Journal of Advanced Scientific Research

Available online through https://sciensage.info

ISSN

0976-9595

Research Article

Exploration of Substituted Thiazolidine-2,4-Diones: Synthesis, Characterization and Antimicrobial Evaluation

Kinjal J. Sabalpara*, Mayur L. Chandera, Chetana M. Rajyaguru, Jatin J. Upadhyay

Matushri Virbaima Mahila Science &Home Science College, Rajkot, Gujarat, India.

*Corresponding author: kinjalsabalpara@gmail.com

Received: 10-04-2025; Accepted: 04-05-2025; Published: 31-05-2025

https://doi.org/10.55218/JASR.2025160503

ABSTRACT

This research article presents a thorough investigation into the synthesis and assessment of a novel series of compounds- thiazolidine-2,4-diones, specifically 5-((3-methyl-5-phenoxy-1-phenyl-1H-pyrazol-4-yl)methylene)-3-((5-(4-nitrophenyl)-1,3,4-oxadiazol-2-yl)methyl)thiazolidine-2,4-dione and other derivatives, focusing on their potential as antibacterial and antifungal agents. The study encompasses a wide array of experiments and analyses aimed at evaluating the antimicrobial activity of these compounds against various gram-positive bacteria (including *Bacillus megaterium* and *Micrococcus* spp.) and gram-negative microorganisms (such as *Escherichia coli* and *Salmonella typhi*). Furthermore, the antifungal activity of the compounds was assessed against *Ganoderma* spp., *Aspergillus niger, A. flavus,* and *Penicillium* spp. The structural identity and purity of the synthesized compounds were verified using different spectroscopic techniques, namely IR, ^{1}H-NMR, ^{13}C-NMR and mass spectrometry. Following the confirmation, the compounds underwent antibacterial and antifungal screening, revealing that KS/5a and KS/5b demonstrated remarkable antibacterial activity compared to other compounds in the series. The minimum inhibitory concentration (MIC) values of KS/5a and KS/5b were determined and found to be below the recommended threshold, indicating their potential as highly effective antibacterial agents.

Keywords: Thiazolidine-2,4-dione, Synthesis, Antibacterial, MIC.

INTRODUCTION

Thiazolidine-2,4-dione (TZD) stands as a significant five-membered heterocyclic ring, incorporating both sulfur and nitrogen atoms. This ring structure features carbonyl groups positioned at the second and fourth positions and is widely distributed in nature in various forms. The diverse biological activities associated with the TZD ring have garnered considerable attention. Notably, this ring structure serves as a cornerstone in the design of drugs aimed at managing diabetes, which is crucial for regulating blood sugar levels in patients. Examples of clinical drugs incorporating the TZD ring include pioglitazone, rosiglitazone, troglitazone and rivoglitazone.[1] Beyond diabetes treatment, synthesized compounds containing the TZD ring have been employed in the development of drugs targeting malaria, microbial infections, viral diseases, oxidative stress, epilepsy, HIV, tuberculosis, cancer and inflammation.[2-6]

Conversely, because of their numerous biological characteristics, including cytotoxicity,[7] antibacterial effects,[8] antioxidant qualities,[9] and anti-inflammatory activity,[10] oxadiazoles and their derivatives have become very desirable targets. One notable example is the 1,3,4-oxadiazole core, which has attracted a lot of attention since its derivatives have a wide range of biological functions. As antidiabetic,[11] antimalarial,[12] antimicrobial,[13] anticancer,[14] analgesic[15] and anti-inflammatory drugs,[16] these derivatives have proven to be effective. Furthermore, this structural fragment is essential to a number of pharmaceutical derivatives that are commercially significant. These include the antiretroviral agent raltegravir,[17] the anticancer drug zibotentan,[18] the hypnotic drug fenadiazole[19] and the antihypertensive agent nesapidil.[20]

In this study, we present the synthesis of 5-((3-methyl-5-phenoxy-1-phenyl-1H-pyrazol-4-yl)methylene)-3-((5-(4-nitrophenyl)-1,3,4-oxadiazol-2-yl)methyl)thiazolidine-2,4-dioneand other derivatives. The newly synthesized compounds were then characterized by elemental analyses, IR, ^{1}H-NMR, ^{13}C-NMR and mass spectrometry. Additionally, the biological activity results of these novel heterocyclic compounds, highlighting their potential as chemotherapeutic agents, are reported. The incorporation of specific substituents in the synthesized compounds provides valuable insights into structure-activity relationships, paving the way for the development of optimized derivatives with enhanced pharmacological properties.

