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Synthesis, Characterization, Docking study and Biological Activity of Some New Thaizolidine-4-one Derivatives

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Abstract:

The present study include the synthesis and characterization of some new Thiazolidine-4-one derivative condensation with primary amine (isonicotinic acid hydrazide, pyrazinoic acid hydrazide and sulphanilamide) in presence of formaldehyde via mannich reaction. The Prepared Compounds GS1-GS13 diagnosed by using IR, ^{1}H-NMR, Mass spectra and elemental analysis. Most of the synthesized compounds were sensitive against gram positive, gram negative bacterial and fungal strains. Among the synthesized molecules, Compound GS7 and GS11 exhibited promising inhibitory activity against all selected fungal strains and gram positive and gram negative bacteria. The in vitro Antioxidant activity of the compounds GS1-GS13 were evaluated by DPPH free radical scavenging assay. Maximum DPPH radical scavenging activity was observed in compound GS1 at 32 ug/ml. The molecular Docking results predicted that thiazolidine-4-one derivatives bind to the active site protein Shikimate kinase, NTMGAM's (PDB ID: 2QMJ) and L-Glutamine:D-fructose-6-phosphateamidotransferase with good interaction energy score for antitubercular, antidiabetic and antimicrobial activity.

Keywords: Thiazolidine-4-one, Antimicrobial, Antidiabetic, Antitubercular

Introduction:

The Chemistry of Heterocyclic Compounds is a logical as that of aliphatic or aromatic compound. There study is of great interest both from the theoretical as well as practical importance.[1] There are various organically dynamic particles containing five-member rings, containing two hetero molecules. Thiazolidines are a class of heterocyclic biological amalgams having a 5 membered saturated ring with a thio ether group at 1 position and an amine group in the 3 position[2,3]. Thiazolidine-4-ones containing thiazole moiety, it had been amalgamated by6-amino coumarin, isatin, primary amines and aromatic aldehydes. Thiazolidine-4-ones has been considered as a magic moiety because it possess almost all types of biological activities such as antifungal[4], antitubercular[5], antimicrobial[6], antioxidant[7], antibacterial[8], cytotoxic[9], anti-inflammatory[10,] analgesic[11], anti YFV (yellow fever virus) activities[12]. 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 with carbonyl group at the fourth position. The carbonyl group of thiazolidine-4-ones is highly un-reactive.[1] The thiazolidine ring has been incorporated into various type of biological compounds either a substituents group or a replacement of another ring. [13]

The aim of this work is to synthesized new compound of thiazolidine-4-one derivatives and studing the biological activity of them.

Experiment:

Melting points were determined by open capillary method on Veego (Model: VMP-D) electronic apparatus and are uncorrected. The IR spectra of the synthesized compounds were recorded Shimandzu 8400-SFT-IR Spectrophotometer using ATRA sampling Technique ^{1}HNMR spectra was obtained on Bruker AV III 500 MHz spectrometer spectra in $CDCl_3$ and chemical shifts are given in parts per million, downfield from Tetramethylsilane (TMS) as an internal standard Mass spectra were obtained from Bruker Impact HD 3050 system instrument at the SPPU, Pune to monitor the reaction as well as to established the identity and purity of reactant and Products, thin layer chromatography was performed on microscopic slides (2 x 7.5 cm) coated with silica gel G F254, using Benzene:Methanol (7:3) solvent system and the spot were visualized under ultra-violet light (254 nm) or exposure to iodine vapours.

