



FACULTY OF SCIENCE  
ENTOMOLOGY DEPARTMENT

# **ANTIPROLIFERATION EFFECT OF CANTHARIDIN EXTRACTED FROM BLISTER BEETLES ON HEPATOCELLULAR CARCINOMA CELL LINE**

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# *Dedication*

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سبحانك لا علم لنا  
إلا ما علمتنا إنك أنت  
العليم العظيم

صدق الله العظيم

سورة البقرة الآية: ٣٢



FIRST AND FOREMOST, THANKS TO ALLAH WHO ENABLED ME TO COMPLETE THIS WORK DESPITE ALL THE PROBLEMS THAT FACED ME.

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*Sarah S. Hegazy*

## Abstract

Hepatocellular carcinoma is one of the most common cancers worldwide, with high prevalence and very low survival rates because of its resistance to conventional anti-cancer therapies. Cantharidin extracted from blister beetles was considered a promising candidate regarding this problem because of its potent medicinal value. Nuclear factor- $\kappa$ B has been linked to a variety of human diseases, particularly cancers. It is constitutively activated in many types of cancer and can exert pro-tumorigenic functions. **This study aimed** to evaluate the anti-cancer effect of cantharidin extracted from the oil blister beetle *in vitro* on human hepatocellular carcinoma and normal human embryonic kidney cell lines (HepG2 and HEK-293). **The materials and methods** involved extracting cantharidin, testing its purity by FT-IR, and testing its cytotoxicity against HepG2, as a hepatocellular carcinoma model, and HEK-293, as normal control. Afterwards, the NF- $\kappa$ B activity was measured in HepG2 cells after 24 and 48 hours. **The results** of the cytotoxicity assay on HepG2 and HEK-293 showed that cantharidin exhibited a high inhibitory effect on HepG2 in a time- and dose-dependent manners, this was evidenced by reduction in viable cells count and a statistically significant reduction in NF- $\kappa$ B activity ( $P < 0.01$ ) when compared with the untreated control. The results were confirmed by microscopical observations of cell morphology and NF- $\kappa$ B fold changes. The direct cytotoxicity of cantharidin was much lower against HEK-293 compared with HepG2, indicating a possible selective behavior. **It was concluded** that cantharidin could be considered a potential anticancer agent against hepatocellular carcinoma.

**Keywords:** Cantharidin, NF- $\kappa$ B, HepG2, HEK-293, Hepatocellular carcinoma.

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## LIST OF ABBREVIATIONS

Abbreviation	Full Term
°C	Degree Celsius
%	Percent
×g	Times Gravity
μL	Microliter
μm	Micrometer
CA	Cantharidin
cDNA	Complementary Deoxyribonucleic Acid
cm	Centimeter
CO <sub>2</sub>	Carbon Dioxide
CRC	Cantharidin-Related Compound
C <sub>t</sub>	Cycle Threshold
DMSO	Dimethyl Sulfoxide
DNA	Deoxyribonucleic Acid
dNTPs	Deoxynucleotide Triphosphates
EDTA	Ethylenediaminetetraacetate
EGF	Epidermal Growth Factor
FT-IR	Fourier-Transform Infrared
g	Gram

<b>h</b>	Hour
<b>HBV</b>	Hepatitis B Virus
<b>HCC</b>	Hepatocellular Carcinoma
<b>HCV</b>	Hepatitis C Virus
<b>IC<sub>50</sub></b>	Median Inhibitory Concentration
<b>IκBα</b>	Nuclear Factor of Kappa Light Polypeptide Gene Enhancer in B-cells Inhibitor, Alpha
<b>km</b>	Kilometer
<b>L</b>	Liter
<b>M</b>	Mean
<b>MDR</b>	Multi-Drug Resistance
<b>mg</b>	Milligram
<b>min</b>	Minute
<b>ml</b>	Milliliter
<b>mM</b>	Millimolar
<b>mm</b>	Millimeter
<b>mRNA</b>	Messenger Ribonucleic Acid
<b>NF-κB</b>	Nuclear Factor-KappaB
<b>nm</b>	Nanometer
<b>OD</b>	Optical Density
<b>PBS</b>	Phosphate-Buffered Saline

<b>PCR</b>	Polymerase Chain Reaction
<b>pH</b>	Potential of Hydrogen
<b>qRT-PCR</b>	Quantitative RT-PCR
<b>RHD</b>	Rel Homology Domain
<b>RNA</b>	Ribonucleic Acid
<b>RNS</b>	Reactive Nitrogen Species
<b>ROS</b>	Reactive Oxygen Species
<b>RT-PCR</b>	Real Time-PCR
<b>SD</b>	Standard Deviation
<b>sec</b>	Second
<b>sqRT-PCR</b>	Semi-quantitative RT-PCR
<b>TAE</b>	Tris-Acetate-EDTA
<b>TNFs</b>	Tumor Necrosis Factors
<b>U</b>	Unit
<b>USA</b>	United States of America
<b>V</b>	Volts

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