# Design and synthesis of novel benzimidazoles containing 1,2,3-triazolesas *in vitro*, anticancer and anti-oxidant agents

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***Abstract***
*A novel series of 2-(1-((1-substitutedphenyl-1H-1,2,3-triazol-4-yl)methoxy)ethyl)-1-((1-substituted phenyl-1H-1,2,3-triazol-4-yl)methyl)-1H-benzo[d]imidazole (3a-j)derivatives was synthesized in moderate to high yields. The structures of all the synthesized compounds were characterized by $^{1}$HNMR, $^{13}$CNMR and Mass spectroscopic methods. The title compounds were screened for their anti-oxidant activity and anti-cancer activity.*

*The cancer activity results reveal that the compounds 3j, 3b and 3f are showing promising activity and remaining compounds exhibited moderate activity against all the tested cancer cell lines. The anti-oxidant activity also shows that the compounds 3c and 3d have shown excellent activity and remaining compounds were also found to exhibit moderate activity against the test organisms employed.*

**Keywords**: Benzimidazole,1,2,3-triazole, anti-oxidant and anti-cancer activity.

## Introduction

The quest for designing novel heterocyclic molecules has become a great challenge for chemists aiming to address the present world demands[1,2]. To meet this target, the medicinal chemists paid attention towards the development of new molecules from natural sources and also from synthetic methodologies[3-5]. Benzimidazole derivatives are an important class of heterocyclic moieties exhibiting various biological activities such as anti-tubercular[6], anti-microbial[7], anti-helminthetic[8], analgesic[9] and anti-tubercular activities[10,11]. Some of the benzimidazole derivatives have been identified as bio-active molecules.

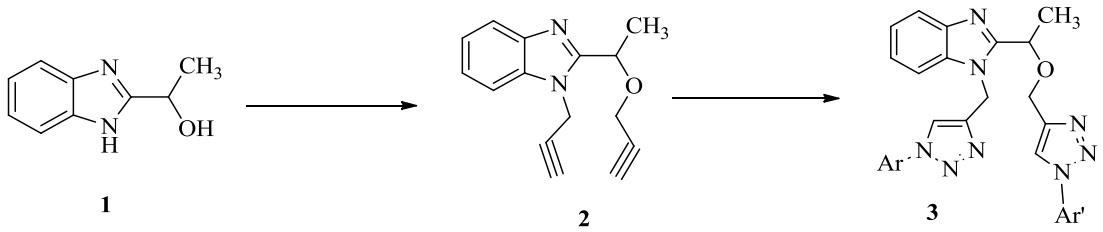
Recently, it was found that the 1,2,3-triazoles occupied a unique position in the field of pharmaceutical chemistry[12-14].1,2,3-triazoles have been identified as anti-inflammatory[15], anticonvulsant[16], antiprotozoal[17] and kinase inhibitors[18]. The derivatives of 1,2,3-triazoles were also proved promising activity in medicinal chemistry[19-21]. Recent research reveals that the combination of 1,2,3–triazoles with other heterocyclic compounds like benimidazoles, pyridine, coumerins and benzofurans enhanced biological activity[22-25]. In recent days, the derivatives of 1,2,3-triazoles have been recognised as most important compounds. Hence, in this direction, we describe the synthesis of novel benzimidazoles containing 1,2,3-triazoles using click chemistry.

## Material and Methods

Melting points were determined using a Cintex apparatus and are uncorrected. All the chemicals and solvents used were purchased from Sigma-Aldrich. Column chromatography was performed using silica gel (60-120 mesh size) purchased from Sigma-Aldrich. Thin layer chromatography was carried out using aluminum sheet pre-coated with silica gel $60F_{254}$ purchased from Merck. Elemental analysis was measured by CHN analyzer (Carlo Erba EA 1108 automatic analyzer). $^{1}$HNMR spectra of compounds were recorded in DMSO-$d_6$ on a Bruker Avance 400 MHz spectrometer. $^{13}$C NMR spectra were recorded with a Mercury plus spectrometer (125MHz). Mass spectra were recorded on a Jeol SX-102 spectrometer (ESI-MS).