Figure: 1

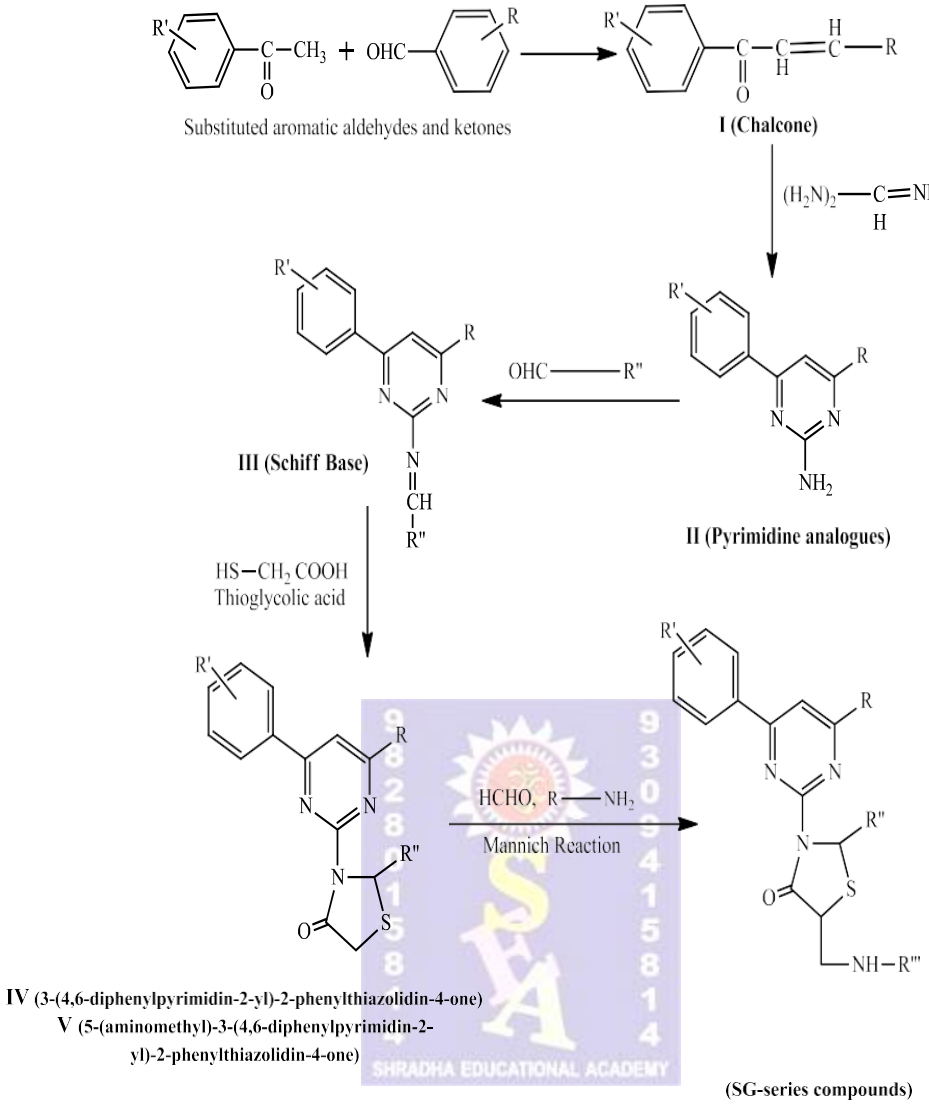


Figure1: (Synthesis of substituted thiazolidine-4-one)

Procedure:

STEP-I: General method for preparation of chalcones (I)

To a solution of 5.5g of sodium hydroxide in 50 ml of distilled water, 30ml of ethanol was added in the flask .The flask was immersed in a bath of crushed ice. After adding 0.1 mol of acetophenone (substituted),thenthemixture was stirred.Then 0.1 mol of aromatic aldehyde was added. This mixture was vigorously stirred for 2-3 h maintained at 25^0C. The reaction mix. After stirring the reaction mixture was kept in the ice chest for 24h & the solid obtained were filtered & washed using cold water until neutral to the litmus. Progress of reaction was monitored by TLC. On completion, there action mixture was neutralized by gradual addition of dil.hydrochloric acid with stirring until neutral to litmus. Crude product recrystallized using rectified spirit.

STEP-II: **General procedure for the preparation of pyrimidines (II)**

A mixture of appropriate chalcones and guanidine hydrochloride in absolute ethanol (10ml) were refluxed on a water bath. The progress of reaction was monitored by TLC. On completion the solvent was completely evaporated and the Residue was poured into ice cold water. The precipitated solid was collected by filtration.

STEP –III: Synthesis of Schiff base of 4-([1, 1'-biphenyl]-4-yl)-N-benzylidene-6-phenylpyrimidin-2-amine(III)

A mixture of 0.01 mol of pyrimidine and aldehyde (0.01 mol) and 2–3 drops of glacial acetic acid in ethanol was refluxed. The progress of reaction was monitored by TLC. The solvent was removed under reduced pressure to afford product Schiff base. Recrystallized from of rectified spirit.

