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Research Article

Tert-butyl Group bearing Murrayanine-chalcone Produced Noteworthy Anti-proliferative Activity against Breast Cancer Cell Line

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Abstract

Cancer is the deadliest disease after cardiovascular diseases and is expected to increase by nearly twice in number by the end of the year 2050. It is rapidly progressing and a majority of the well-known anticancer drugs are in the path of getting resistant. In our previous study, we had rationally designed a hybrid molecule which comprised of murrayanine (carbazole moiety), chalcone, and tert-butyl group, and predicted that that hybridization will lead to enhanced synergistic anti-oxidant activity. The free-radical scavenging screening by DPPH assay was found to be absolutely correct and the chalcone demonstrated nearly analogous scavenging of the reactive species with that of ascorbic acid. Likewise, due to a close association of free-radical species and cancer, the fabricated prop-2-ene-1-one compound having marvelous anti-oxidant activity was screened for anti-proliferative activity against breast cancer MCF-7 cell line using SRB assay and was expected to produce better results than the individual components. The anti-cancer SRB assay of the hybrid compound demonstrated a remarkable anti-proliferative activity with an IC_{50} value of 19.67 µM. The present research will surely motivate the researchers in further developing better chalcone based anti-cancer drugs along with inspiration towards the pharmaceutical product development.

Keywords: Anti-cancer, Anti-proliferative, Anti-oxidant, Chalcone, Murrayanine, Tert-butyl

Introduction

Cancer is the deadliest disease after cardiovascular diseases and is expected to increase by nearly twice in number by the end of the year 2050. It is rapidly progressing and a majority of the well-known anticancer drugs are in the path of getting resistant.[1] While looking at the basic reasons for the proliferation of cancer cells, the free-radicals have been noticed to play a critical role.[2] In the human body, more than 20,000 free-radicals are produced which initiate damage to the deoxyribosyl backbone of DNA and accelerate the oxidation of the polydesaturated fatty acids.[3] In addition to this, prolong exposure to environmental contaminants, lifestyle practices, cigarette smoking, and excessive alcohol consumption intake extremely aggravate the conditions.[4]

Murrayanine, the active carbazole alkaloid present in Murraya koenigii is reported to have potential anti-cancer activity. The semi-synthetically produced derivatives have been found to exhibit much higher anti-proliferative potential as supported from the IC_{50} values.[5,6] Carbazole molecules have been reported to be one of the privileged heterocyclic scaffolds with noteworthy anti-neoplastic attributes.[7] The low-molecular-weight natural scaffold "chalcones" are known for their tremendous anti-cancer, anti-angiogenic, cytoprotective, and miscellaneous activities by modulation of various biochemical pathways.[8] The synthetically prepared anti-oxidants such as 2,6-di-tert-butyl-4-methylphenol (BHT), 2-tert-butyl-4-methoxyphenol (BHA), 2,4,6-tri-tert-butylphenol (TBP), and tert-

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butylhydroquinone (TBHQ) have tert-butyl group which scavenges the free-radicals such as hydroxyl, superoxide, and reactive nitrogen species, etc. by acting as potent reducing agents.[9]

In our previous study, we had rationally designed a hybrid molecule which comprised of murrayanine (carbazole moiety), chalcone, and tert-butyl group, and predicted that that hybridization will lead to enhanced synergistic anti-oxidant activity. The free-radical scavenging screening by DPPH assay was found to be absolutely correct and the chalcone demonstrated nearly analogous scavenging of the reactive species with that of ascorbic acid.[10] Due to a close association of free-radical injury and inflammation, an anti-inflammatory study was also performed using the carrageenan-induced paw edema method in Swiss albino rats which demonstrated encouraging results.[11]

Likewise, due to a close association of free-radical species and cancer, the fabricated prop-2-ene-1-one compound (Figure 1) having marvelous anti-oxidant activity was screened for anti-proliferative activity against breast cancer MCF-7 cell line using SRB assay and was expected to produce better results than the individual components.

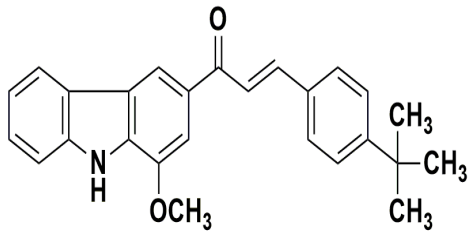

Figure 1.Structure of tert-butyl group bearing murrayanine-chalcone

Materials and Methods

Chemicals and Instrumentation

From HiMedia Ltd., India, the analytical grade chemicals, solvents, and reagents for anti-cancer screening were procured. The (*E*)-3-(4-(tert-butyl) phenyl)-1-(1-methoxy-9H-carbazol-3-yl) prop-2-en-1-one was one of our previous reports and taken from our compound library. For the analysis of SRB Assay, the microplate reader of BioTek Instruments Inc., USA was utilized.