## Results and Discussion

The synthesis of target compounds (3a–j) was accomplished by a sequence shown in scheme 1. The starting compound (1) was synthesized according to reported procedure[26]. Later, the intermediate (2) was treated with propargyl bromide in acetone using $K_2CO_3$. The target compound was synthesized bydipolar cyclo addition of terminal alkyne **(2)** with different substituted aryl azides using a catalytic amount of $CuSO_4.5H_2O$ and sodium ascorbate was refluxed for about 6-8hours using (1:1) aq. BuOH as a green solvent to afford the title compound disubstituted 1,2,3-triazoles (3a–j) in moderate to good yields. The chemical structures of synthesized compounds (3a-j) were confirmed by $^{1}$HNMR, $^{13}$CNMR and mass and elemental (C, H and N) analysis.$^{1}$HNMR spectrum of compound 2 represents the singlets at δ4.62 and 5.89 (-$CH_2$,-$OCH_2$), triplets at δ 2.72, 2.93(≡CH) protons indicate the formation of propargylation. Later the compound 2 undergoes 1,3 dipolar cycloaddition with aromatic azides to afford the corresponding bis 1,2,3 triazoles (3) in good to excellent yield. The HNMR spectrum of compound 3 revealed the new singlet signals at δ value 8.38, 8.42 ppm. With this evidence, the resulting product 1,2,3 bis triazoles are confirmed.



**Scheme 1: (a) propargyl bromide, $K_2CO_3$, Acetone, reflux 6.5h**
**(b): $ArN_3$, $CuSO_4$, $5H_2O$, Sodium ascorbate, reflux, 6-8h.**

**Table 1**
**Compounds and their % yields**

| Compound No. | R=R[1]=Ar | %Yield |
|---|---|---|
| 3a | -$C_6H_5$ | 63 |
| 3b | 3,5-dichloro | 56 |
| 3c | 2-$NO_2$ | 59 |
| 3d | 3,5-dimethyl | 64 |
| 3e | 4-bromo | 52 |
| 3f | 2-trifluoro methyl | 48 |
| 3g | 2,4-dichloro | 53 |
| 3h | 2,4-dimethyl | 72 |
| 3i | 2,3-dimethyl | 67 |
| 3j | 3-$OCH_3$ | 71 |

**Table 2**
**Anti-oxidant activity of compound (3a-j)**

| Compound | DPPH |
|---|---|
| 3a | 22.54±0.13 |
| 3b | 14.18±0.11 |
| 3c | 4.76±0.30 |
| 3d | 4.62±0.42 |
| 3e | 12.54±0.53 |
| 3f | 15.02±0.22 |
| 3g | 16.55±0.26 |
| 3h | 14.19±0.34 |
| 3i | 12.55±0.42 |
| 3j | 16.29±0.51 |
| Ascorbic acid | 3.78±0.43 |

In the mass spectrum, molecular ion peak appeared at m/z 613 and 615 (1:1% intensity), which matches with its molecular formula $C_{27}H_{20}Cl_4N_8O$. Further, the appearance of new peaks at δ value 144.4, 119.1 and 132.8, 119.6 ppm in $^{13}C$ NMR spectrum supported the formation of 1,2,3-triazole ring.

All the newly synthesized compounds were examined for their radical scavenging activity in terms of DPPH method[27]. The compounds were dissolved in DMSO (100µg/ml). The investigation report reveals that the radical scavenging ability of synthesized compounds (3a-j) exhibits significant activity as shown in table 1. Among the tested compounds 3c,3d showed excellent activity, the remaining compounds showed least activity against the test organism employed.

***In vitro* anticancer activity:** All the newly synthesized compounds (3a-j) were further investigated for *in vitro* anticancer activity over MCF-7 (breast), A-549 (lungs) and HeLa (cervical) cell lines using MTT assay[28]. Doxorubicin is used as positive control and the results are shown in table 3. The analogues (3a-3j) were demonstrated with $IC_{50}$ values in the range of 3.12± 0.84 to 44.12 ±10.65µ M respectively, where as the standard drug exhibited $IC_{50}$ values ranging from 2.23± 0.61 to 5.34 ± 0.38µM. Among all the screened compounds, the compounds 3j (MCF-7 = 4.67± 0.22, A-549 = 3.12± 0.84 and HeLa= 6.33± 1.21µM), 3b (MCF-7 =11.42± 3.57, A-549 = 12.16± 4.62 and HeLa = 11.78± 4.89µM) and 3f (MCF-7 =14.42±4.48, A-549=16.84± 6.24 and HeLa =13.94± 6.74 µM) displayed promising activity, whereas, the remaining compounds exhibit moderate to low activity as compared to standard doxorubicin.

