بسم الله الرحمن الرحيم

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Cairo University

Faculty of Veterinary Medicine

Department of Pharmacology

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

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To

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

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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 10,6,1β, 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.

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CONTENTS