RESEARCH ARTICLE

Synthesis, Characterization and Antimicrobial Evaluation of New Substituted Thiazolidinones Bearing Triazole Moiety

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ABSTRACT

Series of thiazolidinone derivatives containing triazole moiety have been synthesized by condensing various substituted aldehydes to form Schiff bases which further reacts with thioglycolic acid undergoes ring condensation to form 3-(3-mercapto-5-((5-methoxy-1H-indol-1-yl)methyl)-4H-1,2,4-triazol-4-yl)-2-substituted phenylthiazolidin-4-one followed by reaction with ethyl chloroacetate to form ethyl 2-((4-(2-subtituted phenyl-4-oxothiazolidin-3-yl)-5-((5-methoxy-1H-indol-1-yl)methyl)-4H-1,2,4-triazol-3-yl)thio)acetate. The synthesized compounds were characterized by elemental analysis, fourier-tranform infrared spectroscopy (FTIR), nuclear magnetic resonance (NMR) and mass spectrometry. All synthesized compounds were evaluated for invitro antibacterial activity against *Staphylococcus aureus*, *Enterococcus faecalis, Escherichia coli, Pseudomonas aeruginosa* and for antifungal activity against *Candida albicans, Aspergillus niger*. The results of synthesized compounds showed that T-III, T-IX, T-X, and T-XVIII have antimicrobial activity when compared to standard drugs. The compounds having p-bromo, p-chloro, p-methoxy and p-nitro groups showed potent antimicrobial agent.

Keywords: Thiazolidinone, Triazole, Synthesis, Characterization, Antimicrobial activity.

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INTRODUCTION

It has long been established that compounds with atoms other than carbon in their ring, known as heterocyclic compounds, exhibit biological activity. With one atom of sulfur, nitrogen, and a carbonyl group, thiazolidinone is another biologically significant heterocyclic ring that has been linked to a variety of pharmacological characteristics. Thiazolidinone is used as an intermediate in the synthesis of several heterocyclic compounds and thus is in great demand.[1–7] In the field of chemistry, 4-thiazolidinone derivatives have attracted a lot of attention. Thiazolidin-4-one ring systems are the fundamental structure of many synthetic pharmaceuticals that have a variety of biological activities, including anti-inflammatory, anticonvulsant, antifungal, anti-thyroid, antitubercular, and antidiabetic effects. Thiazolidine-4-one antibacterial activity is its most potent function. Many clinically used medications have included the 4-thiazolidinone scaffold, which is incredibly adaptable. One of the most valuable heterocyclic molecules from the perspectives of synthetic and medicinal chemistry is indole. Due to its prepared availability, varied compound reactivity, and a broad range of pharmaceutical activities, the basic structure of these platforms has garnered a lot of attention. It has also received significant attention due to its potential as an advantageous platform in medication disclosure and advancement.[8–17] Heterocyclic organic molecules called triazoles have three nitrogen atoms arranged in a five-member ring molecular structure. 1,2,4-triazoles.[18–22] are a significant moiety with biological action. Furthermore, it was noted that due to their numerous biological activities and broad range of therapeutic applications, substituted 1,2,4 triazoles and related N-bridged heterocycles have drawn a lot of attention over the past 20 years. Since the community faces a severe problem with infections brought on by pathogen bacteria and needs effective therapy, as well as the quest for novel antimicrobial medicines, the chemistry of triazole derivatives has been of interest due to its usefulness in the creation of medicine. There is a growing trend of widespread resistance to numerous commercially available antibiotics, and this resistance will only grow with time. Bacterial infections can bring on several of the world's most dangerous illnesses and massive pandemics. It is crucial to create new strategies and antibacterial agents as alternatives to the many antimicrobial therapies now in use due to the rise in bacterial resistance to antibiotic treatment.[23] The management of infectious diseases continues to be a

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significant and difficult problem due to a number of causes, including the emergence of new infectious diseases and the rise in multi-drug resistance microbial pathogens. Even though there are many antibiotics and chemotherapeutics accessible for medical use, the last several decades have seen the growth of both new and old antibiotic-resistant bacterial strains, which has created a significant need for new classes of antibacterial agents. Synthetic organic chemistry has always played an important role in the highly integrated and interdisciplinary process of developing drugs. Molecular manipulation involves the efforts to combine separate groups of similar activity into one compound, leading to synergistic activity. In this context, this study was designed to evaluate the antimicrobial properties of new indolyl triazole derivatives containing thiazolidinone.