MATERIAL AND METHODS

All the chemical compounds and solvents employed in the synthesis of the compound library were sourced from CDH Fine Chemical in Delhi and were utilized without requiring prior additional purification. The progression of reactions was monitored using thin-layer chromatography (TLC) on silica Gel-G plates (G60 F254,

Merck) with a thickness of 0.5 mm. Visualization was facilitated by exposing the plates to UV light at wavelengths of 254, and 365 nm. Melting points were determined using the open capillary method and the reported values were not adjusted for temperature fluctuations. The ^{1}H-NMR spectra of the synthesized compounds were recorded in DMSO-d_6 solvent using a Bruker-Advance-II instrument operating at 400 MHz. Infrared (IR) spectra were acquired using a Shimadzu FTIR-8400 spectrophotometer equipped with a DRS probe and a KBr pallet. Chemical shifts were indicated in parts per million (ppm) relative to the TMS internal standard. Mass spectra were generated using a GCMS-QP 2010 mass spectrometer with a direct inlet probe. These analytical methodologies were employed to deliver comprehensive characterizations of the synthesized compounds, laying the groundwork for further exploration of their potential antimicrobial properties.

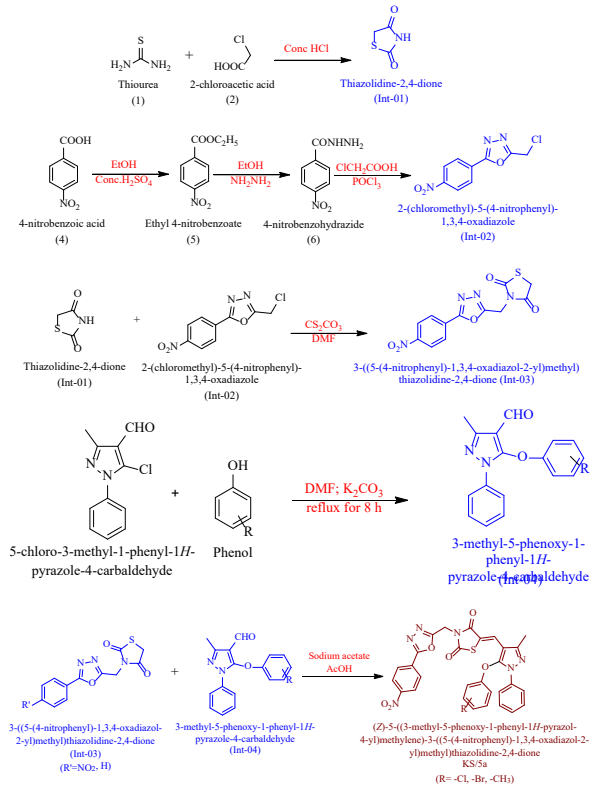
The synthesized compounds underwent *in-vitro* antimicrobial assessment against a range of microorganisms, including gram-positive bacteria (*Bacillus megaterium, Micrococcus spp.*), gram-negative bacteria (*Escherichia coli*, *Salmonella typhi*), and various fungal species (*Ganoderma* spp., *Aspergillus niger*, *Aspergillus flavus* and *Penicillium*) using the agar cup method.

Synthetic Procedure for 5-((3-methyl-5-phenoxy-1-phenyl-1H-pyrazol-4-yl)methylene)-3-((5-(4-nitrophenyl)-1,3,4-oxadiazol-2-yl)methyl) thiazolidine-2,4-dione

