Synthesis, Characterization, Antibacterial, and Antifungal Activity of Novel 2-(2-hydroxy-5-((aryl)-diazenyl)phenyl)-3-(4-hydroxyphenyl)-thiazolidin-4-one

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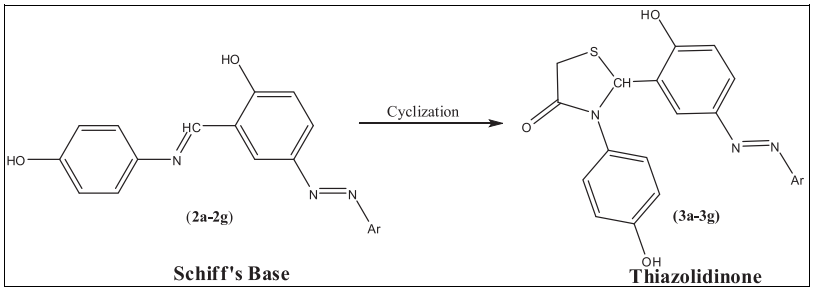

A series of novel thiazolidinones, that is, 2-(2-hydroxy-5-((aryl)-diazenyl)phenyl)-3-(4-hydroxyphenyl)-thiazolidin-4-one, have been synthesized by reaction of various Schiff bases 2-(4-hydroxyphenylimino) methyl)-4-(aryl)diazenyl)phenol with ethanolic thioglycolic acid. Schiff bases were obtained by the reactions of 4-amino phenol with 2-hydroxy-5-((aryl)diazenyl)benzaldehyde. The structures of the newly synthesized compounds were confirmed by IR, ^{1}H NMR, mass spectra, and C, H, N elemental analysis. The thiazolidinone derivatives were evaluated for their antibacterial and antifungal activity.

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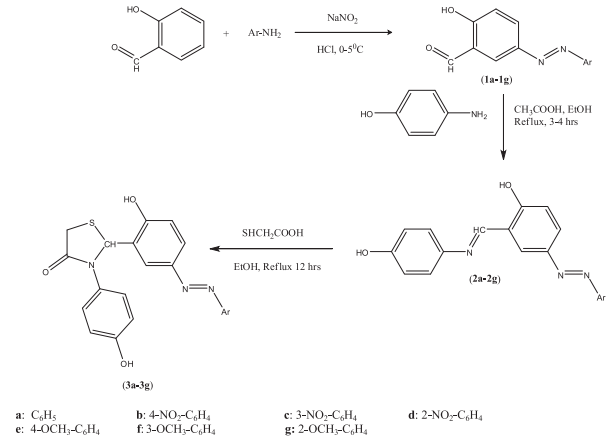
INTRODUCTION

The last few decades have seen a flurry of research activities in the synthesis and development of heterocyclic compounds because of their important biological properties [1]. Heterocyclic compounds containing small rings have been under investigation for a long time because of their important medicinal properties and also contributed to the society from biological and industrial points of view, which help to understand life processes. Among these types of heterocyclic molecules, 4-thiazolidinones have been shown to have various important biological activities such as antibacterial [2], antifungal [3], antioxidant [4], anticancer [5], analgesic [6], anti-inflammatory [7], central nervous system active agent [8], anticonvulsant [9], anti-HIV [10], antitubercular [11], and antiviral activities [12].

Schiff's bases are condensation products of primary amines with carbonyl compounds gaining importance day by day in present scenario. Schiff's bases are the compounds carrying imine or azomethine (–C = N–) functional group and are found to be a versatile pharmacophore for design and development of various bioactive compounds. Schiff's bases exhibit useful biological activities such anti-inflammatory, analgesic, antimicrobial, anticonvulsant, antitubercular, anticancer, antioxidant, anthelmintic, antiglycation, and antidepressant activities. Schiff's bases are also used as catalysts, pigments and dyes, intermediates in organic synthesis, polymer stabilizers, and corrosion inhibitors [13]. It has been found that the activity of azo linkage increases on the incorporation of suitable heterocyclic moiety [14].

The increasing cases of microbial resistance pose a major concern to the pharmaceutical industries and have become a threat for human life worldwide. Moreover, invasive microbial infections caused by multi-drug-resistant Gram-positive and Gram-negative bacteria, fungi, viruses, and other microbes are difficult to diagnose and treat. They are the major cause of morbidity and mortality especially in immune-suppressed and hospital-acquired patients. In such scenario, a pharmacophore hybrid approach for exploration of novel and highly active compounds is an effective and commonly used direction in modern medicinal chemistry. Hybridization of two different bioactive molecules with complementary pharmacophoric functions or with different mechanisms of action often showed synergistic effects [15,16]. This hypothesis was confirmed by the results of our previous studies that allowed identification of the antibacterial and antifungal activity of 4-thiazolidinone derivatives coupled with other heterocyclic fragments in one molecule [17]. In continuation of this theme, we have synthesized new heterocyclic compounds containing pharmacologically attractive 4-thiazolidinone, azo linkage,

Scheme 1. Synthetic route of 2-(2-hydroxy-5-((aryl)-diazenyl)phenyl)-3-(4-hydroxyphenyl)-thiazolidin-4-one (**3a–3g**).



and Schiff's base moieties (Scheme 1) and undertaken the systematic study of these new compounds for their potency as an antibacterial and antifungal agent. Also, these synthesized compounds were characterized using different analytical and spectroscopic techniques.

