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Targeting Telomerase for Human Breast Carcinoma (MCF-7 Cell Lines)

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HUMAN

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ABSTRACT

In the present paper, new pyrimidine derivatives were designed, synthesized, and analyzed in terms of their anticancer properties. Benzimidazole chalcone has been synthesized by reacting acetyl benzimidazole with various heteroaromatic aldehydes. The completion of the reaction is monitored by thin-layer chromatography, and it is then cyclized into the pyrimidine derivative with guanidine hydrochloride. The structures of all synthesized pyrimidine derivatives were further confirmed using infrared spectroscopy, nuclear magnetic resonance, and mass spectroscopy. Tribolium telomerase (PDB ID: 5CQG) with the inbound inhibitor BIBR1532 was used to dock twenty-four designed pyrimidine compounds. The docking score of -10.842 indicated that Compound 12 has more interactions. A native ligand's dock score of -9.148 was discovered. When comparing molecule 12 to the native ligand, it was evident that the latter had a lower binding ability. All the pyrimidine derivatives were evaluated for the cell line (MCF-7) of human breast carcinoma. Pyrimidine derivatives IC-02, IC-12, and IC-08 had IC50 values of 28.19 µg/ml, 31.04 µg/ml, and 38.43 µg/ml, respectively, and were found to be more effective than 5-Flurouracil, which had an IC50 value of 41.56 µg/ml.

INTRODUCTION

A group of illnesses collectively referred to as cancer is characterized by unchecked, rapid, and uncontrolled division of cells.[1] Depending on the patient's medical condition, the type of cancer cells, and the disease's stage, both pharmacologic and non-pharmacologic therapeutic approaches, such as surgery, radiation, and chemotherapy, are required to treat cancer. [2]Almost 10 million deaths globally in 2020 were caused by cancer, making it one of the major causes of mortality.[3]

The main obstacles to cancer treatment are the heterogeneity of certain malignancies, drug resistance, delayed diagnosis, lack of progress in treating early-stage cancer, medications' non-selectivity towards cancer cells, which can cause side effects, and a host of other issues wholly currently unknown.[4] Considering telomerase appears to be essential in almost all cancers to ensure the immortalization of a fraction of cells, including cancer stem cells, it is an appealing target for cancer research. Furthermore, it appears that targeting telomerase would be reasonably safe due to changes in telomere length, cell dynamics, and telomerase expression between normal and cancer tissues.[5]

Specific protein-DNA structures called telomeres are found at the termini of eukaryotic chromosomes. They protect against nuclease degradation and end-to-end fusion of chromosomes. Approximately 4–14 kb of TTAGGG duplex repeats and 150–200 bases of single stranded DNA overhang running 5’ to 3’ towards the end of the chromosome make up the human telomeres.[6] Telomerase has been found in almost every type of cancer, including lymphomas, leukaemias, and melanomas, as well as the most common malignancies of the prostate, breast, lung, colon, bladder, uterus, ovary, and pancreas. Furthermore, telomerase levels have been found to connect with the clinical prognosis of neuroblastomas, leukaemias, and malignancies of the prostate, stomach, and breast in cancer patients.[7]

It is thought that pyrimidine and their derivatives are crucial for pharmaceuticals and agricultural chemicals. Pyrimidine compounds have several remarkable biological properties, notably antimicrobial, [8] antitumor, [9] and antifungal activity.[10] Leukemia and thyroid medications both make extensive use of pyrimidine derivatives. Targeting telomeres and telomerase is crucial for anticancer treatment. Most cancer cells contain telomerase, and 85–90% of human tumours and other tumour-derived cell lines shown telomerase expression. [12] Likewise, 86 percent of carcinoma of breast express telomerase.[13]

By considering these facts in mind, in present work we have designed synthesized pyrimidine and Benzimidazole conjugate derivatives and screened against MCF-7 cell lines for breast cancer.

