



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





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Phytochemical and Pharmacological Studies on Ivy Leaves (*Hedera Helix*).

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(B.V.Sc., Cairo University, 2014)

(M.V.Sc., Cairo University, 2018)

To

(Cairo University, Faculty of Veterinary Medicine)

For The Degree of Ph.D. in Veterinary Medical Sciences (Pharmacology)

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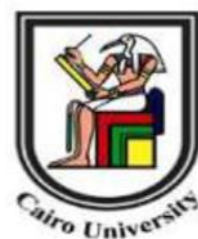
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Abstract

Plants are commonly consumed as natural drugs, and most new clinical trials are recognized most of the previously assumed effects. *Hedera helix* L. (ivy leaves) is an enriched plant from the family *Araliaceae*. Their leaves are extracted and used as the active principle in many herbal preparations. It is traditionally classified as a product for treating a common cold, cough, bronchial disorders, and upper respiratory tract inflammation and infection due to its secretolytic and broncholytic effects.

Our experiment was done to determine the effect of extract from ivy leaves in the treatment of acute lung injury caused by lipopolysaccharides administration intranasally in addition to the detection of the active fraction (saponins or flavonoids). Also, it is done to evaluate the anti-arthritic activity of *Hedera helix* with the detection of secondary metabolites using LC/MS. *In-vitro* antioxidant, antimicrobial, and anti-inflammatory were assumed, and LPS induced an in-vivo acute lung inflammation model in mice. Animals were divided into seven groups randomly (each group containing 10 mice): control negative (saline only), control positive (LPS group), standard (Dexamethasone 2 mg/kg), total ivy ethanolic extract (100, 200 mg/kg), saponin fraction (100 mg/kg), and flavonoid fraction (100 mg/kg), and treated for 7 days. The right lungs were homogenized to determine the levels of SOD, MDA, catalase, interleukins 10,6,1 β , TNF- α , NO, PGE2, and MPO. The left lungs were excised for histopathology and histomorphometry. Immunohistochemistry of Cox-2 and TNF- α levels were measured. Additionally, Western blotting was done to determine phosphorylated MAPK levels.

The anti-arthritic activity was investigated *in-vitro* and *in-vivo*. The *in-vivo* study was done by injection of 0.1 ml of CFA (Complete Freund's Adjuvant) intradermally to induce Adjuvant-induced arthritis. Animals were divided into seven groups randomly (each group containing 7 rats): control negative (saline only), control positive (CFA group), standard (Ibuprofen 5mg/kg), total ivy ethanolic extract (100, 200 mg/kg), saponin fraction (100 mg/kg), and flavonoid fraction (100 mg/kg), and treated for one month. The physical parameters were examined throughout the experiment. Biomarkers of rheumatoid, cytokines of inflammation, antioxidant parameters, and joint enzymes markers (hyaluronidase, and β -glucuronidase enzyme). Histopathological examination for induced paw with edema was examined.

Our data showed that oral administration of ivy ethanolic extract in a dose of 200 mg/kg, and their flavonoids fraction in a dose of 100 mg/kg reduced the pro-inflammatory mediators, and oxidative stress biomarkers induced by LPS significantly ($P < 0.05$). Interestingly, the flavonoids showed promising activity, therefore they are responsible for the action. They also are able to lower the paw's edema, immunological parameters, inflammatory cytokines, joint enzymes markers (hyaluronidase, and β -glucuronidase enzyme), and antioxidant indicators.

In conclusion, standardized ivy leaf extract could be advised for acute lung injury for its antimicrobial, antioxidant, and anti-inflammatory activities. Also, our results suggest that *Hedera helix* extract may be used for the cure of rheumatoid arthritis, which is correlated to its flavonoid content, which can repress all parameters changed by inflammation either oxidative, biochemical, or pathological changes associated with inflammation.

Keywords: *Hedera helix* L., Ivy leaves, Acute lung inflammation, Rheumatoid arthritis, flavonoids, Saponins, LC/MS, CFA.

Dedicated to

My parents

My husband and sons

My brothers and sisters

Who

Shared the responsibility of bringing me up

To be grateful

and

To all those who taught me.

Acknowledgement

First, I would like to extend my thanks to Prof. Dr. Amer Ramadan Ali Ayad, Professor of Pharmacology, Faculty of Veterinary Medicine, Cairo University, for his excellent supervision, encouragement, guidance and valuable instruction that he offered to me while performing this work. His intensive and creative comments have helped me step by step throughout this study and his great help in revising and finishing this thesis indeed, I am very honored and lucky to work under his supervision.

I express my deep gratitude, sincere and heartfelt thanks to my supervisor Prof. Dr. Gehan Mohamed Kamel, Professor of Pharmacology, Faculty of Veterinary Medicine, Cairo University, for her kind co-operation, constant support, untiring patience, stimulating suggestions and encouragement helped me in both, all the time of research work and the writing of this thesis. This thesis would never have to be completed without her help.

I fondly thank with deepest gratitude to Dr. Riham Adel Tawfik Elsheikh, Lecturer of Pharmacognosy, Faculty of Pharmacy, Cairo University, Egypt, for her constant guidance, knowledge on the subject, regular observation, support and encouragement in every step of my thesis work and her great help in revising and finishing this thesis.

*I also appreciate all **staff members** of Pharmacology Department, Faculty of Veterinary Medicine, Cairo University, for their kind cooperation.*

Many thanks are extended to Dr. Alaa Fouad Bakr, Lecturer of Pathology, Faculty of Veterinary Medicine, Cairo University, for her support with great experience throughout our study, with her constant guidance, knowledge of Pathology in this thesis.

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