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DEVELOPMENT OF BENZIMIDAZOLE DERIVATIVES AS TARGET BASED ANTITUMOR DRUGS: AN OVERVIEW

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ABSTRACT

Cancer (also being identified as neoplasm, proliferative activity or tumours), is a world-wide uncontrolled disease affecting almost every part of the world. Cancer can be defined as the excess of reproduction of targeted cells due to abnormality in action of the molecular function or in signal transmissions. Although, various of anticancer drugs were already marketed and in applicable. Most of the drugs identified does not have selective targeted actions which directly or indirectly affects the normal cells of the targeted area. This review surveyed and studied about various of novel synthesized anticancer active drugs targeting selective interacting sites of malignant cells like hCAs, tubulin protiens, Gal-1, EGFR, and so on.

KEYWORDS: Anticancer, Target, hCAs, Tubulin, Galectin-1, EGFR, VEGFR-2, Malignant, Benzimidazole, Hybrids

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INTRODUCTION

Cancer is one of the horrifying illnesses on the planet and for the most part described by unsuppressed cell regeneration. Around the world, one out of six ladies and one of every five men generate neoplasm in their lifetime, while one out of eleven ladies and one out of eight men dies due to cancer. Data collected from the global survey states that 50% of the new cases while great part of the attended cases were observed in Asian population by 2018. It is also assessed that more than 50% of populations with around 21.4 million novel cases along with 13.2 million death each year will happen by 2030. Among all of other neoplasm, breast, colorectal and lungs were found to be performing key role in the prevalence of cancer and causing mortality in patients [1, 2]. Some of the described factors like tobacco, smoking, radiations, substance having amphibole groups and genetic mutations pays the major responsibility for the occurrence of neoplasm in the body. Although availability and application of various of treatment procedures and chemical agents, it continuously causing the death of millions of people globally [3].

In spite of having continuous development in the field of medical technology, well briefed and accurate pathophysiology of the disease. On the other side, large number of attempts and practices were found for proper diagnosis of type of neoplasm which still is not helpful to overcome

the total mortality percentage. Besides, the disease endurance rate will in general be amazingly low in some creating nations. This is because of the mix of both late-stage recognition and constrained access to time and subjective treatment [4]. Radiotherapy, surgical therapy, and chemotherapy are the standard neoplasm treatment methods to show a least bit of effects [5]. Among these, chemotherapy is considered as one of the potentials and first-line requirement for depressing cancer development and annihilation. The vast majority of the chemotherapeutic medications focus on the principle functioning of cell systems and hinder the cell division and in this manner interception in malignancy cell increase. Current clinical anticancer medications in application shows their selectivity for the metabolically active or quick reproducing cells. This resulted in disadvantages, for example, untargeted selectivity between malignancy cells and normal cells [6].

Malignant cells show major effect either on the signal transmission or morphogenetic process for the neoplastic proliferation of tumours. Consequently, attacking in between pathological paths by cytotoxic compounds has been a demonstrated restorative way to approach and performing pharmacological action on tumor development and infection movement of cancer cells. In spite of having cytotoxic activity, the majority of the cytotoxic drugs cause reactions due to their unspecified targeted action toward malignancy cells. Drugs containing higher toxicity effect and intolerant effect are significant impediments to the compelling treatment of malignant growth [7, 8].

Due to presence of these various factors, there is significantly need for the designing, synthesizing and evaluation study novel anticancer drugs with improvised efficacy and minimum adverse reactions to support the recent chemotherapeutic procedures. Determination of various novel compounds or combined drugs dose is necessary to act against this deadly illness. Henceforth, vast exploration of anticancer drugs using research processes underscores for the advancement of proficient chemotherapeutic drugs is a developing path in the field of therapeutic science. The classification of different accessible chemo-therapeutic drugs has been shown in **Table 1** [9].

Heterocyclic pharmacophore benzimidazole is also known as “Skeleton Key” because of its varied active biological properties and synthetic and semi-synthetic applications in medicinal chemistry. It is among the main five most regular five-membered aromatic containing nitrogen heterocycles in U.S. FDA-endorsed pharmaceutical drugs [10]. Benzimidazoles are auxiliary isosteres of nucleobases because of having benzene fused nitrogen heterocycle. And also due to their cooperate involvement with biomolecular targets to generate numerous biological activities, for example, anticancer [11], mitigating [12], antiulcer [13], antihypertensive [14], and anthelmintic [15]. One of the ongoing surveys depicted the medicinal advancement of benzimidazole frameworks during the last quinquennial period [16].

