBalladkaKunhanna*et al.,* synthesized different derivatives of 2-substituted 4-(2,5-dichloro thienyl)-1,3-thiazoles and then evaluated these derivatives for anti-fungal activity against anti-fungal activity against *Aspergillusflavus*, *Aspergillusfumigatus*, *Penicilliummarneffei*and *Trichophytonmentagrophytes*and anti-bacterial activity against *Escherichia coli*, *Staphylococcus aureus*, *Psuedomonusaeruginosa* and*Klebsiellapneumoniae* by disc diffusion method.

Material and methods: In this author synthesized different derivatives of 2-substituted 4-(2,5-dichloro thienyl)-1,3-thiazoles by using 2-Bromo-1-(2,5-dichlorothien-3-yl) ethanone. 2-Bromo-1-(2,5-dichlorothien-3-yl) ethanone was prepared by adding bromine in (2,5-dichlorothien-3-yl) ethanone solution in acetic acid. Make a solution of 2-Bromo-1-(2,5-dichlorothien-3-yl) ethanone, ethanolic LOH and thioamide and the reaction mixture was refluxed for 3 hours. The product was washed, filtered and recrystallized. The reaction was monitored through TLC and the structures of all the derivatives wereconfirmedby spectral analysis.

Result: The result revealed that the compound 8-(4-(2,5-dichlorothiophen-3-yl)thiazol-2-yl)quinolineshowed excellent activity against all microbial strains. The Molecular docking study also showed minimum binding and docking energy for this compound.

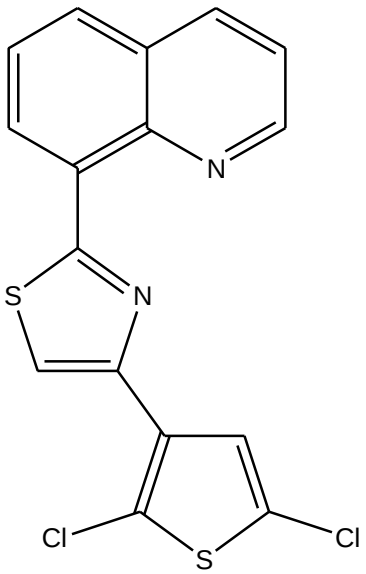

fig. 2.17 8-(4-(2,5-dichlorothiophen-3-yl)thiazol-2-yl)quinoline

2.17 Abdel-Hafez Sh H. *et al.,* synthesized different derivatives of 2-Amino-4-(4 -phenylsulfanyl-phenyl)-thiazole and then evaluated these derivatives for antimicrobial activity against two fungal strains(*Penicilliumoxalicum* and *Aspergillusparasiticus*), two Gram positive bacterial strains (*Streptococcus* and

Staphylococcusaureus) and two Gram negative bacterial strains (*Serratiamarcescems* and *Pseudomonas aeruginosa*) by using the filter paper disc method.

Material and method: In this author synthesized different derivatives of 2-Amino-4-(4 -phenylsulfanyl-phenyl)-thiazole by doing reaction between 4-chloroacetyl diphenyl sulfide and thiourea. Thiazolo-pyrimidines derivatives were prepared by reacting 2-Amino-4-(4 -phenylsulfanyl-phenyl)-thiazole with different arylidinemalonitriles and thiazolo-triazines derivatives were formed by reaction between schiff's bases and phenylisothiocyanate. The reaction was monitored through TLC and the structures of all the derivatives wereconfirmedby spectral analysis.

Result: The result revealed that the compounds 5-(3-(phenylthio)phenyl)thiazol-2-amine, 2-(3-(phenylthio)phenyl)-6H-thiazolo[3,2-a]pyrimidine-5,7-dione,5-amino-2-(3-(phenylthio)phenyl)-7H-thiazolo[3,2-a]pyrimidin-7-one and diethyl 5-(3-(phenylthio)phenyl)thiazol-2-ylcarbonodithioimidate showed both anti-bacterialandanti-fungalactivity from which the compound diethyl 5-(3-(phenylthio)phenyl)thiazol-2-ylcarbonodithioimidate showed maximum anti-bacterialactivity against all bacterial strains and compound 5-(3-(phenylthio)phenyl)thiazol-2-amine showed maximum anti-fungal activity against all fungal strains.

