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# DESIGN, SYNTHESIS, CHARACTERIZATION, MOLECULAR DOCKING STUDIES AND BIOLOGICAL EVALUATION OF BENZIMIDAZOLE CONTAINING 4H-CHROMEN-4-ONE DERIVATIVES

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## ❖ ABSTRACT

Benzimidazole is an interesting pharmacophore which has been extensively studied in medicinal chemistry due to its high affinity towards various enzymes and receptors. Its derivatives have been previously shown to possess a wide range of biological activities including anthelmintic, antihypertensive, antiulcer, as well as anticholinesterase activity. Benzimidazole rings are the most important nitrogen-containing heterocycles, which are widely explored and utilized by the pharmaceutical industry for drug discovery. Due to their special structural features and electron-rich environment, Benzimidazole containing drugs bind to a variety of therapeutic targets, thereby exhibiting a broad spectrum of bioactivities. Numerous benzimidazole based drugs have been extensively used in the clinic to treat various types of diseases with high therapeutic potential. The present study focuses on the design and synthesize of a novel class of (E)-2-(2-(5-nitro-1H-benzo[d]imidazol-2-yl)vinyl)-4H-chromen-4-one derivatives and the characterization was done using IR, 1H NMR, 13C NMR, and mass spectroscopy. Further these novel set of compounds were screened for various pharmacological activities.

**KEYWORDS:** IR, 1H NMR, 13C NMR, and mass spectroscopy.

## ❖ INTRODUCTION

Benzimidazole rings are the most important nitrogen-containing heterocycles, which are widely explored and utilized by the pharmaceutical industry for drug discovery. Due to their special structural features and electron-rich environment, Benzimidazole containing drugs bind to a variety of therapeutic targets, thereby exhibiting a broad spectrum of bioactivities. Numerous benzimidazole based drugs have been extensively used in the clinic to treat various types of diseases with high therapeutic potential. Benzimidazole derivatives play important role in medical field with so many Pharmacological activities such as antimicrobial, antiviral, antidiabetic and anticancer activity. The potency of these clinically useful drugs in treatment of microbial infections and other activities encouraged the development of some more potent and significant compounds.

Benzimidazoles are remarkably effective compounds, extensive biochemical and pharmacological studies have confirmed that these molecules are effective against various strains of microorganisms. Due to their enormous medicinal value, the research and development of benzimidazole-containing drugs is an increasingly active and attractive topic of medicinal chemistry. This review enlightens about the chemistry of different derivatives of substituted benzimidazoles along with their pharmacological activities. Antimicrobial agents / Antibiotics are antibacterial substances produced by various species of micro-organism (bacteria, fungi, and actionomycetes) that suppress the growth of other micro-organisms. They have been designed to inhibit or kill the infecting organism without having measurable effect on the recipient.

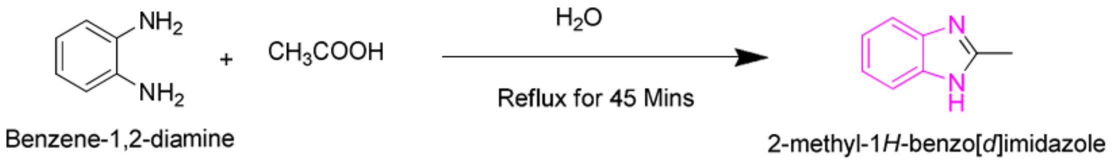
The present study deals with designing of some novel class of (E)-2-(2-(5-nitro-1H-benzo[d]imidazol-2-yl)vinyl)-4H- chromen-4-one Derivatives were synthesized by using of 2-methyl-1H-benzo[d]imidazole, substituted chromone-3-carbaldehyde in presence of GAA. The purity of synthesized compounds was confirmed by Melting Point and TLC using Ethyl Acetate: Petroleum Ether (50:50) as solvent system. The structures of synthesized compounds were confirmed by **FT-IR, $^{1}$H-NMR, $^{13}$C-NMR** and **Mass spectral analysis** the result was correlate The docking study of the synthesized compound was carried out by using **AUTODOCK** software. The synthesized compound were also evaluated for their *in-vitro* anticancer activity by SRB assay method against Human Cancer Cell line A-549.

