INTRODUCTION

Malignant growth is a gathering of ailments including strange cell development with the possibility to attack or spread to different parts of the body. It is a critical and infamous disease in the present world. A dangerous development is a risky disease and but treatable if it is diagnosed at the beginning time. Now a days, various treatment procedures are available for cancer, some of them are surgery [1], radiation therapy [2], chemotherapy, immunotherapy, targeted therapy [3], hormone therapy and stem cell transplant. In light of the impediment of medical procedure and radiotherapy in affecting a solution for disease, chemotherapy has turned out to be progressively essential. Chemotherapy is the use of any drug to treat any disorder. It is the use of any drug to treat any disorder. In any case, to by far most, the word chemotherapy infers drugs used for ailment treatment [4]. Medicinal technique and radiation treatment oust, butcher or damage danger cells in a particular part, anyway chemo can work all through the whole body. This suggests chemo can slaughter harmful development cells that have spread (metastasized) to parts of the body a long way from the primary (fundamental) tumor. Thus, recognizing evidence of a novel solid, specific, and less destructive anticancer expert remains a champion among the most crushing challenges in primary medical care [5].

Antioxidant and molecular docking studies are basic procedures to discover new anticancer experts. Disease avoidance specialists are iotas, trademark or produced, outfitted for working together with free radicals and stopping their chain reactions before crucial essential particles are damaged [6]. The mixes having antioxidant and free radical rummaging properties are considered for use for the balancing activity or treatment of human diseases [7]. A couple of sicknesses, for instance, illness like Alzheimer and Parkinson can be progressed by free radicals [8]. Antioxidants go about as an important assurance against radical mediated noxious quality by getting the free radicals [9]. Molecular docking is a charming structure to appreciate quiet bimolecular correspondences for the rational medicine plan and discovery [10]. Molecular docking is the association of something like two particles to give a consistent adduct. The guideline focus of molecular docking is to achieve ligand-

A variety of amines have been employed to functionalize isobenzofuran-1,3-dione to obtain isoindoline-1,3-dione derivatives in the base free conditions. All the synthesized compounds are screened for their bioactivity through molecular docking, cytotoxicity (against HeLa) and antioxidant activity. ABTS and DPPH are employed to assess the antioxidant activity. Among the synthesized isoindoline-1,3-dione derivatives (3a-k), compound 3e has showed the best antioxidant activity and also exhibited better binding energy when docked with caspase-3 protein. Cytotoxicity of the synthesized compounds was studied against cervical cancer cell line (HeLa) and compound 3e has displayed better activity than other isoindoline derivatives.

Keywords: Isobenzofuran-1,3-dione, Isoindoline-1,3-dione, Molecular docking, Cytotoxicity, HeLa cell lines, Antioxidant activity.
receptor complex with upgraded adjustment and with the objective of having less confining free energy [10]. Various proteins and impetuses are used as targets or receptors in atomic docking.

The discovery and evaluation of organic compounds with a specific pharmacological activity is a necessary task in the drug development process. Among the large variety of organic compounds, heterocyclic compounds have been extensively studied due to their important pharmacological properties and applications [11]. Heterocyclic compounds display an array of interesting properties [12] and exploration of their potency is always worth investigating. Among divergent varieties of heterocyclic compounds, N-heterocyclic compounds [13] occupy centre stage due to their proven bioactivity. Isoindoline-1,3-diones [14] are a group of typical annulated N-heterocyclic compounds which have attracted much attention, in the recent past. They have been widely studied for their anticancer [15], antimicrobial [16], antioxidant [17], anti-inflammatory [18], antipsychotic [19], anticonvulsive [20] and antihypertensive [21] properties. Reports are also available on isoindoline-1,3-diones as enzyme inhibitor towards RS522 [22], cytotoxic activity [23] towards T47D cancer cell line and as a possible 15-lipooxygenase-1-inhibitor [24]. Owing to their interesting properties, isoindoline-1,3-diones are considered as the promising chemical entities whose potential is worth investigating.

