SYNTHESIS AND EVALUATION OF BENZOTHIAZOLYL-PYRAZOLINE CARBOXYLAMIDES AS POTENTIAL ANTICANCER AGENTS

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ABSTRACT
The present investigation, the synthesis of pyrazolines bearing benzothiazole and their evaluation as anticancer agents. A new series of benzothiazole-pyrazoline-1-carboxamides (5a-5p) were synthesized and these compounds were confirmed by IR, NMR, and mass spectroscopy. The compounds were tested for their antitumor activity against HBL-100 cell lines. The synthesized compound 5a–5p showed different levels of anticancer inhibition with the IC50 ranges between 2.55–6.28 µM. The unsubstituted and strong electron donating groups substituted derivatives were observed more potent than compounds substituted with electron withdrawing groups and mild electron donating groups. Among, the electron substituted derivatives, the o-derivatives were exhibited more potent than m- and p-derivatives.

KEY WORDS
synthesis of pyrazolines, carboxamides

INTRODUCTION
Cancer is a major chronic disease, recognized for second foremost cause of death in worldwide.1 As per the world cancer report the international agency for research on cancer (IARC), the cancer rates could raise up to 15 million new cases by 2020. In India, it is the most leading cause for mortality, elaborate in numerous cell signaling pathways and disorganized cell functions like irregular cell proliferation with disturbed apoptosis.2 It is characterized by uncontrollable, irreversible, independent, autonomous, uncoordinated and relatively unlimited and abnormal over growth of tissues3. The common cancers in worldwide are, breast cancer, lung cancer, large intestine cancer, stomach cancer and prostate cancer. Incidence and mortality rates for most cancers are increasing in several countries because of adoption of unhealthy lifestyles, such as smoking, physical inactivity and consumption of high calorie food4. For the treatment of cancer different methods like surgery, radiotherapy and immunotherapy are used.5 Nowadays, the chemotherapeutic agents showed beneficial effects clinically in cancer treatment and showed fatal side effects like bone marrow suppression and some drugs produces alopecia. The cytotoxic and anti-hormonal drugs are the leading chemotherapeutics with significant adverse effects.6 Synthetic organic chemistry has always plays a vital role in combined and multidisciplinary practice for development of anticancer drugs. In recent years, made efforts to synthesize potential anticancer drugs with chemical modifications of known classes of cancer therapeutic agents. Recently, pathogenesis of different types of cancer becomes clearer, more rational methods to the design of newer drugs with no or decreased side effects and lowest possible cost is a potential research area for pharmaceutical industry in worldwide.3 Anticancer drug discovery and development is one of the most essential and rapidly changing avenues for medicinal chemist. The requirement for new chemotherapeutics in cancer is evident due to the limited capacity of drugs to cure or
significantly prolong the survival of patients with disseminated tumors or certain leukemia.

Pyrazoline is a five-membered heterocyclic compound containing two nitrogen atoms in adjacent position and contains two endocyclic double bonds. It is dihydropyrazoline possessing only one endocyclic double bond and unique in their chemical behaviour. Among a wide range of heterocyclic compounds that have been explored for the development new molecules, pyrazolines constitute an interesting class of heterocycles due to their synthetic flexibility and effective biological activities such as anticancer7, antioxidant9, analgesic10, antitubercular11, anticonvulsant12, antimalarial13, antidepressant14, antibacterial15, antifungal16, antifungal17, anticonvulsant18 properties and etc. Benzothiazole belongs to the family of bicyclic heterocyclic compounds having benzene nucleus fused with five-membered ring containing nitrogen and sulfur atoms. Benzothiazole consist of wide variety of biological activities and therapeutic functions including antitubercular12, antibacterial14, antifungal15, antimalarial16, antihistaminic17, antiallergic18, anti-inflammatory19, antidiabetic19, and antidepressant20 activities and etc. In an attempt, to identify new and potent anticancer agents, tried benzothiazole-pyrazole hybrid motif, thus may be exhibit synergetic anticancer effect here to generate new benzothiazolyl-pyrazoline derivatives as anticancer agents using simple methods.