RESULTS AND DISCUSSION

General. An efficient synthesis of series of thiazolidinones, that is, 2-(2-hydroxy-5-((aryl)-diazenyl) phenyl)-3-(4-hydroxyphenyl)-thiazolidin-4-one, has been done by reaction of various Schiff bases, that is, 2-(4-hydroxyphenylimino)methyl)-4-(aryl)diazenyl)phenol with ethanolic thioglycolic acid. Schiff bases were obtained by the reactions of 4-amino phenol with 2-hydroxy-5-((aryl) diazenyl)benzaldehyde. The starting compounds, that is, 2-hydroxy-5-((aryl)diazenyl)benzaldehyde, have been obtained in the similar manner as reported earlier in our previous papers [18]. Physical properties and characterization data of compounds **1a**, **1b**, **1c**, and **1d** have been provided in the literatures [18]. The newly obtained crude products were recrystallized in chloroform. The yield of the products obtained within 70%–85%. The structural elucidation of starting aromatic aldehydes (**1e–1g**), Schiff's bases (**2a–2g**), and thiazoloidinones (**3a–3g**) were done using various spectral and analytical methods such as by IR, ^{1}H NMR, mass spectral, and C, H, N elemental analysis. Formation of Schiff's bases were confirmed with strong signal at 1650–1690 cm^{-1} for the **–**N = C**–** group in the compounds **2a–2g**, whereas the disappearance of such peaks and the appearance of IR frequencies at 650–690 cm^{-1} for the **C-S-C 4-**thiazolodinone group and 1610–1690 cm^{-1} for the C = O confirms the formation of the thiazolidinone ring in the newly synthesized compounds. Resultant data obtained from the ^{1}H-NMR, mass spectra, and elemental analysis confirmed the structure of these compounds.

In-vitro antibacterial and antifungal activity. A new series 2-(2-hydroxy-5-((aryl)-diazenyl)phenyl)-3-(4-hydroxyphenyl)-thiazolidin-4-one (**3a–3g**) have been synthesized and evaluated for their ability to inhibit the growth of different bacterial strains such as *Staphylococcus aureus*, *Bacillus subtilis*, *Pseudomonas sp*., and *Escherichia coli*, whereas antifungal activity was checked against the *Candida albicans* and *Aspergillus niger* strains. The antibacterial and antifungal activities of the compound were evaluated by measuring the zone of inhibition on nutrient agar plates and Sabouraudı's agar plates, respectively. The results were recorded in triplicate using ampicillin as a standard drug for antibacterial activity whereas flucanazole as a standard drug for antifungal activity. The results have been collected in Table 1.

It can be observed from the Table 1 that compounds **3c**, **3d**, **3f**, and **3g** have shown good biological activity, whereas **3b** and **3e** even shown better activity as compared to bioactivity of standard drug against *S. aureus*. Compounds **3d**, **3e**, **3f**, and **3g** posses better bioactivity in comparision with standard drug against *B. subtilis*. Compounds **3c**, **3d**, **3f**, and **3g** posses good antibacterial activity as compared with ampicillin against *Pseudomonas sp*. Gram-negative

Table 1

Biological activities of 2-(2-hydroxy-5-((aryl)-diazenyl)phenyl)-3-(4-hydroxyphenyl)-thiazolidin-4-one.

	Antibacterial activity				Antifungal activity	
	(Zone of inhibition in mm at 500 µg/mL)					
Compound	*S. aureus*	*B. subtilis*	*Pseudomonas sp*.	*E. coli*	*C. albicans*	*A. niger*
3a	5.6	4.8	9.7	14.8	10.5	11.7
3b	9.3	5.2	11.0	17.9	12.4	10.4
3c	8.7	5.8	13.8	14.2	13.7	11.4
3d	8.9	6.9	12.5	15.7	12.7	11.9
3e	10.2	6.4	11.8	18.2	11.8	13.4
3f	8.4	7.0	14.0	14.8	11.0	15.8
3 g	8.9	7.3	13.0	16.3	10.1	14.9
Standard drug	9	6	12	17	13	15

bacterial stains. Compounds **3b**, **3e**, **3d**, and **3g** posses good to better activity against *E. coli* bacterial stains. Thus, it can be concluded that the bacterial activity of the compounds is due to the presence of the thiazolidinone ring present, and it also depends up on the group attached to the ring and its position. When an antifungal study was done, it was observed that compounds **3b**, **3c**, and **3d** posses good activity against *C. albicans*, whereas compounds **3d**, **3e**, and **3f** posses good activity against *A. niger*.