**Table 3**
***In vitro* cytotoxic activity of compounds (3a-j) in ($IC_{50}$ µM)**

| Compound No | R=R[1] | MCF-7 (breast) | A-549 (lung) | HeLa(cervical) |
|---|---|---|---|---|
| 3a | $-C_6H_5$ | 25.15±8.31 | 31.12± 9.31 | 43.56 ±9.67 |
| 3b | 3,5-dichloro | 11.42± 3.57 | 12.16± 4.62 | 11.78± 4.89 |
| 3c | 2-$NO_2$ | 31.52± 11.32 | 29.41± 8.42 | 44.12 ±10.65 |
| 3d | 3,5-dimethyl | 21.22± 6.54 | 19.16± 7.62 | 21.78± 6.88 |
| 3e | 4-bromo | 41.52± 12.32 | 26.41±7.48 | 34.12 ± 8.66 |
| 3f | 2-trifluoro methyl | 14.42± 4.48 | 16.84± 6.24 | 13.94± 6.74 |
| 3g | 2,4-dichloro | 16.41± 3.52 | 19.23± 5.42 | 16.34 ± 5.48 |
| 3h | 2,4-dimethyl | 24.02 ±1.43 | 6.18±1.56 | 7.84 ±2.04 |
| 3i | 2,3-dimethyl | 19.15 ±1.03 | 4.74 ±1.42 | 6.43± 1.67 |
| 3j | 3-$OCH_3$ | 4.67± 0.22 | 3.12± 0.84 | 6.33± 1.21 |
| Doxorubicin | | 3.12 ± 0.41 | 2.23± 0.61 | 5.34 ± 0.38 |

The structure-activity relationships (SAR) studies revealed that the compound 3j containing strong electron releasing 3-methoxy substituent on the phenyl ring attached to triazole skeleton was showed more potent activity than the compounds 3d, 3h and 3i containing weak-electron donating methyl substituted phenyl ring which showed poorer activity. In this context the electron-withdrawing group compound 3b with 3,5-dichloro group on phenyl ring attached to triazole pharmacophore ring exhibited promising anti-cancer activity. Later, the 3,5-dichloro group of phenyl ring of triazole moiety by 2-$NO_2$ and 4-Br (i.e. compounds 3c and 3e) displayed lesser activity than the compound 3b. Nevertheless, the compound 3f containing 2-triflouromethyl group on the phenyl ring of triazole moiety showed improved activity than the compounds 3g. On the other hand, the phenyl ring of triazole skeleton resulting compound 3a exhibited poorer activity.

**General procedure for the preparation of 1-(prop-2-yn-1-yl)-2-(1-(prop-2-yn-1-yloxy) ethyl)-1*H*-benzo[*d*]imidazole (2):** A mixture of 1-(1*H*-benzo[*d*]imidazol-2-yl) ethanol **(1)** (0.05mol) and $K_2CO_3$ (0.15mol) in acetone (30 mL) was treated with propargyl bromide(0.05mol) and the reaction mixture was stirred at room temperature for about 6-8 h. The progress of the reaction was monitored by TLC. After the completion of the reaction, the reaction mixture was poured carefully in ice-cold water (50mL) and extracted with ethyl acetate (2×15mL). The combined organic layer was washed with brine water and dried over anhydrous $Na_2SO_4$ and then the organic layer was filtered, washed and dried under vacuum to give the corresponding compound (2).

**General procedure for the preparation of 2-(1-((1-substituted phenyl-1H-1,2,3-triazol-4-yl)methoxy)ethyl)-1-((1-substitutedphenyl-1H-1,2,3-triazol-4-yl)methyl)-1 H-benzo[*d*]imidazole(3a–3j):** To a stirred solution of compound (2) (1.0 mmol) and aryl azide (2.0 mmol) in aq (1:1)$^t$BuOH (15mL) was added CuI(10mol %) and sodium ascorbate. The reaction mixture was stirred at room temperature for about 8–10 h. After completion of the reaction, the reaction mixture was diluted with water (15mL) and the product was extracted with ethyl acetate (2×15mL). The combined organic layer was washed with brine water and dried over anhydrous $Na_2SO_4$. After filtration, the solvent was evaporated under vacuum and the crude compounds were purified by column chromatography using silica gel (60-120 mesh) and hexane/ethyl acetate gradient system as an eluentto afforded the title compounds.