Table 1: Classification of Anticancer Drugs on the basis of Chemical Structures

Classification	Example
DNA interacting drugs	
Alkylating drugs	Procarbazine, dacarbazine, temozolomide
DNA cleaving drugs	Bleomycin
Cross-linking drugs	Carboplatin, cisplatin, oxaliplatin, cyclophosphamide, ifosfamide
Intercalating drugs	Doxorubicin, epirubicin, mitoxantrone, actinomycin-D
Topoisomerase inhibitors	Camptothecins, anthracyclines, etoposide
Antimetabolites	
Purine based derivatives	Mercaptopurine
Pyrimidine based derivatives	5-fluorouracil
DHFR inhibitors	Methotrexate
Antitubulin drugs	
Taxol	Paclitaxel, docetaxel
Vinca alkaloids	Vincristine, vinblastine, vinorelbine
Tyrosine kinase inhibitors	
Small molecules	Imatinib, gefitinib
Monoclonal antibodies	Trastuzumab
Angiogenesis/ Metastasis inhibitors	
Monoclonal antibody	Bevacizumab

Many known and marketed clinically active drugs consists of heterocycles containing nitrogen with assorted pharmaceutical practices. For example, drugs like rabeprazole and omeprazole (proton pump inhibitors) are in application for the treatment of stomach ulcers [17]. Albendazole and thiabendazole (restraint of tubulin polymerization and hindrance in uptake of glucose) are anthelmintic compounds resulting the deaths of the parasites [18].

Nocodazole (impairment functioning of tubulin polymerization) as an antineoplastic drug. Candesartan (potentially active angiotensin II receptor inhibitor) is utilized for the treatment of hypertension [19]. Bendamustine (alkylating compound) used in the treatment of interminable lymphomas [20]. Dovotininb (interacts with fibroblast development receptor 3 to unequivocally ties to the (FGFR3) and represses their phosphorylation and induces apoptosis) with expected antineoplastic movement [21].

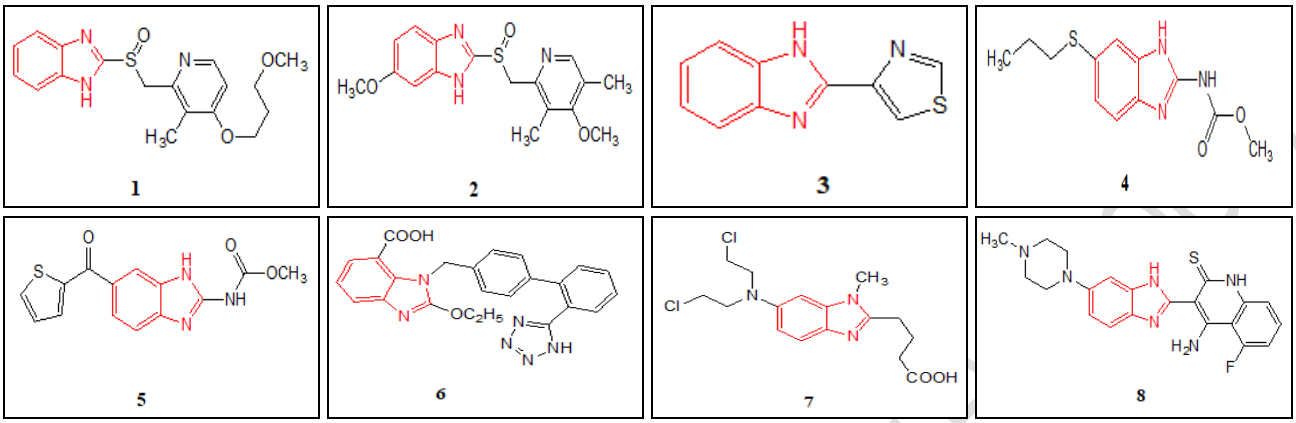

Figure 1: Various Beznimidazole Derivatives as Antiproliferative Agents: 1 Rabeprazole; 2 Omeprazole; 3 Thiabendazole; 4 Albendazole; 5 Nocodazole; 6 Candesartan; 7 Bendamustine and 8 Dovotinib.