Compounds possessing a nitro group on the ring structure are the most active group against *C. albicans*, while the hydroxyphenyl-group possessing derivatives have good activity against *A. niger*. Further biological assessment is also warranted to determine additional biological parameters to have a deeper insight into structure–activity relationship and to optimize the effectiveness of this series of molecules. It would have also been interesting to study bioactivity with a wider range of compounds to establish the importance of the functional groups.

MATERIALS AND METHODS

All the chemicals and solvents were obtained from E-Merck, India (AR grade) and were used without further purification. Melting points were taken in an open capillary tube. IR spectra were recorded on a Shimadzu Dr-8031 instrument. Elemental analyses were carried out using a Perkin-Elmer, CHN elemental analyzer model 2400. ^{1}H NMR spectra of the synthesized compounds were recorded on a Bruker-Avance (300 MHz), Varian-Gemini (200 MHz) spectrophotometer using $CDCl_3$ solvent and TMS as the internal standard. EI-MS spectra were determined on a LCQ ion trap mass spectrometer (Thermo Fisher, San Jose, CA, USA), equipped with an EI source.

General Procedure for the synthesis of 2-Hydroxy-5-((aryl) diazenyl)benzaldehyde (1a–1 g). Aromatic amines (0.01 mol) was added in conc. HCl (5 mL) and boiled for 10 min. The resulting solution was then cooled to 0–5°C in ice bath. Aqueous sodium nitrite ($NaNO_2$) (0.01 mol, 10 mL) solution in the cold condition was added in dropwise manner to this solution. The reaction mixture was then vigorously stirred. The temperature of the reaction mixture was maintained within 0–5°C for at least 1 h to obtain diazonium chloride solution. The resulting diazonium solution was then poured slowly to alkaline suspension of salicylaldehyde in water (10 mL, 0.01 mol) with continuous stirring, keeping the temperature within 0–5°C. The pH of the reaction mixture was maintained within 8 to 10 by simultaneous addition of 10% aqueous sodium hydroxide solution. The resulting reaction mixture was kept unstirred for overnight. The obtained solid precipitate was filtered using Whatman filter paper number 40 and recrystallized using ethanol.

Characterization of 2-hydroxy-5-(*p*-tolyloxy-diazenyl)-benzaldehyde (1e). Yield, 87.16%; m. p.: 125°C; IR (KBr) cm^{-1}: 1055 (Ar-O-CH_3), 1485 (N=N), 1735 (aldehydic C=O), 2855 (aldehydic H-C=), 3455 (Ar-OH); ^{1}H NMR ($CDCl_3$) δ: 2.30 (s, 3H, Ar-CH_3), 6.90 (d, 2H, Ar-CH), 7.10–7.15 (m, 3H, Ar-CH), 7.35 (m, 2H, Ar-CH), 10.40 (s, 1H, Ar-CHO), 11.90 (s, 1H, Ar-OH); elemental analysis of $C_{14}H_{12}N_2O_3$, Calcd. (%): C 65.62, H 4.72, N 10.93; found (%): C 65.60, H 4.80, N 11.05; MS: *m/z* 258 (M^+, 100%).

Characterization of 2-hydroxy-5-(*m*-tolyloxy-diazenyl)-benzaldehyde (1f). Yield, 80.55%; m. p.: 130°C; IR (KBr) cm^{-1}: 1050 (Ar-O-CH_3), 1489 (N=N), 1745 (aldehydic C=O), 2860 (aldehydic H-C=), 3460 (Ar-OH); ^{1}H NMR ($CDCl_3$) δ: 2.35 (s, 3H, Ar-CH_3), 6.75–6.80 (m, 2H, Ar-CH), 7.05 (s, 1H, Ar-CH), 7.15–7.20 (m, 2H, Ar-CH), 7.40–7.45 (m, 2H, Ar-CH), 10.45 (s, 1H, Ar-CHO), 11.80 (s, 1H, Ar-OH); elemental analysis of $C_{14}H_{12}N_2O_3$, Calcd. (%): C 65.62, H 4.72, N 10.93; found (%): C 64.90, H 4.70, N 10.00; MS: *m/z* 257 (M^+, 100%).

