Synthesis, Antimicrobial, Antiproliferative, and Docking Studies of 1,3,4-Oxadiazole Derivatives Containing Benzimidazole Scaffold

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Abstract: Due to chemotherapy failure, drug resistance, and the advent of multiresistant microbes, new antimicrobial and anticancer agents are needed. The present study has synthesized and screened new 1,3,4-oxadiazole derivatives bearing benzimidazole scaffold for antimicrobial and anticancer activities. The structure of final compounds 8-15 was completely established by NMR (1H, 13C), mass, IR, and elemental analysis. From the antimicrobial study, compounds 10 and 15 exhibited promising effects against Gram-positive bacterial strains, S. aureus, and S. epidermidis, with MIC comparable to standard drugs. Also, the same compounds 10 and 15 displayed potent cytotoxicity against MCF-7 breast carcinoma, which was comparable to doxorubicin. Furthermore, docking studies have been performed to explore the binding interaction of the compounds with the target protein.

Keywords: 1,3,4-oxadiazole; benzimidazole; antimicrobial; antiproliferative.

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1. Introduction

Due to chemotherapy failure, the advent of multiresistant microbes, continued use of antibiotics, selectivity, and adverse effects, microbial infection is a major challenge in drug innovation [1-5]. Furthermore, microbial infection is also responsible for the development or progression of cancer due to DNA damage, impaired immunity, and chronic inflammation [6,7] that leads to a decrease in survival rate, extended hospitalization, and treatment disturbances [8]. For example, Helicobacter pylori is a Gram-negative bacteria declared a major cause of gastric carcinoma by the International Agency for Research on Cancer (IARC) [9]. Therefore, drugs with dual modes of action against microbial infection and cancer are crucial for treating these diseases.

Benzimidazole, an isostere of purine nucleotides, is a heterocyclic fused benzene ring with an imidazole ring [10,11]. This scaffold has vast biological activities such as antibacterial, anticancer, and anti-inflammatory [12-16]. Benzimidazole is the building block of many drugs such as valiparib (anticancer), ridinalazole (antibacterial), albendazole (anthelminthic drug), bendamustine (anticancer), and astemizole (antihistamine drug)[17-21] (Figure 1).
Figure 1. Antimicrobial/anticancer drugs containing benzimidazole and 1,3,4-oxadiazole moieties.

On the other hand, 1,3,4-oxadiazoles has been found to exhibit anticancer [22], antimicrobial [23,24], antidiabetic [25], anti-inflammatory [26], antiviral [27] and antitubercular activities [28]. 1,3,4-oxadiazole derivatives have shown promising anticancer and antimicrobial activities through inhibition of different enzymes involved in the pathogenesis of these diseases [29-31]. Thus, incorporating these two heterocycles into a compound could provide new molecules with improved pharmacological activity. In the current work, we report the synthesis, antimicrobial and antiproliferative activities of 1,2,3-oxadiazole derivatives containing benzimidazole scaffold.

2. Materials and Methods

2.1. Chemistry.

The chemicals used were purchased from Sigma Aldrich, USA. Bruker 300 and 850 MHZ spectrophotometer was used for NMR analysis either in DMSO or CDCl3. FT-IR spectra were determined on Thermo Scientific iS50 and melting point on Stuart SMP40 machine. Electron spray ionization mass spectra were carried out using Thermo Scientific-LCQ Fleet (LCF10605) elemental analysis on LEECO Elementar Analyzer. The intermediates 3-6 were prepared by the reported methods [32,33].

2.2. General procedure for the synthesis of 2-\{(5-\{(2-(2-chlorophenyl)-1H-benzimidazol-1-yl)methyl\}-1,3,4-oxadiazol-2-yl)sulfanyl\}-N-(aryl)acetamide (8-15).

A mixture of compound 6 (0.01 mole) and anhydrous potassium carbonate (0.015 mole) was refluxed for 2 hr in dry acetone (50 ml). Then freshly prepared aromatic acetamide 7a-h (0.01 mole) was added to the reaction mixture and continued to reflux for 9-10 hrs. After reaction completion, the mixture was filtered and washed with hot acetone. The filtrate was concentrated and poured into ice; the resulting solid was filtered and recrystallized in a suitable solvent to yield compounds 8-15. The $^1$H NMR (Figure S1-S3), $^{13}$C NMR (Figure S4-S6), and mass spectra (Figure S7-S9) of some final compounds are provided in the supplementary file.
2.2.1. 2-((5-(2-(2-chlorophenyl)-1H-benzimidazol-1-yl)methyl)-1,3,4-oxadia zol-2-yl)thio)-N-phenylacetamide (8).

