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Regular Article

Synthesis and anti-oxidant activity of novel 6,7,8,9 tetra hydro-5H-5-(2'-hydroxy phenyl)-2-(4'-substituted benzylidine)-3-(4-nitrophenyl amino) thiazolo quinazoline derivatives

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In the present study, a series of novel thiazolo quinazoline derivatives were synthesized by condensation of different aromatic aldehydes with 4-nitro aniline. The chemical structures of the synthesized compounds were confirmed by means of IR, ^{1}H-NMR, mass spectroscopy and elemental analyses. These compounds were screened for anti-oxidant activity by DPPH radical assay, nitric oxide scavenging activity and Hydrogen Peroxide scavenging activity. Among the synthesized compounds 5d, 5c and 5b was found to be the most potent anti-oxidant activity.

Key words: Anti-oxidant activity, Benzylidine thiazolo quinazoline, Nitrophenyl amino thiazolo quinazoline, Thiazolo quinazoline

Abbreviations: (DPPH) 1, 1-diphenyl-2-picryl-hydrazyl, (DMF) Dimethyl formamide, (NO) Nitric oxide, (ROS) Reactive oxygen species.

Free radicals are chemical species containing one or more unpaired electrons, most of them being unstable and capable of abstracting electrons from other molecules. The predominant reactive oxygen species and reactive nitrogen intermediates generated by cell metabolism or by exogenous factors include hydrogen peroxide ($\cdot H_2O_2$), the hydroxyl radical ($\cdot OH$), the superoxide anion radical $\cdot(\cdot O_2)$, nitric oxide $\bullet$(NO) and peroxynitrite $\bullet$($ONOO^-$). Oxygen is critical for life on earth. It is produced by plants during photosynthesis, and is necessary for aerobic respiration for animals. In the last few decades, research on free radicals gained more importance (Halliwell, 2008, Sachdev *et al*., 2008, Kamat *et al*., 2006). Oxygen and nitrogen derived free radicals are generated during cellular metabolism and mitochondrial energy production. The oxygen consumption inherent in cell growth leads to the generation of series of reactive oxygen species (ROS). ROS are continuously produced by the body's normal oxygen usage such as respiration and some cell mediated immune functions. ROS such as hydroxyl ions, superoxide anions, and peroxyl radicals, are involved in oxidative damage to cell components (Gulcin, 2006). ROS may be required for normal cell function at physiological concentrations. The consequence of an imbalance of prooxidants and anti-oxidants in the organism, if ROS are not effectively scavenged by cellular

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constituents, they can stimulate free radical chain reactions subsequently damaging the cellular biomolecules such as proteins, lipids and nucleic acids, and finally gaining recognition as a key phenomenon in chronic illnesses (Halliwell *et al*., 1990; Gulcin *et al*., 2003). Therefore the discovery of new safer anti-oxidant drugs becomes essential. Several quinazolines and condensed quinazolines derivatives have associated with a broad range of physiological activities, exhibiting anti-oxidant, analgesic, anti-inflammatory and anti-convulsant (Michael *et al*., 2008; Natalia *et al*., 2007; El-Gazzar *et al*., 2009; Alagarsamy *et al*., 2003; 2006). On the other hand, some thiazole derivatives also have various biological properties like anti-oxidant (Feng Shi *et al*., 2009; Charles *et al*., 2007; Athina *et al*., 2008; Hong *et al*., 2007), anti-inflammatory (Tajana *et al*., 1979), anti-microbial (Shukla *et al*., 1989), anthelmintic (Malesic, 1997) and immunorestoration (McDonald, 1992). Based on prior observations we synthesized a series of compounds (**5a-5f**) containing thiazolo quinazoline which could be effective for antioxidant activity.

Materials and Methods

1,-1-Diphenyl-2-picryl-hydrazine (DPPH) was purchased from Sigma-Aldrich (St. Louis, USA). Ascorbic acid and methanol were purchased from E. Merck (Darmstadt, Germany). The remaining solvents and other chemicals were of purchased from Sigma-Aldrich (St. Louis, USA). The melting points were taken in open capillary tube and are uncorrected. IR spectra were recorded with KBr pellets (ABB Bomem FT-IR spectrometer MB 104 ABB Limited, Bangaluru, India). Proton (^{1}H) NMR spectra (Bruker 400 NMR spectrometer Mumbai, India) were recorded with TMS as internal references. Mass spectral data were recorded with a quadrupol mass spectrometer (Shimadzu GC MS QP 5000, Chennai, India), and microanalyses were performed using a *vario EL* V300 *elemental* analyzer (*Elemental* Analysensysteme *GmbH* Chennai, India). The purity of the compounds was checked by TLC on pre-coated SiO_2 gel (HF_{254}, 200 mesh) aluminium plates (E. Merck) using ethyl acetate: benzene (1 : 3) and visualized in UV chamber. IR, ^{1}H-NMR, mass spectral datas and elemental analysis were consistent with the assigned structures.

