Pakistan J. Zool., pp 1-6, 2020. **DOI**: https://dx.doi.org/10.17582/journal.pjz/20190620180646

Novel Quinolinyl – Sulphonamide Hybrid Schiff Bases as Potent Radical Scavengers to Combat Oxidative Stress

Rubina Munir[1,2]*, Muhammad Zia-ur-Rehman[3], Muhammad Makshoof Athar[1], Noman Javid[1,4], Ayesha Roohi[2] and Syeda Fatima Razavi[2]

[1]Institute of Chemistry, University of the Punjab, Lahore 54590
[2]Department of Chemistry, Kinnaird College for Women, Lahore 54000
[3]Applied Chemistry Research Centre, PCSIR Laboratories Complex, Lahore 54600
[4]Chemistry Department (C-Block), Forman Christian College, Ferozepur Road, Lahore

Article Information
Received 20 June 2019
Revised 30 July 2019
Accepted 17 August 2019
Available online 03 June 2020

Authors' Contribution
MZ and NJ conceived and designed the research scheme. RM executed the synthetic work including characterization and article writing. MMA and NJ helped in data analysis. AR and SFR performed anti-oxidant assay.

Key words
Anti-oxidant, Schiff base, Sulphonamides, DPPH, Radical scavenging.

ABSTRACT

Eight novel quinolinyl-sulphonamide based Schiff bases have been prepared by condensation of substituted 2-chloroquinoline-3-carbaldehydes with sulphonamide substituted benzoic acid hydrazides. Structures of the Schiff bases have been confirmed by spectral techniques including FT-IR, ^{1}H-NMR, ^{13}CNMR, and mass spectroscopies. The purity of compounds has been established by elemental analysis. Free-radical scavenging activity of these compounds has been carried out by DPPH assay that showed these compounds to be effective radical scavengers. The compounds 7a, 7b, 7d, 7f and 7h have exhibited radical scavenging activity better than the reference compound BHT.

INTRODUCTION

Stimulated polymorphonuclear leukocytes, peroxisomes and macrophages produce reactive oxygen species (ROS) during respiration in human body (Bandgar *et al*., 2009; Ceyhan *et al*., 2011). These species (including superoxide anion radicals, hydroxyl radicals and hydrogen peroxide) are routinely removed from the body by action of certain enzymes like catalase, glutathione peroxidase, superoxide dismutase; or nonenzymatic compounds, such as albumin, bilirubin, uric acid and metallothioneins. The abnormal metabolic activity causes "oxidative stress" in which the endogenous enzymes fail to eliminate ROS efficiently resulting these species to attack cell membrane, lipids, proteins, enzymes and DNA (Bandgar *et al*., 2010). Oxidative stress if unrestrained, leads to numerous ailments like cellular aging, reperfusion damage, hepatitis, inflammation, acute pancreatitis, cirrhosis, diabetes, cancer, and many autoimmune diseases (Bandgar *et al*., 2009).

Antioxidants are the natural or synthetic compounds which can control the oxidation processes and are used as stabilizers for polymers, petrochemicals, foods, cosmetics and drugs. Antioxidants are taken as exogenous supplements or medicines to combat the ROS produced inside human body (Kumar and Rawat, 2013). β-Carotene, vitamin C and vitamin E are renowned exogenous antioxidants obtained from natural sources while butylhydroxyanisole, butylhydroxytoluene, gallates, etc. are some synthetic anti-oxidants. There is an increasing curiosity for searching new antioxidants among the researchers, predominantly those anticipated to avoid the presumed toxic effects of reactive oxygen species in human body, as well as the deterioration of foodstuffs (Zaheer *et al*., 2015; Kumar and Rawat, 2013).

Schiff bases are synthesized by condensation reaction between primary amines and carbonyl compounds. These systems are of great interest for researchers as these serve as intermediates for the synthesis of heterocyclic organic compounds as well as catalysts (Rayati *et al*., 2008; Chen *et al*., 2007). Schiff bases of acyl hydrazides have an important role in pharmacology as these have been reported for numerous bio-activities such as antibacterial (Nastasă *et al*., 2015; Ahmad *et al*., 2011), anti-leishmanial (Vargas *et al*., 2018; Vergara *et al*., 2017), anti-oxidant (Zaheer *et al*., 2015; Kotali, 2016), anti-inflammatory and anticancer (Gulzar *et al*., 2018; Li *et al*., 2017) activities. Looking at the biological potential of Schiff bases, the current study was carried out that involves the synthesis of a series of eight novel 2-chloroquinolinyl-sulphonamide hybrid Schiff bases and their in vitro antioxidant potential assay.