## ❖ MATERIALS AND METHODS

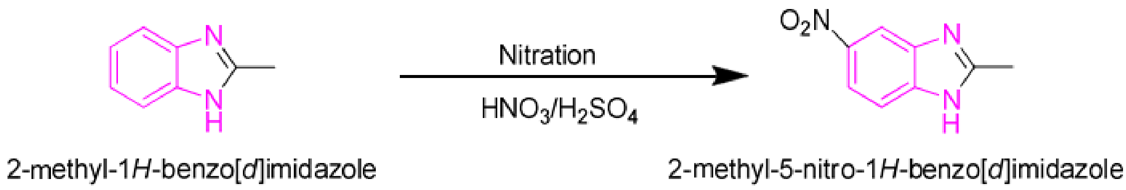
Melting point was determined in capillary tubes and is uncorrected. IR spectra were taken as KBr pellets for solids on Perkin Elmer Spectrum FT-IR. 1H NMR (400MHz) and 13C NMR (100 MHz) spectra were recorded in DMSO-d6 solution with TMS as an internal standard on Bruker instrument. Spin multiplicities are given as s (singlet), d (doublet), t (triplet) and m (multiplet). Coupling constant (J) is given in hertz. Mass spectra were recorded on a thermo Finnigan LCQ Advantage MAX 6000 ESI spectrometer.

**Procedure for the synthesis of title compounds**

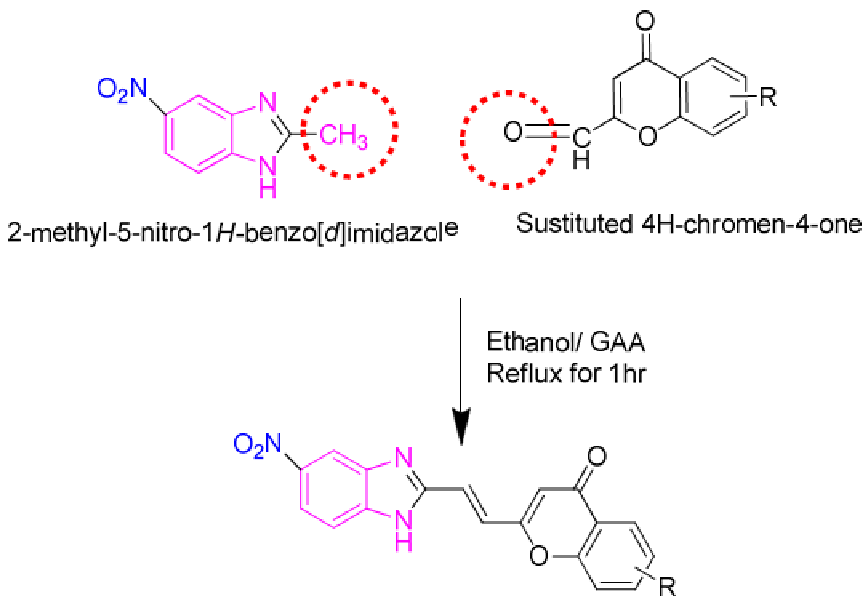
**Step 1:** Synthesis of 2-methyl-1H-benzo[d]imidazole- Place 5.43g of o-phenylene diamine, 20ml of water and 5.4g of acetic acid in RBF. Reflux in a water bath for 45 minutes. Cool and add 10% ammonia solution slowly with constant shaking. Filter the precipitated product. Recrystallize it from 10% aqueous ethanol and activated charcoal.




