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Synthesis, spectral analysis and *in vitro* anticancer activity of 1,2,3-triazole derivatives and their molecular docking studies

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Triazole derivatives are an absolutely essential class of compounds as they are involved in such a diverse range of pharmacological effects. In the field of medical chemistry, these nitrogen-containing heterocycles are used in the role of therapeutic medicines. The molecule with the given name has been synthesized by using click chemistry [Copper-Catalyzed Azide-Alkyne Cycloaddition (CuAAC)] with 1-propargyl-6-methoxy benzimidazolone as the dipolarophile and benzylazide as the dipole. A majority of the compounds show moderate to excellent efficacy when tested for anticancer properties against several cancer cell lines. The MCF-7 cell line is the most resistant to compounds **1a** and **1e**, with an IC_{50} value of 1.82 and 1.90 µM respectively. In contrast, the MDA - MB-231 and HeLa cell lines respond favorably to compounds **IVb**, **IVc** and **IVd**. Compound **IVa** is docked in the active site with EGFR as the target molecule. ^{1}H and ^{13}C NMR, IR and ESI-HRMS have been used to determine the structures of the newly synthesized compounds.

Keywords: Triazole, 1,3-Dipolar cycloaddition, Click reaction, Anticancer activity

The triazoles are a class of heterocyclic organic compounds with a wide range of biological activity[1]. Hydrogen bonds coordinated with metal ions or hydrophobic contacts may also be used by triazole derivatives to attach to enzymes or receptors[2]. This has made for a favourable and productive environment for studies of triazoles in pharmacology. In addition, 1,2,3-triazole derivatives are well-known starting materials for the synthesis of several useful drugs[3]. Indeed, effective anticancer, antibacterial, and anti-HIV activities have been shown in heterocyclic compounds bearing this pattern[4-6].

Cytotoxic, antiviral, antibacterial, and anticancer activities are only few of the many biological capabilities of 1,2,3-triazole-based derivatives[7-10]. To this end, we set out to identify innovative, stable, cost-effective, and physiologically active compounds for the synthesis of 1,2,3-triazole derivatives of pyrrolo[2,3-d]pyrimidine[11-14]. Study after study has focused on this particular facet[15]. The synthesis of new compounds with biological activity under moderate and convenient conditions has gained substantial attention in organic synthesis in recent years due to the good yields and high selectivity of the related products[16]. However, there is a dearth of literature on the synthesis of such molecules[17]. There is currently no publication on the synthesis of 1,2,3-triazole derivatives of phenyl benzo[d]imidazole in the accessible literature[18].

Results and Discussion

We used Electrothermal 9002 melting point equipment to get an accurate reading. The FTS-6000 BIO-RAD apparatus could record IR spectra as well. Spectra of ^{1}H and ^{13}C NMR were recorded in DMSO-d_6 using a Bruker AC-300. The units for chemical shifts (ppm) and coupling constants (*J*) were both hertz (Hz). For mass spectrometry, we employed micromass LCT (electrospray ionization, positive mode) spectrometers (HRES-MS). On aluminum sheets of SDS silica gel 60 F254,0.2 mm 4-Dimethylaminopiridinium, TLC was used to track the progress of all reactions.

6-Methoxy-1-phenyl-1*H*-benzo[d]imidazol-2(3*H*)-one is reacted with propargyl bromide, dimethyl formamide, benzylthio trifluoromethyl benzoic acid, and potassium carbonate reacted at RT to give 5-methoxy-3-phenyl-1-(prop-2-ynyl)-1*H*-benzo[d] imidazol-2(3*H*)-one. In this study, we report the synthesis of a novel 1-((1-benzyl-1*H*-1,2,3-triazol-4-yl) methyl)-5-methoxy-3-phenyl-1*H*-benzo[d]imidazol-2 (3*H*)-one through the click chemistry of copper-catalyzed azide-alkyne cycloaddition (CuAAC) employing benzyl azide and 5-methoxy-3-phenyl-1-

(prop-2-ynyl)-1*H*-benzo[d]imidazol-2(3*H*)-one in a water/ethanol (1:1) combination (Scheme 1).