All the synthesized isoindoline-1,3-dione derivatives were thoroughly analyzed and their structures are confirmed using FTIR, NMR (1H and 13C) and mass spectrosopy techniques. For all the synthesized compounds, molecular docking, antioxidant and cytotoxicity studies were carried out to evaluate their bioactivity.

**EXPERIMENTAL**

All the chemicals and reagents employed for the synthesis of isoindoline-1,3-dione derivatives (3a-k) were purchased from Sigma-Aldrich. All the reagents and solvents were obtained from Aldrich and used without further purification. Doxorubicin was purchased from Pfizer Pharma, India. ABTS was purchased from Nice chemicals Ltd., India. 1H and 13C NMR spectra were recorded on a Bruker FT-500 using tetramethylsilane (TMS) as an internal standard. The IR spectra were recorded on a Shimadzu FTIR spectrophotometer using KBr (4000-400 cm⁻¹). The compounds were purified by column chromatography using silica gel (100-200 mesh) and petroleum ether:ethyl acetate (7:3).

**Synthesis of isoindoline-1,3-dione derivatives (3a-k):**

To a solution of isobenzofuran-1,3-dione (1.48 g, 10 mmol) in methanol (4 mL/1 mmol) at room temperature was added aliphatic or aromatic amine (10 mmol) and the reaction mixture was refluxed at 65 ºC for 4 h. After completion of the reaction as indicated by the TLC, the reaction was cooled to room temperature and purified by column chromatography using petroleum ether:ethyl acetate (7:3).

**2-(4-(4-Aminobenzyl)phenyl)isoindoline-1,3-dione (3a):**

White solid; m.p.: > 300 ºC; yield: 1.968 g, 60 %; IR (KBr, νmax, cm⁻¹): 717 (C-H), 1373 (C-N), 1512 (C=C), 1720 (C=O); 1H NMR (500 MHz, DMSO-d₆): 7.91-8.10 (2H, Ar-phenolic), 7.6-7.7 (2H, Ar-phenolic), 6.3-7.8 (8H, Ar-benzene), 4.00 (2H, -NH₂), 3.33 (2H, CH₂). 13C NMR (125 MHz, DMSO-d₆): 127, 131 (6C, Ar-phenolic), 137, 130, 125 (3C, CN, C-CH₂, C-CH₃), 128.8, 128.4, 128.2, 124 (8C, Ar-benzene), 148 (1C, CNH₂), 54.1 (1C, CH₂), 167.5 (3C, C=O); MS (EI): m/z [M+H]+: Calcd. for C₁₅H₁₀N₂O₄: 282.2509; found: 282.2504.

**4-(1,3-dioxoisoindolin-2-yl) benzoic acid (3b):**

White solid; m.p.: 290 ºC; yield: 1.78 g, 67 %; IR (KBr, νmax, cm⁻¹): 713 (C-H), 1300 (C-N), 1378 (C=C), 1714 (C=O); 1H NMR (500 MHz, DMSO-d₆): 7.61-7.62 (2H, Ar-phenolic), 7.91-8.00 (2H, Ar-phenolic), 7.92-7.93 (2H, Ar-phenolic), 8.00-8.10 (2H, Ar-benzene), 8.10 (1H, OH); 13C NMR (125 MHz, DMSO-d₆): 127, 131, 130 (6C, Ar-phenolic), 146 (1C, CN), 121, 124, 135 (5C, Ar-benzene), 171, 167.12 (3C, C=O); MS (EI): m/z [M+H]+: Calcd. for C₁₅H₁₀N₂O₄: 282.3639; found: 282.3601.