Thiazolidine 2,4- dione (Int-01) and 2-(chloromethyl)-5-(4-nitrophenyl)-1,3,4-oxadiazole (Int-02) have been synthesized by the reported methods. In the second stage of the reaction, a DMF solution is prepared by mixing Int-01 and Int-02 in a suitable amount, followed by CS_2CO_3 is added to the reaction mixture carefully for the synthesis of 3-((5-(4-nitrophenyl)-1,3,4-oxadiazol-2-yl)methyl) thiazolidine-2,4-dione (Int-03). Next, phenylhydrazine and ethyl-3-oxobutanoate are refluxed to prepare 3-methyl-1-phenyl-1H-pyrazol-5(4H)-one. The resulting substance is mixed with DMF and $POCl_3$ and further refluxed for 8 hours which yields 5-chloro-3-methyl-1-phenyl-1H-pyrazole-4-carbaldehyde. K_2CO_3 and DMF, along with phenol, are further added to the reaction mixture and the reaction mass is refluxed again for 8 hours, which finally produces 3-methyl-5-phenoxy-1-phenyl-1H-pyrazole-4-carbaldehyde (Int-04). For the synthesis of the final product in the final stage, a solution of 0.01 mole of 3-((5-(4-nitrophenyl)-1,3,4-oxadiazol-2-yl)methyl) thiazolidine-2,4-dione and 0.01 mole of 3-methyl-5-phenoxy-1-phenyl-1H-pyrazole-4-carbaldehyde in 1.0 mL of hot acetic acid was made. This solution was treated with 0.01 mole (0.338 g) of sodium acetate and refluxed for 1.5 hours. Pouring the mixture into water and recrystallizing the solid from ethyl acetate yielded the desired product, 5-((3-methyl-5-phenoxy-1-phenyl-1H-pyrazol-4-yl)methylene)-3-((5-(4-nitrophenyl)-1,3,4-oxadiazol-2-yl)methyl) thiazolidine-2,4-dione, KS/5a.

General Synthetic Procedure for Substituted Thiazolidine-2,4-diones

A series of compounds-KS/5b to KS/5j was synthesized by taking various substituted phenols in the second stage as shown in Figure 1.



Reaction scheme

Figure 1: Synthesis of new thiazolidine-2,4-dione derivatives

Antibacterial Activity

Fresh bacterial cultures were prepared and cultivated in nutrient broth. These cultures were then evenly spread onto sterile Muller-Hinton agar plates using sterile swabs. Wells with a diameter of 1-cm were carefully created in the agar plates. Standard antibiotics were dissolved in sterile distilled water to achieve a final concentration of 200 µg/mL, while synthetic compounds were dissolved in DMSO to a final concentration of 1-mg/mL before being added to the wells in 0.1 mL volumes. To facilitate proper diffusion, the plates were initially incubated at 4°C for 20 minutes before further incubation at 37°C for 24 hours for bacterial cultures. DMSO controls were included for comparison purposes. Following incubation, the zones of inhibition were visually examined and measured, allowing for the evaluation of the antimicrobial effectiveness of the synthesized compounds against the bacterial cultures.

Antifungal Activity

Fresh fungal cultures were prepared and cultivated in potato dextrose broth. These cultures were then evenly spread onto sterile potato dextrose agar plates using sterile swabs. Wells with a diameter of 1-cm were carefully created in the agar plates. Standard antibiotic, nystatin, was dissolved in sterile distilled water to achieve a final concentration of 200 µg/mL, while synthetic compounds were dissolved in DMSO to a final concentration of 1-mg/mL before being added to the wells in 0.1 mL volumes. To facilitate proper diffusion, the plates were initially incubated at 4°C for 20 minutes before further incubation at 30°C for 48 hours for fungal cultures. DMSO controls were

included for comparison purposes. Following the incubation, the zones of inhibition were visually examined and measured, allowing for the evaluation of the antimicrobial effectiveness of the synthesized compounds against the fungal cultures.

The bioassay investigation into the *in-vitro* antibacterial activity of the newly synthesized compounds (KS/5a–KS/5j) yielded noteworthy results. These compounds demonstrated significant potential against the tested microorganisms, surpassing the effectiveness of conventional medications. Table 1 provides further validation of their remarkable activity, with compounds KS/5a and KS/5b notably standing out for their efficacy. The presence of active compounds within these substances contributes significantly to their potent activity against the tested microorganisms. By analyzing the structural features of these active compounds, we can pinpoint specific groups that enhance their overall efficacy. These findings underscore the substantial promise of compounds KS/5a and KS/5b as potent antibacterial agents.

