Research Article

ANTICANCER STUDIES OF NOVEL 2, 4-DISUBSTITUTED -1, 5 -DIPHENYL -1H-IMIDAZOLE DERIVATIVES

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ABSTRACT

In the present work a series of novel 2,4-disubstituted -1, 5 -diphenyl substituted -1H-imidazole derivatives were screened for anticancer activity using human liver cancer cell line. Derivatives were evaluated for anticancer activities against Hep G2 (Human liver cancer) cell lines. Newly synthesized compounds A-IVn, A-IVo, B-IVb, B-IVc, B-IVd, and B-IVe showed highly significant cytotoxic activity. Compound containing diphenyl substitution with 2-F,3-NO₂, 4-Cl, 4-Br,4-OH, 3-Cl, 3-Cl, 2-NO₂ and 2-Cl showed higher anticancer activity against Hep G2 (Human liver cancer) cell lines 5-Fluorouracil was used as standard drug for anticancer evaluation.

Keywords: Anticancer, Liver Cancer cell line, Imidazole

INTRODUCTION

The drug that are available, are given in combination to show their effect so it is felt worthwhile to synthesize and evaluate some chemical entities which can be helpful in the treatment of cancer¹. This research study may also prove to be useful to minimize adverse effect of the drugs. This study may be used to innovate site specific novel molecule and the molecules that will have low /no toxic effect as compared to existing drug.

In worldwide, second most leading death occur due to cancer after heart disease. Imidazole plays an important part in the development of new drug for treatment of cancer². They have wide range of biological activities. They are well known anti inflammatory³ antidepressant⁴, anticancer⁵⁻⁶, antitubercular⁷ antiviral⁷⁻⁸, antihypertensive⁹ anthelmintic¹⁰, antihistaminic¹¹,

In view of such report and in continuation to our work on the imidazole derivatives as anticancer agent.

Cancer is the class of disease in which a group of cell displays uncontrolled growth. The traditional anticancer drugs are the basis for drug development for cancer in which imidazole is an important nucleus. The leading causes were lung cancer, stomach cancer, liver cancer and breast cancer. The most important applications of imidazole derivatives is their used as material for treatment of denture stomatitis and in cancer.^{12,13}

MATERIALS AND METHODS

Following novel 2, 4-disubstituted -1, 5 -diphenyl substituted -1H-imidazole derivatives were screened for anticancer activities. (A-IVk-o) and (B-IVa-j).

Table 1

Code no.	STRUCTURES	Code no.	STRUCTURES
A-IVk		B-IVd	

A-IVl		B-IVe
A-IVm		B-IVf
A-IVn		B-IVg
A-IVo		B-IVh
B-IVa		B-IVI

IN VITRO ANTICANCER ACTIVITY (MTT ASSAY)¹⁴

MATERIAL

Hep G2 (Human liver cancer) cell lines, CO₂ incubator, Elisa plate reader, inverted phase contrast microscope etc.

METHOD

Cancer cell cultures

Hep G2 (Human liver cancer) cell lines were purchased from NCCS, Pune, India. All cell lines were grown and maintained in suitable (MEM) media and were grown and subcultured in medium supplemented with 10% fetal bovine serum, 1% L-Glutamine, 1% penicillin streptomycin –streptomycin-amphotericin-B antibiotic solution. All cells were trypsinated using trypsin-EDTA solution and seeded in 96 well plates.

The newly prepared synthesized compounds were evaluated for their in vitro cytotoxic effects against Hep G2 (Human liver cancer cell line), by the standard MTT (3-(4,5-dimethylthiazol-

2-yl)-2,5-diphenyl tetrazolium bromide) assay using 5-FU (5-Fluorouracil) as a positive control.

The Hep G2 (Human liver cancer) was maintained in MEM medium supplemented with 10 % fetal bovine serum. The cells were plated at a density of 1×10^5 cells per well in a 96-well plate, and cultured for 24 h at 37 °C. The cells were subsequently exposed to 10 µg. The plates were incubated for 48 h, and cell proliferation was measured by adding 10 µL of MTT (thiazolyl blue tetrazolium bromide) dye (5 mg ml⁻¹ in phosphate-buffered saline) 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 200 µl DMSO, and absorbance was read at 490 nm. The results were compared with the standard drug inhibitors 5-fluorouracil. (10 µg). Lastly percent cytotoxicity of the compounds was calculated by using the following formula.

Percent Cytotoxicity = $\frac{\text{Reading of control} - \text{Reading of treated cells}}{\text{Reading of control}} \times 100$

RESULT

Table 2: Anticancer activity of synthesized compound against HepG2 cell lines

Compound no.	% Inhibition	Compound no	% Inhibition
A-IVk	66.46	B-IVd	89.29
A-IVl	76.36	B-IVe	81.48
A-IVm	65.98	B-IVf	73.14
A-IVn	96.91	B-IVg	72.35
A-IVo	94.87	B-IVh	66.97
B-IVa	74.72	B-IVi	79.77
B-IVb	80.63	B-IVj	56.46
B-IVc	93.89	5 FU (10 µg)	79.31

DISCUSSION

Novel 2, 4-disubstituted -1, 5 -diphenyl substituted -1H-imidazole derivatives were synthesized (A-IVk-o) and (B-IVa-j). The synthesized compounds were characterized by IR, ¹H NMR, Mass spectra. The newly synthesized compounds were evaluated for anticancer activities against Hep G2 (Human liver cancer) cell lines. Newly synthesized compounds A-IVn, A-IVo, B-IVb, B-IVc, B-IVd, and B-IVe showed highly significant cytotoxic activity. Compound containing diphenyl substitution with 2-F, 3-NO₂, 4-Cl, 4-Br, 4-OH, 3-Cl, 3-Cl, 2-nitro and 2-Cl showed higher anticancer activity against Hep G2 (Human liver cancer) cell lines. 5-Fluorouracil was used as standard drug for anticancer evaluation.

CONCLUSION

Newly screened compounds A-IVn, A-IVo, B-IVb, B-IVc, B-IVd, and B-IVe showed highly significant cytotoxic activity. Compound containing biphenyl substitution with 2-F, 3-NO₂, 4-Cl, 4-Br, 4-OH, 3-Cl, 3-Cl, 2-nitro and 2-Cl showed higher anticancer activity against Hep G2 (Human liver cancer) cell lines. 5-Fluorouracil was used as standard drug for anticancer evaluation. From the above study it could be concluded that the synthesized derivatives could provide a search light for further development of novel potent anticancer agents and could use for the design and development of new anticancer agents. This has been noticed so far that modification on imidazole moiety displayed important biological activity. It will be exciting to observe that these modifications can utilize for development of potent anticancer agent in future.

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