JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

Synthesis of novel series of 3-(4,6-dimethyl pyrimidine-2-yl)-2-phenylthiazolidine-4-one analogous and Antimicrobial activity

J.JAGADEESH[1], Dr. KRISHNARAO [1*]

1*.Department of organic chemistry, PRISM PG&DG College (Affiliated to Andhra University), Visakhapatnam, India, 530016

ABSTRACT:

We have designed and synthesized a series of novel series of new 3-(4, 6-dimethylpyrimidine-2-yl)-2-phenylthiazolidine-4-one analogous synthesized by 2,6-dimethylpyrimidine-2-amine (1mmol) with mercaptoaceticacid (3mmol). and various substituted aromatic aldehyde (2mmol) in presence of DCC in MDC under reflux. The 2,6-dimethylpyrimidine-2-amine can be obtained from a mixture of acetyl acetone and guanidine in presence of methane sulfonic acid as catalyst as well as solvent at 1100C. These novel derivatives were evaluated by spectral data such as elemental analysis, 1H NMR and mass spectral data. In addition to the antibacterial and antifungal activity of these derivatives was evaluated against two Gram-positive bacteria (Staphylococcus aureus and Bacillus subtilis), two-Gram negative bacteria(Escherichia coli and Pseudomonas aeruginosa), and two fungal isolate (Candida albicans).examined by antimicrobial activity

KEYWORDS:

2,6-dimethylpyrimidine-2-amine,acetylacetone,guanidine,Methanesulfonicacid,Arylaldehyde, mercaptoaceticacid.

INTRODUCTION:

The chemistry of heterocyclic compounds is as logical as that of aromatic compounds. The study of heterocyclic compounds is of an interest both from the theoretical as well as practical importance. Various heterocyclic compounds such as alkaloids, essential amino acids, hemoglobin, hormones, vitamins, large number of synthetic drugs and dyes having heteroaromatic ring systems. There are large number of synthetic heterocyclic compounds, like furan, piperidine, pyridine, pyrrole, pyrrolidine, thiophene, and thiazole having important application & many are important intermediates in synthesis. Heterocyclic containing sulphur and nitrogen atoms in the core structure, it shows number of pharmacologically and biologically active compounds

Thiazolidine-4-ones are derivatives of thiazolidine which is five member heterocyclic rings with a thiogroup and amine group. Thiogroup are always in one, amine group at third position and keto group at fourth position. Thiazolidine-4-ones are usually solids, often melting with decomposition but the attachment of an alkyl group to the nitrogen lowers the melting point. Thiazolidine-4-ones are derivatives of thiazolidine

Thiazolidine-4-ones are important compounds due to their broad range of biological properties viz; Antibacterial**(1-5)**, Antimicrobial**(6-10)**,Antifungal**(3,6)**, Antioxidant**(11),** Analgesic**(7)**,Anti-inflammatory**(7)**,AntiYFV(yellowfevervirus)activity(2), Antitubercular(2,13), Cytotoxic(11),

We have designed and synthesized a series of novel series of new 3-(4, 6-dimethylpyrimidine-2-yl)-2-phenylthiazolidine-4-one analogous synthesized by 2,6-dimethylpyrimidine-2-amine (1mmol) with mercaptoaceticacid (3mmol). and various substituted aromatic aldehyde (2mmol) in presence of DCC in MDC under reflux. The 2,6-dimethylpyrimidine-2-amine can be obtained from a mixture of acetyl acetone and guanidine in presence of methane sulfonic acid as catalyst as well as solvent at 110^0C. These novel derivatives were evaluated by spectral data such as elemental analysis, 1H NMR and mass spectral data. In addition to the antibacterial and antifungal activity of these derivatives was evaluated against two Gram-positive bacteria (Staphylococcus aureus and Bacillus subtilis), two-Gram negative bacteria(Escherichia coli and Pseudomonas aeruginosa), and two fungal isolate (Candida albicans).examined by antimicrobial activity.

2. MATERIAL AND METHODS:

All chemicals, reagents and solvents were purchased from Merck chemicals. Melting points newly synthesized derivatives were determined by open capillary tubes on a MPA 120 –Automated Melting Points apparatus and are uncorrected. The ^{1}H-NMR spectra were recorded on Varian NMR 400 MHz spectrometer using TMS as internal standard and the chemical shifts are expressed in ppm. The products were purified by column chromatography using silica gel (100 meshes, S.D Fine, India). Thiazolidine4-one was prepared as, the two steps as stated below. Time-of-Flight Mass Spectrometer. The progress of the reaction was monitored on TLC, using pre-coated Kieselgel 60 F254 plates) and the compounds were visualized using UV light.The bacterial cultures were purchased from Microbial type Culture Collection, Institute of Microbial Technology, Chandigarh, India. Dimethyl sulfoxide (DMSO) and Streptomycin and Fluconozole) were used as negative and positive controls, respectively. The experiments were carried out in triplicates.