Anti-Cancer Screening

The anti-breast cancer screening was performed by Sulforhodamine B (SRB) assay against cell line MCF-7 using capecitabine as the positive control. According to the protocol given by Padole *et al*., the study was carried out. In the RPMI1640 media, the procured cell lines were cultured at 37°C under a low CO_2 atmosphere (5%) in the presence of 10% fetal bovine serum. By using the 96-well plates, the live cells were harvested, counted, and plated. At 4°C, the live cells were treated with the test compound in presence of 10% trichloroacetic acid solution to fix. The live cells were treated by deionized water and stained with 0.4% SRB solution for the duration of 15 min. The unbound stain in wells was removed by treating with the glacial acetic acid solution and dried thoroughly at room temperature. The bound protein stain was solubilized by using tris-base (tris(hydroxymethyl)aminomethane) solution and the optical density was measured at 540 nm by utilizing the microplate reader. The IC_{50} values were estimated accordingly.[12]

Results and Discussion

Anti-Proliferative Activity

The anti-cancer SRB assay of the hybrid compound demonstrated a remarkable anti-proliferative activity with an IC_{50} value of 19.67 µM while the positive control had an IC_{50} value of 6.82 µM. The high activity of the compound may be due to the synergistic free-radical scavenging potentials of the carbazole, chalcone, and tert-butyl group. However, the compound did not produce analogous or better pharmacological activity than the positive control. From the study, it was evidenced that hybridization of multiple dynamic scaffolds significantly amplified the hydroxyl, superoxide, etc. scavenging activity.

Table 1.Anti-proliferative activity of tert-butyl containing murrayanine-chalcone molecule against MCF-7 cell line

Compounds	IC_{50} value (µM)
Chalcone	19.67
Capecitabine	6.82

Conclusion

This interesting study revealed the potential of chalcone compound in exhibiting anti-proliferative activity against breast cancer cell line MCF-7 by its free-radical scavenging potentials. The hybridization strategy proved to be an effective way of enhancing the anti-cancer activity by expressing the cumulative or synergistic effects of the multiple scaffolds. The present research will surely motivate the researchers in further developing better chalcone based anti-cancer drugs along with inspiration towards the pharmaceutical product development.

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Conflict of Interest: None

References

1. Mahapatra DK, Bharti SK. *Handbook of Research on Medicinal Chemistry: Innovations and Methodologies*. Apple Academic Press, New Jersey. 2017.
2. Mahapatra DK, Bharti SK. *Drug Design*. Tara Publications Private Limited, New Delhi. 2016.

3. Shivhare RS, Mahapatra DK, Nair RR et al. Schiff's base derivatives of murrayanine demonstrated enhanced anti-oxidant activity than its parent moiety. *Indian J Pharm Edu Res* 2016; 50(4): 9-15.
4. Mahapatra DK, Shivhare RS. Synthesizing an anti-oxidant principle 2-(((1-methoxy-9H-carbazol-3-yl)methylene)amino)isoindoline-1,3-dione from N-aminophthalimide and murrayanine. *Inventi Med Chem* 2017; (4): 1-3.
5. Mahapatra DK, Dadure KM, Shivhare RS. MCF-7 cell line screening of some uracil containing murrayanine based (thio)-semicarbazide hybrids. *Innovat Int J Med Pharm Sci* 2018; 3(5): 14-6.
6. Mahapatra DK, Das D, Shivhare RS. Substituted thiazole linked murrayanine-Schiff's base derivatives as potential anti-breast cancer candidates: Future EGFR kinase inhibitors. *Int J Pharm Sci Drug Res* 2017; 9(3): 139-44.
7. Bashir M, Bano A, Ijaz AS, Chaudhary BA. Recent developments and biological activities of n-substituted carbazole derivatives: a review. *Molecules* 2015; 20(8): 13496-517.
8. Mahapatra DK, Bharti SK, Asati V. Anti-cancer chalcones: structural and molecular targets perspectives. *Eur J Med Chem* 2015; 98: 69-114.
9. Murakami Y, Kawata A, Katayama T et al. Anti-inflammatory Activity of the Artificial Antioxidants 2-Tert-butyl-4-methoxyphenol (BHA), 2, 6-Di-tert-butyl-4-methylphenol (BHT) and 2, 4, 6-Tri-tert-butylphenol (TBP), and their various combinations. *In vivo* 2015; 29(2): 197-206.
10. Mahapatra DK, Shivhare RS. Substituting tert-butyl group on murrayanine-chalcone scaffold produced tremendously high anti-oxidant activity than the individual components. *Int J Anal Med Chem* 2018; 1(1): 1-5.
11. Mahapatra DK, Shivhare RS, Borkar SS. Tert-butyl Group Substitution in the Ring-B of murrayanine-chalcone leads to higher expression of edema reduction. (Communicated).
12. Padole CD, Amdare MD, Jogdand KR et al. Discovery of 4-methyl-2-oxo-2H-chromen-7-yl-2-benzamidoacetate as anti-proliferative agent. *Int J Ayur Pharm Chem* 2018; 8(1): 62-8.

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