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SYNTHESIS, CHARACTERIZATION AND ANTIOXIDANT ACTIVITY OF SOME NEW 4-THIAZOLIDINONYL-4*H*-1, 2, 4-TRIAZOLE DERIVATIVES.

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Abstract:
Schiff bases of 1,2,4-triazoles have been found to possess extensive pharmacological activities and 4-thiazolidinone is considered as a biologically important active scaffold that possesses almost all types of biological activities. A rapid and efficient synthesis of 4-thiazolidinone fused with 1,2,4-triazole has been developed. In this view we have synthesized different new compounds in which 4-oxo-thiazolidines coupled with 1,2,4-triazole ring. 4-amino-1,2,4-triazole on condensation with different aryl aldehyde produced different Schiff bases (comp. 2) which on cycloaddition with mercaptoacetic acid produced 4-(2-aryl-4-oxo-thiazolidinyl)-4*H*-1,2,4-triazole (compound 3). All synthesized compounds were characterized by their spectral studies FTIR, ^{1}HNMR, ^{13}CNMR and elemental analysis. These all new synthesized 1,2,4-triazole derivatives evaluated for their antioxidant activities. Some of the compounds have shown better antioxidant activity than ascorbic acid.

Keywords: 1,2,4-triazole, Schiff base, 4-thiazolidinone, DPPH, antioxidant.

Introduction

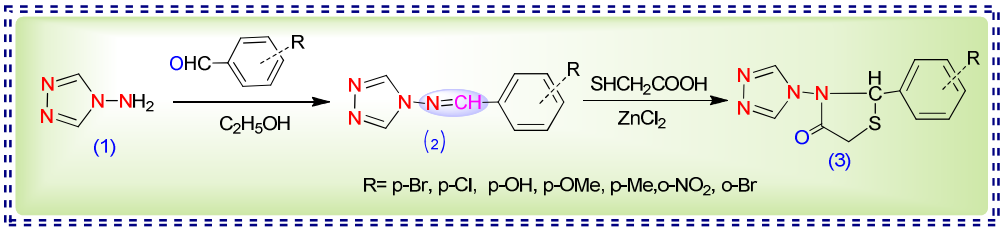
The chemistry of 4-amino-1,2,4-triazoles and their fused heterocyclic derivatives has received considerable attention owing to their synthetic and effective biological importance.[i] It is well known that the 1,2,4-triazoles and their derivatives constitute an important class of organic compounds with diverse agricultural, industrial and biological activities.[ii] For example, a large number of 1,2,4-triazole-containing ring system have been incorporated into a wide variety of therapeutically interesting drug candidates including anti-inflammatory,[iii] CNS stimulants,[iv] antitubercular,[v] antitumor[vi] antimicrobial agents[vii] and antimycotic[viii] activity such as Fluconazole, Itraconazole, Voriconazole. Also, there are other known drugs containing the 1,2,4-triazole group e.g. Triazolam (CNS depressant, anticonvulsant), Alprazolam, Etizolam, (anxiolytic), Furacylin (antibacterial) Anastazole (anticancer) and Ribavirin(antiviral) have reported. 1, 2, 4- triazole have drawn great attention to medicinal chemists from two decades due to its wide variety of activity, low toxicity and good pharmacokinetic and pharmacodynamics profiles.[ix]

Compounds containing an azomethine group (-CH=N-), known as Schiff's bases are formed by the condensation of a primary amine with a carbonyl compound. Schiff's bases derived from triazole were reported to possess antimicrobial[x], antioxidant[xi] antianxiety, anti-depressant, antiinflammatory[xii], plant growth regulatory activity.[xiii] Thiazolidinones are the derivatives of thiazolidine which belong to an important group of heterocyclic compounds containing sulfur and nitrogen in a five membered ring with a carbonyl group at the 4-position. The literature survey revealed that 4-thiazolidinone and their derivatives were possessed a wide range of pharmacological activities such as anti-inflammatory, analgesic, anticonvulsant, antimicrobial local and spinal anesthetics, CNS stimulants, hypnotics, anti HIV, hypoglycemic, antitumor activity.[xiv-xv]

Damage to cells caused by free radical is believed to play a central role in the aging process and in disease progression. antioxidants are our first line to defense against free radical damage, the need for antioxidants become even more critical with increased exposure to free radicals, pollution, cigarette smoke, drugs, illness and even stress can increase free radical exposure. [xvi]

1,1-diphenyl-2-picryl-hydrazyl (DPPH) is a stable free radical which has an unpaired valence electron at one atom of nitrogen bridge which produce a violet solution in ethanol, scavenging of DPPH radical is the basis of the popular DPPH antioxidant assay, this free radical stable at room temperature is reduced in the presence of an antioxidant molecule , giving rise to colourless ethanol solution. The use of the DPPH assay provides an easy and rapid way to evaluate antioxidants by spectrophotometry. [xvii- xviii]