STEP –IV: **Synthesis of - (3-(4, 6-diphenylpyrimidin-2-yl)-2-phenylthiazolidin-4-one)(IV)**

A mixture of appropriate (0.01 mol) **N**-(4-methoxy benzylidine)-4, 6-diphenylpyrimidine 2-amine, thioglycolic acid (0.015 mol) and a pinch of anhydrous ZnCl2 in dry 1, 4-dioxane was refluxed for 12–14 h. The reaction mixture was cooled and neutralized with 10% sodium bicarbonate solution. The separated solid was filtered and then washed with water and recrystallized from ethanol.

STEP–V Synthesis of (5-(aminomethyl)-3-(4,6-diphenylpyrimidin-2-yl)-2-phenyl thiazolidin-4-one) (V)

An equimolar quantity (0.004 mol) of substituted amine in 10 ml of ethanol was added to slurry containing product IV and aq. formaldehyde solution dissolve in10ml of ethanol. There action mixture was stirredfor1hat room temperature and refrigerated for 48 h the product was separated by suction filtration and recrystallize from ethanol.

Table 1. Physical and analytical data of synthesized selected Thiazolidine-4-one derivatives (GS-series)

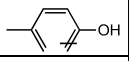
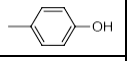
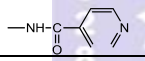
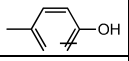
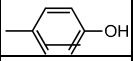
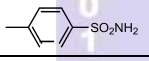
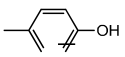
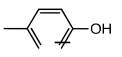
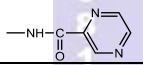
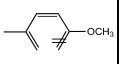
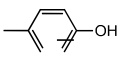
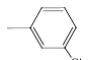
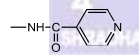
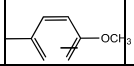
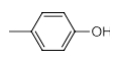
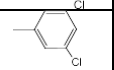
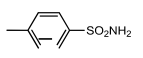
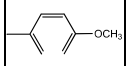
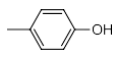
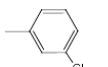
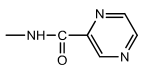
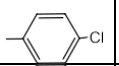
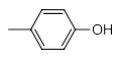
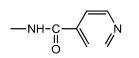
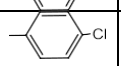
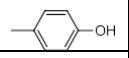
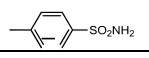
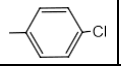
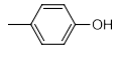
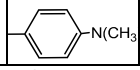
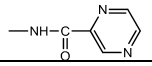
Sr .No	R	R’	R’’	R’’’	Comp Code	Mol.formula	Mol.Wt.	M.P (^{0}C)	R_f Value	% Yield
1	-H				GS1	C32H24N6O4SCl	623.45	101-103	0.56	74.84
2	-H				GS2	C30H23N7O4SCl	612.45	102-105	0.47	78.51
3	-H				GS3	C32H23N5O5S2Cl	670.44	108-110	0.53	68.52
4					GS6	C34H28N6O3SCl	635.45	109-111	0.50	62.54
5					GS7	C32H27N6O3SCl	610.45	115-117	0.58	78.24
6					GS8	C33H29N6O4S2Cl	672.45	119-121	0.54	64.36
7					GS11	C31H23N6O3S2Cl	629.9	120-122	0.60	68.57
8					GS12	C30H22N6O3SCl	616.9	125-127	0.53	69.43
9					GS13	C32H23N5O4S2Cl 2	675.9	124-126	0.51	61.98

Table 2. IR Spectral, ^{1}HNMR and Mass spectral Data of Selected Compound of GS series.