Yield: 72%; M.p.: 124-126 ºC; IR (vmax, cm⁻¹): 3381, 2987, 1687, 1588, 1497, 1041; 1H NMR (850 MHz, DMSO-d6): δ 4.85 (s, 2H, S-CH2), 5.33 (s, 2H, N-CH2), 7.08-8.15 (m, 13H, Ar-H), 11.61 (s, 1H, NH); 13C NMR (213 MHz, DMSO-d6): δ 37.04, 48.35, 111.12, 116.98, 117.88, 122.61, 122.87, 124.25, 127.17, 127.48, 129.65, 130.01, 130.85, 131.94, 132.32, 134.42, 139.21, 147.57, 149.03, 160.18, 161.18, 170.31; ESI +ve MS (m/z): 475 (M+H)+; Elemental analysis for C23H18ClN3O2S: Calcd: C, 51.93; H, 3.07; N, 12.63; O, 5.77; S, 5.78. Obs: C, 60.53; H, 3.84 N, 14.70; O, 6.72; S, 6.73.

2.2.2. 2-((5-(2-(2-chlorophenyl)-1H-benzimidazol-1-yl)methyl)-1,3,4-oxadia zol-2-yl)thio)-N-(4-methoxyphenyl)acetamide (9).

Yield: 85%; M.p.: 278-279 ºC; IR (vmax, cm⁻¹): 3382, 3140, 1649, 1623, 1585, 1498, 1023; 1H NMR (850 MHz, DMSO-d6): δ 3.88 (s, 3H, OCH3), 4.86 (s, 2H, S-CH2), 5.34 (s, 2H, N-CH2), 7.10-8.15 (m, 12H, Ar-H), 11.65 (s, 1H, NH); 13C NMR (213 MHz, DMSO-d6): δ 37.03, 48.37, 55.58, 112.36, 116.88, 119.47, 121.89, 123.68, 125.12, 126.93, 127.29, 127.68, 129.50, 130.35, 131.75, 132.31, 134.78 139.07, 147.87, 148.83, 160.20, 161.23, 170.54; ESI +ve MS (m/z): 505 (M+H)+; Elemental analysis for C23H20ClN3O2S: Calcd: C, 59.34; H, 3.98; N, 13.84; O, 9.49; S, 6.34. Obs: C, 59.36; H, 3.96; N, 13.83; O, 9.52; S, 6.35.

2.2.3. 2-((5-((2-(2-chlorophenyl)-1H-benzimidazol-1-yl)methyl)-1,3,4-oxadia zol-2-yl)sulfanyl)-N-(3-bromophenyl)acetamide (10).

Yield: 70%; M.p.: 145-146 ºC; IR (vmax, cm⁻¹): 3384, 3143, 1644, 1624, 1584, 1498, 1435, 1042; 1H NMR (850 MHz, DMSO-d6): δ 4.87 (s, 2H, S-CH2), 5.34 (s, 2H, N-CH2), 7.08-8.15 (m, 12H, Ar-H), 11.60 (s, 1H, NH); 13C NMR (213 MHz, DMSO-d6): δ 37.03, 48.37, 111.14, 116.87, 118.41, 122.62, 123.68, 124.21, 127.15, 127.29, 127.65, 130.01, 130.35, 131.75, 132.32, 134.41, 139.05, 147.54, 148.03, 160.19, 161.13, 170.23; ESI +ve MS (m/z):556 (M+H)+; Elemental analysis for C23H17BrClN3O2S: Calcd: C, 51.95; H, 3.09; N, 12.62; O, 5.77; S, 5.78. Obs: C, 51.93; H, 3.07 N, 12.63; O, 5.78; S, 5.76.

2.2.4. 2-((5-((2-(2-chlorophenyl)-1H-benzimidazol-1-yl)methyl)-1,3,4-oxadia zol-2-yl)sulfanyl)-N-(3-bromophenyl)acetamide (11).