**2-(1-((1-phenyl-1*H*-1,2,3,-triazol-4-yl)methoxy)ethyl)-1-((1-phenyl-1*H*-1,2,3-triazol-4-yl)methyl)-1*H*-benzo[*d*] imidazole (3a):** M.P:287-289$^o$C;$^1$HNMR(400MHz, DMSO-$d_6$,δ ppm): 1.56 (d, *J*= 4.2Hz, 3H,-$CH_3$), 4.32 (q,1H,-CH), 4.55 (s, 2H, -$CH_2$), 5.78 (s, 2H, -$CH_2$), 7.29-7.36 (m,2H,Ar-H),7.36 (d, *J*= 4.4Hz, 1H,Ar-H),7.43(d, *J*= 4.6Hz, 1H,Ar-H),7.48 (d, *J*= 4.7Hz, 1H,Ar-H),7.57 (d, *J*= 4.8Hz, 1H,Ar-H), 7.62 (t,1H,Ar-H), 7.66 (d, *J*=4.9Hz, 1H,Ar-H), 7.72 (t,1H,Ar-H), 7.75 (d,*J*=4.6Hz,1H,Ar-H),7.78 (d,*J*=4.9Hz, 1H,Ar-H), 7.82 (t,1H,Ar-H), 7.85-7.92 (m,2H, Ar-H), 8.17 (s,1H,triazol-H), 8.21 (s,1H,triazol-H); $^{13}$C NMR (125 MHz, DMSO-$d_6$,δ ppm): 23.4, 42.0, 59.7, 63.8, 114.1, 118.4, 119.3, 119.9, 120.3, 120.8, 121.3, 122.5, 123.0, 125.1,127.3, 128.0, 129.2, 129.8, 130.1, 132.2, 136.2, 138.2, 139.8, 140.4, 141.5, 152.3, 158.1; MS: *m/z* 476 $(M+H)^+$; Anal. Cal. for $C_{27}H_{24}N_8O$: C, 68.05; H, 5.08; N,23.51. Found: C, 68.03; H, 5.08; N, 23.50 %.

**2-(1-((1-(3,5-dichlorophenyl)-1*H*-1,2,3,-triazol-4-yl)methoxy)ethyl)-1-((1-(3,5-dichloro phenyl) -1*H*-1,2,3-triazol-4-yl)methyl)-1*H*-benzo[*d*] imidazole(3b):** M.P:272-274$^o$C;$^1$HNMR (400MHz, DMSO-$d_6$,δ ppm): 1.78 (d, *J*= 4.45Hz, 3H,-$CH_3$), 4.50 (q,1H,-CH), 4.62 (s, 2H, -$CH_2$), 5.89 (s, 2H, -$CH_2$), 7.30 (d, *J*=5.4Hz, 1H, Ar-H), 7.36 (d, *J*=5.9Hz, 1H, Ar-H), 7.38-7.43 (m,2H, Ar-H), 7.47 (s,1H, Ar-H), 7.56 (s,1H, Ar-H), 7.60 (s,1H, Ar-H), 7.65 (s, 1H, Ar-H), 7.72 (s,1H, Ar-H), 7.78 (s,1H, Ar-H), 8.38 (s,1H,triazol-H), 8.42 (s,1H,triazol-H); $^{13}$C NMR (125 MHz, DMSO-$d_6$,δ ppm): 27.4, 46.2,63.3, 66.8, 113.2, 115.3, 117.2, 118.2, 118.7, 119.0, 119.6, 122.0, 122.5, 123.3, 125.1, 126.1, 135.2, 135.4, 135.9, 136.2, 138.6, 139.0, 140.2, 141.2, 142.4, 152.2, 157.1;MS: *m/z* 613 $(M+H)^+$, 615 $(M+2)^+$;Anal. Cal. for $C_{27}H_{20}Cl_4N_8O$: C, 52.79; H, 3.28; N,18.24. Found: C, 52.78; H, 3.28; N, 18.23 %.

**2-(1-((1-(2-nitrophenyl)-1*H*-1,2,3,-triazol-4-yl)methoxy) ethyl)-1-((1-(2-nitrophenyl)-1*H*-1,2,3-triazol-4-yl)methyl )-1*H*-benzo[*d*]imidazole (3c):** M.P:310-312$^{o}$C; $^{1}$HNMR (400MHz, DMSO-$d_6$,δ ppm): 1.61 (d, *J*=5.3Hz, 3H,-$CH_3$), 4.55 (q,1H,-CH), 4.62 (s, 2H,-$CH_2$), 5.65 (s, 2H, -$CH_2$),7.38 (t,1H,Ar-H), 7.45 (t,1H,Ar-H),7.49 (t,1H,Ar-H), 7.56 (t,1H,Ar-H), 7.60 (t,1H,Ar-H), 7.64 (t,1H,Ar-H), 7.69 (d, *J*=5.7Hz, 1H,Ar-H), 7.72 (d, *J*=5.9Hz, 1H,Ar-H), 7.78 (d, *J*=6.1Hz, 1H,Ar-H), 7.83 (d, *J*=6.5Hz, 1H,Ar-H), 7.87 (d, *J*=6.9Hz, 1H,Ar-H), 7.92 (d, *J*=7.1Hz, 1H,Ar-H), 8.35 (s,1H,triazol), 8.39 (s,1H,triazol); $^{13}$CNMR (125 MHz, DMSO-$d_6$, δ ppm): 22.4, 43.0, 59.1, 65.2, 114.1, 119.4, 120.2, 121.3, 122.4, 123.1, 125.1, 125.8, 127.1, 127.9, 128.4, 129.0, 132.4,132.7, 133.1, 134.1, 137.6, 139.4, 140.0, 142.2, 144.3, 152.2, 157.1;MS: *m*/*z* 567 $(M+H)^+$; Anal. Cal. for $C_{27}H_{22}N_{10}O_5$: C, 57.24; H, 3.91; N, 24.72. Found: C, 57.24; H, 3.90; N, 24.72 %.