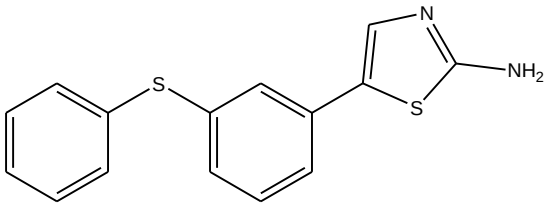

fig. 2.18a 5-(3-(phenylthio)phenyl)thiazol-2-amine

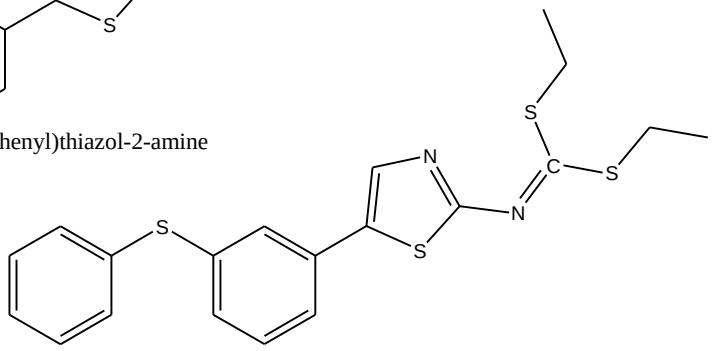

fig. 2.18b diethyl 5-(3-(phenylthio)phenyl)thiazol-2-ylcarbonodithioimidate

2.18 Al- Saadi Mohammed S. *et al.,* prepared different derivatives of 2,4,5-polysubstituted thiazoles and then evaluated these derivatives for their antimicrobial activity against two fungal strains (*Candida albicans* and *Aspergillusniger*), three gram negative bacterial strains (*Escherichia coli*, *Pseudomonas aeruginosa* and *Klebsiella pneumonia*) and three gram positive bacterial strains (*Staphylococcus aureus*, *Bacillus subtilis* and *Bacillus cereus*) by using the agar diffusion method.

Material and methods: In this author synthesized 2,4,5-polysubstituted thiazoles derivatives by warming thiazole with acetic anhydride and different aldehydes or any

different groups for 1 hour. The product was washed, filtered and recrystallized. The reaction was monitored through TLC and the structures of all the derivatives wereconfirmedby spectral analysis.

Result: The result revealed that the compounds 1-(2-acetamido-4-methylthiazole-5-carbonyl)-4-(4-fluorophenyl)thiosemicarbazide, 1-(2-acetamido-4-methylthiazole-5-carbonyl)-4-phenylthiosemicarbazide and 4-(4-fluorophenyl)-1-(2-(3-(4-fluorophenyl)thioureido)-4-methylthiazole-5-carbonyl)thiosemicarbazideshowed tremendousantimicrobial action against all bacterial and fungous strains.

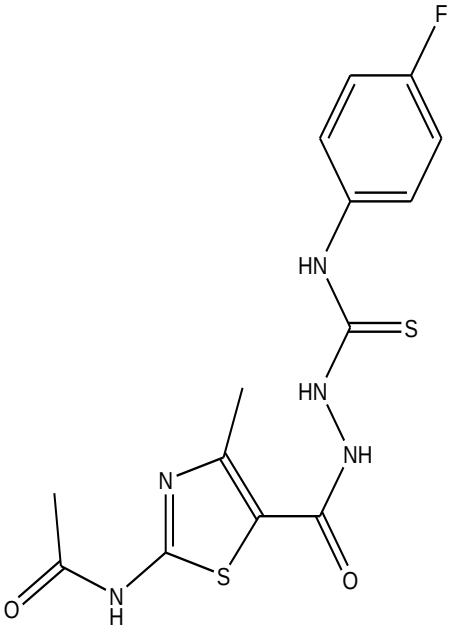

fig. 2.19a 1-(2-acetamido-4-methylthiazole-5-carbonyl)-4-(4-fluorophenyl)thiosemicarbazide