Characterization of 2-hydroxy-5-(*m*-tolyloxy-diazenyl)-benzaldehyde (1g). Yield, 80.55%; m. p.: 132°C; IR (KBr) cm^{-1}: 1060 (Ar-O-CH_3), 1490 (N=N), 1740 (aldehydic C=O), 2852 (aldehydic H-C=), 3455 (Ar-OH); ^{1}H NMR ($CDCl_3$) δ: 2.10 (s, 3H, Ar-CH_3), 6.85–6.95 (m, 3H, Ar-CH), 7.05–7.10 (m, 2H, Ar-CH), 7.40 (t, 2H, Ar-CH), 10.40 (s, 1H, Ar-CHO), 11.90 (s, 1H, Ar-OH); elemental analysis of $C_{14}H_{12}N_2O_3$, Calcd. (%): C 65.62, H 4.72, N 10.93; found (%): C 65.50, H 4.75, N 10.80; MS: *m/z* 257 (M^+, 100%).

General procedure of synthesis of 2-(4-hydroxyphenylimino) methyl)-4-(aryl)diazenyl)phenol (2a–2g). Equimolar amount of 2-hydroxy-5-((aryl)diazenyl)benzaldehyde (**1a–1g**) (0.002 mol) and 4-amino phenol (0.002 mol) was dissolved in ethanol (10 mL), and the reaction mixture was refluxed for 3–4 h. The completion of the reaction was monitored by TLC. After the completion of reaction, it was poured in ice-cold water, and the solid precipitate was separated out. The solid deposited was separated by filtration. The crude product obtained was recrystallized from chloroform.

Characterization of 2-(4-hydroxyphenylimino)-methyl)-4-(phenyldiazenyl)-phenol (2a). Yield: 85%; m. p.: 70°C; IR (KBr) cm^{-1}: 1420 (C=C), 1450 (N=N), 1640 (–C=N–), 2350 (Ar-CH), 3100 (Ar-OH), 3210 (Ar-OH); ^{1}H NMR ($CDCl_3$): δ=6.80 (d, 2H, Ar-CH), 7.10–7.30 (m, 4H, Ar-CH), 7.60 (t, 2H, Ar-CH), 8.70 (d, 1H, Ar-CH), 8.80 (d, 2H, Ar-CH), 9.10 (s, 1H, Ar-CH), 9.30 (s, 1H, N=CH), 9.50 (s, 1H, Ar-OH), 11.30 (s, 1H, Ar-OH); elemental analysis of $C_{19}H_{15}N_3O_2$, Calcd. (%): C 71.91, H 4.76, N 13.24; found (%): C 71.90, H 4.70, N 13.20; MS: *m/z* 317.10 (M^+, 100%).

Characterization of 2-(4-hydroxyphenylimino)-methyl)-4-(4-nitrophenyl)-diazenyl)-phenol (2b). Yield: 80%; m. p.: 85°C; IR (KBr) cm^{-1}: 1310 (Ar-NO_2), 1440 (C=C),

1470 (N=N), 1670 (–C=N–), 2370 (Ar-CH), 3110 (Ar-OH), 3220 (Ar-OH); ^{1}H NMR ($CDCl_3$): δ=6.90 (d, 2H, Ar-CH), 7.10–7.20 (m, 3H, Ar-CH), 7.80 (d, 2H, Ar-CH), 8.30 (q, 2H, Ar-CH), 8.70 (d, 1H, Ar-CH), 9.00 (s, 1H, Ar-CH), 9.20 (s, 1H, N=CH), 9.60 (s, 1H, Ar-OH), 11.40 (s, 1H, Ar-OH); elemental analysis of $C_{19}H_{14}N_4O_4$, Calcd. (%): C 62.98, H 3.89, N 15.46; found (%): C 62.90, H 3.80, N 15.40; MS: *m/z* 362.00 (M^+, 100%).

Characterization of 2-(4-hydroxyphenylimino)-methyl)-4-(3-nitrophenyl)-diazenyl)-phenol (2c). Yield: 75%; m. p.: 82°C; IR (KBr) cm^{-1}: 1330 (Ar-NO_2), 1430 (C=C), 1480 (N=N), 1650 (–C=N–), 2390 (Ar-CH), 3120 (Ar-OH), 3220 (Ar-OH); ^{1}H NMR ($CDCl_3$): δ=6.85 (d, 2H, Ar-CH), 7.20–7.25 (m, 3H, Ar-CH), 7.90 (t, 1H, Ar-CH), 8.40 (q, 1H, Ar-CH), 8.70–8.80 (m, 2H, Ar-CH), 9.05 (s, 1H, Ar-CH), 9.30 (s, 1H, N=CH), 9.55 (s, 1H, Ar-OH), 11.30 (s, 1H, Ar-OH); elemental analysis of $C_{19}H_{14}N_4O_4$, Calcd. (%): C 62.98, H 3.89, N 15.46; found (%): C 62.80, H 3.80, N 15.30; MS: *m/z* 362.10 (M^+, 100%).