**2-(Aminomethyl)isoindoline-1,3-dione (3c):**

White solid; m.p.: 190 ºC; yield: 1.31 g, 69 %; IR (KBr, νmax, cm⁻¹): 719 (C-H), 1316 (C-N), 1397 (C=C), 1709 (C=O), 3064 (C-H); 1H NMR (500 MHz, DMSO-d₆): 1.71 (2H, NH₂), 3.35, 3.85 (2H, NH₂). 13C NMR (125 MHz, DMSO-d₆): 36.7, 54.1 (2C, CH₂, CH₃), 123.5, 131.8, 134.9 (4C, Ar-phenolic), 168.2 (2C, C=O); MS (EI): m/z [M+H]+: Calcd. for C₁₅H₁₀N₂O₃: 267.0531; found: 267.0012.

**2-(Methyl-5-nitrophenyl)isoindoline-1,3-dione (3d):**

White solid; m.p.: 213 ºC; yield: 1.80 g, 64 %; IR (KBr, νmax, cm⁻¹): 788 (C-H), 1345 (C-N), 1544 (C=C), 1710 (C=O); 1H NMR (500 MHz, DMSO-d₆): 7.9-8.0 (2H, Ar-phenolic), 7.6-7.7 (2H, Ar-phenolic), 7.52-7.79 (2H, Ar-benzene), 8.4 (1H, Ar-benzene), 2.35 (3H, CH₃); 13C NMR (125 MHz, DMSO-d₆): 129, 131, 132 (6C, Ar-phenolic), 141 (1C, C-NO₂), 137 (1C, CN), 18.5 (1C, CH₂), 128, 130.0, 130.1 (3C, Ar-benzene), 139 (1C, C-CH₂), 167 (2C, C=O); MS (EI): m/z [M+H]+: Calcd. for C₁₅H₁₁N₂O₃: 282.4259; found: 282.4254.
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Ar-phthalic), 7.6-7.8 (2H, Ar-phthalic), 6.2-6.8 (2H, Ar-benzene), 7.6-7.9 (6H, Ar-benzene), 3.36 (2H, NH3); 13C NMR (125 MHz, DMSO-d6): 127, 131 (6C, Ar-phthalic), 142, 140, 130 (3C, CN, CS, SC), 128-7, 128.3, 128.2, 125 (8C, Ar-benzene), 154 (1C, CNH, C), 166 (2C, C=O); MS (EI): m/z [M+H]+: Calcd. for C30H23N2O5S: 378.4011; found: 378.4014.

2-Benzylisoindoline-1,3-dione (3f): White solid; m.p.: 115 °C, yield: 1.50 g, 63 %; IR (KBr, νmax, cm−1): 717 (C-H), 1329, 131 (6C, Ar-phthalic), 1381 (1C, H2C-N), 1450 (3H, Ar-benzene), 154, 124.1, 131, 135 (6C, Ar-phthalic), 139, 124.6 (2C, CN, C-COOH), 110, 110.3, 113 (3C, Ar-benzene), 166, 169 (3C, C=O), 146 (1C, C-NH), MS (EI): m/z [M+H]+: Calcd. for C14H9NO2: 223.0789; found: 223.0709.

2-(Pyridin-2-yl)isoindoline-1,3-dione (3g): White solid; yield: 1.40 g, 62 %; IR (KBr, νmax, cm−1): 781 (C-H), 1377 (C-N), 1454 (C-C), 1711 (C=O), 3045 (C-H); 1H NMR (500 MHz, DMSO-d6): 7.53-7.56 (3H, Ar-phthalic), 7.96-8.03 (2H, Ar-phthalic); 13C NMR (125 MHz, DMSO-d6): 132.5, 124.1, 139.1 (3C, Ar-benzene), 124.5, 131.8, 135.8 (6C, Ar-phthalic), 146.4, 149.8 (2C, C-N), 166.9 (2C, C=O); MS (EI): m/z [M+H]+: Calcd. for C14H10N2O4: 282.2509; found: 282.2504.