**EXPERIMENTAL**

**Chemistry**

Melting points were determined using Thermonik Melting Point Apparatus (Campbell electronics, India) by capillary method and are uncorrected. Infrared (IR) spectra were taken on a Fourier Transform Infrared Spectrophotometer IR-Prestige 21 (Shimatsu Corporation, Japan) from 4000-400 cm⁻¹ using KBr discs. ¹H NMR spectra were recorded at 400 MHz in DMSO-δ₆ using a Bruker Avance 400 instrument (Bruker Instruments Inc., USA). Chemical shifts were measured at 6 units (ppm) relative to tetramethylsilane (TMS). Fast-atom bombardment (FAB) mass spectra were recorded on a Jeol SX 102/DA-6000 mass spectrometer (Jeol Ltd Akishima, Tokyo, Japan) using argon/xenon (6 kV, 10 mA) as FAB gas, m-nitrobenzyl alcohol as matrix, and 10 kV as accelerating voltage at room temperature. Elemental analysis was performed on a Vario EL III Elemental Analyser (Elementar, Germany) using sulfanilamide as standard. All chemicals were purchased from Merck, Spectrochem or CDH, India. Solvents were of reagent grade and were purified and dried by standard procedure. Reactions were monitored by thin-layer chromatography on silica gel plates in either iodine or UV chambers. Intermediates were characterized by IR spectroscopic analysis and elemental analysis for CHN. In the elemental analysis, the observed values were within ±0.4% of the calculated values. Final compounds were characterized by ¹H NMR and FAB mass spectrometry (MS). The final yields and the physicochemical data of the compounds 5a-5p are presented in Table 1.

**General procedure for synthesis of 2-amino-benzothiazoles:**

A solution of aniline (0.03 M) in 95% acetic acid (20 ml) was added to a solution of KSCN (0.12 M) in 95% acetic acid (20 ml). The reaction mixture was cooled to 0 °C and a solution of Br₂ (1.6 ml) in acetic acid (10 ml) was added over 90 minutes; during the addition the temperature should not raise to 5 °C. After addition, the stirring for about 3 hr at 10-15 °C, and then poured into hot water (300 ml). Separated hydrogen bromide salt was filtered, washed with acetic acid and dried. It was dissolved in hot water and neutralizes with 26% ammonium hydroxide solution, filtered the solid product, washed with water and recrystallized from ethanol22.

**General procedure for the synthesis of chalcones (2a-2p)**

To a solution of suitably substituted benzaldehyde (0.01 M) and acetonophene (0.01 M) in ethanol (10 ml) was added aqueous solution of potassium hydroxide (60%) drop wise with continuous stirring at 0 °C over a period of 15 minutes. The reaction mixture was kept at room temperature for about 48 h with occasional shaking. After 48 h it was poured into ice-cold water, and then neutralized to pH 2 using 6 N hydrochloric acid. The yellow precipitate obtained was filtered, washed, dried, and recrystallized from dry methanol. The intermediates 2a-2p were obtained.
General procedure for the synthesis of 3,5-diaryl-4,5-dihydro-1H-pyrazole (3a-3p)

Appropriate chalcone (1–2) was treated with 10 times excess of hydrazine hydrate in dry ethanol and refluxed for 3–6 h. The hot reaction mixture was then poured into ice-cold water. The solid separated out was filtered, washed, dried and recrystallized from ethanol to afford respective pyrazoline (3a-3p).

General procedure for the synthesis of N-(1,3-benzothiazol-2-yl)-3-(substituted phenyl)-5-phenyl-4,5-dihydro-1H-pyrazole-1-carboxamide (5a-5p):

**Scheme. 1**

![Scheme 1 Diagram](image)

**Reagents and condition:** (a). Acetophenone, KOH (60%), stirring at 0 °C, 15 min, 48 hr, RT; (b) NH₂NH₂, ethanol, reflux 3–6 h; (c). Phenyl chloroformate, trimethylamine, THF, stirring at below 5 °C, 1 hr; (d). 2-amino benzothiazole, THF, stirring, RT, 3 hrs.

**N-(1,3-benzothiazol-2-yl)-3,5-diphenyl-4,5-dihydro-1H-pyrazole-1-carboxamide (5a):**

IR (KBr, cm⁻¹): 3148 (Ar-H), 3089, 2865 (C-H), 1616 (C=N), 1233 (C-N), 1264 (C-S); 

¹H NMR (300 MHz, CDCl₃, δ ppm): 3.36 (d, 2H, CH₂), 5.44 (t, 1H, CH₂), 6.78-7.36 (m, 14H, ArH), 9.02 (s, 1H, NH); 

FAB-MS (m/z): 399 [m+1]+; 

Elemental analyses Found (Calcd.): C 69.12 (69.32) H 4.56 (4.55) N 14.03 (14.06)