In Silico Modeling and Virtual Screening

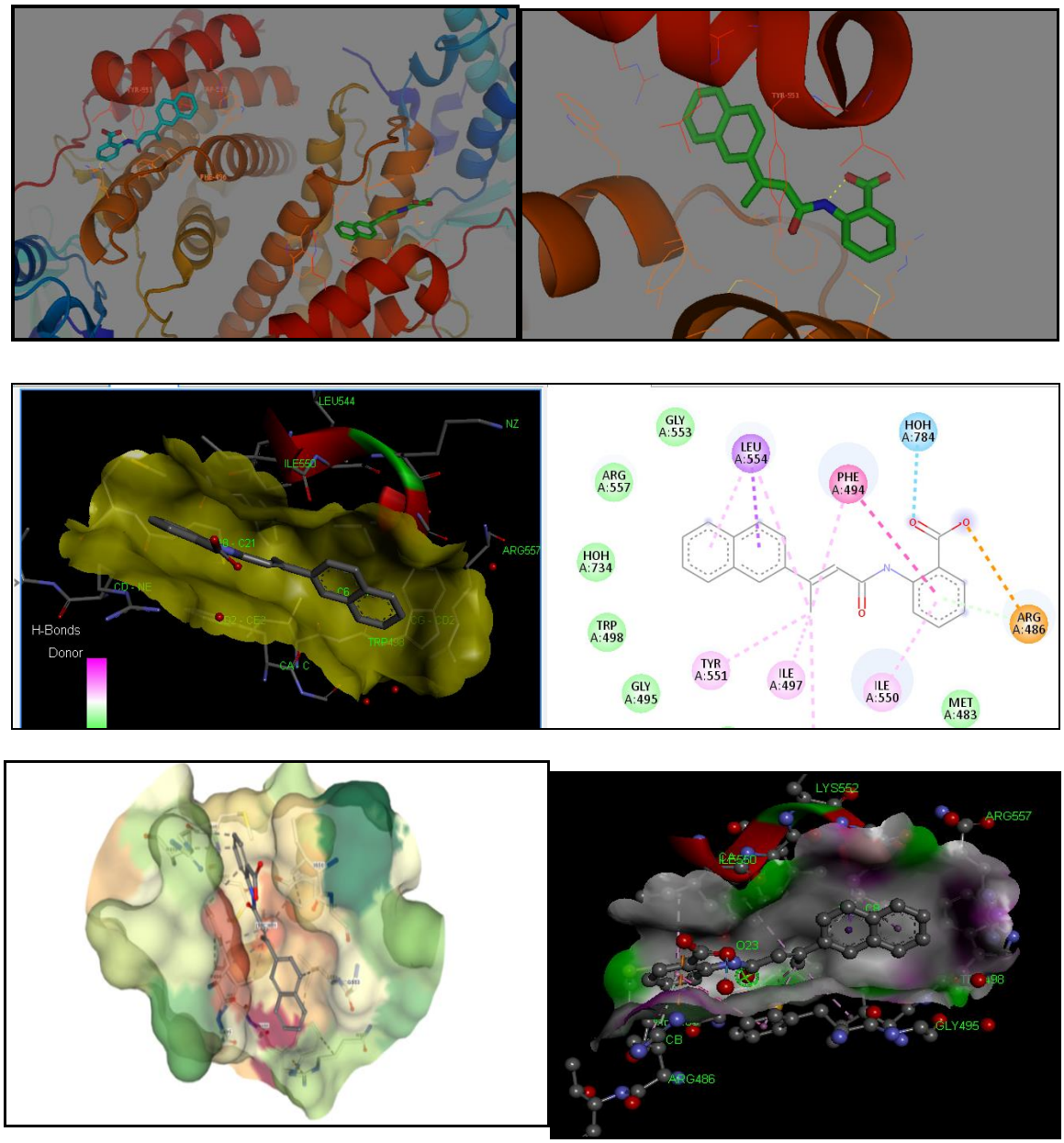


Figure 1: 5CQG Tribolium telomerase's structure in combination with the extremely selective inhibitor BIBR153

This study used a structure-based virtual screening method that combined MD pharmacophore modeling and docking studies to identify potential telomerase inhibitors from our internal library of pyrimidine derivatives. The full-length catalytic subunit of telomerase

from Tribolium castaneum was combined with the compound BIBR1532 (PDB 5CQG) in the first step. The amide groups of asparagine (Asn) and glutamine (Gln), as well as the imidazole ring in histidine (His), aspartic acid (Asp), and glutamic acid (Glu), were optimized in the crystal structure once the whole structure was completed and refined. The protonation states of histidine, glutamic acid (Glu), and aspartic acid (Asp) were predicted.

Table 1: Docking score of pyrimidine derivatives on Telomerase.

DDD ID Ligand ID	**Docking Score on 5CQG**
1	-9.262
2	-9.442
3	-8.113
4	-7.306
5	-6.954
6	-7.873
7	-8.161
8	-8.124
9	-8.589
10	-8.283
11	-9.268
12	-10.842
Native ligand	-9.148

Table 2: Interaction of amino acid.

Sr. No.	**Ligand ID**	**Docking Score**	**Interacting amino acid with type of interaction**
1	12	-10.842	GLN 549(H-Bond), ILE 550 (H-Bond), PHE 494(H-Bond), TYR 551(Pi-Pi stacking), PHE 494(Pi-Pi stacking)
5	2	-9.442	PHE 494 (Pi-Pi stacking), ASP 493(H-Bond), ASP 493(salt bridge)