Characterization of 2-(4-hydroxyphenylimino)-methyl)-4-(2-nitrophenyl)-diazenyl)-phenol (2d). Yield: 78%; m. p.: 80°C; IR (KBr) cm^{-1}: 1320 (Ar-NO_2), 1410 (C=C), 1450 (N=N), 1660 (–C=N–), 2380 (Ar-CH), 3100 (Ar-OH), 3210 (Ar-OH); ^{1}H NMR ($CDCl_3$): δ=6.80 (d, 2H, Ar-CH), 7.15–7.30 (m, 3H, Ar-CH), 7.90–8.20 (m, 2H, Ar-CH), 8.30–8.35 (q, 2H, Ar-CH), 8.75 (d, 1H, Ar-CH), 9.10 (s, 1H, Ar-CH), 9.15 (s, 1H, N=CH), 9.45 (s, 1H, Ar-OH), 11.25 (s, 1H, Ar-OH); elemental analysis of $C_{19}H_{14}N_4O_4$, Calcd. (%): C 62.98, H 3.89, N 15.46; found (%): C 62.80, H 3.70, N 15.40; MS: *m/z* 362.00 (M^+, 100%).

Characterization of 2-(4-hydroxyphenylimino)-methyl)-4-((4-methoxyphenyl)-diazenyl)phenol (2e). Yield: 84%; m. p.: 95°C; IR (KBr) cm^{-1}: 1035 (Ar-O-CH_3), 1410 (C=C), 1480 (N=N), 1660 (–C=N–), 2360 (Ar-CH), 3130 (Ar-OH), 3250 (Ar-OH); ^{1}H NMR ($CDCl_3$): δ=3.83 (s, 3H, O-CH_3), 6.80 (d, 2H, Ar-CH), 7.20–7.25 (m, 5H, Ar-CH), 7.85 (d, 2H, Ar-CH), 8.70 (d, 1H, Ar-CH), 9.10 (s, 1H, Ar-CH), 9.30 (s, 1H, N=CH), 9.50 (s, 1H, Ar-OH), 11.25 (s, 1H, Ar-OH); elemental analysis of $C_{20}H_{17}N_3O_3$, Calcd. (%): C 69.15, H 4.93, N 12.10; found (%): C 69.45, H 5.05, N 12.05; MS: *m/z* 349.35 (M^+, 100%).

Characterization of 2-(4-hydroxyphenylimino)-methyl)-4-((3-methoxyphenyl)-diazenyl)phenol (2f). Yield: 70%; m. p.: 93° C; IR (KBr) cm^{-1}: 1045 (Ar-O-CH_3), 1430 (C=C), 1450 (N=N), 1690 (–C=N–), 2380 (Ar-CH), 3120 (Ar-OH), 3260 (Ar-OH); ^{1}H NMR ($CDCl_3$): δ=3.80 (s, 3H, O-CH_3), 7.15–7.20 (m, 4H, Ar-CH), 7.35 (t, 1H, Ar-CH), 7.55 (d, 2H, Ar-CH), 8.75 (d, 1H, Ar-CH), 9.00 (s, 1H, Ar-CH), 9.15 (s, 1H, N=CH), 9.45 (s, 1H, Ar-OH), 11.20 (s, 1H, Ar-OH); elemental analysis of $C_{20}H_{17}N_3O_3$, Calcd. (%): C 69.15, H 4.93, N 12.10; found (%): C 68.95, H 4.95, N 12.15; MS: *m/z* 347.65 (M^+, 100%).

Characterization of 2-(4-hydroxyphenylimino)-methyl)-4-((2-methoxyphenyl)-diazenyl)phenol (2g). Yield: 68%; m. p.: 91°C; IR (KBr) cm^{-1}: 1040 (Ar-O-CH_3), 1440 (C=C), 1480 (N=N), 1670 (–C=N–), 2370 (Ar-CH), 3110 (Ar-OH), 3230 (Ar-OH); ^{1}H NMR ($CDCl_3$): δ=3.90 (s, 3H, O-CH_3), 7.15–7.20 (m, 4H, Ar-CH), 7.65 (d, 1H, Ar-CH), 7.95 (d, 1H, Ar-CH), 8.80 (d, 1H, Ar-CH), 9.10 (s, 1H, Ar-CH), 9.20 (s, 1H, N=CH), 9.45 (s, 1H, Ar-OH), 11.35 (s, 1H, Ar-OH); elemental analysis of $C_{20}H_{17}N_3O_3$, Calcd. (%): C 69.15, H 4.93, N 12.10; found (%): C 69.25, H 5.00, N 12.20; MS *m/z* 346.65 (M^+, 100%).

