Journal of the Korean Chemical Society
2012, *Vol. 56, No. 3*
Printed in the Republic of Korea
http://dx.doi.org/10.5012/jkcs.2012.56.3.341

Synthesis and Antimicrobial Evaluation of Some Novel 2-(4-Chlorophenylimino) thiazolidin-4-one Derivatives

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(Received February 6, 2012; Accepted May 7, 2012)

ABSTRACT. A series of 2-(4-chlorophenylimino)-5-((3-(*p*-substituted phenyl)-1-phenyl-1*H*-pyrazol-4-yl) methylene) thiazolidin-4-one (**3a-h**) compounds were prepared from the 2-(4-chlorophenylimino) thiazolidin-4-one (**1**) and 1-phenyl-3-(*p*-substituted phenyl)-1*H*-pyrazole-4-carbaldehyde (**2a-h**). All compounds were characterized by elemental (C, H, N) analysis and spectral (FT-IR, ^{1}H NMR and GC-MS) analysis. These newly synthesized compounds were screened for their antibacterial and antifungal activities. Antimicrobial activity was observed and evaluated against the bacterial strains like *Escherichia coli* (MTCC 443), *Pseudomonas aeruginosa* (MTCC 1688), *Staphylococcus aureus* (MTCC 96), *Streptococcus pyogenes* (MTCC 442) and against the fungal strains like *Candida albicans* (MTCC 227), *Aspergillus niger* (MTCC 282) and *Aspergillus clavatus* (MTCC 1323). All the synthesized compounds were found to possess moderate to excellent antimicrobial activity against above selected strains.

Key words: 2-(4-Chlorophenylimino) thiazolidin-4-one, Antibacterial activity, Anti fungal activity, Vilsmeier-Haack reaction, Knoevenagel condensation reaction

INTRODUCTION

For more than a century, heterocyclic compounds are known to have significant and important place in organic chemistry. These compounds are the part and parcel of many important biochemical processes and are the constituents of main compounds like DNA, RNA, amino acids, purines, pyrimidine bases and vitamins in live cells. It has been established that more than half of the therapeutic agents available till date consist of sulphur and/ or nitrogen containing heterocyclic moieties and these have dragged the attention of chemists due to their broad spectrum biological activities and usage in various fields of pharmacy.

The biological and therapeutic properties of thiazolidinone have immensely initiated the synthesis of many derivatives of this moiety. 4-thiazolidinone derivatives are well known for their variety of pharmacological properties such as antibacterial,[1] anticonvulsant,[2] sedative,[3] antimycobacterial,[4,5] anti-tuberculosis,[6,7] anti-inflammatory,[8-10] anti-HIV,[11-13] anti tumor,[14] anti diabetic activity.[15,16]

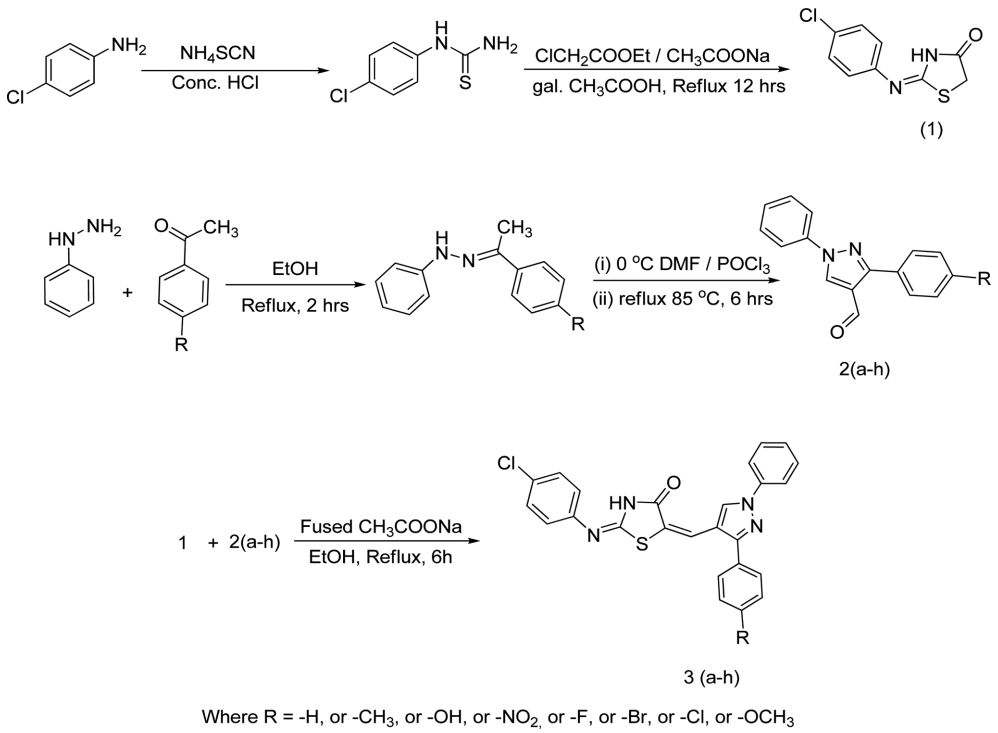
It is always interesting for medicinal chemist to synthesize more potent compounds. Various derivatives of pyrazoles are already synthesized and screened for various pharmacological activities like antimicrobial,[17-21] anticonvulsant,[22] anti inflammatory,[23-25] antimalerial[26] and antiviral activity.[27]

