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ARTICLE

Synthesis of Some New 5-Indolylidene-4-thiazolidinone Derivatives of 1,2,4-triazole as Potent Antioxidant and Antifungal Agents

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ABSTRACT

A series of 1,2,4-triazolyl-4-(5-indolylidene)-thiazolidinone derivatives were synthesized and screened for their antifungal and antioxidant activity. Among these synthesized compounds **3d**, **3g** showing good antifungal activity and compounds **3b**, **3d**, **3f** and **3h** have high % antioxidant activity with lower IC_{50} value of 11.21, 20.89, 17.51 and 14.05 respectively. We report the antioxidant potential of the said class of compound in which free radical is generated by methelenic and 2nd carbon of thiazolidinone ring. The antifungal activity reported against *A. niger, C. albicans* and *A. flavus.* The antioxidant activity of all the synthesized compounds was screened by H_2O_2, DPPH scavenging and by phosphomolybdenum method with respect to ascorbic acid.

KEYWORDS

1,2,4-Triazole, Schiff base, 4-Thiazolidinone, Antifungal activity.

INTRODUCTION

4-Thiazolidinones are the derivatives of thiazolidine which belong to an important group of heterocyclic compounds containing sulfur and nitrogen in five membered ring with a carbonyl group at the 4-position. The literature survey revealed that 4-thiazolidinone and their 5-arylidene derivatives containing compounds were incorporate with a large range of pharmacological activities such as antimicrobial, analgesic, anticonvulsant, anti-inflammatory, local and spinal anesthetics, CNS stimulants, hypnotics, anti HIV, hypoglycemic and antitumor activity *etc*. [1-6]. The chemistry of 4-amino-1,2,4-triazoles and their fused heterocyclic derivatives has received considerable attention owing to their synthetic and effective biological importance [7]. It is well known that the 1,2,4-triazoles and their derivatives have number of applications in agricultural, biological industrial fields [8,9]. For example, a large number of 1,2,4-triazole-containing ring systems have wide range of therapeutically important activities including anti-inflammatory [10], CNS stimulants [11], antitubercular [12], antitumor [13] and antimicrobial agents *etc*. [14,15].

Damage to cells caused by free radical is believed to play a central role in the aging process and in disease progression. Antioxidants are compounds capable to either delay or inhibit

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the oxidation processes which occur under the influence of atmospheric oxygen or reactive species. Antioxidants are involved in the defense mechanism of the organism against the pathologies associated to the attack of the free radicals. Recently, antioxidants have attracted considerable attention in relation to radicals and oxidative stress [16].

Here we are reporting the synthesis of new triazole bearing aryl-4-oxo-thiazolidine moiety at position 4 and then their 5-indolylidene-thiazolidinone derivatives have been synthesized. All the synthesized compounds were characterized by their physical and spectral studies. Thus in search for new biodynamic potent molecule it assumed to incorporate thiazolidinone moiety with triazole nucleus and to study their antioxidant activity. In the present work, the synthesis of a new series of 5-indolylidenyl-thiazolidin-4-one derivatives of 1,2,4-triazoles with evaluation of their antifungal activity and DPPH, H_2O_2 radical scavenging capability and total antioxidant capacity is described.

EXPERIMENTAL

High quality commercial reagents and anhydrous solvents were used for synthesis of all the compounds. Follow up of the reactions and the purity of the compounds was checked by ascending TLC on precoated silica-gel in plates and the spots were rendered visible by exposing the plates to UV light. The FTIR spectra were recorded (ν_{max}, cm^{-1}) on Shimadzu FTIR 8400 spectrophotometer in KBr. ^1H and ^{13}C NMR spectra (data reported in δ ppm) were recorded on a Bruker Avance II-400 MHz and Jeol series JNM-ECX-500 NMR spectrometer using TMS as internal standard. The absorbance of compounds were reported in Systronic 2201 double beam UV-visible spectrophotometer.