MATERIALS AND METHODS

Reagents and general methods

Schiff bases were prepared from acyl hydrazides and

* Corresponding author: organist94@gmail.com
0030-9923/2020/0001-0001 $ 9.00/0

2-chloroquinoline-3-carbaldehydes according to Figure 1. All the commercial reagents were used without further purification. All the solvents used were reagent or HPLC grade. Melting points were recorded on Gallenkamp melting point apparatus in an open capillary. IR spectra were recorded on Agilent Technologies Cary 630 FTIR. ^{1}H-NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded in DMSO-d_6 on Brücker Avance NMR instrument taking TMS as internal standard. Elemental analysis was carried out on LECO 630-200-200 TRUSPEC CHNS micro analyzer. TLC was performed on aluminum plates coated with silica gel 60 F_{254} (Merck) in an appropriate eluent system. Visualization was performed using ultraviolet light.

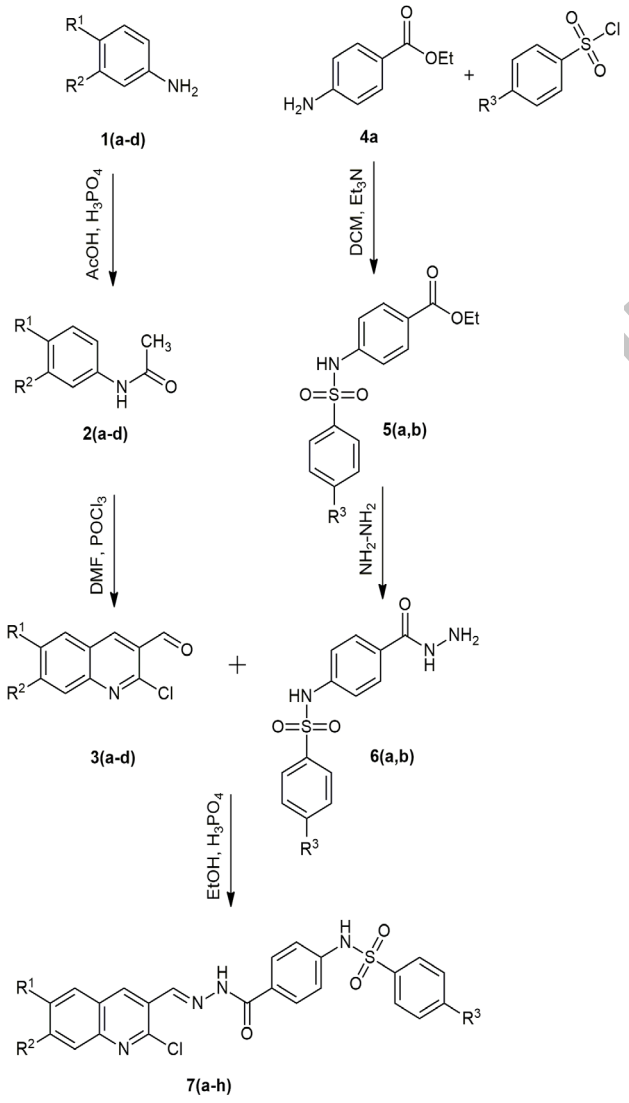

Fig. 1. Synthesis of quinolinyl-sulphonamide hybrid Schiff bases.

Synthesis of compounds 2(a-e)

Substituted aniline (1 mol) was refluxed in glacial acetic acid (118 mL; 2 mol) with catalytic amount of H_3PO_4 for 6 h after. After completion of the reaction, the reaction mixture was poured into ice cold water with stirring. The product was filtered, washed with excess cold water and recrystallized from boiling water.

Synthesis of compounds 3(a-d)

Vilsmeyer reagent was prepared by dropwise addition of $POCl_3$ (65.3 mL, 107.45 g, 0.70 mol) to DMF (19.3 mL, 18.26 g, 0.25 mol) with constant stirring at 0°C. Acetanilide 2 (0.10 mol) was then added and the reaction mixture was heated at 70-80°C for 8-18 h. The reaction mixture was poured on crushed ice cautiously and stirred for 20 min. The precipitated aldehyde 3 was filtered, washed with excess water and recrystallized from ethyl acetate (Meth-Cohn *et al*., 1979).

Synthesis of compounds 5(a,b)

Substituted sulphonyl chloride (50 mmol) was dissolved in dichloromethane (10 mL) and the solution was maintained at 0°C. To this solution, a mixture of ethyl 4-aminobenzoate (50 mmol), triethylamine (6.97 mL; 50 mmol) and dichloromethane (10 mL) was added dropwise and stirred for 3 h. Excess solvent was removed under vacuum leaving behind the crude product that was recrystallized from ethanol (Shafiq *et al*., 2011).

