



بسم الله الرحمن الرحيم

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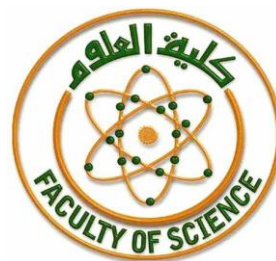
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بقسم التوثيق الإلكتروني بمركز الشبكات وتكنولوجيا المعلومات دون أدنى

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Antitumor Efficacy of Gallic Acid-Coated Gallium Nanoparticles on Hepatocellular Tumor Model

A Thesis

Submitted in the Fulfillment of the Degree of Ph.D. in Biochemistry

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بسم الله الرحمن الرحيم

" رَبِّ أَوْزِعْنِي أَنْ أَشْكُرَ نِعْمَتَكَ الَّتِي
أَنْعَمْتَ عَلَيَّ وَعَلَىٰ وَالِدَيَّ وَأَنْ أَعْمَلَ صَالِحًا
تَرْضَاهُ وَأَصْلِحْ لِي فِي ذُرِّيَّتِي ۖ إِنِّي تُبْتُ
إِلَيْكَ وَإِنِّي مِنَ الْمُسْلِمِينَ "

صدق الله العظيم

" سورة الأحقاف...آيه رقم ١٥ "

Declaration

- *I declare that the work of this thesis is a record that has been done by myself.*
- *This thesis has not been submitted for a degree at this or any other university.*

Dedication

To my Mother, my Father, my Husband

And

To my Children

*For their love, encouragement, help and
prayers, during the course of my life, that
made my studies possible*

and to them I owe everything.

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Antitumor Efficacy of Gallic Acid-Coated Gallium Nanoparticles on Hepatocellular Tumor Model

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Abstract

In the fight against cancer, cisplatin (CDDP) is most widely used as a clinical mainstay for the chemotherapy of various human cancers. Meanwhile, its cytotoxic profile, serious side effects, as well as drug resistance limit its widespread application. The goal of precision medicine is to generate better responses in the clinic, otherwise, to tailor an optimized therapeutic program based on the biology of the disease. In recent years, green nanotechnology has been demonstrated to be promising in this scenario. Accordingly, a novel gallium-based nanocomplex, namely gallic acid-coated gallium nanoparticles (GA-GaNPs), has been currently developed and evaluated for its antineoplastic efficacy alone and/or combined with CDDP. A precise structural characterization of the emergent GA-GaNPs nanocomplex has been evident *via* a panel of physicochemical analyses. In essence, the work comprised a series of both *in vitro* and *in vivo* investigations. The test compounds were *in vitro* biologically evaluated for cytotoxicity upon human hepatocellular HepG2 cancer cell line using the tetrazolium MTT assay. Considering the hallmarks of cancer, the *in vivo* therapeutic efficacy of such treatments against a chemical hepatocarcinogenesis model was further evaluated by tracking 4-axes mechanistic aspects, including iron homeostasis aspects, gene expression aspects, biological markers aspects, and routine preclinical aspects.

In tandem, the work also implied a histopathological survey upon liver biopsies of the whole studied groups. Basically, the *in vitro* results established that GA-GaNPs exhibited superior anticancer potential than CDDP, as it recorded a lower IC₅₀ value. Else more, the results of the *in vivo* experiment highlighted that GA-GaNPs treatment could diminish key hallmarks of cancer by ameliorating most of the investigated biomarkers. This was well-appreciated with the histopathological alteration findings of the liver architectures of the treated groups. Collectively, the existing results could speculate that the reaction of Ga(NO₃)₃ with GA, following the principles of green synthesis of nanoparticles, resulted in super-additive anticarcinogenic effects. In conclusion, our findings suggest that novel biogenic Ga-based nanocomplexes may potentially present new hope for the development of alternative liver cancer therapeutics, which should attract further scientific and pharmaceutical interest.

Keywords Hepatocellular carcinoma (HCC), Cisplatin (CDDP), Green nanotechnology, Gallium (Ga), Gallic acid (GA).