Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2017, 9(7):179-187

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Microwave Assisted Synthesis of 1, 2, 3-Triazole Tethered Pyrazolines and their Pharmacological Studies

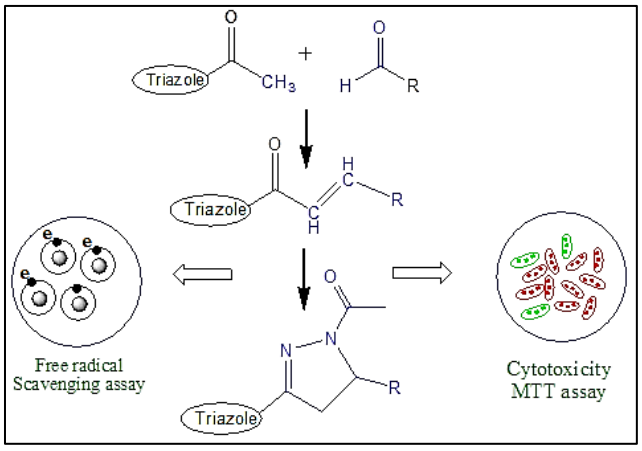
Vishwanath Turukarabettu[1], Balakrishna Kalluraya[1*] and Prashantha Naik[2]

[1]*Department of Chemistry, Mangalore University, Mangalagangothri, Karnataka, India*
[2]*Department of Bioscience, Mangalore University, Mangalagangothri, Karnataka, India*

ABSTRACT

A novel series of 1-(3-(1-(p-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl)-5-aryl-4,5-dihydropyrazol-1-yl)ethanone was prepared from 1-(1-(p-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl)-3-arylprop-2-en-1-one and hydrazine hydrate in acetic acid under microwave irradiation. The structure of propeonone and pyrazoline derivatives was elucidated by FT-IR, ^{1}H-NMR, ^{13}C NMR, mass spectral data and CHN analysis. The antioxidant and cytotoxic activities of newly synthesized compounds were tested by in-vitro method and compounds 7, 9 and 10 are found to be the promising anticancer agents.

Graphical Abstract



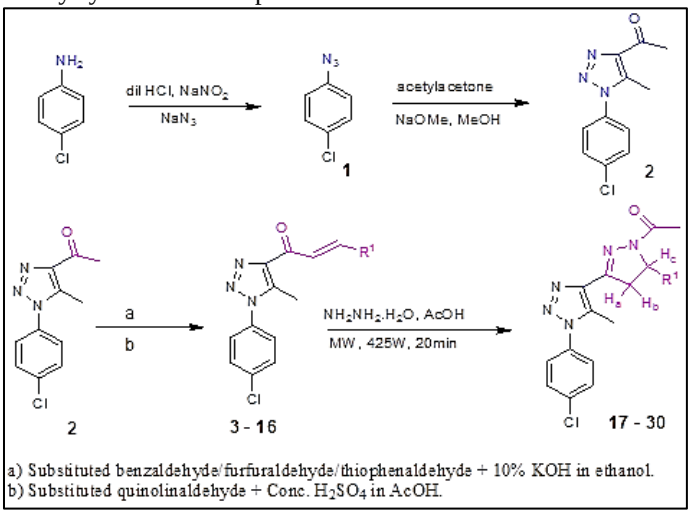
Keywords: Antitumor; Antioxidant; Claisen-Schmidt condensation; Propeonone; 1,2,3-triazoles

---

INTRODUCTION

In oncology, the drug specificity and resistance to chemotherapeutic agents is a key challenge to fight against cancer cells. Generally anticancer drugs destroy tumor cells as well as normal cells due to their lack of selectivity. Therefore, the researchers are more interested in the discovery of new antineoplastic agents with high selectivity in destroying of tumor cells or to limit their proliferation [1]. 1,2,3-Triazole and pyrazole derivatives are reported as possible anticancer [1,2], antibacterial [3-5], anti-inflammatory [6,7] and antiviral drugs [8,9]. Microwave (MW) energy provides a convenient and rapid technique in the conversion of reactants into products with no solvent or

minimum use of solvent [4,10-14]. The separation of products from the reaction mixture requires simple filtration or quenching the contents into water. So MW reaction was considered to be an energetically sustainable technique. Prompted by these observations and in continuation of our search for new pyrazole derivatives [15-19], a series of 4,5-dihydro-pyrazolines containing 1,2,3-triazole has been prepared (Scheme 1) and characterized by spectral and analytical techniques. The newly synthesized compounds were also screened for anti-oxidant and cytotoxicity study.



Scheme 1: Synthesis of chalcone (3-16) and pyrazoline (17-30) derivatives

EXPERIMENTAL SECTION

The progress of reactions was monitored by TLC on silica gel G-Al backed and observed under UV light. The microwave irradiation was performed in a Catalyst^{TM} CATA 2R MW oven with 85-850 W variable power levels. Melting points were determined using DSC-SDT Q600 instrument. FTIR spectra were recorded on a Shimadzu FTIR 157 spectrophotometer. The NMR spectra were recorded on Agilent VNMRS-400MHz NMR spectrometer using TMS as internal standard. Chemical shift values are reported in parts per million (δ), coupling constants (*J*) are reported in Hertz (Hz). Mass spectra were recorded on a Shimadzu 8030 mass spectrometer. Elemental analyses (C, H, N) were carried out in Vario-EI elementar III instrument and the results were found to be in good agreement (± 0.3%) with the calculated values.

Preparation of 1-Azido-*p*-Chlorobenzene (1)

4-Chloroaniline 0.51 g (4.0 mmol) in dilute HCl was cooled to 0°C. $NaNO_2$ 0.27 g (4.0 mmol) in 5 cm^3 water was added dropwise and stirred. Immediately NaN_3 0.32 g (5 mmol) in 5 cm^3 water was added dropwise below 5°C. After 30 minutes the reaction mixture was extracted with CH_2Cl_2 and washed repeatedly with saline solution. Dried over sodium sulphate and dichloromethane was removed to get a dark liquid. Yield 80%.