MATERIALS AND METHODS

Chemicals

Every chemical used in the synthesis was bought from Merck and Sigma-Aldrich. The remaining reagents and solvents were all of analytical quality and were obtained from different commercial suppliers.

Instrumentation

Melting points are uncorrected and were measured using the Perfit melting point instrument. The Shimadzu IR instrument was used to record the infrared spectra of compounds by using KBr discs. Using TMS (Sigma-Aldrich) as an internal standard, the Bruker spectroscopic DPX-300 NMR captured the ^{1}H-NMR (400 MHz) spectra. The instrument used to obtain the mass spectra was the JEOL-JMS-DX 303. The Perkin-Elmer 24℃ analyzer was used to perform elemental studies (C, H, and N). Every chemical was within ±0.4% of the values predicted by theory. TLC plates coated with silica gel G were used for thin-layer chromatography (Merck).

Synthesis

General method of preparation of ethyl-N- indolyl acetate

In a 100 mL dry conical flask, 1.1 g of indole (0,01 mole) was dissolved in 10 mL of acetone. This was mixed with 1.2 mL (0.01 moles) of ethyl chloroacetate. After adding 2.3 g of potassium carbonate, the liquid was covered with cotton and given a 24-hour stir with a magnetic stirrer. After pouring the mixture into around 100 mL of ice water, it was refrigerated for the entire night. After that, ether was used to extract the ester that had been produced above, and an ester was obtained by discarding the ether.

General method of preparation of N-Indolyl acetyl hydrazine

In 0.96 mL of hydrazine hydrate (0.01 mole) was added to above formed 2 g of indoly ester (0.01 mole), and the mixture was refluxed for a duration of 12 to 16 hours. After adding the aforementioned mixture to a beaker filled with ice-cold water, it was refrigerated for the entire night. The product underwent filtration at the pump, multiple ice-cold water washes, and 100% alcohol recrystallization. Yield: 89%, melting point: 49℃.

General method of preparation of 2-(2-(5-methoxy-1H-indol-1-yl)acetyl)hydrazine-1-carbodithioic acid, potassium salt

About 50 mL of pure ethanol contained 0.03 moles of potassium hydroxide dissolved in it. After the mixture had cooled in an ice bath, above formed hydrazide (0.02 mole) was added and mixed together. This was mixed continuously while little amounts of carbon disulfide (0.025 mole) were added. For 16 hours at room temperature, the reaction mixture was constantly stirred. After precipitating potassium dithiocarbazinate, it was filtered, cleaned with anhydrous ether, and vacuum-dried. The resulting potassium salt was utilized in the following stage without undergoing additional purification. Yield: 82%.

Synthesis of 4-amino-5-((5-methoxy-1H-indol-1-yl)methyl)-4H-1,2,4-triazole-3-thiol

A solution of above-formed potassium dithiocarbazinate (0.02 mole) and hydrazine hydrate 99% (0.04 mole) in 50 mL of ethanol was refluxed for ten to 15 hours while being shaken periodically. As the hydrogen sulfide gas evolved, the reaction mixture's hue turned light green. During the reaction procedure, a homogenous mixture was produced. After cooling the reaction mixture to room temperature (20 mL), it was diluted with cold water. The necessary triazole formed as a white precipitate upon acidification with dilute hydrochloric acid. It underwent filtration, a cold water wash, drying, and recrystallization from DMSO to achieve purification. Using toluene:ethyl acetate:formic acid (5:4:1, v/v/v) as the solvent system, TLC examination revealed that the chemical was homogenous, yield: 73%, melting point: 210℃.

Synthesis of 4-(benzylideneamino)-5-((5-methoxy-1H-indol-1-yl)methyl)-4H-1,2,4-triazole-3-thiol

In a round-bottom flask, an equal volume of the above-formed compound (0.01 mole) and aldehyde (0.01 mole) was taken in 30 mL of 100% ethanol, and four drops of glacial acetic acid were added. After that, it refluxed for 10 hours. After cooling the reaction mixture to room temperature (RT), the suspension was transferred to ice-cold water. The resultant product was filtered, repeatedly cleaned with cold water, and refined by recrystallization from ethanol to produce compound crystals with a cream color. TLC analysis with a solvent solution of n-Hexane: Petroleum ether (60–40) (6:4 v/v). Yield: 69%, Melting point: 152℃.