We have reported the synthesis of new triazole bearing aryl-4-oxo-thiazolidine moiety at position 4 as shown in Scheme 1. All synthesized compounds were characterized by their spectral studies and elemental analysis. Thus in search for new biodynamic potent molecule it was thought to incorporate some additional heterocyclic moieties in triazole nucleus and study their biological and pharmacological activity. In the present work the synthesis and DPPH radical scavenging essay of certain new triazolo Schiff bases derivatives bearing aryl moiety is described.



Scheme 1– Synthesis of 4-(4-substitutedphenyl-4-oxo-thiazolidinyl)-4*H*-1,2,4-triazoles

Experimental

Mps were recorded using an electrothermal melting point apparatus and are uncorrected. The elemental analysis (C, H and N) of the reported compounds agrees with the calculated values and was within ±0.4-0.8% of theoretical values. 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 taken on a SHIMADZU FTIR 8400 spectrophotometer in KBr. ^{1}H NMR spectra (data reported in δ-ppm) were recorded on a Bruker Avance II-400 MHz, with TMS as internal reference in $CDCl_3$ and DMSO-d6. High quality commercial reagents and anhydrous solvent were used for synthesis of all the compounds.

Synthesis and Characterization

General procedure for the Synthesis of Schiff bases of 1,2,4- triazole (2)[xix]

The 1,2,4-triazole Schiff bases were synthesized by condensation 4-amino-4*H*-1,2,4-triazole with aromatic aldehydes in ethanol (Scheme 1) . An equimolar mixture of 4-amino-1,2,4-triazole compound **1** (0.02 mol) and aromatic aldehyde (0.02 mol) in ethanol 20 ml was refluxed for 2-4 hrs. The excess of solvent was distilled off under reduced pressure. The residue was cooled. The solid thus obtained was filtered, dried and recrystallized from methanol. The completion of the reaction was monitored by TLC using Chloroform and MeOH (8:2) as eluent.

Synthesis of 4-(4-bromobenzylidene-amino)-4*H*-1,2,4-triazole (Comp.2a)

White solid, Yield:80%, Rf-0.66, m.p.155-160 ^{o}C; IR(KBr) 1616 cm^{-1}(H–C=N), 3122 cm^{-1} (Ar,CH-strech.); 610 cm^{-1} (Ar-Br). ^{1}H NMR ($CDCl_3$) 7.3–7.8 (m, 4H, Ar–H), 9.21 (s, 1H, H–C=N), 9.11(s,2H,triazole)ppm.; ^{13}C NMR ($CDCl_3$) 127-138 (m,Ar-C), 168.4 (s,1C,N=CH), 157.1 (s,2C,C=N triazole), Anal. Calcd. for $C_9H_7N_4Br$; C, 43.05; H, 2.81; N,22.31. Found: C, 43.17; H, 3.16; N, 20.45.

Synthesis of 4-(4-chlorobenzylidene-amino)-4*H*-1,2,4-triazole (Comp.2b)

White solid, Yield:78%, Rf-0.69, m.p. 96-110 ^{o}C; IR (KBr) 1610 cm^{-1}(H–C=N), 3105 cm^{-1} (Ar,CH-strech.); 773cm^{-1} (Ar-Cl). ^{1}H NMR ($CDCl_3$) 7.2–7.8 (m, 4H, Ar–H), 9.18 (s, 1H, H–C=N), 9.13(s,2H,triazole) ppm.; ^{13}C NMR ($CDCl_3$) 126-138 (m,Ar-C), 168 (s,1C,N=CH), 157.3 (s,2C,C=N triazole), Anal. Calcd. for $C_9H_7N_4Cl$; C, 52.31; H, 3.41; N,22.11. Found: C, 51.14; H, 3.19; N, 21.65.

Synthesis of 4-(4-hydroxybenzylidene-amino)-4*H*-1,2,4-triazole (Comp.2c)

Brown solid, Yield:81%, Rf-0.52, m.p. 120-140 ^{o}C; IR (KBr) 1645 cm^{-1}(H–C=N), 3080 cm^{-1} (Ar,CH-strech.); 1311cm^{-1} (Ar-OH). ^{1}H NMR ($CDCl_3$) 6.9–7.8 (m, 4H, Ar–H), 9.23 (s, 1H, H–C=N), 9.15(s,2H,triazole), 5.43(s,1H,p-OH) ppm.; ^{13}C NMR ($CDCl_3$) 115-132 (m,Ar-C), 168.4 (s,1C,N=CH), 157.2 (s,2C,C=N triazole), 162(s,1C,C-OH) Anal. Calcd. for $C_9H_8N_4O$; C, 57.44; H, 4.28; N,8.50. Found: C, 56.18; H, 4.13; N, 9.25.