Synthesis of compounds 6(a,b)

The esters 5 (10 mmol) was refluxed in ethanol (50 mL) with hydrazine monohydrate (50 mmol) till the reaction went to completion. The product was obtained upon removing solvent and hydrazine under vacuum that was recrystallized using absolute ethanol.

General procedure for the synthesis of N-(4-(2-((2-chloroquinolin-3-yl)methylene)hydrazinecarbonyl) phenyl)benzenesulfonamide 7(a-h)

Equimolar quantities of substituted aldehydes 3 (10 mmol) and the sulphonamide hydrazides 6(a,b) were refluxed in ethanol with catalytic amount of H_3PO_4. The precipitated Schiff bases were filtered, washed with hot ethanol and dried.

N-(4-(2-((2-Chloro-6-methylquinolin-3-yl) methylene) hydrazinecarbonyl) phenyl) benzenesulfonamide (7a)

Yield 74%. Dirty Yellow solid. Decomposes above 300 °C. FTIR: 3227 (NH), 3031 (CH-Imine), 2921 (CH), 1643 (C=O), 1607 (C=N), 1331 (SO_2 Antisym.), 1158 (SO_2 Sym.). ^{1}H NMR (DMSO-d_6, 300 MHz) δ = 2.34 (s, 3H, CH_3), 7.23 (d, J = 8.7 Hz, 2H, Ar*H*), 7.37 (dd, J

= 8.4 Hz, 1.5 Hz, 1H, Ar*H*), 7.55 – 7.67 (m, 4H, Ar*H*), 7.80 – 7.88 (m, 5H, Ar*H*), 8.36 (s, 1H, Ar*H*), 8.65 (s, 1H, N=C*H*), 10.79 (s, 1H, N*H*), 11.96 (s, 1H, N*H*) ppm. ^{13}C NMR δ = 20.9, 115.5, 118.8, 119.4, 125.8, 127.2, 128.7, 128.8, 129.5, 129.9, 131.8, 133.0, 133.7, 134.9, 137.5, 139.8, 141.4, 143.0, 161.4, 162.8 ppm. Anal. calculated for $C_{24}H_{19}ClN_4O_3S$: C, 60.19; H, 4.00; N, 11.70; S, 6.69; Found: C, 60.30; H, 4.12; N, 11.85; S, 6.77. MS m/z: 479.1 $[M + 1]^+$, 481.1 $[M + 1]^+ + 2$.

N-(4-(2-((2-Chloro-6-methylquinolin-3-yl)methylene) hydrazinecarbonyl)phenyl)-4-methylbenzenesulfonamide (7b)

Yield 78%. Pale Yellow solid. Mp 288 °C. FTIR: 3330 (NH), 3149 (NH), 3047 (CH-Imine), 2927 (CH), 1643 (C=O), 1606 (C=N), 1336 (SO_2 Antisym.), 1162 (SO_2 Sym.). ^{1}H NMR (DMSO-d_6, 300 MHz) δ = 2.33 (s, 3H, CH_3), 2.34 (s, 3H, CH_3), 7.20 – 7.26 (m, 3H, Ar*H*), 7.37 (d, *J* = 8.1 Hz, 3H, Ar*H*), 7.62 (s, 1H, Ar*H*), 7.73 (d, *J* = 8.1 Hz, 2H, Ar*H*), 7.81 (d, *J* = 8.7 Hz, 2H, Ar*H*), 8.36 (s, 1H, Ar*H*), 8.65 (s, 1H, N=C*H*), 10.71 (s, 1H, N*H*), 11.96 (s, 1H, N*H*) ppm. ^{13}C NMR δ = 20.9, 21.4, 115.5, 118.6, 119.4, 125.8, 127.2, 128.5, 128.8, 129.5, 130.3, 131.8, 133.0, 134.9, 136.9, 137.5, 141.6, 143.0, 144.1, 161.4, 162.8 ppm. Anal. calculated for $C_{25}H_{21}ClN_4O_3S$: C, 60.91; H, 4.29; N, 11.36; S, 6.50; Found: C, 60.95; H, 4.40; N, 11.45; S, 6.64. MS m/z: 493.1 $[M + 1]^+$, 495.1 $[M + 1]^+ + 2$.