RESULTS AND DISCUSSION

A series of novel compounds, KS/5a to KS/5j was synthesized by mixing 3-((5-(4-nitrophenyl)-1,3,4-oxadiazol-2-yl)methyl) thiazolidine-2,4-dione and 3-methyl-5-phenoxy-1-phenyl-1H-pyrazole-4-carbaldehyde in an AcOH solution and sodium acetate, followed by the addition of aldehyde derivatives which produced the desirable product 5-((3-methyl-5-phenoxy-1-phenyl-1H-pyrazol-4-yl)methylene)-3-((5-(4-nitrophenyl)-1,3,4-oxadiazol-2-yl)methyl) thiazolidine-2,4-dione(KS/5a) and in the similar way KS/5a to KS/5jwere prepared as illustrated in Table 1. The structures of KS/5a to KS/5j were established on the basis of their spectral data (Mass spectra, IR, ^{1}H-NMR and ^{13}C-NMR).

Characterization of the Synthesized Compounds

5-((3-methyl-5-phenoxy-1-phenyl-1H-pyrazol-4-yl) methylene)-3-((5-(4-nitrophenyl)-1,3,4-oxadiazol-2-yl) methyl)thiazolidine-2,4-dione(KS/5a)

^{1}H-NMR (400 MHz, DMSO-d_6) in δ ppm**:** 2.36–2.50 (a; 3H, Singlet), 4.92 (b; 2H, Singlet), 6.88 (c; 2H, Doublet), 6.90 (d; 1H, dd, 8Hz), 7.0-7.29 (e; 2H, Doublet), 7.30 (f; 1H, dd, 8Hz), 7.43 (g; 2H, Doublet), 7.97 (h; 2H, Doublet), 8.03 (i; 1H, Singlet), 8.74 (j; 4H, Doublet). ^{13}C-NMR (400 MHz, DMSO-d_6) δ-ppm**:** 177.94 (s), 168.43 (s), 165.66 (s), 162.07 (s), 153.43 (s), 150.05 (s), 147.39 (s), 141.26 (s), 138.57 (s), 135.30 (s), 132.08 (s), 130.13 – 129.91 (m), 129.54 – 129.14 (m), 127.56 – 127.34 (m), 126.57 (s), 124.90 (s), 124.79 – 124.57 (m), 121.90 (t, J = 7.1 Hz), 118.97 – 118.57 (m), 89.90 (s), 43.02 (s), 5.56 (s). FTIR (KBr, ν_{max}, cm^{-1}): 3471, 3223, 3115, 3039, 2964, 2870, 2196, 1633, 1600, 1525, 1487, 1394, 1219, 1184, 1070, 1051, 1012, 858, 813, 746, 617 and 488. Elemental analysis: C (59.99%), H (3.37%), N (14.58%), O (16.63%), S (5.42%) MS (m/z): 580; M.F.: $C_{29}H_{20}N_6O_6S$; M.P.: 168-170, %yield: 90%.

5-((3-(4-chlorophenoxy)-4-methyl-1-phenyl-1H-pyrazol-4-yl)methylene)-3-((5-(4-nitrophenyl)-1,3,4-oxadiazol-2-yl) methyl)thiazolidine-2,4-dione (KS/5b)

^{1}H-NMR (400 MHz, DMSO-d_6) in δ ppm: 2.36-2.50 (a; 3H, Singlet), 4.92 (b; 2H, Singlet), 6.98 (c; 2H, Doublet), 7.01 (d; 1H, dd, 8Hz), 7.09-7.29 (e; 2H, Doublet), 7.30 (f; 1H, dd, 8Hz), 7.43 (g; 2H, Doublet), 7.97 (h; 2H, Doublet), 8.03 (i; 1H, Singlet), 8.74 (j; 4H, Doublet). ^{13}C-NMR (400 MHz, DMSO-d_6) δ-ppm 177.94 (s), 168.43 (s), 165.66 (s), 162.07 (s), 152.37 (s), 150.05 (s), 147.39 (s), 141.26 (s), 138.57 (s), 135.30 (s), 132.08 (s), 131.71 (s), 130.02 – 129.62 (m), 129.54 – 129.14 (m), 127.56 – 127.34 (m), 126.57 (s), 124.79 – 124.57 (m), 121.90 (t, J = 7.1 Hz), 120.50 – 120.10 (m), 89.90 (s), 43.02 (s), 5.56 (s). FTIR (KBr, ν_{max}, cm^{-1}): 3458, 3323, 3259, 3213, 3066, 2960, 2874, 2198, 1664, 1595, 1516, 1456, 1392, 1332, 1265, 1224, 1128, 1070, 1022, 817, 754, 682 and 515. Elemental analysis: C (56.61%), H (3.13%), Cl (5.56%), N (13.86%), O (14.61 %), S (6.21%) MS (m/z): 614; M.F.: $C_{29}H_{19}ClN_6O_6S$; M.P.: 156-158, %yield: 88%.