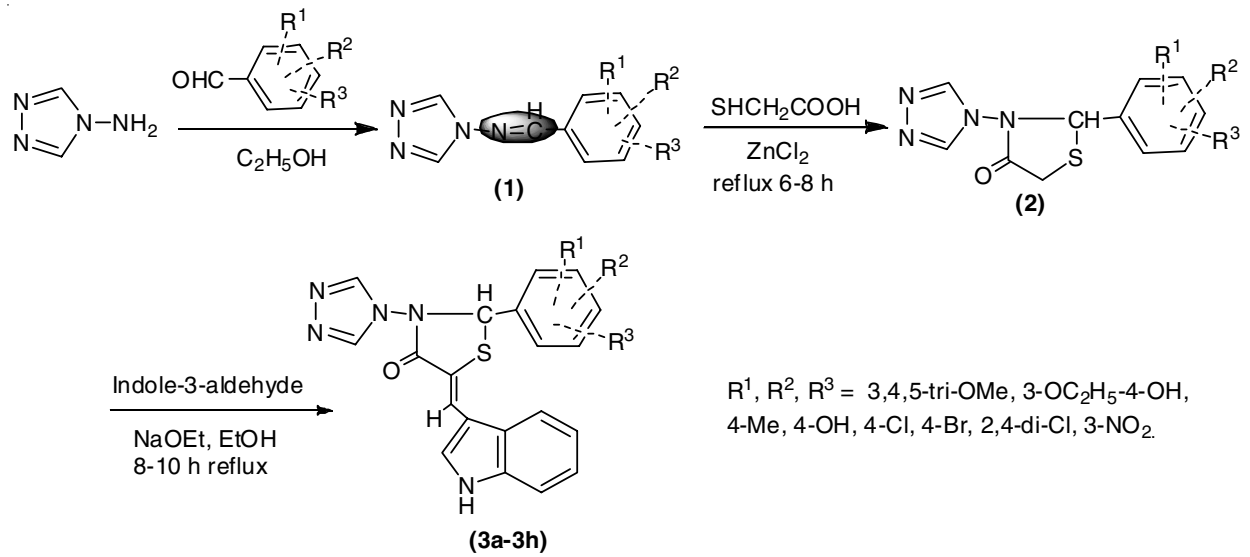
General procedure for the synthesis of 4-(4-substituted-benzylideneamino)- 4*H*-1,2,4-triazoles (Schiff bases, 1a-h): The 1,2,4-triazole Schiff bases were synthesized by condensation of 4-amino-4*H*-1,2,4-triazole with aromatic aldehydes in presence of 2-3 drops of glacial acetic acid (**Scheme-I**). An equimolar mixture of 4-amino-1,2,4-triazole (**1**) (0.02 mol) and different aromatic aldehydes (0.02 mol) in ethanol 20 mL was refluxed for 2-4 h [17]. The completion of the reaction was monitored by TLC using chloroform and methanol (8:2) as eluent. The excess of solvent was evaporated thus the solid obtained was dried and recrystallized from methanol.

General procedure for synthesis of 4-(4-substituted-phenyl-4-oxo-thiazolidinyl)-4*H*- 1,2,4-triazole (2a-h): A solution of 4-(4-substituted-benzylideneamino)-4*H*-1,2,4-triazoles (**1a-h**) (0.02 mol) in 25 mL ethanol, thioglycolic acid (0.02 mol) added in presence of a pinch of anhydrous $ZnCl_2$ stirred and refluxed the mixture for about 5-7 h. After completion of the reaction, the reaction mixture poured into ice cold water and a saturated solution of $NaHCO_3$ added. Then filtered the solution and washed the solid product [18,19]. The product was filtered, dried and finally recrystallized by ethanol to give compounds (**2a-h**).

General procedure for synthesis of 5-(1*H*-indolylidene)-3-(4*H*-1,2,4-triazolyl)-2-(substituted phenyl) thiazolidin-4-one (3a-h): In a solution of 4-(4-substitutedphenyl-4-oxo-thiazolidinyl)-4*H*-1,2,4-triazoles (**2a-h**, 0.02 mol) in 20 mL ethanol, indole-3-carboxaldehyde (0.02 mol) was added with stirring then 0.1 g of sodium ethoxide was added and refluxed the mixture at 90 °C for 7-10 h [20]. The reaction was monitered by TLC using $CHCl_3$ and MeOH in 8:2 as eluent. After completion the reaction, we kept the reaction mixture for 1 h at room temperature for evaporation of solvent. The obtained solid product was purified using column chromatography with $CHCl_3$ and MeOH in 8:2 to give compounds **3a-h**.

Characterization of synthesized compounds 3a-h

5-(1*H*-Indolylidene)-3-(4*H*-1,2,4-triazolyl)-2-(3,4,5-trimethoxyphenyl)thiazolidin-4-one (3a): Off white solid, yield: 78 %, m.p.: 195 °C, $C_{23}H_{21}N_5O_4S$, IR (KBr, ν_{max}, cm^{-1}): 1685 (-C=O thiazolidinone), 3350 (N-CH thiazolidinone), 3102 (Ar, C-H), 2850 (C-S-C cyclic), 3430 (NH-indole) 761 (Ar-OCH_3). ^1H NMR (500 MHz, DMSO-d_6, δ ppm): 7.15 (s, 2H, Ar–H), 3.8-3.9 (s, 9H, -OCH_3), 4.82 (s, 1H, HC-N), 9.06(s, 2H, triazole), 9.8 (s, 1H, indolyl NH). ^{13}C NMR (125 MHz, δ ppm): 105 (2C, Ar-C), 140, 153 (3C, Ar -C-OCH_3), 56-60 (3C, -O$\underline{C}H_3$), 175 (1C, C=O), 125 (1C, arylidinonyl), 138.9 (2C,



Scheme-I: Synthesis of 4-(5-indolylidene-4-substituted phenyl-4-oxo-thiazolidinyl)-4*H*-1,2,4-triazoles

C=N triazole), 165 (1C, C-S), 75 (1C, N-CH thiazolidinone). Elemental analysis: C, 59.60; H, 4.57; N, 15.11; O, 13.81; S, 6.92.