Synthesis of 4-(4-methylbenzylidene-amino)-4*H*-1,2,4-triazole (Comp.2d)

Light Yellow solid, Yield:72%, Rf-0.52, m.p. 135-165 ^{o}C; IR (KBr) 1610 cm^{-1}(H–C=N), 3112 cm^{-1} (Ar,CH-strech.); 773cm^{-1}, 2990 cm^{-1} (Ar-CH_3). ^{1}HNMR ($CDCl_3$) 7.3–7.9 (m, 4H, Ar–H), 9.22 (s, 1H, H–C=N), 9.15(s,2H,triazole), 2.34(s,3H,p-CH_3) ppm.; ^{13}CNMR ($CDCl_3$) 126-138 (m,Ar-C), 168.5 (s,1C,N=CH), 156.8 (s,2C,C=N triazole), 21.3(s,3H,-CH_3) Anal. Calcd. for $C_{10}H_{10}N_4$; C,64.5; H, 5.41; N,30.09. Found: C, 63.18; H, 4.68; N, 29.57.

Synthesis of 4-(4-methoxybenzylidene-amino)-4*H*-1,2,4-triazole (Comp.2e)

Cream solid, Yield:79%, Rf-0.45, m.p. 85-100 ^{o}C; IR (KBr) 1604 cm^{-1}(H–C=N), 3180 cm^{-1} (Ar,CH-strech.); 1173cm^{-1} (Ar-OCH_3). ^{1}HNMR ($CDCl_3$) 7.0–7.9 (m, 4H, Ar–H), 9.21 (s, 1H, H–C=N), 9.11(s,2H,triazole), 3.83(s,3H,-OCH_3) ppm.; ^{13}CNMR ($CDCl_3$) 127-130 (m,Ar-C),168.8 (s,1C,N=CH), 157.3 (s,2C,C=N triazole), 56.8(s,1C,-OCH_3) Anal. Calcd. for $C_{10}H_{10}N_4O$; C, 59.44; H, 4.98; N,27.70. Found: C, 58.18; H, 4.58; N, 29.25.

Synthesis of 4-(3-nitrobenzylidene-amino)-4*H*-1,2,4-triazole (Comp.2f)

Off white solid, Yield:83%, Rf-0.63, m.p. 180-200 ^{o}C; IR (KBr) 1607 cm^{-1}(H–C=N), 3164 cm^{-1} (Ar,CH-strech.); 1350cm^{-1} (Ar-NO_2). ^{1}H NMR ($CDCl_3$) 7.3–8.3 (m, 4H, Ar–H), 9.22 (s, 1H, H–C=N), 8.45(s,2H,triazole) ppm.; ^{13}C NMR ($CDCl_3$) 124-150 (m,Ar-C), 156 (s,1C,C-NO_2)168.1 (s,1C,N=CH), 157.3 (s,2C,C=N triazole), Anal. Calcd. for $C_9H_7N_5O_2$; C, 49.77; H, 3.28; N,14.73. Found: C, 48.78; H, 4.13; N, 13.25.

Synthesis of 4-(2-bromobenzylideneamino)-4*H*-1,2,4-triazole (Comp.2g)

White solid, Yield:76%, Rf-0.52, m.p. 185-195 ^{o}C; IR (KBr) 1625 cm^{-1}(H–C=N), 3130 cm^{-1} (Ar,CH-strech.); 615cm^{-1} (Ar-Br). ^{1}H NMR ($CDCl_3$) 7.3–7.8 (m, 4H, Ar–H), 8.76 (s, 1H, H–C=N), 9.11(s,2H,triazole) ppm.; ^{13}C NMR ($CDCl_3$) 121-138 (m, Ar-C),164.5 (s,1C,N=CH),

157.2 (s,2C,C=N triazole), Anal. Calcd. for $C_9H_7N_4Br$; C, 43.05; H, 2.81; N,22.30. Found: C, 43.18; H, 3.03; N, 22.25.

General procedure for synthesis of 4-(4-substitutedphenyl-4-oxo-thiazolidinyl)-4*H*-1,2,4-triazole (Comp. 3)[xx]

A solution of [4-(4-substitutedbenzylideneamino)-4*H*-1,2,4-triazoles **2** (0.02 mol) in 25 ml ethanol, thioglycolic acid (0.02 mol) added in presence of a pinch of anhy.$ZnCl_2$ stirred the mixture for about 5-6 hrs. Then the reaction mixture poured in to ice cold water and a saturated solution of $NaHCO_3$ added. Then filtered the solution and washed the solid product. The product were filtered, dried and finally recrystallized by ethanol compound (3a-3g).