Chemistry

The synthetic strategy leading to the key intermediate and the target compounds are illustrated in **Scheme 2**. 6,7,8,9 tetra hydro-5H-5-(2'-hydroxy phenyl) thiazolo (2, 3-*b*) quinazolin-3(2*H*)-one **3** prepared by the equimolar quantities of each (0.039 mol) of cyclohexanone and salicylaldehyde (0.039 mol) were taken in a beaker, to this sodium hydroxide solution was added to make the solution alkaline, this was shaken and kept aside. The solid thus obtained, was filtered, washed with water and recrystallized from absolute ethanol. A mixture of 2-hydroxy benzylidine cyclohexanone ring **1** (0.039 mol) thiourea (0.03 mol) and potassium hydroxide (2.5g) in ethanol (100 mL) was heated under reflux for 3h. The reaction mixture was concentrated to half of its volume, dilute with water, then acidified with dilute acetic acid and kept overnight. The solid thus obtained, was filtered, washed with water and recrystallized from ethanol to give 4-hydroxy phenyl 3, 4, 5, 6, 7, 8-hexahydro quinazolin-2-thione **2**. The chloroacetic acid (0.096 mol) was melted on a water bath and thione (0.009 mol) added to it portion wise to maintain its homogeneity. The homogeneous mixture was further heated on a water bath for 30 min and kept overnight. The solid thus obtained was washed with water until neutralized and crystallized from ethanol to give 6,7,8,9 tetra hydro-5H-5-(2'-hydroxy phenyl) thiazolo (2,

3-*b*) quinazolin-3(2*H*)-one **3** (Sharma *et al*., 1991). A mixture of **3** (0.002 mol)**,** substituted benzaldehyde (0.002 mol) and anhydrous sodium acetate (0.2g 0.002 mol) in glacial acetic acid (10 mL) was heated under reflux for 4h. The reaction mixture was kept overnight and the solid, thus separated, was filtered, washed with water and recrystallized from ethanol to furnish of 6,7,8,9 tetra hydro-5H-5-(2'-hydroxy phenyl)-2-(4'-substituted benzylidine) thiazolo (2,3-b) quinazolin-3(2H)-one **4**. Equimolar quantities (0.004 mol) of compound **4** treated with thionyl chloride and DMF to get chloro derivative and then coupled with *p*-nitro anilines in DMF at 80^0C and quenched in ice-water to get the product were separated by filtration, vaccum dried and recrystallized from warm ethanol to yields 6,7,8,9 tetra hydro-5H-5-(2'-hydroxy phenyl)-2-(4'-substituted benzylidine)-3-(4-nitrophenyl amino) thiazolo quinazoline (**5a-5f**) **Scheme 2**. The spectral data IR, ^{1}H NMR, mass spectroscopy and elemental analyses were used to ascertain the structures of all the compounds.

^{1}H NMR spectra were recorded for all the target compounds. The ^{1}H NMR spectra were recorded for the representative key intermediate **3**. The 6,7,8,9 tetra hydro-5H-5-(2-hydroxy phenyl) thiazoloquinazolin-3-one. Yield: 71%; m.p.153-155 °C; IR (KBr, cm^{-1}): 3402 (phenolic OH), 3046 (Ar-CH), 1719 (C=O), 1462 (C=C) cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 6.61-6.89 (m,4H Ar-H), 5.71 (s, 1H; -CH) 9.91 (s, 1H; Ar-OH), 3.76 (s, 2H; -CH_2) 1.6-2.42 (m, 8H; CH_2, CH_2, CH_2, CH_2).EI-MS m/z (M+): 300 (Calcd for $C_{16}H_{16}N_2O_2S$; 300.38). Anal. Calcd for $C_{16}H_{16}N_2O_2S$; C, 63.98; H, 5.37; N, 9.32; Found: C, 63.92; H, 5.28; N, 9.30.

*6,7,8,9 tetra hydro-5H-5-(2'-hydroxy phenyl)-2-benzylidine thiazolo (2, 3-b) quinazolin-3(2H)-one (**4**)*

Yellow solid; Yield: 82%; mp. 153-155 °C; IR : 3450 (O-H), 3051 (Ar-CH), 1724 (C=O), 1472 (C=C) cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 6.92-7.56 (m, 9H, Ar-H), 6.63 (s, 1H, =CH), 5.81 (s, 1H, H-5), 9.74 (s, 1H, Ar-OH), 1.58-2.67 (m, 8H, 4 × CH_2); EI-MS (m/z): 377 (M+); (Calcd for $C_{23}H_{20}N_2O_2S$; 377.48). Anal. Calcd for $C_{23}H_{20}N_2O_2S$, C, 71.11; H, 5.19; N, 7.21; Found: C, 71.19; H, 5.26; N, 7.14.