**N-(1,3-benzothiazol-2-yl)-5-(2-hydroxyphenyl)-3-phenyl-4,5-dihydro-1H-pyrazole-1-carboxamide (5b):**

IR (KBr, cm⁻¹): 3079 (Ar-H), 3056, 2918 (C-H), 1616 (C=N), 1463 (C-N), 1256 (C-S), 1315 (C-O), 2794 (O-H); 

¹H NMR (300 MHz, CDCl₃, δ ppm): 3.56 (d, 2H, CH₂), 5.88 (t, 1H, CH₂), 6.92-7.18 (m, 4H, ArH), 7.34-7.52 (m, 9H, ArH), 8.82 (Ar-OH), 9.06 (s, 1H, NH); 

FAB-MS (m/z): 415 [M+1]+; 

Elemental analyses Found (Calcd.): C 66.40 (66.65); H 4.37 (4.38); N 13.50 (13.52)
N-(1,3-benzothiazol-2-yl)-5-(3-hydroxyphenyl)-3-phenyl-4,5-dihydro-1H-pyrazole-1-carboxamide (5c):

IR (KBr, cm⁻¹): 3082 (Ar-H), 3056, 2851 (C-H), 1629 (C=N), 1460 (C=N), 1286 (C-S), 1308 (C-O), 2796 (O-H); ¹H NMR (300 MHz, CDCl₃, δ ppm): 3.58 (d, 2H, CH₂), 5.72 (t, 1H, CH₂), 6.96-7.16 (m, 4H, ArH), 7.38-7.44 (m, 9H, ArH), 8.88 (Ar-OH), 9.08 (s, 1H, NH); FAB-MS (m/z): 415 [M+1]⁺; Elemental analyses Found (Calcd.): C 67.32 (67.27); H 4.69 (4.70); N 13.07 (13.05)

N-(1,3-benzothiazol-2-yl)-5-(4-hydroxyphenyl)-3-phenyl-4,5-dihydro-1H-pyrazole-1-carboxamide (5d):

IR (KBr, cm⁻¹): 3025 (Ar-H), 2998 (Ar-CH₃), 2960 (C-H), 2860 (C-H), 1629 (C=N), 1286 (C-S), 1308 (C-O), 2790 (O-H); ¹H NMR (300 MHz, CDCl₃, δ ppm): 3.60 (s, 3H, OCH₃), 3.64 (d, 2H, CH₂), 5.72 (t, 1H, CH₂), 7.36 (m, 9H, ArH), 8.74 (Ar-OH), 9.16 (s, 1H, NH); FAB-MS (m/z): 415 [M+1]⁺; Elemental analyses Found (Calcd.): C 66.46 (66.50); H 4.38 (4.38); N 13.49 (13.54)

N-(1,3-benzothiazol-2-yl)-5-(2-methoxyphenyl)-3-phenyl-4,5-dihydro-1H-pyrazole-1-carboxamide (5e):

IR (KBr, cm⁻¹): 3121 (Ar-H), 3051, 2851 (C-H), 1632 (C=N), 1471 (C-N), 1281 (C-S), 1310 (C-O); ¹H NMR (300 MHz, CDCl₃, δ ppm): 3.50 (s, 3H, -O-CH₃), 3.42 (d, 2H, CH₂), 5.80 (t, 1H, CH₂), 6.82-7.02 (m, 4H, ArH), 7.24-7.36 (m, 9H, ArH), 9.16 (s, 1H, NH); FAB-MS (m/z): 429 [M+1]⁺; Elemental analyses Found (Calcd.): C 67.32 (67.27); H 4.69 (4.70); N 13.05 (13.07)

N-(1,3-benzothiazol-2-yl)-5-(3-methoxyphenyl)-3-phenyl-4,5-dihydro-1H-pyrazole-1-carboxamide (5f):

IR (KBr, cm⁻¹): 2998 (Ar-H), 3062, 2870 (C-H), 1670 (C=N), 1264 (C-N), 1298 (C-S), 1346 (C-O); ¹H NMR (300 MHz, CDCl₃, δ ppm): 3.55 (s, 3H, -O-CH₃), 3.48 (d, 2H, CH₂), 5.88 (t, 1H, CH₂), 6.90-7.14 (m, 4H, ArH), 7.32-7.42 (m, 9H, ArH), 9.18 (s, 1H, NH); FAB-MS (m/z): 429 [M+1]⁺; Elemental analyses Found (Calcd.): C 67.34 (67.27); H 4.71 (4.70); N 13.09 (13.07)