5-(1*H*-Indolylidene)-3-(4*H*-1,2,4-triazolyl)-2-(3-ethoxy-4-hydroxyphenyl)thiazolidin-4-one (3b): Yellowish crystals, yield: 75 %, $C_{22}H_{19}N_5O_3S$, m.p.: 170 °C, IR (KBr, ν_{max}, cm^{-1}): 1690 (-C=O thiazolidinone), 3425 (N-CH, thiazolidinone), 2780 (C-S-C, cyclic), 3480 (NH-indole), 3120 (Ar, C-H), 768 (Ar-OCH_3). ^{1}H NMR (500 MHz, DMSO-d_6, δ ppm): 1.3 (t, 3H, CH_3), 4.0 (q, 2H, -OCH_2), 4.85 (s, 1H, HC-N), 9.04 (s, 2H, triazole), 4.1(br. peak 1H, -OH), 8.06 (s, 1H, arylidinyl H), 7.1-8.8 (m, aromatic-H), 9.8 (s, 1H, indolyl-NH). ^{13}C NMR (125 MHz, δ ppm): 125 (1C, arylidene C), 15(1C, CH_3), 65 (1C, -OCH_2), 147 (C-OH), 185 (1C, C=O), 145 (2C, C=N triazole), 137(1C, C-S), 79.6 (1C, N-CH thiazolidinone) 118-139 (aromatic C).

5-(1*H*-Indolylidene)-3-(4*H*-1,2,4-triazolyl)-2-(4-methylphenyl)thiazolidin-4-one (3c): Light yellow solid, yield: 63 %, $C_{21}H_{17}N_5OS$, m.p.: 85 °C; IR (KBr, ν_{max}, cm^{-1}): 1726 (-C=O thiazolidinone), 3362 (N-CH, thiazolidinone), 3102 (Ar, C-H), 2850 (C-S-C cyclic), 3430 (NH, indole) 2970 (Ar-CH_3). ^{1}H NMR (500 MHz, DMSO-d_6, δ ppm): 2.4 (s, 3H, Ar-CH_3), 4.3 (s, 1H, HC-N), 9.11(s, 2H, triazole), 9.87 (s, 1H, indolyl NH), 7.1–8.3 (m, 10H, Ar–H), ^{13}C NMR (125 MHz, δ ppm): 153 (3C, Ar C-CH_3), 23 (1C, CH_3), 157 (1C, C=O), 123 (1C, arylidinonyl), 140 (2C, C=N triazole), 165 (1C, C-S), 68 (1C, N-CH thiazolidinone), 108-158 (12C, Ar-C).

5-(1*H*-Indolylidene)-3-(4*H*-1,2,4-triazolyl)-2-(4-hydroxy-phenyl)thiazolidin-4-one (3d): Off white solid, yield: 79 %, $C_{20}H_{15}N_5O_2S$, m.p.: 130 °C; IR (KBr, ν_{max}, cm^{-1}): 1755 (-C=O thiazolidinone), 3328 (N-CH, thiazolidinone), 2750 (C-S-C, cyclic), 3470 (NH, indole), 3120 (Ar, C-H), 3600 (-OH). ^{1}H NMR (500 MHz, DMSO-d_6, δ ppm): 5.12 (s, 1H, HC-N), 9.06 (s, 2H, triazole), 4.08 (br. peak 1H, -OH), 7.5 (s, 1H, arylidinyl H), 7.2-8.5 (m, aromatic-H), 9.9 (s, 1H, indolyl-NH). ^{13}C NMR (125 MHz, δ ppm): 127 (1C, arylidene C), 150 (C-OH), 184.5 (1C, C=O), 149 (2C, C=N triazole), 135.6 (1C, C-S), 85.5 (1C, N-CH thiazolidinone), 110-140 (8C, aromatic C).