Preparation of 1-[1-(*p*-chlorophenyl)-4-5-methyl-1H-1,2,3-triazol-4-yl]ethanone (2)

Compound 1 1 g (6.5 mmol) and acetyl acetone 0.65 g (6.5 mmol) in 30 cm^3 of methanol in a round bottomed flask was cooled to 0°C. Sodium methoxide 0.37 g (7.0 mmol) was added to the mixture in portions and the contents were heated on a water bath. The solid formed was filtered off, dried and recrystallized in ethanol. Yield 75%; MP 92-94°C ([20] 93-94°C).

Preparation of 1-((*p*-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl)-3-substituted phenylprop-2-en-1-one (3-14)

Triazolyl ketone 2 0.47 g (2.0 mmol) and substituted aryl aldehyde (1.0 mmol) was dissolved in 20 cm^3 ethanol and stirred with 2 cm^3 10% KOH solution. The solid separated was collected by filtration, washed with aqueous ethanol, dried and recrystallized from ethanol. The propeonones prepared according to this procedure are,

1-(1-(p-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl)-3-phenylprop-2-en-1-one (3):
White solid; Yield 85%; mp 170-172°C ([21] 171-173°C); FT-IR (KBr) $\bar{\nu}$: 3044 (C-H), 1656 (C=O), 1597 (C=C) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 2.67 (s, 3H, CH_3), 7.40-7.45 (m, 5H), 7.57 (d, 2H, 6.8 Hz), 7.71 (d, 2H, 7.6 Hz), 7.89 (d, 1H, 16.4 Hz, α-CH), 8.05 (d, 1H, 16 Hz, β-CH); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 10.37, 122.83, 126.53, 128.82, 129.98, 130.68, 133.85, 134.85, 136.21, 138.51, 143.88, 144.09, 184.26; MS m/z: 323.60 (M^++1).

1-(1-(p-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl)-3-(p-biphenyl)prop-2-en-1-one (4):
White crystalline; Yield: 80%; mp 177-179°C; FT-IR (KBr) $\bar{\nu}$: 3035 (C-H), 1655 (C=O), 1595 (C=C) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 2.68 (s, 3H, CH_3), 7.37-7.67 (m, 9H), 7.56 (d, 2H, 8.8 Hz), 7.79 (d, 2H, 8.4 Hz), 7.94 (d, 1H, 15.6 Hz, α-CH), 8.10 (d, 1H, 16 Hz, β-CH); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 10.40, 122.40, 126.91, 128.92, 130.03, 130.67, 133.75, 134.84, 136.24, 138.41, 143.80, 144.08, 184.15; MS m/z: 399.50 (M^++1); (M.F.-). Analy. found (calcd) for $C_{24}H_{18}N_3OCl$: C 71.89 (72.09), H 4.53 (4.54), N 10.50 (10.51).

1-(1-(p-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl)-3-(3,4-dihydroxyphenyl)prop-2-en-1-one(5):
White crystalline; Yield: 80%; mp 152-155°C; FT-IR (KBr) $\bar{\nu}$: 3487 (O-H), 2947 (C-H), 1629 (C=O), 1602 (C=C) cm^{-1}; ^1H NMR(400 MHz, $CDCl_3$) δ: 2.68 (s, 3H, CH_3), 5.02 (s, 1H, OH), 5.13 (s, 1H, OH), 7.68-7.71 (m, 3H), 7.58 (d, 2H, 8.0 Hz), 7.73 (d, 2H, 7.6 Hz), 7.90 (d, 1H, 16.4 Hz, α-CH), 8.04 (d, 1H, 16 Hz, β-CH); ^{13}C NMR(400 MHz, $CDCl_3$) δ : 10.25, 122.91, 123.73, 123.89, 124.83, 125.93, 128.15, 132.54, 135.92, 138.51, 143.87, 150.2, 184.25; MS m/z: 355.70 (M^++1); Analy. found (calcd) for $C_{18}H_{14}N_3O_3Cl$: C 60.84 (60.77), H 3.88 (3.97), N 11.80 (11.81).

1-(1-(p-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl)-3-(3,4-dimethoxyphenyl)prop-2-en-1-one(6):
White crystalline; Yield: 81%; mp 174-176°C; FT-IR (KBr) $\bar{\nu}$: 3057 (C-H), 1654 (C=O), 1570 (C=C) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 2.66 (s, 3H, CH_3), 3.92 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 6.88 (d, 1H, 8.8 Hz), 7.25-7.57 (m, 7H), 7.85 (d, 1H, 15.6 Hz, α-CH), 7.92 (d, 1H, 16 Hz, β-CH); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 10.36, 56.01, 56.06, 109.9, 111.04, 120.67, 124.02, 126.53, 127.93, 129.98, 133.91, 136.22, 138.34, 149.3, 151.58, 184.16; MS: m/z = 383.60 (M^++1). Analy. found (calcd) for $C_{20}H_{18}N_3O_3Cl$: C 62.53 (62.58), H 4.65 (4.73), N 10.88 (10.95).

1-(1-(p-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl)-3-(p-fluorophenyl)prop-2-en-1-one (7):
White crystalline; Yield: 73%; mp 200-202°C; FT-IR (KBr) $\bar{\nu}$: 3055 (C-H), 1666 (C=O), 1587 (C=C) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 2.67 (s, 3H, CH_3), 7.08-7.45 (m, 4H, F-Ar), 7.55 (d, 2H, 8.8 Hz), 7.70 (d, 2H, 8.8 Hz), 7.85 (d, 1H, 16 Hz, α-CH), 7.98 (d, 1H, 5.6 Hz, β-CH); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 10.28, 122.26, 127.45, 129.37, 130.10, 131.57, 135.64, 135.39, 143.67, 144.04, 184.18; MS m/z: 341.66 (M^++1); Analy. found (calcd) for $C_{18}H_{13}N_3OFCl$: C 63.07 (63.26), H 3.96 (3.83), N 12.14 (12.29).

1-(1-(p-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl)-3-(p-bromophenyl)prop-2-en-1-one (8):
White crystalline; Yield: 75%; mp 195-197°C; FT-IR (KBr) $\bar{\nu}$: 3025 (C-H), 1669 (C=O), 1560 (C=C) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 2.68 (s, 3H, CH_3), 7.40 (d, 2H, 8.0), 7.47 (d, 2H, 6.8 Hz), 7.56 (d, 2H, 8.0 Hz), 7.75 (d, 2H, 8.6 Hz), 7.78 (d, 1H, 16.2 Hz, α-CH), 8.01 (d, 1H, 16.0 Hz, β-CH); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 10.26, 122.33, 130.04, 130.39, 132.26, 133.13, 135.68, 143.68, 144.01, 184.20; MS m/z: 401.45 (M^+), 403.30 (M^++3), 405.35 (M^++4); Analy. found (calcd) for $C_{18}H_{13}N_3OBrCl$: C 53.57 (53.69), H 3.30 (3.25), N 10.27 (10.44).