Looking to the importance of above mentioned thiazolidin-4-one derivatives, we intend to synthesize new entities like 2-(4-chlorophenylimino)-5-((3-(*p*-substituted phenyl)-1-phenyl-1*H*-pyrazol-4-yl)methylene)thiazolidin-4-one (**3a-h**) using 2-(4-chlorophenylimino) thiazolidin-4-one (**1**) and 1-phenyl-3-(*p*-substituted phenyl)-1*H*-pyrazole-4-carbaldehyde (**2a-h**).

RESULTS AND DISCUSSION

Chemical Characterization

In the present investigation, we have synthesized, characterized the novel 2-(4-chlorophenylimino)-5-((3-(*p*-substitutedphenyl)-1-phenyl-1*H*-pyrazol-4-yl)methylene) thiazolidin-4-one (**3a-h**) derivatives and studied their antimicrobial activity. 4-chloro aniline was reacted with ammonium thiocyanate to produce 4-Chlorophenyl thiourea, which was further reacted with mono chloro acetic acid to produce 2-(4-chlorophenylimino) thiazolidin-4-one (**1**). 1-phenyl-3-(*p*-substituted phenyl)-1*H*-pyrazole-4-carbaldehyde (**2a-h**) compounds were synthesized from *p*-substituted acetophenone, phenyl hydrazine, phosphorous oxychloride and formaldehyde using the Vilsmeier-Haack reaction. Substituted acetophenone was reacted with phenyl hydrazine to produce hydrazones, which was further



***Scheme* 1.** Schematic representation of synthesis of 2-(4-chlorophenylimino)-5-((3-(p-substituted phenyl)-1-phenyl-1*H*-pyrazol-4-yl) methylene) thiazolidin-4-one (**3a-h**).

reacted with formylating solution (Dimethyl formamide and phosphorous-oxychloride solution) to produce 1-phenyl-3-(*p*-substituted phenyl)-1*H*-pyrazole-4-carbaldehyde. 2-(4-chlorophenylimino) thiazolidin-4-one (**1**). 1-phenyl-3-(*p*-substituted phenyl)-1*H*-pyrazole-4-carbaldehyde (**2a-h**) were subjected to Knoevenagel condensation reaction to produce 2-(4-chlorophenylimino)-5-((3-(*p*-substituted phenyl)-1-phenyl-1*H*-pyrazol-4-yl) methylene) thiazolidin-4-one (3a-h) (*Scheme* 1). All the synthesized compounds were characterized by elemental analysis, FT-IR, NMR and Mass spectroscopy. The IR Spectra of synthesized compounds (**3a-h**) is interpreted by assigning expected bands to the synthesized compounds. The band observed around 1360-1320 cm^{-1} is attributed to C=S stretching vibration of thiazole ring and bands at ~1600-1510 cm^{-1} is attributed to C=N stretching vibration of pyrazole moiety. Strong band in the region 1725-1670 cm^{-1} is attributed to -C=O stretching of thiazolidinone ring. ^{1}H-NMR and Mass spectral data of compound (**3a-h**) are shown in characterization data of Experimental section. Chemical shift δ at around 8.66-8.60 ppm is due to the presence of -C=CH group in pyrazole ring. The entire series compounds were quantitatively analyzed for C, H, and N and results were found satisfactorily.