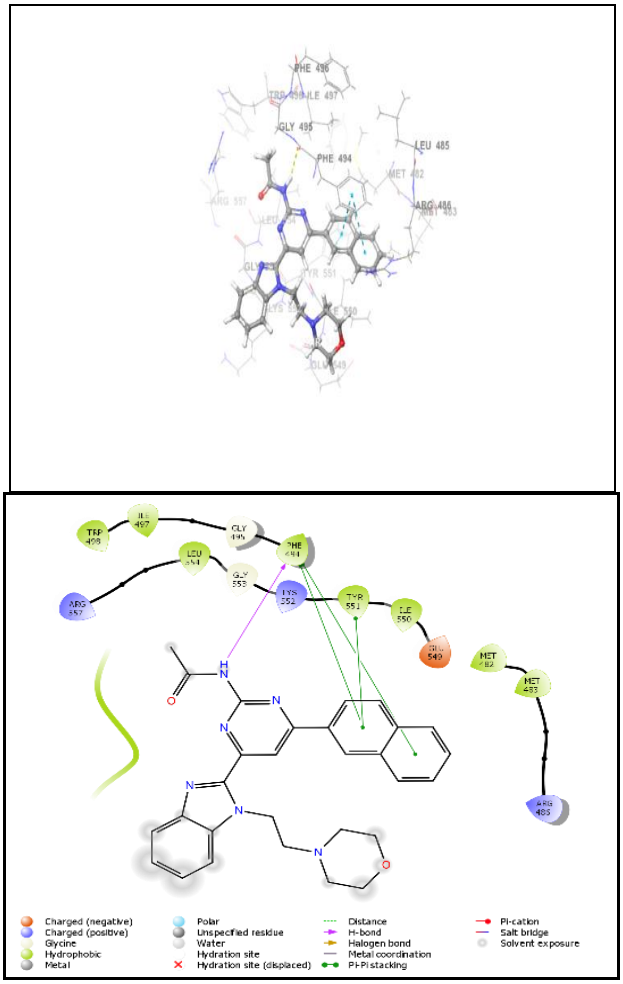


Figure 2: Compound bound to 5CQG: a 3D and 2D interaction diagram

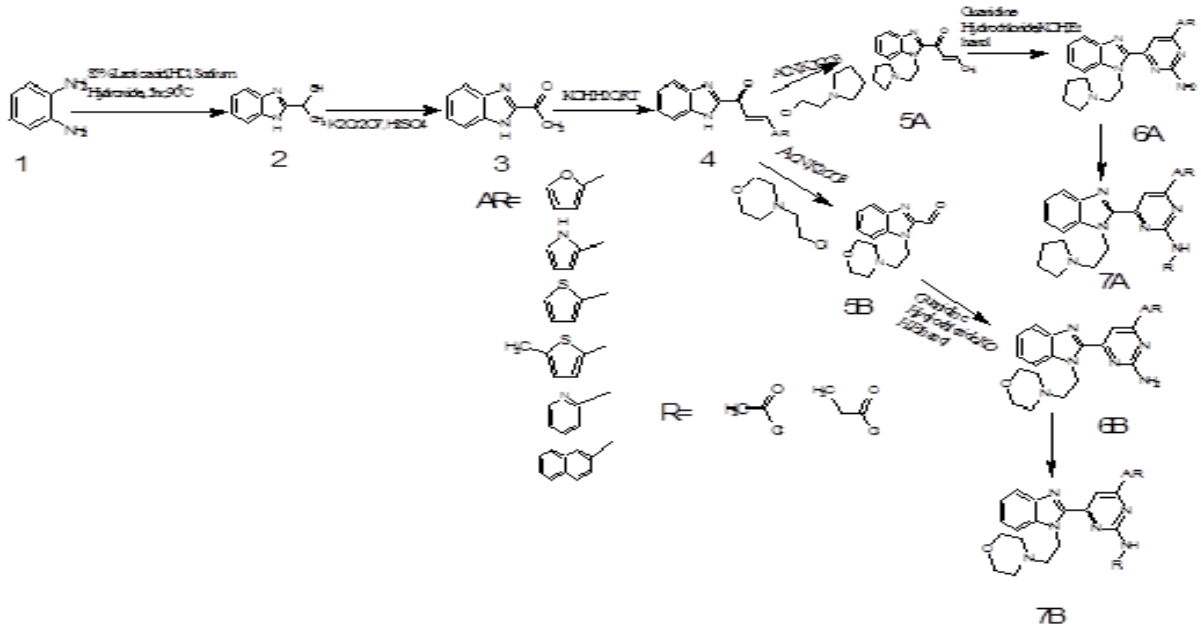
Tribolium telomerase (PDB ID: 5CQG) with inbound inhibitor BIBR1532, was used to dock twenty-four designed pyrimidine compounds. Docking Sco. -10.842 indicated that Compound-12 has more interactions. A native ligand's dock S.-9.148 was discovered. When comparing molecule 12 to the native ligand, it was evident that the latter had a lower binding ability.

Using a different approach, the 12 molecules that were chosen aligned with the three-dimensional structure of tribolium telomerase in conjunction with the extremely selective inhibitor BIBR1532 (PDB ID: 5CQG), an essential enzyme anti-cancer drugs. Molecular docking done protein's binding pocket, Compound 12 was shown the highest binding affinity.