**Step 2:** 2-methyl-5-nitro-1H-benzo[d]imidazole- 2-methyl-1H-benzo[d]imidazole adds 5 mL of Con. $HNO_3$, 5 mL of Con $H_2SO_4$ and reflux for 30 mins. After that pour the reaction mixture into cold water and shack vigorously. The yellow colour of 2-methyl-5-nitro-1H-benzo[d]imidazole was precipitated out.



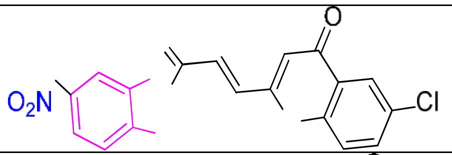
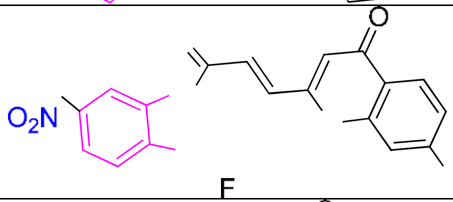
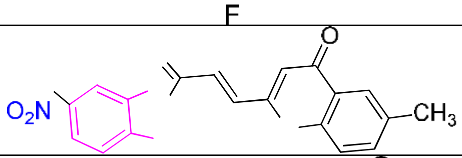
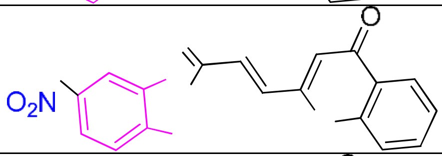
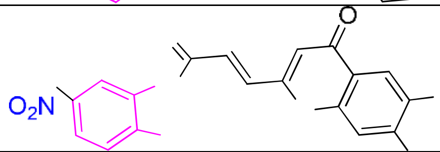
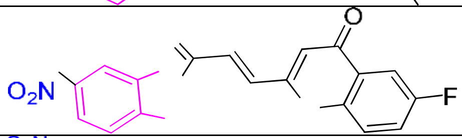
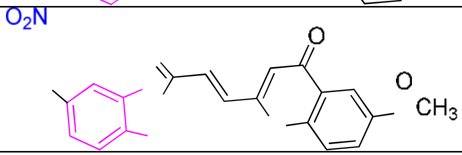
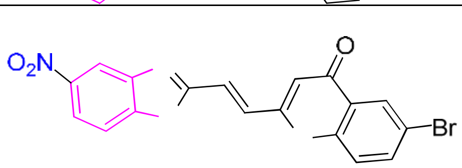

**Step 3:** (E)-2-(2-(5-nitro-1H-benzo[d]imidazol-2-yl)vinyl)-4H-chromen-4-one Derivatives- 1mmole of 2-methyl-1H-benzo[d]imidazole and add 1mmole of various substituted chromen 3 carboldehyde dissolved in ethanol. Add 10 mL of Glacial Acetic acid and reflux for 1 hr. The completion of reaction monitor by using TLC using ethyl acetate andpetroleum ether (50:50) as mobile phase. Upon completion of reaction, the reaction mixture was filtered, washed with acetic acid or ethanol and dry using vacuum.




(E)-2-(2-(5-nitro-1H-benzo[d]imidazol-2-yl)vinyl)-4H-chromen-4-one Derivatives

| Sr. No | Compound code | R |
|---|---|---|
| 1 | R1 | 6-Cl |
| 2 | R2 | 7-F |
| 3 | R3 | 6-CH3 |
| 4 | R4 | -H |
| 5 | R5 | 6,7-Cl |
| 6 | R6 | 6-F |
| 7 | R7 | 6-OCH3 |
| 8 | R8 | 6-Br |