5-(1*H*-Indolylidene)-3-(4*H*-1,2,4-triazolyl)-2-(4-chlorophenyl)thiazolidin-4-one (3e): White solid, yield: 72 %, $C_{20}H_{14}N_5OSCl$, m.p.: 180 °C; IR (KBr, ν_{max}, cm^{-1}): 1725 (-C=O thiazolidinone), 3348 (N-CH, thiazolidinone), 2720 (C-S-C, cyclic), 3410 (NH, indole), 3135 (Ar, C-H), 772 (Ar-Cl). ^{1}H NMR (500 MHz, DMSO-d_6, δ ppm): 5.16 (s, 1H, HC-N), 9.08 (s, 2H, triazole), 7.96 (s, 1H, arylidinyl H), 7.3-8.4 (m, 9H, aromatic-H), 9.9 (s, 1H, indolyl-NH). ^{13}C NMR (125 MHz, δ ppm): 128 (1C, arylidene C), 185 (1C, C=O), 145 (2C, C=N triazole), 135 (1C, C-S), 145 (C, C-Cl), 86 (1C, N-CH thiazolidinone), 108-162 (aromatic C).

5-(1*H*-Indolylidene)-3-(4*H*-1,2,4-triazolyl)-2-(4-bromophenyl)thiazolidin-4-one (3f): Brown solid, yield: 76 %, $C_{20}H_{14}N_5OSBr$, m.p.: 145 °C; IR (KBr, ν_{max}, cm^{-1}): 1645 (-C=O thiazolidinone), 3340 (N-CH, thiazolidinone), 2932 (C-S-C, cyclic), 3326 (NH, indole), 640 (Ar-Br). ^{1}H NMR (500 MHz, DMSO-d_6, δ ppm): 4.92 (s, 1H, HC-N), 9.10 (s, 2H, triazole), 7.9 (s, 1H, arylidinyl H), 7.0-8.2 (m, 9H, aromatic-H), 9.81 (s, 1H, indolyl-NH). ^{13}C NMR (125 MHz, δ ppm): 128 (1C, arylidene C), 175 (1C, C=O), 143 (2C, C=N triazole), 135 (1C, C-S), 135 (C, C-Br), 83 (1C, N-CH thiazolidinone), 115-153 (aromatic C).

5-(1*H*-Indolylidene)-3-(4*H*-1,2,4-triazolyl)-2-(2,4-dichlorophenyl)thiazolidin-4-one (3g): White solid, yield: 71 %, $C_{20}H_{13}N_5OSCl_2$, m.p.: 150 °C; IR (KBr, ν_{max}, cm^{-1}): 1720 (-C=O thiazolidinone), 3345 (N-CH, thiazolidinone), 2715 (C-S-C, cyclic), 3450 (NH, indole), 3135 (Ar, C-H), 770 (Ar-Cl). ^{1}H NMR (500 MHz, DMSO-d_6, δ ppm): 5.12 (s, 1H, HC-N), 9.1 (s, 2H, triazole), 7.5 (s, 1H, arylidinyl H), 7.3-8.4 (m, 8H, aromatic-H), 9.9 (s, 1H, indolyl-NH). ^{13}C NMR (125 MHz, δ ppm): 125 (1C, arylidene C), 176 (1C, C=O), 143 (2C, C=N triazole), 137 (1C, C-S), 165-168 (2C, C-Cl), 85.5 (1C, N-CH thiazolidinone), 108-158 (aromatic C).

5-(1*H*-Indolylidene)-3-(4*H*-1,2,4-triazolyl)-2-(3-nitrophenyl)thiazolidin-4-one (3h): Off white solid, yield: 66 %, $C_{20}H_{14}N_6O_3S$, m.p.: 165 °C; IR (KBr, ν_{max}, cm^{-1}): 1735 (-C=O thiazolidinone), 3370 (N-CH, thiazolidinone), 3110(Ar, C-H), 2846 (C-S-C, cyclic), 3340 (NH, indole), 761(Ar-NO_2). ^{1}H NMR (500 MHz, DMSO-d_6, δ ppm): 4.86 (s, 1H, HC-N), 9.12 (s, 2H, triazole), 7.5 (s, 1H, arylidinyl H), 7.3-8.3 (m, aromatic-H), 9.86 (s, 1H, indolyl-NH). ^{13}C NMR (125 MHz, δ ppm): 121 (1C, arylidene C), 169 (1C, C=O), 143 (2C, C=N triazole), 137 (1C, C-S), 83 (1C, N-CH thiazolidinone), 108-158 (aromatic C), 150 (1C, C-NO_2).

Evaluation of antifungal activity: The stock solutions were prepared by dissolving of 500 µg of each synthesized compound in 1 mL of dimethyl sulfoxide as solvent and different dilute solutions have made from this solution. The antifungal activity of the synthesized compounds was evaluated and MIC determines by the microbroth dilution method [20]. The antifungal activity was evaluated against human pathogenic fungal strains, such as *C. albicans* (MTCC 227), *A. flavus* (MTCC 277), *A. niger* (MTCC 282), which are often encountered clinically and were compared with standard drugs like fluconazole. The zone of inhibition was measured in millimeter. The MIC was determined by measuring the absorbance of microtiter plates at 530 nm. The optical density from each well was compared with optical density from the positive control wells, the lowest concentration with optical density, < 0.1 signifies inhibition and considered as MIC [21].