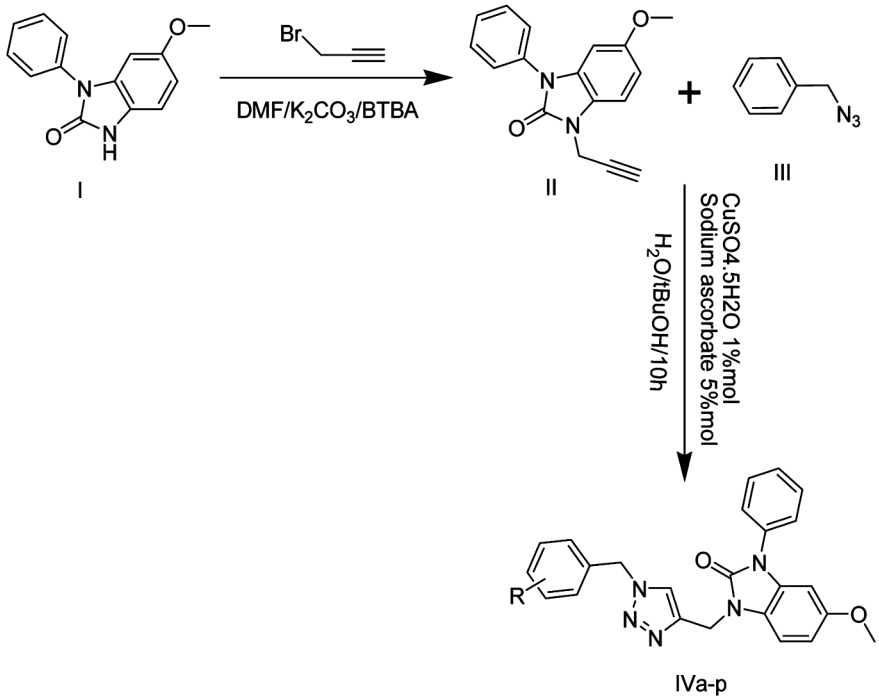
Anticancer activity of compounds IV(a-p) was evaluated by monitoring their capacity to inhibit the growth of tumor cell lines in 96-well plates by cell-mediated reduction of tetrazolium salt to water-insoluble crystal formation. Doxorubicin was used as a standard. The MTT tests were used to measure cytotoxicity against a panel of four human tumor cell lines: A549, derived from human alveolar adenocarcinoma epithelial cells, Hela derived from human cervical cancer cells, MDA-MB-231, derived from human breast adenocarcinoma cells, and HEK 293 (normal human embryonic kidney cell line). Absorbance data for dose-response curves were used to calculate inhibitory concentration (IC_{50}) values. The median (and standard deviation) IC_{50} values (in μM) from three independent experiments are shown. The majority of the synthesized compounds displayed a significant cytotoxic effect on all the cell lines tested (Table 1), with the potencies of some compounds being on par with the gold standard, doxorubicin. The MCF-7 cell line was the most sensitive to the tested drugs (IVa and IVe had the lowest IC_{50}values, at 1.82 and 1.90 μM, respectively), while the MDA-MB-231 and Hela cell lines showed the greatest promise (IVb, IVc, IVd, IVf, IVj, IVh, IVi, IVk, IVl, IVm, IVn, IVo, and IVp).

Molecular Docking

A molecular modeling study where One of the compound IVa was docked in the active site with EGFR as the target revealed has strong interactions (Saeedi, *et al*., 2018) [19], could be seen in Fig. 1. One strong hydrogen bond are formed *via* –OH moieties of MET 769 with the distance of 2.14A° with Binding Energy -9.97 Kcal/mol and Inhibition Constant 49.28nm. IVb, IVc is with Binding Energy -10.62 Kcal/mol, -10.19 Kcal/mol and Inhibition Constant 16.42, 33.74 nm. Schrodinger's maestro v9.5 vizualizer was used to create the visuals, and AUTODOCK 4.2 was used for the docking analysis.

***In vitro* anticancer activity**

The compounds IV(a-p) were tested for their anticancer properties by measuring their ability to suppress the proliferation of tumor cell lines in 96-well plates by cell-mediated reduction of tetrazolium salt to water-insoluble crystal formation, with doxorubicin serving as the reference. The MTT tests



R=IVa;H, IVb;4-OH, IVc;4-Ome, IVd;4-Cl, IVe;4-NO_2, IVf;3-NO_2, IVg;3-CF_3, IVh; 3-F, IVi;2-NO_2,Br, IVj; 4-I, Ik;3Br, IVm;3,5-CH_3, IVn;3,5-NO_2, IVo;3-CN, IVp;3-Cl, 5-NO_2