1-(1-p-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl)-3-(p-nitrophenyl)prop-2-en-1-one (9):
Light yellow crystalline; Yield: 80%; mp 242-244°C; FT-IR (KBr) $\bar{\nu}$: 3051 (C-H), 1664 (C=O), 1612 (C=C), 1500 (asym. NO_2), 1409 (sym. NO_2) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 2.68 (s, 3H, CH_3), 7.41 (d, 2H, 8.8 Hz), 7.46(d, 2H, 8.8 Hz), 7.52 (d, 2H, 8.6 Hz), 7.68 (d, 2H, 8.8 Hz), 7.83 (d, 1H, 16 Hz, α-CH), 7.99 (d, 1H, 16.2 Hz, β-CH); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 10.39, 122.82, 126.48, 128.83, 130.08, 133.85, 136.61, 138.05, 143.75, 144.08, 149.7, 184.24; MS m/z: 368.76 (M^++1); Analy. found (calcd) for $C_{18}H_{13}N_4O_3Cl$: C 58.49 (58.62), H 3.51 (3.55), N 15.16 (15.19).

1-(1-(p-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl)-3-(p-chlorophenyl)prop-2-en-1-one (10):
White crystalline; Yield: 81%; mp 197-199°C; FT-IR (KBr) $\bar{\nu}$: 3033 (C-H), 1669 (C=O), 1598 (C=C) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 2.66 (s, 3H, CH_3), 7.47-7.68 (m, 8H), 7.81 (d, 1H, 16 Hz, α-CH), 8.03 (d, 1H, 15.6 Hz, β-CH); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 10.37, 122.84, 127.33, 129.35, 129.39, 131.03, 132.14, 135.64, 137.81, 143.20, 184.20; MS m/z: 341.66 (M^++1); Analy. found (calcd) for $C_{18}H_{13}N_3OCl_2$: C 60.32 (60.35), H 3.68 (3.66), N 11.69 (11.73).

1-(1-(p-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl)-3-(p-(dimethylamino)phenyl)prop-2-en-1-one (11):
Yellow crystalline solid; Yield: 69%; mp >240 (decomp.) FT-IR (KBr) $\bar{\nu}$ = 3051 (C-H), 1672 (C=O), 1574 (C=C) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 2.68 (s, 3H, CH_3), 2.81 (s, 6H, $N(CH_3)_2$), 7.44 (d, 2H, 8.4), 7.46 (d, 2H, 8.6 Hz), 7.50 (d, 2H, 8.6 Hz), 7.52 (d, 2H, 8.0 Hz), 7.80 (d, 1H, 16 Hz, α-CH), 7.91 (d, 1H, 16.0 Hz, β-CH); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 10.38, 45.14, 120.23, 122.86, 126.53, 127.94, 130.67, 133.83, 134.86, 137.92, 143.74, 149.60, 184.35; MS m/z: 366.50 (M^++1); Analy. found (calcd) for $C_{20}H_{19}N_4O_1Cl$: C 65.45 (65.48), H 5.28 (5.22), N 15.19 (15.27).

1-(1-(p-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl)-3-(p-tolyl)lprop-2-en-1-one (12):
White crystalline solid; Yield 75%; mp 156-158°C, [21] 155°C; Analy. found (calcd) for $C_{19}H_{16}N_3OCl$: C 67.69 (67.56), H 4.71 (4.77), N 12.38 (12.44).

1-(1-(p-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl)-3-(furan-2-yl)prop-2-en-1-one (13):
Pale yellow crystals; Yield: 65%; mp 262-264°C; FT-IR (KBr) $\bar{\nu}$: 3055 (C-H), 1662 (C=O), 1584 (C=C) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 2.65 (s, 3H, CH_3), 6.62 (d, 6.4 Hz, 1H, furan-4H), 6.70 (m, 1H, furan-3H), 6.81 (d, 2H, 7.0 Hz), 7.70 (d, 2H, 8.0 Hz), 7.76 (d, 1H**,** furan-5H), 7.78 (d, 1H, 16.2 Hz, α-CH), 8.00 (d, 1H, 16.0 Hz, β-CH); ^{13}C NMR(400 MHz, $CDCl_3$) δ: 10.35, 112.65, 116.21, 120.74, 126.54, 129.93, 133.89, 136.20, 138.33, 144.09, 145.21, 151.81, 184.12; MS m/z: 401.45 (M^+), 403.30 (M^++3), 405.35 (M^++4); Analy. found (calcd) for $C_{16}H_{12}N_3O_2Cl$: C 61.20 (61.25), H 3. 87 (3.86), N 13.35 (13.39).

1-(1-(p-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl)-3-(thiophen-2-yl)prop-2-en-1-one (14):
Pale yellow crystals; Yield: 62%; mp 243°C; FT-IR (KBr) $\bar{\nu}$: 3056 (C-H), 1664 (C=O), 1586 (C=C) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 2.66 (s, 3H, CH_3), 6.64 (d, 6.6 Hz, 1H, thiophene-4H), 6.74 (m, 1H, thiophene-3H), 6.82 (d, 2H, 7.6 Hz), 7.72 (d, 2H, 8.6 Hz), 7.77 (m, 1H, thiophene-2H), 7.92 (d, 1H, 16.0 Hz, α-CH), 8.01 (d, 1H, 16.0 Hz, β-CH); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 10.34, 112.66, 116.20, 120.73, 126.56, 129.96, 133.86, 136.20, 138.35, 144.10, 145.22, 151.80, 184.12; MS m/z: 329.43 (M^+); Analy. found (calcd) for $C_{16}H_{12}N_3OClS$: C 58. 20 (58.27), H 3.65 (3.67), N 12.70 (12.74).