*6,7,8,9 tetra hydro-5H-5-(2'-hydroxy phenyl)-2-benzylidine-3-(4-nitrophenyl amino) thiazolo quinazoline (**5a**)*

Pale solid; Yield: 78%; mp. 157-159 °C IR : 3461 (O-H), 3029 (Ar-CH), 1492 (C=C), 1316 (N-H bending), 3391 (N-H stretching) cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 6.74-7.13 (m, 13H, Ar-H), 6.32 (s, 1H, =CH),5.59 (s, 1H, H-5), 9.81 (s, 1H, Ar-OH), 4.42 (s, 1H, thiazole), 7.26 (s, 1H, N-H), 1.46-2.42 (m, 8H, 4 × CH_2); EI-MS (m/z): 510 (M+); (Calcd for $C_{29}H_{26}N_4O_3S$; 510.61). Anal. Calcd for $C_{29}H_{26}N_4O_3S$; C, 68.21; H, 5.13; N, 10.97; Found: C, 68.26; H, 5.19; N, 10.82.

*6,7,8,9 tetra hydro-5H-5-(2'-hydroxy phenyl)-2-(4'-hydroxybenzylidine)-3-(4-nitrophenyl amino) thiazolo quinazoline (**5b**)*

Pale yellow solid; Yield: 72%; mp. 151-153 °C IR : 3467 (O-H), 3021 (Ar-CH), 1497 (C=C), 1312 (N-H bending), 3391 (N-H stretching) cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 6.74-7.29 (m, 12H, Ar-H), 6.36 (s, 1H, =CH),5.62 (s, 1H, H-5), 9.87 (s, 2H, Ar-OH), 4.46 (s, 1H, thiazole), 7.42 (s, 1H, N-H), 1.46-2.42 (m, 8H, 4 × CH_2); EI-MS (m/z): 556 (M+); (Calcd for $C_{30}H_{26}N_4O_5S$; 556.63). Anal. Calcd for $C_{30}H_{26}N_4O_5S$; C, 64.73; H, 5.07; N, 10.07; Found: C, 64.79; H, 5.11; N, 10.12.

*6,7,8,9 tetra hydro-5H-5-(2'-hydroxy phenyl)-2-(4'-hydroxy-5'-methoxy benzylidine)-3-(4-nitrophenyl amino) thiazolo quinazoline (**5c**)*

Pale yellow solid; Yield: 76%; mp. 156-158 °C IR : 3464 (O-H), 3027 (Ar-CH), 1494 (C=C), 1306 (N-H bending), 3396 (N-H stretching) cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 6.72-7.23 (m, 12H, Ar-H), 6.36 (s, 1H, =CH),5.62 (s, 1H, H-5), 9.89 (s, 1H, Ar-OH), 4.46 (s, 1H, thiazole), 3.78 (s, 3H –OCH_3), 7.29 (s, 1H, N-H), 1.46-2.42 (m, 8H, 4 × CH_2); EI-MS (m/z): 540 (M+); (Calcd

for $C_{30}H_{28}N_4O_4S$; 540.18). Anal. Calcd for $C_{30}H_{28}N_4O_4S$; C, 66.65; H, 5.22; N, 10.36; Found: C, 66.67; H, 5.25; N, 10.38.

*6,7,8,9 tetra hydro-5H-5-(2'-hydroxy phenyl)-2-(3', 4', 5'-tri methoxy benzylidine)-3-(4-nitrophenyl amino) thiazolo quinazoline (**5d**)*

Cream solid; Yield: 71%; mp. 187-189 °C IR : 3429 (O-H), 3027 (Ar-CH), 1413 (C=C), 1334 (N-H bending), 3313 (N-H stretching) cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 6.72-7.21 (m, 10H, Ar-H), 6.27 (s, 1H, =CH), 5.72 (s, 1H, H-5), 9.91 (s, 1H, Ar-OH), 4.42 (s, 1H, thiazole), 3.32 (s, 9H,–OCH_3), 7.47 (s, 1H, N-H), 1.34-2.46 (m, 8H, 4 × CH_2); EI-MS (m/z): 600 (M+); (Calcd for $C_{32}H_{32}N_4O_6S$; 600.68). Anal. Calcd for $C_{32}H_{32}N_4O_6S$; C, 63.98; H, 5.37; N, 9.33; Found: C, 63.81; H, 5.39; N, 9.37.