Scheme 1 — Schematic illustration of the synthesis of the compound

Table 1 — *In vitro* anticancer activity of compounds

Compd	IC_{50} values in µM				HEK 293
	A549	Hela	MDAMB231	MCF-7	>100
IVa	6.02	5.32	6.29	1.82	>100
IVb	7.08	3.72	4.11	10.27	>100
IVc	>100	3.66	4.13	>100	>100
IVd	12.09	2.88	3.87	>100	>100
IVe	6.01	5.15	6.45	1.90	>100
IVf	7.06	3.62	4.10	10.26	>100
IVg	>100	3.64	4.11	>100	>100
IVh	12.05	2.85	3.85	>100	>100
IVi	7.06	3.72	4.10	10.25	>100
IVj	>100	3.65	4.12	>100	>100
IVk	6.06	3.62	4.10	9.26	>100
IVl	>100	3.64	4.11	>100	>100
IVm	11.05	2.85	2.85	>100	>100
IVn	7.06	3.72	4.10	10.25	>100
IVo	>100	2.65	3.12	>100	>100
IVp	7.06	2.62	4.10	9.26	>100
Doxorubicin	0.459	0.509	0.91	1.07	>100

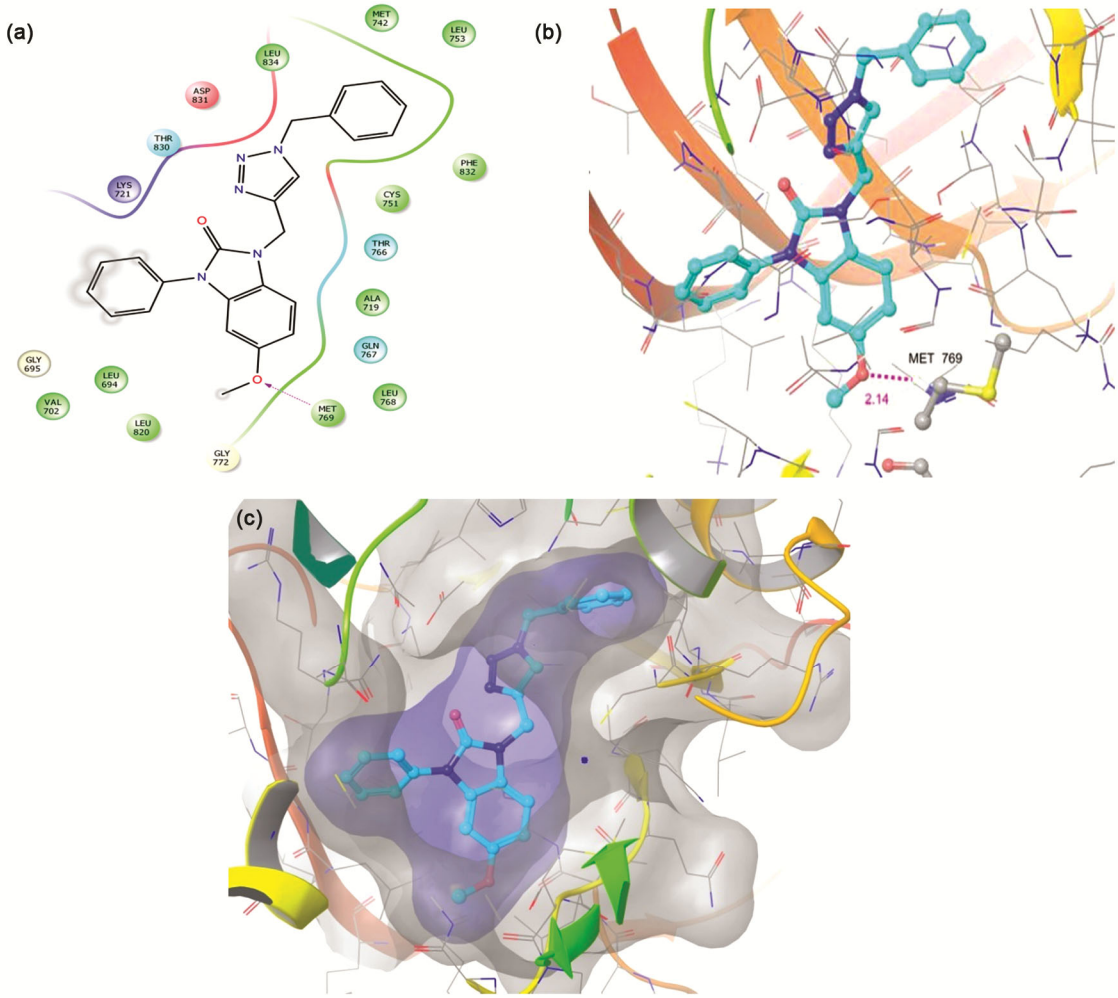


Fig. 1 — (a) represents 2D interactions of compound IVa, (b) represents 3D H-bond interaction formed by the compound (IVa) with MET 769 residue, whereas (c) represents 3D Surface area interactions of compound (IVa)