Antimicrobial Evaluation

Antimicrobial drugs known for high potential therapeutic characteristics are always in demand. To establish newly synthesized entities as potential therapeutic candidates appropriate scientific loom, perfect experimental set ups and precisely planned execution of methods is required. Antimicrobial activity of synthesized compounds was performed against four different bacterial strains like, *E.coli, P.aeruginosa, S.aureus* and *S.pyogenes* and three different fungi like, *C.albicans, A.niger* and *A.clavatus*. Ampicillin and Griseofulvin were used as positive control drugs for selected bacteria and fungi respectively. Solvent control was also studied to know the effect of solvent on activity on selected microorganisms.

Antibacterial Activity

The results of antibacterial screening of newly synthesized compounds are presented in *Table* 1. Results reveal that four selected bacterial strains like, *E. coli, P. aeruginosa, S. aureus and S. pyogenes* has shown different patterns of activities against the control drugs. For, *E. coli*, compound 3e (R'=4-F) possessed good activity, while compounds 3c, 3d, 3f and 3h (R'=4-OH, 4-NO_2, 4-Br and 4-OCH_3 respectively) possessed moderate activity when

***Table* 1.** Antibacterial and Antifungal activity of compounds **(3a-h)**

		Bacterial Strains				Fungal Strains		
		E. coli (MTCC 443)	*P. aeruginosa* (MTCC 1688)	*S. aureus* (MTCC 96)	*S. pyogenes* (MTCC 442)	*C. albicans* (MTCC 227)	*A. niger* (MTCC 282)	*A. clavatus* (MTCC 1323)
Comp. Code	-R	Minimum Inhibition Concentration (MIC) µg/ml						
3a	-H	500	500	200	200	250	500	>1000
3b	$-CH_3$	500	500	250	250	500	500	1000
3c	-OH	250	250	500	500	1000	>1000	>1000
3d	$-NO_2$	200	250	1000	1000	250	500	500
3e	-F	100	100	250	500	500	500	500
3f	-Br	250	250	500	500	500	>1000	>1000
3g	-Cl	500	250	500	500	250	500	1000
3h	$-OCH_3$	250	200	200	100	100	500	500
Ampicillin		100	100	250	100			
Griseofulvin						500	100	100

compared to the standard drug ampicillin. In case of *P. aeruginosa*, compound 3e (R'=4-F) showed good activity while compounds 3c, 3d, 3f, 3g and 3h (R'=4-OH, 4-NO_2, 4-Br, 4-Cl and4-OCH_3 respectively) showed moderate activity when compared to the standard drug ampicillin. Compounds 3d possessed excellent activity and compounds 3a, 3b, 3e and 3h (R'=4-H, 4-CH_3, 4-F and 4-OCH_3 respectively) possessed good activity when compared to the standard drug ampicillin in case of *S. aureus*. For, *S. pyogenes*, compound 3h (R'=4-OCH_3) possessed good activity while compound 3a and 3b (R'=4-H and 4-CH_3) possessed moderate activity as compared to the standard drug ampicillin. Out of all the synthesized compounds, compound 3h showed good activity for all bacterial strains as compared to parent compounds 1 and 2g (*Fig.* 1). However the other synthesized compounds showed specificity towards a particular microbial strain thereby revealing a random inhibition potential pattern

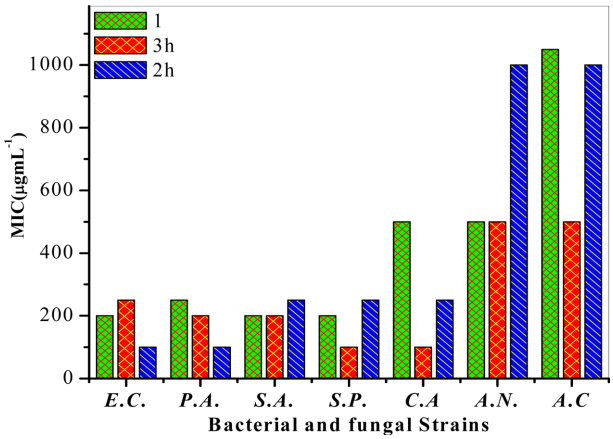


***Fig.* 1.** Comparative Study of Antibacterial activity for compounds 3h, 2h and 1.

when compared with their parental compounds (1 and 2g) (*Table* 2).