Yield: 60%; M.p.: 165-166 ºC; IR (vmax, cm⁻¹): 3384, 3093, 1704, 1644, 1618, 1584, 1475, 1429, 1048; 1H NMR (850 MHz, DMSO-d6): δ 4.80 (s, 2H, S-CH2), 5.29 (s, 2H, N-CH2), 7.06-8.02 (m, 12H, Ar-H), 11.61 (s, 1H, NH); 13C NMR (213 MHz, DMSO-d6): δ 33.28, 46.96, 111.98, 115.26, 120.98, 122.76, 127.16, 127.21, 127.29, 127.72, 128.19, 132.41, 133.04, 134.50, 135.05, 139.32, 148.31, 149.55, 160.28, 161.19, 170.34; ESI +ve MS (m/z):556 (M+H)+; Elemental analysis for C24H17BrClN3O2S: Calcd: C, 51.95; H, 3.09; N, 12.62; O, 5.77; S, 5.78. Obs: C, 51.96; H, 3.10; N, 12.61; O, 5.79; S, 5.79.

2.2.5. 2-((5-((2-(2-chlorophenyl)-1H-benzimidazol-1-yl)methyl)-1,3,4-oxadia zol-2-yl)sulfanyl)-N-(4-bromophenyl)acetamide (12).

Yield: 65%; M.p.: 110-111 ºC; IR (vmax, cm⁻¹): 3389, 3094, 1706, 1644, 1622, 1599, 1478, 1432, 1047; 1H NMR (850 MHz, DMSO-d6): δ 4.77 (s, 2H, S-CH2), 5.28 (s, 2H, N-CH2), 7.05-7.90 (m, 12H, Ar-H), 11.38 (s, 1H, NH); 13C NMR (213 MHz, DMSO-d6): 35.97, 46.75.
2.2.6. 2-({5-[2-(2-chlorophenyl)-1H-benzimidazol-1-yl)methyl]-1,3,4-oxadiazol-2-yl}sulfanyl)-N-(2-methylphenyl)acetamid (13).

Yield: 65%; M.p.: 132-133 ºC; IR (ν_max, cm⁻¹): 3401, 2763, 1705, 1646, 1617, 1562, 1477, 1434, 1048; ¹H NMR (850 MHz, DMSO-d₆): δ 2.19 (s, 3H, Ar-CH₃), 4.77 (s, 2H, S-CH₂), 5.18 (s, 2H, N-CH₂), 7.04-7.87 (m, 12H, Ar-H), 10.95 (s, 1H, NH); ¹³C NMR (213 MHz, DMSO-d₆): δ 17.64, 34.82, 45.26, 112.65, 124.95, 126.12, 127.16, 127.29, 127.62, 128.15, 128.26, 129.82, 130.04, 131.28, 133.12, 133.60, 133.82, 135.66, 136.05, 148.77, 149.70, 161.21, 161.51, 170.39; ESI +ve MS (m/z): 490 (M+H)⁺; Elemental analysis for C_{25}H_{20}ClN₅O₂S: Calcd: C, 61.28; H, 4.11; N, 14.29; O, 6.53; S, 6.54. Obs: C, 61.29; H, 4.10; N, 14.31; O, 6.51; S, 6.53.

2.2.7. Methyl-2-{{{[5-[2-(2-chlorophenyl)-1H-benzimidazol-1-yl)methyl]-1,3,4-oxadiazol-2-yl}sulfanyl}acetyl}amino}benzoate (14).

Yield: 60%; M.p.: 133-134 ºC; IR (ν_max, cm⁻¹): 3391, 3146, 2952, 1701, 1647, 1621, 1584, 1498, 1435, 1044; ¹H NMR (850 MHz, DMSO-d₆): δ 3.87 (s, 3H, O-CH₃), 4.78 (s, 2H, S-CH₂), 5.28 (s, 2H, N-CH₂), 7.05-7.98 (m, 12H, Ar-H), 11.64 (s, 1H, NH); ¹³C NMR (213 MHz, DMSO-d₆): δ 35.97, 47.92, 52.31, 110.4, 111.7, 120.38, 120.42, 124.68, 126.78, 127.27, 127.55, 127.80, 129.45, 130.72, 131.93, 134.41, 138.73, 148.15, 149.74, 160.15, 162.59, 169.79, 171.02; ESI +ve MS (m/z): 534 (M+H)⁺; Elemental analysis for C_{26}H_{20}ClN₅O₄S: Calcd: C, 58.48; H, 3.78; N, 13.12; O, 11.98; S, 6.00. Obs: C, 58.47; H, 3.79; N, 13.10; O, 11.99; S, 6.02.

2.2.8. 2-({5-[2-(2-chlorophenyl)-1H-benzimidazol-1-yl)methyl]-1,3,4-oxadiazol-2-yl}sulfanyl)-N-(2-chlorophenyl)acetamid (15).