MATERIALS AND METHODS

For synthesis, recrystallization, and assessment, AR-grade chemicals and solvents were used entirely. The synthesized compounds' melting points were determined at a gradient of 10°C/min using melting point equipment (REMI apparatus). Preparative TLC plates, model TLC Silica Gel 60 F254 from Merck KGaA Darmstadt, were used for thin layer chromatography. On a Bruker, the FTIR spectra of the synthesized derivatives were recorded. All the compounds' infrared spectra showed absorption bands that matched the expected structures of their synthesized derivatives. The synthesized compounds' H1-NMR spectra in DMSO were recorded at 300 MHz using the Bruker Advance DPX 300 NMR spectrometer. Using an electrospray ionizer, the mass spectra of the synthesized compounds are recorded on ZQ-4000.

Synthetic Scheme:



1. Synthesis of Benzimidazole Ethanol

Lactic acid (3.96 g, 44.0 mmol) and o-phenylenediamine (4.32 g, 40.0 mmol) were added to RBF in conjunction with hydrochloric acid (4.0 N, 25 ml). After that, it was allowed to have reflux for a period of six hours. A dilute sodium hydroxide solution is then used to neutralize it. To obtain the intended chemical, IC-01 A1 (6.15 g) in 95% yield as an off-white solid, the reaction mass was filtered.

2. Synthesis of Acetyl-Benzimidazole

Following a 20-minute reaction time (RT), K2Cr207 (19.8 g, 150 mmol) was gradually added to a solution of 1-(1H-Benzo[d]imidazol-2-yl) ethanol (8.1 g, 50 mmol) in dil.H2S04 (5%; 40 ml). After stirring for an additional two hours, aqueous NH3 was added to the mixture to lower its pH to 6.0–6.5. A pure product was obtained by drying (5.76 g, 72%) and recrystallized in ethyl acetate.

3. Synthesis of Benzimidazole Chalcone.

The 2-acetyl benzimidazole (0.02 mol) in ethanol (20 ml) stirring solution was mixed with 8 ml of a 10% sodium hydroxide solution. After that, 0.02 mmol of an aromatic or heteroaromatic aldehyde was added to it. The resultant liquid was constantly swirled at room temperature for five hours. Filtration has been carried out in order to get the necessary components via the reaction mixture.

4. Synthesis of N-Pyrrolidine or N-Morpholine Derivatives of Benzimidazole Chalcone

Potassium carbonate (5.0 equiv), benzimidazole derivative (1.0 equiv), and acetonitrile (10 ml) were all transferred to a round-bottom flask. After whirling for ten minutes, add either 2-Chloroethyl Pyrrolidine hydrochloride (1.1 equiv) or 2-chloroethyl Morpholine hydrochloride (1.1 equiv). Reflux the two ingredients for a total of six hours, and the mass was partitioned between ethyl acetate and water. The organic layer was then separated and concentrated using chromatography to provide the desired chemical.

5. Synthesis of Pyrimidine derivatives

Following the stirring of a reaction mixture containing guanidine hydrochloride (1.5 equiv.) and N-pyrrolidine or N-morpholin benzimidazole derivatives (1.0 equiv.) in ethanol (10 mL), at room temperature, a solution containing sodium hydroxide (2.0 equiv.) in water (1 ml) was added. The reaction was completed, yielding a brown solid.

6. Synthesis of N-Acetyl or Propionyl Pyrimidine derivatives

After adding one equivalent of potassium carbonate and benzimidazole pyrimidine (1 equi) to 25 millilitres of dry acetone, acetyl chloride (0.097 g, 1.23 mmol) was produced. the mixture being agitated and five milliliters of water being used to quench it. To acquire the final

Compound, the precipitate was isolated by filtering the reaction mass and purified using column chromatography.

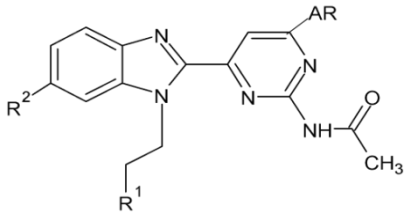
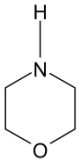
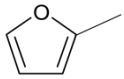
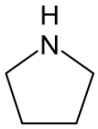
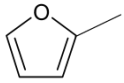
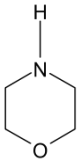
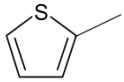
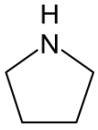
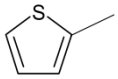
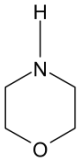
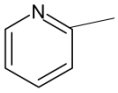
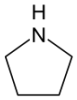
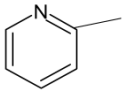
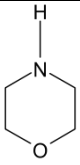
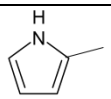
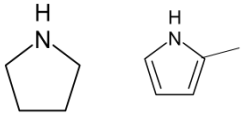
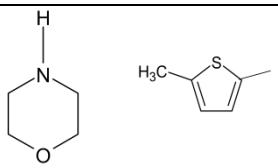
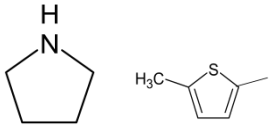
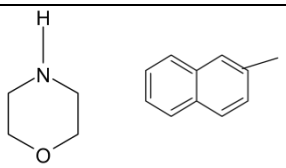
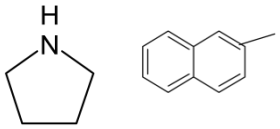


Table 3: Designed pyrimidine and benzimidazole conjugate and physicochemical parameter.