Antifungal Activity

Antifungal screening of data of newly synthesized compounds are reported in *Table* 1. To carryout antifungal study, three different fungal strains like *C. albicans, A. niger, and A. clavatus* were selected. For, *C. albicans,* compound 3h (R'=4-OCH_3) possessed excellent activity, compounds 3a, 3d and 3g (R'=4-H, 4-NO_2 and 4-Cl respectively) possessed very good activity, compounds 3b, 3e and 3f (R'=4-CH_3, 4-F and 4-Br respectively) possessed good activity, while compounds 3b, 3e and 3f (R'=4-CH_3, 4-F and 4-Br respectively) possessed moderate activity as compared to the standard drug, Griseofulvin. Amongst all the synthesized compounds, compound 3d (R'=4-NO_2) 3g (R'=4-Cl) and 3h (R'=4-OCH_3) showed good to very good activity for all fungal strains compared to parent compounds (1 and 2g) (*Fig.* 1). However, the other synthesized compounds showed specificity towards particular microbial strain thereby revealed random inhibition potential behavior when compared to their parental compounds (1 and 2g) (*Table* 2).

CONCLUSION

Novel series of 2-(4-chlorophenylimino)-5-((3-(*p*-substituted phenyl)-1-phenyl-1*H*-pyrazol-4-yl)methylene)thiazolidin-4-one (3a-h) compounds were synthesized from 2-(4-chlorophenylimino) thiazolidin-4-one (**1**) and 1-phenyl-3-(*p*-substituted phenyl)-1*H*-pyrazole-4-carbaldehydes (**2a-h**). Analytical and spectral data obtained (CHN/S and FT-IR, ^{1}H-NMR, GC-MS) for all the synthesized com-

***Table* 2.** Antibacterial and Antifungal activity of the synthesized compounds **[(1) and (2a-h)]**

		Bacterial Strains				Fungal Strains		
		E. coli (MTCC 443)	*P. aeruginosa* (MTCC 1688)	*S. aureus* (MTCC 96)	*S. pyogenes* (MTCC 442)	*C. albicans* (MTCC 227)	*A. niger* (MTCC 282)	*A. clavatus* (MTCC 1323)
Compound Code	-R	Minimum Inhibition Concentration (MIC) μg/ml						
1		200	250	200	200	500	500	>1000
2a	-H	50	200	200	200	500	>1000	>1000
2b	$-CH_3$	100	200	200	200	250	500	500
2c	-OH	200	200	250	250	500	1000	1000
2d	$-NO_2$	250	250	500	500	500	>1000	>1000
2e	-F	500	500	250	250	500	1000	1000
2f	-Br	200	250	100	200	>1000	500	500
2g	-Cl	250	250	250	250	>1000	200	200
2h	$-OCH_3$	100	100	250	250	250	1000	1000
Ampicillin		100	100	250	100			
Griseofulvin						500	100	100

pounds were in full conformity with their proposed structures. Comparison of the antimicrobial results of synthesized compounds (**3a-h**), it is concluded that the pyrazole derivatives of 2-(4-chlorophenylimino) thiazolidin-4-one (**1**) has improved their antimicrobial activity when compared with parent compounds. Most of the compounds were found to be active against tested micro-organism. A series of 2-(4-chlorophenylimino)-5-((3-(*p*-substituted phenyl)-1-phenyl-1*H*-pyrazol-4-yl) methylene) thiazolidin-4-one compounds (**3a-h**) exhibited moderate to excellent activity.