4.1. Preparation of 2,6-dimethylpyrimidine-2-amine(3):

The mixture of acetyl acetone **(1)** and guanidine **(2)** taken in dry and clean 100mL RBF.The catalytic amount of Methane Sulphonicacid introduced in a RBF and total set fitted on magnetic stirrer. The reaction maintained at 110^0C in two hours. The reaction mixture was monitored in TLC (ethylacetae: n-hexane).After completion of reaction, the reaction mixture poured in a ethylacetae in a beaker and extracted .The crude washed with a saturated solution of $NaHCO_3$.The crude separated from column chromatography and recrystallization with ethanol and get compound **(3)** as shown in **Scheme**-I.

Characterization of 2,6-dimethylpyrimidine-2-amine:

paleyellowsolid,yield-93%;^{1}HNMR(400MHz,$CDCl_3$)ppm:7.7.125(s,1H,Pyrimidinesring),6.127 (s,2H,NH_2),1.962(s,6H,$(CH_3)_2$).^{13}CNMR(100MHz,$CDCl_3$)ppm:160.08,157.92,120.15,23.92. LCMS(m/z):122.31(M^+-H): 128.41; molecular formulae: C_6H_9N.Elemental Analysis: calculated: C- 58.45, H-7.36 ,N-34.19 ; Obtained: C-58.38 ,H-7.35 ,N-58.48.

4.1.2Preparation of 3-(4,6-dimethylpyrimidine-2-yl)-2-phenylthiazolidine-4-one analogous:

General Procedure for the Synthesis of Compounds (6a–6l).

A solution of 2,6-dimethylpyrimidine-2-amine (1mmol) **(3)** and various substituted aromatic aldehyde (1.5mmol) **(4)** was stirred in MDC under RT conditions for 5min, followed by the addition of mercaptoaceticacid (2.5mmol) **(5)**. After 5 min, DCC (2mmol) was added to the reaction mixture at RT and the reaction mixture stirred for an additional 5 hr RT room temp. DCU was removed by filtration, the filtrate was concentrated to dryness under reduced pressure, and the residue was extracted with ethylacetate. The organic layer was successively washed 5% aqueous sodium hydrogen carbonate and then finally with brine. The organic layer was dried over sodium sulphate and the solvent was removed under reduced pressure to get desired the products **(6a–6f).**The progress of the reaction was monitored by TLC, using the solvent system Ethylacetate: Hexane (5:5).

4.1.3Characterization of 3-(4,6-dimethylpyrimidine-2-yl)-2-phenylthiazolidine:

1) 3-(4,6-dimethylpyrimidine-2-yl)-2-phenylthiazolidine-4-one(6a):

Colorlessolid,yield-79%;^{1}HNMR(400MHz,$CDCl_3$)ppm:7.38-7.26(m,5H,Ar-H),7.18(s,1H, Pyrimidinesring),6.15(s,1H,-CH-),3.42-3.23(m,2H,-CH-),1.87(s,6H$(CH_3)_2$).^{13}CNMR(100 MHz,$CDCl_3$)ppm:167.44,158.74,155.68,129.73,128.15,127.36,126.65,119.79,64.38,30.45,23.92.LCMS(m/z):128 .41; molecularformulae: $C_{15}H_{15}N_3O$3ElementalAnalysis: calculated: C- 63.13, H-5.30 ,N-14.73 ; Obtained: C-63.05 ,H-5.29 ,N-14.82.

2) 3-(4,6-dimethylpyrimidine-2-yl)-2(4-hydroxyphenyl)thiazolidine-4-one(6b):

Paleyellowsolid,yield-87%;^{1}HNMR(400MHz,$CDCl_3$) ppm:8.97 (s,1H,-OH),7.41-7.29(m,4H,Ar-H),7.20(s,1H,Pyrimidinesring),6.04(s,1H,-CH-),3.35-3.18(m,2H,-CH-),1.80(s,6H,$(CH_3)_2$). ^{13}CNMR(100MHz,$CDCl_3$)ppm:166.62,157.77,154.38,130.92,129.66,128.48,120.94,118.36,63. 62,31.58,23.19.LCMS(m/z):302.13(M^++H);Molecularformulae:$C_{15}H_{15}N_3O_2S$;Elemental Analysis :calculated:C-59.78,H-5.02,N-13.94; Obtained: C- 59.71,H- 5.01 ,N-14.06.