Preparation of 1-((*p*-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl)-3-(substituted quinolin-3-yl)prop-2-en-1-one (15-16)
Triazolyl ketone 2 0.47 g (2.0 mmol) and substituted quinoline aldehyde (2.0 mmol) was dissolved in acetic acid 20 cm^3 and added 2 drops of Conc. H_2SO_4. The mixture was stirred at room temperature for 2 h and allowed to stand for a day. The precipitate was filtered off, washed with ethanol, dried and recrystallized from DMF-ethanol mixture.

1-(1-(p-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl)-3-(2-hydroxyquinolin-3-yl)prop-2-en-1-one (15):
Yellow crystals; Yield: 74%; mp 156-158°C; FT-IR (KBr) $\bar{\nu}$: 3040 (C-H), 1669 (C=O), 1576 (C=C) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 2.67 (s, 3H, CH_3), 6.05 (s, 1H, OH), 7.52 (d, 2H, 8.7 Hz), 7.58 (d, 2H, 8.8 Hz), 7.52-7.64 (m, 5H), 7.80 (d, 1H, 15.8 Hz, α-CH), 8.10 (d, 1H, 16.0 Hz, β-CH); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 10.35, 122.86, 123.35, 125.40, 127.43, 128.65, 130.08, 131.82, 133.04, 135.75, 138.52, 143.90, 144.06, 147.16, 149.75, 176.28, 185.21; MS m/z: 390.45 (M^++1); Analy. found (calcd) for $C_{21}H_{15}N_4O_2Cl$: C 64. 42 (64.54), H 3.79 (3.87), N 14.26 (14.34).

1-(1-(p-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl)-3-(2-hydroxy-6-methylquinolin-3-yl)prop-2-en-1-one (16):
Yellow crystals; Yield: 75%; mp 162-164°C; FT-IR (KBr) $\bar{\nu}$: 3045 (C-H), 1666 (C=O), 1576 (C=C) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 2.31 (s, 3H, CH_3), 2.68 (s, 3H, CH_3), 6.06 (s, 1H, OH), 7.53 (d, 2H, 8.6 Hz), 7.59 (d, 2H, 8.6 Hz), 7.54-7.67 (m, 5H), 7.82 (d, 1H, 16.0 Hz, α-CH), 8.11 (d, 1H, 16.0 Hz, β-CH); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 10.35, 27.14, 122.85, 123.36, 125.41, 127.45, 128.65, 130.09, 131.83, 133.10, 135.76, 143.89, 144.05, 147.18, 149.76, 176.28, 185.21; MS m/z: 404.66 (M^++1); Analy. found (calcd) for $C_{22}H_{17}N_4O_2Cl$: C 65.20 (65.27), H 4.25 (4.23), N 13.80 (13.84).

Preparation of 1-(3-(1-(*p*-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl)-5-aryl-4,5-dihydro pyrazol-1-yl)ethanone (17-30)
Propeonone 3-16 (1.0 mmol), hydrazine hydrate (1.0 mmol) and glacial acetic acid 5 cm^3 were taken in a round bottomed flask equipped with reflux condensor. The contents were irradiated with microwave at 510 watt for 15

minutes. Cooled the reaction flask and contents were poured on to ice cold water. The precipitate was collected by filtration, washed with water and dried. The crude product was recrystallized in DMF-ethanol mixture.

1-(3-(1-(4-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl)-5-phenyl-4,5-dihydropyrazol-1-yl)etha none (17): White crystals; Yield: 87%; mp 159-161°C; FT-IR (KBr) $\overline{\nu}$: 3053 (C-H), 1672 (C=O), 1502 (C=N) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 2.37 (s, 3H, CH_3), 2.58 (s, 3H, CH_3), 3.46 (dd, 1H, 4.4 Hz and 18.8 Hz, H_a), 3.90 (dd, 1H, 12.0 Hz and 18.8 Hz, H_c), 5.56 (dd, 1H, 4.4 Hz and 11.6 Hz, H_b), 7.22-7.33 (m, 5H), 7.42 (d, 2H, 8Hz), 7.55 (d, 2H, 8.8 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 10.49, 21.95, 43.38, 58.97, 125.63, 126.36, 127.69, 128.86, 129.99, 133.39, 134.14, 136.09, 138.25, 141.48, 149.25, 168.66; MS m/z: 379.65 (M^++1); Analy. found (calcd) for $C_{20}H_{18}N_5OCl$: C 63.16 (63.24), H 4.70 (4.78), N 18.32 (18.44).

1-(3-(1-(p-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl)-5-(p-biphenyl)-4,5-dihydropyrazol-1-yl) ethanone (18):
White solid; Yield: 84%; mp 108-110°C; FT-IR (KBr) $\overline{\nu}$: 3030 (C-H), 1668 (C=O), 1572 (C=N) cm^{-1}; ^1H NMR(400 MHz, $CDCl_3$) δ: 2.40 (s, 3H, CH_3), 2.65 (s, 3H, CH_3), 3.51 (dd, 1H, 4.4 Hz and 18.8 Hz, H_a), 3.93 (dd, 1H, 12.0 Hz and 18.8 Hz, H_c), 5.60 (dd, 1H, 4.4 Hz and 11.6 Hz, H_b), 7.30-7.57 (m, 13H); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 10.49, 21.95, 43.37, 58.95, 125.62, 126.36, 127.67, 128.88, 129.97, 130.15, 132.69, 133.40, 134.15, 136.07, 138.24, 141.47, 149.26, 168.66; LCMS m/z: 455.25 (M^+); Analy. found (calcd) for $C_{26}H_{22}N_5OCl$: C 68.51 (68.49), H 4.82 (4.86), N 15.32 (15.36).

1-(3-(1-(p-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl)-5-(3,4-dihydroxyphenyl)-4,5-dihydro pyrazol-1-yl)ethanone (19):
White crystals; Yield: 80%; mp 205°C; FT-IR (KBr) $\overline{\nu}$: 3210 (O-H), 3025 (C-H), 1673 (C=O), 1595 (C=N) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 2.41 (s, 3H, CH_3), 2.60 (s, 3H, CH_3), 3.47 (dd, 1H, 4.4 Hz and 18.8 Hz, H_a), 3.92 (dd, 1H, 12.0 Hz and 18.8 Hz, H_c), 5.58 (dd, 1H, 4.4 Hz and 11.6 Hz, H_b), 5.60 (s, 1H, OH), 5.61(s,1H, OH), 7.26-7.57 (m, 7H); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 10.50, 21.93, 43.40, 59.10, 125.67, 126.73, 128.81, 130.15, 135.92, 137.37, 149.81, 168.65; MS m/z: 411.66 (M^++1); Analy. found (calcd) for $C_{20}H_{18}N_5O_3Cl$: C 58.28 (58.33), H 4.39 (4.41), N 16.93 (17.0).

