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Investigating the anticancer activity of PPAPs on hepatocellular carcinoma cells in vitro and vivo

Ali Mohammed

Degree in Pharmaceutical Science, China

Hepatocellular carcinoma (HCC) is a common malignant tumor with high recurrence and mortality rates. New and effective anti-cancer drugs are urgently needed. In this study, we aimed to evaluate the anticancer activity of ten compounds, Polycyclic polyprenylated acylphloroglucinols (PPAPs), in vitro on HCC cells HepG2 and Huh-7and a normal cell line (L-02), followed by in vivo studies. PPAPs are bioactive compounds present in the genus Hypercom that have potential pharmacological properties, including anticancer activity. The initial results show among ten compounds, 3, 5, 7, and 8 exhibited strong cytotoxic activity by inhibiting cell viability while having almost low cytotoxicity on normal L02 cells. We will further investigate the effects of these compounds on colony formation, cell cycle G2/M phase arrest, and cell apoptosis of HCC cells. We will also evaluate the anticancer activity of these compounds in animal models. Mechanistically, we anticipate that one or more of these compounds will trigger intense DNA damage by suppressing the MAPK signaling pathway. The study will also evaluate the mechanisms underlying the hepatoprotective effects of these compounds. Furthermore, we expect a combination of these compounds with sorafenib to significantly induce synergistic cytotoxicity in HCC cells. Our objective is to identify a novel chemotherapeutic drug that can be administered either alone or in combination therapy for HCC treatment from among these ten compounds. Additionally, we will evaluate the PPAPs for their neuroprotective and hepatoprotective properties. Overall, our study will provide valuable insights into the anti-cancer activity of PPAPs from the genus Hypericum and their potential use as a new therapeutic approach for the treatment of liver cancer. The results of this study will contribute to the development of new drugs to treat this devastating disease and improve the quality of life for patients suffering from liver cancer.

Biography

Ali Mohammed doing a Ph.D. degree in Pharmaceutical Sciences in China. My research work in master focused on the discovery of β-cyclocitral-derived mono-carbonyl curcumin analogs as anti-hepatocellular carcinoma agents via suppression of MAPK signaling pathway, which was published in Bioorganic Chemistry in 2023 (https://doi.org/10.1016/j.bioorg.2023.106358). I also contributed to two other projects related to my research work that were published in reputed journals. These projects include the synthesis and biological evaluation of novel N-substituted benzamides as anti-migration agents for the treatment of osteosarcoma (https://doi.org/10.1016/j.ejmech.2021.113203) and the discovery of novel sanjuanolide derivatives as chemotherapeutic agents targeting castration-resistant prostate cancer.