**Table 1: Physico-chemical properties of synthesized compound.**

| Comp. | Structure | Mol. Formula | | Melting Point | Appearance |
|---|---|---|---|---|---|
| R1 |  | C18H10Cl N3O4 | 367 | 218-220$^0$C | Orange solid |
| R2 |  | C18H10F N3O4 | 351 | 210-212$^0$C | Yellow solid |
| R3 |  | C19H13N 3O4 | 347 | 200-202$^0$C | Orange solid |
| R4 |  | C18H11N 3O4 | 333 | 220-222$^0$C | Orange solid |
| R5 |  | C18H9Cl2 N3O4 | 402 | 220-222$^0$C | Orange solid |
| R6 |  | C18H10F N3O4 | 351 | 219-221$^0$C | Orange solid |
| R7 |  | C19H13N 3O5 | 363 | 216-218$^0$C | Orange solid |
| R8 |  | C18H10B rN3O4 | 412 | 218-220$^0$C | Orange solid |

➢ **Spectral data of synthesized compounds**

- **R1: (E)-6-chloro-2-(2-(5-nitro-1H-benzo[d] imidazol -2-yl)vinyl)-4H-chromen-4-one**

$^1$**H NMR**- (400 MHz, DMSO) δ 8.39 (s, 1H), 8.07 (d, J = 7.1 Hz, 1H), 8.10 (m, 2H), 7.86 – 7.77 (m, 3H) 6.39 – 6.37 (d, 1H), 6.65 (s, 1H), 5.0 (s, NH).

$^{13}$**NMR** (101 MHz, DMSO) δ 178.5, 163.2, 155.3, 144.3, 145.0, 141.5, 139.8, 136.4, 145.0, 130. 6, 129.0, 128.8, 125.5, 125.3, 119.6, 118.6, 116.1, 112.2.

**IR (KBr):** 3158, 3095, 1634, 1644, 724; ESI-MS: m/z 367.74;

**Elemental Analysis:** C, 58.79; H, 2.74; Cl, 9.64; N, 11.43; O, 17.40.

- **R2: (E)-7-fluoro-2-(2-(5-nitro-1H-benzo[d]imidazol-2-yl)vinyl)-4H-chromen-4-one**

**$^1$H NMR** (400 MHz, DMSO) δ 8.39 (s,1H), 8.17 (d, *J* = 7.1 Hz, 1H), 8.10 (m, 2H), 7.56 7.67 (m, 3H) 6.36 – 6.31 (d, 1H),6.65 (s, 1H), 5.0 (s, NH).
**$^{13}$NMR** (101 MHz, DMSO) δ 178.5, 163.2, 155.3, 144.3, 145.0, 141.5, 139.8, 136.4, 145.0, 130. 6, 128.7, 128.8, 125.5, 125.3, 119.6, 117.6, 116.1, 111.2.
**IR (KBr):** 3157, 3095, 1644, 1317, 1124, 824, 726; ESI-MS: m/z 351;
**Elemental Analysis:** C, 61.54; H, 2.87; F, 5.41; N, 11.96; O, 18.22.

- **R3 : (E)-6-methyl-2-(2-(5-nitro-1H-benzo[d]imidazol-2-yl)vinyl)-4H-chromen-4- one**

**$^1$H NMR** (400 MHz, DMSO) δ 8.29 (s, 1H), 8.07 (d, J = 7.1 Hz, 1H), 8.10 (m, 2H), 7.56 – 7.67 (m, 3H) 6.36 – 6.31 (d, 1H), 6.65 (s,1H), 5.0 (s, NH), 2.33 (T, 3H).
**$^{13}$NMR** (101 MHz, DMSO) δ 178.5, 163.2, 155.3, 144.3, 145.0, 141.5, 139.8, 136.4, 145.0, 130. 6, 128.7, 128.8, 125.5, 125.3, 119.6, 117.6, 116.1,111.2. 20.98.
**IR (KBr):** 3158, 3095, 2940, 1644, 1435, 1374, 834, 637; ESI-MS: m/z 347;
**Elemental Analysis:** C, 65.70; H, 3.77; N, 12.10; O, 18.43.