N-(4-(2-((2-Chloro-6-methoxyquinolin-3-yl)methylene) hydrazinecarbonyl)phenyl)benzenesulfonamide (7c)

Yield 90%. Beige Powder. Mp 272 °C. FTIR: 3291 (NH), 3054 (CH-Imine), 2931 (CH), 1645 (C=O), 1608 (C=N), 1337 (SO_2 Antisym.), 1153 (SO_2 sym.). ^{1}H NMR (DMSO-d_6, 300 MHz) δ = 3.90 (s, 3H, OCH_3), 7.25 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.48 (dd, *J* = 9.0 Hz, 2.7 Hz, 1H, Ar*H*), 7.56 – 7.67 (m, 4H, Ar*H*), 7.82 – 7.88 (m, 5H, Ar*H*), 8.83 (s, 1H, Ar*H*), 8.85 (s, 1H, N=C*H*), 10.82 (s, 1H, N*H*), 12.11 (s, 1H, N*H*) ppm. ^{13}C NMR δ = 56.2, 107.1, 118.8, 124.7, 126.7, 127.2, 128.5, 128.7, 129.5, 129.6, 129.9, 133.7, 134.7, 139.7, 141.6, 143.7, 146.3, 158.5, 163.2 ppm. Anal. calculated for $C_{24}H_{19}ClN_4O_4S$: C, 58.24; H, 3.87; N, 11.32; S, 6.48; Found: C, 58.36; H, 4.01; N, 11.41; S, 6.60. MS m/z: 495.1 $[M + 1]^+$, 497.1 $[M + 1]^+ + 2$.

N-(4-(2-((2-Chloro-6-methoxyquinolin-3-yl)methylene) hydrazinecarbonyl)phenyl)-4-methylbenzenesulfonamide (7d)

Yield 95%. Beige Powder. Mp 264 °C. FTIR: 3286 (NH), 3037 (CH-Imine), 2931 (CH), 1645 (C=O), 1609 (C=N), 1340 (SO_2 Antisym.), 1149 (SO_2 Sym.). ^{1}H NMR (DMSO-d_6, 300 MHz) δ = 2.33 (s, 3H, CH_3), 3.90 (s, 3H, OCH_3), 7.24 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.37 (d, *J* = 8.4 Hz, 2H, Ar*H*), 7.47 (dd, *J* = 9.3 Hz, 2.7 Hz, 1H, Ar*H*), 7.65 (d, *J* = 1.8 Hz, 1H, Ar*H*), 7.73 (d, *J* = 8.1 Hz, 2H, Ar*H*), 7.82 – 7.88 (m, 3H, Ar*H*), 8.83 (s, 1H, ArH), 8.84 (s, 1H, N=C*H*), 10.74 (s, 1H, N*H*), 12.10 (s, 1H, N*H*) ppm. ^{13}C NMR δ = 21.4, 56.2, 107.1, 124.7, 126.6, 127.2, 128.3, 128.6, 129.5, 129.6, 130.3, 134.7, 136.9, 141.8, 142.9, 143.7, 144.1, 146.3, 158.5, 163.0 ppm. Anal. calculated for $C_{25}H_{21}ClN_4O_4S$: C, 58.99; H, 4.16; N, 11.01; S, 6.30; Found: C, 59.05; H, 4.23; N, 11.10; S, 6.36. MS m/z: 509.1 $[M + 1]^+$, 511.1 $[M + 1]^+ + 2$.

N-(4-(2-((2-Chloro-7-methoxyquinolin-3-yl)methylene) hydrazinecarbonyl)phenyl)benzenesulfonamide (7e)

Yield 77%. Yellow Brown powder. Mp 279°C. FTIR: 3247 (NH), 3052 (CH-Imine), 2923 (CH), 1643 (C=O), 1607 (C=N), 1334 (SO_2 Antisym.), 1161 (SO_2 Sym.). ^{1}H NMR (DMSO-d_6, 300 MHz) δ = 3.83 (s, 3H, OCH_3), 6.83 – 6.86 (m, 2H, Ar*H*), 7.22 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.55 – 7.67 (m, 3H, Ar*H*), 7.75 – 7.86 (m, 5H, Ar*H*), 8.39 (s, 1H, Ar*H*), 8.63 (s, 1H, N=C*H*), 10.78 (s, 1H, N*H*), 11.89 (s, 1H, N*H*) ppm. ^{13}C NMR δ = 56.0, 98.3, 112.2, 113.8, 118.8, 122.5, 127.2, 128.8, 129.5, 129.9, 131.1, 133.7, 135.3, 139.8, 141.4, 141.5, 143.2, 161.8, 162.3, 162.7 ppm. Anal. calculated for $C_{24}H_{19}ClN_4O_4S$: C, 58.24; H, 3.87; N, 11.32; S, 6.48; Found: C, 58.41; H, 3.93; N, 11.53; S, 6.61. MS m/z: 495.1 $[M + 1]^+$, 497.1 $[M + 1]^+ + 2$.