were used to measure cytotoxicity against a panel of four human tumor cell lines: A549, derived from human alveolar adenocarcinoma epithelial cells, Hela derived from human cervical cancer cells, MDA-MB-231, derived from human breast adenocarcinoma cell, and HEK 293 (normal human embryonic kidney cell line). Inhibitory concentration (IC50) values were determined by graphing absorbance data for dose-response curves. The IC50 values (in μM) are shown as the average standard deviation of three separate trials. Table 1 shows that the majority of the produced compounds had a notable cytotoxic impact on all the cell lines evaluated, with several compounds having potencies equivalent to the gold standard doxorubicin. Among the studied compounds IVa and IVe exhibited most strong action against MCF- 7 cell line with IC_{50} value of 1.82 1.90 μM, whilst IVb, IVc, IVd, IVf, IVj, IVh, IVi, IVj, IVk, IVl, IVm, IVn, IVo and IVp showed promising activity against MDA- MB-231 and Hela cell lines.

Experimental Section

1-((1-Benzyl-1*H*-1,2,3-triazol-4-yl)methyl)-5-methoxy-3-phenyl-1*H*-benzo[d]imidazol-2(3*H*)-one, IVa: A combination of copper(II) sulfate pentahydrate (300 mg, 1.23 mmol), sodium ascorbate (490 mg, 2.47 mmol), benzyl azide (660 mg, 4.94 mmol), and ethanol (15 mL) and water (10 mL) was added to a solution of 5-methoxy-3-phenyl-1-(prop-2-ynyl)-1*H*-benzo[d]imidazol-2(3*H*)-one(490 mg, 2.47 mmol). At RT, the reaction mixture was agitated for 12 hours before the solvent was evaporated at low pressure. A separating funnel was used to remove the organic layer from the acquired residue after it was rinsed with CH_2Cl_2 (15 mL) and H_2O (20 mL). Three separate extractions of CH_2Cl_2 (10 mL) were made from the aqueous layer. The product was produced as colorless crystals (500 mg) with a yield of 70% after drying with anhydrous sodium sulphate and removing the solvent. Yield 70%. m.p. 190-192°C. IR (KBr): 1780-1765 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.82 (s, 3H, OCH_3), 4.42 (s, 2H, CH_2), 4.91 (s, 1H, CH_2), 6.82 (s, 1H, Ar-H), 7.05 (m, 5H, Ar-H), 7.18 (dd, *J*=2.5, 3.4Hz, 4H, Ar-H), 7.43 (m, 3H, Ar-H), 8.02 (s, 2H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 35.15, 50.17, 56.04, 102.83, 110.06, 124.50, 125.93, 127.54, 128.52, 129.65, 130.31, 135.94, 136.23,138.73, 154.70, 157.38; MS: (M+H): *m*/*z* 411.56. Found: 411.25. Anal. Cacld for $C_{24}H_{21}N_5O_2$: C, 70.06; H, 5.14; N, 17.02. Found: C, 70.09; H, 5.18; N, 17.05%.

1-((1-(4-Hydroxybenzyl)-1*H*-1,2,3-triazol-4-yl) methyl)-5-methoxy-3-phenyl-1*H*-benzo[d]imidazol-2(3*H*)-one, IVb: Yield 65%. m.p. 182-184°C. IR (KBr): 1770-1765, 3000-3700 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.81 (s, 3H, OCH_3), 4.09 (s, 1H, OH), 4.42 (s, 2H, CH_2), 5.04 (s, 2H, CH_2), 6.93 (m, 3H, Ar-H), 7.10 (m, 4H, Ar-H), 7.36(m, 4H, Ar-H), 7.62(s, 1H, CH), 8.01 (s, 1H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.13, 35.15, 50.17, 56,04, 102.83, 110.49, 113.06, 124.50, 125.93, 128.42, 129.65, 130.31, 133.41, 135.94, 136.35, 138.73, 154.70, 157.38; MS: (M+H): *m*/*z* 427.46. Found: 427.16. Anal. Cacld for $C_{24}H_{21}N_5O_3$: C, 67.44; H,4.95; N, 16.38. Found: C, 67.48; H, 4.97; N,16.40%.