- **R4 : (E)-2-(2-(5-nitro-1H-benzo[d]imidazol-2-yl)vinyl)-4H-chromen-4-one**

**$^1$H NMR** (400 MHz, DMSO) δ 8.29 (s, 2H), 8.07 (d, J = 7.1 Hz, 2H), 8.10 (m, 2H), 7.67 (s, 1H), 7.56 – 7.47 (m, 4H), 6.36 – 6.31 (d,2H), 6.65 (s, 2H), 5.0 (s, NH),.
**$^{13}$NMR** (101 MHz, DMSO) δ 178.5, 163.2, 155.3, 144.3, 145.0, 141.5, 139.8, 136.4, 145.0, 130.6, 128.7, 128.8, 125.5, 125.3, 119.6, 118.2, 115.90, 111.2.
**IR (KBr):** 3159, 1641, 1499, 1215, 824, 725, 637; ESI-MS: m/z 333;
**Elemental Analysis:** C, 64.86; H, 3.33; N, 12.61; O, 19.20.

- **R5 : (E)-6,7-dichloro-2-(2-(5-nitro-1H-benzo[d]imidazol-2-yl)vinyl)-4H-chromen- 4-one**

**$^1$H NMR** (400 MHz, DMSO) δ 8.49 (s, 2H), 8.37 (d, J = 7.1 Hz, 2H), 8.14 (m, 2H), 7.77 (s, 1H), 7.46 – 7.37 (m, 3H), 6.36 – 6.31 (d,2H), 6.55 (s, 2H), 5.2 (s, NH).
**$^{13}$NMR** (101 MHz, DMSO) δ 178.5, 163.2, 155.3, 144.3, 145.0, 141.5, 139.8, 136.4, 145.0, 130. 6, 128.7, 128.8, 125.5, 125.3, 119.6, 118.2, 115.90, 115.2.
**IR (KBr):** 1644, 1468, 1336, 824, 725, 637; ESI-MS: m/z 402;
**Elemental Analysis:** C, 53.75; H, 2.26; Cl, 17.63; N, 10.45; O, 15.91.

- **R6 : (E)-6-fluoro-2-(2-(5-nitro-1H-benzo[d]imidazol-2-yl)vinyl)-4H-chromen-4-one**

**$^1$H NMR** (400 MHz, DMSO) δ 8.39 (s, 1H), 8.17 (d, J = 7.1 Hz, 1H), 8.10 (m, 2H), 7.56 – 7.67 (m, 3H) 6.36 – 6.31 (d, 1H), 6.65 (s, 1H), 5.0 (s, NH).
**$^{13}$NMR** (101 MHz, DMSO) δ 178.5, 163.2, 155.3, 144.3, 145.0, 141.5, 139.8, 136.4, 145.0, 130. 6, 128.7, 128.8, 125.5, 125.3, 119.6, 117.6, 116.1, 111.2.
**IR (KBr):** 3157, 3095, 1644, 1317, 1124, 824, 726; ESI-MS: m/z 351;
**Elemental Analysis:** C, 61.54; H, 2.87; F, 5.41; N, 11.96; O, 18.22.

- **R7: (E)-6-methoxy-2-(2-(5-nitro-1H-benzo[d]imidazol-2-yl)vinyl)-4H-chromen-4- one**

**$^1$H NMR** (400 MHz, DMSO) δ 8.39 (s, 1H), 8.17 (d, J = 7.1 Hz, 1H), 8.10 (m, 2H), 7.56 – 7.67 (m, 3H) 6.36 – 6.31 (d, 1H), 6.65 (s,2H), 5.0 (s, NH) 3.90 (m, 3H).
**$^{13}$NMR** (101 MHz, DMSO) δ 178.5, 163.2, 155.3, 144.3, 145.0, 141.5, 139.8, 136.4, 145.0, 130. 6, 128.7, 128.8, 125.5, 125.3, 119.6, 117.6, 116.1, 111.2.
**IR (KBr):** 3157, 3011, 2980, 2927, 1644, 1574, 1156, 1317, 937, 637; ESI-MS:m/z 363;
**Elemental Analysis:** C, 62.81; H, 3.61; N, 11.57; O, 22.02.

