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Synthesis of novel α-naphthol hydroxamate derivatives as anticancer agents

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Chemotherapy is one of the treatment options for cancer. A major problem in cancer chemotherapy is the lack of selective toxicity of many commonly used anti-cancer agents towards tumor tissue compared to normal tissue. Studies have shown that α-naphthol is selectively toxic to cultures of human tumor tissue compared to normal tissues *in-vitro*. Hence, this study was conducted to synthesize a series of new hydroxamate derivatives containing α-naphthol nucleus by the reaction of naphthol acetic acid with amino acid methyl ester derivatives which were directly reacted with hydroxyl amine at room temperature. Structures of these compounds were confirmed by standard studies of IR, 1H-NMR, 13C-NMR, MS and elemental analysis. The cytotoxicity of the synthesized compounds were studied using the MTT assay in 4 human cancer cell lines, including HepG2, PC-3, HT-29 and MCF-7. Among the compounds, N-hydroxy-2-(2-(naphthalen-1-yloxy) acetamido)-3-phenylpropanamide; had exhibited significant cytotoxicity against almost all the used cells including the normal cells (WRL-68). N-hydroxy-3-(4-hydroxyphenyl)-2-(2-(naphthalen-1-yloxy) acetamido) propanamide has shown cytotoxicity to HepG2 cells alone with an IC50 of 12.17 μg/ml. The next significant compound which showed cytotoxicity was (N1-hydroxy-2-(2-(naphthalen-1-yloxy) acetamido) pentanediamide. Further studies have shown that the cell death observed was closely associated with generation of reactive oxygen species (ROS). In this study, other napthol derivatives have shown significant increase in the level of ROS in concentration dependent manner in treated cells. In conclusion, the study has shown that among the synthesized compounds, ((N-hydroxy-2-(2-(naphthalen-1-yloxy)acetamido)-3-phenylpropanamide; and (N-hydroxy-3-(4-hydroxyphenyl)-2-(2-(naphthalen-1-yloxy) acetamido) propanamide; hold the potential for further research.

Biography

Hafiz Makeen is an Assistant Professor in the Department of Clinical Pharmacy, College of Pharmacy, Jazan University, Saudi Arabia. He has completed his PhD in Cancer Therapeutics in 2012 from the University of Bradford, UK. He has completed his Master's degree in Clinical Pharmacy in 2002 from the College of Pharmacy, King Saud University, Riyadh, KSA. Currently, he is the Vice Dean for clinical affairs at the College of Pharmacy, Jazan University, KSA. His area of research in addition to clinical pharmacy is cancer research and drug delivery to solid tumors.

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