Early in 1954, Tamm Folkers *et al.*, found that 5, 6- dichloro- 1-β-D-ribofuranosyl benzimidazole (DRB) acts multiple targeting actions on DNA & RNA viruses which resulted in the synthesis of antiviral drugs from halogenated benzimidazole nucleosides [22]. DRB hinders cell RNA polymerase II, influencing the different cell forms in such manner to cause more cytotoxicity than antiviral. Albendazole and thiabendazole were identified by Slayden et al. which interfere and inhibits the Mtb cell division forms [23]. Later on, Kumar *et al.*, worked on the formation of novel benzimidazole derivatives to act as the FtsZ protein inhibitor, which will have action against both sensitivity and drug resistant Mtb [24].

Target-based Benzimidazole Derivatives

Galectin-1 Inhibitors

In spite of being communicated in different physiological and pathophysiological effects by galectin-1 (Gal-1), it is highly effective various of biological activities. Galectin-1 is a homo-dimeric lectin protein of 14KDa, majorly responsible for an incidence of signal transmission paths, immunity response leading to the development of cancer cells, neurological and immune disorders [25]. Gal-1 has a property to identify carbohydrates for selective action for β-galactosides. Inactivation of Gal-1 has been viewed as one of the effectively helpful methodologies for the treatment of neoplasm, as it shows a significant action in tumor progression and metastasis by regulating different biological activities viz. angiogenesis, apoptosis, relocation, and cell immune escape [26]. This Gal-1 expression has been accounted for in numerous malignant cell types like the brain, breast, osteosarcoma, lung, prostate, melanoma, and so on [27].

Gal-1 plays a role in neoplastic mutations by forming interactions with cancer-genes (H-Ras) and generate Ras-intervene signal transduction including RAF1 and extracellular regulated kinase (ERK).Gal-1 multivalently intervenes tumor cell-ECM adhesion at the essential site by connecting cell surface of glycoproteins (integrins) and glycosylated proteins in the ECM (laminin and fibronectin) [28]. Thus, Gal-1 is considered as a prominent target for the advancement of new helpful pharmacological treatment of cancer cells.

Novel derivative series of 1-benzyl-1H-benzimidazole have been synthesized to act on the Gal-1-intercepting anti-tumour drugs agents. Desired compound 9 shows potential activity against MCF-7 & MDA-MB-231 (breast), HCT-116 (colorectal), DU-145 (prostate) and A-459 (lung) within the range of 10.69-14.04μM. The target compound 9 showed significant growth inhibition against breast cancer (MCF-7) cells with an IC_{50} value of 7.01±0.20μM. Moreover, in-vitro Gal-1 articulation in cell supernatant of MCF-7 cells with compound 9 was estimated in enzymatic GAL-1 ELISA studies and found to

subordinate decrease from 10-300μM. The objective compound demonstrated Gal-1-intervened apoptosis, which was affirmed by morphological modification in MCF-7 on treatment with cells like blebbing, cell divider twisting, and cell shrinkage. It can be well understood by Acridine Orange/Ethidium Bromide (AO/EB) staining, DAPI nucleic acid staining, mitochondrial membrane potential, annexin V/propidium iodide dual staining assay, and dichloro-fluorescein (DCF) fluorescence assay. In cell cycle studies, the desired compound specifically with MCF-7 cell progression at the G2/M stage and S stage.

Further, the binding interaction of synthesized compound toward Gal-1 was affirmed by surface plasmon resonance, fluorescence spectrum data and the binding constant value (Ka) of 1.2×104 M^{-1} was seen in fluorescence spectroscopic studies, while the equilibrium constant (KD) value of 5.76×10^{-4} M was seen in surface plasmon resonance. Interaction of synthesized compounds with Gal-1 was affirmed by RP-HPLC studies and found to show 85.44% binding [29, 30].