N-(4-(2-((2-Chloro-7-methoxyquinolin-3-yl)methylene) hydrazinecarbonyl)phenyl)-4-methylbenzenesulfonamide (7f)

Yield 83%. Brownish Yellow solid. Mp 298 °C. FTIR: 3346 (NH), 3206 (NH), 3063 (CH-Imine), 2915 (CH), 1638 (C=O), 1618 (C=N), 1340 (SO_2 Antisym.), 1159 (SO_2 Sym.). ^{1}H NMR (DMSO-d_6, 300 MHz) δ = 2.34 (s, 3H, CH_3), 3.83 (s, 3H, OCH_3), 6.83 – 6.87 (m, 2H, Ar*H*), 7.21 (d, *J* = 8.4 Hz, 2H, Ar*H*), 7.37 (d, *J* = 8.4 Hz, 2H, Ar*H*), 7.71 – 7.76 (m, 3H, Ar*H*), 7.80 (d, *J* = 8.7 Hz, 2H, Ar*H*), 8.39 (s, 1H, Ar*H*), 8.63 (s, 1H, N=C*H*), 10.70 (s, 1H, N*H*), 11.89 (s, 1H, N*H*) ppm. ^{13}C NMR δ = 56.0, 98.2, 112.2, 113.8, 118.6, 122.5, 127.2, 128.7, 129.5, 130.3, 131.1, 135.3, 136.9, 141.5, 143.2, 144.1, 161.8, 162.3, 162.7 ppm. Anal. calculated for $C_{25}H_{21}ClN_4O_4S$: C, 58.99; H, 4.16; N, 11.01; S, 6.30; Found: C, 58.90; H, 4.09; N, 10.96; S, 6.19. MS m/z: 509.1 $[M + 1]^+$, 511.1 $[M + 1]^+ + 2$.

N-(4-(2-((2,7-Dichloroquinolin-3-yl)methylene) hydrazinecarbonyl)phenyl)benzenesulfonamide (7g)

Yield 77%. Pale Yellow solid. Mp 280 °C. FTIR: 3261 (NH), 3030 (CH-Imine), 1645 (C=O), 1605 (C=N), 1334 (SO_2 Antisym.), 1156 (SO_2 Sym.). ^{1}H NMR (DMSO-d_6,

300 MHz) δ = 7.23 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.24 – 7.38 (m, 2H, Ar*H*), 7.55 – 7.65 (m, 3H, Ar*H*), 7.80 – 7.86 (m, 5H, Ar*H*), 8.46 (s, 1H, Ar*H*), 8.63 (s, 1H, N=C*H*), 10.80 (s, 1H, N*H*), 12.10 (s, 1H, N*H*) ppm. ^{13}C NMR δ = 114.8, 118.4, 118.8, 123.0, 126.2, 127.2, 128.6, 129.6, 129.9, 131.3, 133.7, 134.6, 135.9, 139.7, 140.2, 141.5, 142.4, 161.3, 162.8 ppm. Anal. calculated for $C_{23}H_{16}Cl_2N_4O_3S$: C, 55.32; H, 3.23; N, 11.22; S, 6.42; Found: C, 55.54; H, 3.40; N, 11.41; S, 6.59. MS m/z: 499.0 $[M + 1]^+$, 501.0 $[M + 1]^+ + 2$, 503.0 $[M + 1]^+ + 4$.

N-(4-(2-((2,7-Dichloroquinolin-3-yl)methylene) hydrazinecarbonyl)phenyl)-4-methylbenzenesulfonamide (7h)

Yield 73%. Pale Yellow solid. Mp 215 °C. FTIR: 3305 (NH), 3035 (CH-Imine), 2915 (CH), 1651 (C=O), 1607 (C=N), 1346 (SO_2 Antisym.), 1156 (SO_2 Sym.). ^{1}H NMR (DMSO-d_6, 300 MHz) δ = 2.33 (s, 3H, CH_3), 7.20 – 7.28 (m, 3H, Ar*H*), 7.36 – 7.38 (m, 3H, Ar*H*), 7.72 (d, *J* = 8.1 Hz, 2H, Ar*H*), 7.81 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.90 (d, *J* = 8.4 Hz, 1H, Ar*H*), 8.46 (s, 1H, Ar*H*), 8.63 (s, 1H, N=C*H*), 10.72 (s, 1H, N*H*), 12.11 (s, 1H, N*H*) ppm. ^{13}C NMR δ = 21.4, 114.8, 118.4, 118.6, 123.0, 126.2, 127.2, 128.5, 129.6, 130.3, 131.3, 134.6, 135.9, 136.9, 140.2, 141.6, 142.4, 144.1, 161.4, 162.8 ppm. Anal. calculated for $C_{24}H_{18}Cl_2N_4O_3S$: C, 56.15; H, 3.53; N, 10.91; S, 6.25; Found: C, 56.19; H, 3.61; N, 11.03; S, 6.33. MS m/z: 513.1 $[M + 1]^+$, 515.0 $[M + 1]^+ + 2$, 517.0 $[M + 1]^+ + 4$.