General procedure of synthesis of 2-(2-hydroxy-5-((aryl)-diazenyl)phenyl)-3-(4-hydroxyphenyl)-thiazolidin-4-one (3a–3g). Equimolar amount of 2-(4-hydroxyphenylimino) methyl)-4-(aryl)diazenyl)phenol (**2a–2g**) (0.002 mol) and thioglycolic acid (0.002 mol) was dissolved in ethanol (10 mL), and the reaction mixture was refluxed for 14–16 h. The completion of the reaction was monitored by TLC. After the completion of reaction, it was poured in ice-cold water, and the solid precipitate was separated out. Collect the solid deposit by filtration and the crude product was recrystallized from chloroform.

Characterization of 2-(2-hydroxy-5-((phenyl)-diazenyl)phenyl)-3-(4-hydroxyphenyl)thiazolidin-4-one (3a). Yield: 70%; m. p.: 110°C; IR (KBr) cm^{-1}: 670 (C-S-C, 4-thiazolidinone), 730 (1, 2 disubstituted benzene ring), 1230 (C-N), 1440 (C=C), 1470 (N=N), 1610 (C=O, thiazolidinone), 2370 (Ar-CH), 3110 (Ar-OH), 3220 (Ar-OH); ^{1}H NMR ($CDCl_3$): δ=3.95–4.05 (m, 2H, S-CH_2-C thiazolidinone ring); 6.45 (s, 1H, S-CH-N, thiazolidinone ring), 7.10–7.15 (m, 3H, Ar-CH), 7.30–7.35 (m, 3H, Ar-CH), 7.50–7.60 (m, 4H, Ar-CH), 8.20 (d, 2H, Ar-CH), 9.50 (s, 1H, Ar-OH), 9.70 (s, 1H, Ar-OH); elemental analysis of $C_{21}H_{17}N_3O_3S$, Calcd. (%): C 64.43, H 4.38, N 10.73, S 8.19; found (%): C 64.40, H 4.30, N 10.50, S 8.10; MS: *m/z* 391.00 (M^+, 100%).

Characterization of 2-(2-hydroxy-5-((4-nitro-phenyl)-diazenyl) phenyl)-3-(4-hydroxyphenyl)-thiazolidin-4-one (3b). Yield: 75%; m. p.: 120°C; IR (KBr) cm^{-1}: 680 (C-S-C, 4-thiazolidinone), 740 (1, 2 disubstituted benzene ring), 1250 (C-N), 1315 (Ar-NO_2), 1420 (C=C), 1460 (N=N), 1630 (C=O, thiazolidinone), 2360 (Ar-CH), 3170 (Ar-OH), 3210 (Ar-OH); ^{1}H NMR ($CDCl_3$): δ=3.90–4.00 (m, 2H, S-CH_2-C thiazolidinone ring), 6.50 (s, 1H, S-CH-N, thiazolidinone ring), 7.00–7.10 (m, 3H, Ar-CH), 7.35 (d, 2H, Ar-CH), 7.50 (t, 1H, Ar-CH), 7.70 (s, 1H, Ar-CH), 7.90 (d, 2H, Ar-CH), 8.40 (d, 2H, Ar-CH), 9.40 (s, 1H, Ar-OH), 9.60 (s, 1H, Ar-OH); elemental analysis of $C_{21}H_{16}N_4O_5S$, Calcd. (%) : C 57.79, H 3.70, N 12.84, S 7.35; found (%): C 57.50, H 3.50, N 12.70, S 7.30; MS: *m/z* 436.00 (M^+, 100%).

Characterization of 2-(2-hydroxy-5-((3-nitrophenyl)-diazenyl) phenyl)-3-(4-hydroxyphenyl)-thiazolidin-4-one (3c). Yield: 72%; m. p.: 120°C; IR (KBr) cm^{-1}: 680 (C-S-C,

4-thiazolidinone), 750 (1, 2 disubstituted benzene ring), 1260 (C-N), 1340 (Ar-NO_2), 1420 (C=C), 1480 (N=N), 1690 (C=O, thiazolidinone), 2350 (Ar-CH), 3170 (Ar-OH), 3280 (Ar-OH); ^{1}H NMR ($CDCl_3$): δ = 3.85–3.90 (q, 2H, S-CH_2-C thiazolidinone ring), 6.55 (s, 1H, S-CH-N, thiazolidinone ring), 7.05 (m, 3H, Ar-CH), 7.30 (d, 2H, Ar-CH), 7.55 (q, 1H, Ar-CH), 7.75 (d, 1H, Ar-CH), 7.95–8.10 (m, 2H, Ar-CH), 8.20–8.30 (m, 2H, Ar-CH), 9.50 (s, 1H, Ar-OH), 9.75 (s, 1H, Ar-OH); elemental analysis of $C_{21}H_{16}N_4O_5S$, Calcd. (%): C 57.79, H 3.70, N 12.84, S 7.35; found (%): C 57.70, H 3.60, N 12.80, S 7.20; MS: *m/z* 436.00 (M^+, 100%).