EXPERIMENTAL

Laboratory chemicals used were supplied by Ranbaxy Ltd, India. The melting points of the synthesized products were measured using automated Mettler Toledo FP 62 melting point apparatus (Metter Toledo-Switzerland) in open-glass capillary and were reported uncorrected. Compound purity was checked by thin layer chromatography (TLC). Ethyl acetate: methanol (1:9) solvent system was used as mobile phase in TLC and the spots were monitored under simple UV light chamber. The FT-IR spectra of synthesized compounds were recorded using KBr-pallets technique on a Perkin Elmer - Spectrum GX FT-IR System (PE-USA) in range of 4000-400 cm^{-1}. ^1H spectra were recorded using 200 MHz Bruker Avance DPX NMR system. Chemicals shifts were expressed in δ (ppm) relative to Tetramethylsilane (TMS) as an internal standard using DMSO-d_6 as solvent. Elemental analyses of these novel compounds were performed on Perkin Elmer-2400 CHNS/O analyzer (PE-USA). Results of elemental analysis of all compounds were in well agreement with the theoretical values. The mass spectra were scanned with the help of sophisticated Shimadzu QP2010 spectrometer (Shimadzu-Japan), which was equipped with a direct inlet probe and mass detector system which was operated at 70 eV.

Biological Assay

Antibacterial activity:

The novel compounds were evaluated with different bacterial and fungal strains. Antibacterial activity was tested against gram positive bacteria *Staphylococcus aureus (MTCC-96)* and *Streptococcus pyogenes* (MTCC-442) and gram negative *Escherichia coli* (MTCC-443) and *Pseudomonas aeruginosa* (MTCC-1688). Thiazoles are known for inhibiting protein synthesis in bacteria by binding to the complex formed between 23S rRNA and ribosomal protein L11, thereby restricting the action of GTP dependent elongation factors.[30] Antibacterial activity was carried out by serial broth dilution method.[31] The standard strains used for the antimicrobial activity were procured from Institute of Microbial Technology, Chandigarh, India. The compounds (**3a-h**) were screened for their antibacterial activity in triplicate against *Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa,* and *Streptococcus pyogenes* at different concentrations of 1000, 500, 200,100, 50, 25, 12.5 μg/ml as shown in (*Table* 1). The novel compounds which were found to be active in primary screening were diluted to obtain 100, 50, 25, 12.5 μg/ml concentrations. The growths of bacterial cultures were monitored after 24 and 48 h. The lowest concentration, which showed no growth after spot subculture was considered as MIC for each drug. The highest dilution showing at least 99% inhibition is taken as MIC. The test

mixture contained ~10^8 cells/ml. The standard drug used in this study was 'ampicillin' and it showed MIC at 100, 100, 250, and 100 μg/ml for evaluating antibacterial activity against *E. coli, P. aeruginosa, S. aureus* and *S. pyogenes* respectively.

Antifungal activity:

Same compounds were tested for antifungal activity in triplicate against *Candida albicans*, *Aspergillus niger*, and *Aspergillus clavatus* at various concentrations of 1000, 500, 200, and 100 μg/ml as shown in (*Table* 1). The results were recorded in the form of primary and secondary screening. The synthesized compounds were diluted to 1000 μg/ml as a stock solution. The synthesized compounds which were found to be active in this primary screening were further tested in a second set of dilution against all microorganisms. The lowest concentration, which showed no growth after spot subculture was considered as MIC for each drug and the highest dilution showing at least 99% inhibition wass taken as MIC. The test mixture contained ~10^8 spores/ml. ''Griseofulvin'' was used as a standard drug for antifungal activity and its MIC values are at 500, 100 and 100 μg/ml for *Candida albicans*, *Aspergillus niger*, and *Aspergillus clavatus*, respectively.

General Synthetic Methods

(i) Synthesis of 2-(4-chlorophenylimino) thiazolidin-4-one (1): The titled compound was prepared according to method reported earlier.[28]

(ii) Synthesis of 1-phenyl-3-(p-substituted phenyl)-1H-pyrazole-4-carbaldehydes (2a-h): Was carried out according to methods given in literature.[29]

(iii) Synthesis of 2-(4-chlorophenylimino)-5-((3-(p-substituted phenyl)-1-phenyl-1H-pyrazol-4-yl) methylene) thiazolidin-4-one (3a-h): To a solution of 2-(4-chlorophenylimino)thiazolidin-4-one (1) (10 mM) in ethanol and anhydrous sodium acetate (10 mM), 1-phenyl-3-(*p* substituted phenyl)-1*H*-pyrazole-4-carbaldehyde (**2a-h**) (10 mM) was added. The reaction mixture was heated and refluxed for 6 h. A bright yellow crystalline product was formed and the excess solvent was removed at reduced pressure. Crude product was washed with plenty of water, isolated by filtration and re-crystallized from ethanol to get compounds (**3a-h**).