1-((1-(4-Methoxybenzyl)-1*H*-1,2,3-triazol-4-yl) methyl)-5-methoxy-3-phenyl-1*H*-benzo[d]imidazol-2(3*H*)-one, IVc: Yield 69%. m.p. 191-193°C. IR (KBr): 1775-1765 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.83 (s, 3H, OCH_3), 4.42 (s, 1H, CH_2), 5.02 (s, 2H, CH_2), 6.84 (s, 1H, Ar-H), 7.02 (m, 5H, ArH), 7.19 (m, 4H, Ar-H), 7.47(m, 4H, Ar-H), 7.50 (s, 1H, CH), 8.23 (s, 2H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 35.15, 50.17, 56.23, 102.23, 110.49, 113.06, 124.50, 125.93, 126.46, 128.42, 129.13, 129.65, 130.31, 135.94, 138.73, 154.70, 157.38, 158.83; MS: (M+H): *m*/*z* 441.18. Found: 441.48. Anal. Cacld for $C_{25}H_{23}N_5O_3$: C, 68.01; H,5.25; N, 15.86. Found: C, 68.05; H, 5.29; N,15.89%.

1-((1-(4-Chlorobenzyl)-1*H*-1,2,3-triazol-4-yl) methyl)-5-methoxy-3-phenyl-1*H*-benzo[d]imidazol-2(3*H*)-one, IVd: Yield 80%. m.p. 193-195°C. IR (KBr): 1780-1770, 850-550 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.83 (s, 3H, OCH_3), 4.42 (s, 1H, CH_2), 4.96 (s, 2H, CH_2), 6.84 (s, 1H, Ar-H), 7.08 (m, 4H, Ar-H), 7.31 (m, 4H, Ar-H), 7.46 (m, 3H, Ar-H), 7.49 (s, 1H, Ar-H), 8.32 (s, 1H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 35.15, 50.17, 56.04, 102.23, 110.49, 113.06, 124.50, 125.93, 128.42, 129.21, 129.65, 130.62, 133.21, 134.39, 135.94, 138.73, 154.70, 157.38, 230.01; MS: (M+H): *m*/*z* 445.91. Found: 445.17. Anal. Cacld for $C_{24}H_{20}ClN_5O_2$: C, 64.65; H,4.52; N, 15.71. Found: C, 64.68; H, 4.55; N,15.74%.

1-((1-(4-Nitrobenzyl)-1*H*-1,2,3-triazol-4-yl) methyl)-5-methoxy-3-phenyl-1*H*-benzo[d]imidazol-2(3*H*)-one, IVe: Yield 79%. m.p. 192-195°C. IR (KBr): 1770-1765, 1600-1550 cm^{-1}; ^{1}H NMR

(400 MHz, DMSO-d_6): δ 3.81 (s, 3H, OCH_3), 4.42 (s, 1H, CH_2), 5.09 (s, 2H, CH_2), 6.83 (d, *J*=1.2Hz, 2H, Ar-H), 7.05 (s, 1H, Ar-H), 7.16 (m, 4H, Ar-H), 7.42 (m, 3H, Ar-H), 7.63 (s, 1H, Ar-H), 8.06 (m, 3H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 35.15, 50.17, 56.04, 102.23, 110.49, 113.06, 124.58, 125.93, 128.51, 129.65, 130.31, 135.94, 138.73, 143.70, 154.70, 157.38; MS: (M+H): *m*/*z* 456.45. Found: 456.15. Anal. Cacld for $C_{24}H_{20}N_6O_4$: C, 63.15; H,4.42; N, 18.41. Found: C, 63.15; H, 4.45; N,18.44%.

1-((1-(3-Nitrobenzyl)-1*H*-1,2,3-triazol-4-yl) methyl)-5-methoxy-3-phenyl-1*H*-benzo[d]imidazol-2(3*H*)-one, (IVf):Yield 75%. m.p. 194-196°C. IR (KBr): 1775-1765, 1650-1550 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.81 (s, 3H, OCH_3), 4.42 (s, 1H, CH_2), 5.10 (s, 2H, CH_2), 6.83 (d, *J*=0.9Hz, 2H, Ar-H), 7.05 (s, 1H, Ar-H), 7.16 (m, 3H, Ar-H), 7.36 (m, 3H, Ar-H), 7.44 (s, 2H, Ar-H), 7.90 (m, 2H, Ar-H), 8.01 (s, 1H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 35.15, 50.53, 56.04, 102.83, 110.49, 113.06, 122.69, 124.50, 124.84, 125.93, 128.42, 129.65, 130.31, 130.72, 134.37, 135.94, 138.38, 138.73, 148.79, 154.70, 157.38; MS: (M+H): *m*/*z* 456.45. Found: 456.72. Anal. Cacld for $C_{24}H_{20}N_6O_4$: C, 63.15; H,4.42; N, 14.02. Found: C, 63.16; H, 4.44; N,14.05%.