4)3-(4,6-dimethylpyrimidine-2-yl)-2-(4-hydroxy-3-methoxyphenyl)thiazolidine-4-one(6c):

Colourlesssolid,yield-87%;^{1}HNMR(400MHz,$CDCl_3$)ppm:9.16(s,1H,-OH),7.41(s,1H,Ar-H),7.27 (d,J=7.6Hz,1H,Ar-H),),7.14(s,1H,pyrimidine),6.89(d,J=8.0Hz,1H,Ar-H),6.04(s,1H,-CH-),3.542 (s,3H,-OCH_3),3.50-3.38(m,6H,$(-CH_3)_2$),1.873(s,6H,$(-CH_3)_2$);^{13}CNMR(100MHz,$CDCl_3$)ppm: 166.92,158.68,155.36,140.64,136.78,129.62,128.14,124.61,121.72,119.77,116.62,64.67,55.26,31.36,LCMS(m/z):

330.44(M-H);Molecularformulae:$C_{16}H_{17}N_3O_3S$;ElementalAnalysis:calculated: C-57.99 ,H-5.17,N-12.68 ;Obtained: C-57.92 ,H-5.16 , N-12.75.

5)3-(4,6-dimethylpyrimidine-2-yl)-2-(3,4,5-trimethoxyphenyl)thiazolidine-4-one(6d):

Colorlesssolid,yield-90%;^{1}HNMR(400MHz,$CDCl_3$)ppm:7.194(s,1H,pyrimidine),7.106-6.916 (m,2H,Ar-H),6.143(s,1H,-CH-),3.645(s,9H,$(OCH_3)_3$),3.462-3.286(m,2H,-CH_2),1.862(s,6H, $(CH_3)_2$);^{13}CNMR(100MHz,$CDCl_3$)ppm:166.16,158.74,155.28,150.62,135.34,130.54,128.64, 125.72,120.48,65.62,59.14,55.25,31.55,23.42;LCMS(m/z):375.05;Molecularformulae: $C_{18}H_{21}N_3O_4S$; Elemental Analysis: calculated: C-57.58,H-5.64,N-11.19 ; Obtained: C-57.50 ,H-5.63 ,N-11.28.

9)2-(4-chlorophenyl)-3-(4,6-dimethylpyrimidine-2-yl)-thiazolidine-4-one (6e):

colourlesssolid,yield-86%;^{1}HNMR(400MHz,$CDCl_3$)ppm:7.41-7.29(m,4H,Ar-H),7.22(s,1H, pyrimidinering),6.09(s,1H,-CH-),3.79-3.56(m,2H,,-CH_2-),1.98(s,6H,$(CH_3)_2$),^{13}CNMR (100MHz,$CDCl_3$)ppm:165.82,157.16,155.42,132.37,129.99,128.67,120.98,64.66,32.98, 23.09.LCMS(m/z):320.17(M+2);molecularformulae:$C_{15}H_{14}ClN_3OS$;ElementalAnalysis: calculated: C- 56.33 , H-4.41 ,N-13.14 ; Obtained: C-56.26,H-4.40 ,N-13.21

10) 2-(4-bromophenyl)-3-(4,6-dimethylpyrimidine-2-yl)-thiazolidine-4-one(6f):

paleyellowsolid,yield-85%;^{1}HNMR(400MHz,$CDCl_3$)ppm:7.62-7.41(s,2H,Ar-H),7.22(s,1H, pyrimidine),7.06(m,2H,Ar-H),6.12(s1H,-CH-),3.62-3.41(m,2H.-CH_2-),1.74(s,6H,$(CH_3)_2$); ^{13}CNMR(100MHz,$CDCl_3$)ppm:166.74,158.62,156.73,133.67,129.44,122.66,120.94,64.72, 31.09,22.96;LCMS(m/z):363.42(M+H);molecularformulae:$C_{15}H_{14}BrN_3OS$;ElementalAnalysis: calculated: C-49.46,H-3.86 ,N-11.61; Obtained: C-49.40,H-3.85 ,N-11.68.