Characterization Data

(i) 2-(4-chlorophenylimino)-5-((1,3-diphenyl-1H-pyrazol-4-yl)methylene)thiazolidin-4-one (3a): Yield 72%; Yellow crystalline solid; mp 214-216 ºC; IR (KBr, cm^{-1}) ν: 3408 (NH- Stretching), 3120, 2995 (Ar-H stretching, pyrazole -H stretching), 1707 (C=O stretching), 1536, 1496, 1445 (C=N, C=C, aromatic ring), 1340 (C=S stretching), 693 (C-S-C linkage); ^{1}H NMR (DMSO) δ (ppm): 8.65 (s, 1H, -C=CH group in pyrazole ring), 8.18-7.06 (m, 16H, Ar-H, C-NH, -C=CH); MS: m/z: 456 (M^+), 305, 276, 215, 172; Analytical calculations for $C_{25}H_{17}ClN_4OS$ (456.0) (%): C, 65.71; H, 3.75; N, 12.26; S, 7.02; Found: C, 65.58; H, 3.67; N, 12.32; S, 7.12.

(ii) 2-(4-chlorophenylimino)-5-((1-phenyl-3-p-tolyl-1H-pyrazol-4-yl)methylene)thiazolidin-4-one (3b): Yield 79%; Yellow crystalline solid; mp 154-156 ºC; IR (KBr, cm^{-1}) ν: 3417 (NH- Stretching), 3120, 3060 (Ar-H stretching, pyrazole -H stretching), 1711 (C=O stretching), 1521, 1491, 1451 (C=N, C=C, aromatic ring), 1359 (C=S stretching), 685 (C-S-C linkage); ^{1}H NMR (DMSO) δ (ppm): 8.61 (s, 1H, -C=CH group in pyrazole ring), 8.08-7.05 (m, 15H, Ar-H, C-NH, -C=CH), 2.38 (s, 3H, Ar-CH_3 in pyrazole ring); MS: m/z: 469 (M^+), 438, 276, 215, 122; Analytical calculations for $C_{26}H_{19}ClN_4OS$ (470.0) (%): C, 66.30; H, 4.07; N, 11.90; S, 6.81; Found: C, 66.12; H, 4.17; N, 11.77; S, 6.96.

(iii) 2-(4-chlorophenylimino)-5-((3-(4-hydroxyphenyl)-1-phenyl-1H-pyrazol-4-yl)methylene) thiazolidin-4-one (3c): Yield 82%; Yellow crystalline solid; mp 210-212 ºC; IR (KBr, cm^{-1}) ν: 3343 (NH- Stretching), 3110, 3066 (Ar-H stretching, pyrazole -H stretching), 1683 (C=O stretching), 1519, 1492, 1447 (C=N, C=C, aromatic ring), 1358 (C=S stretching), 688 (C-S-C linkage); ^{1}H NMR (DMSO) δ (ppm): 8.61 (s, 1H, -C=CH group in pyrazole ring), 7.96-7.04 (m, 16H, Ar-OH, C-NH, -C=CH); MS: m/z: 472 (M^+), 276, 215, 173, 140; Analytical calculations for $C_{25}H_{17}ClN_4O_2S$ (472.0) (%): C, 63.49; H, 3.62; N, 11.85; S, 6.78; Found: C, 63.32; H, 3.48; N, 11.65; S, 6.61.

(iv) 2-(4-chlorophenylimino)-5-((3-(4-nitrophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene) thiazolidin-4-one (3d): Yield 68%; Yellow crystalline solid; mp 138-140 ºC; IR (KBr, cm^{-1}) ν: 3417 (NH- Stretching), 3122, 3075 (Ar-H stretching, pyrazole -H stretching), 1712 (C=O stretching), 1531, 1494 (C=N, C=C), 1349 (C=S stretching), 686 (C-S-C linkage); ^{1}H NMR (DMSO) δ (ppm): 8.66 (s, 1H, -C=CH group in pyrazole ring), 8.40-7.02 (m, 15H, Ar-H, C-NH, -C=CH); MS: m/z: 501 (M^+), 290, 257, 190, 121; Analytical calculations for $C_{25}H_{16}ClN_5O_3S$ (501.0) (%): C, 59.82; H, 3.21; N, 13.95; S, 6.39; Found: C, 59.74; H, 3.22; N, 13.72; S, 6.47.