2-(4-Chlorophenyl)isoindoline-1,3-dione (3k): White solid; m.p.: 201 °C, yield: 1.80 g, 70 %; IR (KBr, νmax, cm−1): 708 (C-H), 1390 (C-N), 1491 (C=C), 1714 (C=O), 3067 (C-H); 1H NMR (500 MHz, DMSO-d6): 7.90-7.95 (2H, Ar-benzene), 7.50-7.55 (2H, Ar-benzene), 7.4-7.5 (2H, Ar-phthalic), 7.90-8.03 (2H, Ar-phthalic); 13CNMR (125 MHz, DMSO-d6): 123.5, 128.4 (4C, Ar-benzene), 127.8, 132.0, 132.3 (6C, Ar-phthalic), 129.5 (1C, C-Cl), 135.1 (1C, C-N), 167.5 (2C, C=O); MS (EI): m/z [M+H]+: Calcd. for C13H9ClN2O2: 257.0249; found: 257.0214.

Molecular docking studies: Three dimensional structure of Caspase-3 was found as a complex with Y195A showed in Fig. 1. This was retrieved from the PDB (Protein Data Bank). Caspase-3 [25] receptor was docked with different ligands (3a-k) standard) using Hex 8.0.0 docking software [26,27]. It is an interactive Molecular Graphics Program that calculates and displays possible docking modes of pairs of protein and DNA molecules and also analyzes protein-ligand docking. Hex docking was carried out by setting appropriate parameters such as twist range-360, grid dimension-0.6 and distance range-40 and correlation type of shape complementarily and electrostatics. The binding energy of the compounds 3a-k and the caspase inhibitor III (standard) has been tabulated.

In vitro Antioxidant activity: The compounds 3a-k were tested for in vitro antioxidant activity by DPPH and ABTS methods.

Fig. 1. (a) HeLa cell line protein Caspase-3 complex with Y195A retrieved from PDB (PDB ID: 4QTX) (b) The 2D structure of Caspase Inhibitor III retrieved from PDB
**RESULTS AND DISCUSSION**

Isoindoline-1,3-dione derivatives were synthesized from isobenzofuran-1,3-dione in the absence of a base or a Lewis acid. For the preparation of desired isoindoline-1,3-dione derivatives a variety of aliphatic and aromatic amines have been employed and the reaction was carried out by refluxing in methanol for 4 h (Scheme-I). A tedious workup procedure is required to remove the base from the reaction mixture. In order to circumvent the workup procedure, a base-free method was adopted for the synthesis of isoindoline-1,3-dione derivatives. Reaction optimization was carried out to select the suitable solvent and the results are tabulated in Table-1. It is clear that the reactions carried out in halogenated solvents resulted in poor yields, whereas methanol and ethanol are found to be the preferred choice of solvents for this chemical transformation. Further, methanol was selected over ethanol due to its low boiling point, which makes it easier to evaporate it after the completion of reaction. After reaction optimization, isobenzofuran-1,3-dione was subjected to reaction with a variety of amines and the results are shown in Table-2. It was observed that even under the slightly altered reaction conditions, the desired products are formed smoothly and in good yields. Aliphatic amines, substituted aromatic as well as heterocyclic amines functionalized isobenzofuran-1,3-dione to give isoindoline-1,3-dione derivatives. All the synthesized compounds were thoroughly analyzed and their structures are confirmed using FTIR, NMR (¹H and ¹³C), and mass spectroscopy techniques.

**Synthesis of isoindoline-1,3-dione derivatives**

**TABLE-I**

| Entry | Solvent          | Yield (%) |
|-------|------------------|-----------|
| 1     | Dichloromethane  | 20        |
| 2     | Chloroform       | 18        |
| 3     | Tetrahydrofuran  | 37        |
| 4     | Acetone          | 65        |
| 5     | Methanol         | 71        |
| 6     | Ethanol          | 68        |
| 7     | Isopropyl alcohol| 57        |
| 8     | Toluene          | 48        |

*Yield corresponding to the isolated product either by column chromatography or recrystallization.