- **R8 : (E)-6-bromo-2-(2-(5-nitro-1H-benzo[d]imidazol-2-yl)vinyl)-4H-chromen-4- one**

**$^1$H NMR** (400 MHz, DMSO) δ 8.49 (s, 1H), 8.27 (d, J = 7.1 Hz, 1H), 8.20 (m, 2H), 7.56 – 7.67 (m, 3H) 6.36 – 6.31 (d, 1H), 6.65 (s, 1H), 5.0 (s, NH).
**$^{13}$NMR** (101 MHz, DMSO) δ 179.01, 163.2, 155.3, 144.3, 145.0, 141.5, 139.8, 136.4, 145.0, 130. 6, 128.7, 128.8, 125.5, 125.3, 119.6, 117.6, 116.1, 111.2**.**
**IR (KBr):** 3157, 3095, 1644, 1317, 1124, 824, 726; ESI-MS: m/z 412;
**Elemental Analysis:** C, 52.45; H, 2.45; Br, 19.39; N, 10.19; O, 15.53.

## ❖ Biological Evaluation

### Anticancer activity

The cell lines were grown in RPMI 1640 medium containing 10% fetal bovineserum and 2 mM L-glutamine. For present screening experiment, cells were inoculated into 96 well microtiter plates in 100 μ L at plating densities as shown in the study details above, depending on the doubling time of individual cell lines. After cell inoculation, the microtiter plates were incubated at 37° C, 5 % CO2, 95 % air and 100 % relative humidity for 24 h prior to addition of experimental drugs. Experimental drugs were initially solubilize in dimethyl sulfoxide at 100mg/ml and diluted to 1mg/ml using water and stored frozen prior to use. At the time of drug addition, an aliquote of frozen concentrate (1mg/ml) was thawed and diluted to 100 μg/ml, 200 μg/ml, 400 μg/ml and 800 μg/ml with complete medium containing test article. Aliquots of 10 μl of these different drug dilutions were added to the appropriate micro titer wells already containing 90 μl of medium, resulting in the required final drug concentrations i.e.10 μg/ml, 20 μg/ml, 40 μg/ml, 80 μg/ml. After compound addition, plates were incubated at standard conditions for 48 hours and assay was terminated by the addition of cold TCA. Cells were fixed in situ by the gentle addition of 50 μl of cold 30 % (w/v)

TCA (final concentration, 10 % TCA) and incubated for 60 minutes at 4°C. The supernatant was discarded; the plates were washed five times with tap water and air dried. Sulforhodamine B (SRB) solution (50 µl) at 0.4 % (w/v) in 1 % acetic acid was added to each of the wells, and plates were incubated for 20 minutes at room temperature. After staining, unbound dye was recovered and the residual dye was removed by washing five times with 1 % acetic acid. The plates were air dried. Bound stain was subsequently eluted with 10 mM trizma base, and the absorbance was read on an plate reader at a wavelength of 540 nm with 690 nm reference wavelength.

Percent growth was calculated on a plate-by-plate basis for test wells relative to control wells. Percent Growth was expressed as the ratio of average absorbance of the test well to the average absorbance of the control wells * 100.

Using the six absorbance measurements [time zero (Tz), control growth (C), and test growth in the presence of drug at the four concentration levels (Ti)], the percentage growth was calculated at each of the drug concentration levels. Percentage growth inhibition was calculated as.

**[Ti/C] x 100 %**

In this study Adriamycin used as standard drug. The **Table 2** shows the SRB Assay of tested compounds against Human Lung Cancer Cell Line A-549. And the **Table 3** represents the LC50, TGI and GI50 values of the tested compound.