**2-(1-((1-(3,5-dimethylphenyl)-1*H*-1,2,3,-triazol-4-yl)me thoxy)ethyl)-1-((1-(3,5-dimethyl phenyl)-1*H*-1,2,3-triazol -4-yl)methyl)-1*H*-benzo[*d*]imidazole (3d):** M.P:266-268$^{o}$C; $^{1}$HNMR (400MHz, DMSO-$d_6$,δ ppm): 1.52 (d, *J*= 4.2Hz, 3H,-$CH_3$), 2.32 (s, 3H,-$CH_3$), 2.34 (s, 3H,-$CH_3$), 2.41 (s, 3H,-$CH_3$), 2.44 (s, 3H,-$CH_3$), 4.48 (q,1H,-CH), 4.52 (s, 2H, -$CH_2$), 5.56 (s, 2H, -$CH_2$), 6.95 (s,1H, Ar-H), 7.15 (s,1H, Ar-H), 7.20 (s,1H, Ar-H), 7.25 (s,1H, Ar-H), 7.28 (s,1H, Ar-H), 7.35 (s,1H, Ar-H), 7.46-7.58(m,2H, Ar-H), 7.58(d,2H, Ar-H), 8.22 (s,1H,triazol-H), 8.31 (s,1H,triazol-H); $^{13}$C NMR (125 MHz, DMSO-$d_6$,δ ppm): 20.1, 20.9, 21.2, 21.8, 23.1, 42.0, 59.3, 64.5, 112.1, 119.2, 119.6, 122.0, 122.5, 123.1, 124.2, 125.3, 125.6, 125.9, 127.2, 128.5, 136.2, 137.2, 137.6, 138.4, 139.4, 139.7, 139.9, 140.4, 141.2, 153.3, 156.1;MS: *m*/*z* 533 $(M+H)^+$; Anal. Cal. for $C_{31}H_{32}N_8O$: C, 69.90; H, 6.06; N, 21.04. Found: C, 69.88; H, 6.05; N, 21.02 %.

**2-(1-((1-(4-bromophenyl)-1*H*-1,2,3,-triazol-4-yl)methox y)ethyl)-1-((1-(4-bromophenyl)-1*H*-1,2,3-triazol-4-yl)me thyl)-1*H*-benzo[*d*] imidazole (3e):** M.P:256-258$^{o}$C;$^{1}$HNMR (400MHz, DMSO-$d_6$,δ ppm): 1.67 (d, *J*= 4.6Hz, 3H,-$CH_3$), 4.67 (q,1H,-CH), 4.78 (s, 2H, -$CH_2$), 5.84 (s, 2H, -$CH_2$), 7.49-7.56 (m,4H, Ar-H), 7.66 (d, *J*=6.0Hz, 1H, Ar-H), 7.69 (d, *J*=6.2Hz, 1H, Ar-H), 7.72 (d,*J*=6.3Hz, 1H, Ar-H), 7.77 (d, *J*=6.5Hz, 1H, Ar-H), 7.82 (d, *J*=6.3Hz, 1H, Ar-H), 7.85 (d, *J*=6.9Hz, 1H, Ar-H), 7.89 (d, *J*=7.1Hz, 1H, Ar-H), 7.93 (d, *J*=7.34Hz, 1H, Ar-H), 8.45 (s,1H,triazol-H), 8.52 (s,1H,triazol-H); $^{13}$CNMR (125 MHz, DMSO-$d_6$,δ ppm): 22.4, 44.3, 61.8, 64.3, 114.1, 119.3, 119.6, 120.0, 120.5, 120.8, 121.2, 121.7, 121.9, 122.0, 122.5, 123.2, 132.3, 132.9, 133.2, 134.1, 135.1, 136.4, 138.2, 141.4, 143.2, 153.3, 158.1;MS: *m*/*z* 632$(M+H)^+$,634 $(M+2)^+$;Anal. Cal. for $C_{27}H_{22}Br_2N_8O$: C, 51.12; H, 3.50; N, 17.67. Found: C, 51.11; H, 3.50; N, 17.66 %.

