بسم الله الرحمن الرحيم

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تم رفع هذه الرسالة بواسطة / مني مغربي أحمد

بقسم التوثيق الإلكتروني بمركز الشبكات وتكنولوجيا المعلومات دون أدنى مسئولية عن محتوى هذه الرسالة.

ملاحظات: لا يوجد

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

Presented By

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(M.Sc. in Biochemistry, 2015)

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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.

Acknowledgment

First and foremost, cordial thanks to Allah.

No words could express my sincere appreciation and deepest thanks to ***Prof. Dr. Ahmed M. Salem***, Professor of Biochemistry, Faculty of Science, Ain Shams University, for his endless help, fatherly attitude, creative thinking, valuable suggestions, and constant encouragement throughout this research work. Without his support, the performance of this work would be difficult.

I am so grateful to ***Prof. Dr. Eman I. Kandil***, Professor of Biochemistry, Faculty of Science, Ain Shams University, for her spiritual and practical guidance, her enthusiastic encouragement and revision of every detail, as well as profound reading of the manuscript. Actually, she was more than a supervisor, she was a teacher who inspired me and pushed me forward.

Also, I am deeply indebted and sincerely thankful to ***Prof. Dr. Somaya Z. Mansour***, Professor of Biochemistry, Radiation Biology Department, Atomic Energy Authority, for suggesting the point, instructive guidance, tremendous concern and care, and invaluable practical assistance. I am very much honored to have her as my supervisor.

I would like to express my deep thanks to ***Prof. Dr. Sawsan M. El-sonbaty***, Professor of Biochemistry, Radiation Biology Department, Atomic Energy Authority, for her sustained encouragement, great assistance, and kind help in preparing the novel nanocomplex used in this research work.

My sincere thanks and regards to ***Dr. Fatma S. Moawed***, Assistant Professor of Biochemistry, Radiation Biology Department, Atomic Energy Authority, for her help during the fulfillment of the biological experiments, and tremendous encouragement. I am very pleased to deal with her.

I would also like to acknowledge ***Prof. Dr. Adel B. Kholousy***, Professor of Pathology, Cairo University, for his great effort in the histopathological examination of liver biopsies of the whole studied rat groups.

Besides my advisors, I would like to thank the staff members of the Biochemistry Department, Faculty of Science, Ain Shams University and Atomic Energy Authority for their support and help.

Also, great thanks and gratitude to ***My Husband***, his patience and continuous encouragement were the dynamo that gave me the power to accomplish my work.

Last but not least, no words could express my sincere appreciation and deepest thanks to ***My Mother and Father*** for their sincere help and encouragement during the course of my life. I ask Allah to bless them. I dedicate this thesis to them and to my husband.

Nihal M. Mansour

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Biography

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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 paraclinical 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 IC_{50} 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 $Ga(NO_3)_3$ 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).