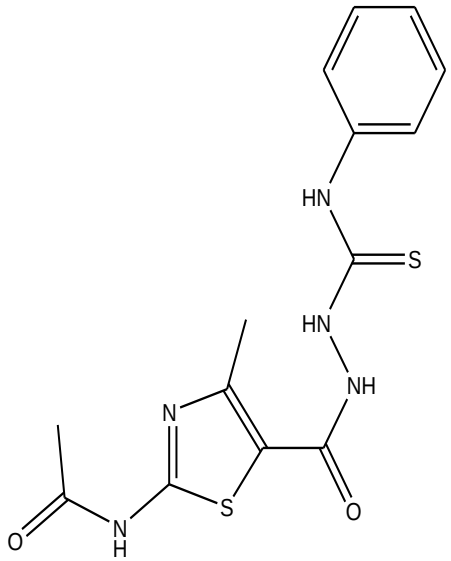

fig. 2.19b 1-(2-acetamido-4-methylthiazole-5-carbonyl)-4-phenylthiosemicarbazide

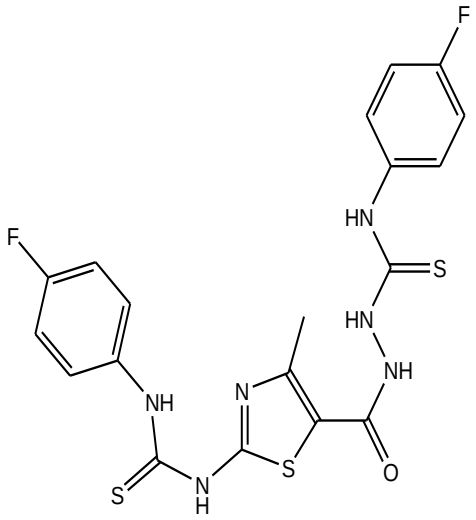

fig. 2.20c 4-(4-fluorophenyl)-1-(2-(3-(4-fluorophenyl)thioureido)-4-methylthiazole-5-carbonyl)thiosemicarbazide

2.19 PawarChandrakant D *et al.*, synthesized different derivatives of ethyl 2-(2-(4-substituted) acetamido)-4-subtituted-thiazole-5-carboxylate and then evaluated these derivatives for antimicrobial activity against three bacterial strains(Bacillus subtilis, Staphyllococcusaureus and Esherichia coli) and three fungal strains(Candida albicans, Aspergillusflavus and Aspergillusnigar) by the agar diffusion method.

Material and method: In this author synthesized different derivatives of ethyl 2-(2-(4-substituted) acetamido)-4-subtituted-thiazole-5-carboxylate by using reagents 2,6-leutidine, DMAP, di-chloromethane and Chloroacetyl chloride at temperature 0°c. The reaction was monitored through TLC and the structures of all the derivatives wereconfirmedby spectral analysis.

Result: The result revealed that the compounds 2-(2-(4-benzylpiperidin-1-yl)acetamido)thiazol-5-yl propionate, 2-(2-(4-benzylpiperidin-1-yl)acetamido)-4-cyclopropylthiazol-5-yl propionate, 2-(2-(4-benzylpiperidin-1-yl)acetamido)-4-phenylthiazol-5-yl propionate and 2-(2-(4-phenylpiperidin-1-yl)acetamido)thiazol-5-yl propionate showed excellent antimicrobial activity against all bacterial and fungal strains.

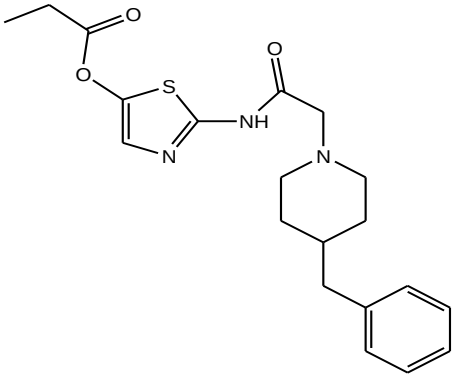

fig. 2.20a 2-(2-(4-benzylpiperidin-1-yl)acetamido)thiazol-5-yl propionate

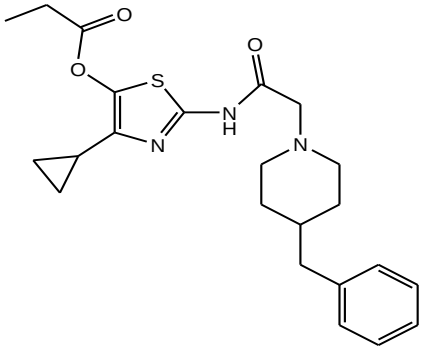

fig. 2.20b 2-(2-(4-benzylpiperidin-1-yl)acetamido)-4-cyclopropylthiazol-5-yl propionate