**Table 2: The SRB Assay of tested compounds against Human Lung Cancer Cell Line A-549.**

| Code | Human Lung Cancer Cell Line A-549 | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | % Control Growth | | | | | | | | | | | | | | | |
| | Drug Concentrations (µg/ml) | | | | | | | | | | | | | | | |
| | Experiment 1 | | | | Experiment 2 | | | | Experiment 3 | | | | Average Values | | | |
| | 10 | 20 | 40 | 80 | 10 | 20 | 40 | 80 | 10 | 20 | 40 | 80 | 10 | 20 | 40 | 80 |
| **R1** | **86.7** | **96.7** | **62.5** | **18.3** | **101.9** | **113.2** | **84.1** | **34.7** | **93.2** | **92.4** | **42.5** | **12.8** | **93.9** | **100.8** | **63.0** | **21.9** |
| R2 | 91.2 | 89.5 | 85.6 | 95.3 | 101.3 | 104.9 | 112.6 | 93.0 | 90.8 | 92.4 | 88.9 | 95.2 | 94.4 | 95.6 | 95.7 | 94.5 |
| R5 | 91.2 | 87.6 | 75.6 | 66.9 | 102.7 | 104.9 | 104.3 | 56.3 | 90.1 | 90.6 | 61.2 | 49.9 | 94.7 | 94.3 | 80.4 | 57.7 |
| **R6** | **96.2** | **88.5** | **77.0** | **33.5** | **110.4** | **111.7** | **98.6** | **51.0** | **96.2** | **102.0** | **81.7** | **33.5** | **100.9** | **100.7** | **85.8** | **39.4** |
| R7 | 94.9 | 85.6 | 80.0 | 43.3 | 104.8 | 97.6 | 102.6 | 75.1 | 93.6 | 111.8 | 82.3 | 96.2 | 97.8 | 98.3 | 88.3 | 71.5 |
| ADR | 10.0 | 5.1 | -8.4 | -1.2 | 8.4 | 5.0 | 10.4 | 6.1 | 4.7 | 2.6 | -3.1 | 5.4 | 7.7 | 4.2 | -0.4 | 3.4 |

**Table 3: LC50, TGI and GI50 values of the tested compound-**

| Sample code | Drug concentrations (µg/ml) calculated from graph | | |
|---|---|---|---|
| | LC50 | TGI | GI50* |
| R1 | NE | >80 | 55.1 |
| R2 | NE | >80 | >80 |
| R5 | NE | >80 | >80 |
| R6 | NE | >80 | 71.9 |
| R7 | NE | >80 | >80 |
| ADR | NE | <10 | <10 |

## ❖ Molecular Docking

Molecular docking is the process of arranging molecules in specific configurations to engage with a receptor. Autodock 1.5.4 is a software suite to develop in Scripps Research Institute. This software is used for modeling flexible small molecule such as drug molecule binding to receptor proteins. The current version of Autodcok uses genetic algorithm for the conformational search and is a suitable method for the docking studies. Scripps Research Institute has developed a Graphical User Interface (GUI) using Python 2.5 language, and it is called Autodock Tool (ADT). ADT is used to prepare, run and analyze the docking stimulation, in addition to its several features necessary for modeling studies. In order to gain more insight on the binding mode of the compounds with MAP Kinase docking studies using Auto Dock 4.0.1 were carried out. Top scoring molecules from the largest cluster were considered for interaction studies. The crystallographic structure of MAP kinase, which is retrieved from the RCSB Protein Data Bank (PDB code 1CM8) serves as docking receptor, and all the designed compounds are selected as ligand molecules. Before docking the screened ligands in to the protein active site, the protein was prepared by deleting the substrate cofactor as well as the crystallographically observed water molecules and then protein was defined for generating the grid. All molecules were drawn using ChemDraw Ultra 8.0 tool and energy minimized using Chem 3D Ultra 8.0 software.