Yield: 60%; M.p.: 110-111ºC; IR (ν_max, cm⁻¹): 3385, 3093, 1707, 1644, 1623, 1584, 1499, 1431, 1047; ¹H NMR (850 MHz, DMSO-d₆): δ 4.80 (s, 2H, S-CH₂), 5.40 (s, 2H, N-CH₂), 7.06-7.85 (m, 12H, Ar-H), 11.64 (s, 1H, NH); ¹³C NMR (213 MHz, DMSO-d₆): δ 34.56, 46.90, 113.19, 115.17, 120.86, 121.38, 125.91, 126.08, 127.99, 130.40, 130.68, 131.93, 133.56, 133.65, 134.89, 147.76, 149.86, 160.86, 161.03, 170.22; ESI +ve MS (m/z): 510 (M+H)⁺; Elemental analysis for C_{24}H_{17}Cl₂N₅O₂S: Calcd: C, 56.48; H, 3.36; N, 13.72; O, 6.27; S, 6.28.Obs:C, 56.49; H, 3.34; N, 13.70; O, 6.30; S, 6.28.

2.3. Antiproliferative activity.

Compounds (8-15) were evaluated for antiproliferative effect by MTT assay on HepG2, HCT-116, and MCF-7 cancer cell lines. Tamoxifen and doxorubicin were used as standard anticancer drugs. The activity was performed according to our published work [20], and the results are presented in Table 1.
2.4. Antimicrobial activity.

The antimicrobial activity was performed against four bacterial strains, *Staphylococcus aureus* (*S. aureus*, ATCC 25923), *S. epidermidis* (*S. epidermidis*, ATCC 12228), *Escherichia coli* (*E. Coli*, ATCC 25992), *Klebsiella pneumoniae* (*K. pneumoniae*, ATCC 700603) and one fungal strain, *Candida albicans* (*C. albicans*) by well diffusion method as previously published [34]. The results are shown in Table 2.

2.5. Molecular docking studies.

The Molecular docking was performed by Glide-tools as previously reported [35]. The results are presented in Table 3, and Figure 2.

3. Results and Discussion

3.1. Chemistry.

The final compounds (8-15) were obtained by the condensation of 1,3,4-oxadiazole-2-thiol (6) with different chloro acetamides using (7a-h) potassium carbonate in dry acetone. The key intermediate, 1,3,4-oxadiazole-2-thiol (6), was subsequently prepared by the fusion of 2-chloro benzaldehyde (1) with o-phenylene diamine (2) using sodium metabisulfite at 120 °C followed by the esterification with ethylchloroacetate, reaction with hydrazine monohydrate and refluxing in ethanol with KOH and CS₂ (Scheme 1).

![Scheme 1. Synthetic scheme for the synthesis of 1,3,4-oxadiazole derivatives containing benzimidazole scaffold.](https://biointerfaceresearch.com/)

The formation of the key intermediate (6) was confirmed by mass spectrometry, which showed a molecular ion peak at 343 [M+H]⁺. The formation of final 1,3,4-oxadiazole-linked benzimidazole hybrids (8-15) was confirmed by using different analytical techniques such as IR, NMR, mass, and elemental analysis. The IR spectrum exhibited an absorption band at 3210-
3177 cm\(^{-1}\) for N-H benzimidazole and 1581-1546 cm\(^{-1}\) for C=\(\equiv\)N of oxadiazole ring stretching, respectively. The presence of carbonyl group (C=O) was confirmed by the appearance of strong stretching at 1689-1664 cm\(^{-1}\), which was observed after S-alkylation and the disappearance of the S-H signal in the IR spectrum. In \(^1\)H NMR spectrum, the appearance of two signals as a singlet at \(\delta\) 4.77-4.87 ppm and \(\delta\) 5.18-5.40 ppm was assigned to S-CH\(_2\) and -N-CH\(_2\)- groups, respectively. The aromatic region appeared in the range 7.04-8.15 ppm, and NH in the range 10.95-11.64 ppm in \(^1\)H NMR. At the same time, \(^13\)C NMR revealed downfield signals for C=O, 160.04-161.21 ppm for C=\(\equiv\)N of 1,3,4-oxadiaozle ring. Besides these confirmatory peaks, aromatic carbons were found in the range 110.4-149.86 ppm, N-CH\(_2\) signal in the range 45.26-48.37 ppm, and S-CH\(_2\) peaks in the range 33.28-37.03 ppm. All the final compounds were confirmed by electrospray ionization mass spectrometry which displayed desired molecular ion peaks of the compounds.