11)3-(4,6-dimethylpyrimidine-2-yl)-4-oxothiazolidine-2-yl) benzonitrile (6g):

colourlesssolid,yield-80%;1HNMR(400MHz,CDCl3)ppm:7.71-7.41(m,4H,Ar-H),7.28(s,1H, Pyrimidines),6.15(s,1H,-CH-),3.77-3.61(m,2H,-CH_2-),1.87(s,6H,(CH3)$_2$),^{13}CNMR(100MHz, $CDCl_3$):166.98,159.42,157.36,130.76,129.62,126.08,121.48,117.66,64.76,32.61,23.53;LCMS (m/z):310.29(M^+);Molecularformulae:$C_{15}H_{14}N_4OS$;ElementalAnalysis:calculated:C-61.92,H-4.55 ,N-18.05;Obtained: C-61.86,H-4.54 ,N-18.13.

3. BIOLOGICAL EVALUATION:

3.2.1. Antibacterial assay: 100 mL sterile conical flask of nutrient broth was inoculated with the test organisms and incubated at 37^0 C over night. By using a sterile pipette, 0.6 mL of the broth culture of each test organism was added to 60 mL of molten agar, mixed well and maintained at 45^0C. Sterile agar test plates of each test organism were prepared by pouring inoculated medium with uniform thickness. The agar was allowed to set and harden and wells of 4 mm diameter were cut at equidistant using a sterile cork borer. Agar plugs were removed. 100 lg/mL of test solutions **(6a–l)** were prepared in DMSO and were introduced into the wells using micropipette. The plates were kept at room temperature for 2 h for better diffusion of solution into the medium. The plates were incubated for 36h at37^0C. After incubation the diameter of inhibitory zones formed around each well was measured in millimeter (mm) using antibiotic zone scale. The assay was carried out in duplicate.DMSO was used as control and the antibacterial activity of the test compounds was compared with standard **"Streptomycin**".

3.2.2. Antifungal assay

Sterile molten potato dextrose agar (PDA) medium was inoculated with 50 lL of fungal spore suspension aseptically and maintained at 45^0Ctemperature. The inoculated medium was mixed well and poured immediately in sterilized petriplates. Then five wells of 6 mm diameter were punched using sterile borer and filled with 100 lg/mL of test compounds **(6a-l)** as well as sterile DMSO 100% as negative control. Plates were incubated for 24 h at 37^0C. Antifungal activity was determined by measuring the zone of inhibition. The zones produced by the test compounds were compared with the "**ketoconazol"**.

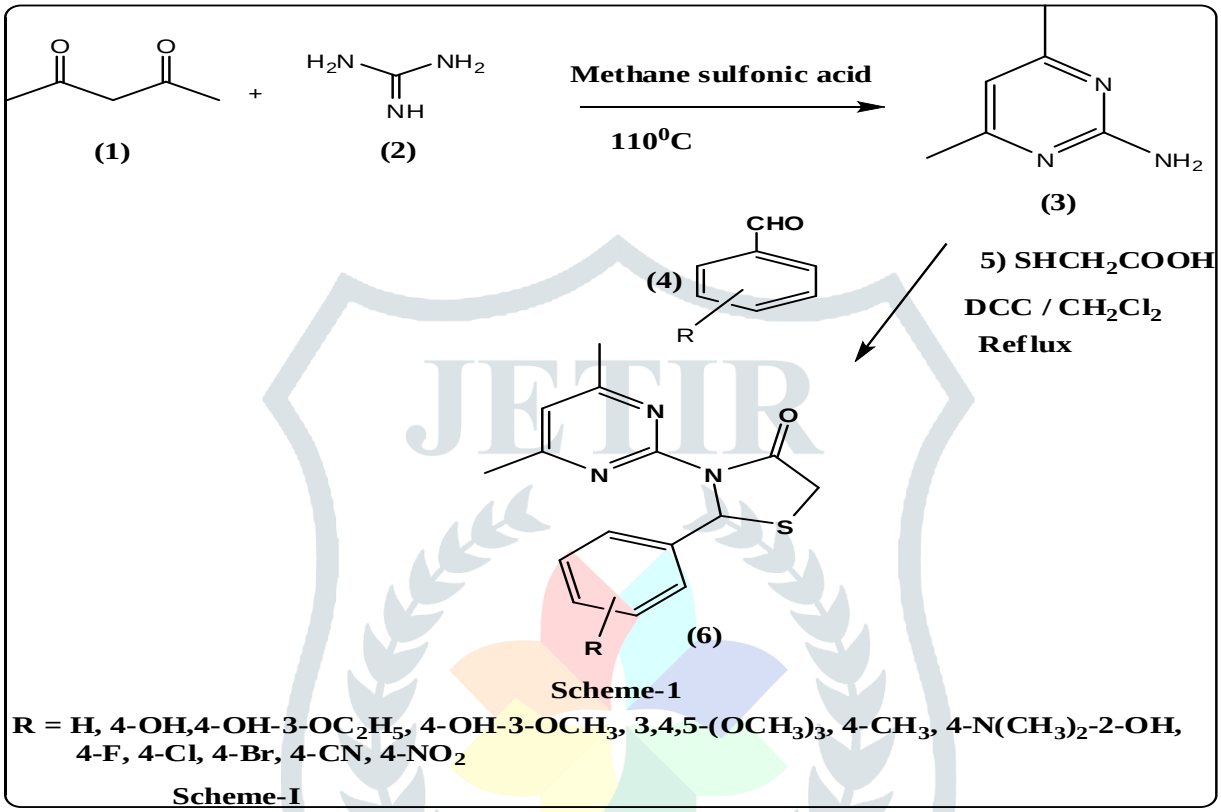
RESULTS AND DISCUSSION:

Chemistry:

3-(4, 6-dimethylpyrimidine-2-yl)-2-phenylthiazolidine-4-oneanalogous were synthesized in two steps. In the first step, 2, 6-dimethylpyrimidine-2-amine was synthesized by the reaction of 1,3-diketones(acetyl acetone)with guanidine in the presence of methanesulfonic acid. Finally, second step **(6a–6l)** were synthesized

by reaction of the compounds of 2,6-dimethylpyrimidine-2-amine with substituted aromatic aldehyde and mercaptoaceticacid acids, using DCC in CH_2Cl_2as intra molecular cyclizing agent at reflux as shown **scheme-I.**

In the first step, 2, 6-dimethylpyrimidine-2-amine was synthesized, the catalyst Bronstd acid can be used due it act as catalyst as well as solvent and it also be used for easy handling and workup during the reaction It is also commercial available ,the reaction condition enhanced by it.



Scheme-1

R = H, 4-OH,4-OH-3-OC_2H_5, 4-OH-3-OCH_3, 3,4,5-$(OCH_3)_3$, 4-CH_3, 4-$N(CH_3)_2$-2-OH, 4-F, 4-Cl, 4-Br, 4-CN, 4-NO_2

Scheme-I

In the step, the reagent DCC used, it is an intermolecular cyclizing reagent and it can dissolve in MDC, the reaction carried out RT to reflux during this reaction. The rate of reaction enhanced by this reagent and the yield of the product increased compared with other reagent such as CDI (carbonyl di imidazole) and dehydrating reagents as shown in **Table-I**.In this reaction, there are electron donating groups; electron withdrawing groups' substituted aromatic aldehyde can be used. The yield of the derivatives can be obtained whether the aromatic compound having electron donating group compared with electron withdrawing group.

Table-I : Reaction of 2, 6-dimethylpyrimidine-2-amine with 3, 4, 5-trimethoxybenzaldehyd *in* different catalyst in CH_2Cl_2 using at reflux.

Entry	Various Catalyst	Time(hrs)	Yield(%)

1	**CDI**	**6**	**75**
2	**DCC**	**3.5**	**90**
3	**P_2O_5**	**10**	**68**
4	**PTS**	**8**	**50**

For optimization of the amount of catalyst required for this reaction, 3, 4, 5-trimethoxybenzaldehyd was used as a model compound and different amounts of catalyst were tested under the same conditions. It was found that 2 mol% of catalyst was enough for a desired yield of the product **(Table -I1)**. On the other hand, an amount of catalyst more than 2 mol% did not increase the yield of desired product.

To examine the effect of solvent for this model reaction, we have also performed the reaction in different organic solvents reflux with 2 mol% of DCC. As shown in **Table-II**, DCM is most suitable solvent for this procedure. Consequently the reaction was carried out in DCM with 2 mol% of DCC for the preparation of titled compounds **(6a-6l)**.

Table-II: Reaction of 2, 6-dimethylpyrimidine-2-amine with 3, 4, 5-trimethoxybenzaldehyd *in* CH_2Cl_2 using different amounts of catalyst at reflux.