1-((1-(3-(Trifluoromethyl)benzyl)-1*H*-1,2,3-triazol-4-yl)methyl)-5-methoxy-3-phenyl-1*H*-benzo [d]imidazol-2(3*H*)-one, IVg: Yield 85%. m.p. 193-196°C. IR (KBr): 1770-1765 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.77 (s, 3H, OCH_3), 4.42 (s, 1H, CH_2), 5.49 (s, 2H, CH_2), 6.83 (d, *J*=0.2Hz, 2H, Ar-H), 7.05 (s, 1H, Ar-H), 7.27 (m, 4H, Ar-H), 7.44 (m, 4H, Ar-H), 7.55 (s, 1H, Ar-H), 8.12 (s, 2H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 35.15, 50.43, 56.04, 102.83, 110.49, 113.06, 123.59, 124.14, 124.50, 125.93, 126.27, 128.46, 129.65, 130.31, 131.84, 132.29, 135.94, 137.06, 138.38, 138.73, 154.70, 157.38; MS: (M+H): *m*/*z* 479.45. Found: 479.55. Anal. Cacld for $C_{25}H_{20}F_3N_5O_2$: C, 62.63; H,4.20; N, 14.69. Found: C, 62.64; H, 4.24; N,14.72%.

1-((1-(3-Fluorobenzyl)-1*H*-1,2,3-triazol-4-yl) methyl)-5-methoxy-3-phenyl-1*H*-benzo[d]imidazol-2(3*H*)-one, IVh: Yield 81%. m.p. 192-194°C. IR (KBr): 1780-1775, 1400-1300 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.81 (s, 3H, OCH_3), 4.42 (s, 1H, CH_2), 5.61 (s, 2H, CH_2), 6.92 (m, 4H, Ar-H), 7.05 (s, 1H, Ar-H), 7.17 (m, 4H, Ar-H), 7.36 (m, 3H, Ar-H), 7.63 (s, 1H, Ar-H), 8.16 (s, 1H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 35.15, 50.43, 56.04, 102.83, 110.49, 113.66, 115.88, 123.95, 124.50, 125.93, 128.42, 129.49, 130.31, 135.94, 137.96, 138.73, 154.70, 158.29; MS: (M+H): *m*/*z* 429.45. Found: 429.16. Anal. Cacld for $C_{24}H_{20}FN_5O_2$: C, 67.12; H,4.69; N, 14.42. Found: C, 67.14; H, 4.44; N,14.46%.

1-((1-(2-Nitrobenzyl)-1*H*-1,2,3-triazol-4-yl) methyl)-5-methoxy-3-phenyl-1*H*-benzo[d]imidazol-2(3*H*)-one, IVi: Yield 75%. m.p. 195-196°C. IR (KBr): 1780-1775, 1440-1300 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.81 (s, 3H, OCH_3), 4.42 (s, 1H, CH_2), 5.17 (s, 2H, CH_2), 6.83 (m, 3H, Ar-H), 7.06 (s, 1H, Ar-H), 7.43 (m, 4H, Ar-H), 7.50 (m, 3H, Ar-H), 7.78 (s, 1H, Ar-H), 8.01 (s, 2H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 35.15, 50.81, 56.04, 102.83, 110.49, 113.06, 124.50, 125.93, 126.24, 126.83, 128.42, 129.65, 130.31, 130.68, 133.84, 134.20, 135.94, 138.73, 150.84, 154.70, 157.38; MS: (M+H): *m*/*z* 456.45. Found: 456.20. Anal. Cacld for $C_{24}H_{20}N_6O_4$: C, 63.15; H, 4.42; N, 18.41. Found: C, 63.19; H, 4.45; N,18.45%.