5-((3-methyl-5-phenoxy-1-phenyl-1H-pyrazol-4-yl) methylene)-3-((5-phenyl-1,3,4-oxadiazol-2-yl)methyl) thiazolidine-2,4-dione(KS/5c)

^{1}H-NMR (400 MHz, DMSO-d_6) in δ ppm: 2.36-2.50 (a; 3H, Singlet), 4.92 (b; 2H, Singlet), 6.98 (c; 2H, Doublet), 7.01 (d; 1H, dd, 8Hz), 7.09-7.29 (e; 2H, Doublet), 7.30 (f; 1H, dd, 8Hz), 7.43 (g; 2H, Doublet), 7.74 (j; 5H, Doublet) 7.97 (h; 2H, Doublet), 8.03 (i; 1H, Singlet). ^{13}C-NMR (400 MHz, DMSO-d_6) δ-ppm 177.94 (s), 168.43

Table 1: Physical parameters of KS/5a to KS/5j

Code	*Molecular formula*	*Substitution*	*M.W.*	*M.P.(^{0}C)*	*%Yield*
KS/5a	$C_{29}H_{20}N_6O_6S$	R=NO_2, R'=H	580	168–170	90
KS/5b	$C_{29}H_{19}ClN_6O_6S$	R=NO_2, R'=4-Cl	614	156–158	88
KS/5c	$C_{29}H_{21}N_5O_4S$	R=H, R'=H	535	175–177	85
KS/5d	$C_{29}H_{20}ClN_5O_4S$	R=H, R'= 4-Cl	570	170–173	81
KS/5e	$C_{29}H_{20}BrN_5O_4S$	R=H, 37=Br	613	148–151	78
KS/5f	$C_{29}H_{20}Cl_2N_5O_4S$	R=H, R'=2,4-Cl_2	603	155–157	75
KS/5g	$C_{29}H_{19}BrN_6O_6S$	R=NO_2, R'= 4-Br	658	178–181	89
KS/5h	$C_{29}H_{18}Cl_2N_6O_6S$	R=NO_2, R'= 2,4-Cl_2	648	163–165	73
KS/5i	$C_{29}H_{18}Br_2N_6O_6S$	R=NO_2, R'= Br_2	736	138–140	55
KS/5j	$C_{30}H_{22}N_6O_6S$	R=NO_2, R'=4-CH_3	594	141–143	45

Table 2: Biological assay of the synthesized compounds

Code	*Antibacterial activity*				*Antifungal activity*			
	Antibacterial activity (zone in cm), concentration: 1 mg/mL				*Antifungal activity (zone in cm), concentration: 1-mg/mL*			
	*Gram +*ve *Bacteria*		*Gram –*ve *bacteria*					
	B. megaterium	*Micrococcus spp.*	*S. typhi.*	*E. coli.*	*Penicillium spp.*	*Ganoderma spp.*	*A. niger*	*A. flavus*
KS/5a	2.3	2.0	0.8	2.5	2.1	2.9	1.5	1.4
KS/5b	2.2	2.0	1.0	2.7	2.1	2.9	1.6	2.0
KS/5c	-	-	0.5	1.0	2.1	2.0	1.8	1.4
KS/5d	1.2	2.0	1.5	-	-	1.3	1.0	1.6
KS/5e	1.1	0.7	-	1.6	1.4	0.1	0.3	1.1
KS/5f	-	1.5	1.2	-	1.3	-	1.4	0.8
KS/5g	1.0	1.0	1.1	-	1.2	2.4	1.5	1.3
KS/5h	1.0	0.4	-	1.2	0.8	0.8	1.0	1.1
KS/5i	2.1	1.1	1.4	2.2	2.4	2.0	0.8	1.0
KS/5j	1.0	2.1	1.7	-	-	1.4	2	3.2
Streptomycin (200 µg/mL)	3.0	2	2	3.2	-	-	-	-
Ciprofloxacin (200 µg/mL)	3.8	4	4	3	-	-	-	-
Nystatin (200 µg/mL)	-	-	-	-	3.2	4	3.5	3.8

