Cairo University

Faculty of Veterinary Medicine

Comparative pathological study on the anti-inflammatory effect of prednisolone and myrrh extract in a model of autoimmune disease using silica

A thesis submitted by:

Dina Emad Eldeen Mohamed ElMosbah

(Bachelor's degree of Veterinary Science 2016)

Faculty of Veterinary Medicine

Cairo University

For

The Degree of M.V.Sc

In pathology (General, special and postmortem)

Under the Supervision of

Prof. Dr. Hala Mohamed Farouk ElMiniawy

Professor of Pathology
Faculty of Veterinary Medicine
Cairo University

Dr. Marwa Mohamed Salah El-Din Ibrahim Khattab

Assistant Professor of Pathology
Faculty of Veterinary Medicine
Cairo University

2020

Cairo University
Faculty of Veterinary Medicine
Department of Pathology

Supervision Sheet

Prof. Dr. Hala Mohamed Farouk Elminiawy

Professor of Pathology Faculty of Veterinary Medicine Cairo University

Dr. Marwa Mohamed Salah El-Din Ibrahim khattab

Assistant Professor of Pathology Faculty of Veterinary Medicine Cairo University

Cairo University
Faculty of Veterinary Medicine
Department of Pathology

Name: Dina Emad Eldeen Mohamed ElMosbah
Birth date: 3/8/1993
Place of Birth: Cairo
Nationality: Egyptian
Scientific degree: Master's Degree (M.V. Sc)
Specification: Pathology

Thesis title: Comparative pathological study on the anti-inflammatory effect of prednisolone and myrrh extract in a model of autoimmune disease using silica

Supervisors:

Prof. Dr. Hala Mohamed Farouk ElMiniawy
Professor of Pathology, Faculty of Veterinary Medicine, Cairo University

Dr. Marwa Mohamed Salah El-Din Ibrahim Khattab
Assistant Professor of Pathology, Faculty of Veterinary Medicine, Cairo University

Abstract

This study investigates the role of silica exposure by different routes and doses in developing autoimmune diseases in non-susceptible rats and the therapeutic effect of myrrh as a natural medicine compared to prednisolone. The autoimmune disease model in rats was induced by injecting 5mg crystalline sodium silicate suspension subcutaneously once weekly for 20 weeks, then the rats treated either with myrrh extract or prednisolone or with both for 6 weeks. Detection of serum anti-nuclear antibodies (ANA), liver and kidney function tests, Matrix metalloproteinase activity (MMP-2, MMP-9 and MMP13), oxidative stress biomarkers, genetic expression of TNF-α, and Bcl-2, histopathology and immunohistochemistry of TNF-α expression in kidney tissue were performed. All silica treated groups showed a significant increase in ANA, oxidative stress markers, TNF, MMP, and creatinine. Histopathology revealed vasculitis and fibrinoid degeneration of blood vessels in different organs and immune-mediated glomerulonephritis in silica treated groups. Furthermore TNF-α expression was significantly decreased in treated groups.

Interestingly, the myrrh didn’t produce hepatic lesions and improved the side effect of prednisolone in liver when taken in combination. In conclusion, both 5 mg subcutaneously and 7 mg oral silica-induced autoimmune disease in non-susceptible rats. Myrrh extract possessed anti-inflammatory properties and counteracted the side effect of prednisolone on the liver. Myrrh extract can serve as a conjunctive therapy with prednisolone to treat autoimmune diseases.

Keywords: Rats; silica; autoimmune diseases; prednisolone; Myrrh; histopathology; matrix metalloproteinases ; TNF-α; ANA

Dedication

I would like to dedicate this work to my father, my mother, my aunt Dina, my brother and sisters, whom I am indebted to them for my happiness in my life.

Acknowledgment

I wish to present my respect, deepest gratitude and appreciation to ***Prof. Dr. Hala M.F. ElMiniawy*** *Professor of Pathology, Faculty of Veterinary Medicine, Cairo University for planning this research program, sincere supervision, wise scientific advices and encouragement during this study which made this thesis in the best way.*

I am extremely grateful to ***Dr. Marwa S. Khattab*** *Assistant Professor of Pathology, Faculty of Veterinary Medicine, Cairo University for her valuable advices, continuous encouragement and constructive criticism. She offered continuous help and support.*

I would like to express my appreciation to ***Huda O. AbuBakr*** *Assistant Professor of Biochemistry, Faculty of Veterinary Medicine, Cairo University for her kind and actual scientific help in this work.*

I feel very grateful to ***Shimaa R. Emam*** *Lecturer of pharmachology, Faculty of Veterinary Medicine, Cairo University for her kind and actual scientific help in this work.*

I would like to thank all staff members of the Department of Pathology for their encouragement during this work.

Finally, my thanks are sent to every kind hand that extended to help me to allow the fulfillment of this work.

CONTENTS

	Item	Page number
1-	**List of tables……...……..**	I
2-	**List of Figures……...……**	II- VI
3-	**List of Abbreviations…….……...**	VII- IX
4-	**Introduction…….**	1-2
5-	**Review article……...……**	3-25
6-	**Thesis Paper (1) ….……...……**	26-39
7-	**Thesis Paper (2) ...……...……**	40-65
8-	**Thesis Paper (3) ...…….……...……**	66-87
9-	**Discussion…….**	88-89
10	**Conclusions……...**	90
11	**English Summary……..**	91-92
12	**References……..**	93-95
13	**Arabic Summary……**	

List of tables

NO.	Legend	Page
1	Liver and kidney function tests in different groups at 3 weeks post treatment.	72
2	Liver and kidney function tests in different groups at 6 weeks post treatment.	73

List of figures

NO.	Title	Page
Paper (1)		
1	photomicrograph of stomach, intestine, and liver sections of rats in different groups. (a) normal histological structure of stomach in G1 group (100X), (b) edema, congestion, and moderate mononuclear cells infiltration in lamina propria and submucosa of the stomach in G2 rats, (c) severe diffuse and focal mononuclear inflammatory cells in T. muscularis mucosa of stomach in G3 group (200X), (d) normal histological structure of intestine in G1 group, (e) goblet cells and epithelial cells hyperplasia as well as moderate mononuclear inflammatory cells infiltration in lamina propria and submucosa of the intestine in G2 group, (f) desquamation and necrosis of the enterocyte and intestinal glands with heavy infiltration of mononuclear inflammatory cells in Lamina propria and submucosa in G3 group (200X), (g) normal histological structure of hepatic tissue in G1 group (100X), (h) congestion of hepatic sinusoids with focal inflammatory cells aggregation in G2 group, (i) diffuse vacuolar degeneration of hepatocytes in G3 group (200X) (H and E stain).	31
2	Boxplot of stomach and intestine lesions score. (a) Inflammatory cells infiltration in the stomach. (b) Inflammatory cells infiltration in the intestine. (c) Epithelial hyperplasia in the intestine. (d) Goblet cell loss in the intestine. The boxes are the interquartile range (IQR). The medians are	33