Sr. No.	Code	R^1	AR	R^2	a_acc	a_don	logP(o/w)	Weight
1.	**IC-01**			H	6	1	1.42	432.4
2.	**IC-02**			H	5	1	2.38	416.4
3.	**IC-03**			H	6	1	2.23	448.5
4.	**IC-04**			H	5	1	3.203	432.5
5.	**IC-05**			H	7	1	1.63	443.51
6.	**IC-06**			H	6	1	2.597	427.51
7.	**IC-07**			H	6	2	1.798	431.5

							
8.	**IC-08**		H	5	2	2.76	415.5
9.	**IC-09**		H	6	1	2.414	462.5
10.	**IC-10**		H	5	1	3.38	446.5
11.	**IC-11**		H	6	1	3.966	492.5
12.	**IC-12**		H	5	1	4.932	476.5

RESULTS AND DISCUSSION:

Spectral data of the Synthesized Compound:

1. Compound Name: *N*-(4-(Furan-2-yl)-6-(1-(2-morpholinoethyl)-1*H*-benzo[*d*]imidazol-2-yl) pyrimidin-2-yl) acetamide (0.19 g, 35% yield) as a white solid.

IR: 3253(NH Stretch) 2812(CH Stretch), 1681(C=O Stretch), 1585(C=C Stretch), 1470(CH Bending)

NMR Interpretation (δ ppm) 2.2(d,4H,3H),2.5(t,2H CH2 of ethylene side chain),3.1(s,4H CH2 of Morpholine),5.2(s,2H CH2 of ethylene side chain),7.4(m,2H CH of Benzene),7.6(m,2H CH of Benzene),7.7(d,1H CH of Naphthalene),7.8(d,1H CH of Naphthalene),8.0(d,1H CH of Naphthalene),8.1(d,1H CH of Naphthalene),8.197(d,1H CH of Naphthalene),8.4(d,1H CH of Naphthalene),8.6(s,1H CH of Naphthalene),8.9(s,1H CH of Pyrimidine),10.95(1H NH of Amide)

Mass: 493.40

2. Compound Name: N-(4-(furan-2-yl)-6-(1-(2-(pyrrolidin-1-yl) ethyl)-1H-benzo[d]imidazol-2-yl) pyrimidin-2-yl) acetamide (0.19 g, 33% yield), a yellowish white solid.

IR: 3254(NH Stretch), 2812(CH Stretch), 1684(C=O Stretch), 1585(C=C Stretch), 1457(CH Bending)

NMR Interpretation (δ ppm)1.4(s,4H),1.9(s,3H),2.3(d,7H),2.7(t,2H),5.2(t,2H CH2 of Naphthalene),7.4(m,2H CH of Benzene),7.6(m,2H CH of Benzene),7.8(m,2H CH of Naphthalene),8.0(d,1H CH of Naphthalene),8.1(m,2H CH of Naphthalene),8.7(d,1H CH of Naphthalene),8.5(s,1H CH of Naphthalene),8.9(s,1H CH of Pyrimidine), 10.9(s1H NH of amide)

Mass: 477.50

3. Compound Name: *N*-(4-(1-(2-Morpholinoethyl)-1*H*-benzo[*d*]imidazol-2-yl)-6-(thiophen-2-yl) pyrimidine-2-yl) acetamide (0.20 g, 36% yield).

IR: 3260(NH Stretch), 2812(CH Stretch), 1682(C=O Stretch), 1587(C=C Stretch), 1468(CH Bending)

NMR Interpretation (δ ppm) 2.2(s, 7H CH3 and CH2 of Morpholine),

3.1(s,4H CH2 of Morpholine),3.3(s,2H Morpholine side chain),5.2(t,2H Morpholine side chain) ,6.8(m,1H Benzene),7.2(t,1H Furan CH),7.5(d,1H Benzene),7.7(d,1HBenzene),7.8(q,1H Furan CH),8.0(s,1H Furan CH),8.2(s,1H Pyrimidine CH),10.9(s,1H amide NH)

Mass: 451.4

4. Compound Name: *N*-(4-(1-(2-(Pyrrolidin-1-yl) ethyl)-1*H*-benzo[*d*]imidazol-2-yl)-6-(thiophen-2-yl) pyrimidin-2-yl) acetamide (0.21 g, 38% yield) a white solid.