1-(3-(1-p-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl)-5-(3,4-dimethoxyphenyl)-4,5-dihydro pyrazol-1-yl)ethanone (20):
White needles; Yield: 78%; mp 146-148°C; FT-IR (KBr) $\overline{\nu}$: 3026 (C-H), 1677 (C=O), 1592 (C=N) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 2.37 (s, 3H, CH_3), 2.64 (s, 3H, CH_3), 3.83 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 3.47 (dd, 1H, 4.4 Hz and 18.8 Hz, H_a), 3.87 (dd, 1H, 11.2 Hz and 18.4 Hz, H_c), 5.50 (dd, 1H, 4.8 Hz and 12.4 Hz, H_b), 6.78-6.81 (m, 3H), 7.42 (d, 2H, 8.4 Hz), 7.55 (d, 2H, 8.8 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 10.36, 10.47, 21.97, 41.56, 43.31, 55.94, 58.76, 109.5, 111.47, 117.67, 126.35, 129.89, 133.31, 134.16, 136.12, 138.29, 148.57, 149.22, 168.71; MS m/z: 439.65 (M^++1); Analy. found (calcd) for $C_{22}H_{22}N_5O_3Cl$: C 60.01 (60.07), H 5.10 (5.04), N 15.88 (15.92).

1-(3-(1-(p-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl)-5-(p-fluorophenyl)-4,5-dihydropyrazol-1-yl)ethanone (21):
White crystals; Yield: 83%; mp 183-185°C; FT-IR (KBr) $\overline{\nu}$: 2996 (C-H), 1649 (C=O), 1581 (C=N) cm^{-1}; ^1H NMR(400 MHz, $CDCl_3$) δ: 2.36 (s, 3H, CH_3), 2.64 (s, 3H, CH_3), 3.44 (dd, 1H, 4.4 Hz and 18.8 Hz, H_a), 3.89 (dd, 1H, 11.6 Hz and 18.8 Hz, H_c), 5.54 (dd, 1H, 4.8 Hz and 11.6 Hz, H_b), 6.97 (t, 2H, 8.8 Hz), 7.20 (m, 2H), 7.42 (d, 2H, 7.2 Hz), 7.55 (d, 2H, 8.8 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 10.50, 21.96, 43.37, 58.96, 125.66, 126.36, 127.71, 128.87, 129.96, 133.44, 134.14, 136.08, 138.3, 141.51, 149.26, 168.67; MS m/z: = 397.60 (M^++1); Analy. found (calcd) for $C_{20}H_{17}N_5OFCl$: C 60.35 (60.38), H 4.27 (4.31), N 17.55 (17.60).

1-(3-(1-(p-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl)-5-(p-bromophenyl)-4,5-dihydropyrazol-1-yl)ethanone (22):
White crystals; Yield: 84%; mp 127-129°C; FT-IR (KBr) $\overline{\nu}$: 2997 (C-H), 1660 (C=O), 1580 (C=N) cm^{-1}; ^1H NMR(400 MHz, $CDCl_3$) δ: 2.37 (s, 3H, CH_3), 2.65 (s, 3H, CH_3), 3.46 (dd, 1H, 4.4 Hz and 18.8 Hz, H_a), 3.90 (dd, 1H, 11.6 Hz and 18.8 Hz, H_c), 5.56 (dd, 1H, 4.8 Hz and 11.6 Hz, H_b), 7.22 (t, 2H, 8.8 Hz), 7.44 (d, 2H), 7.46 (d, 2H, 7.6 Hz), 7.62 (d, 2H, 8.6 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 10.48, 21.94, 43.39, 58.96, 125.62, 126.34, 127.70, 128.84, 129.96, 133.40, 135.98, 141.43, 149.26, 168.63; MS m/z: 457.55 (M^++1), 459.50 (M^++2), 461.60 (M^++4); Analy. found (calcd) for $C_{20}H_{17}N_5OBrCl$: C 52.38 (52.36), H 3.75 (3.74), N 15.25 (15.27).

1-(3-(1-(p-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl)-5-(p-nitrophenyl)-4,5-dihydropyrazol-1-yl)ethanone (23):

Light yellow solid; Yield: 81%; mp 224°C (decomp.); FT-IR (KBr) $\overline{\nu}$: 3005 (C-H), 1663 (C=O), 1580 (C=N), 1570 (asym. NO_2), 1350 (sym. NO_2) cm^{-1}; ^1H NMR(400 MHz, $CDCl_3$) δ: 2.38 (s, 3H, CH_3), 2.67 (s, 3H, CH_3), 3.48 (dd, 1H, 4.6 Hz and 18.8 Hz, H_a), 3.90 (dd, 1H, 11.6 Hz and 18.8 Hz, H_c), 5.58 (dd, 1H, 4.7 Hz and 11.6 Hz, H_b), 7.42 (d, 2H), 7.46 (d, 2H, 7.6 Hz), 7.52 (t, 2H, 8.0 Hz), 7.68 (d, 2H, 8.6 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 10.53, 21.97, 43.36, 59.06, 125.61, 126.37, 127.72, 130.11, 133.43, 134.17, 136.15, 138.28, 142.65, 151.19, 159.8, 168.69; MS m/z: 424.40 (M^+); Analy. found (calcd) for $C_{20}H_{17}N_6O_3Cl$: C 56.27 (56.54), H 3.96 (4.03), N 19.67 (19.78).

1-(3-(1-(p-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl)-5-(p-chlorophenyl)-4,5-dihydropyrazol-1-yl)ethanone (24):

White crystals; Yield: 80%; mp 176°C (decomp.); FT-IR (KBr) $\overline{\nu}$: 3010 (C-H), 1672 (C=O), 1571 (C=N) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 2.34 (s, 3H, CH_3), 2.65 (s, 3H, CH_3), 3.44 (dd, 1H, 4.4 Hz and 18.8 Hz, H_a), 3.89 (dd, 1H, 12.0 Hz and 18.6 Hz, H_c), 5.53 (dd, 1H, 4.6 Hz and 11.6 Hz, H_b), 7.42-7.50 (m, 8H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 10.49, 21.94, 43.39, 58.96, 125.62, 126.37, 127.70, 128.88, 130.06, 133.37, 134.17, 136.12, 139.40, 142.57, 152.7, 168.68; MS m/z: 413.56 (M^++1); Analy. found (calcd) for $C_{20}H_{17}N_5OCl_2$: C 58.00 (57.98), H 4.15 (4.14), N 16.88 (16.90).