*6,7,8,9 tetra hydro-5H-5-(2'-hydroxy phenyl)-2-(5'-nitro benzylidine)-3-(4-nitrophenyl amino) thiazolo quinazoline (**5e**)*

Yellow solid; Yield: 79%; mp. 154-156 °C IR : 3467 (O-H), 3026 (Ar-CH), 1486 (C=C), 1311 (N-H bending), 3397 (N-H stretching) cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 6.77-7.23 (m, 12H, Ar-H), 6.24 (s, 1H, =CH), 5.69 (s, 1H, H-5), 9.89 (s, 1H, Ar-OH), 4.42 (s, 1H, thiazole), 7.23 (s, 1H, N-H), 1.41-2.46 (m, 8H, 4 × CH_2); EI-MS (m/z): 555 (M+); (Calcd for $C_{29}H_{25}N_5O_5S$; 555.6). Anal. Calcd for $C_{29}H_{25}N_5O_5S$; C, 62.69; H, 4.54; N, 12.60; Found: C, 62.54; H, 4.49; N, 12.59.

*6,7,8,9 tetra hydro-5H-5-(2'-hydroxy phenyl)-2-(4'-nitro benzylidine)-3-(4-nitrophenyl amino) thiazolo quinazoline (**5f**)*

Pale yellow solid; Yield: 71%; mp. 152-154 °C IR : 3461 (O-H), 3021 (Ar-CH), 1493 (C=C), 1309 (N-H bending), 3392 (N-H stretching) cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 6.73-7.21 (m, 12H, Ar-H), 6.33 (s, 1H, =CH), 5.67 (s, 1H, H-5), 9.81 (s, 1H, Ar-OH), 4.46 (s, 1H, thiazole), 7.19 (s, 1H, N-H), 1.46-2.42 (m, 8H, 4 × CH_2); EI-MS (m/z): 555 (M+); (Calcd for $C_{29}H_{25}N_5O_5S$; 555.6). Anal. Calcd for $C_{29}H_{25}N_5O_5S$; C, 62.69; H, 4.54; N, 12.60; Found: C, 62.62; H, 4.51; N, 12.67.

Antioxidant Screening

DPPH radical scavenging activity

DPPH solution, 1 mmol/L, was prepared by dissolving 31.54 mg DPPH in 95% v/v buffered methanol (40 mL of 0.1 mol/L acetate buffer (pH 5.5) with 60 mL of methanol) and made up to 50 mL with buffered methanol. DPPH scavenging activity was assessed using the method of (Hatano *et al*., 1988; Gow Chin *et al*., 1995). The synthesized compounds (**5a-5f**) at different concentrations such as 0.2, 0.4, 0.6, 0.8, 1.0 mL (200, 400, 600, 800 and 1000 µg/mL) were made up to 4 mL with distilled water. 1 mL of DPPH (1 mmol, 3.953×10^{-10} µg/mL) was added to each test tube, shaken and the reaction mixture was kept at 30^0 C for 30 minutes. Absorbance of the resulting solution was measured spectrophotometrically at 517 nm. The effect of ascorbic acid (vitamin C) on DPPH was also assessed for comparison with that of synthesized compounds (**5a-5f**). A buffered methanolic dilution (0.2, 0.4, 0.6, 0.8, 1.0 mL) of 1 mg/mL ascorbic acid was made to 4 mL with distilled water. 1mL DPPH radical (1 nmol/L) was added to each tube and same procedure as in DPPH scavenging experiment was followed. The absorbance measured for the control solution (Buffered methanol with DPPH) was in the range 0.500 ± 0.040 (Sharma *et al*., 2009). Antiradical activity was expressed as inhibition percentage (I %) and calculated using the following equation:

Inhibition Percentage = [(Absorbance control – Absorbance sample)/ Absorbance control] × 100

Nitric oxide scavenging activity

Nitric oxide scavenging activity was measured spectrophotometrically (Govindarajan *et al*., 2003). The reaction mixture (3 mL) containing 2 mL of an aqueous solution of sodium nitroprusside (5 mmol/L), 0.5 mL phosphate buffer saline as a good solvent for DPPH, and different concentrations (200 µg/mL-1000 µg/

mL, 0.5 mL) of the synthetic compounds (**5a-5f**) or the standard solution (rutin, 0.5 mL) were incubated at 25°C for 30 minutes. A control without the test compound, but with an equivalent amount of buffered methanol, was taken. After 30 min, 1.5 mL of the incubated solution was removed and diluted with 1.5 mL Griess reagent (1% sulphanilamide, 2% phosphoric acid and 0.1% N-1-naphthylethylenediamine dihydro chloride). Absorbance of the chromophore formed during diazotization of the sulphanilamide with nitrite and subsequent coupling with N-1-naphthylethylene diamine dihydrochloride was measured at 546 nm and the percentage scavenging activity was measured with reference to the standard.