IR (KBr): 3190 cm^{-1} (Aromatic C-H Stretching), 3022 cm^{-1} (Aliphatic C-H Stretching) 1597 cm^{-1} (C=N Stretching) 1550 cm^{-1} (Aromatic C=C Stretching), 756 cm^{-1} (C-S bending).

Synthesis of 3-(3-mercapto-5-((5-methoxy-1H-indol-1-yl) methyl)-4H-1,2,4-triazol-4-yl)-2-phenyl thiazolidin-4-one

Thioglycolic acid (0.01 mol) was taken in a round bottom flask and an equimolar solution of the above-formed compound (0.01 mol) was dissolved in 1,4-dioxane (25 mL). A 200 mg little amount of fused $ZnCl_2$ was added to the reaction mixture. The round-bottom flask's contents refluxed for a full day. After cooling, the reaction mixture was treated with ice-cold water that contained sodium bicarbonate in order

to eliminate any unreacted thioglycolic acid. The resultant product was then filtered, cleaned with water, and allowed to crystallize again in DMSO. Solvent system used for TLC was Benzene:Chloroform:Ethanol (5:2:3). Yield- 65%, melting point- 115°C

FTIR (KBr): 3155 cm^{-1} (Ar-CH), 1688 cm^{-1} (C=O), 1602 (C-N), 1555(C=C), 747 cm^{-1}(C-S-C); *1H*-NMR (DMSO-d6): δ 3.6 (d, *2H*, -CH2 of thiazolidinone), 7.4–7.9 (m, 8H, ArH), 8.4 (s, *1H*, -NCHS), 3.7 (s, 3H, O-CH3). 7.8-CH-CH(Triazole).

Synthesis of ethyl 2-((4-(2-subtituted phenyl-4-oxothiazolidin-3-yl)-5-((5-methoxy-1H-indol-1-yl)methyl)-4H-1,2,4-triazol-3-yl)thio)acetate

Using 25 mL of ethanol and above formed compound (0.01 mole), ethyl chloroacetate (0.01 mole) was added. The mixture was then agitated for one hour at room temperature and refluxed for 4 hours while triethylamine (0.01 mole) was present. A solid was then formed by removing the solvent at a lower pressure. Ethanol and water (1:2) were used to recrystallize the material. n-Hexane:Methanol (7:3 v/v) was used as the solvent system for the TLC analysis.Yield: 69%, melting point: 100 to 102°C. The physical data of the synthesized compounds shown in (Table 1). Like wise other substituted thiazolidinones (TI – TXXV) were synthesized (Figure 1).

Ethyl 2-((4-(2-phenyl-4-oxothiazolidin-3-yl)-5-((5-methoxy-1H-indol-1-yl)methyl)-4H-1,2,4-triazol-3-yl)thio)acetate (T-I)

FTIR (KBr): 3142 cm^{-1} (Ar-CH), 1653 cm^{-1} (C=O), 1604 cm^{-1} (C-N), 1531(C=C), 717 cm^{-1}(C-S-C); *1H*-NMR (DMSO-d6): δ 3.8 (d, *2H*, -CH2 of thiazolidinone), 7.4–7.6 (m, 8H, ArH), 8.6 (s, *1H*, -NCHS), 3.4 (s, 3H, O-CH3). 7.7-CH-CH(Triazole), MS m/z: 525 [M+]. Anal. Calcd for $C_{25}H_{27}N_5O_4S_2$:C, 57.12; H, 5.18; N, 13.32. Found:C, 57.01; H, 5.09; N, 13.28%.

Ethyl 2-((4-(2-(4-hydroxyphenyl)-4-oxothiazolidin-3-yl)-5-((5-methoxy-1H-indol-1-yl)methyl)-4H-1,2,4-triazol-3-yl) thio)acetate (T-II)

FTIR (KBr): 3344 cm^{-1} (Ar-OH), 3246 cm^{-1} (Ar-CH), 1697 cm^{-1} (C=O), 1602 cm^{-1} (C-N), 522 cm^{-1} (C-S-C); *1H*-NMR (DMSO-d6): δ 3.2 (d, *2H*, -CH2 of thiazolidinone), 7.3–7.6 (m, 8H, ArH), 8.3 (s, *1H*, -NCHS), 3.2 (s, 3H, O-CH3). 7.4 (m,2H, CH-CH Triazole), MS m/z: 541.2 [M+]. Anal. Calcd for $C_{25}H_{26}BrN_5O_4S_2$:C, 55.44; H, 5.02; N, 12.93. Found:C, 55.31; H, 4.93; N, 12.89%.