Anti-oxidant assay: Free radical scavenging activity

Various amounts of the test compounds (5µg/mL, 10µg/mL and 20µg/mL, 40µg/mL, 60µg/mL, 80µg/mL and 100µg/mL) were mixed with 3mL methanolic solution of DPPH (0.1mM). The mixture was shaken vigorously and allowed to stand at room temperature for one an hour. The absorbance was measured at 517 nm in the spectrophotometer against methanol as a blank (Lee *et al.*, 2007). The capability to scavenge the DPPH radical was calculated using the following equation:

$$\text{DPPH Scavenging effect (\%)} = \frac{A_0 - A_1}{A_0} \times 100$$

Where, A_0 is the absorbance of the control reaction and A_1 is the absorbance in the presence of the samples or standards. IC_{50} was calculated by linear regression method.

RESULTS AND DISCUSSION

The structures of the synthesized compounds were interpreted by spectral techniques including IR, NMR and Mass spectra. The presence of a strong C=N band in the range 1633–1598 cm^{-1} confirmed the formation of Schiff bases. The NH stretching bands for hydrazide as well sulphonamide were observed between 3330 cm^{-1} to 3247 cm^{-1}. Imine CH was observed at 3063 – 3030 cm^{-1} and carbonyl around 1651–1638 cm^{-1}. The sulphonamide functionality was confirmed from absorption bands at 1340 – 1334 cm^{-1} and 1162 – 1153 cm^{-1} due to SO_2 stretching vibrations.

Table I.- Substituents and yields of quinolinyl - sulphonamides hybrid Schiff bases 7(a-h).

Entry	Compound	R^1	R^2	R^3	Yield (%)
1	7a	- CH_3	- H	- H	74
2	7b	- CH_3	- H	- CH_3	78
3	7c	- OCH_3	- H	- H	90
4	7d	- OCH_3	- H	- CH_3	95
5	7e	- H	- OCH_3	- H	77
6	7f	- H	- OCH_3	- CH_3	83
7	7g	- H	- Cl	- H	77
8	7h	- H	- Cl	- CH_3	73

In ^{1}H-NMR spectra, three separate peaks for CONH, S-NH and N=CH protons were observed. The CONH proton gave peak at 12.11–11.89 ppm and S-NH proton at 10.80 – 10.70 ppm, respectively while the singlet of N=CH was observed at 8.85 – 8.63 ppm. The peaks of aromatic protons appeared at 8.83 – 6.83 ppm depending upon the substitution pattern on quinoline and phenyl ring. The methyl protons of quinoline were observed at 2.37 – 2.33 ppm while -OCH_3 protons emerged at 3.93 – 3.80 ppm for compounds 7c-7f. ^{13}C NMR spectra supplemented the ^{1}HNMR data for confirmation of the proposed structures. The C=O carbon gave peak near 163.2 – 162.7 ppm while the N=CH carbon at 162.3 – 158.5 ppm in all the compounds. Methyl carbon appeared at 20.9 ppm 21.4 ppm while –OCH_3 carbon at 56.2 ppm and 56.0 ppm depending upon the position of these substituents on quinoline and phenyl ring.

The $[M+1]^+$ peaks of all the synthesized derivatives were in good agreement with their suggested structures. Mass spectra of the compounds confirmed the molar masses of all the compounds.

DPPH anti-oxidant assay

In the current study, the *in vitro* antioxidant activity of the synthesized Schiff bases was measured by the DPPH (1,1-diphenyl-2-picrylhydrazyl) radical scavenging protocol. This spectrophotometric method measures the decrease in absorbance of methanolic DPPH solution in the presence of antioxidant compound at 517 nm (Sumrra *et al*., 2018).

Table II.- Radical scavenging activity of quinolinyl - sulphonamides hybrid Schiff bases 7(a-h).

Entry	Compound	IC_{50} Value (µM)
1	7a	19.49
2	7b	16.94
3	7c	29.66
4	7d	18.92
5	7e	23.57
6	7f	19.88
7	7g	41.67
8	7h	18.54
9	BHT	19.88

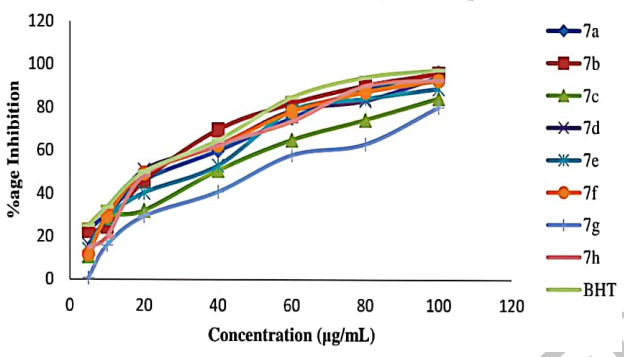

Fig. 2. DPPH anti-oxidant activity of quinolinyl-sulphonamide hybrid Schiff bases.