Hydrogen Peroxide scavenging activity

The ability of test compounds to scavenge hydrogen peroxide was determined according (Sanchez, 2001; Famey *et al*., 1998). The solution of hydrogen peroxide (20 mmol) was prepared in phosphate buffer saline (pH 7.4). 1 mL of various concentrations (200 µg/mL-1000 µg/mL) of test compounds and standard were added to 2 mL of hydrogen peroxide. Absorbance of hydrogen peroxide at 230 nm was determined 10 min later against a blank solution containing the phosphate buffer saline without hydrogen peroxide. H_2O_2 radical scavenging ability of test and standard compounds (vitamin E) was calculated by

% Scavenged [H_2O_2] = [(Absorbance control - Absorbance sample)/ Absorbance control] × 100

Results and Discussion

Chemistry

The synthesized series of heterocycles, **4** and **5a-5f** by the reaction of **3** with appropriate aromatic aldehydes and *p* –nitro aniline in the presence of anhydrous sodium acetate and DMF as presented in Scheme 1. The IR, ^{1}H-NMR, mass spectroscopy and elemental analysis for the new compound is in accordance with the assigned structures. The IR spectra of compounds **4** showed stretching bands of keto group at 1715-1740 cm^{-1}. In **5a-5f**, stretching and bending NH bands of thiazolo quinazoline moiety appear at 3300-3400 cm^{-1}, 1300-1350 cm^{-1} respectively. The recorded IR spectra of representative compounds **5a-5f** showed missing of keto group bands. This clearly envisages that the keto group of **4** is converted in to secondary NH. The proton magnetic resonance spectra of thiazolo quinazoline and their corresponding derivatives have been recorded in $CDCl_3$. In this **5a-5f** NH signal of 3-(4-nitro phenyl) amino thiazolo quinazoline moiety appear at 7.19-7.67 (s) ppm respectively. The position and presence of NH signal in the ^{1}H-NMR spectra of final compounds conforms the secondary NH proton in thiazolo quinazoline moiety. This clearly envisages that thiazole-3-one moiety involve in 3-(4-nitro phenyl) amino formation. All these observed facts clearly demonstrate that 3rd position of keto group in thiazole ring is converted in to secondary amino group as indicated in **scheme 2** and conforms the proposed structure (**5a -5f**).

Anti-oxidant Testing

Compounds **5a-5f** was tested for anti-oxidant property by DPPH, nitric oxide and Hydrogen Peroxide scavenging methods. The observed data of the anti-oxidant activity is given in **Figure 1-3.**

DPPH radical scavenging is considered a good *in vitro* model and is widely used to conveniently assess antioxidant efficacy. In its radical form, DPPH has an absorbance at 515 nm which disappears when DPPH is reduced by an antioxidant compound or a radical species to become a stable diamagnetic molecule. As a result, the color changes from purple to yellow. This color change is taken as an indication of the hydrogen

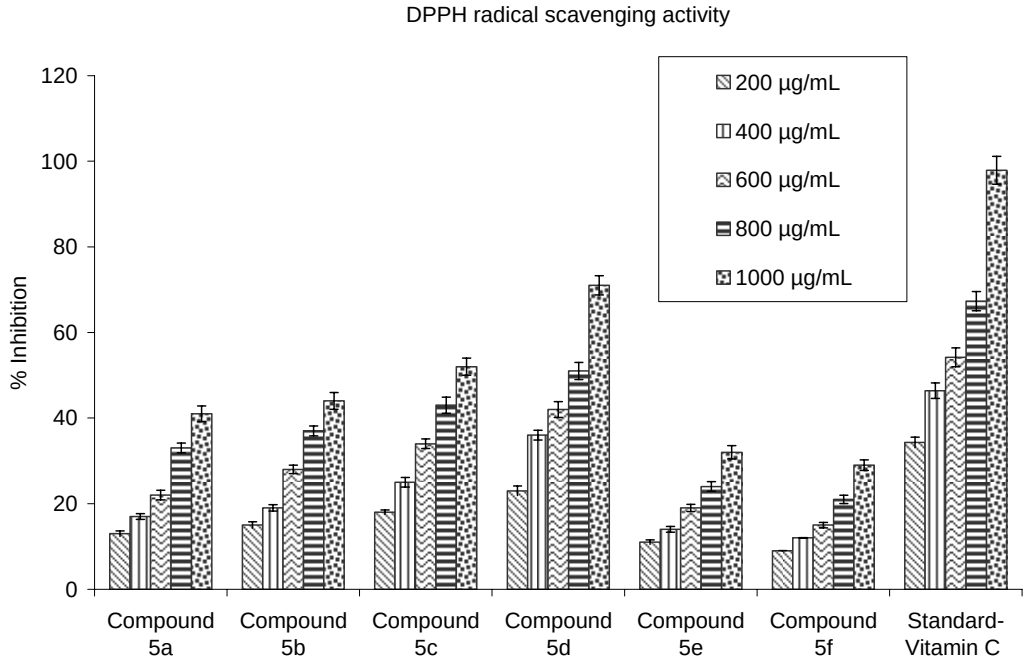


Figure 1. Scavenging effect of synthesized compounds (**5a-5f**) and standard vitamin C on 1, -1′-diphenyl-2-picryl hydrazyl (DPPH) radical. Results are the means ± S.D of five parallel measurements.