Compound	IR (KBr) cm^{-1}	^{1}H-NMR (δ ppm)	MS (FAB positive ion mode) m/z
GS1	3055.35 (Ar-CH), 1595.18(C=C Ar) , 1670.41(C=O), 3500-3000(Ar-OH), 3250.16 (N-H(Sec.	7.842 (1H NH), 7.260 (1H NH) 7.654 (2H Ar-H) 8.006 (2H Ar-H), 1.254 (2H CH_2), 0.869 (1H thazo.ring),	590.65

	Stretch) 1357.93 (Ar,ter. C-N amine) 1066.67 (N-N hydrizide) 3495.13 (NH str. Of hydrazide)	2.249 (1H thiazo.ring CH), 6.990 (2H Ar-H), 7.441(2H Ar-H) 5.310 (1H -OH), 7.561 & 7.457 (1H Ar-H), 7.532, 7.430 & 7.107 (1H Ar-H), 4.811 (1H, OH) 8.194 (1H Ar-H)	
GS11	3015.80 (Ar-CH), 1580.72 (C=C), 1646.30 (C=O), 3500-3000 (Ar-OH), 3229.91(NH stretch), 1344.43 (Ar-CN ter. Amine), 1090.78 (N-N hydrizide) 3401.58 (NH hydrizide), 747.44 (C-Cl)	6.0 & 5.4 (1H NH), 7.755 & 7.957 (2H Ar-H) 0.869 (2H CH_2) 1.240 & 2.61 (1H thiazo.ring) 6.883 & 7.521 (2H, Ar-H), 2.983 (CH_3 al) 7.385, 7.888, 6.923, 6.773, 7.478 (Ar-H), 5.10 (OH)	652.17
GS12	3191.33 (Ar-CH), 1588.43 (C=C), 1644.37 (C=O), 3500-3000 (Ar-OH), 3257.88 (NH sec.), 1342.50 (C-N amine), 1322.25 (S=Oasym), S=O (Sym), 1293.31 (Ar-CN ter.) 813.99 (C-Cl)	9.5-9.7 (2H SO_2NH_2), 7.961 & 7.891 (Ar-H), 3.085 (1H NH), 0.869 (2H CH_2), 1.299 (1H thiazo.ring CH), 2.598 (1H thiazo.ring CH), 6.884 (2H Ar-H), 7.485 (2H Ar-H), 5.431 (6H Ar-NH-CH_3), 6.580, 7.791, 6.771, 7.565 & 7.36 (1H Ar-H), 4.77 (1H OH)	687.23

Table 3. IR Spectral data of selected derivative of thiazolidine-4-one

Compound GS 2		Compound GS 3		Compound GS6		Compound GS7		Compound GS8	
Observed frequency(cm^{-1})	Infrared Assignments	Observed frequency (cm^{-1})	Infrared Assignments	Observed frequency (cm^{-1})	Infrared Assignments	Observed frequency(cm^{-1})	Infrared Assignments	Observed frequency(cm^{-1})	Infrared Assignments
3038.83	Ar-CH	3000.37	Ar-CH	3063.06	Ar-CH	3000	Ar-CH	3091.99	Ar-CH
1575.89	C=C(Ar)	1588.43	C=C(Ar)	1597.11	C=C(Ar)	1593.31	C=C(Ar)	1550.82	C=C(Ar)
1646.30	C=O	1666.55	C=O	1643.41	C=O	1683.94	C=O	1681.98	C=O
3500-3000	Ar-OH	3500-3000	Ar-OH	3500-3000	Ar-OH	3500-3000	Ar-OH	3541.42	Ar-OH
3261.74	NH(Sec.)	3200.01	NH(Sec.)	3209.66, 3147.93	NH(Sec.)	3211.59, 3279.32	NH(Primary Stretch)	1313.57	Ar-C-N (ter.mines)
1342.50	CN(Amines)	1277.88	Ar,C-N (ter. amines)	1365.65	Ar,C-N (ter.amines)	1360.68	CN(Amines)	1037.74	NNstr .hydrazide
1325.14	S=O asym.Str.	1090.78	N-Nstr.hydrazide	1091.75	NNstr.hydrazide	1317.23	S=Oasym.Str.	3400.62	-NHstr. hydrazide
1168.90	S=Osym.Str.	3399.65	-NHstr. hydrazide	3531.78	-NHstr. hydrazide	1148.41	S=Osym.Str.	775.41	C-Cl
1291.39	Ar,ter. –C-N			817.85	-C-Cl	825.44	-C-Cl		

Docking Study: [14-20]