Evaluation of antioxidant activity

DPPH radical scavenging activity [22-24]**:** The radical scavenging activity of the synthesized compounds against stable free radical 2.2-diphenyl-2-picrylhydrazyl hydrate (DPPH, Sigma-Aldrich) was determined spectrophotometrically. When DPPH reacts with antioxidant compounds, which can donate hydrogen, it is reduced. Following the reduction, its deep violet colour in methanol bleached to yellow, showing a significant absorption decrease at 517 nm. Then 1 mL of various concentration (25, 50, 100 and 200 µg/mL) of the compounds **3a-h** dissolved in methanol were added to 1 mL of ethanol solution of DPPH. The mixture was shaken vigorously and allowed to stand at room temperature for 30 min. Then the absorbance was measured at 517 nm in a spectrophotometer (Systronic 2201 Double Beam UV-visible spectrophotometer). Ascorbic acid was used as the reference. All tests and analyses were done in three replicates and the results were

averaged. Free radical DPPH inhibition in percentage (AA %) was calculated as follows:

$$\text{DPPH radical scavenging activity (\%)} = \frac{A_{control} - A_{test}}{A_{control}} \times 100 \quad (1)$$

where $A_{control}$ is the absorbance of the control sample (DPPH solution without test sample) and A_{test} is the absorbance of the test sample (DPPH solution + test compound).

Hydrogen peroxide (H_2O_2) scavenging activity: Hydrogen peroxide may enter into the human body through inhalation of vapour or mist and through eye or skin contact. H_2O_2 is rapidly decomposed into oxygen and water and this may produce hydroxyl radicals (OH) that can initiate lipid peroxidation and cause DNA damage in the body [25,26].

The H_2O_2 scavenging ability of the test compound was determined according to the method of Ruch *et al*. [27,28]. A solution of H_2O_2 (40 mM) was prepared in phosphate buffer (pH 7.4). 25, 50, 100 and 200 µg/mL concentrations of the test compounds in 3.4 mL phosphate buffer were added to H_2O_2 solution (0.6 mL, 40 mM). The absorbance value of the reaction mixture was recorded at 230 nm. The percent of scavenging of H_2O_2 was calculated by using eqn. 2:

$$H_2O_2 \text{ scavenging activity (\%)} = \frac{A_{control} - A_{test}}{A_{control}} \times 100 \quad (2)$$

where $A_{control}$ is the absorbance of the control sample (H_2O_2 solution without test sample) and A_{test} is the absorbance of the test sample (H_2O_2 solution + test compound).

Total antioxidant capacity by phosphomolybdenum method: This method is based on the reduction of phosphomolybdic acid to phosphomolybdenum green complex by sodium sulfide. In this method Mo(VI) reduced to Mo(V) by the tested compounds, followed by formation of a green phosphate/Mo(V) complex at acid pH [29].

An aliquot of 0.1 mL of the test solution in DMSO was mixed with 1 mL of a reagent solution (0.6 M sulfuric acid, 28 mM sodium phosphate and 4 mM ammonium molybdate). The test tubes were capped and incubated at 95 °C for 90 min. The samples were cooled at room temp. and then absorbance was measured at 695 nm against the blank. The blank solution was containing 1 mL of the reagent solution and an appropriate volume DMSO. The total antioxidant capacity of the tested compounds was calculated according to the eqn. 1.

RESULTS AND DISCUSSION

Compounds **3a-h** were successfully synthesized and characterized quantitatively and qualitatively by using FTIR, ^{1}H NMR and ^{13}C NMR spectroscopy. When the Schiff bases of 1,2,4-triazole on reaction with equimolar amount of thioglycolic acid in the presence of $ZnCl_2$ as a catalyst in the trace amount, gives the cycloaddition reaction and produced a five membered 4-thiazolidinone ring, as compound **2a-h**. When all these compounds **2a-h** underwent the Knoevenagel condensation reaction with indole-3-carboxaldehyde in the presence of sodium ethoxide (C_2H_5ONa) to afford the compounds **3a-h** (**Scheme-I**). In the ^{1}H NMR spectra of the these compounds, we have found the disappearance of two methylene protons of compounds **2a-h** and an appearance of a new signal for arylidene H in the range of 7.5-8.1δ ppm and a peak for 1H of indolyl -NH- group in the range of 9.1-9.95 in the ^{1}H NMR, and a new signals for arylidene C in range of 121-129 δ ppm in the ^{13}C NMR spectra of compounds **3a-h**. These all above facts clearly confirmed the synthesis of all newly 5-arylidene derivatives of 4-thiazolidnones as final products.