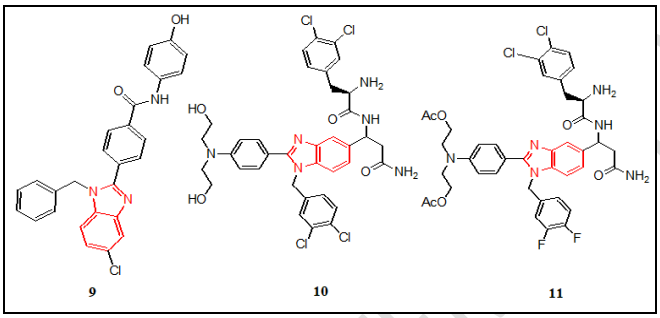

Figure 2: Benzimidazole derivatives synthesized targeting Galectin-1

Tsung-Chieh Shih *et al.*, described a novel Gal-1 inhibitor 10, which was found through the One-Bead-Two-Compound library. The binding interaction of targeted Gal-1 with 10 was affirmed by LC-MS/MS logical and pull-down assay. The interaction complication in between 10 with Gal-1 specifically diminishes membrane-based H-Ras and K-Ras pathways, resulted in the induction of apoptosis process. The 10 showed a synergistic impact in combining with paclitaxel against a large number of the human malignancy cell lines like for example, pancreatic disease, ovarian malignant growth, and breast malignancy cells *in-vitro*. The reaction of paclitaxel with 10 proficiently lessens the development of ovarian malignant growth xenografts in athymic mice *in-vivo* (**Figure 2**).

A similar group was reported a stronger Gal-1 inhibitor 11, it hinders resistant alteration of prostate tumour cell development and infringement functioning. 11 attacks on Gal-1 as an allosteric inhibitor and diminishes Gal-1 binding affinity to their binding target accomplices and furthermore causes depression in Akt and AR signal transmitting pathways. *In=vivo potency* of LLS3 targeted study indicates adequacy in both androgen receptor-positive and negative xenograft models [31, 32].

Tubulin Protein Inhibitors

Tubulin is part of the family groups of globular proteins. In between the presence of various form of isoforms, α-and β-tubulins are the most well-known individuals from tubulin. The cell protein tubulin is a significant protein for replication. Microtubules are empty filaments consisting of head and tail polar sequential arrangement of α-and β-tubulins as the constituent subunits. It also contains 13 dynamic protofilaments arranged parallelly along with the axis of microtubule structure which might give constant transportation for cell content via motor proteins (dynein and kinesin). Basic structure of microtubules is an essential piece of the cell skeleton and dependable for the upkeep of cell shape, motility and intracellular transmission of the vesicles, mitochondria, and different segments [33, 34]. In addition, cell division includes the duplication of DNA and the isolation of the imitated chromosomes into two haploids.

The detachment of these chromosomes occurs in mitotic stage which is done by the microtubules. In the development of the microtubule, the (+)ve end is ceased by β-tubulin while the (-)ve end is discontinued by α-tubulin. They can be found either by polymerization or depolymerization process. They can either abbreviate or extend in a hypothetical pattern by contraction or expansion of α/β-tubulin heterodimers from the end point of microtubules. This activity can be identified as "dynamic precariousness" [35, 36]. Microtubules contains the activity to develop constantly until the free tubulin level is over a perilous level. The evaluative concentration at (+)ve ending is more in comparison with (-)ve end point (which initially stops development). With the effect of drugs on cells, cells might halt developing and initiate their constriction. This modifying alterations from development to shrinkage can be defines as “catastrophe”.

Later, a contracting microtubule may end up and then initiate to develop once more which is known as "salvage". During mitotic cell division, the chromosomes are isolated by the mitotic shaft, which is framed from tubulin microtubules. Tubulin elements have a significant activity in cell division. Few drugs influenced on the micro tubulin elements and causes either polymerization or depolymerization and cell replication alterations. Thus, at the molecular mechanism stage, tubulin is considered as attentive and dependable approaches for structuring novel anticancer drugs.