1-((1-(4-Iodobenzyl)-1*H*-1,2,3-triazol-4-yl)methyl)-5-methoxy-3-phenyl-1*H*-benzo[d]imidazol-2(3*H*)-one, IVj: Yield 72%. m.p. 193-195°C. IR (KBr): 1770-1760, 600-650 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.83 (s, 3H, OCH_3), 4.42 (s, 2H, CH_2), 5.28 (s, 2H, CH_2), 6.83 (m, 3H, Ar-H), 7.05 (s, 4H, Ar-H), 7.17 (m, 3H, Ar-H), 7.22 (s, 1H, Ar-H), 7.78 (s, 1H, Ar-H), 8.04 (s, 1H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 19.44, 35.15, 45.80, 56.04, 102.83, 110.49, 113.06, 124.50, 126.06, 126.39, 128.35, 129.65, 130.39, 135.94, 136.76, 138.73, 154.70, 157.38; MS: (M+H): *m*/*z* 537.35. Found: 537.07. Anal. Cacld for $C_{24}H_{20}IN_5O_2$; C, 53.65; H, 3.75; N, 13.03. Found: C, 53.68; H, 3.79; N, 13.05%.

1-((1-(3-Bromobenzyl)-1*H*-1,2,3-triazol-4-yl) methyl)-5-methoxy-3-phenyl-1*H*-benzo[d]imidazol-2(3*H*)-one, IVk: Yield 73%. m.p. 194-196°C. IR (KBr): 1775-1760, 650-700 cm^{-1}; ^{1}H NMR (100 MHz, DMSO-d_6): δ 3.83 (s, 3H, OCH_3), 5.42 (s, 2H, CH_2), 4.97 (d, *J*=3.2Hz, 2H, CH_2), 7.07 (t, *J*=7.4Hz, 4H, Ar-H), 7.29 (d, *J*=4.9, 3H, Ar-H), 7.46 (m, 4H, Ar-H), 8.23 (s, 2H, Ar-H); ^{13}C NMR

(100 MHz, DMSO-d_6): δ 35.15, 50.43, 56.04, 102.03, 110.49, 113.06, 124.50, 124.99, 125.93, 127.56, 128.42, 129.65, 130.50, 135.94, 138.73, 139.05, 154.70, 157.38; MS: (M+H): *m*/*z* 489.08. Found: 489.30. Anal. Cacld for $C_{24}H_{20}BrN_5O_2$: C, 58.79; H, 4.11; N, 14.28. Found: C, 58.82; H, 4.15; N,14.32%.

1-((1-(2-Hydroxybenzyl)-1*H*-1,2,3-triazol-4-yl) methyl)-5-methoxy-3-phenyl-1*H*-benzo[d]imidazol-2(3*H*)-one, IVl: Yield 76%. m.p. 196-198°C. IR (KBr): 1750-1740, 3550-3450 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.73 (s, 3H, OCH_3), 5.40 (s, 2H, CH_2), 5.0 (s, 1H, OH), 6.66 (m, 3H, Ar-H), 7.05 (m, 4H, Ar-H), 7.37 (m, 3H, Ar-H), 7.43 (m, 3H, Ar-H), 8.02 (s, 2H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 35.16, 50.43, 56.04, 102.83, 110.49, 113.06, 115.75, 121.56, 124.50, 125.93, 128.42, 129.65, 130.31, 131.42, 135.94, 137.21, 138.73, 154.70, 155.74, 157.38; MS: (M+H): *m*/*z* 427.16. Found: 427.47. Anal. Cacld for $C_{24}H_{21}N_5O_3$: C, 67.44; H, 4.95; N, 16.38. Found: C, 67.46; H, 4.98; N,16.40%.

1-((1-(3,5-Dimethylbenzyl)-1*H*-1,2,3-triazol-4-yl) methyl)-5-methoxy-3-phenyl-1*H*-benzo[d]imidazol-2(3*H*)-one, IVm: Yield 77%. m.p. 193-195°C. IR (KBr): 1760-1740, 3550-3450 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.91 (s, 6H, CH_3), 3.81 (s, 3H, OCH_3), 5.13 (s, 2H, CH_2), 5.04 (m, 2H, CH_2), 6.90 (m, 3H, Ar-H), 7.05 (m, 3H, Ar-H), 7.36 (m, 4H, Ar-H), 8.23 (s, 2H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 35.15, 50.17, 56.04, 102.03, 110.49, 113.06, 115.94, 124.58, 125.93, 126.51, 128.42, 129.59, 129.97, 130.31, 135.94, 138.73, 154.70, 156.76, 157.38; MS: (M+H): *m*/*z* 439.16. Found: 439.57. Anal. Cacld for $C_{26}H_{25}N_5O_2$: C, 71.05; H, 5.73; N, 15.93. Found: C, 71.09; H, 5.74; N,15.95%.