IR: 2995(CH Stretch), 1678(C=O Stretch),1604(C=C Stretch), 1483 (CH Bending)

NMR:1.4(s,4HCH2 of Pyrrolidine),2.2(s,3H CH3 of Amide),2.3(s,4HCH2 of Pyrrolidine),2.7(t,2H CH2 of ethylene side chain),5.1(t,2H CH2 of ethylene side chain),6.7(1H CH of Furan),7.1(t,1H CH of Furan),7.4(m,1H CH of Benzene),7.6(m,1H CH

of benzene),7.7(m,1H CH of Benzene),8.0(s,1H CH of Furan),8.1(s,1H CH of Pyrimidine),10.8(s,1H NH Of amide)

Mass: 435

5. Compound Name: *N*-(4-(1-(2-Morpholinoethyl)-1*H*-benzo[*d*]imidazol-2-yl)-6-(pyridin-2-yl) pyrimidin-2-yl) acetamide (0.15 g, 27% yield) as a light brown.

IR:3350(NH Stretch),2950(CH Stretch),1715(C=O Stretch) 1588, (C=C Stretch)1496 (CH Bending)

NMR:2.2(d,7H CH3 of amide and CH2 of Morpholine),3.1(s,4H CH2 of Morpholine),5.2(s,2H CH2 of Ethylene side chain),7.1(t,1H CH of Thiophene),7.3(t,1H CH of Benzene),7.6(d,1H CH of Benzene),7.8(q,1H CH of Benzene),7.9(d,1H CH of Thiophene),8.2(d,1H CH of Thiophene),8.3(s,1H CH of Pyrimidine),10.8(s,1H NH of amide)

Mass:467.40

6. Compound Name: *N*-(4-(Pyridin-2-yl)-6-(1-(2-(pyrrolidin-1-yl) ethyl)-1*H*-benzo[*d*]imidazol-2-yl) pyrimidine-2-yl) acetamide (0.14 g, 25% yield)

IR: 3178 Secondary amine N-H stretch 1679 C=O stretch 1583 C=C stretch 1464 C-H Bending

NMR: 1.6(s 4H CH2 of Pyrrolidine) 2.3(s3H CH3 of amide linkage) 2.6(s 4H CH2 of Pyrrolidine) 3(s 2H CH2 of Pyrrolidine side chain) 5.2(t 2H Pyrrolidine side chain) 7.4(m 2H CH of Benzene) 7.6(m1H CH of Pyridine) 7.8(m2H CH of Benzene) 8(m1H CH of Pyridine) 8.4(d1H CH of Pyridine) 8.8(d1H CH of Pyridine) 8.9(1H CH of Pyrimidine) 11(s1H NH of Amide)

Mass: 428.4

7. Compound Name: *N*-(4-(1-(2-Morpholinoethyl)-1*H*-benzo[*d*]imidazol-2-yl)-6-(1*H*-pyrrol-2-yl) pyrimidine-2-yl) acetamide (0.14 g, 25% yield), which was a dark brown solid

IR: 3213 Secondary amine N-H stretch 2820 C-H stretch (Asymmetric) 1685 C=O stretch 1586 C=C stretch 1416 C-H Bending

NMR: 10(s 1H NH of amide) 8.2(s 1H CH of Pyrimidine) 7.9(q 2H CH of Pyrrole) 7.3(m 2H CH of Benzene) 7.1(s 2H CH of benzene) 6.2(s1H CH of Pyrrole) 5.2(t 2H CH2 of Pyrrolidine side chain) 3.1(s 4H CH2 of Pyrrolidine) 2.3(m 6H CH3 of amide)

Mass: 432.4

8. Compound Name: *N*-(4-(1*H*-Pyrrol-2-yl)-6-(1-(2-(pyrrolidin-1-yl) ethyl)-1*H*-benzo[*d*]imidazol-2-yl) pyrimidine-2-yl) acetamide 0.24 g, 22% yield was a brown solid.

IR: 3213 Secondary amine N-H stretch 2881 C-H stretch (Asymmetric) 2824 C-H stretch (Symmetric) 1709 C=O stretch 1590 C=C stretch 1419 C-H Bending

NMR: 10.64(s1H NH of amide) 8.2(s 1H CH of Pyrimidine) 7.8(d 2H CH of Pyrrolidine)7.4(q 2H CH of Benzene) 7.1(s 2H CH of Pyrrolidine) 6.2(s1H CH of Benzene) 5.1(s 2H CH2 of Morpholine) 2.2(s 3H CH3 of amide)

Mass: 416.4

9. Compound Name: *N*-(4-(5-Methylthiophen-2-yl)-6-(1-(2-morpholinoethyl)-1*H*-benzo[*d*]imidazol-2-yl) pyrimidine-2-yl) acetamide 0.19 g, 35% yield as a light brown solid

IR: 3289 Secondary amine N-H stretch 2801 C-H stretch (Asymmetric)