Zhang *et al.*, reported a derivative series of substituted-1,2-diarylbenzimidazole and evaluated their activity as anticancer agents. Among the other studied compounds, compound 12 has been found to show critical cytotoxicity against human malignant growth cells likely against A549, HepG2, HeLa, and MCF-7 cells. The resulted data shows the effects on GI_{50} range as 0.71–2.41μM which additionally, shows cytotoxicity towards ordinary cells. The apoptosis occurrence by the synthesized compound was affirmed by morphological alterations on HepG2 and HeLa-treated with cells like cell wall disruption, blebbing, and cell contraction. Each data was precisely calculated after apoptosis study using mitochondrial membrane potential, annexin V/propidium iodide dual staining assay, and dichlorofluorescein (DCF) fluorescence assay. In cell cycle investigation, the desired synthesized compound specifically restrained cell development at the G2/M stage. Further, the tested compound demonstrated notable hindrance of microtubule polymerization with an IC_{50} estimation of 8.47μM. The docking evaluation of synthesized compound were performed to affirm the interaction with microtubule protein [37].

Miao *et al.*, synthesized a novel series of 2-aryl-benzimidazole- based dehydroabietic acid analogues as potent cytotoxic drugs by causing hindrance on tubulin polymerization. The targeted compounds structure was identified and confirmed by elemental and analytical test procedures. The desired compound 13 indicated noticeable hindrance against the growth progression of SMMC-7721 (hepatocarcinoma malignant cells) with an IC_{50} estimation of 0.08±0.01μM.

Additionally, this compound indicated potent cytotoxicity in between the limit of 0.04–0.07μM against MDA-MB-231 (Breast Malignant cells), HeLa (cervical malignant cells), and CT-26 (colon malignant cells). The apoptosis process was evaluated using various of techniques like ROS levels analysis, loss of mitochondrial film potential, and cell cycle testing to affirm the acceptance of apoptosis in SMMC-7721 cells. In cell cycle analysis, the desired compound specifically inhibits the tumor development at the G2/M stage. Furthermore, the synthesized compound causes hindrance of microtubule polymerization with an IC_{50} of 5μM. The docking studies shows the selectivity binding to tubulin protein dependent on solid electronic communications between the objective mixes and tubulin [38].

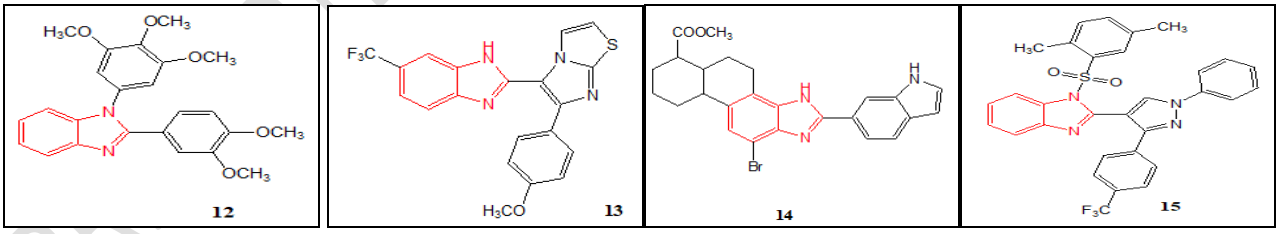

Figure 3: Tubulin Targeting Benzimidazole Derivatives

Wang *et al.*, found a series of benzimidazole containing benzsulfamide pyrazole ring structures as potential tubulin polymerization inhibitors. The derived compound 14 inhibited the cell growth in A549 (lung malignant cells) with an IC_{50} estimation of 0.15±0.05μM. Moreover, it also creates the disruptive actions in HepG2, and MCF-7 cell lines concentration ranging in between 0.17–0.33μM. Detailed study of synthesized derivatives demonstrated huge restraint of microtubule polymerization with an IC_{50}valueas 1.52μM. In cell cycle analytical study, this compound 14 specifically targeted A549 to hinder the cell development at G2/M stage. The derived compound initiated A549 cell apoptosis which was easily understood under the study of annexin V/propidium iodide dual staining assay and cell cycle analysis (**Figure 3**) [39]. A series of imidazo[2,1-b]thiazole-benzimidazole subsidiaries was explained by Baig *et al.*, as antitumor agents

by acting on tubulin polymerization. The synthesized compound 15 has shown cytotoxicity against A549(human lung malignant cell) with an IC_{50}range as 1.08µM. Additionally, it also showed effective cytotoxic activity against DU-145 (prostate malignant cells), MCF-7 (breast malignant cell), A549 (lung disease), and HeLa (cervical disease) in the IC_{50} value of 1.65–7.55µM. Compound 15 particularly disrupts A549 cell development at the G2/M stage during cell cycle analysis. Apoptosis process by the synthesized compound was affirmed by structural alteration in A549-dealt with cells like blebbing, disruption of cell wall, and cell shrinkage. These all process were identified and determined by Hoechst staining, mitochondrial layer potential, annexin V/propidium iodide dual staining test. Moreover, microtubule assembly was hindered by the synthesized compound with an IC_{50}value of 1.68µM [40].