Characterization of 2-(2-hydroxy-5-((2-nitrophenyl)-diazenyl) phenyl)-3-(4-hydroxyphenyl)-thiazolidin-4-one (3d). Yield: 65%; m. p.: 115°C; IR (KBr) cm^{-1}: 660 (C-S-C, 4-thiazolidinone), 770 (1, 2 disubstituted benzene ring), 1230 (C-N), 1325 (Ar-NO_2), 1440 (C=C), 1470 (N=N), 1660 (C=O, thiazolidinone), 2380 (Ar-CH), 3140 (Ar-OH), 3250 (Ar-OH); ^{1}H NMR ($CDCl_3$): δ = 3.95–4.05 (q, 2H, S-CH_2-C thiazolidinone ring), 6.50 (s, 1H, S-CH-N, thiazolidinone ring), 7.00–7.05 (m, 3H, Ar-CH), 7.30 (d, 2H, Ar-CH), 7.50 (q, 1H, Ar-CH), 7.75 (d, 1H, Ar-CH), 7.90–8.05 (m, 2H, Ar-CH), 8.25–8.35 (m, 2H, Ar-CH), 9.40 (s, 1H, Ar-OH), 9.65 (s, 1H, Ar-OH); elemental analysis of $C_{21}H_{16}N_4O_5S$, Calcd. (%): C 57.79, H 3.70, N 12.84, S 7.35; found (%): C 57.60, H 3.40, N 12.60, S 7.10; MS: *m/z* 436.00 (M^+, 100%).

Characterization of 2-(2-hydroxy-5-((4-methoxyphenyl)-diazenyl) phenyl)-3-(4-hydroxy-phenyl)-thiazolidin-4-one (3e). Yield: 80%; m. p.: 110°C; IR (KBr) cm^{-1}: 650 (C-S-C, 4-thiazolidinone), 770 (1, 2 disubstituted benzene ring), 1060 (Ar-O-CH_3), 1250 (C-N), 1440 (C=C), 1470 (N=N), 1670 (C=O, thiazolidinone), 2340 (Ar-CH), 3130 (Ar-OH), 3260 (Ar-OH); ^{1}H NMR ($CDCl_3$): δ = 3.80 (s, 3H, O-CH_3), 4.00–4.10 (q, 2H, S-CH_2-C thiazolidinone ring), 6.45 (s, 1H, S-CH-N, thiazolidinone ring), 7.10–7.15 (m, 3H, Ar-CH), 7.25 (d, 2H, Ar-CH), 7.35 (d, 2H, Ar-CH), 7.50 (d, 1H, Ar-CH), 7.80 (s, 1H, Ar-CH), 8.85 (d, 2H, Ar-CH), 9.55 (s, 1H, Ar-OH), 9.85 (s, 1H, Ar-OH); elemental analysis of $C_{22}H_{19}N_3O_3S$, Calcd. (%): C 65.17, H 4.72, N 10.36, S 7.91; found (%): C 65.10, H 4.70, N 10.30, S 7.80; MS: *m/z* 405.00 (M^+, 100%).

Characterization of 2-(2-hydroxy-5-((3-methoxyphenyl)-diazenyl) phenyl)-3-(4-hydroxyphenyl)-thiazolidin-4-one (3f). Yield: 70%; m. p.: 125°C; IR (KBr) cm^{-1}: 680 (C-S-C, 4-thiazolidinone), 750 (1, 2 disubstituted benzene ring), 1060 (Ar-O-CH_3), 1230 (C-N), 1410 (C=C), 1450 (N=N), 1650 (C=O, thiazolidinone), 2380 (Ar-CH), 3170 (Ar-OH), 3250 (Ar-OH); ^{1}H NMR ($CDCl_3$): δ = 3.90 (s, 3H, O-CH_3), 4.05–4.15 (q, 2H, S-CH_2-C thiazolidinone ring), 6.55 (s, 1H, S-CH-N, thiazolidinone ring), 7.05–7.15 (m, 3H, Ar-CH), 7.15-7.40 (m, 5H, Ar-CH), 7.50–7.55 (m, 2H, Ar-CH), 7.75 (s, 1H, Ar-CH), 9.40 (s, 1H, Ar-OH), 9.75 (s, 1H, Ar-OH), elemental analysis of $C_{22}H_{19}N_3O_3S$, Calcd. (%): C 65.17, H 4.72, N 10.36, S 7.91; found (%): C 64.90, H 4.50, N 10.10, S 7.50; MS *m/z* 405.10 (M^+, 100%).