(s), 165.66 (s), 162.07 (s), 153.43 (s), 150.05 (s), 141.26 (s), 138.57 (s), 135.30 (s), 131.57 (s), 130.13 – 129.91 (m), 129.54 – 129.26 (m), 129.26 – 128.85 (m), 127.18 – 126.97 (m), 126.62 (d, J = 11.2 Hz), 124.90 (s), 121.90 (t, J = 7.1 Hz), 118.97 – 118.57 (m), 89.90 (s), 43.02 (s), 5.56 (s). FTIR (KBr, ν_{max}, cm^{-1}): 3426, 3335, 3070, 2960, 2874, 2193, 1656, 1591, 1518, 1485, 1454, 1392 1325, 1259, 1184, 1130, 1072, 1030, 898, 786, 752 and 605. Elemental analysis: C (63.02%), H (3.95%), N (15.08%), O (11.97%), S (5.99%) MS (m/z): 535; M.F.: $C_{29}H_{21}N_5O_4S$; M.P.: 175-177, %yield: 85%.

Through a series of analytical techniques like ^1H & ^{13}C-NMR, IR and Mass spectral analysis, we scrutinized the structures of KS/5a to KS/5j, confirming their congruence with the anticipated results. Specifically, the mass spectrometric value [m/z = 580.12 (M^+)] for KS/5a closely corresponds to the molecular formula $C_{29}H_{20}N_6O_6S$. FTIR data provides information on the stretching frequencies of various functional groups (KBr, vmax, cm^{-1}): 3471, 3223, 3115, 3039, 2964, 2870, 2196, 1633, 1600, 1525, 1487, 1394, 1219, 1184, 1070, 1051, 1012, 858, 813, 746, 617, 488. ^1H-NMR (400 MHz, DMSO-d_6) in δ ppm: 2.36-2.50 (a; 3H, Singlet), 4.92 (b; 2H, Singlet), 6.88 (c; 2H, Doublet), 6.90 (d; 1H, dd, 8Hz), 7.0-7.29 (e; 2H, Doublet), 7.30 (f; 1H, dd, 8Hz), 7.43 (g; 2H, Doublet), 7.97 (h; 2H, Doublet), 8.03 (i; 1H, Singlet), 8.74 (j; 4H, Doublet).

All the synthesized compounds showed characteristic absorption bands in the range of 3402 to 3415cm^{-1} for >N-H stretching, 4.90 to 5.20 ppm, which can be attributed to the methylene group, 1070 cm^{-1} for C-N frequencies, 2964 cm^{-1} for C-H stretching (asymmetric), 2870 cm^{-1} for C-H stretching (symmetric), 3039 cm^{-1} for aromatic C-H stretching, 1447 cm^{-1} for C-H def. (symmetric). ^1H-NMR spectra exhibited multiplets in the range of 6.97 to 8.20 δ ppm for the protons of aromatic rings and 8.0 to 8.20 for CH=N. The molecular mass of the compounds was confirmed from the mass spectrometry as the calculated mass was in accordance with the observed mass. The observed molecular weights of particular compounds were showing (M+1) molecular ion peak.

Antimicrobial Activity

Following the confirmation, the synthesized compounds KS/5a to KS/5j underwent antibacterial and antifungal screening, wherein a variety of bacterial and fungal species were utilized in the investigation. The bacterial strains encompassed gram-positive bacteria such as *B. megaterium* and various *Micrococcus* species, alongside gram-negative bacteria including *E. coli* and S. *typhi*. The antifungal activity of the compounds was assessed against fungal strains such as *Ganoderm*a spp., *A. niger*, *A. flavus* and *Penicillium* spp. This selection of microbial strains was deliberately diverse, aiming to provide a comprehensive assessment of the antimicrobial potential of the synthesized compounds, revealing that KS/5a and KS/5b demonstrated remarkable antibacterial activity compared to other compounds in the series. The minimum inhibitory concentration (MIC) values of KS/5a and KS/5b were determined against *B. megaterium, S. typhi, Micrococcus* spp. and *E. coli.* and were found to be below the recommended threshold, indicating their potential as highly effective antibacterial agents.

These findings underscore the potential of these compounds as promising candidates for further investigation, including determining their minimum inhibitory concentration (MIC), and their prospective use as effective therapeutic agents.