Synthesis of 4-(4-bromophenyl-4-oxo-thiazolidinyl)-4*H*-1,2,4-triazole (Comp.3a)

White solid, Yield:70%, Rf-0.61, m.p.200-220 ^oC; IR(KBr) 1710 cm^{-1} (>C=O stretch.of thiazoli-dinone), 3122 cm^{-1} (Ar,CH-strech.), 2970 cm^{-1} (CH_2-S streching), 610 cm^{-1} (Ar-Br). ^{1}HNMR (DMSO) 7.13–7.82 (m, 4H, Ar–H), 5.63 (s, 1H, HC-N), 9.10(s,2H,triazole), 4.05(s,2H,-CH_2S), 2.5(t,2H,$COCH_2$ thiazol.) ppm; ^{13}CNMR (DMSO) 125.8-132.1(m,Ar C), 156.7(s,1C,C=O), 138.8(s,2C,C=N triazole), 39.5(m,1C,CH_2S), 78.8(t,1C,N-CH thiazolidinone) Anal. Calcd. for $C_{11}H_8N_4OSBr$; C, 40.75; H, 2.49; N,4.94. Found: C, 41.17; H, 2.56; N, 4.45.

Synthesis of 4-(4-chlorophenyl-4-oxo-thiazolidinyl)-4*H*-1,2,4-triazole (Comp.3b)

White solid, Yield:78%, Rf-0.63, m.p.75-80 ^oC; IR(KBr) 1712 cm^{-1} (>C=O stretch.of thiazolidinone), 3115 cm^{-1} (Ar,CH-strech.), 2950 cm^{-1} (CH_2-S streching), 768 cm^{-1} (Ar-Cl). ^{1}HNMR (DMSO) 7.1–7.43 (m, 4H, Ar–H), 5.93 (s, 1H, HC-N), 9.10(s,2H,triazole), 4.05(s,2H,-CH_2S), 2.5(t,2H,$COCH_2$ thiazol.) ppm; ^{13}CNMR (DMSO) 125.8-132.1 (m,Ar-C), 156.7(s,1C,C=O), 138.8(s,2C,C=N triazole), 39.5(m,1C,CH_2S), 78.8(t,1C,N-CH thiazolidinone) Anal. Calcd. for $C_{11}H_8N_4OSCl$; C, 47.23; H, 2.88; N,11.62. Found: C, 47.17; H, 2.66; N, 11.52.

Synthesis of 4-(4-hydroxyphenyl-4-oxo-thiazolidinyl)-4*H*-1,2,4-triazole (Comp.3c)

Cream solid, Yield:78%, Rf-0.67, m.p.100-120^oC; IR(KBr) 1680 cm^{-1} (>C=O stretch.of thiazoli-dinone), 3135 cm^{-1} (Ar,CH-strech.), 2982 cm^{-1} (CH_2-S streching), 1290 cm^{-1} (Ar-OH). ^{1}HNMR (DMSO) 6.7–7.8 (m, 4H, Ar–H), 5.35(s,1H,-OH), 5.65(s, 1H, HC-N), 9.10 (s,2H, tria-zole), 4.08(s,2H,-CH_2S), 2.56(t,2H,$COCH_2$ thiazol.) ppm; ^{13}CNMR (DMSO) 115.8-132.1 (m,Ar-C), 143.5(s,1c,C-OH), 157.2 (s,1C,C=O), 138.4 (s,2C,C=N triazole), 39.5 (m,1C,CH_2S), 78.5 (t,1C,N-CH thiazolidinone), Anal. Calcd. for $C_{11}H_9N_4O_2S$; C, 50.57; H, 3.47; N,12.25. Found: C, 51.27; H, 3.56; N, 12.35.

Synthesis of 4-(4-methylphenyl-4-oxo-thiazolidinyl)-4*H*-1,2,4-triazole (Comp.3d)

Light brown solid, Yield:67%, Rf-0.51, m.p.60-70 ^oC; IR(KBr) 1716 cm^{-1} (>C=O stretch.of thiazolidinone), 3125 cm^{-1} (Ar,CH-strech.), 2970 cm^{-1} (CH_2-S streching), 2970cm^{-1}(Ar-CH_3). ^{1}HNMR (DMSO) 7.1–7.5 (m, 4H, Ar–H), 2.8 (s,3H,-CH_3), 5.65 (s, 1H, HC-N), 9.10 (s,2H,triazole), 4.15 (s,2H,-CH_2S), 2.5 (t,2H,$COCH_2$ thiazol.) ppm; ^{13}CNMR (DMSO) 125.8-138.7 (m,Ar-C),21.3(s,1C,CH_3), 156.8(s,1C,C=O), 137.8(s,2C,C=N triazole), 39.5 (m,1C,CH_2S), 78.8 (t,1C,N-CH thiazolidinone), Anal. Calcd. for $C_{12}H_{11}N_4OS$; C, 55.58; H, 4.28; N,6.17. Found: C, 54.86; H, 4.55; N, 6.16.