Present study aim towards development of new therapeutic moieties containing thiazolidine-4-one for the treatment of Mycobacterium tuberculosis infection, diabetes mellitus, microbial infection. The Ligands were docked in the selected targets using the GRIP docking method from Vlife MDS. The ligands were docked in the active site for the targets which was identified using the co-crystal ligand from the PDB. The ligands were rotated by 15 degrees and an exhaustive methods was used to screen different poses of ligands using the PLP scoring function. The PLP scoring function provides a good weightage to the hydrogen bonding interactions which are the most desired interactions between the ligand and the target. **Antitubercular activity:** *Shikimate kinase* is an essential enzyme in several pathogenic bacteria and does not have any counter part

in human cells, thus making it an attractive target for the development of new antibiotics. The crucial interactions of the substrate and product binding and the enzyme activities that are essential for catalytic turnover of the Mycobacterium tuberculosis *shikimate kinase* enzyme (Mt-SK) have been investigated by structural and computational studies.**. Diabetes:** *(N-terminal maltase glucoamylase), Human maltase-glucoamylase* (MGAM) is one of the two enzymes responsible for catalyzing the last glucose-releasing step in starch digestion. Thus PDB ID 2QMJ was selected asatarget for docking of compounds for anti-diabetic screening **Antimicrobial:** *GlcN-6-P synthase* as described by the reported reference. The pdb enzyme file of receptor was downloaded from the RCSB Protein Data Bank (PDB code 1MOQ) and used as a fixed molecule. The docking study of the potent active thiazolidine-4-one derivatives toward antimicrobial species inside the active pocket of L-Glutamine:D-fructose-6-phosphate amido transferase, the active target for antimicrobial agents was explored. Results of docking study was depicted in **Table 4.**

Table 4. Docking score of thiazolidine-4-one derivative for Anti-Tubercular, Antidiabetic and Antimicrobial activity

Compound code	Tubercular Interaction	Antidiabetic activity	Antimicrobial activity
	Docking score	Docking score	Docking Score
GS1	-29.707261	105.811132	1.852601
GS2	-24.089490	12.450631	43.873639
GS3	-39.048571	104.183210	6.532034
GS4	15.267315	91.160337	110.941799
GS5	49.530517	156.411515	82.421198
GS6	43.425921	19.467906	-10.706952
GS7	-18.968123	97.746974	6.862944
GS8	12.991728	33.962804	55.064335
GS9	-21.772201	57.802448	35.561462
GS10	1.574863	14.724713	5.348551
GS11	41.891160	50.176605	77.665601
GS12	4.360460	55.398410	50.43.8341
GS13	97.159404	155.795102	130.629519

Biological Activity:

Antimicrobial Activity:

Determination of Zone of Inhibiton:

The zone of inhibition of selected test compound of AS and SA series against gram positive bacteria S. Aureus, S. epidermis and gram negative bacteria *Klebsiella, E.Coli* was determined by well diffusion method. In this assay measure diameter inhibition of zone using measuring device to each test substance required to inhibit the growth of micro-organism was determined. Standard Antifungal drug Fluconazole and standard Antibacterial drug Ciprofloxacin was tested at concentration of 10 ug/ml and 30 ug/ml. The plate were inspected visually to determine the growth of the organism as indicated by turbidity. Zone of Inhibition value of each tested compound were recorded in table. 5 & 6

Table 5: Results of zone of inhibition of bacteria of selected thiazolidine-4-ones

CompoundCode	Meanzoneof inhibition(inmm)			
	Gram+vebacteria		Gram–vebacteria	
	S.Aures	***S.Epidermis***	***Klebsiella***	***E.coli***

Conc.In□g/ml	75	50	25	10	5	75	50	25	10	5	75	50	25	10	5	75	50	25	10	5
GS1	17	15	13	10	8	17	16	14	12	9	29	26	22	18	13	15	10	-	-	-
GS2	21	19	17	9	-	21	20	16	10	-	43	39	35	29	24	23	21	10	-	-
GS3	23	20	18	15	10	23	20	18	15	12	40	38	35	30	24	25	22	20	10	-
GS6	20	18	14	13	11	20	17	13	11	10	40	38	35	30	24	13	10	-	-	-
GS7	24	21	18	10	7	24	20	16	14	8	40	38	35	30	24	12	-	-	-	-
GS8	25	22	20	18	13	25	23	20	17	12	38	33	29	25	20	10	-	-	-	-
GS11	17	14	13	10	5	18	15	12	8	5	40	37	33	29	25	12	-	-	-	-
GS12	15	13	10	8	-	15	13	10	8	-	45	40	38	30	26	25	22	20	10	-
GS13	24	22	20	17	15	26	24	21	18	15	42	39	35	30	28	28	23	19	14	-
Ciprofloxacin (10µg)	26					26					30					32				