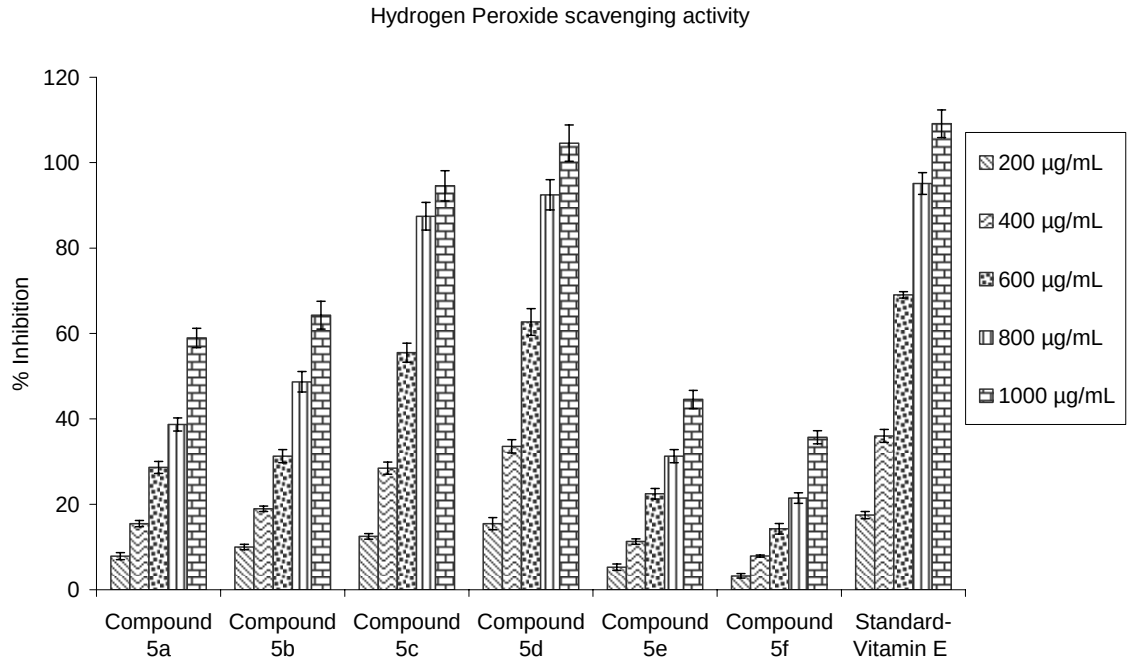


Figure 2. Effect of synthesized compounds (**5a-5f**) and vitamin E on hydrogen peroxide scavenging activity. Results are the means ± S.D of five parallel measurements