CONCLUSION

A series of heterocyclic systems, thiazolidine-2,4-diones was synthesized with moderate to high yields. The synthetic compounds were characterized by analytical techniques like ^{1}H-NMR,^{13}C-NMR, IR spectroscopy and mass spectrometry. They were further assessed against the selected bacterial and fungal strains using standard drugs as the references. KS/5a and KS/5b showed high antibacterial efficacy. Other compounds showed low to moderate biological activity. These findings underscore the potential of these compounds as promising candidates for further investigation, including determining their MIC, and their prospective use as effective therapeutic agents.

ACKNOWLEDGMENTS

The authors are thankful to the Principal, M.V.M Science and Home Science College Rajkot.

REFERENCES

1. Desai NC, Pandit UP, Dodiya A. Thiazolidinedione compounds: A patent review (2010–present). Expert opinion on therapeutic patents. 2015 Apr 3;25(4):479-88. Available from: doi.org/10.1517/13543776.2014.1001738
2. Chadha N, Bahia MS, Kaur M, Silakari O. Thiazolidine-2, 4-dione derivatives: Programmed chemical weapons for key protein targets of various pathological conditions. Bioorganic & Medicinal Chemistry. 2015 Jul 1;23(13):2953-74. Available from: doi.org/10.1016/j.bmc.2015.03.071
3. Liu XF, Zheng CJ, Sun LP, Liu XK, Piao HR. Synthesis of new chalcone derivatives bearing 2, 4-thiazolidinedione and benzoic acid moieties as potential anti-bacterial agents. European journal of medicinal chemistry. 2011 Aug 1;46(8):3469-73. Available from: doi.org/10.1016/j.ejmech.2011.05.012
4. Hu CF, Zhang PL, Sui YF, Lv JS, Ansari MF, Battini N, Li S, Zhou CH, Geng RX. Ethylenic conjugated coumarin thiazolidinediones as new efficient antimicrobial modulators against clinical methicillin-resistant Staphylococcus aureus. Bioorganic chemistry. 2020 Jan 1;94:103434. Available from: doi.org/10.1016/j.bioorg.2019.103434
5. Youssef AM, White MS, Villanueva EB, El-Ashmawy IM, Klegeris A. Synthesis and biological evaluation of novel pyrazolyl-2, 4-thiazolidinediones as anti-inflammatory and neuroprotective agents. Bioorganic & medicinal chemistry. 2010 Mar 1;18(5):2019-28. Available from: doi.org/10.1016/j.bmc.2010.01.021
6. Naim MJ, Alam MJ, Nawaz F, Naidu VG, Aaghaz S, Sahu M, Siddiqui N, Alam O. Synthesis, molecular docking and anti-diabetic evaluation of 2, 4-thiazolidinedione based amide derivatives. Bioorganic chemistry. 2017 Aug 1;73:24-36. Available from: doi.org/10.1016/j.bioorg.2017.05.007
7. Saïd AB, Romdhane A, Elie N, Touboul D, Jannet HB, Bouajila J. Design, synthesis of novel pyranotriazolopyrimidines and evaluation of their anti-soybean lipoxygenase, anti-xanthine oxidase, and cytotoxic activities. Journal of Enzyme Inhibition and Medicinal Chemistry. 2016 Nov 1;31(6):1277-85. Available from: doi.org/10.3109/14756366.2015.1118684
8. Rai NP, Narayanaswamy VK, Govender T, Manuprasad BK, Shashikanth S, Arunachalam PN. Design, synthesis, characterization, and antibacterial activity of {5-chloro-2-[(3-substitutedphenyl-1, 2, 4-oxadiazol-5-yl)-methoxy]-phenyl}-(phenyl)-methanones. European journal of medicinal chemistry. 2010 Jun 1;45(6):2677-82. Available from: doi.org/10.1016/j.ejmech.2010.02.021
9. Ningaiah S, Bhadraiah UK, Keshavamurthy S, Javarasetty C. Novel pyrazoline amidoxime and their 1, 2, 4-oxadiazole analogues: Synthesis and pharmacological screening. Bioorganic & Medicinal Chemistry Letters. 2013 Aug 15;23(16):4532-9. Available from: doi.org/10.1016/j.bmcl.2013.06.042