Entry	%Amount of catalyst	Time(hrs)	Yield(%)
1	**2**	**2.5**	**90**
2	**2.5**	**3.5**	**90**
3	**3.5**	**4**	**90**
4	**5**	**4**	**90**

Table-III: Reaction of 2, 6-dimethylpyrimidine-2-amine with 3, 4, 5-trimethoxybenzaldehyd using different solvents, prompted by DCC RT reflux**.**

Entry	Solvent	Time (hrs)	Yield(%)
1	**Ethanol**	**3**	**72**
2	**Methanol**	**4.5**	**68**
3	**DMF**	**3.5**	**73**
4	**Acetonitrile**	**5**	**76**
5	**CH_2Cl_2**	**2.5**	**90**

4.2. BIO EVALUATION:

4.2.1. Antimicrobial activity:

The newly synthesized and well characterized compounds (6a-l) were screened for in vitro antibacterial activity against Gram positive bacterium (Bacillus subtilis), Gram negative bacteria (Escherichia coli, Klebsiella pneumonia, Pseudomonas aureoginosa) and antifungal activity against Aspergillums Niger, Candida albicans using agar well diffusion assay and zones of inhibition of the test Compounds were expressed in mm as shown in Table.

4.2.2. Antibacterial activity:

The in vitro antibacterial activity of the newly synthesized derivatives **(6a-6l)** was compared with standard**" Streptomycin''** as collected in (**Table-IV).** .As indicated in **Table-IV,** most of the synthesized derivatives generally exhibited potent activity against all the tested bacterial strains. Compound **"6c and 6e"** showed excellent antibacterial activity against gram-positive bacterial strains viz; E.coli, P.aeruginosa and gram negative bacterial strains viz; B.subtilis, and Staphylococcus aureus with zones of inhibition of **20,19,2120** mm and **21, 20, 21,20mm** respectively. The compound 6jshowed good activity against the bacterial stains such as E.coli, B.subtilis, and Staphylococcusaureus are **21, 19** and **20**mm respectively. The derivatives 6b, 6d, 6g and 6h showed moderate active potent against bacterial stains. 6a,6k and 6l showed low activity against bacterial stains .These results reveals that the compounds having electron releasing groups showed good activity than the compounds having electron withdrawing groups.

Antifungal activity:

The in vitro antifungal activity of the newly synthesized derivatives **(6a-6g)** was compared with standard drug**" Ketonozole.''** as collected in (**Table-V).** The in vitro antifungal activity of the newly synthesized derivatives **(6a-6g)** was studied against A.ngier and C.albicans. Compound **6i** exhibited significant antifungal activity **(A. Niger, C.albicans and Aspergillusfavu**s,**)**. Compounds **6C** and **6f** showed significant activity against "A.ngier" than the fungal strain "C.albicans". 6**b** and 6**d** were found to be moderately active against tested fungal strain. Compounds **3a** have demonstrated significant antifungal activity comparable to standard. From the results it is evident that most of the compounds showed significant activity and few are moderately active as shown in **Table-V**.

Table-IV: Antibacterial activity of the newly synthesized compounds (6a-g):
Zones of inhibition (mm)[a] of compounds 6a–6l against tested bacterial strains and fungal strains:

Compound	Anti Bacterial Activity			
	Gram(+ve) bacteria		Gram(-ve) bacteria	
	E. c.	P.a.	B. s.	S.a.
6a	**09**	**11**	**10**	**13**
6b	**14**	**13**	**14**	**15**

6c	**20**	**19**	**21**	**20**
6d	**15**	**14**	**14**	**16**
6e	**21**	**20**	**21**	**20**
6f	**19**	**18**	**18**	**19**
6g	**18**	**16**	**15**	**19**
Streptomycin	**25**	**25**	**25**	**25**
DMSO				

Streptomycin was used as standard. a 100 lg/mL of compound in each well.

Values are average of three readings, Escherichia coli, Pseudomonas aureoginosa,B. s.-Bacillus subtilis , S. a-Staphylococcus aureus,

Table-V: Antifungal activity of the synthesized compounds (6a-g)
Zones of inhibition (mm)[a] of compounds (6a–6l) against tested fungal strains:

Entry	Antifungal activity		
	A .n.	**C.a.**	**A. f.**
6a	08	05	04
6b	18	16	17
6c	19	15	17
6d	18	15	14
6e	17	16	14
6f	19	14	15
6g	17	15	13
Ketonozole	22	22	22
DMSO			

Values are the average of three readings. Ketoconazol was used as standard.
a 100 lg/mL of compound in each well.
A .n,- Aspergillus Niger(NCIM-1375), C. a- Candida albicans(NCIM-2475),
A. f- Aspergillusfavus (NCIM-479).).