N-(1,3-benzothiazol-2-yl)-5-(4-methoxyphenyl)-3-phenyl-4,5-dihydro-1H-pyrazole-1-carboxamide (5g):

IR (KBr, cm⁻¹): 3082 (Ar-H), 3056, 2844 (C-H), 1684 (C-N), 1436 (C-N), 1236 (C-S), 1287 (C-O); ¹H NMR (300 MHz, CDCl₃, δ ppm): 3.60 (s, 3H, -OCH₃), 3.54 (d, 2H, CH₂), 5.66 (t, 1H, CH₂), 6.84-7.08 (m, 4H, ArH), 7.24-7.38 (m, 9H, ArH), 9.16 (s, 1H, NH); FAB-MS (m/z): 429 [M+1]⁺; Elemental analyses Found (Calcd.): C 67.39 (67.27); H 4.69 (4.70); N 13.10 (13.07)

N-(1,3-benzothiazol-2-yl)-5-(2-methylphenyl)-3-phenyl-4,5-dihydro-1H-pyrazole-1-carboxamide (5h):
Elemental analyses Found (Calcd.): C 63.76 (63.81); H 3.97 (3.96); N 12.96 (12.94)

IR (KBr, cm⁻¹): 3130 (Ar-H), 3084, 2919 (C-H), 1636 (C=N), 1398 (C-N), 1264 (C-S); ¹H NMR (300 MHz, CDCl₃, δ ppm): 2.22 (s, 3H, -CH₃), 3.20 (d, 2H, CH₂), 5.28 (t, 1H, -CH), 6.72-6.84 (m, 4H, ArH), 6.98-7.14 (m, 9H, ArH), 9.12 (s, 1H, NH); FAB-MS (m/z): 413 [M+H]+;

Elemental analyses Found (Calcd.): C 69.80 (69.88); H 4.87 (4.89); N 13.60 (13.58)

N-(1,3-benzothiazol-2-yl)-5-(3-methylphenyl)-3-phenyl-4,5-dihydro-1H-pyrazole-1-carboxamide (5i):

IR (KBr, cm⁻¹): 3094 (Ar-H), 3060, 2941 (C-H), 1662 (C=N), 1468 (C-N), 1270 (C-S); ¹H NMR (300 MHz, CDCl₃, δ ppm): 2.28 (s, 3H, -CH₃), 3.24 (d, 2H, CH₂), 5.26 (t, 1H, -CH), 6.50-6.74 (m, 4H, ArH), 6.92-7.10 (m, 9H, ArH), 9.06 (s, 1H, NH); FAB-MS (m/z): 413 [M+1]+;

Elemental analyses Found (Calcd.): C 69.76 (69.88); H 4.90 (4.89); N 13.59 (13.58)

N-(1,3-benzothiazol-2-yl)-5-(4-methylphenyl)-3-phenyl-4,5-dihydro-1H-pyrazole-1-carboxamide (5j):

IR (KBr, cm⁻¹): 3070, 2954 (C-H), 1676 (C=N), 1454 (C-N), 1263 (C-S); ¹H NMR (300 MHz, CDCl₃, δ ppm): 2.22 (s, 3H, -CH₃), 3.30 (d, 2H, CH₂), 5.28 (t, 1H, -CH), 6.54-6.78 (m, 4H, ArH), 7.12-7.39 (m, 9H, ArH), 9.04 (s, 1H, NH); FAB-MS (m/z): 413 [M+1]+;

Elemental analyses Found (Calcd.): C 69.80 (69.88); H 4.87 (4.89); N 13.60 (13.58)

N-(1,3-benzothiazol-2-yl)-5-(2-chlorophenyl)-3-phenyl-4,5-dihydro-1H-pyrazole-1-carboxamide (5k):

IR (KBr, cm⁻¹): 3048, 2846(C-H), 1624 (C=N), 1284 (C-N), 1200 (C-S), 812 (C-Cl); ¹H NMR (300 MHz, CDCl₃, δ ppm): 3.42 (d, 2H, CH₂), 5.90 (t, 1H, CH), 7.33-7.44 (m, 4H, ArH), 7.92-8.08 (m, 9H, ArH), 9.24 (s, 1H, NH); FAB-MS (m/z): 433 [M+1]+;