Carbonic Anhydrase Inhibitors

The hCAs enzyme (human carbonic anhydrases) being a part pf α-family of carbonic anhydrases class, existed in 16 diverse isoforms [41]. In light of their area in the body, they are characterized into cytosolic hCAs, transmembrane hCAs, mitochondrial-bound hCAs, secretory hCAs, and chemically latent isoforms, which are considered as CA-related proteins (CARPs) [42]. Among all the forms of hCAs, the hCA isoforms IX & XII expressed their significant actions for different types of malignant cell formations. Both isoforms are tumor-linked transmembrane bound enzymes, specifically hypoxic cancers, which resulted as significant target for developing different types of cancers [43].

They have also shown their contributed activities in the process of angiogenesis, metastasis, tumour development and proliferative development of malignant cells [44]. These hCAs dependent cancer development activities, centring the focus of researchers around the improvement of different heterocycles that specifically target tumor-linked hCAs isoforms IX and XII for efficient treating drugs cancer treatment [45].

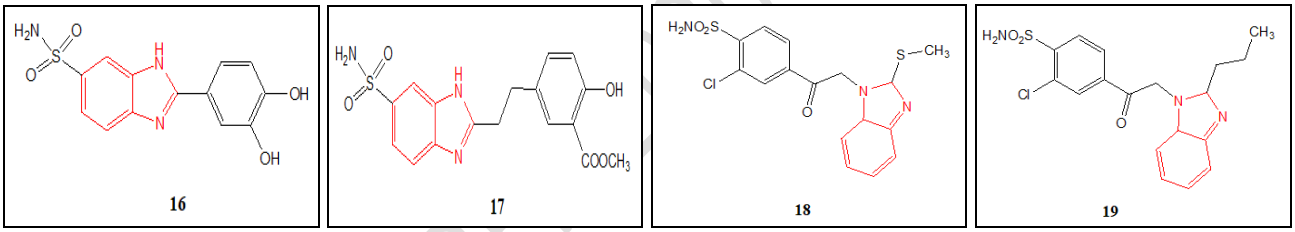

Figure 4: Benzimidazole Derivatives as hCAs Targeting Anticancer Drugs

During various of research work in target hCAs isoforms for anticancer activity, 2-substituted-benzimidazole-6-sulfonamides series was defined as having an anticancer property by biological evaluation against four physiologically targeted hCAs (CA-I, CA-II, CA-IX and CA-XII). The inhibitory activity analysis of hCAs demonstrated that this novel series of benzimidazole-based sulfonamide analogues showed specific hindrance toward tumor-linked isoforms (CA-IX &CA-XII). Compound 16 a derivative of benzimidazole-based sulfonamide analogue series has been observed having potent interference at low concentration of drugs against hCA-IX and hCA-XII isoform within the K_i (inhibitory constant) value of 2.2µM and 22.3µM.Alternatively, compound 17displayed potent resistance at less concentration against hCA-IX and hCA-XII, with K_i value of 5.9µM and 7.9µM individually [46]. Asta Zubriene *et al.*, have described the synthesis of novel benzenesulfonamides with benzimidazole derivatives targeting selective human carbonic anhydrase (hCA-I, II, VII, XII, & XIII) as inhibitors. The desired compounds were obtained from the reaction of pre-prepared benzimidazole derivatives with various phenacyl bromides. The synthesized compounds 18 & 19 were assessed against five physiologically significant hCA isoforms (CA-I, CA-II, CA-VII, CA-XII& CA-XIII). These compounds have showed a promising inhibitory activity at a lower concentration against targeted hCAs with a K_i range of 1.67–66.7Mm (**Figure 4**) [47].