1-(3-(1-(p-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl)-5-(p-(dimethylamino)phenyl)-4,5-dihydropyrazol-1-yl)ethanone (25):

Yellow needles; Yield: 67%; mp 253°C (decomp.); FT-IR (KBr) $\overline{\nu}$: 3100 (C-H), 1671 (C=O), 1590 (C=N) cm^{-1}; ^1H NMR(400 MHz, $CDCl_3$) δ: 2.28 (s, 3H, CH_3), 2.68 (s, 3H, CH_3), 2.80 (s, 6H, $N(CH_3)_2$), 3.46 (dd, 1H, 4.4 Hz and 18.6 Hz, H_a), 3.91 (dd, 1H, 11.4 Hz and 18.6 Hz, H_c), 5.54 (dd, 1H, 4.7 Hz and 11.8 Hz, H_b), 7.40 (d, 2H, 7.6 Hz), 7.46 (d, 2H, 7.6 Hz), 7.50 (t, 2H, 8.4 Hz), 7.57 (d, 2H, 8.0 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 10.49, 21.95, 43.37, 45.31, 58.96, 125.62, 126.37, 127.70, 128.82, 130.07, 133.26, 133.55, 138.06, 148.41, 168.71; MS m/z: 422.55 (M^++1); Analy. found (calcd) for $C_{23}H_{23}N_6OCl$: C 62.38 (62.48), H 5.39 (5.48), N 19.84 (19.87).

1-(3-(1-(p-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl)-5-(p-tolyl)-4,5-dihydropyrazol-1-yl)ethanone (26):

White crystals; Yield: 76%; mp 192-195°C; FT-IR (KBr) $\overline{\nu}$: 3050 (C-H), 1669 (C=O), 1585 (C=N) cm^{-1}, ^1H NMR(400 MHz, $CDCl_3$) δ: 2.27 (s, 3H, CH_3), 2.33 (s, 3H, CH_3), 2.68 (s, 3H, CH_3), 3.44 (dd, 1H, 4.4 Hz and 18.8 Hz, H_a), 3.87 (dd, 1H, 11.6 Hz and 18.8 Hz, H_c), 5.48 (dd, 1H, 4.6 Hz and 11.6 Hz, H_b), 7.41-7.76 (m, 8H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 10.49, 21.95, 24.09, 43.35, 59.05, 125.61, 126.39, 127.70, 128.84, 129.97, 133.36, 134.15, 136.13, 139.26, 141.57, 150.16, 168.62; MS m/z: 393.65 (M^++1); Analy. found (calcd) for $C_{21}H_{20}N_5OCl$: C 64.07 (64.04), H 5.13 (5.12), N 17.77 (17.78).

1-(3-(1-(p-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl)-5-(furan-2-yl)-4,5-dihydropyrazol-1-yl)ethanone (27):

Pale creamy crystals; Yield: 81%; mp 200°C; FT-IR (KBr) $\overline{\nu}$: 2979 (C-H), 1658 (C=O), 1577 (C=N) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: δ2.33 (s, 3H, CH_3), 2.61 (s, 3H, CH_3), 3.75 (dd, 2H, 6.8 Hz and 10.8 Hz, H_a), 3.76 (m, 1H, H_c), 5.64 (dd, 1H, 7.2 Hz and 10 Hz, H_b), 6.30-7.29 (m, 3H, furan), 7.42 (m, 2H), 7.54 (d, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 10.46, 21.94, 39.31, 52.37, 107.74, 110.51, 126.37, 129.98, 133.46, 134.12, 136.06, 138.14, 142.05, 149.42, 151.91, 168.78; MS m/z: 369.55 (M^++1); Analy. found (calcd) for $C_{18}H_{16}N_5O_2Cl$:): C 58.35 (58.46), H 4.32 (4.36), N 18.77 (18.94).

1-(3-(1-(p-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl)-5-(thiophen-2-yl)-4,5-dihydropyrazol-1-yl)ethanone (28):

Pale creamy crystals; Yield: 80%; mp 185-187°C; FT-IR (KBr) $\overline{\nu}$: 2980 (C-H), 1659 (C=O), 1575 (C=N) cm^{-1}; ^1H NMR(400 MHz, $CDCl_3$) δ: 2.33 (s, 3H, CH_3), 2.61 (s, 3H, CH_3), 3.75 (m, 2H, 6.6 Hz and 10.6 Hz, H_a), 3.76 (m, 1H, H_c), 5.64 (dd, 1H, 7.2 Hz and 10.4 Hz, H_b), 6.30-7.29 (m, 3H, furan), 7.42 (m, 2H), 7.54 (d, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 10.47, 21.93, 39.31, 52.38, 107.75, 110.53, 126.49, 130.04, 133.48, 134.11, 136.08, 138.14, 142.46, 149.44, 151.93, 168.76; MS m/z: 385.57 (M^++1); Analy. found (calcd) for $C_{18}H_{16}N_5OClS$: C 55.97 (56.03), H 4.15 (4.18), N 18.10 (18.15).

1-(3-(1-(p-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl)-5-(2-hydroxyquinolin-3-yl)-4,5-dihydro pyrazol-1-yl)ethanone (29):

Light yellow crystals; Yield: 70%; mp 133-135°C; FT-IR (KBr) $\bar{\nu}$: 3055 (C-H), 1662 (C=O), 1574 (C=N) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 2.26 (s, 3H, CH_3), 2.67 (s, 3H, CH_3), 3.45 (dd, 1H, 4.6 Hz and 18.6 Hz, H_a), 3.46 (dd, 1H, 11.6 Hz and 18.6 Hz, H_c), 5.46 (dd, 1H, 4.8 Hz and 11.8 Hz, H_b), 6.07 (s, 1H, OH), 7.42 (d, 2H, 8.7), 7.50 (d, 2H, 8.8 Hz), 7.54-7.67 (m, 5H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 10.51, 21.97, 43.40, 58.93, 125.67, 126.52, 125.43, 126.98, 129.54, 130.76, 135.17, 135.52, 137.48, 157.69, 167.64, 168.69; MS: m/z = 446.75 (M^++1); Analy. found (calcd) for $C_{23}H_{19}N_6O_2Cl$: C 61.77 (61.82), H 4.19 (4.29), N 18.82 (18.81).