1680 C=O stretch 1587 C=C stretch 1461 C-H Bending

NMR: 2.2(d, 6H CH2 of Pyrrolidine) 2.5(d3H CH3 of amide) 3.1(s 4H CH2 of Pyrrolidine) 5.2(s2H CH2 of side chain) 6.9(s1H CH of Thiophene) 7.3(m1H CH of benzene) ,7.7(m2H CH of Benzene) 8.0(s1H CH of Thiophene) 8.2(s1H CH of Pyrimidine) 10.75(s1H NH of Amide)

Mass: 463.3

10. Compound Name: *N*-(4-(5-Methylthiophen-2-yl)-6-(1-(2-(pyrrolidin-1-yl) ethyl)-1*H*-benzo[*d*]imidazol-2-yl) pyrimidine-2-yl) acetamide (0.19 g, 35% yield) as a light-yellow solid

IR: 2964 C-H stretch (Asymmetric 1671 C=O stretch 1582 C=C stretch 1468 C-H Bending

NMR: 1.4(s 4H CH2 of Pyrrolidine) 2.2(s 6H CH3 of Methyl and CH2 of Pyrrolidine) 2.5(d 3H CH3 of Thiophene) 2.6(s 2H CH2 of Pyrrolidine side chain) 5.1(s 2H CH2 of Pyrrolidine

side chain) 6.9(s1H CH of Thiophene) 7.3(m 2H CH of Benzene) 7.7(m 2H CH of Benzene) 8.0(s 1H CH of Thiophene) 8.2(s1H CH of amide) 10.7(s1H NH of Amide)

Mass: 447.3

11. Compound Name: *N*-(4-(1-(2-Morpholinoethyl)-1*H*-benzo[*d*]imidazol-2-yl)-6-(naphthalen-2-yl) pyrimidin-2-yl) acetamide 0.20 g, 37% yield as a white solid

IR: 3253(NH Stretch) 2812(CH Stretch), 1681(C=O Stretch), 1585(C=C Stretch),1470(CH Bending)

NMR: 2.2(d,4H,3H),2.5(t,2H CH2 of ethylene side chain),3.1(s,4H CH2 of Morpholine),5.2(s,2H CH2 of ethylene side chain),7.4(m,2H CH of Benzene),7.6(m,2H CH of Benzene),7.7(d,1H CH of Naphthalene),7.8(d,1H CH of Naphthalene),8.0(d,1H CH of Naphthalene),8.1(d,1H CH of Naphthalene),8.197(d,1H CH of Naphthalene),8.4(d,1H CH of Naphthalene), 8.6(s,1H CH of Naphthalene),8.9(s,1H CH of Pyrimidine),10.95(1H NH of Amide)

Mass: 493.40

12. Compound Name: *N*-(4-(Naphthalen-2-yl)-6-(1-(2-(pyrrolidin-1-yl) ethyl)-1*H*-benzo[*d*]imidazol-2-yl) pyrimidin-2-yl) acetamide 0.39 g, 36% yield as a light-yellow solid.

IR: 3254(NH Stretch), 2812(CH Stretch), 1684(C=O Stretch), 1585(C=C Stretch), 1457(CH Bending)

NMR: 1.4(s, 4H), 1.9(s, 3H), 2.3(d, 7H),2.7(t,2H),5.2(t,2H CH2 of Naphthalene), 7.4(m, 2H CH of Benzene), 7.6(m, 2H CH of Benzene),7.8(m,2H CH of Naphthalene),8.0 (d,1H CH of Naphthalene),8.1(m,2H CH of Naphthalene),8.7(d,1H CH of Naphthalene),8.5(s,1H CH of Naphthalene),8.9(s,1H CH of Pyrimidine), 10.9(s1H NH of amide)

Mass: 477.5

ANTICANCER ACTIVITY:

The therapeutic potential of all synthesized pyrimidine compounds was evaluated against the breast cancer cell line (MCF-7) for human breast carcinoma. It is compared with 5-Fluro Uracil (a standard anticancer drug), and cytotoxicity has been investigated in the same way. The *half maximal inhibitory concentration (*IC50 value) was determined using the MTT (3-

(4, 5-dimethylthiazol-6-yl)-6, 5-diphenyl tetrazolium bromide) assay. For assessing a compound's potential anticancer activity, the MTT assay's IC50 value (the dose required to cause a fifty percent reduction in the survival value) is employed. Table 4 lists the IC50 values of synthesized pyrimidine derivatives.

Pyrimidine derivatives IC-02, IC-12 and IC-08 had IC50 values 28.19 µg/ml and 31.04 µg/ml and 38.43 µg/ml respectively and were found more effective than 5-Flurouracil, which had an IC50 value of 41.56 µg/ml.