3.2. Antiproliferative activity.

The final molecules (8-15) were screened for cytotoxicity HepG2, HCT-116, and MCF-7 cancer cell lines using an MTT assay (Table 1). Tamoxifen and doxorubicin were used as reference drugs for the activity [20].

Table 1. Cytotoxicity (IC\(_{50}\), \(\mu\)M) of 8-15 against MCF-7, HepG2, and HCT-116 cancerous cells.

<table>
<thead>
<tr>
<th>Compds</th>
<th>IC(_{50}) ((\mu)M)</th>
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<tbody>
<tr>
<td></td>
<td>MCF-7</td>
</tr>
<tr>
<td>8</td>
<td>64.37</td>
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<td>9</td>
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<td>15</td>
<td>1.53</td>
</tr>
<tr>
<td>Tamoxifen</td>
<td>18.94</td>
</tr>
<tr>
<td>doxorubicin</td>
<td>1.45</td>
</tr>
</tbody>
</table>

IC\(_{50}\) is the mean ± standard deviation performed in triplicate experiments; Doxorubicin and tamoxifen are positive reference drugs.

It was found that compounds 10 and 15 were the most active toward MCF-7 cells. Among these compounds, 10 (9.10 fold), 14 (1.78 fold), and 15 (12.37 fold) exhibited better cytotoxicity on MCF-7 cells than tamoxifen. At the same time, compared to doxorubicin, compound 15 (IC\(_{50}\) = 1.53 \(\mu\)M) exhibited comparable cytotoxicity to doxorubicin, while compound 10 (IC\(_{50}\) = 2.08 \(\mu\)M) was 0.94 times active to doxorubicin (IC\(_{50}\) = 1.45 \(\mu\)M). The remaining compounds displayed moderate activity. Against HepG2 cancer cells, compounds 10 and 15 have shown significant antiproliferative activity with IC\(_{50}\) 6.69 \(\mu\)M and 4.37 \(\mu\)M, respectively. All the compounds except 8 were better than tamoxifen (IC\(_{50}\) = 21.96 \(\mu\)M), with IC\(_{50}\) in the range 3.36-20.71 \(\mu\)M. Against colorectal HCT-116 cancer cells, two compounds (10 and 15) were most active with IC\(_{50}\) 5.38 and 2.78 \(\mu\)M, respectively. Compound 15 (IC\(_{50}\) = 2.78 \(\mu\)M) exhibited comparable cytotoxicity to doxorubicin (IC\(_{50}\) = 2.12 \(\mu\)M), whereas compounds 10, 11, and 15 with IC\(_{50}\) in the range 2.35-16.97 \(\mu\)M were found to be better than tamoxifen (IC\(_{50}\) = 24.26 \(\mu\)M) in killing the cancer cells. It was noted that compounds 10 and 15 bearing bromo at meta and chlorine at the ortho position, respectively, were the most promising against all the tested cell lines.
3.3. Antimicrobial activity.

All the final synthesized molecules (8-15) were screened for antimicrobial activity against four bacterial strains, *Staphylococcus aureus* (S. aureus, ATCC 25923), *S. epidermidis* (S. epidermidis, ATCC 12228), *Escherichia coli* (E. Coli, ATCC 25992), *Klebsiella pneumoniae* (K. pneumoniae, ATCC 700603) and one fungal strain, *Candida albicans* (C. albicans) by well diffusion method [34]. The antimicrobial activity is presented in the form of inhibition zone and minimum inhibitory concentration in Table 2.

<table>
<thead>
<tr>
<th>Compd.</th>
<th>S. aureus</th>
<th>S. epidermidis</th>
<th>E. coli</th>
<th>K. pneumoniae</th>
<th>C. albicans</th>
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<tbody>
<tr>
<td></td>
<td>ZI</td>
<td>MIC</td>
<td>ZI</td>
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<tr>
<td>Amox.</td>
<td>28</td>
<td>12.5</td>
<td>30</td>
<td>12.5</td>
<td>16</td>
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<tr>
<td>Flucon.</td>
<td>NT</td>
<td>NT</td>
<td>NT</td>
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</table>

NT: not tested. Amox.: amoxicillin-standard antibacterial drug; Flucon.: fluconazole-positive control for antifungal activity.

