ANTICANCER STUDIES OF NOVEL 2-IODO-4-HYDROXYMETHYL-1, 5-DIPHENYL SUBSTITUTE-1-H-IMIDAZOLE DERIVATIVES.

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ABSTRACTS:
The aim of the present study was the evaluation for anticancer activity of 2-iodo 4-hydroxy methyl-1, 5 diphenyl substituted 1-H-imidazole derivatives(C-IVa-j). Then identification of novel anti-cancer agents that can potently target cancer cells. Cancer is one of the major causes of death worldwide irrespective of the sex. The imidazole nucleus in general and its chemistry has Attention due to outstanding biological activities. In the present reports synthesized series of novel derivatives 2-iodo 4-hydroxy methyl 1, 5 diphenyl substituted 1-H-imidazole derivatives(C-IVa-j) and evaluated for their in vitro cytotoxic effects against MDA MB 4355 (Human breast cancer cell), by the MTT assay. The results were compared with the standard drug inhibitors 5 fluorouracil (10μg/ml). Compound no. C-IVc (41.00), C-IVf (49.72)and C-IVg(57.18) exhibited significant inhibitory activities against MDA MB 4355 (breast cancer) cancer cell lines at 20μg/mL concentration compared to the positive control 5-FU (54.33%) respectively. The results indicated that Compounds containing diphenyl substitution with, 4-Br, 3-OH, 2-NO2 and 2,4-dinitro showed potent anti cancer activity.

KEYWORDS: Imidazole, Anticancer, Human breast cancer cell, MTT assay.

INTRODUCTION
Imidazole and its derivatives have attracted considerable interests in recent years for their versatile properties in chemistry and pharmacology. In the present time imidazole plays an important part in the development of new drug for treatment of cancer activity. Nitrogen containing heterocyclic ring in imidazole possesses biological and pharmaceutical importance. Imidazole (1,3-diaza-2,4-cyclopentadiene) is a planar five-member ring system with 3C and 2N atom in 1 and 3 positions. The simplest member of the imidazole family is imidazole itself, a compound with molecular formula C3H4N2. The systemic name for the compound is 1, 3 diazole, one of the annular N bear a H atom and can be regarded as a pyrole type N. It is soluble in water and other polar solvents. It exists in two equivalent tautomeric forms because the hydrogen atom can be located on either of the two nitrogen atoms.1

Its derivatives possess extensive spectrum of biological activities such as antibacterial2, antitubercular3, anticancer4-6, antifungal7-9, analgesic10-11, anti-inflammatory12 and anti-HIV activities13.
2.0 MATERIAL AND METHODS

2.1 MATERIAL
All the reagents, chemicals and solvents were purchased from S.D fine, Sigma Aldrich and Spectrochem Mumbai. Cancer cell line MDA MB 4355 (Human breast cancer) cell line was procured from NCCS, Pune, India. cell lines were grown and maintained in suitable ( L-15- media and were grown and subcultured in medium supplemented with 10% fetal bovine serum,1% L-Glutamine.1% penicillin streptomycin –streptomycin-amphotericine-B antibiotic solution. All cells were trypsinated using trypsin-EDTA solution and seeded in 96 well plates. The results were compared with the standard drug 5-fluorouracil (10 μg/ml).

2.2 METHOD
All newly synthesized compounds were evaluated for their in vitro anticancer effects against MDA MB 4355 (Human breast cancer), by the standard MTT assay using 5-FU (5-Fluorouracil) as a positive control. Test compounds were prepared in DMSO (0.2%) and Controls were performed with medium alone. The MDA MB 4355 (Human breast cancer) was maintained in L-15-media supplemented with 10 % fetal bovine serum. The cells were plated at a density of 1 × 105 cells per well in a 96-well plate, and cultured for 24 h at 37 °C. The cells were subsequently exposed to 20 μg/ml. The plates were incubated for 24 h, and cell proliferation was measured by adding 10 μL of MTT (thiazolyl blue tetrazolium bromide) dye (5 mg ml-1 in phosphate per well. The plates were incubated for a further 4 h at 37 °C in a humidified chamber containing 5% CO2. Formazan crystals formed due to reduction of dye by viable cells in each well were dissolved in 100 μL DMSO, and absorbance was read at 490 nm. The results were compared with the standard drug inhibitors 5 fluorouracil. (10μg/ml). Lastly a percent cytotoxicity of compound was calculated by using following formula.¹⁴

Percent Cytotoxicity = Reading of control - Reading of treated cells/Reading of control X 100
RESULT
Table no. 1. Anticancer activity of synthesized compound against MDA MB 4355 (breast cancer) cancer cell line

<table>
<thead>
<tr>
<th>Compound (20 μg/ml)</th>
<th>% inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>C-I Vα</td>
<td>37.12</td>
</tr>
<tr>
<td>C-I Vb</td>
<td>39.12</td>
</tr>
<tr>
<td>C-I Vc</td>
<td>41.00</td>
</tr>
<tr>
<td>C-I Vd</td>
<td>35.68</td>
</tr>
<tr>
<td>C-I Ve</td>
<td>34.30</td>
</tr>
<tr>
<td>C-I Vf</td>
<td>49.72</td>
</tr>
<tr>
<td>C-I Vg</td>
<td>57.18</td>
</tr>
<tr>
<td>C-I Vh</td>
<td>9.34</td>
</tr>
<tr>
<td>C-I Vi</td>
<td>10.66</td>
</tr>
<tr>
<td>C-I Vj</td>
<td>11.76</td>
</tr>
<tr>
<td>5-FU (10 μg/ml)</td>
<td>54.33</td>
</tr>
</tbody>
</table>

DISCUSSION
As per table indicated that prepared all the synthesized 2-iodo 4-hydroxy methyl, 1, 5 diphenyl substituted 1 -H-imidazole derivatives were evaluated for in vitro anticancer activity against MDA MB 4355 (Human breast cancer), by the standard MTT assay. Imidazole is a nitrogen containing heterocyclic ring which possesses biological and pharmaceutical importance. Imidazole ring consists of variety of important natural product like histidine and purine.

Imidazole derivatives have an important application in cancer treatment and an important agent used in medicinal chemistry.[15] Compounds C-I Vc (41.00), C-I Vf (49.72) and C-I Vg (57.18) exhibited significant inhibitory activities against MDA MB 4355 (breast cancer) cancer cell lines at 20 μg/mL concentration compared to the positive control 5-FU (54.33%). The results indicated that Compounds containing diphenyl substitution with 4-Br, 3-OH, 2-NO2 and 2,4-dinitro showed potent anti cancer activity.

CONCLUSION
Our results clearly demonstrate that a synthesized imidazole derivative suppresses the cell proliferation. Moreover the possible improvement in the activity can be achieved by slight modification in the substituent on imidazole nucleus. Various recent new drugs developments in imidazole derivatives show better effect. Thus imidazole derivatives offer better pharmacodynamic characteristics. This has been noticed so far that modification on imidazole moiety displayed important biological activity. Various recent new drugs developments in imidazole derivatives show better effect with less toxicity. It will be exciting to observe that these modifications can utilized for development of potent anticancer derivatives in future.

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REFERENCES