ANTICANCER ACTIVITY RESULT:

Table 4: Cytotoxic effect of standard and pyrimidine derivatives

Sr. No.	Sample No.	Concentration (µg/ml)	OD	Mean	% inhibition	IC 50 (µg/ml))
1	Control		1.238 1.477 1.320	1.345		
2	Std. 5 FU	10	0.223 0.315 0.259	0.265	80.29	41.56
		40	0.303 0.351 0.301	0.318	76.35	
		100	0.365 0.387 0.398	0.383	71.52	
3	IC 1	10	0.322 0.354 0.260	0.312	76.80	44.69
		40	0.352 0.287 0.345	0.328	75.61	
		100	0.286 0.392 0.397	0.358	73.38	
4	IC 2	10	0.258 0.287 0.272	0.272	79.77	28.19
		40	0.286 0.361 0.380	0.342	74.57	
		100	0.325 0.364 0.362	0.350	73.97	

5	IC 3	10	0.303 0.293 0.358	0.318	76.35	56.14
		40	0.351 0.382 0.295	0.330	75.46	
		100	0.416 0.371 0.642	0.476	64.60	
6	IC4	10	0.560 0.513 0.289	0.520	61.33	48.54
		40	0.570 0.651 0.431	0.552	58.95	
		100	0.627 0.455 0.718	0.666	50.48	
7	IC5	10	0.512 0.306 0.787	0.535	60.22	42.98
		40	1.190 0.617 0.447	0.751	46.84	
		100	0.521 1.275 1.241	1.012	24.75	
8	IC6	10	0.516 0.513 0.289	0.439	67.36	45.61
		40	0.326 0.446 0.688	0.486	63.86	
		100	0.435 0.723 0.617	0.591	56.05	
9	IC7	10	0.669 0.431 0.992	0.698	48.10	58.94
		40	0.340 1.023 0.746	0.703	47.73	
		100	1.381 0.806 0.850	1.012	24.75	
10	IC8	10	0.453 0.784 0.477	0.571	57.54	38.43
		40	0.622	0.646	51.97	

			0.787 0.530			
		100	0.847 0.404 0.866	0.705	47.58	
11	IC9	10	0.336 0.348 0.338	0.340	74.72	49.50
		40	0.244 0.442 0.524	0.403	70.03	
		100	0.786 0.698 0.441	0.641	52.34	
12	IC10	10	0.268 0.211 0.456	0.311	76.87	55.95
		40	0.269 0.403 0.278	0.316	76.50	
		100	0.467 0.253 0.337	0.352	73.82	
13	IC11	10	0.513 0.512 0.569	0.534	60.29	43.91
		40	0.538 0.581 0.546	0.555	58.73	
		100	0.632 0.552 0.588	0.590	56.13	
14	IC12	10	0.629 0.501 0.509	0.546	59.40	31.04
		40	0.542 0.503 0.663	0.569	57.69	

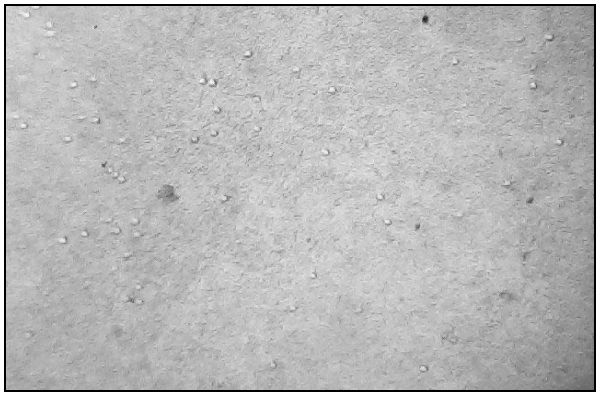


Figure 3: Cytotoxic effect of IC-12

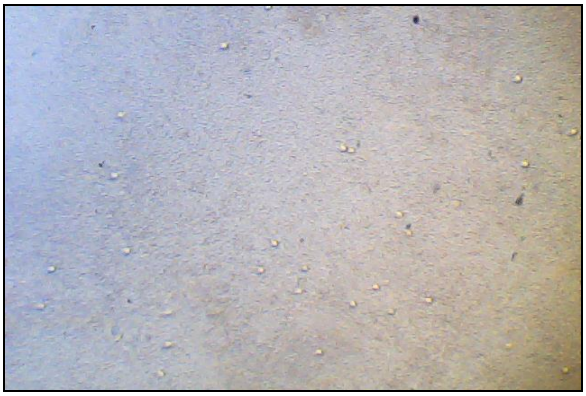


Figure 4: Cytotoxic effect of 5-Flurouracil

CONCLUSION

Benzimidazole Chalcone derivatives were cyclized by using guanidine hydrochloride to obtain pyrimidine derivatives. All the pyrimidine derivatives were evaluated for cell line (MCF-7) for human breast carcinoma. Pyrimidine derivatives IC-02, IC-12 and IC-08 had IC50 values 28.19 µg/ml and 31.04 µg/ml and 38.43 µg/ml respectively and were found more effective than 5-Flurouracil, which had an IC50 value of 41.56 µg/ml.

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