Synthesis of 4-(4-methoxyphenyl-4-oxo-thiazolidinyl)-4*H*-1,2,4-triazole (Comp.3e)

Brown solid, Yield:79, Rf-0.59, m.p.160-170 ^oC; IR(KBr) 1704 cm^{-1} (>C=O stretch.of thiazolidinone), 3112 cm^{-1} (Ar,CH-strech.), 2955 cm^{-1} (CH_2-S streching), 761 cm^{-1} (Ar-OCH_3). ^{1}HNMR (DMSO) 6.8–7.9 (m, 4H, Ar–H),3.8(s,3H,-OCH_3) 5.62 (s, 1H, HC-N), 9.10(s,2H,triazole), 4.15(s,2H,-CH_2S), 2.8(t,2H,$COCH_2$ thiazol.) ppm; ^{13}CNMR (DMSO) 125.8-138.7(m,Ar-C), 21.3(s,1C,CH_3), 158.4(s,1C,C=O), 137.8(s,2C,C=N triazole), 38.5 (m,1C,CH_2S), 83.4(t,1C,N-CH thiazolidinone) Anal. Calcd. for $C_{12}H_{11}N_4O_2S$; C, 52.35; H, 4.03; N,11.62. Found: C, 51.17; H, 4.16; N, 11.45.

