شبكة المعلومات الجامعية

# بسم اللّه الرحمن الرحيم



# شبكة المعلومات الجامعية

# التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

# جامعة عين شمس

## التوثيق الإلكتروني والميكروفيلم

# قسم

## نقسم باللّه العظيم أن المادة التي تم توثيقها وتسجيلها علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات

# يجب أن

## تحفظ هذه الأقراص المدمجة بعيدا عن الغبار

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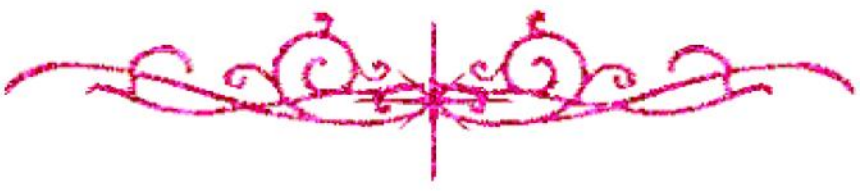
# بعض الوثائق الأصلية تالفة



# بالرسالة صفحات
# لم ترد بالأصل

# PHARMACOLOGICAL STUDY OF PROTECTIVE EFFECT OF METHYL PALMITATE IN EXPERIMENTALLY-INDUCED MYOCARDIAL INFARCTION

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**Submitted for the partial fulfillment of Master's degree in Pharmaceutical Sciences**
**(Pharmacology & Toxicology)**

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**2020**

## Examination Board Approval Sheet

- **Title of the Master's Degree thesis in Pharmaceutical Science (Pharmacology and Toxicology):**

Pharmacological study of protective effect of methyl palmitate in experimentally-induced myocardial infarction

- **Name of candidate:**

Ahmed Badreldin Abdelaal Hamed

- **Submitted to:**

Pharmacology and Toxicology Department, Faculty of Pharmacy, Ain Shams University.

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**Date: 21 / 3 / 2020**

# ACKNOWLEDGMENT

*First of all, no words can express my deep thanks to* ***Allah****.*

*I would like to express my deep and sincere gratitude to my supervisor* ***Prof. Dr. Samar Azab****, Professor of Pharmacology & Toxicology, Faculty of Pharmacy, Ain Shams University, for her keen supervision, valuable guidance and continuous encouragement throughout the whole study. I am profoundly grateful for her support and valuable instructions throughout this work.*

*I would like to express my deep and sincere thanks to my supervisor* ***Dr. Yousra Abdel-Mottaleb****, Lecturer of Pharmacology & Toxicology Faculty of Pharmaceutical Sciences and Pharmaceutical Industries, Future University in Egypt, for her keen supervision, valuable guidance and helpful comments and discussion during the whole study.*

## *ACKNOWLEDGMENT*

*I owe special thanks to my supervisor* ***Dr. Eman Mantawy****, Lecturer of Pharmacology & Toxicology, Faculty of Pharmacy, Ain Shams University, for her kind supervision and her continuous guidance and support throughout the whole study. Also, I am profoundly grateful for her indispensable help during the practical work.*

*I am greatly thankful to* ***Ass. Prof. Dr. Wesam El-Bakly****, Associate Professor of Pharmacology & Therapeutics, Faculty of Medicine, Ain Shams University, for her guidance leading to completion of this study. A special thanks is paid to her for providing me with advice and facilities to complete the practical work throughout this study.*

*I am deeply indebted to* ***Prof. Dr. Adel Bakeer****, Professor of Pathology, Faculty of Veterinary Medicine, Cairo University, for his great effort in accomplishing the part of the histopathological technique.*

## *ACKNOWLEDGMENT*

*Finally, my profound gratitude goes to my **family** for encouraging me to pursue this academic achievement. I am forever indebted to them for their blessings, encouragement & endless support.*

***Ahmed Badreldin Hamed***

# *ABSTRACT*

## *ABSTRACT*

Myocardial infarction (MI) is an acute condition of sudden ischemic necrosis of the myocardium that results from the critical imbalance between the coronary blood supply and the myocardium demand. Oxidative stress is an important pathogenic event in MI, where the generated reactive oxygen species (ROS) cause cellular destruction. Moreover, apoptosis and the inflammatory cascades play major roles in the pathogenesis of MI.

The present study was designed to assess the potential cardioprotective effect of the naturally occurring fatty acid ester methyl palmitate (MP) against isoproterenol (ISO)-induced MI in rats and the possible underlying molecular mechanisms.The study was carried out in two consequent phases, the first phase screened the cardioprotective dose of MP in ISO-intoxicated rats. In the second phase, forty male Sprague dawley rats were treated with either MP (150 mg/kg, p.o) 3 times/week on alternative days for 2 weeks and/or 2 consecutive doses of ISO separated by 24 hours (85 mg/kg, s.c.) on the $13^{th}$ and $14^{th}$ days.

Different cardiotoxicity and oxidative stress markers were assessed. Moreover, endothelial nitric oxide synthase (eNOS) content was determined. In addition, cardiac expression of caspase 3, Bax and Bcl-2 was assessed to detect apoptosis. To assess inflammation, ELISA measurement of toll like receptor 4 (TLR-4) and tumor necrosis factor-alpha (TNF-α), as well as the immunohistochemical detection of nuclear factor kappa B (NF-κB) and cyclooxygenase-2 (COX-2) were performed as well.

Cardiotoxicity and oxidative stress markers were significantly ameliorated by pretreatment with MP. Furthermore, MP pretreatment significantly elevated eNOS levels, decreased the expression of the pro-apoptotic markers but increased that of Bcl-2 and mitigated TLR-4 activation and the other inflammatory markers. Additionally, histopathological examination and electrocardiogram confirmed the cardioprotective effect of MP.

Collectively, these findings indicate that MP possesses a potential cardioprotective effect against ISO-induced MI.

**Keywords:** Myocardial infarction; Methyl Palmitate; Oxidative stress; Apoptosis; TLR-4; Inflammation

# *Contents*