Epidermal Growth Factor Receptor (EGFR) Inhibitors

The EGFR (Epidermal Growth Factor Receptor) is a sub-categorized family ErbB-1, ErbB-2, ErbB-3, ErbB-4 of ErbB class of tyrosine kinase receptors [48]. The interior ligands like EGF and TGF$_\alpha$ takes part in maintaining epithelial tissue progressions and homeostasis processes by

developing signal transmissions to cells by collaborating with EGFR receptors [49, 50]. In epithelial malignancies, excess of formation of EGFR ligands in cancerous cells creates stimulation or modification of EGFR receptors to produce the development, metastasis and intrusion [51, 52]. In the current project work, a series of benzimidazole-based triazole and thiadiazole analogues was synthesized and assessed as specific EGFR inhibitors. The single-crystal X-beam crystallographic analysis has been performed to affirm the molecular structure of the desired compound.

On biological evaluation screening, they have shown potential antiproliferative properties against EGFR kinase in comparison with standard drug erlotinib. On observation, compound 20 shows potent inhibitory actions on EGFR kinase on MCF-7 (breast cancer cell). On docking evaluation studies demonstrated that the compound indicated two-hydrogen holding associated with the residue of LYS721 and THR830 at the interaction site of EGFR tyrosine kinase [53]. Akhtar *et al.*, announced the benzimidazole-oxadiazole hybrid compounds as specific EGFR and erbB2 receptor inhibitors.

In-vitro studies, compound 21causes a potential inhibitory activity with an IC_{50} of 5.0µM onMCF-7 (breast malignant growth cells). The synthesized compound generates hindrance of EGFR and erbB2 receptor at 0.081µM and 0.098µM individually. Many of these synthesized compounds have shown high cytotoxic activities against selective human malignancy cell lines. During cell cycle analysis, the synthesized compound specifically targets MCF-7 cell progression at the G2/M stage [54].

Akhtar *et al.*, synthesized a novel series by treating benzimidazole-based pyrazole derivatives through a one-pot multicomponent reaction and analysing their biological activities for anticancer activities. On evaluating their anticancer activity against MCF-7, MDA-MB231, A549, HepG2, and HaCaT cell lines specifically targeting EGFR receptors. Compound 22 showed promising cytotoxicity against the A549 (lung malignant cell lines) with an IC_{50} estimation of 2.2 mM and the EGFR receptor inhibited by an IC_{50} of 0.97 mM. This synthesized compound shows targeted action on A549 cell development at the G2/M stage during cell cycle analysis. It also hinders the development of lung malignancy cells by inducing apoptosis process [55]. Yuan *et al.*, reported a library of 6-amide- 2-aryl benzoxazole / benzimidazole derivatives and evaluated their inhibitory activity against VEGFR-2. The library of mixes displayed specific anticancer action against the HepG2 (hepatocellular carcinoma), and HUVECs (umbilical vein endothelial cells) over the A549 (lung malignant cell) and MDA-MB-231(breast cancer) cell lines. Many of these synthesized compounds have shown great hindrance in the progression of HepG2 and HUVEC cell lines with 1.47 mM and 2.57 mM in IC_{50}value, separately. Compound 23 indicated against angiogenesis process (79% restraint at 10 nM/eggs) by chick chorioallantoic membrane (CAM) assay and expressed its action by VEGFR-2 kinase hindrance with an IC_{50} of 0.051mM (**Figure 5**) [56].