1-(3-(1-(p-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl)-5-(6-methyl-2-hydroxyquinolin-3-yl)-4,5-dihydropyrazol-1-yl)ethanone (30):

Light yellow crystals; Yield: 72%; mp 127-129°C; FT-IR (KBr) $\bar{\nu}$: 2926 (C-H), 1654 (C=O), 1577 (C=N) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 2.27 (s, 3H, CH_3), 2.43 (s, 3H, CH_3), 2.67 (s, 3H, CH_3), 3.45 (dd, 1H, 4.4 Hz and 11.8 Hz, H_a), 3.86 (dd, 1H, 11.4 Hz and 18.6 Hz, H_c), 5.51 (dd, 1H, 4.6 Hz and 11.8 Hz, H_b), 6.03 (s, 1H, OH), 7.42 (d, 2H, 8.6), 7.49 (d, 2H, 8.0 Hz), 7.52-7.60 (m, 4H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 10.50, 20.29, 21.96, 43.41, 58.92, 125.66, 126.53, 125.44, 126.99, 128.63, 130.85, 133.64, 135.25, 136.98, 157.17, 167.54, 168.65; MS m/z: 460.45 (M^+); Analy. found (calcd) for $C_{24}H_{21}N_6O_2Cl$: C 62.46 (62.54), H 4.70 (4.59), N 18.20 (18.23).

Experimental Protocol for Biological Activity

Antioxidant activity (DPPH radical scavenging assay):

(Brand-Williams method [22]): 10 mg/mL of each test sample and standard was taken in different test tubes, dissolved in minimum volume of DMSO and the volume was adjusted to 2.5 mL using ethanol. The DPPH control was prepared using the same procedure. Freshly prepared 1 mL of 0.1 mM DPPH solution was added to test solutions and vortexed thoroughly and left in dark for 30 min. The absorbance of stable DPPH radical was measured at 517 nm. Radical scavenging activity was expressed as the percentage inhibition of DPPH. The results are given in (Table 1).

Cytotoxic Activity [3-(4, 5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay (Mosmann [23]):

Cell lines: HeLa (Batch No. P80) and HSC-I (Batch No. PN12) were procured from National Center for Cell Sciences (NCCS), Pune, India. Initially, a wide range of concentration of the test compound in a log increment (1 to1000 µg/mL) dissolved in DMSO was used for cytotoxicity tests. Based on the results of these tests, subsequent tests were performed with concentrations in a narrow range, viz., 10 to 100 µg/mL (linear order). The conventional anticancer drug, cyclophosphamide (0.5 to 10.0 µg/mL) was used as the positive control. HeLa and HSC-1 cells were seeded in 96-well flat bottom tissue culture plates at a density of approximately 1x104 cells per well and allowed to attach to the plate for 24 hr at 37°C. The growth medium was aspirated off and substituted with the fresh medium containing the selected concentrations of the test compounds and CP. Control wells contained 200 µL of the medium. After exposing the cells to the test samples for 24 hours, the cells were grown for another 24 hr in the fresh medium. At the end, the cells in the microtiter wells were treated with 50 µL of MTT solution and incubated for 4 hr in a humidified atmosphere at 37°C. MTT was aspirated from the wells and replaced with 200 µL of DMSO to all of the wells to dissolve MTT-formazan crystals. In the spectroscopic studies, the absorbance was recorded at wavelength of 570 nm with the aid of Double beam UV-VIS spectrophotometer. For each test sample, the IC_{50} value was determined from the dose response curves. The assay was performed in triplicate for each of the test samples and mean IC_{50} values were calculated and are presented in (Table 1).

RESULTS AND DISCUSSION

The FT-IR spectrum of 3-16 has shown absorption band at ~1650cm^{-1} and ~1600cm^{-1} due to the carbonyl (C=O) and alkene (HC=CH) stretching respectively. The 1-(3-(1-(*p*-chlorophenyl)-5-methyl-1*H*-1,2,3-triazol-4-yl)-5-aryl-4,5-dihydropyrazol-1-yl)ethanone 17-30 the IR absorption bands were seen at ~1660 cm^{-1} and ~1580 cm^{-1} due to the amide carbonyl (C=O) and imine (C=N) stretching respectively. The proton NMR spectrum of compound 3-16 showed two doublets at δ 7.8 - 8.1 ppm with a coupling constant *J*= 15-16 Hz indicating the trans geometry for the propeonone group. In the proton NMR spectrum of 17-30, the methyl protons of acetyl group resonated at δ 2.25 ppm as singlet while the triazolyl methyl protons came into resonance at δ 2.67 ppm as a singlet. The three

pyrazoline ring protons are magnetically non-equivalent and appeared as doublet of doublet. The two C4 protons resonated as doublet of doublet at δ 3.3-3.45 ppm (*J*= 4.4 and 18.6 Hz) and δ 5.5 ppm (*J*= 4.8 and 11.6 Hz) respectively indicating the magnetic non-equivalency. The chiral C5 proton resonated as a doublet of doublet at δ 5.5 ppm due to vicinal coupling with the two protons of the C4 position of the pyrazoline ring with *J* = 11.6 and 18.8 Hz. In the ^{13}C NMR spectrum of 3 - 16, the carbonyl carbon peak was seen at 184 ppm while in 17-30 the amide carbonyl carbon peak was observed at 168 ppm. The mass spectrum of 3-30 has shown molecular ion (M^+) peak and (M^++2) peak with relative intensity of 3:1 due to the presence of chlorine atom.

Antioxidant Activity

Most of the pyrazolines 17 - 30 have shown moderate to good antioxidant activity and similarly the intermediates 5, 15 and 16 have shown considerable activity. The antioxidant property was increased when propeonones were converted to pyrazolines. Further it was observed that only hydroxyl group containing substituents have shown increased antioxidant activity.