Elemental analyses Found (Calcd.): C 63.62 (63.81); H 3.95 (3.96); N 12.92 (12.94)

N-(1,3-benzothiazol-2-yl)-5-(3-chlorophenyl)-3-phenyl-4,5-dihydro-1H-pyrazole-1-carboxamide (5l):

IR (KBr, cm⁻¹): 3060, (Ar-H), 3028, 2952 (C-H), 1620 (C=N), 1285 (C-N), 1216 (C-S), 818 (C-Cl); ¹H NMR (300 MHz, CDCl₃, δ ppm): 3.34 (d, 2H, CH₂), 5.82 (t, 1H, CH), 7.26-7.58 (m, 4H, ArH), 7.94-8.30 (m, 9H, ArH), 9.26 (s, 1H, NH); FAB-MS (m/z): 433 [M+1]+;

Elemental analyses Found (Calcd.): C 63.76 (63.81); H 3.97 (3.96); N 12.96 (12.94)

N-(1,3-benzothiazol-2-yl)-5-(4-chlorophenyl)-3-phenyl-4,5-dihydro-1H-pyrazole-1-carboxamide (5m):
Anticancer studies (MTT assay) Compounds 5a-5p were evaluated for their anticancer activity on HT-29 cell lines using MTT assay by serial double dilution method in 96-well plate. Cells seeded in plate at 5000 cells/well. Different dilutions of test and standard (0.1–100 μM) were made with growth medium in such a way that the final DMSO concentration is around 0.5%. 100 mL of cell suspension and 100 mL of test and standard were transferred aseptically to each well. The plate was then incubated at 37 °C for 72 h in CO₂ incubator. After incubation, 20 mL of MTT was added to each well and plate was wrapped in aluminum foil to prevent the oxidation of the dye. The plate was again incubated for 2 h. 80 mL of lysis buffer was added to each well and the plate was placed on a shaker overnight. The absorbance was recorded on the ELISA reader at 562 nm wavelength. The absorbance of the test was compared with that of DMSO control to get the percentage inhibition and IC₅₀ values are calculated by plotting a graph between log concentrations and percentage inhibition value. All the studies were performed in duplicate and results were presented in Table 1.

The plate was again incubated for 2 h. 80 mL of lysis buffer was added to each well and the plate was placed on a shaker overnight. The absorbance was recorded on the ELISA reader at 562 nm wavelength. The absorbance of the test was compared with that of DMSO control to get the percentage inhibition and IC₅₀ values are calculated by plotting a graph between log concentrations and percentage inhibition value. All the studies were performed in duplicate and results were presented in Table 1.

N-(1,3-benzothiazol-2-yl)-5-(2-nitrophenyl)-3-phenyl-4,5-dihydro-1H-pyrazole-1-carboxamide (5n):

IR (KBr, cm⁻¹): 3080 (Ar-H), 3060, 2860 (C-H), 1634 (C=C), 1646 (C=N), 1466 (C-N), 1240 (C-S); ¹H NMR (300 MHz, CDCl₃, δ ppm): 3.26 (d, 2H, CH₂), 5.34 (t, 1H, -CH), 6.96-7.26 (m, 9H, ArH), 8.14-8.28 (m, 4H, ArH), 9.16 (s, 1H, NH); FAB-MS (m/z): 443 [M+1]⁺; Elemental analyses Found (Calcd.): C 63.79 (63.81); H 3.95 (3.96); N 12.93 (12.94)

N-(1,3-benzothiazol-2-yl)-5-(3-nitrophenyl)-3-phenyl-4,5-dihydro-1H-pyrazole-1-carboxamide (5o):

IR (KBr, cm⁻¹): 3120 (Ar-H), 3058, 2900 (C-H), 1624 (C=N), 1464 (C-N), 1244 (C-S); ¹H NMR (300 MHz, CDCl₃, δ ppm): 3.30 (d, 2H, CH₂), 5.30 (t, 1H, -CH), 6.98-7.14 (m, 9H, ArH), 7.98-8.26 (m, 4H, ArH), 9.18 (s, 1H, NH); FAB-MS (m/z): 444 [M+1]⁺; Elemental analyses Found (Calcd.): C 62.26 (62.29); H 3.85 (3.86); N 15.76 (15.79)

N-(1,3-benzothiazol-2-yl)-5-(4-nitrophenyl)-3-phenyl-4,5-dihydro-1H-pyrazole-1-carboxamide (5p):