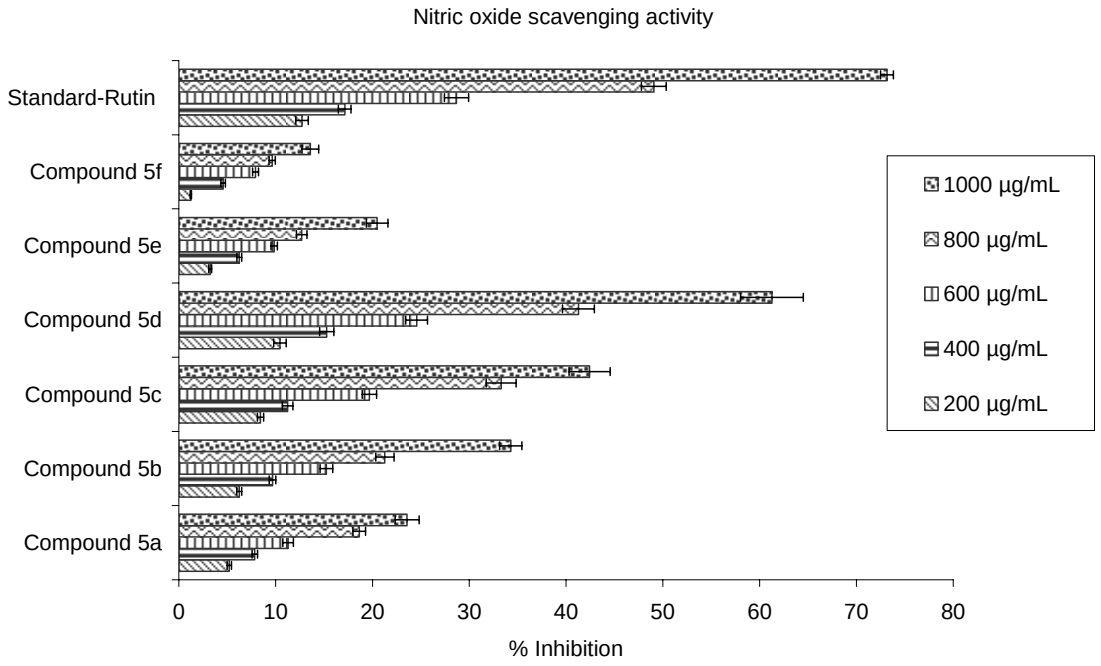
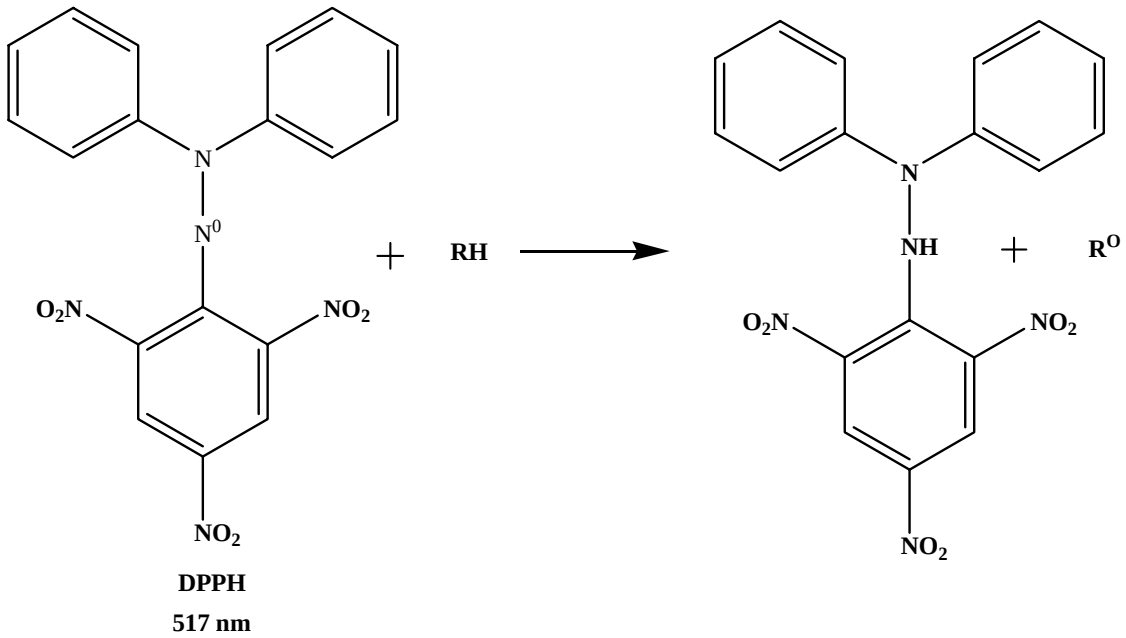
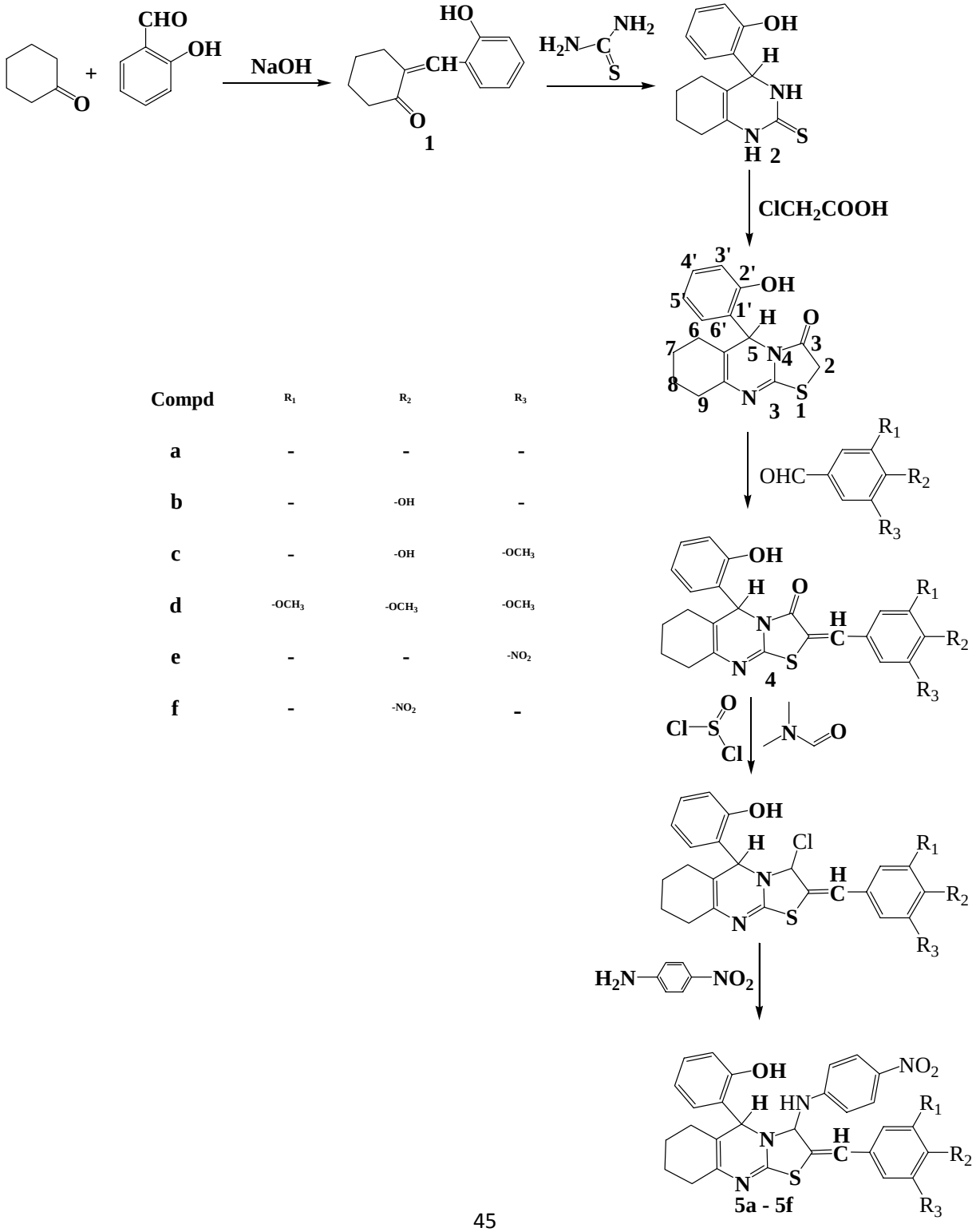