Ethyl 2-((4-(2-(4-bromophenyl)-4-oxothiazolidin-3-yl)-5-((5-methoxy-1H-indol-1-yl)methyl)-4H-1,2,4-triazol-3-yl)thio) acetate (T-III)

FTIR (KBr): 3245 cm^{-1} (Ar-CH), 1698 cm^{-1} (C=O), 1601 cm^{-1} (C-N), 521 cm^{-1} (C-Br), 746 cm^{-1}(C-S-C); *1H*-NMR (DMSO-d6): δ 3.7 (d, *2H*, -CH2 of thiazolidinone), 7.2–7.6 (m, 8H, ArH), 8.7 (s, *1H*, -NCHS), 3.3 (s, 3H, O-CH3). 7.9 (m,2H, CH-CH Triazole), MS m/z: 604 [M+]. Anal. Calcd for $C_{25}H_{26}BrN_5O_4S_2$:C, 49.67; H, 4.33; N, 11.58. Found:C, 49.49; H, 4.22; N, 11.50%.

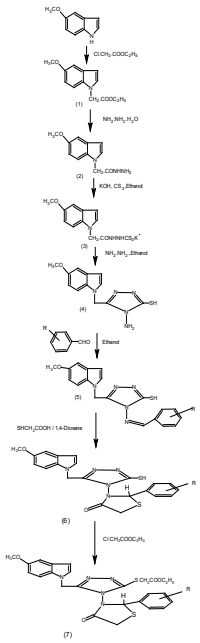

Figure 1: Synthetic route to thiazolidinones

Ethyl 2-((4-(2-(3-hydroxyphenyl)-4-oxothiazolidin-3-yl)-5-((5-methoxy-1H-indol-1-yl)methyl)-4H-1,2,4-triazol-3-yl) thio)acetate (T-IV)

FTIR (KBr): 3340 cm^{-1} (Ar-OH), 3240 cm^{-1} (Ar-CH), 1696 cm^{-1} (C=O), 1601 cm^{-1} (C-N), 529 cm^{-1} [1](C-S-C); *1H*-NMR (DMSO-d6): δ 3.6 (d, *2H*, -CH2 of thiazolidinone), 71–7.6 (m, 8H, ArH), 8.5 (s, *1H*, -NCHS), 3.7 (s, 3H, O-CH3). 7.7(m,2H, CH-CH Triazole), MS m/z: 541.4 [M+]. Anal. Calcd for $C_{25}H_{26}BrN_5O_4S_2$:C, 55.44; H, 5.02; N, 12.93. Found:C, 55.35; H, 4.92; N, 12.84%.

Ethyl 2-((4-(2-(2-hydroxyphenyl)-4-oxothiazolidin-3-yl)-5-((5-methoxy-1H-indol-1-yl)methyl)-4H-1,2,4-triazol-3-yl) thio)acetate (T-V)

FTIR (KBr): 3346 cm^{-1} (Ar-OH), 3236 cm^{-1} (Ar-CH), 1691 cm^{-1} (C=O), 1605 cm^{-1} (C-N), 524 cm^{-1} [1](C-S-C); *1H*-NMR (DMSO-d6): δ 3.4 (d, *2H*, -CH2 of thiazolidinone), 7.2–7.6 (m, 8H, ArH), 8.4 (s, *1H*, -NCHS), 3.5 (s, 3H, O-CH3). 7.5(m,2H, CH-CH Triazole), MS m/z: 541.9 [M+]. Anal. Calcd for $C_{25}H_{26}BrN_5O_4S_2$:C, 55.44; H, 5.02; N, 12.93. Found:C, 55.35; H, 4.93; N, 12.85%.