**Molecular docking studies:** Bioinformatics is ascending as a basic gadget in the field of pharmaceutical and prescription improvement with the colossal unconstrained formation of APL. Caspase (cysteine aspartic protease) is a family of protease enzymes...
| Entry | Substrate 1 | Amine 2   | Product 3     | Yield<sup>b</sup> |
|-------|-------------|-----------|---------------|------------------|
| a     |             | H<sub>2</sub>N-Ph-Ph-N<sub>2</sub> | N<sub>2</sub>O-Ph-Ph-N<sub>2</sub> | 60               |
| b     |             | H<sub>2</sub>N-Ph-OH | N<sub>2</sub>O-Ph-COOH | 67               |
| c     |             | H<sub>2</sub>N-NH<sub>2</sub> | N<sub>2</sub>O-Ph-NH<sub>2</sub> | 69               |
| d     |             | H<sub>3</sub>C-Ph-N<sub>2</sub> | N<sub>2</sub>O-Ph-CH<sub>3</sub>N<sub>2</sub> | 64               |
| e     |             | H<sub>2</sub>N-Ph-SO<sub>2</sub>-Ph-N<sub>2</sub> | N<sub>2</sub>O-Ph-SO<sub>2</sub>-Ph-NH<sub>2</sub> | 64               |
| f     |             | H<sub>2</sub>N-Ph | N<sub>2</sub>O-Ph-Ph | 63               |
| g     |             | H<sub>2</sub>N-Py | N<sub>2</sub>O-Py | 62               |
| h     |             | H<sub>2</sub>N-Ph | N<sub>2</sub>O-Ph | 71               |
| i     |             | H<sub>2</sub>N-Ph | N<sub>2</sub>O-Ph | 60               |
| j     |             | H<sub>2</sub>N-Ph-COOH | N<sub>2</sub>O-Ph-COOH | 65               |
playing essential roles in programmed cell death (including apoptosis, pyroptosis and necroptosis) and inflammation. Caspase-3 has been found to be necessary for normal brain development as well as its typical role in apoptosis, where it is responsible for chromatin condensation and DNA fragmentation [35].

All the synthesized compounds 3a-k were defined as ligands and the molecular docking was performed using caspase-3 as a receptor in Hex 8.0.0 software. After molecular docking, calculated binding free energies (Kcal/mol) were observed for each ligand (Table-3). The comparison of binding free energies shows that compound 3e has the best interaction with caspase-3 (Fig. 2). Higher the negative $E_{\text{total}}$ value, stronger is the interaction between ligand and receptor, which leads to activation of receptors. The compound 3g displayed hydrogen bond interactions with the active site of the protein as showed in Fig. 3.

Among eleven isoindoline-1,3-dione derivatives, compounds

| Compd. | Hela cell line protein (Receptor) | Docking score $E_{\text{total}}$ value (KJ/mol) | $E_{\text{shape}}$ (energy content of the protein) | $E_{\text{force}}$ (binding energy of ligand) |
|--------|---------------------------------|---------------------------------------------|---------------------------------------------|---------------------------------------------|
| 3a     | Casepase-3                      | -249.3                                      | -249.3                                      | 0.0                                         |
| 3b     | Casepase-3                      | -212.6                                      | -212.6                                      | 0.0                                         |
| 3c     | Casepase-3                      | -193.7                                      | -193.7                                      | 0.0                                         |
| 3d     | Casepase-3                      | -234.7                                      | -234.7                                      | 0.0                                         |
| 3e     | Casepase-3                      | -291.6                                      | -291.6                                      | 0.0                                         |
| 3f     | Casepase-3                      | -210.3                                      | -210.3                                      | 0.0                                         |
| 3g     | Casepase-3                      | -216.7                                      | -194.5                                      | -22.2                                       |
| 3h     | Casepase-3                      | -229.7                                      | -229.7                                      | 0.0                                         |
| 3i     | Casepase-3                      | -179.2                                      | -179.2                                      | 0.0                                         |
| 3j     | Casepase-3                      | -229.0                                      | -229.0                                      | 0.0                                         |
| 3k     | Casepase-3                      | -260.6                                      | -260.6                                      | 0.0                                         |
| Standard | Casepase-3                    | -320.3                                      | -320.3                                      | 0.0                                         |