Table 6: Results of zone of inhibition of fungi of selected thiazolidine-4-ones:

Compound Code	Meanzoneof inhibition(inmm)									
	A.niger					*A.flavus*				
Conc.In □g/ml	75	50	25	10	5	75	50	25	10	5
GS1	33	23	21	23	23	42	32	22	18	22
GS2	34	24	19	14	14	42	32	22	12	12
GS3	32	22	20	22	22	43	33	23	13	23
GS6	38	28	22	18	18	47	37	27	17	17
GS7	34	24	20	24	24	43	33	23	13	23
GS8	33	23	21	23	23	41	31	30	28	15
GS11	32	29	23	20	17	45	35	25	15	10
GS12	34	24	22	14	14	46	36	26	16	10
GS13	37	27	21	17	12	48	38	28	18	13
Fluconazole(30µg)	26					26				

Antioxidant Activity:

When DPPH reacts with antioxidant compounds, which can donate hydrogen, it is reduced. Succeeding the reduction, its deep violet color in methanol bleached to yellow, showing a significant absorption decrease at 517 nm. Then 3ml of various concentrations (2, 4,8,16 and 32 µg/ml) of the compounds (GS1-GS13) dissolved in ethanol were added to 1ml of ethanol solution of DPPH (40□g/ml). After a 30 minute incubation period at room temperature, the

absorbance was read against a blank at 517nm (Shimadzu UV-Vis spectrophotometer) Ascorbic acid was used as the reference compound. All tests and analyses were done in three replicates and the results were averaged. Free radical DPPH inhibition in percentage (AA %) was calculated as follows:

$$\text{Scavenging Effect (\%)} = \frac{\text{Absorbance}_{\text{Control}} - \text{Absorbance}_{\text{sample}}}{\text{Absorbance}_{\text{Control}}} \text{ X } 100$$

Table 7: Data of % Scavenging Activity at Different Concentrations for selected Thiazolidine-4-one

Sr.No	Sample	% Scavenging Activity At Different Concentrations				
		2µg/mL	4µg/mL	8µg/mL	16µg/mL	32µg/mL
1.	Ascorbic Acid	19.70±0.36	25.92±1.19	37.96±0.38	55.77±0.26	89.61±0.36
2.	GS1	19.28± 0.51	30.53***±0.55	32.72***±0.56	47.59***±0.84	83.54***±0.40
3.	GS2	18.50±1.82	30.12***±0.33	41.24***±0.61	56.21±0.77	62.22***±0.52
4.	GS3	18.49±1.82	25.63±0.40	32.61***±0.58	47.72***±0.71	63.62***±0.53
5.	GS6	17.48*±0.60	26.53±0.51	30.94***±0.51	39.21***±0.76	67.99***±0.63
6.	GS7	17.20**±0.80	32.59***±0.54	41.26***±0.54	53.81***±0.32	58.63***±0.77
7.	GS8	18.41±1.77	29.53***±0.43	39.6***±0.77	47.45***±0.71	59.06***±0.98
8.	GS11	27.2***±0.96	36.53***±0.70	43.16***±0.35	53.53***±0.30	67.19***±1.03
9.	GS12	19.75±0.13	29.05***±0.58	31.42***±0.61	38.64***±0.63	56.59***±0.72
10.	GS13	22.23**±1.27	36.13***±0.48	40.83***±0.67	57.26**±0.17	63.07***±0.68

Table 7: Data of IC50 of antioxidant activity for selected thiazolidine-4-one:

Sample	IC50µg/ml(n=6)						Mean ±SD
AA	14.3	14.35	14.22	14.27	14.02	14.23	14.23±0.11
GS1	15.9511	15.8072	15.9321	17.7092	16.18	16.003	16.1±0.71
GS2	21.28	21.23	21.684	20.001	20.89	21.07	21.00±0.56
GS3	21.28	21.23	20.684	20.88	20.29	21.07	20.90±0.37
GS6	20.26	20.19	21.48	21.51	21.55	21.38	21.06±0.65
GS7	20.45	20.38	19.66	20.45	20.44	19.99	20.22±0.33
GS8	20.17	20.81	20.21	20.81	22.75	21.52	21.04□0.97
GS11	21.77	21.85	20.87	21.96	22.75	21.52	21.78±0.61
GS12	25.82	26.72	25.86	25.87	24.92	25.97	25.86±0.57
GS13	26.41	26.22	26.72	27.07	26.31	26.3	26.50±0.32

Result and Discussion:

Initial chalcones were synthesized by using differently substituted acetophenone and aromatic

aldehyde following Claisen-Schmidt‟s condensation reaction. Substituted thiazolidine-4-ones were formed by condensing pyrimidines with appropriately substituted aldehyde to form Schiff base, followed by cyclization with thioglycolic acid. Finally the target compound 5-(amino methyl)-3-(4,6-diphenyl pyrimidin-2-yl)-2-phenyl thiazolidin-4-one) of 5-substituted thiazolidine-4-ones (GS1-GS13) were obtained by condensation with primary amine (isonicotinic acid hydrazide, pyrazinoic acid hydrazide and sulphanilamide) in presence of formaldehyde via well-known mannich reaction. Structures of all derivatives have been elucidated by ^{1}H-NMR, HRMS and IR spectral measurements. The results obtained from this study confirmed that the product has formed. The solid state IR (ATR, cm^{-1}) spectra of these compounds reveal a characteristic N-H (secondary stretch) 3200-3250.16of hydrazide and aromatic Stretch between 3150-3050 cm^{-1}. The amine group of thiazolidine ring (C-N) group present in the thiazolidine ring reveal peaks at 1350-1000 cm^{-1} .The C=C group of Aromatic ring showed stretching vibrations at around 1600and 1475cm^{-1}. C=O (ketone) group reveal peaks at 1725-1705 cm-1. The ^{1}H NMR spectra of all targetderivatives (GS1-GS21) were recorded in $CDCl_3$. ^{1}H NMR has revealed signal around at δ 3.50-3.64 accounting for thiazolidine nucleus. Signal for the aromatic protons were present in between δ 8 and 7. Thus, all the protons were accounted for the respective structures. Mass spectra were also in accordance with the proposed structures. Newly synthesized derivatives of selected GS1-GS13 were tested for in vitro Antibacterial, Antifungal and Antioxidant activity. From the structure of potent antimicrobial compounds amongst the synthesized series it has been observed that groups like–Cl,-OH and OCH_3 at substituent on phenyl ring as well as isonicotinic acid hydrazide/sulphanilamide on thiazolidine-4-one positively contributes for antimicrobial potential. GS3, GS8 and GS13exhibited promising activity GS1, GS2,GS7, GS11, GS12, exhibit moderate, activity against *S Aureus*. GS3, GS6, GS7,GS8, GS11 exhibit potent activity against *S. Epidermis* .GS2, GS3, GS6, GS7,GS8, GS11, GS12and GS13 exhibited promising activity against *Klebsiell* and GS2,GS3, GS12 and GS13 against *E. coli,* gram negative bacteria. The compounds GS1,GS2, GS3, GS6, GS7, GS8, GS11 GS12, and GS13 exhibited promising activity against fungi *A. niger* and *A. flavus*. The DPPH radical scavenging efficacy of GS1 analogue showing maximum effect of 83.54 %, respectively. Where as for its substituted counterpart and chloro analogue, the moderate free radical scavenging activity was GS7 (20.22□0.134) and 58.63 %, at a concentration of 32 µg/ml, respectively.