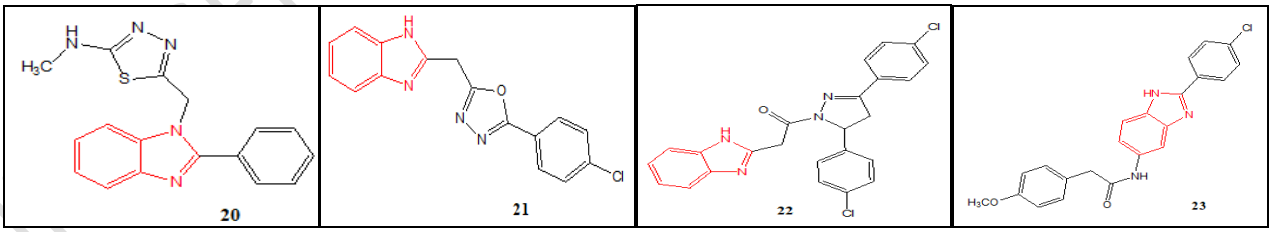

Figure 5: Epidermal Growth Factor Receptor targeting benzimidazole based drugs

Miscellaneous Agents

Wu *et al.* incorporated a series of novel benzimidazole-2-substituted phenyl or pyridine propyl ketene subordinates where two (24 & 25) of these synthesized compounds shows potent inhibitory activity against HCT116 (colorectal), MCF-7 (breast), and HepG2 (liver) cell lines. These compounds have shown successful restraint activity of tumor development in BALB/c mice withHCT116(colon carcinoma cells) [57]. Reddy *et al.*, reported a series of pyrazole-incorporating benzimidazole hybrids and observed as potential antiproliferative action against A549 (lung), MCF-7 (breast), and HeLa (cervical) cell lines. Compounds 26 and 27 indicated as effective inhibitor against all the cell lines tried, with IC_{50}

values in between 0.83–1.81μM [58]. Gowda *et al.*, synthesized a novel series of 1-(4-methoxy phenethyl)-1H-benzimidazole-5-carboxylic acid and the compound 28induced cell apoptosis in K562 and CEM (leukemic cell lines), by means of S/G2 cell cycle inhibiting; down regulations of CDK2, Cyclin B1 and PCNA; cleavage of PARP; and elevated levels of DNA strand breaks [59]. Akhtar *et al.*, describes a series of benzimidazole-linked oxadizole hybrids which on screening for their anticancer and in vitro EGFR and erbB2 receptor inhibition assay. While compound 29 & 30 shown prominent activity (**Figure 6**) [54].

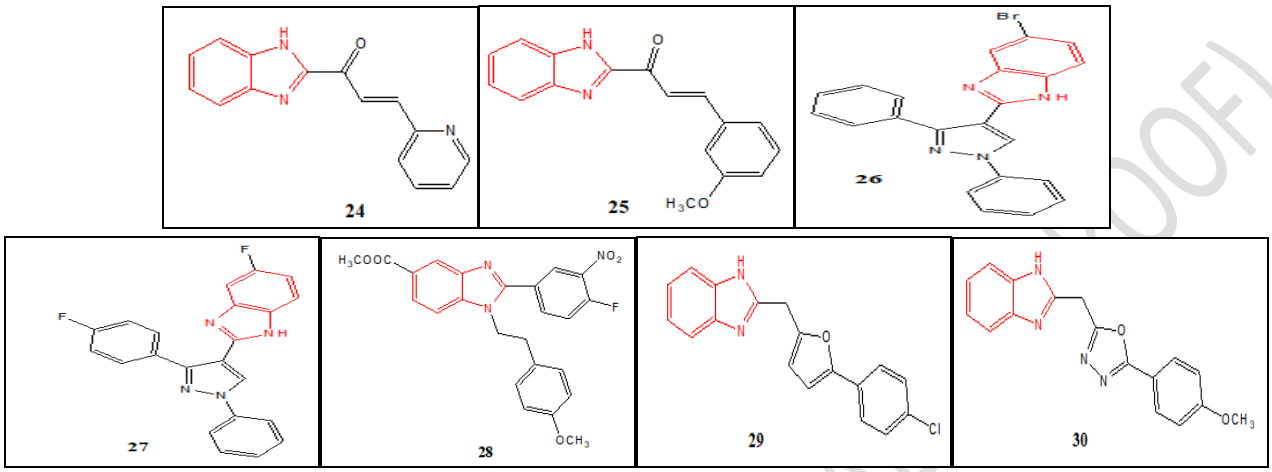

Figure 6: Potentially active antiproliferative drugs targeting various of binding sites

CONCLUSION

Lightening the detailed study of novel benzimidazole based derivatives for the selective targeting for cancerous cells. Many of these synthesized and biologically screened compounds have shown selective target action while some have shown unselective targeted activity. Thus, significant requirement for development of novel series of benzimidazole for selective target activity along with no or minute adverse effects.

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CONFLICT OF INTEREST

None

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