The antimicrobial results showed that the tested compounds showed moderate to promising activity against the tested microbial strains. Among the tested compounds, most of the compounds showed better activity against the Gram-positive strains compared to Gram-negative strains. Two compounds (10 and 15) from the series showed promising activity against both types of tested strains, comparable to the standard drug amoxicillin. Compound 10 showed zone of inhibition 28, 20, 14, and 14 mm, whereas compound 15 showed 30, 28, 14, 16 mm against *S. aureus*, *S. epidermidis*, *E. coli*, and *K. pneumoniae*, respectively, at 200 μL/disc. Compounds that showed more than 10 mm zone of inhibition were further evaluated for their MIC; the tested compounds showed MIC in the 200 – 12.5 μL/disc range. Two compounds 10 and 15 among the series, showed good MIC; compound 10 showed 25, 50, 100, and 100 μL/disc against *S. aureus*, *S. epidermidis*, *E. coli*, and *K. pneumoniae* respectively, whereas compound 15 displayed 12.5, 12.5, 50 and 25 μL/disc against *S. aureus*, *S. epidermidis*, *E. coli*, and *K. pneumoniae* respectively compared to standard drugs with MIC 12.5, 12.5, 50 and 25 μL/disc respectively. Antifungal activity of the tested compounds was found to be moderate with a zone of inhibition of 8–14 mm and MIC 50-100 μL/disc. It was noted that compounds 10 and 15 were the most promising molecules against the Gram-positive *S. aureus* bacteria.

3.4. Molecular docking studies.

To explore the binding interaction of the compounds, the molecular docking of the final compounds (8-15) has been performed with the EGFR protein (PDB 1M17) using erlotinib as a reference standard [31]. Erlotinib is reported to exhibit interaction with vital amino acids such as Phe699, Met96, Met964, Lys721, Cys773, Leu977, Asn784, Gln958, Val702, Gln962, Leu820, Met769, Asn818, H-bonds with Gln767, and Leu768 in EGFR binding pocket. The binding free energies ΔG of 1,3,4-oxadiazole derivatives (8-15) are tabulated in Table 3.
Table 3. The docking scores (kcal/mol) of compounds (8-15) against EGFR kinase.

<table>
<thead>
<tr>
<th>Compd.</th>
<th>ΔG</th>
<th>RMSD</th>
<th>Eplace</th>
<th>Econf</th>
<th>Eele</th>
<th>LE</th>
<th>Ki</th>
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<td>5.09</td>
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<td>-10.82</td>
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ΔG: Free binding energy of the ligand from a given conformer, Econf and Eplace: are free binding energy for the conformer and receptor; RMSD: Root Mean Square Deviation; Eele: Electrostatic interaction with the receptor, L.E.: Ligand efficiency. Ki: Inhibition constant.

It was observed that these compounds showed higher binding energy (-8.09 to -8.41 Kcal/mol) than erlotinib. Compounds 10 and 15 bearing meta-bromo and ortho-chloro, respectively, interacted with the binding pocket through the formation of H-bond with Gly772 & Cys773 for 10 and Asp831 for 15. The results of the docking study were in agreement with biological study results indicating that compounds 10 and 15 could be used as leads for antimicrobial and anticancer agents (Figure 2).

Figure 2. Binding interaction of erlotinib and compounds 10, 15 against EGFR kinase.

4. Conclusions

A series of novel 1,3,4-oxadiazole derivatives bearing benzimidazole scaffold have been successfully prepared by the alkylation of 5-((2-(2-chlorophenyl)-1H-benzo[d]imidazol-1-yl)methyl)-1,3,4-oxadiazole-2-thiol (6) with different chloroacetamides. The antimicrobial results showed that compounds 10 (MIC= 25 μL/disc) and 15 (MIC= 12.5 μL/disc) were most potent against S.aureus. The antiproliferative activity displayed that compound 15 (IC₅₀= 1.53 μM) exhibited comparable cytotoxicity to doxorubicin, while compound 10 (IC₅₀= 2.08 μM) was 0.94 times active to doxorubicin (IC₅₀= 1.45 μM) against MCF-7 cells. The docking study further supported the biological activities exhibited by compounds 10 and 15. It can be concluded that compounds 10 and 15 could be used as antimicrobial and anticancer lead candidates.

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Conflicts of Interest

The authors declare no conflict of interest.

References


Figure S1. $^1$H NMR of compound 12.

Figure S2. $^1$H NMR of compound 13.
Figure S3. $^1$H NMR of compound 15.

Figure S4. $^{13}$C NMR of compound 12.
Figure S5. $^{13}$C NMR of compound 13.

Figure S6. $^{13}$C NMR of compound 15.
Figure S7. Mass spectrum of compound 12.

Figure S8. Mass spectrum of compound 13.
Figure S9. Mass spectrum of compound 15.