Figure 3 Scavenging effect of synthesized compounds (**5a-5f**) and standard rutin on nitric oxide radical. Results are the means ± S.D of five parallel measurements

Scheme – 1



Scheme -2



Compd	R_1	R_2	R_3
a	-	-	-
b	-	-OH	-
c	-	-OH	$-OCH_3$
d	$-OCH_3$	$-OCH_3$	$-OCH_3$
e	-	-	$-NO_2$
f	-	$-NO_2$	-

donating ability of the tested compounds. Antioxidants can react with DPPH and produce 1, 1-diphenyl-2-picryl-hydrazine Scheme **1** (Blois, 1958). The antioxidant activity of thiazoloquinazoline in general can be explained due to the presence of substituted aromatic aldehyde groups at the second position of thiazole ring. The reducing abilities of the examined compounds were determined by their interaction with the free stable radical 1,-1-diphenyl-2-picryl-hydrazine (DPPH) at five different concentrations for 30 min. The highest scavenger activity observed in compound **5d** is probably due to the presence of methoxy groups at positions 3, 4 and 5 in aromatic ring (**Figure 1**). The better activity of compound **5c** having hydroxyl group at *p*- position in the aromatic ring, has high electron-releasing properties (positive mesomeric effect is higher than negative inductive effect) and it activates aromatic ring. The same is valid for **5b** also. Generally, carboxyl and nitro groups are electron-withdrawing substituents which, deactivate the aromatic ring and have no capability to bind free radicals. The better scavenger activity of **5e** in comparison with **5f** is probably due to the lower electron-withdrawing effect of *m*-nitro group than that of *p*-nitro group. This could be the explanation of the good antioxidative activity of **5d** and **5c** and of the lower activity of **5f**. The cellular toxicity of nitric oxide has been associated with its reaction derivatives, especially peroxynitrite which could lead to DNA fragmentation and protein modification. Thus, nitric oxide scavengers could lower the risk of cellular and tissue damages associated with excessive nitric oxide production. The *in vitro* scavenging activities of the compound **5f** against nitric oxide at 1000 μg/mL was weak due to the electron withdrawing group ($-NO_2$). The remaining compounds having electron donating groups like **5d, 5c** and **5b** showed better scavenging activity against nitric oxide free radicals at the same concentration, compared to the standard drug rutin (**Figure 3**). All the synthesized compounds evaluated in this study exhibited concentration–dependent inhibition of hydrogen peroxide activity, which was also dependent on electron releasing nature of the compounds (**Figure 2**). The compound **5d** potently inhibited hydrogen peroxide activity at low concentration. Moreover the compounds **5c** and **5b** also inhibited hydrogen peroxide activity for the same reason. The weakest inhibitory activity was observed for the compounds **5f** and **5e** due to electron withdrawing nature of the substituent.

Conclusion

Several new thiazolo quinazolines were synthesized in moderate to good yield. The antioxidant properties of these molecules were evaluated by three methods. The prominent antioxidant effectiveness of the studied compounds seems to be related to the presence of electron donating group substituents in the aromatic rings. In the future, further studies with different substituents will be performed.

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