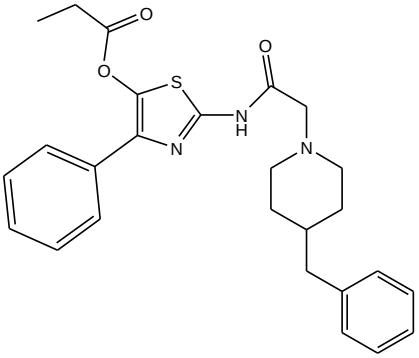

fig. 2.20c 2-(2-(4-benzylpiperidin-1-yl)acetamido)-4-phenylthiazol-5-yl propionate

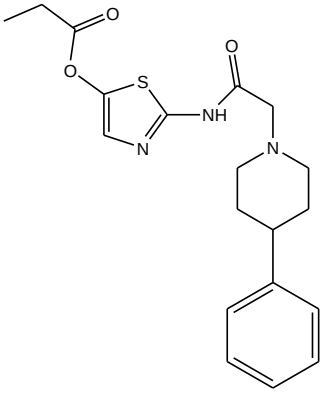

fig. 2.20d 2-(2-(4-phenylpiperidin-1-yl)acetamido)thiazol-5-yl propionate

2. Summary

Thizaole is an aromatic heterocyclic compound.Thiazole structure made up of three carbon atoms, with one nitrogen atom and with one sulfur atom which is arranged in the form of a ring. Thiazole is used in the manufacturing of an anti.microbial agents, anti-inflammatory agents, pesticides, insecticides dyeing agents, etc. various research has been done for thiazole as an antimicrobial agents such as in article 2.1 compounds5-Amino-2-oxo-7-phenyl-3,7-dihydro-2H-pyrano[2,3-d]thiazole-6-carbonitrile,5-Amino-7-(naphthalen-2-yl)-2-oxo-3,7-dihydro-2H-pyrano[2,3-d]thiazole-6-carbonitrile and 5-Amino-7-(2-hydroxynaphthalen-1-yl)-2-oxo-3,7-dihydro-2H-pyrano[2,3-d]thiazole-6-carbonitrile, in article 2.2 compound 1-[(5E)-4-[2-(3-{2-[(2E)-5-acetyl-2-[(Z)-2-[1-(pyridin-2-yl)ethylidene]hydrazin-1-ylidene]-2,3-dihydro-1,3,4-thiadiazol-3-yl]phenoxy}propoxy)phenyl]-5-[(Z)-2-[1-(pyridin-2-yl)ethylidene]hydrazin-1-ylidene]-4,5-dihydro-1,3,4-thiadiazol-2-yl]ethan-1-one, in article 2.3 compounds 6-phenylimidazo[2,1-b]thiazole-5-carbaldehyde and (E)-1-(furan-2-yl)-3-(6-phenylimidazo[2,1-b]thiazol-5-yl)prop-2-en-1-one, in article 2.4 compound 3-(4-Methyl-2-(methylamino)thiazol-5-yl)-7-phenyl-5H-thiazolo[3,2-a]pyrimidin-5-one, in article 2.5 compounds containing p-tolyl moiety, in article 2.6 compounds (2E,2Z)-5-((Z)-phenyldiazenyl)-2-(2-(2,3-dihydrothiochromen-4-ylidene)hydrazono)-4-methylthiazol-3(2H)-amine and (2E,2Z,NZ)-5-((Z)-phenyldiazenyl)-N-(3,4-dihydronaphthalen-2(1H)-ylidene)-2-(2-(2,3-dihydrothiochromen-4-ylidene)hydrazono)-4-methylthiazol-3(2H)-amine, in article 2.7 compound Ethyl 2-(2-(4-phenylthiazol-2-yl)hydrazono)propanoate, in article 2.8 compounds 2-chloro-3-(3-(2-chlorophenyl)-1-(4-(naphthalen-2-yl)thiazol-2-yl)-4,5-dihydro-1H-pyrazol-5-yl)quinolone, 2-chloro-3-(3-(2-fluorophenyl)-1-(4-(naphthalen-2-yl)thiazol-2-yl)-4,5-dihydro-1H-pyrazol-5-yl)quinolone and 2-chloro-3-(3-(3-fluorophenyl)-1-(4-(naphthalen-2-yl)thiazol-2-yl)-4,5-dihydro-1H-pyrazol-5-yl)quinolone, in article 2.9 compound N-(4-methylthiazol-2-yl)-2-(5-nitro-2,3-dihydrobenzo[d]oxazol-2-ylthio)acetamide, in article 2.10 compound 2-(4-Methylpiperazin-1-yl)-N-(thiazol-2-yl) acetamideand 