**Table 4: Energy minimization table of Ligand and MAP kinase Interaction.**

| Code | Binding Energy (Kcal/mol) | Inhibition | Vdw. Desolvation Energy | Intermol Energy | Ligand Efficiency | Electrostatic Energy | Total Internal |
|---|---|---|---|---|---|---|---|
| R1 | -7.79 | 2.04 | -7.66 | -8.96 | -0.31 | -1.3 | 1.19 |
| R2 | -7.95 | 6.75 | -7.83 | -8.25 | -0.27 | -0.42 | 0.32 |
| R3 | -7.28 | 6.42 | -6.95 | -8.28 | -0.26 | -1.33 | -0.44 |
| R4 | -6.41 | 20.04 | -7.48 | -7.6 | -0.25 | -0.12 | -0.044 |
| R5 | -7.19 | 5.36 | -8.71 | -8.38 | -0.28 | -0.32 | -0.42 |
| R6 | -7.76 | 2.05 | -7.73 | -8.95 | -0.3 | -1.23 | -0.41 |
| R7 | -7.35 | 4.1 | -8.71 | -8.54 | -0.28 | 0.17 | -0.44 |
| R8 | -6.58 | 14.98 | -7.89 | -8.07 | -0.24 | -0.19 | -0.43 |
| Diclofenac | -7.18 | 14.32 | -8.98 | -9.02 | -0.32 | -0.18 | -0.32 |
| Imatinib | -7.27 | 53.99 | -11.29 | -11.65 | -0.43 | -0.19 | -0.54 |

## ❖ RESULT AND DISCUSSION

A series of novel class of (E)-2-(2-(5-nitro-1H-benzo[d]imidazol-2-yl)vinyl)-4H- chromen-4-one Derivatives were synthesized by using of 2-methyl-1H-benzo[d]imidazole, substituted chromone-3-carbaldehyde in presence of GAA. The purity of synthesized compounds was confirmed by Melting Point and TLC using Ethyl Acetate: Petroleum Ether (50:50) as solvent system. The structures of synthesized compounds were confirmed by FT-IR, $^{1}$H-NMR, $^{13}$C-NMR and Mass spectral analysis the result was correlated with the expected structure. The Physico-chemical properties of synthesized compound were represented in **Table 1.**

Synthesized compounds R1, R2, R3, R6 and R7 were evaluated for anticancer activity by SRB assay method against Human Cancer Cell line A-549. All tested compound exhibit moderate to good percentage of growth inhibition of Human Lung Cancer Cell Line A-549 when compared with the control drug Adriamycin. The SRB Assay of tested compounds against Human Lung Cancer Cell Line A-549 was shown in **Table 2** and **Table 3** represents LC50, TGI and GI50 values of the tested compound.

The docking study of the synthesized compound was carried out by using **AUTODOCK** software version 4.2 working system against target enzyme **MAP Kinase** as per the literature survey. The docking result of the synthesized compounds showed binding score in active site of MAP Kinase between **7.0** and **7.90 K Cal/mol**. Compounds **R1, R2, R6,** and **R7** were found to have significant binding score against target enzyme MAP Kinase, compared to standard drugs such as **Imatinib** and **Diclofenac.** The Energy minimization data of Ligand and MAP kinase Interaction was shown in **Table 4.**

## ❖ CONCLUSION

The present study deals with designing of some novel (E)-2-(2-(5-nitro-1H- benzo[d]imidazol-2-yl)vinyl)-4H-chromen-4-one Derivatives on the basis reaction between 2-methyl-1H-benzo[d]imidazole, substituted chromone-3-carbaldehyde in presence of GAA. The Synthesized compound were evaluated for their in-vitro anticancer activity by SRB assay method against Human Cancer Cell line A-549. From the result the compound **R1** and **R6** allowed only 21.9 and 39.4 of % cell growth at the concentration of 80µg/mL. Whereas other compounds has showed **57-94** of **%** cell growth. From the above, it may conclude that the substitution on the Coumarin nucleus alter the biological activity. The un-substituted **(R4)** and **Flouro (R6)** and **Chloro (R1)** substituted Coumarin derivatives were found to be potent by producing biological activity.

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