1-((1-(3,5-Dinitrobenzyl)-1*H*-1,2,3-triazol-4-yl) methyl)-5-methoxy-3-phenyl-1*H*-benzo[d]imidazol-2(3*H*)-one, IVn: Yield 72%. m.p. 183-185°C. IR (KBr): 1770-1760, 1570 – 1490 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.83 (s, 3H, OCH_3), 4.42 (s, 2H, CH_2), 5.01 (s, 2H, CH_2), 7.05 (m, 3H, Ar-H), 7.42 (m, 6H, Ar-H), 8.33 (m, 3H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 35.15, 50.99, 56.04, 102.03, 110.49, 113.03, 118.79, 124.50, 125.93, 128.38, 129.65, 130.31, 135.94, 136.82, 138.73, 145.02, 154.70, 157.38; MS: (M+H): *m*/*z* 501.14. Found: 501.45. Anal. Cacld for $C_{24}H_{19}N_7O_6$: C, 57.48; H, 3.82; N, 19.55. Found: C, 57.52; H, 3.85; N,19.57%.

3-((4-((1,2-Dihydro-6-methoxy-2-oxo-1-phenyl-benzo[d]imidazol-3-yl)methyl)-1*H*-1,2,3-triazol-1-yl)methyl)benzonitrile, IVo: Yield 75%. m.p. 186-187°C. IR (KBr): 1760-1740, 2280 – 2200 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.83 (s, 3H, OCH_3), 4.42 (s, 2H, CH_2), 5.47 (s, 2H, CH_2), 7.06 (m, 3H, Ar-H), 7.16 (m, 4H, Ar-H), 7.53 (m, 5H, Ar-H), 8.02 (s, 1H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 35.15, 50.43, 56.04, 102.83, 110.49, 113.06, 117.13, 119.29, 124.50, 125.93, 127.40, 128.42, 129.65, 130.01, 130.31, 131.24, 132.71, 135.94, 138.23, 138.73, 154.70, 157.38; MS: (M+H): *m*/*z* 436.16. Found: 436.47. Anal. Cacld for $C_{25}H_{20}N_6O_2$: C, 68.80; H, 4.62; N, 19.25. Found: C, 68.83; H, 4.65; N,19.27%.

1-((1-(3-Chloro-5-nitrobenzyl)-1*H*-1,2,3-triazol-4-yl)methyl)-5-methoxy-3-phenyl-1*H*-benzo[d] imidazol-2(3*H*)-one, IVp: Yield 76%. m.p. 186-187°C. IR (KBr): 1770-1765, 2280 – 2500, 600-550 cm^{-1}; (400 MHz, DMSO-d_6): δ 3.82 (s, 3H, OCH_3), 4.97 (s, 2H, CH_2), 5.05 (s, 2H, CH_2), 6.83 (m, 3H, Ar-H), 7.16 (m, 4H, Ar-H), 7.41 (m, 4H, Ar-H), 8.01 (s, 1H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 35.15, 50.99, 56.04, 102.03, 110.49, 113.06, 122.41, 123.19, 124.50, 125.93, 128.42, 129.65, 130.31, 134.19, 134.73, 135.94, 138.73, 140.95, 149.07, 154.70, 157.38; MS: (M+H): *m*/*z* 490.12. Found: 410.91. Anal. Cacld for $C_{24}H_{19}ClN_6O_4$: C, 58.72; H, 3.90; N, 17.12. Found: C, 58.75; H, 3.94; N,17.15%.

Conclusion

In conclusion, we present a novel, unambiguous synthesis of the title compound by click chemistry (Copper-Catalyzed Azide-Alkyne Cycloaddition (CuAAC)). And assessed for their anticancer activity. Compounds 1a and 1e had the highest IC_{50}values against the MCF-7 cell line, at 1.82 and 1.90 μM, respectively. Compounds IVb, c, and IVd exhibited promising activity against the MDA- MB-231 and Hela cell lines.

Supplementary Information

Supplementary information is available in the website http://nopr.niscpr.res.in/handle/123456789/58776.

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Conflict of Interest

Declaring that there are no potential conflicts of interest.

Supporting Information

^{1}H and ^{13}C NMRspectra and mass spectra of the synthesized compounds are provided in Supplementary Information. Supplementary information is available in the website http://nopr.niscpr.res.in/handle/123456789/58776.

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