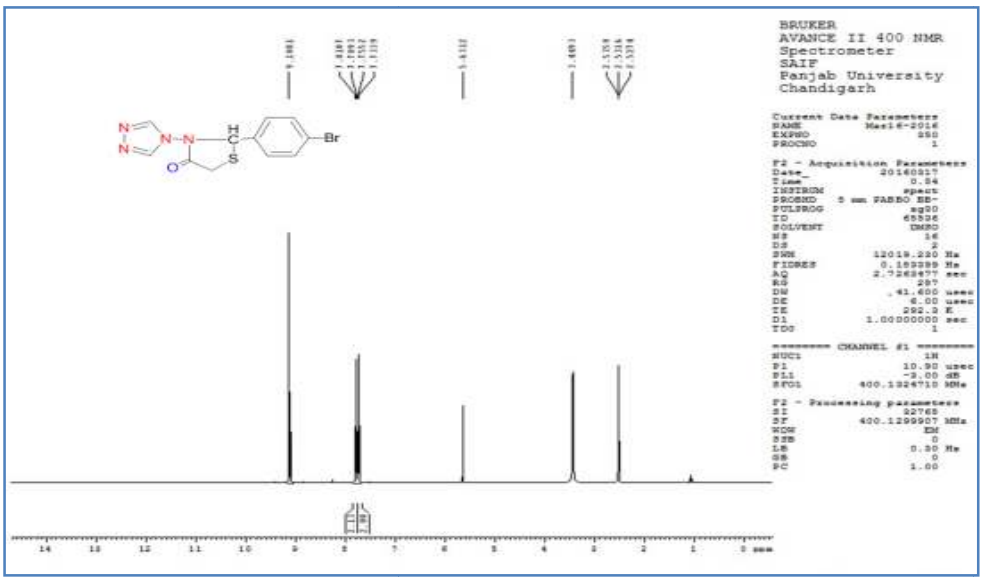


Figure 1. ^{1}HNMR spectra of compound 3a

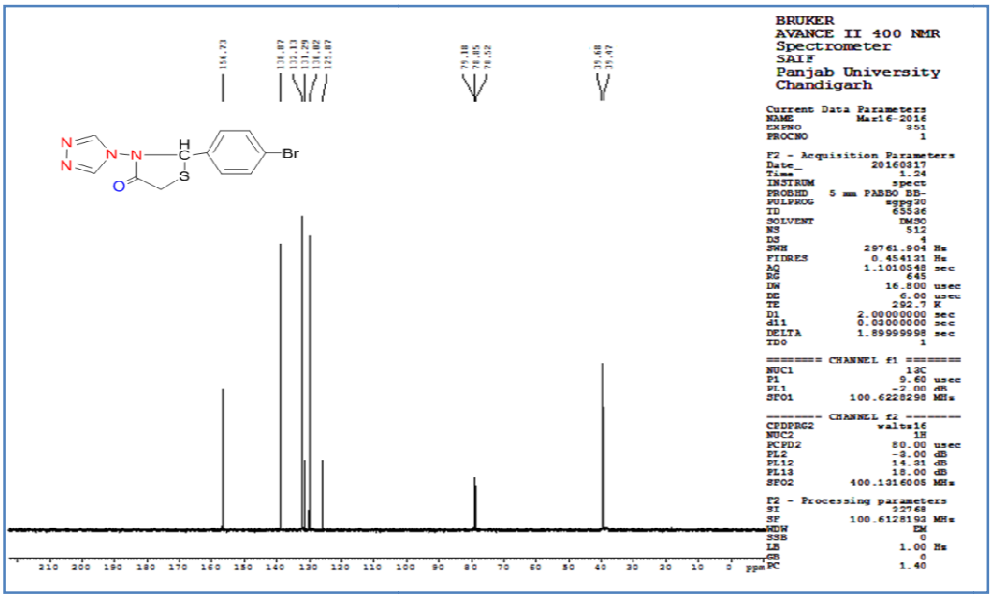


Figure 2. ^{13}CNMR spectra of compound 3a

Synthesis of 4-(2-nitrophenyl-4-oxo-thiazolidinyl)-4*H*-1,2,4-triazole (Comp.3f)

White solid, Yield:65%, Rf-0.56, m.p.70-90 ^{o}C; IR(KBr) 1717 cm^{-1} (>C=O stretch.of thiazolidinone), 3105 cm^{-1} (Ar,CH-strech.), 2980 cm^{-1} (CH_2-S streching), 1345 cm^{-1} (Ar-NO_2). ^{1}HNMR (DMSO) 7.5–8.2 (m, 4H, Ar–H), 5.62 (s, 1H, HC-N), 9.10(s,2H,triazole), 2.46(s,2H,-CH_2S), 3.53(t,2H,$COCH_2$ thiazol.)ppm; ^{13}CNMR (DMSO) 125.8-138.7(m,Ar-C), 140.3(s,1C,C-NO_2) 156.7(s,1C,C=O), 138.3(s,2C,C=N triazole), 39.06 (s,1C,CH_2S), 78.4 (t,1C, N-CH thiazolidinone) Anal. Calcd. for $C_{11}H_8N_5O_3S$; C, 45.51; H, 2.79; N.24.13, Found: C, 45.37; H, 2.66; N.23.98.

Synthesis of 4-(2-bromophenyl-4-oxo-thiazolidinyl)-4*H*-1,2,4-triazole (Comp.3g)

Off white solid, Yield:77%, Rf-0.65, m.p.160-170 ^{o}C; IR(KBr) 1723 cm^{-1} (>C=O stretch.of thiazolidinone), 3128cm^{-1} (Ar,CH-strech.), 2977 cm^{-1} (CH_2-S streching), 616 cm^{-1} (Ar-Br). ^{1}HNMR (DMSO) 7.13–7.50 (m, 4H, Ar–H), 5.65 (s, 1H, HC-N), 9.10(s,2H,triazole) 4.05(s,2H,-CH_2S), 2.6(t,2H,$COCH_2$ thiazol.) ppm; ^{13}CNMR (DMSO) 120.8-140.1 (m,Ar-C), 156.2 (s,1C,C=O), 138.3(s,2C,C=N triazole), 39.5(m,1C,CH_2S), 78.8(t,1C,N-CH thiazolidinone) Anal. Calcd. for $C_{11}H_8N_4OSBr$; C, 40.75; H, 2.49; N,4.94. Found: C, 41.13; H, 2.46; N, 4.73.

Free Radical Scavenging Activity (DPPH Assay)[xi]

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 color in methanol bleached to yellow, showing a significant absorption decrease at 517 nm. Then 1 mL of various concentration (5, 10, 25 and 50µg/ml) of the compounds (3a-3g) dissolved in methanol were added to 1 mL of ethanol solution of DPPH. After a 30 min incubation period at room temperature, the absorbance was read against a blank at 517 nm (Systronic 2201 Double Beam UV-Vis spectrophotometer) Ascorbic acid was used as the reference compound. 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:

$$\% \text{ of radical scavenging activity} = [(A_{control} - A_{test}) / A_{control}] \times 100$$

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).