Ethyl 2-((4-(2-(4-chlorophenyl)-4-oxothiazolidin-3-yl)-5-((5-methoxy-1H-indol-1-yl)methyl)-4H-1,2,4-triazol-3-yl)thio) acetate (T-IX)

FTIR (KBr): 3178 cm^{-1} (Ar-CH), 1670 cm^{-1} (C=O), 1547 cm^{-1} (C-N), 561 cm^{-1} (C-Cl), 756 cm^{-1} (C-S-C); *1H*-NMR (DMSO-d6): δ 3.5 (d, *2H*, -CH2 of thiazolidinone), 7.5–7.8 (m, 8H, ArH), 8.8 (s, *1H*, -NCHS), 3.4 (s, 3H, O-CH3). 7.9(m,2H, CH-CH Triazole), MS m/z: 560.09 [M+]. Anal. Calcd for $C_{25}H_{26}ClN_5O_4S_2$:C,53.61; H, 4.68; N, 12.50. Found:C, 53.50; H, 4.60; N, 12.45%.

Table 1: Physical data of synthesized compounds

S. No.	*Compound*	*R*	*Molecular formula*	*Molecular weight*	*%Yeild*	*M.P.(ºC)*	*Rf value*
1	T-I	H	$C_{25}H_{27}N_5O_4S_2$	525.64	69	100-102	0.62
2	T-II	4-OH	$C_{25}H_{27}N_5O_5S_2$	541.64	65	182-185	0.60
3	T-III	4-Br	$C_{25}H_{26}BrN_5O_4S_2$	604.54	70	188-190	0.71
4	T-IV	3-OH	$C_{25}H_{27}N_5O_5S_2$	541.64	61	166-168	0.82
5	T-V	2-OH	$C_{25}H_{27}N_5O_5S_2$	541.64	62	151-153	0.69
6	T-VI	2-Cl	$C_{25}H_{26}ClN_5O_4S_2$	560.09	52	189-191	0.77
7	T-VII	4-CH_3	$C_{26}H_{29}N_5O_4S_2$	539.67	69	208=210	0.77
8	T-VIII	2-NO_2	$C_{25}H_{26}N_6O_6S_2$	570.64	52	198-200	0.58
9	T-IX	4-Cl	$C_{25}H_{26}ClN_5O_4S_2$	560.09	67	118-120	0.71
10	T-X	4-OCH_3	$C_{26}H_{29}N_5O_5S_2$	555.67	49	140-142	0.67
11	T-XI	3-NO_2	$C_{25}H_{26}N_6O_6S_2$	570.64	62	188-200	0.59
12	T-XII	3,4(OCH_3)$_2$	$C_{27}H_{29}N_5O_6S_2$	585.69	57	149-152	0.71
13	T-XIII	3,4(Cl)$_2$	$C_{25}H_{25}Cl_2N_5O_4S_2$	594.53	68	159-161	0.81
14	T-XIV	4-N(CH_3)$_2$	$C_{27}H_{32}N_6O_4S_2$	568.71	58	143-145	0.66
15	T-XV	3,4,5(OCH_3)$_3$	$C_{28}H_{33}N_5O_7S_2$	615.72	53	151-155	0.61
16	T-XVI	2-OCH_3	$C_{26}H_{29}N_5O_5S_2$	555.67	68	111-113	0.72
17	T-XVII	3-OCH_3	$C_{26}H_{29}N_5O_5S_2$	555.67	62	109-111	0.77
18	T-XVIII	4-NO_2	$C_{25}H_{26}N_6O_6S_2$	570.64	72	203-205	0.51
19	T-XIX	4-OH-3-OCH_3	$C_{26}H_{29}N_5O_6S_2$	571.67	53	165-168	0.77
20	T-XX	3,4(OH)$_2$	$C_{25}H_{27}N_5O_6S_2$	557.64	62	158-160	0.61
21	T-XXI	2-OH-4-OCH_3	$C_{26}H_{29}N_5O_6S_2$	571.67	63	169-171	0.71
22	T-XXII	3-Cl	$C_{25}H_{26}ClN_5O_4S_2$	560.09	69	123-125	0.61
23	T-XXIII	4-N(C_2H_5)$_2$	$C_{29}H_{36}N_6O_4S_2$	596.76	65	153-156	0.73
24	T-XXIV	2,4-(OCH_3)$_2$	$C_{27}H_{31}N_5O_6S_2$	585.69	48	171-173	0.74
25	T-XXV	4(OC_2H_5)	$C_{27}H_{31}N_5O_5S_2$	569.69	56	182-184	0.59