Molecular Docking and Scoring

Antitubercular activity of thiazolidine-4-one derivative done by docking 117 Ligands in the“Crystal Structure Of *Shikimate Kinase* From Mycobacterium Tuberculosis In Complex With Mg adp And Pt (Ii) At1.8 Angstrom Resolution”(PDB ID: 1L4U) using GRIP docking Facility of **Vlife MDS 4.3.** The PDB was cleaned and optimized before using for docking studies. The binding site was analyzed considering the Co-crystal ligand. According to co-crystal ligand, reported binding site includes GLY12, GLY14, SER 16, THR17, ARG 110, ARG117, ARG153. The Docking studies carried out on the Co-crystal ligand to *Shikimate Kinase* revealed that the binding modes of the compounds to the target. The docking scores ranging from-59.08 to-35.44 which indicate that all the compounds have good binding *Shikimate Kinase*. The analysis of the docking results of the co-crystal with the *Shikimate Kinase* indicates major Hydrogen bonding interactions with GLY12, LYS15, SER 16 and THR17 Charge Interaction with ARG110 and hydrophobic interactions GLY12,THR17, ARG110 and PRO155 residues of *Shikimate Kinase*. The docking scores and the interactions of top scoring compounds are as indicated in Table 4. The best docked pose of the molecule GS12 is as shown in **Figure 2**. PDB ID 2QMJ was selected as a target for docking of compounds for anti-diabetic screening. The results of docking study are depicted in Table 2. For Antimicrobial activity The docking study of the potent active derivatives toward antimicrobial species inside the active pocket of L-Glutamine:D-fructose-6-phosphate amido transferase, the active target for antimicrobial agents was explored. As

described by the X-ray study, the binding pocket of target enzyme including the following subsequent residues, cysteine300, glycine301, threonine302 serine303, serine347, glutamine348, serine349, threonine352, valine399, serine401, alanine602 and lysine 603 as shown in Figure 3.

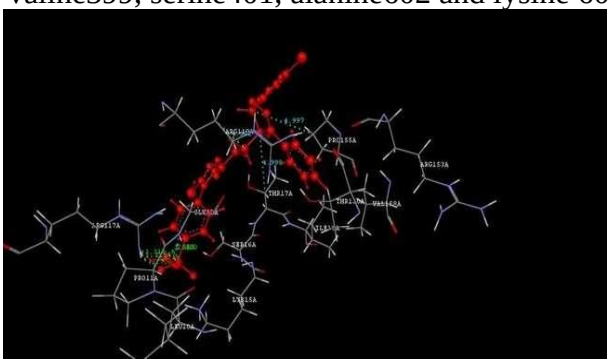


Figure 2: Docking interactions for the GS 13 molecule with Shikimate Kinase (RED colour ball and stick)

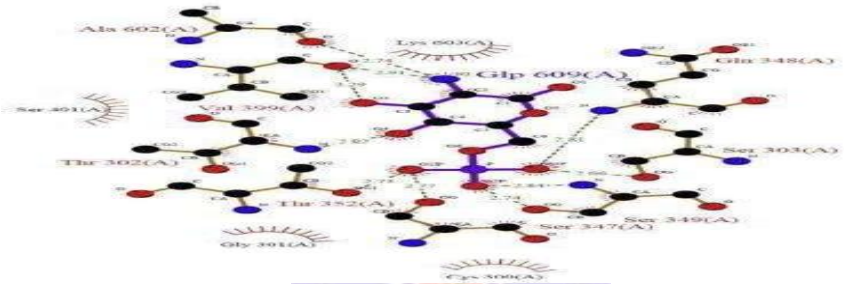


Figure 3: The binding of glucoASmine-6-phosphate inside the active site of target enzyme

Conclusion:

The present study includes the synthesis and characterization of some new thiazolidine-4-one derivative through condensation with primary amine (isonicotinic acid hydrazide, pyrazinoic acid hydrazide and sulphanilamide) in presence of formaldehyde via mannich reaction. These compounds were characterized with various spectral method like IR and ^{1}HNMR. The obtained result indicated that the synthesized compound possessed relatively high to moderate Antioxidant, Antibacterial and antifungal activity. groups like–Cl,-OH and OCH_3 at substituent on phenyl ring as well as isonicotinic acid hydrazide/sulphanilamide on thiazolidine-4-one positively contributes for antimicrobial potential. The selected derivative of GS1-GS13 screened for Anti-tubercular and Anti-diabetic activity using GRIP docking method from Vlife MDS. As we consider all result obtained from Antibacterial, antifungal and docking studies together we can say the thiazolidine -4-one derivative are active bacteria and fungi.

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