5. CONCLUSION:

In this study new heterocyclic compounds such as the thiazolidine-4-one structure from2, 6-dimethylpyrimidine-2-amin with substituted aromatic aldehyde and mercaptoaceticacid acids, using DCC in CH_2Cl_2as ntramolecularcyclizing agent at reflux . 2, 6-dimethylpyrimidine-2-amine was synthesized by the reaction of 1,3-diketones(acetyl acetone)with guanidine in the presence of Methanesulphonic acid. The structure of the new compounds was evaluated using spectral methods (^{1}H-NMR, ^{13}C-NMR, LCMS).the newly derivative evaluated there in vitro antibacterial as well as antifungal activities.

5. ACKNOWLEDGEMENTS

The authors gratefully acknowledge to the management of PRISM PG&DG College Visakhapatnam, India, for laboratory support. The authors also gratefully thank both referees for their helpful critical suggestions

REFERENCES:

1. R. C. Sharma and D. Kumar, "Synthesis of some newthiazolidin-4-ones as possible antimicrobial agents," *Journal ofIndian Chemical Society*, vol. 77, no. 10, pp. 492–493, 2000.
2. Vinita V mulwad, Abib Ali Mir, Hitesh T Parmar. Synthesis and antimicrobial screeningof 5-benzylidine-2-imino-3-(2-oxo-2H-benzopyran-6-yl)-thiazolidine-4-one and its derivatives. Ind J Chem, 2009, 48(B): 137-141.
3. Visagaperumal D, R Jaya Kumar, R Vijayaraj, N Anbalgan. Microwave induced synthesis of some new 3-substituted-1,3-thiazolidin-4-ones for their potent antimicrobial and antitubercular activities. Int J Chem Tech Res, 2009, 1(4): 1048-1051
4. Hui-Ling Liu, Zongcheng Li and Thorleif Anthonsen. Synthesis and fungicidalactivity of 2-imino-3-(4-arylthiazol-2-yl)-thiazolidine-4-ones and their 5-arylidenederivatives. Molecules, 2000, 5: 1055-1061.
5. Vandana Tiwari, Jyotsna Meshram, Parvez Ali. Microwave assisted synthesis Of quinolinyl thiazolidinones using Zeolite as an efficient and recyclable activationsurface: SAR and Biological activity. Der Pharma Chemica, 2010, 2 (3): 187-195.
6. Milan Cacic, Maja Molnar and Nela Draca. Design and synthesis of some thiazolidine--ones based on (7-hydroxy-2-oxo-2H-chromen-4-yl) acetic acid. Molecule, 2009, 14: 2501-2513
7. Kandapalli Venkata Gowri Cchandra Shekar, Vajja Sambasiva Rao. Solvent freemicrowave accelerated synthesis of heterocyclic thiazolidine-4-ones as antimicrobial and antifungal agents. Bull Korean Chem Soc, 2010, 35 (5): 1219-1222.
8. Gurupadyya BM, Gopal M, Padmashali B, and Manohara YN. Synthesis and pharmacologicalevaluation of azetidin-2-ones and thiazolidin-4-ones encompassing benzthiazole. Ind J Pharm Sci, 2008, 70 (5): 572-577.
9. Ketan Mistry and K R Desai. Microwave assisted rapid and efficient synthesis ofnitrogen and sulphur containing heterocyclic compounds and their pharmacologicalevaluation. Ind J Chem, 2006, 45(B): 1762-1766.
10. Sharanabasppa B Patil, Naganna M Goudgaon. Synthesis pf 3-(1-benzyl-1H-benzo [D] imidazole-2-L-amino)-2-(3-Aryl-1-phenyl-1H-pyrazol-4-yl) Thiazolidine-4-one and their antimicrobial activities. I J P S R, 2010, (1): 50-60.
11. Parmeshwaran Manojkumar, Gopalkrishnan Subbuchettiar. Synthesis

of coumarinheterocyclic derivatives with antioxidant activity and *invitro* cytotoxic activity against tumour cells. Acta Pharm, 2009, 59: 159-170.