**2-(1-((1-(2-(trifluoromethyl)phenyl)-1*H*-1,2,3,-triazol-4-yl)methoxy)ethyl)-1-((1-(2-(trifluoromethyl)phenyl)-1*H*-1,2,3-triazol-4-yl)methyl)-1*H*-benzo[*d*]imidazole(3f):** M. P:271-273$^{o}$C; $^{1}$HNMR (400MHz, DMSO-$d_6$,δ ppm): 1.82 (d, *J*= 4.0Hz, 3H,-$CH_3$), 4.62 (q,1H,-CH), 4.68 (s, 2H, -$CH_2$), 5.74 (s, 2H, -$CH_2$), 7.53 (d, *J*= 5.3Hz 1H,Ar-H), 7.57 (d, *J*= 5.6Hz, 1H,Ar-H), 7.62 (t,1H,Ar-H), 7.65 (t,1H,Ar-H), 7.68-7.74 (m,2H,Ar-H), 7.79 (d, *J*= 5.7Hz, 1H,Ar-H), 7.84 (t,1H,Ar-H),7.88 (d, *J*= 5.9Hz, 1H,Ar-H), 7.93(d, *J*= 6.0Hz, 1H,Ar-H), 7.97(t,1H,Ar-H), 8.12(t,1H,Ar-H), 8.46 (s,1H,triazol-H), 8.57 (s,1H,triazol-H);$^{13}$CNMR (125 MHz, DMSO-$d_6$,δ ppm): 22.4, 43.0, 61.2, 65.2, 114.1, 119.6, 120.3, 120.9, 121.9, 122.1, 122.5, 123.1, 123.6, 123.9, 127.1, 127.8, 128.4, 129.2, 130.3, 131.3, 133.5, 134.2, 135.9, 136.5, 138.6, 142.4, 145.0, 154.4, 159.1;MS: *m*/*z* 613 $(M+H)^+$; Anal. Cal. for $C_{29}H_{22}F_6N_8O$: C, 56.86; H, 3.63; N,18.29. Found: C, 56.85; H, 3.62; N, 18.28 %.

**2-(1-((1-(2,4-dichlorophenyl)-1*H*-1,2,3,-triazol-4-yl)meth oxy)ethyl)-1-((1-(2,4-(dichloro phenyl)-1*H*-1,2,3-triazol-4-yl)methyl)-1*H*-benzo[*d*]imidazole(3g):** M.P:282-284$^{o}$C; $^{1}$HNMR (400MHz, DMSO-$d_6$,δ ppm): 1.78 (d, *J*= 5.2Hz, 3H,-$CH_3$), 4.58 (q,1H,-CH), 4.93 (s, 2H, -$CH_2$), 5.36 (s, 2H, -$CH_2$), 7.38 (d, *J*=5.4Hz, 1H,Ar-H), 7.44 (d,*J*= 5.6Hz, 1H,Ar-H), 7.53 (t,1H,Ar-H), 7.62 (t,1H, Ar-H), 7.62 (d, *J*= 5.9Hz, 1H, Ar-H), 7.66 (d, *J*= 6.1Hz,1H,Ar-H), 7.72 (d, *J*= 6.3Hz, 1H, Ar-H), 7.78 (d, *J*= 6.6Hz, 1H,Ar-H), 7.84(s,1H, Ar-H), 7.93 (s, 1H, Ar-H), 8.24 (s,1H,triazol-H), 8.29 (s,1H,triazol-H); $^{13}$CNMR (125MHz, DMSO-$d_6$,δ ppm): 22.4, 43.0, 62.1, 65.5, 114.1, 120.4, 121.2, 122.8, 123.4, 124.1, 127.0, 127.8, 128.2, 128.8, 130.4, 130.9, 132.9, 133.5, 134.2, 135.1, 137.3, 138.3, 139.1, 142.4, 144.0, 153.5, 158.4;MS: *m*/*z* 612 $(M+H)^+$, 614 (M+2); Anal. Cal. for $C_{27}H_{20}Cl_4N_8O$: C, 52.79; H, 3.28; N, 18.24. Found: C, 52.78; H, 3.27; N, 18.28 %.