Ethyl 2-((4-(2-(4-methoxyphenyl)-4-oxothiazolidin-3-yl)-5-((5-methoxy-1H-indol-1-yl)methyl)-4H-1,2,4-triazol-3-yl) thio)acetate (T-X)

FTIR (KBr): 3161 cm^{-1} (Ar-CH), 1678 cm^{-1} (C=O), 1602 cm^{-1} (C-N), 567 cm^{-1} (C-Cl), 755 cm^{-1} (C-S-C); ^1H-NMR (DMSO-d6): δ 3.2 (d, *2H*, -CH2 of thiazolidinone), 7.2–7.8 (m, 8H, ArH), 8.7 (s, *1H*, -NCHS), 3.3 (s, 3H, O-CH3). 7.8(m,2H, CH-CH Triazole), MS m/z: 555.4[M+]. Anal. Calcd for $C_{26}H_{29}N_5O_5S_2$:C, 56.20; H, 5.26; N, 5.19. Found:C, 56.09; H, 5.19; N, 12.51%.

Ethyl 2-((4-(2-(2-methoxyphenyl)-4-oxothiazolidin-3-yl)-5-((5-methoxy-1H-indol-1-yl)methyl)-4H-1,2,4-triazol-3-yl) thio)acetate (T-XVI)

FTIR (KBr): 31975 cm^{-1} (Ar-CH), 1673 cm^{-1} (C=O), 1603 cm^{-1} (C-N), 784 cm^{-1} (C-S-C); ^1H-NMR (DMSO-d6): δ 3.5 (d, *2H*, -CH2 of thiazolidinone), 7.4-7.9 (m, 8H, ArH), 8.6 (s, *1H*, -NCHS), 3.4 (s, 3H, O-CH3). 7.9(m,2H, CH-CH Triazole), MS m/z: 555.1 [M+]. Anal. Calcd for $C_{26}H_{29}N_5O_5S_2$:C, 56.20; H, 5.26; N, 5.19. Found:C, 56.09; H, 5.19; N, 12.51%.

Ethyl 2-((4-(2-(3-methoxyphenyl)-4-oxothiazolidin-3-yl)-5-((5-methoxy-1H-indol-1-yl)methyl)-4H-1,2,4-triazol-3-yl) thio)acetate (T-XVII)

FTIR (KBr): 3197 cm^{-1} (Ar-CH), 1671 cm^{-1} (C=O), 1604 cm^{-1} (C-N), 780 cm^{-1} (C-S-C); ^1H-NMR (DMSO-d6): δ 3.4 (d, *2H*, -CH2 of thiazolidinone), 7.4–7.8 (m, 8H, ArH), 8.7 (s, *1H*, -NCHS), 3.5 (s, 3H, O-CH3). 7.8(m,2H, CH-CH Triazole), MS m/z: 555.2 [M+]. Anal. Calcd for $C_{26}H_{29}N_5O_5S_2$:C, 56.20; H, 5.26; N, 5.19. Found:C, 56.09; H, 5.19; N, 12.51%.

Ethyl 2-((4-(2-(4-nitrophenyl)-4-oxothiazolidin-3-yl)-5-((5-methoxy-1H-indol-1-yl)methyl)-4H-1,2,4-triazol-3-yl)thio) acetate (T-XVIII)

FTIR (KBr): 3167 cm^{-1} (Ar-CH), 1655 cm^{-1} (C=O), 1629 cm^{-1}(C-N), 1540 cm^{-1} (N-O), 759 cm^{-1} (C-S-C); ^1H-NMR (DMSO-d6): δ 4.3 (d, *1H*, CH, thiazolidinone), 7.5–7.8 (m, 8H, ArH), 8.5 (s, *1H*, -NCHS), 4.7 (s, 3H, O-CH3). MS m/z: 570.2 [M+]. Anal. Calcd for $C_{26}H_{28}ClN_5O_5S$: C, 52.62; H, 4.59; N, 14.73. Found :C, 52.51; H, 4.50; N, 14.69%.