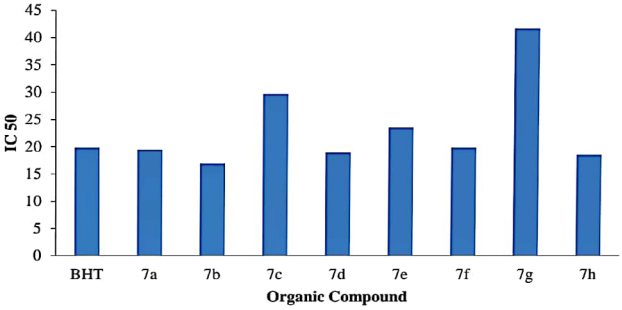

Fig. 3. IC_{50} of quinolinyl-sulphonamide hybrid Schiff bases compared to BHT.

Compound 7c, 7e and 7g exhibited moderate anti-oxidant activity with IC_{50} value 29.66, 23.57 and 41.67, respectively. The rest compounds exhibited better antioxidant activity than 7c, 7e and 7g. The Schiff base 7f exhibited activity equal to reference compound BHT (IC_{50} = 19.88 µg/mL). The synthesized compounds 7a, 7b, 7d, and 7h exhibited antioxidant activity even better than BHT (Table II). The quinolinyl – sulphonamide hybrid Schiff base 7b was found to be the most potent compound with IC_{50} values 16.94 µg/ mL. These compounds can be considered as the paramount anti-oxidants as IC_{50} values lower than 10 mg/mL is considered to be effective in antioxidant properties (Kumar and Rawat, 2013). Figures 2 and 3 show the percentage antioxidant activity at various concentrations and IC_{50} of the synthesized Schiff bases with reference to BHT, respectively.

CONCLUSION

Eight novel Schiff bases have been synthesized and characterized by using FTIR, ^{1}HNMR, ^{13}CNMR and mass spectroscopies. All the compounds exhibited DPPH scavenging activity. Antioxidant activity data of the synthesized quinolinyl – sulphonamide hybrid Schiff bases by DPPH radical scavenging assay confirmed the antioxidant potential of these compounds. Five compounds showed excellent potential even better than the reference BHT out of which compound 7b was found to be the most effective anti-oxidant with IC_{50} 16.94 µg/mL.

ACKNOWLEDGEMENT

The authors are grateful to Higher Education Commission of Pakistan for providing funding for this research.

Statement of conflict of interest

The authors declare no conflict of interest.

REFERENCES

Ahmad, N., Zia-ur-Rehman, M., Siddiqui, H.L., Ullah, M.F. and Parvez, M., 2011. Microwave assisted synthesis and structure–activity relationship of 4-hydroxy-N′-[1-phenylethylidene]-2H/2-methyl-1, 2-benzothiazine-3-carbohydrazide 1, 1-dioxides as anti-microbial agents. *Eur. J. med. Chem.*, **46**: 2368-2377. https://doi.org/10.1016/j.ejmech.2011.03.020

Bandgar, B.P., Gawande, S.S., Bodade, R.G., Gawande, N.M. and Khobragade, C.N., 2009. Synthesis and biological evaluation of a novel series of pyrazole chalcones as anti-inflammatory, antioxidant and antimicrobial agents. *Bioorg. med. Chem.*, **17**: 8168-8173. https://doi.org/10.1016/j.bmc.2009.10.035

Bandgar, B.P., Gawande, S.S., Bodade, R.G., Totre, J.V. and Khobragade, C.N., 2010. Synthesis and biological evaluation of simple methoxylated chalcones as anticancer, anti-inflammatory and antioxidant agents. *Bioorg. med. Chem.*, **18**: 1364-

1370. https://doi.org/10.1016/j.bmc.2009.11.066

Ceyhan, G., Celik, C., Uruş, S., Demirtaş, İ., Elmastaş, M. and Tümer, M., 2011. Antioxidant, electrochemical, thermal, antimicrobial and alkane oxidation properties of tridentate Schiff base ligands and their metal complexes. *Spectrochim. Acta A*, **81**: 184-198. https://doi.org/10.1016/j.saa.2011.05.106