12. Jubie S, Gowramma B, Nitin KM, Jawahar N, Kalirajan R, Gomathy S. Synthesis and biological evaluation of some 3-(methoxy phenyl)-2-aryl Thizolidin-4-one derivative.Ind J Pharma Sci, 2009, 1 (1): 32-38.
13. Dharmrajan sriram, Perumal Yogeeshwari, Ashok Kumar TG. Microwave-assistedSynthesis and anti YFV activity of 2,3-diaryl-1-3-thiazolidin-4-one. J Pharmaceut Sci, 2005, 8 (3): 426-429
14. Aamer Saeed, Naeem Abbas, Ulrich Florke. Synthesis and antibacterial activity ofsome novel 2-arollimino-3-aryl-thizolidin-4-one. J Braz Chem Soc, 2007, 18 (3): 559-565.
15. R. K. Rawal, Y. S. Prabhakar, S. B. Katti, and E. De Clercq,"2-(Aryl)-3-furan-2-ylmethyl-thiazolidin-4-ones as selectiveHIV-RT Inhibitors," *Bioorganic and Medicinal Chemistry*, vol.
16. 13, no. 24, pp. 6771–6776, 2005.
17. R. Ottaná, E. Mazzon, L. Dugo et al., "Modeling and biologicalevaluation of 3,3□-(1,2-ethanediyl)bis[2-(4-methoxyphenyl)-thiazolidin-4-one], a new synthetic cyclooxygenase-2 inhibitor,"*European Journal of Pharmacology*, vol. 448, no. 1, pp.71–80, 2002.
18. E. Piscapo, M. V. Diurno, R. Gagliardi, and O. Mazzoni,"Studies on heterocyclic ompounds: 1,3-thiazolidin-4-onederivatives. IV. Biological activity of variously substituted 2,3-diaryl-1,3-thiazolidin-4-ones," *Bollettino Della Societa Italianadi Biologia Sperimentale*, vol. 65, no. 9, pp. 853–859, 1989.
19. S. Desai, P. B. Desai, and K. R. Desai, "Synthesis of newheterocyclic thiazolidinone and azetidinone compounds andtheir anticancer activity," *Heterocyclic Communications*, vol. 5,no. 4, pp. 385–387, 1999.
20. R. B. Lesyk and B. S. Zimenkovsky, "4-thiazolidones: centenarianhistory, current status and perspectives for modern organicand medicinal chemistry," *Current Organic Chemistry*, vol. 8,no. 16, pp. 1547–1577, 2004.
21. M. V. Diurno, O. Mazzoni, F. Capasso, A. A. Izzo, andA. Bolognese, "Synthesis and pharmacological activity of2-(substituted phenyl)-32 or 3-[(4-substituted phenyl-4-hydroxy)piperidino]ethyl or propyl-1,3-thiazolidin-4-ones,"*Farmaco*, vol. 52, no. 4, pp. 237–241, 1997.
22. N. Ergenc and G. Capan, "Synthesis and anticonvulsant activityof new 4-thiazolidone and 4- thiazoline derivatives," *Farmaco*,vol. 49, no. 6, pp. 449–451, 1994.
23. S. Desai, R. Desai, and N. Chandra Desai, "Vitamin A interventionin the □ar Desert," *Indian Journal of Ophthalmology*, vol.51, no. 4, pp. 361–363, 2003.
24. R. C. Sharma and D. Kumar, "Synthesis of some newthiazolidin-4-ones as possible antimicrobial agents," *Journal ofIndian Chemical Society*, vol. 77, no. 10, pp. 492–493, 2000.
25. T. M. de Aquino, A. P. Liesen, R. E. A. da Silva et al., "Synthesis,anti-*Toxoplasma gondii* and antimicrobial activities of benzaldehyde4-phenyl-3-thiosemicarbazones and 2-

(phenylmethylene)hydrazono]-4-oxo-3-phenyl-5-thiazolidineaceticacids,"*ioorganicand Medicinal Chemistry*, vol. 16, no. 1, pp. 446–456,2008.

26. M. S. A. El-Gaby, G. A. M. El-Hag Ali, A. A. El-Maghraby,M. T. Abd El-Rahman, and M. H. M. Helal, "Synthesis,characterization and in vitro antimicrobial activity of novel2-thioxo-4-thiazolidinones and 4,4□-bis(2-thioxo-4-thiazolidinone-3-yl)diphenylsulfones," *European Journal of MedicinalChemistry*, vol. 44, no. 10, pp. 4148–4152, 2009.
27. K. G. Desai, J. P. Raval, and K. R. Desai, "Neat reactiontechnology for the synthesis of 4-oxo-thiazolidines derivedfrom 2-SH-benzothiazole and antimicrobial screening of somesynthesized 4-thiazolidinones," *Journal of the Iranian ChemicalSociety*, vol. 3, no. 3, pp. 233–241, 2006.
28. P. R. Kumar, M. S. Yadav, M. M. Kumar, and T. S. Rao, "Synthesisand antimicrobial activity of some new substituted aryloxy-4-thiazolidinones," *E-Journal of Chemistry*, vol. 3, no. 1, pp. 44–48,2006.