**2-(1-((1-(2,4-dimethylphenyl)-1*H*-1,2,3,-triazol-4-yl) methoxy)ethyl)-1-((1-(2,4-dimethyl phenyl)-1*H*-1,2, 3-triazol-4-yl)methyl)-1*H*-benzo[*d*]imidazole (3h):** M.P:278-280$^{o}$C;$^{1}$HNMR (400MHz, DMSO-$d_6$,δ ppm): 1.62 (d, *J*= 3.4Hz, 3H,-$CH_3$),2.23 (s, 3H,-$CH_3$), 2.28 (s, 3H,-$CH_3$), 2.32 (s, 3H,-$CH_3$), 2.35 (s, 3H,-$CH_3$), 4.61 (q,1H,-CH), 4.68 (s, 2H, -$CH_2$), 5.20 (s, 2H, -$CH_2$), 6.78(s, 1H, Ar-H), 6.83 (s, 1H, Ar-H), 7.10(d, 1H, *J*= 4.4Hz, Ar-H), 7.16 (d, 1H, *J*= 4.6Hz, Ar-H), 7.32-7.46 (m, 3H, Ar-H), 7.52 (d, *J*= 4.5Hz, 1H, Ar-H), 7.57 (d, 1H, *J*= 4.7Hz, Ar-H), 7.63 (d, *J*= 4.9Hz,1H, Ar-H), 8.18 (s,1H,triazol-H), 8.23 (s,1H,triazol-H); $^{13}$CNMR (125 MHz, DMSO-$d_6$,δ ppm): 18.9,19.2,20.4, 21.1, 21.8, 42.0, 59.2, 63.8, 113.1, 118.3, 120.2, 122.4, 122.9, 123.2, 123.8, 124.1, 125.1, 126.2, 130.5, 131.0, 132.3, 133.2, 135.2, 135.9, 136.4, 139.6, 137.4, 141.2, 142.0, 152.2, 155.6; MS: *m*/*z* 533 $(M+H)^+$; Anal. Cal. for $C_{31}H_{32}N_8O$: C, 69.90; H, 6.06; N, 21.04. Found: C, 69.88; H, 6.06; N, 21.00 %.

**2-(1-((1-(2,3-dimethylphenyl)-1*H*-1,2,3,-triazol-4-yl) methoxy)ethyl)-1-((1-(2,4-dimethyl phenyl)-1*H*-1,2, 3-triazol-4-yl)methyl)-1*H*-benzo[*d*]imidazole (3i):** M.P:289-291$^{o}$C;$^{1}$HNMR (400MHz, DMSO-$d_6$,δ ppm): 1.59 (d, *J*= 3.4Hz, 3H,-$CH_3$), 2.25 (s, 3H,-$CH_3$), 2.32 (s, 3H,-$CH_3$), 2.36 (s, 3H,-$CH_3$), 2.41 (s, 3H,-$CH_3$), 4.58

(q,1H,-CH), 4.66 (s, 2H, -$CH_2$), 5.14 (s, 2H, -$CH_2$), 6.73 (d, *J*= 4.1Hz, 1H, Ar-H), 6.79 (d, *J*= 4.4Hz, 1H, Ar-H), 6.86 (d, *J*= 4.6Hz,1H, Ar-H), 6.94 (d, *J*= 4.8Hz, 1H, Ar-H),7.04 (t, 1H, Ar-H),7.10 (t, 1H, Ar-H), 7.31(t, 1H, Ar-H), 7.36(t, 1H, Ar-H), 7.42(d, *J*= 4.9Hz, 1H, Ar-H), 7.47(d, *J*= 4.6Hz,1H, Ar-H), 8.05 (s,1H,triazol-H), 8.12 (s,1H,triazol-H); $^{13}$C NMR (125 MHz, DMSO-$d_6$,δ ppm): 17.3, 17.9, 19.2, 19.7, 22.4, 43.1, 59.5, 64.2, 115.1, 117.1, 117.9, 118.4, 120.2, 122.4, 122.9, 123.1, 124.4, 125.1,127.2, 128.7, 133.2, 134.0, 136.2, 138.3, 138.9, 139.3, 139.9, 140.1, 142.0, 153.2, 155.4; MS: *m*/*z* 533 $(M+H)^+$; Anal. Cal. for $C_{31}H_{32}N_8O$: C, 69.90; H, 6.06; N, 21.04. Found: C, 69.88; H, 6.06; N, 21.00 %.