Fig. 2. Compound 3e interaction with caspase-3 receptor

Fig. 3. Compound 3g interaction with caspase-3 receptor
3c and 3k have the best binding energy of -291.6 KJ/mol and -260.0 KJ/mol, respectively, which is close to the binding energy of standard [caspase inhibitor III (-320.3 KJ/mol)]. The compound 3g showed hydrogen bond interactions to the active site of protein. This molecular docking gives accurate understanding for ligand and receptor binding interaction, which can be employed for developing new drugs against cancer.

**in vitro Antioxidant activity:** The antioxidant properties of these compounds were evaluated by two different *in vitro* methods namely, DPPH radical scavenging activity and ABTS radical scavenging activity. The DPPH and ABTS scavenging activities of all the synthesized compounds was screened at different concentrations by dissolving the compounds in methanol.

**DPPH radical scavenging activity:** The activity was assessed by measuring its electron donating ability to DPPH, which was indicated by changes in absorbance of the solution of different concentrations at 517 nm. All the synthesized derivatives (3a-k) exhibited increased DPPH inhibitory percentage with the increase in concentration of standard antioxidants as shown in Fig. 4. It is understood that the lower the absorbance of the reaction mixture, the higher is the free radical scavenging activity. Among all the analyzed compounds, compound 3e have exhibited the highest inhibition (92 %) and the other compounds have shown inhibition in the range of 58-80 % at a concentration of 5 mM during the time duration of 90 min. The IC50 values of compounds 3a-k scavenging DPPH radical is presented in Table-4 and the results show that the compound 3e has better DPPH radical activity (IC50 1.74 mM) than the other synthesized compounds. It can be seen from Table-4 that compounds 3a, 3c and 3h also have better scavenging activity (IC50) on DPPH radical. The compound 3g shows less scavenging activity (IC50 4.75 mM).

**ABTS radical scavenging activity:** The antioxidant property of the tested samples was evaluated at different concentrations. From Fig. 5, it was clear that all the isoindoline-1,3-dione derivatives (3a-k) exhibited increased ABTS inhibitory percentage with the increase in concentration of standard antioxidants. Hence, it was assumed that they should be able to donate electrons to free radicals in the actual biological system. Among all the tested antioxidants, compound 3e has exhibited the highest inhibition of 96 % and other compounds showed inhibition in the range of 58-82 % at a concentration of 5 mM during the time duration of 90 min. The IC50 values of compounds 3a-k scavenging ABTS radical is presented in Table-4 and the results showed that the compound 3e has better ABTS radical activity (IC50: 1.69 mM) than the other synthesized compounds. It can be seen from Table-4 that compounds 3a, 3c and 3h also have better scavenging activity (IC50) on ABTS radical. The compound 3g shows less scavenging activity (IC50: 4.68 mM).

**TABLE-4**

| Compound | DPPH assay | Mean | 30 min | 60 min | 90 min |
|----------|------------|------|--------|--------|--------|
| 3a       | 4.59       |      | 2.78   | 2.65   | 3.34   |
| 3b       | 4.92       |      | 4.41   | 4.28   | 4.53   |
| 3c       | 2.93       |      | 2.84   | 2.80   | 2.85   |
| 3d       | 4.91       |      | 4.69   | 4.28   | 4.62   |
| 3e       | 1.96       |      | 1.80   | 1.74   | 1.83   |
| 3f       | 5.00       |      | 4.80   | 4.63   | 4.81   |
| 3g       | 4.89       |      | 4.78   | 4.75   | 4.80   |
| 3h       | 3.64       |      | 2.99   | 1.85   | 2.82   |
| 3i       | 5.00       |      | 4.23   | 4.06   | 4.43   |
| 3j       | 4.81       |      | 4.00   | 3.62   | 4.14   |
| 3k       | 4.28       |      | 3.81   | 3.71   | 3.93   |