The compounds **3a-h** were screened for their antifungal and antioxidant activity. The antifungal activity results showed that compounds **3d** and **3f** exhibit good activity against *A. flavus*, compounds **3d**, **3f** and **3g** exhibit good activity against *C. albicans*, while compounds **3c** and **3e** exhibit good activity against *A. niger* with lowest value (Table-1). It is also found that thiazolidinone and their arylidene derivatives containing –Cl, –Me and –OH group exhibited good antifungal activity.

TABLE-1
ANTIFUNGAL ACTIVITY AND DPPH SCAVENGING ACTIVITY OF SYNTHESIZED COMPOUNDS

Comp.	-R	Antifungal activity (MIC value in µg/mL)		
		C. albicans	*A. niger*	*A. flavus*
3a	3,4.5-tri-OCH_3-	125	125	250
3b	3-OEt-4-OH-	125	250	125
3c	4-CH_3-	100	31.2	62.5
3d	4-OH-	62.5	125	31.2
3e	4-Cl-	125	62.5	62.5
3f	4-Br-	32.5	125	62.5
3g	2,4-di-Cl-	26.5	152.5	125
3h	3-NO_2-	62.5	125	100
Fluconazole	–	25	25	25

These synthesized thiazolidinone derivatives have shown promising antioxidant activities by scavenging of H_2O_2 and DPPH radical and by reduction of Mo(IV) to Mo(V). Free radical scavenging activity of the 1,2,4-triazole derivatives is concentration dependent, the radical scavenging activity increases with concentration and lower IC_{50} value reflects better protective action. From results, it may be postulated that compounds **3a-h** were able to reduce the stable free radical DPPH to diphenylpicrylhydrazine exhibiting better free radical scavenging activity than the standard antioxidant ascorbic acid.

Some compounds have found to have low IC_{50} value (for DPPH radicals scavenging) which is comparable to the ascorbic acid (Table-2) compounds **3b** (11.21 µg/mL), **3h** (14.05 µg/mL) and **3f** (17.51 µg/mL) have found lowest IC_{50} value comparable to ascorbic acid (9.4 µg/mL). From results of H_2O_2 assay (Table-2), it is found that the compounds **3b**, **3d**, **3f** and **3h** have good antioxidant activity. The structure activity relationship showed that the antioxidant activity of these 1,2,4-triazole derivatives could be due to that consists of atom with low electronegativity and species with relatively small ionization energy compounds **3b**, **3d**, **3f** and **3h** have higher antioxidant activity due to 3-OEt-4–OH, 4-Br, 4-OH and 3–NO_2 group present with the phenyl ring. It suggested that these compounds could have great importance as therapeutic agents in preventing or slowing the progress of aging and age associated oxidative stress related degenerative diseases.

TABLE-2
ANTIOXIDANT ACTIVITIES OF SYNTHESIZED COMPOUNDS (**3a-h**)

Compounds	IC_{50} (µg/mL)	H_2O_2 scavenging activity (%)		DPPH Scavenging activity (%)		Total antioxidant capacity (%)	
		100 µg/mL	200 µg/mL	100 µg/mL	200 µg/mL	100 µg/mL	200 µg/mL
3a	67.18	55.17	64.18	63.13	71.92	55.98	72.52
3b	11.21	81.16	92.91	72.18	90.68	70.13	89.35
3c	83.71	70.62	82.17	53.36	68.53	53.18	60.52
3d	20.89	80.15	91.59	71.62	80.94	70.64	91.28
3e	75.09	61.23	70.18	60.33	75.08	57.15	68.35
3f	17.51	81.22	95.39	73.99	93.17	69.82	89.32
3g	66.20	46.58	67.37	64.2	81.26	57.55	78.81
3h	14.05	78.38	95.26	76.28	92.13	72.71	93.26
Ascorbic acid	9.40	83.58	97.80	82.18	97.68	85.11	96.56

Conclusion

A simple and straightforward synthetic procedures were adopted for the synthesis of newly 3-(4*H*-1,2,4-triazol-3-yl)-2-(4-substitued-phenyl)thiazolidin-4-one (**2a-h**) and 3-(4*H*-1,2,4-triazol-3-yl)-2-(4-substitued-phenyl)-5-(indolylidene)thiazolidin-4-one (**3a-h**) derivatives from the Schiff bases of 1,2,4-triazoles. The compounds have been characterized by spectral methods such as FT-IR, ^{1}H NMR, ^{13}C NMR and Mass spectrometer. All the synthesized compounds have been investigated for their antifungal and antioxidant activity. Some of these compounds have good to moderate antifungal activity and most of these compounds were found to be significant scavengers of free radicals. From results of DPPH assay, it found that the compounds **3b**, **3d**, **3f** and **3h** showed excellent antioxidant activity with lower IC_{50} value which is comparable to ascorbic acid. These results obtained by preliminary screening of antioxidant activity suggested that the molecules from 5-arylideno-indolyl-thiazolidin-4-one class might serve as interesting compounds which could have great importance as therapeutic agents in preventing or slowing the progress of aging and age associated oxidative stress related degenerative diseases.