DPPH radicals react with suitable reducing agents as a result of which the electrons become paired off forming the corresponding hydrazine (Figure 3). The solution therefore loses colour stoichometrically depending on the number of electrons taken up. Substances capable of donating electrons/hydrogen atoms are able to convert DPPH (Purple) into their non- radical form 1, 1-diphenyl-2- picrylhydrazine (Yellow), a reaction which can be followed spectrophotometrically. Free radical scavenging activity of the 1,2,4-triazole derivatives is concentration dependent, as the concentration of the test compounds increases, the radical scavenging activity increases and lower IC_{50} value reflects better protective action. From results, it may be postulated that compounds (3a- 3g) were able to reduce the stable free radical DPPH to diphenylpicrylhydrazine exhibiting better free radical scavenging activity than the standard antioxidant Ascorbic acid.

Figure 3- Mechanisms for antioxidants to scavenge DPPH radical

Result and Discussion

The condensation of 4-amino-1,2,4-triazole with different aryl aldehyde furnished 4-arylidine-1,2,4-triazole (Schiff base) (**2a-g**). Compound 2 on cycloaddition with mercaptoacetic acid in presence of anhy. $ZnCl_2$ give [4-(2-aryl-4-oxo-thiazolidinyl)-1,2,4

triazole (**3a-g**). All the compounds were characterized by analytical and spectroscopic methods.

In the IR spectrum of compounds showed absorption peak at 1580-1620 cm^{-1} occurred by N=CH linkage and a peak at 3120 cm^{-1} for aromatic C-H streching . The ^1H NMR (δ) spectrum of compounds showed a singlet at 4.43 was assigned to (-CH_2) proton and a Singlet at 9.11 occurred by N=CH proton in arylidenes derivative.

A multiplet was observed at 7.12 was assigned to different aromatic proton of 4-(2-aryl-4-oxo-thiazolidinyl)-1,2,4-triazole moiety. The structure of the 4-oxo-thiazolidinone obtained was established by its ^{1}HNMR spectrum 4.05 (s, 2H, S-CH_2), 2.5 (t,2H,$COCH_2$ thiazol.) a singlet and a triplet at 5.63 and 3.21 ppm for N-CH and CH_2 protons of respectively.

In the DPPH Free radical scavenging activity, compounds (3a-3g) were evaluated for their free radical scavenging activity with ascorbic acid as standard compound. The IC_{50} was calculated for each compound as well as ascorbic acid as standard and summarized in table 1 and shown in figures (4-7). The scavenging effect increased with the increasing concentrations of test compounds. The IC_{50} value for compounds 3a,3c and 3e were 44 µg/ml, 44.5 µg/ml and 63 µg/ml respectively less than ascorbic acid (68 µg/ml). Structure activity relationship study showed that the antioxidant activity of these 1,2,4-triazole derivatives could be due to that consist of atoms with low electronegativity and species with relatively small ionization energies compounds 3a and 3c have higher antioxidant activity due to bromide atom and -OH group As shown in figure. The most active compound was 3a and 3c that show highest antioxidant activity reached to 94.16% and 93.51% (IC_{50}= 44 and 44.5µg/ml) at concentration 50µg/ml that may be due to thiazolidinone ring which possess a high biological activity .

