Effect of Celecoxib on Immunological Liver Injury and Depression Induced by Specific Liver Antigen and Complete Freund's Adjuvant in C57BL/6 Mice

Thesis for partial fulfillment of the master degree of Pharmacology and Therapeutics

By

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بسم الله الرحمن الرحيم

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم الحكيم

صدق الله العظيم

سورة البقرة الآية: ٣٢

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Esraa ELnahas

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List of Abbreviations

C57BL/6	C57 black 6 mice
CLD	Chronic liver disease
HCV	Hepatitis C virus
HBV	Hepatitis B virus
TNF-α	Tumor necrosis factor α
NF-κB	Nuclear factor κB
COX-2	Cyclooxygenase-2
PGE-2	Prostaglandin E2
S-100	Supernatant of syngeneic liver homogenate at 100.000g
CFA	Complete freund's adjuvant
PBS	Phosphate buffered saline
EAH	Experimental autoimmune hepatitis
NSF	Novelty-Suppressed Feeding test
TST	Tail suspension test
FST	Forced swimming test
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
Hyp	Hepatic tissue Hydroxyproline
AIH	Autoimmune hepatitis

List of Abbreviations (continue)	
LSP	Liver specific lipoprotein
IFN	Interferon
CYP2C9	Cytochrome P4502C9
eLMA	Exploratory locomotor activity
ANOVA	One way analysis of variance
LPS	Lipopolysaccharide
Con A	Concavalin A
CCl_4	Carbon tetrachloride
HSCs	hepatic stellate cells

Introduction and Aim of the work

INTRODUCTION

Liver is the target of numerous acute and chronic inflammatory processes (***Manns& Obermayer-Straub, 1997***). It is the principal "residence of metabolic clearing" for exogenous drugs and endogenous chemicals that would harm the body such as cholesterol, steroid hormones, fatty acids, and proteins ***(Parkinson, 2001).***

Inflammatory liver injury due to viral infection, autoimmune etiology or intoxication with drugs is mediated by the activation of the innate and/or specific immune response. Inflammatory liver injury may also develop as a part of a systemic inflammatory response (***Liu et al., 2006***).

Chronic liver disease (CLD) is usually caused by chronic injury to the liver with different etiologic agents such as hepatotropic viruses including hepatitis C virus (HCV) and hepatitis B virus (HBV), autoimmune hepatitis, alcoholic liver disease, fatty liver, and other etiologic processes ***(Weinstein et al., 2011).***

HBV and HCV infections are the most common causes of liver diseases worldwide and both induce immune mediated acute and chronic necroinflammatory liver disease (***Rehermann& Nascimbeni, 2005).*** Chronic hepatitis is characterized by the