Cytotoxicity Studies

Few of the selected compounds were tested for their cytotoxic activity against human cervical cancer HeLa cell line and squamous cell carcinoma of human skin HSC-1 cell line. All the tested compounds were active against both the cell lines. The compounds containing flurophenyl 7, nitrophenyl 9 and chlorophenyl substituents 10 have shown good cytotoxic activity for both HeLa cell line and HSC-1 cell lines. It indicates that the activity of the tested compounds was influenced considerably by the nature of the substituents on the aryl group. Among the tested compounds, 7 can be identified as the most promising compound against both cancer cell lines.

Table 1: Antioxidant activity and cytotoxicity data of compounds 3-30

Compd	Antioxidant activity (%)	Compd	Antioxidant activity (%)	Compd	Cytotoxicity(%) aIC50- µg/mL HeLa cell line	Cytotoxicity (%) aIC50- µg/mL HeLa cell line
3	21	17	47	3	30.4	37.09 ± 0.7
4	22	18	46	7	18.7 ± 1.8	17.4 ± 1.3
5	73	19	85	9	21.4 ± 2.4	36.5 ± 3.1
6	37	20	54	10	19.2 ± 2.2	24.7 ± 3.7
7	30	21	48	13	67.5 ± 3.6	55.3 ± 4.5
8	26	22	46	16	43.9 ± 3.2	29.6 ± 3
9	47	23	52	17	50.0 ± 2.1	61.8 ± 1.2
10	29	24	53	21	41.7 ± 0.9	47.1 ± 1.5
11	38	25	51	23	43.5 ± 0.4	41.7 ± 1.6
12	24	26	49	24	44.8 ± 1.2	38.27 ± 0.5
13	39	27	44	27	54.3 ± 4.2	70.2 ± 5.1
14	40	28	46	30	37.5 ± 2.9	41.9 ± 4.2
15	54	29	64	-	-	-
16	57	30	67	-	-	-
BHT[a]	96	-	-	CP[c]	5.2 ± 0.18	4.6 ± 0.15

[a] Butylated hydroxytoluene; [b] IC_{50} - concentration that induced 50% growth inhibition and values were obtained from dose-response curves, mean of triplicate wells; [c] cyclophosphamide.

CONCLUSION

A series of propeonones 1 - 16 was prepared by acid or base catalyzed condensation reaction and pyrazolines 17 - 30 were prepared by MW irradiation. The purity and structures of synthesized compounds have been elucidated by FT-IR, ^{1}H NMR, ^{13}C NMR and Mass spectral techniques. All data were in accordance with proposed structures. The pyrazolines 17-30 have shown good antioxidant property than propeonones 3-16. However, among the tested compounds the cytotoxic activity of intermediates was better than pyrazolines. Compounds containing substituents such as fluorine, chlorine and nitro groups on the aryl ring have shown good cytotoxic activity.

ACKNOWLEDGEMENT

The authors are thankful to PURSE, USIC -Mangalore University, NMR Centre- Mysore University and SAIF Punjab University for providing spectral analysis facility.

REFERENCES

[1] M Karabacak; MD Altintop; HI Ciftci; R Koga; M Otsuka; M Fujitha; A Ozdemir. *Molecules*. **2015**, 20, 19066-19084.
[2] Nithinchandra; B Kalluraya; S Shetty; M Babu. *J Chem Pharm Res.* **2013**, 5, 307-313.
[3] BD Mistry; KR Desai; SM Intwala. *Indian J Chem Sect B*. **2015**, 54B, 128-134.
[4] D Azarifar; M Shaebanzadeh. *Molecules*. **2002**, 7, 885-895.
[5] NM Chavhan; PV Badadhe; SN Shelke. *IJIRSET*. **2015**.
[6] S Rollas; SG Kücükgüzel. *Molecules*, **2007**, 12, 1910-1939.
[7] MA Rahman; AA Siddiqui. *Int J Pharm Sci Drug Res.* **2010**, 2, 165-175.
[8] Q Wang; TR Chan; R Hilgraf; VV Fokin; KB Sharpless; MG Finn. *J Am Chem Soc.* **2003**, 125, 3192-3193.
[9] SS Gupta; KS Raja; E Kaltgrad; E Strable; MG Finn. *Chem Commun.* **2005**, 4315-4317.
[10] M Kuntal; KA Yadvendra. *Bioorg Med Chem*. **2009**, 19, 2688-2692.
[11] L Pelle; T Jason; W Bernard; W Jacob. *Tetrahedron*. **2001**, 57, 9225-9283.
[12] A Saber; M Driowya; S Alaoui; H Marzag; L Demange; E Alvarez; R Benhida; K Bougrin. *Chem Het Comp*. **2016**, 52, 31-36.
[13] SS Sulthana; SA Antony; C Balachandran; SS Shafi. *Bioorg Med Chem*. **2015**, 25, 2753-2757.
[14] A Pradhan; H Goyal; N Khan. *Asian J Sci Technol.* **2015**, 6, 1673-1676.
[15] AM Isloor; B Kalluraya; R Mahadeva; MR Abdul. *J Saudi Chem Soc*. **2000**, 4, 265-270.
[16] B Kalluraya; RM Chimbalkar; G Rai; G Rai; S Shalini. *J Ind Chem.* **2001**, 2, 39-46.
[17] B Kalluaya; AM Isloor; PV Frank; RL Jagadeesha. *Indian J Heterocycl Chem*. **2004**, 13, 245-248.
[18] M Babu; B Kalluraya; KS Girisha; Nithinchandra; Sathyamurthy; B Prasad; V Narayana; S Shalini. *Indian J Heterocycl Chem*. **2013**, 23, 39-43.
[19] VHS Jois; B Kalluraya; KS Girisha. *J Serb Chem*. **2014**, 79, 1469-1475.
[20] NT Pokhodylo; RD Savka;VS Matiichuk; ND Obushak. *Russ J Gen Chem*. **2009**, 79, 309-314.
[21] D Wang-Jun; G Zhong-Lian; D Hong-Ru; D Heng-Shan. *Indian J Heterocycl Chem*. **2009**, 19, 51-57.
[22] W Brand-Williams; ME Cuvelier; C Berset. *LWT-Food Sci Technol*. **1995**, 28, 25-30.
[23] TJ Mosmann. *J Immunol Meth*. **1983**, 65, 55-63.