Table 2: Antibacterial activity of thiazolidinone compounds

S. No	*Thiazolidinone derivative*	*Substitution at R*	*Minimum inhibitory concentration (µg/mL)*			
			Gram-positive bacteria		*Gram-negative bacteria*	
			S. aereus ATCC6538	*E. faecalis ATCC 2912*	*E. coli ATCC8739*	*P. aeruginosa ATCC9027*
1	T-I	H	50	50	100	50
2	T-II	4-OH	12.5	12.5	12.50	12.50
3	T-III	4-Br	6.25	6.25	6.25	6.25
4	T-IV	3-OH	50	50	50	25
5	T-V	2-OH	100	50	100	50
6	T-VI	2-Cl	12.5	12.5	12.5	50
7	T-VII	4-CH_3	50	100	100	50
8	T-VIII	2-NO_2	12.5	12.5	12.5	50
9	T-IX	4-Cl	6.25	6.25	6.25	6.25
10	T-X	4-OCH_3	6.25	12.5	6.25	12.5
11	T-XI	3-NO_2	12.5	12.5	50	50
12	T-XII	3,4$(OCH_3)_2$	12.5	50	100	100
13	T-XIII	3,4$(Cl)_2$	12.5	12.5	12.5	12.5
14	T-XIV	4-N$(CH_3)_2$	50	100	50	100
15	T-XV	3,4,5$(OCH_3)_3$	12.5	25	50	50
16	T-XVI	2-OCH_3	100	50	100	50
17	T-XVII	3-OCH_3	25	50	50	50
18	T-XVIII	4-NO_2	6.25	6.25	6.25	6.25
19	T-XIX	4-OH-3-OCH_3	25	50	50	50
20	T-XX	3,4$(OH)_2$	50	25	50	50
21	T-XXI	2-OH-4-OCH_3	50	25	50	12.5
22	T-XXII	3-Cl	25	12.5	6.25	12.5
23	T-XXIII	4-N$(C_2H_5)_2$	50	100	100	100
24	T-XXIV	2,4-$(OCH_3)_2$	50	25	12.5	12.5
25	T-XXV	4(OC_2H_5)	100	100	100	50
26	Std	Penicillin	6.25	6.25	6.25	6.25

Ethyl 2-((4-(2-(3-chlorophenyl)-4-oxothiazolidin-3-yl)-5-((5-methoxy-1H-indol-1-yl)methyl)-4H-1,2,4-triazol-3-yl)thio) acetate (T-XXII)

FTIR (KBr): 3171 cm^{-1} (Ar-CH), 1671 cm^{-1} (C=O), 1546 (C-N), 564 cm^{-1} (C-Cl), 754 cm^{-1} (C-S-C); ^{1}*H*-NMR (DMSO-d6): δ 3.4 (d, *2H*, -CH2 of thiazolidinone), 7.5–7.9 (m, 8H, ArH), 8.9 (s, *1H*, -NCHS), 3.2 (s, 3H, O-CH3). 7.8(m,2H, CH-CH Triazole), MS m/z: 560.01 [M+]. Anal. Calcd for $C_{25}H_{26}ClN_5O_4S_2$:C,53.61; H, 4.68; N, 12.50. Found:C, 53.51; H, 4.61; N, 12.43%.

Antimicrobial Evaluation

The antibacterial studies of thiazolidinediones derivatives were carried out against gram-positive microorganism *Staphylococcus aureus*, *E. faecalis* and gram-negative microorganism *Pseudomonas aeruginosa*, *Escherichia coli,* while the antifungal study of synthesized derivatives was carried out against *C. abicans and Aspergillus niger.* The *in-vitro* antimicrobial activity was assessed under standard operating circumstances by disc diffusion technique using the Muller Hinton Agar medium. Newly grown cultures of microorganisms were put onto Muller Hinton agar plates in a laminar flow cabinet and incubated for 24 hours at 37°C. Before the drug solution was soaked onto sterile discs of Whatman filter paper No. 1 (6 mm diameter), it was dissolved in dimethylsulfoxide (DMSO). After that, the discs were placed over of the previously prepared plates and allowed to incubate for 24 hours at 37°C, the diameter of the zone of inhibition was measured in mm. As a disc impregnated with DMSO was used as a negative control. To compare the activity, the

antibiotics penicillin and fluconazole were used as standard for determination of antibacterial and antifungal activity, respectively.