10. Farooqui M, Bora R, Patil CR. Synthesis, analgesic and anti-inflammatory activities of novel 3-(4-acetamido-benzyl)-5-substituted-1, 2, 4-oxadiazoles. European journal of medicinal chemistry. 2009 Feb 1;44(2):794-9. Available from: doi.org/10.1016/j.ejmech.2008.05.022
11. Bhutani R, Pathak DP, Kapoor G, Husain A, Iqbal MA. Novel hybrids of benzothiazole-1, 3, 4-oxadiazole-4-thiazolidinone: Synthesis, in silico ADME study, molecular docking and in vivo anti-diabetic assessment. Bioorganic chemistry. 2019 Mar 1;83:6-19. Available from: doi.org/10.1016/j.bioorg.2018.10.025
12. Al-Wahaibi LH, Kumar NS, El-Emam AA, Venkataramanan NS, Ghabbour HA, Al-Tamimi AM, Percino J, Thamotharan S. Investigation of potential anti-malarial lead candidate 2-(4-fluorobenzylthio)-5-(5-bromothiophen-2-yl)-1, 3, 4-oxadiazole: Insights from crystal structure, DFT, QTAIM and hybrid QM/MM binding energy analysis. Journal of Molecular Structure. 2019 Jan 5;1175:230-40. Available from: doi.org/10.1016/j.molstruc.2018.07.102
13. Khalilullah H, Khan S, Nomani MS, Ahmed B. Arab J Chem 2016, 9. S1029. Available from: doi.org/10.1016/j.arabjc.2011.11.009
14. Sławiński J, Szafrański K, Pogorzelska A, Żołnowska B, Kawiak A, Macur K, Belka M, Bączek T. Novel 2-benzylthio-5-(1, 3, 4-oxadiazol-2-yl) benzenesulfonamides with anticancer activity: Synthesis, QSAR study, and metabolic stability. European Journal of Medicinal Chemistry. 2017 May 26;132:236-48. Available from: doi.org/10.1016/j.ejmech.2017.03.039
15. Husain A, Ahmad A, Alam MM, Ajmal M, Ahuja P. Fenbufen based 3-[5-(substituted aryl)-1, 3, 4-oxadiazol-2-yl]-1-(biphenyl-4-yl) propan-1-ones as safer antiinflammatory and analgesic agents. European journal of medicinal chemistry. 2009 Sep 1;44(9):3798-804. Available from: doi.org/10.1016/j.ejmech.2009.04.009
16. Amir M, Kumar S. Synthesis and evaluation of anti-inflammatory, analgesic, ulcerogenic and lipid peroxidation properties of ibuprofen derivatives. Acta Pharmaceutica. 2007 Mar 1;57(1):31. Available from: 10.2478/v10007-007-0003-y
17. Savarino A. A historical sketch of the discovery and development of HIV-1 integrase inhibitors. Expert opinion on investigational drugs. 2006 Dec 1;15(12):1507-22. Available from: doi.org/10.1517/13543784.15.12.1507
18. James ND, Growcott JW. Zibotentan. Drugs of the Future. 2009;34(8). Available from: 10.1358/dof.2009.34.8.1400202
19. Varshney H, Ahmad A, Rauf A, Sherwani A, Owais M. Multistep synthesis of 1-[{(5-alkenyl/hydroxyalkenylsubstituted)-1, 3, 4-oxadiazol-2-yl}-methyl]-2-methyl-1 H-benzimidazole series and in vitro anticancer screening, SAR studies. Medicinal Chemistry Research. 2015 Mar;24:944-53. Available from: doi.org/10.1007/s00044-014-1162-2
20. Desai NC, Bhatt N, Somani H, Trivedi A. Synthesis, antimicrobial and cytotoxic activities of some novel thiazole clubbed 1, 3, 4-oxadiazoles. European Journal of Medicinal Chemistry. 2013 Sep 1;67:54-9. Available from: doi.org/10.1016/j.ejmech.2013.06.029s

HOW TO CITE THIS ARTICLE: Sabalpara KJ, Chandera ML, Rajyaguru CM, Upadhyay JJ. Exploration of Substituted Thiazolidine-2,4-Diones: Synthesis, Characterization and Antimicrobial Evaluation. *J Adv Sci Res*. 2025;16(05): 14-18 **DOI:** 10.55218/JASR.2025160503