2-(2-Methyl-1H-imidazol-1-yl)-N-(thiazol-2-yl), in article 2.11 compound 4-(1,10-Biphenyl-4-yl)-2-(2,3,5-trichlorophenyl)-1,3-thiazole, in article 2.12 compound 5-acetyl4-methyl-2-(3-pyridyl)thiazole, in article 2.13 compounds 2-[3-cyclopropyl-5-(p-substitutedphenyl)-4,5-dihydropyrazol-1-yl]-N-[4-(p-substitutedphenyl)-thiazol-2-yl]-acetamides, in article 2.14 compounds 2-(2-(4-(4-Bromophenyl)thiazol-2-yl)hydrazono)-1,2-diphenylethanol, 1-Cyclohexylidene-2-(4-(4-methoxyphenyl) thiazol-2-yl) hydrazine and 1-(4-(4-Bromophenyl) thiazol-2-yl)-2-cyclohexylidenehydrazine, in article 2.15 compounds N-[4-(4-Nitro-phenyl)-thiazol-2-yl]-benzamide and 4-Methoxy-N-[4-(4-nitro-phenyl)-thiazol-2-yl]-benzamide, in article 2.16 compound 2-(3-Hydroxyphenyl)benzo[d]thiazole, in article 2.17 compound 8-(4-(2,5-dichlorothiophen-3-yl)thiazol-2-yl)quinolone, in article 2.18 compounds 5-(3-(phenylthio)phenyl)thiazol-2-ylcarbonodithioimidateand5-(3-(phenylthio)phenyl)thiazol-2-amine, in article 2.19 compounds 1-(2-acetamido-4-methylthiazole-5-carbonyl)-4-(4-fluorophenyl)thiosemicarbazide, 1-(2-acetamido-4-methylthiazole-5-carbonyl)-4-phenylthiosemicarbazide and 4-(4-fluorophenyl)-1-(2-(3-(4-fluorophenyl)thioureido)-4-

methylthiazole-5-carbonyl)thiosemicarbazideand in article 2.20 compounds 2-(2-(4-benzylpiperidin-1-yl)acetamido)thiazol-5-yl propionate, 2-(2-(4-benzylpiperidin-1-yl)acetamido)-4-cyclopropylthiazol-5-yl propionate, 2-(2-(4-benzylpiperidin-1-yl)acetamido)-4-phenylthiazol-5-yl propionate and 2-(2-(4-phenylpiperidin-1-yl)acetamido)thiazol-5-yl propionate showed excellent antimicrobial activity. From the above articles it has confirmed that thiazole moiety has antimicrobial activity and we can prepare thousands of derivatives containing thiazole ring with good yield which may have high chances of antimicrobial activity.

3. CONCLUSION

Thizaole is an aromatic heterocyclic compound. Thiazole structure made up of three carbon atoms, with one nitrogen atom and with one sulfur atom which is arranged in the form of a ring.Thiazole is used in the manufacturing of an anti.microbial agents, anti-inflammatory agents, pesticides, insecticides dyeing agents, etc. From the above articles (2.1-2.20) it has confirmed that thiazole moiety has antimicrobial activity and we can prepare thousands of derivatives containing thiazole ring with good yield which may have high chances of antimicrobial activity.

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