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REFERENCES

1. A.K. Jain, A. Vaidya, V. Ravichandran, S.K. Kashaw and R.K. Agrawal, Recent Developments and Biological Activities of Thiazolidinone Derivatives: A Review, *Bioorg. Med. Chem.*, **20**, 3378 (2012); https://doi.org/10.1016/j.bmc.2012.03.069.
2. F. Hassan, A.B. Hameed, A. Alshanon, B.S. Abdullah, H.Z. Huri, N. Hairunisa and E. Yousif, Antitumor Activity for Gold(III) Complex by High Content Screening Technique (HCS) and Cell Viability Assay, *Asian J. Biochem.*, **10**, 252 (2015); https://doi.org/10.3923/ajb.2015.252.266.
3. V. Sindhi, V. Gupta, K. Sharma, S. Bhatnagar amd R. Kumari and N. Dhaka, Potential Applications of Antioxidants-A Review, *J. Pharm. Res.*, **7**, 828 (2013); https://doi.org/10.1016/j.jopr.2013.10.001.
4. A. Gupta, R. Singh, P.K. Sonar and S.K. Saraf, Novel 4-Thiazolidinone Derivatives as Anti-Infective Agents: Synthesis, Characterization and Antimicrobial Evaluation, *Biomed. Res. Int.*, **2016**, Article ID 8086 (2016); https://doi.org/10.1155/2016/8086762.
5. S.K. Srivastava, A. Jain and S. Srivastava, Synthesis and Biological Significance of 2-Mercaptobenzoxazole Derivatives, *J. Indian Chem. Soc.*, **83**, 1118 (2006).
6. S.K. Srivastava, R. Yadav and S.D. Srivastava, Synthesis of Some New 2-Mercaptobenzothiazolyl-2-oxoazetidines as Antimicrobial and Anthelmintic agents, *J. Indian Chem. Soc.*, **81**, 342 (2004).
7. I. Awad, A. Abdel-Rahman and E. Bakite, Synthesis and Application of Some New Heterocyclo-S-Triazole Derivatives as Antimicrobial Agents, *J. Chem. Technol. Biotechnol.*, **51**, 483 (2008); https://doi.org/10.1002/jctb.280510406.
8. H.M. Dalloul, Reaction of Nitrilimines with Pyruvaldehyde Hydrazones: Synthesis and Antimicrobial Evaluation of Some New 1,2,4-Triazole Derivatives, *J. Chem.*, **2015**, Article ID 593738 (2015); https://doi.org/10.1155/2015/593738.
9. Z.A. Kaplancikli, T.G. Zitouni, A. Ozdemir and G. Revail, *Eur. J. Med. Chem.*, **43**, 115 (2008); https://doi.org/10.1016/j.ejmech.2007.03.019.
10. M.W. Akhter, M.Z. Hassan and M. Amir, Synthesis and Pharmacological Evaluation of 3-Diphenylmethyl-6-substituted-1,2,4-triazolo[3,4-*b*]-1,3,4-thiadiazoles: A Condensed Bridgehead Nitrogen Heterocyclic System, *Arab. J. Chem.*, **7**, 955 (2014); https://doi.org/10.1016/j.arabjc.2014.05.036.
11. S. Shenone, O. Bruno, A. Ranise, W. Bondavalli, G. Falcone, L. Giordano and M.R. Vitelli, 3-Arylsulphonyl-5-arylamino-1,3,4-thiadiazol-2(3*H*)-ones as Anti-inflammatory and Analgesic Agents, *Bioorg. Med. Chem.*, **9**, 2149 (2001); https://doi.org/10.1016/S0968-0896(01)00121-3.
12. S.D. Joshi, H.M. Vagdevi, V.P. Vaidya and G.S. Gadaginamath, Synthesis of New 4-Pyrrol-1-yl Benzoic Acid Hydrazide Analogs and Some Derived Oxadiazole, Triazole and Pyrrole Ring Systems: A Novel Class of Potential Antibacterial and Antitubercular Agents, *Eur. J. Med. Chem.*, **48**, 1989 (2008); https://doi.org/10.1016/j.ejmech.2007.11.016.
13. O. Pintilie, L. Profire, V. Sunel and P.A. Popa, Synthesis and Antimicrobial Activity of Some New 1,3,4-Thiadiazole and 1,2,4-Triazole Compounds having a D,L-Methionine Moiety, *Molecules*, **12**, 103 (2007); https://doi.org/10.3390/12010103.
14. R. El-Sayed, Synthesis, Antibacterial and Surface Activity of 1,2,4-Triazole Derivatives, *Indian J. Chem.*, **45B**, 738 (2006).
15. P. Molyneux, The Use of Stable Free Radical Diphenylpicrylhydrazyl (DPPH) for Estimating Antioxidant Activity, *Songklanakarin J. Sci. Technol.*, **26**, 211 (2004).
16. A.M. Pisoschi and G.P. Negulescu, Methods for Total Antioxidant Activity Determination: A Review, *Biochem. Anal. Biochem.*, **1**, 106 (2011); https://doi.org/10.4172/2161-1009.1000106.
17. X. Li, X.-Q. Li, H.-M. Liu, X.-Z. Zhou and Z.-H. Shao, Synthesis and Evaluation of Antitumor Activities of Novel Chiral 1,2,4-Triazole Schiff Bases Bearing γ-Butenolide Moiety, *Org. Med. Chem. Lett.*, **2**, 26 (2012); https://doi.org/10.1186/2191-2858-2-26.
18. T. Khan and R. Yadav, Synthesis, Characterization and Antioxidant Activity of Some New 4-Thiazolidinonyl-4*H*-1,2,4-Triazole Derivatives, *Heterocycl. Lett.*, **6**, 757 (2016).
19. R. Yadav, S.D. Srivastava and S.K. Srivastava, Synthesis, Antimicrobial and Antiinflammatory Activities of 4-Oxothiazolidines and their 5-Arylidenes, *Indian J. Chem.*, **44B**, 1262-1266 (2005).