Characterization of 2-(2-hydroxy-5-((2-methoxyphenyl)-diazenyl) phenyl)-3-(4-hydroxy-phenyl)-thiazolidin-4-one (3g). Yield: 65%; m. p.: 115°C; IR (KBr) cm^{-1}: 690 (C-S-C, 4-thiazolidinone), 780 (1, 2 disubstituted benzene ring), 1055 (Ar-O-CH_3), 1270 (C-N), 1420 (C=C), 1460 (N=N), 1680 (C=O, thiazolidinone), 2390 (Ar-CH), 3150 (Ar-OH), 3290 (Ar-OH); ^{1}H NMR ($CDCl_3$): δ = 3.80 (s, 3H, O-CH_3), 4.85–4.95 (q, 2H, S-CH_2-C thiazolidinone ring), 6.50 (s, 1H, S-CH-N, thiazolidinone ring), 6.90 (d, 1H, Ar-CH), 6.95–7.05 (m, 3H, Ar-CH), 7.20–7.25 (m, 1H, Ar-CH), 7.45–7.50 (m, 2H, Ar-CH), 7.70 (s, 1H, Ar-CH), 7.95 (d, 1H, Ar-CH), 9.45 (s, 1H, Ar-OH), 9.70 (s, 1H, Ar-OH); elemental analysis of $C_{22}H_{19}N_3O_3S$, Calcd. (%) : C 65.17, H 4.72, N 10.36, S 7.91; found (%): C 65.00, H 4.60, N 10.20, S 7.60; MS: *m/z* 405.00 (M^+, 100%).

Biological activity. Antibacterial and antifungal activities were tested for newly synthesized 2-(2-hydroxy-5-((aryl)-diazenyl)phenyl)-3-(4-hydroxyphenyl)-thiazolidin-4-one (**3a–3g**) using the well diffusion method against the different Gram-positive and Gram-negative bacterial stains and fungi stains. Different bacterial stains used for the screening were *S. aureus* (Gram-positive), *B. subtilis* (Gram-positive), *Proteus vulgaris*. (Gram-negative) and *E. coli* (Gram-negative). Antifungal activities of these compounds were also tested against *C. albicans* and *A. niger*. The stock solutions of thiazolidinone derivatives or standard drug in dimethyl sulfoxide (100 μg/mL) were prepared for the study. The sterilized Petri dishes and agar medium were used in the present work. The antibacterial activities of compounds were evaluated by measuring the zone of inhibition on nutrient agar plate. Muller Hinton agar was used in the antibacterial study, whereas Sabouraud's Dextrose agar was used for the antifungal activity study. The composition of nutrient agar medium to culture the bacterial strains used in the present study was: peptone (10 gm), agar powder (20 gm), sodium chloride powder (10 gm), beef extract (5 gm), and distilled water (1000 mL). The pH of the nutrient agar medium was adjusted to 7.2. The nutrient agar medium was mixed well and was autoclaved at 15 lbs pressure at 120°C for at least 15 min.

In the sterilized agar medium, 10 mL of one day old bacterial/fungal cultures were added. Bacterial or fungal culture were inoculated into nutrient broth and incubated at (37 ± 2) C on rotary shaker at 100 rpm. After 36-h incubation, bacterial suspensions were used for further tests. This media were poured in Petri dishes and allowed to set. Two wells were created using a 5 mm cork borer. In this well, 0.1 mL of test samples/standards were filled.

All the nutrient agar plates were incubated at 37 C for 24 h in antibacterial study and at 37 C for 48 h in antifungal activity study. The plates were observed for clear zone of inhibition. Then, diameters of the zone of inhibition for these compounds were measured. The biological activities were tested for at least three times for all the compounds against all microorganisms, and the average value has been reported in Table 1.

CONCLUSION

In the present research work, we have synthesized series of thiazolidinones, that is, 2-(2-hydroxy-5-((aryl)-diazenyl) phenyl)-3-(4-hydroxyphenyl)-thiazolidin-4-one, by reaction of various Schiff bases 2-(4-hydroxyphenylimino) methyl)-4-(aryl)diazenyl)phenol with ethanolic thioglycolic acid in good yields. Schiff bases were obtained by the reactions of 4-amino phenol with 2-hydroxy-5-((aryl)diazenyl) benzaldehyde. The structure of the newly synthesized compounds was confirmed by IR, ^{1}H NMR, mass spectral, and C, H, N elemental analysis. The thiazolidinone derivatives were evaluated for their antibacterial and antifungal activities by well diffusion method in triplicate. These compounds have shown promising biological activities against Gram-positive and Gram-negative bacterial stains. Also, antifungal activities have also been shown of these compounds. These compounds could be useful as templates for further development through modification to design more potent antimicrobial and antifungal agents.

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