| Compound | ABTS assay | Mean | 30 min | 60 min | 90 min |
|----------|------------|------|--------|--------|--------|
| 3a       | 4.53       |      | 2.75   | 2.63   | 3.30   |
| 3b       | 4.94       |      | 4.30   | 4.23   | 4.49   |
| 3c       | 2.92       |      | 2.75   | 2.70   | 2.79   |
| 3d       | 4.94       |      | 4.70   | 4.30   | 4.64   |
| 3e       | 2.00       |      | 1.78   | 1.69   | 1.82   |
| 3f       | 5.00       |      | 4.76   | 4.66   | 4.80   |
| 3g       | 4.86       |      | 4.70   | 4.68   | 4.74   |
| 3h       | 3.60       |      | 2.95   | 1.80   | 2.78   |
| 3i       | 5.00       |      | 4.20   | 4.02   | 4.40   |
| 3j       | 4.76       |      | 3.98   | 3.63   | 4.12   |
| 3k       | 4.20       |      | 3.80   | 3.61   | 3.87   |
in vitro Cytotoxicity activity: The compounds 3a-k was screened for in vitro cytotoxicity against human cervical cancer cell line (HeLa) using the MTT assay. Doxorubicin was used as the standard drug in this assay. All the analyzed compounds (3a-k) exhibited inhibition (cytotoxicity) activity on HeLa cells. At a concentration of 6 µg/mL, no cytotoxic effect was observed when tested against the cells (cells survival were more than 90 %); but at a concentration of 85 µg/mL, the compounds were effective on Hela cells. The compound 3e has exhibited the maximum inhibition (91 %) at a concentration of 85 µg/mL and its viability was 09 % as shown in Fig. 6c. Doxorubicin has exhibited an inhibition of 84 % and viability of 16 % at the same concentration of 85 µg/mL. Compounds 3a, 3b, 3d, 3f, 3g, 3i, 3j and 3k displayed better inhibition percentage than the standard drug in the used concentration of 85 µg/mL. The result of cytotoxic activity was expressed in terms of half-inhibition concentration (IC50), which denotes the concentration required to inhibit 50 % of Hela cells. The IC50 value of compound 3e shows better results (IC50: 20 µg/mL) than the other compounds. Compounds 3a, 3b, 3d and 3k show better IC50 values than the standard drug doxorubicin as seen in Table-5.

| Compound | IC50 (µg/mL) | Compound | IC50 (µg/mL) |
|----------|-------------|----------|-------------|
| 3a       | 22.5        | 3g       | 32.3        |
| 3b       | 23.2        | 3h       | 42.0        |
| 3c       | 42.6        | 3i       | 32.0        |
| 3d       | 22.4        | 3j       | 40.3        |
| 3e       | 20.0        | 3k       | 22.4        |
| 3f       | 36.8        | Doxorubicin | 26.4        |

Conclusion

A series of isindoline-1,3-dione derivatives (3a-k) have been synthesized in the base free conditions with appreciable yields. The synthesized compounds were screened for their in vitro antioxidant activity employing the DPPH and ABTS methods. In this screening, compound 3e exhibited better inhibition efficiency in DPPH and ABTS methods. Among the studied compounds, 3e was the one with the best binding energy of -291.6 Kcal/mol which is close to the binding energy of the standard. The entire set of compounds was also evaluated for their in vitro cytotoxicity against human cervical cancer cell line (HeLa). All the synthesized compounds exhibited inhibition (cytotoxicity) against HeLa cells and compound 3e exhibited the maximum inhibition and its viability was 9 %. Compounds 3a, 3b, 3d and 3k show better IC50 values than the standard drug doxorubicin. Some drugs are available for treating cancer cells, there is still a need for safe and effective drugs. Therefore, the synthesized fluorescein derivatives and phenolphthalein derivatives might turn out to be a potential lead for the development of drug molecules having cytotoxicity activity.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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