20. R. Dua, S.K. Srivastava and S.D. Srivastava, Synthesis, Characterization and Antimicrobial Activity of 4-Oxothiazolidines and 5-Arylidene Derivatives of 2-Methylimidazoles, *Macroheterocycles*, **3**, 82 (2010); https://doi.org/10.6060/mhc2010.1.82.
21. M.A. Shakhatreh, M.L. Al-smadi, O.F. Khabour, F.A. Shuaibu, E.I. Hussein and K.H. Alzoubi, Study of the Antibacterial and Antifungal Activities of Synthetic Benzyl Bromides, Ketones and Corresponding Chalcone Derivatives, *Drug Design, Develop. Ther.*, **10**, 3653 (2016); https://doi.org/10.2147/DDDT.S116312.
22. H. Matsuda, T. Wang, H. Managi and M. Yoshikawa, Structural Requirements of Flavonoids for Inhibition of Protein Glycation and Radical Scavenging Activities, *Bioorg. Med. Chem.*, **11**, 5317 (2003); https://doi.org/10.1016/j.bmc.2003.09.045.
23. S.F. Barbuceanu, D.C. Illies, G. Saramet, V. Uivarosi, C. Draghici and V. Radulescu, Synthesis and Antioxidant Activity Evaluation of New Compounds from Hydrazinecarbothioamide and 1,2,4-Triazole Class Containing Diarylsulfone and 2,4-Difluorophenyl Moieties, *Int. J. Mol. Sci.*, **15**, 10908 (2014); https://doi.org/10.3390/ijms150610908.
24. A.A. Hameed and F. Hassan and F. Hassan, Synthesis, Characterization and Antioxidant Activity of Some 4-Amino-5-phenyl-4H-1,2,4-triazole-3-thiol Derivatives, *Int. J. Appl. Sci. Technol.*, **4**, 202 (2014).
25. T. Tsuneda, J. Miyake and K. Miyatake, Mechanism of H_2O_2 Decomposition by Triphenylphosphine Oxide, *ACS Omega*, **3**, 259 (2018); https://doi.org/10.1021/acsomega.7b01416.
26. D. Babu, P. Gurumurthy, S.K. Borra and K.M. Cherian, Antioxidant and Free Radical Scavenging Activity of Triphala Determined by Using Different *in vitro* Models, *J. Med. Plants Res.*, **7**, 2898 (2013).
27. R.J. Ruch, S.J. Cheng and J.E. Klaunig, Prevention of Cytotoxicity and Inhibition of Intercellular Communication by Antioxidant Catechins Isolated from Chinese Green Tea, *Carcinogenesis*, **10**, 1003 (1989); https://doi.org/10.1093/carcin/10.6.1003.
28. S. Keser, S. Celik, S. Turkoglu, O. Yilmaz and I. Turkoglu, Hydrogen Peroxide Radical Scavenging and Total Antioxidant Activity of Hawthorn, *Chem. J.*, **2**, 9 (2012).
29. P. Prieto, M. Pineda and M. Aguilar, Spectrophotometric Quantitation of Antioxidant Capacity through the Formation of Phosphomolybdenum Complex: Specific Application to the Determination of Vitamin E, *Anal. Bioch.*, **269**, 337 (1999); https://doi.org/10.1006/abio.1999.4019.