IR (KBr, cm⁻¹): 3098 (Ar-H), 3062, 2940 (C-H), 1626 (C-N), 1464 (C-N), 1260 (C-S); ¹H NMR (300 MHz, CDCl₃, δ ppm): 3.26 (d, 2H, CH₂), 5.28 (t, 1H, -CH), 6.92-7.14 (m, 9H, ArH), 7.88-8.29 (m, 4H, ArH), 9.16 (s, 1H, NH); FAB-MS (m/z): 444 [M+1]⁺; Elemental analyses Found (Calcd.): C 62.52 (62.29); H 3.85 (3.86); N 15.82 (15.79)

Pharmacology

Anticancer studies (MTT assay) Compounds 5a-5p were evaluated for their anticancer activity on HT-29 cell lines using MTT assay by serial double dilution method in 96-well plate. Cells seeded in plate at 5000 cells/well. Different dilutions of test and standard (0.1–100 μM) were made with growth medium in such a way that the final DMSO concentration is around 0.5%. 100 mL of cell suspension and 100 mL of test and standard were transferred aseptically to each well. The plate was then incubated at 37 °C for 72 h in CO₂ incubator. After incubation, 20 mL of MTT was added to each well and plate was wrapped in aluminum foil to prevent the oxidation of the dye.

The plate was again incubated for 2 h. 80 mL of lysis buffer was added to each well and the plate was placed on a shaker overnight. The absorbance was recorded on the ELISA reader at 562 nm wavelength. The absorbance of the test was compared with that of DMSO control to get the percentage inhibition and IC₅₀ values are calculated by plotting a graph between log concentrations and percentage inhibition value. All the studies were performed in duplicate and results were presented in Table 1.
Results and Discussion:

Chemistry

The compounds were synthesized as shown in Scheme 1 according to previously reported method.22 The synthesis of chalcones (2a-2p) was carried out at room temperature by reacting with different substituted acetophenone and benzaldehyde in the presence of base by conventional Claisen–Schmidt condensation. These chalcones were then reacted with hydrazine in ethanol using catalytic amount of concentrated sulphuric acid offered 3a-3p. The solid compound so obtained was filtered and purified by recrystallization from ethanol. The final pyrazoline derivatives 5a-5p were obtained by the reaction of appropriate pyrazoline 3a–3p with phenyl chloroformate followed by 2-amino benzothiazole in THF at room temperature. The pyrazoline derivatives were characterized by their spectral studies using IR, $^1$H NMR, and FAB-MS. All the synthesized pyrazoline compounds gave satisfactory analytical and spectroscopic data, which were in full consistent with their depicted structures. The structures of pyrazolines (5a-5p) were confirmed through the IR, $^1$H NMR, FAB-MS spectral data. In the elemental analysis of CHN, the observed values were within ±0.4% of the calculated values.

Anticancer activity

The in vitro anticancer screening of pyrazolines 5a–5p was done by means of MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] assay using HBL-100 cancer cell line. After 24 h incubation at 37 °C under a humidified 5% CO$_2$ to allow cell attachment, the cancer cells in the wells were, respectively, treated with target compounds at various concentrations for 48 h. The experiment was done in triplicate and the inhibitory concentration (IC$_{50}$) values were calculated from a dose response curve. IC$_{50}$ is the concentration in ‘µM’ required for 50% inhibition of cell growth as compared to that of untreated control. The cell viability was measured with the purple formazan that was metabolized from MTT mitochondrial dehydrogenase, which is active only in live cells. The data reported in Table 1 indicates that compound 5a–5p showed different levels of anticancer inhibition with the IC$_{50}$ ranges between 2.55-6.28 µM. The unsubstituted and strong electron donating groups substituted derivatives were observed more potent than compounds substituted with electron withdrawing groups and mild electron donating groups. Among, the electron substituted derivatives, the o-derivatives were exhibited more potent than m- and p-derivatives

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</table>

Table. 1: Physical data of 5a-5p and anticancer activity against HBL-100
The present investigation synthesized 16 molecules (5a–bp) and characterized based on its physical and spectral data. The synthesized compounds were exhibited wide range of potent to moderate anticancer activity against HBL-100 cell line by MTT assay method. Furthermore, our preliminary results which support the anticancer potential of the synthesized compounds, suggest that generating hybrid compounds containing N-benzothiazole-pyrazolines are a promising new approach of developing an effective anticancer agent.

REFERENCES:


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