(v) 2-(4-chlorophenylimino)-5-((3-(4-fluorophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene) thiazolidin-4-one (3e): Yield 74%; Yellow crystalline solid; mp 283-285 ºC; IR (KBr, cm^{-1}) ν: 3408 (NH- Stretching), 3123, 3010 (Ar-

H stretching, pyrazole -H stretching), 1670 (C=O stretching), 1599, 1521, 1450 (C=N, C=C, aromatic ring), 1338 (C=S stretching), 684 (C-S-C linkage), ^{1}H NMR (DMSO) δ (ppm): 8.61 (s, 1H, -C=CH group in pyrazole ring), 7.95-7.05 (m, 15H, Ar-H, C-NH, -C=CH); MS: m/z: 474 (M^+), 323, 294, 233, 152; Analytical calculations for $C_{25}H_{16}ClFN_4OS$ (474.0) (%): C, 63.22; H, 3.40; N, 11.80; S, 6.75; Found: C, 63.43; H, 3.25; N, 11.56; S, 6.82.

(vi) 5-((3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-2-(4-chlorophenylimino)thiazolidin-4-one (3f): Yield 79%; Yellow crystalline solid; mp 134-136 ºC; IR (KBr, cm^{-1}) ν: 3411 (NH- Stretching), 3121, 3025 (Ar-H stretching, pyrazole -H stretching), 1672 (C=O stretching), 1594, 1521, 1444 (C=N, C=C, aromatic ring), 1338 (C=S stretching), 684 (C-S-C linkage); ^{1}H NMR (DMSO) δ (ppm): 8.61 (s, 1H, -C=CH group in pyrazole ring), 7.96-7.04 (m, 15H, Ar-H, C-NH, -C=CH); MS: m/z: 534 (M^+), 474, 356 , 294, 152; Analytical calculations for $C_{25}H_{16}BrClN_4OS$ (534.0) (%): C, 56.04; H, 3.01; N, 10.46; S, 5.98;. Found: C, 55.89; H, 3.11; N, 10.54; S, 6.17.

(vii) 2-(4-chlorophenylimino)-5-((3-(4-methoxyphenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)thiazolidin-4-one (3g): Yield 87%; Yellow crystalline solid; mp >300 ºC; IR (KBr, cm^{-1}) ν: 3410 (NH- Stretching), 3125, 3000 (Ar-H stretching, pyrazole -H stretching), 1700 (C=O stretching), 1596, 1496, 1443 (C=N, C=C, aromatic ring), 1337 (C=S stretching), 685 (C-S-C linkage); ^{1}H NMR (DMSO) δ (ppm): 8.61 (s, 1H, -C=CH group in pyrazole ring), 7.96-7.04 (m, 15H, Ar-H, C-NH, -C=CH); MS: m/z: 490 (M^+), 310, 275, 231, 152; Analytical calculations for $C_{25}H_{16}Cl_2N_4OS$ (490.0) (%): C, 61.11; H, 3.28; N, 11.40; S, 6.53; Found: C, 61.29; H, 3.34; N, 11.67; S, 6.71.

(viii) 5-((3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-2-(3,4-dichlorophenylimino) thiazolidin-4-one (3h): Yield 85%; Yellow crystalline solid; mp >300 ºC; IR (KBr, cm^{-1}) ν: 3401 (NH- Stretching), 3117, 3038 (Ar-H stretching, pyrazole -H stretching), 1723 (C=O stretching), 1585, 1524, 1438 (C=N, C=C, aromatic ring), 1331 (C=S stretching), 686 (C-S-C linkage), ^{1}H NMR (DMSO) δ (ppm): 8.61 (s, 1H, -C=CH group in pyrazole ring), 7.96-7.04 (m, 15H, Ar-H, C-NH, -C=CH), 3.84 (s, 3H, Ar-OCH_3 in pyrazole ring); MS: m/z: 486 (M^+), 335, 306, 263, 152; Analytical calculations for $C_{26}H_{19}ClN_4O_2S$ (486.0) (%): C, 64.13; H, 3.93; N, 11.51; S, 6.58; Found: C, 64.29; H, 3.82; N, 11.44; S, 6.34.

Acknowledgements. Authors are thankful to Micro Care laboratory and TRC, Surat, India for carrying out microbial studies.

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