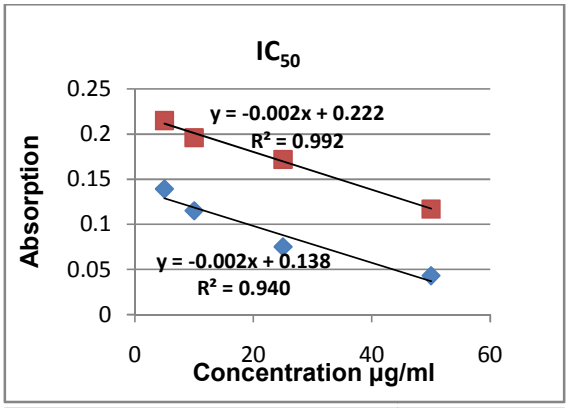


Figure 4- IC_{50} for Compound 3a and 3b

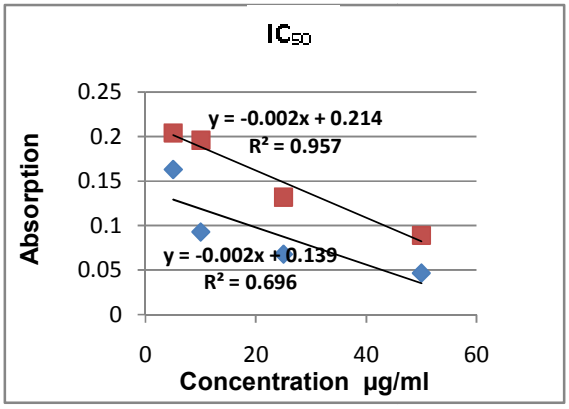


Figure 5- IC_{50} for Compound 3c and 3d

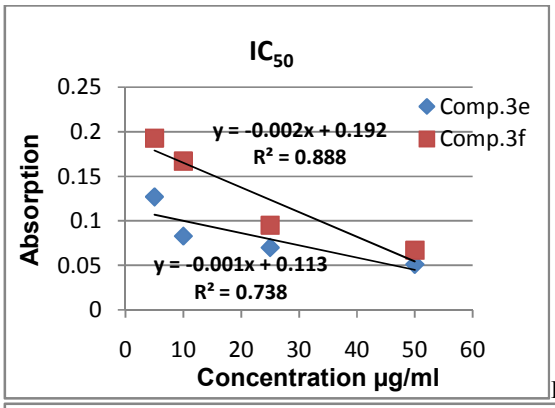


Figure 6- IC_{50} for Compound 3e and 3f

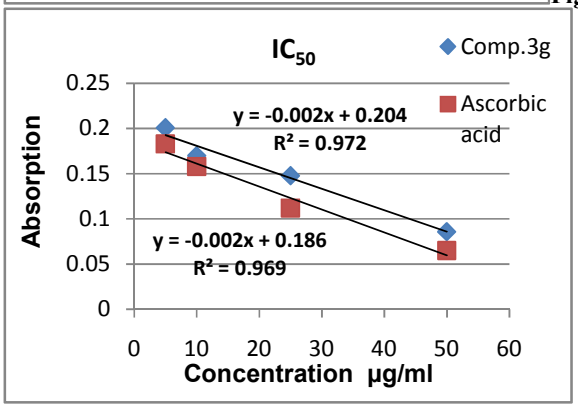


Figure 7- IC_{50} for Compound 3g and Ascorbic

Table 1: IC_{50} Values for Compounds(3a-3g) and Standard Ascorbic Acid

Compounds	IC_{50} (µg/ml)
3a	44
3b	86
3c	44.5
3d	82
3e	63
3f	71
3g	77
Ascorbic Acid	68

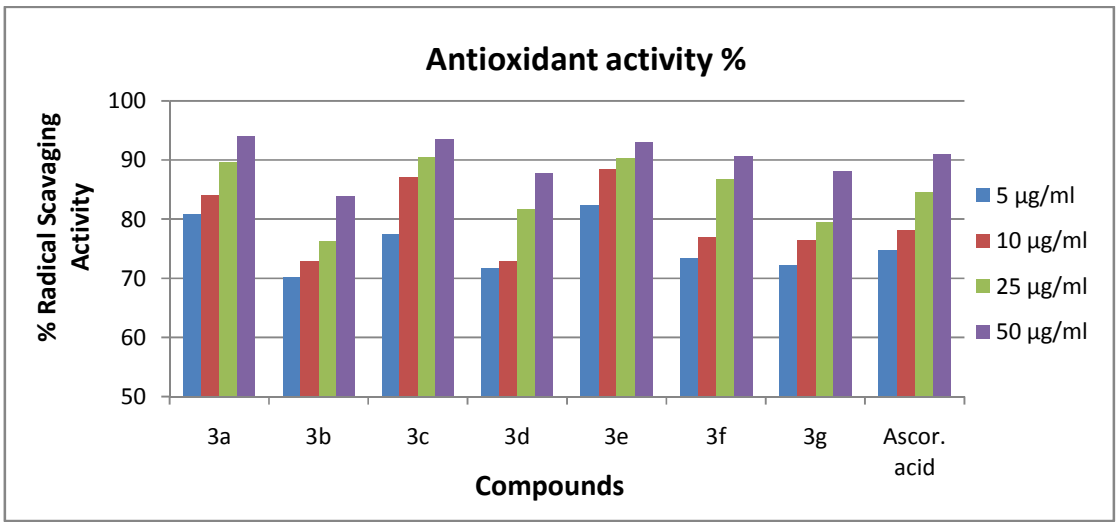


Figure 8. Antioxidant Activity of Compounds (3a-3g) at Different Concentration by Using Stable Free radical DPPH Assay.

Conclusion

In summary compounds (3a-3g) were successfully synthesized and characterized quantitatively and qualitatively by using FTIR, ^{1}HNMR, ^{13}CNMR spectroscopy and microelement analysis .4 -(4-aryl-4-oxo-thiazolidinyl)-4*H*-1,2,4-triazole derivatives have shown promising antioxidant activities. The IC_{50} value was determined for each compound. From results of DPPH assay, it found that compounds 3a,3c and 3e have strong antioxidant activity compared to the ascorbic acid and 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. Compounds (3d,3f) is also showed good antioxidant activity.

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