**2-(1-((1-(3-methoxyphenyl)-1*H*-1,2,3,-triazol-4-yl)methoxy)ethyl)-1-((1-(3-methoxyphenyl)-1*H*-1,2,3-triazol-4-yl)methyl)-1*H*-benzo[*d*]imidazole (3j):** M.P: 271-273°C;$^1$HNMR (400MHz, DMSO-$d_6$,δ ppm): 1.69 (d, *J*= 4.3Hz, 3H,-$CH_3$), 3.86 (s, 3H,-$OCH_3$), 3.91 (s, 3H,-$OCH_3$), 4.68 (q,1H,-CH), 4.82 (s, 2H, -$CH_2$), 5.34 (s, 2H, -$CH_2$), 6.72(d, *J*= 4.6Hz,1H, Ar-H), 6.79 (d, *J*= 4.9Hz,1H, Ar-H), 6.86 (s, 1H,Ar-H), 6.94 (s, 1H,Ar-H), 7.04 (t, 1H,Ar-H), 7.10 (d, *J*= 5.0Hz, 1H, Ar-H),7.16 (d, *J*= 5.3Hz,1H,Ar-H),7.21(t,1H,Ar-H), 7.38(t, 1H, Ar-H), 7.45 (t,1H,Ar-H),7.52 (d, *J*=4.9Hz,1H, Ar-H),7.59 (d, *J*=5.2Hz, 1H, Ar-H),8.24 (s,1H,triazol-H), 8.31 (s,1H,triazol-H); $^{13}$C NMR (125 MHz, DMSO-$d_6$,δ ppm): 22.4. 43.4, 58.4, 60.0, 61.7, 63.1, 107.4, 108.3, 112.1, 113.4, 113.9, 115.2, 116.1, 118.4, 119.0, 123.2, 124.3, 125.1, 133.2, 134.2, 136.3, 139.0, 140.4, 142.2, 143.2, 153.1, 158.2, 160.1, 162.3; MS: *m*/*z* 537 $(M+H)^+$; Anal. Cal. for $C_{29}H_{28}N_8O_3$: C, 64.91; H, 5.26; N, 20.88. Found: C, 64.90; H, 5.26; N, 20.87 %.

**DPPH free radical scavenging assay:** The antioxidant activity of compounds was measured in terms of hydrogen donating or radical scavenging ability using the stable free radical DPPH method. 200 ml aliquots of sample at different concentrations were mixed with 1.8 ml of the DPPH solution (0.5 mM). The reaction mixture was allowed to stand at room temperature for 30 minutes and absorbance was measured at 517nm using UV-VIS spectrophotometer. Control solution consisting of DPPH and DMSO without compounds was used as blank. Ascorbic acid was used as standard. The percentage inhibition of DPPH radical was calculated by comparing the results of the test with those of the control and results are summarized in table 2.

**Anti-cancer assay - MTT protocol:** The anti-cancer activity of the synthesized compounds was determined using the MTT assay $1\times10^4$ cell/well were seeded in 200 mL DMEM, supplemented with 10% FBS in each well of 96-well micro culture plates and incubated for 24 hours at 37°C in a $CO_2$ incubator.

Compounds diluted to the desired concentrations in culture medium were added to the well with respective vehicle control. After 48 hours in incubation, 10mL MTT (3-(4,5-dimethyl thiazol-2-yl)-2,5-diphenyl tetrazolium bromide) (5mg/mL) was added to each well and the plates were further incubated for four hours. Then the supernatant from each well was carefully removed, formation crystals were dissolved in 100 mL of DMSO and absorbance at 570 nm wavelength was recorded and the values are summarized in table 3.

## Conclusion

In conclusion, the synthesis of some novel 2-(1-((1-substitutedphenyl-1*H*-1,2,3-triazol-4-yl)methoxy)ethyl)-1-((1-substitutedphenyl-1*H*-1,2,3-triazol-4-yl)methyl)-1*H*-benzo[*d*]imidazole (3a-j)derivatives was synthesized in moderate to high yields(3a–j). The *in vitro* anti-cancer activity of these compounds (3a-j) over three human cancer cell lines namely HeLa(cervical cancer), MCF-7 (breast cancer) and A-549 (lung cancer) using doxorubicin was used as standard. The compounds 3j, 3b and 3f showed promising activity against all the cell lines were compared with the positive control.

The compounds 3c and 3d displayed excellent antioxidant activity against test organism employed. The remaining compound exhibit lesser to moderate activity against all the tested cancer cell lines.

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