Determination of the minimal inhibitory concentration

The disc diffusion technique technique was used to calculate the minimal inhibitory concentration (MIC). Gradient amounts of tested components were combined with a predetermined quantity of sterile molten agar (Muller Hinton agar) to create a stock solution in DMSO. After making the microbial suspension (105 CFU/mL), it was added to test plates containing synthesized compound solution in DMSO and incubated for 24 hours at 37°C. Once the incubation time was over, the MIC values were ascertained. Every measurement was made three times, with the average serving as the final reading. A positive control of 6.25 µg/mL of antibiotic penicillin was used for antibacterial as shown in (Table 2) and 12,5 µg/mL of fluconazole for antifungal activity as shown in (Table 3) whereas a negative control of 100 mL of DMSO was employed. The MIC was defined as the test substance's concentration at which no observable bacterial or fungal growth could be seen on the plate.

RESULT AND DISCUSSION

Chemistry

Fourier transform infrared (FTIR) spectroscopy revealed the main features of the synthesized compounds. Proton nuclear magnetic resonance (^{1}H-NMR) ascertained the main structural characteristics. Mass spectrometry shows base peaks that are similar or almost match their molecular mass. A comprehensive examination of the mass spectra shows some significant differences. Additionally, many fragment peaks appear at different m/z ranges. The percentages of carbon, nitrogen and

Table 3: Antifungal activity of thiazolidinedione compounds

S. No.	*Thiazolidinone derivative*	*Substitution at R*	*Minimum inhibitory concentrations (µg/mL)*	
			Fungus	
			C. albicans ATCC 10231	*Aspergillus niger ATCC 10581*
1	T-I	H	100	100
2	T-II	4-OH	12.5	12.5
3	T-III	4-Br	12.5	12.5
4	T-IV	3-OH	200	100
5	T-V	2-OH	100	200
6	T-VI	2-Cl	23	25
7	T-VII	4-CH_3	50	100
8	T-VIII	2-NO_2	25	12.5
9	T-IX	4-Cl	12.5	12.5
10	T-X	4-OCH_3	12.5	12.5
11	T-XI	3-NO_2	12.5	12.5
12	T-XII	3,4$(OCH_3)_2$	25	12.5
13	T-XIII	3,4$(Cl)_2$	25	50
14	T-XIV	4-N$(CH_3)_2$	50	100
15	T-XV	3,4,5$(OCH_3)_3$	50	50
16	T-XVI	2-OCH_3	50	25
17	T-XVII	3-OCH_3	50	25
18	T-XVIII	4-NO_2	12.5	12.5
19	T-XIX	4-OH-3-OCH_3	25	50
20	T-XX	3,4$(OH)_2$	25	25
21	T-XXI	2-OH-4-OCH_3	50	50
22	T-XXII	3-Cl	12.5	25
23	T-XXIII	4-N$(C_2H_5)_2$	200	200
24	T-XXIV	2,4-$(OCH_3)_2$	50	50
25	T-XXV	4(OC_2H_5)	100	200
26	Std	Flucanozole	12.5	12.5

hydrogen in the compounds were determined by elemental analysis and the results were consistent with theoretical value.

Antimicrobial Activity

Antibacterial activity

The antibacterial activity results revealed that compounds T-III, T-IX, T-XVIII displayed equipotent activity compared with the standard drug. The compounds with p-hydroxy, p-chloro and p-nitro groups exhibited the most potent antimicrobial agent.

Antifungal activity

The antifungal activity results revealed that compound T-II. T-III, T-IX, , T-X, T-XI, T-XVIII exhibited equipotent activity compared with the standard drug. Compounds with electron-withdrawing groups such as bromo, chloro methoxy and electron-donating group such as nitro demonstrated the highest antifungal activity.

CONCLUSION

In the present study, a highly efficient and simple procedure for the synthesis of ethyl 2-((4-(2-substituted phenyl -4-oxothiazolidin-3-yl)-5-((5-methoxy-1H-indol-1-yl)methyl)-4H-1,2,4-triazol-3-yl)thio)acetate, (TI-TXXV), where indolyl and 1,2,4-triazole rings are attached, was developed. The adopted method is easy, inexpensive and gives good yields. On the basis of antibacterial and antifungal tests, it can be said that most of the compounds are active against bacteria and fungi when compared with standard drugs.

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