Chen, Y., Ruppel, J.V. and Zhang, X.P., 2007. Cobalt-catalyzed asymmetric cyclopropanation of electron-deficient olefins. *J. Am. chem. Soc.*, **129**: 12074-12075. https://doi.org/10.1021/ja074613o

Gulzar, A., Mahmud, T., Munir, R. and Anjum, A., 2018. Anti-cancerous and anti-inflammatory activities of some novel schiff bases derived from 2-[(1,3-benzothiazol-2-yl)sulfanyl]-*n*-[4-(hydrazinecarbonyl)phenyl]acetamide. *Pakistan J. Zool.*, **50**: 1003-1009. https://doi.org/10.17582/journal.pjz/2018.50.3.1003.1009

Kotali, A., Nasiopoulou, D., Tsoleridis, C., Harris, P., Kontogiorgis, C. and Hadjipavlou-Litina, D., 2016. Antioxidant Activity of 3-[*N*-(Acylhydrazono) ethyl]-4-hydroxy-coumarins. *Molecules*, **21**: 138. https://doi.org/10.3390/molecules21020138

Kumar, D. and Rawat, D.S., 2013. Synthesis and antioxidant activity of thymol and carvacrol based Schiff bases. *Bioorg. med. Chem. Lett.*, **23**: 641-645. https://doi.org/10.1016/j.bmcl.2012.12.001

Lee, Y.L., Yen, M.T. and Mau, J.L., 2007. Antioxidant properties of various extracts from *Hypsizigus marmoreus*. *Fd. Chem.*, **104**: 1-9. https://doi.org/10.1016/j.foodchem.2006.10.063

Li, F.Y., Wang, X., Duan, W.G. and Lin, G.S., 2017. Synthesis and in vitro anticancer activity of novel dehydroabietic acid-based acylhydrazones. *Molecules*, **22**: 1087. https://doi.org/10.3390/molecules22071087

Meth-Cohn, O., Narine, B. and Tarnowski, B., 1979. A versatile new synthesis of quinolines and related fused pyridines. Part II. *Tetrahed. Lett.*, **20**: 3111-3114. https://doi.org/10.1016/S0040-4039(01)95334-1

Nastasă, C., Tiperciuc, B., Duma, M., Benedec, D. and Oniga, O., 2015. New hydrazones bearing thiazole scaffold: Synthesis, characterization, antimicrobial, and antioxidant investigation. *Molecules*, **20**: 17325-17338. https://doi.org/10.3390/molecules200917325

Rayati, S., Torabi, N., Ghaemi, A., Mohbbi, S., Wojtczak, A. and Kozakiewicz, A., 2008. Vanadyl tetradentate Schiff base complexes as catalyst for C–H bond activation of olefins with tertbutylhydroperoxide: Synthesis, characterization and structure. *Inorg. Chem. Acta*, **361**: 1239-1245. https://doi.org/10.1016/j.ica.2007.08.004

Shafiq, M., Zia-ur-Rehman, M., Khan, I.U., Arshad, M.N. and Khan, S.A., 2011. Synthesis of novel anti-bacterial 2, 1-benzothiazine 2, 2-dioxides derived from methyl anthranilate. *J. Chil. Chem. Soc.*, **56**: 527-531. https://doi.org/10.4067/S0717-97072011000100001

Sumrra, S.H., Kausar, S., Raza, M.A., Zubair, M., Zafar, M.N., Nadeem, M.A., Mughal, E.U., Chohan, Z.H., Mushtaq, F. and Rashid, U., 2018. Metal based triazole compounds: Their synthesis, computational, antioxidant, enzyme inhibition and antimicrobial properties. *J. mol. Struct.*, **1168**: 202-211. https://doi.org/10.1016/j.molstruc.2018.05.036

Vargas, E., Echeverri, F., Upegui, Y., Robledo, S. and Quiñones, W., 2018. Hydrazone derivatives enhance antileishmanial activity of thiochroman-4-ones. *Molecules*, **23**: 70. https://doi.org/10.3390/molecules23010070

Vergara, S., Carda, M., Agut, R., Yepes, L.M., Vélez, I.D., Robledo, S.M. and Galeano, W.C., 2017. Synthesis, antiprotozoal activity and cytotoxicity in U-937 macrophages of triclosan–hydrazone hybrids. *Med. Chem. Res.*, **26**: 3262-3273. https://doi.org/10.1007/s00044-017-2019-2

Zaheer, M., Zia-ur-Rehman, M., Jamil, N., Arshad, M.N., Siddiqui, S.Z. and Asiri, A.M., 2015. Efficient green synthesis of N′-benzylidene-2-(2-fluorobiphenyl) propanehydrazides: crystal structure and anti-oxidant potential. *J. chem. Res.*, **39**: 668-673. https://doi.org/10.3184/174751915X14452514747565