HEMODYNAMIC STUDY OF A NEW **CALCIUM CHANNEL BLOCKER** AMLODIPINE

Thesis Submitted for the Partial Fulfillment of the Master Degree in Pharmacology

By

Khaled Abdel Fattah Mahmoud

M.B., B.Ch (December, 1989) Demonstrator of Pharmacology & Therapeutic Dept. Faculty of Medicine-Ain Shams University 5~80°

Supervised by

Prof. Dr. Mahdy Salama Abou Zeid

Professor of Pharmacology Faculty of Medicine-Ain Shams University

Prof. Dr. Ahmed Shaaban Abou Seif

Professor of Pharmacology Faculty of Medicine-Ain Shams University

Dr. Boshra Mohammed Shalaby

Assistant Professor of Pharmacology Faculty of Medicine-Ain Shams University

> **Faculty of Medicine** Ain Shams University 1997



يسم الله الرحمن الرحيم

قالوا سبحانك لا علم لنا إلا ما علمتنا، إنكأنت الغليم المكيم

صدق الله العظيم

سورة البقرة، الآية ٣٢



Acknowledgment

I wish to offer my sincere thanks and gratitude to Prof. Dr. Mahdy Salama Abou Zeid, Professor of Pharmacology, Faculty of Medicine, Ain Shams University, for his experienced supervision, persistent effort, continuous guidance, fruitful criticism and valuable help throughout the present work.

I am also much obliged and deeply indebted to Prof. Dr. Ahmed Shaaban Abou Seif, Professor of Pharmacology, Faculty of Medicine, Ain Shams University, for his keen interest, advice, valuable help and pertinent observations on this work.

I want also to express my sincere gratitude to Dr. Boshra Mohammed Shalaby, Assistant Professor of Pharmacology, Faculty of Medicine, Ain Shams University, for her valuable advice and help in this work.

My deepest thanks and great gratitude to Dr. Laila Allam, Assistant Professor of Pharmacology, Faculty of Medicine, Ain Shams University, for her valuable advice, help and time she gave me in this work.

Lastly, I wish to extend my deepest thanks to all my professors and colleagues in the Pharmacology Department, Faculty of Medicine, Ain Shams University.



List of Contents

		Page
•	Introduction	1
•	Aim of the Work	23
•	Materials and Methods	24
•	Results	42
•	Discussion	103
•	Summary and Conclusion	113
•	English Abstract	117
•	References	118
•	Arabic Summary	
•	Arabic Abstract	



List of Tables

Page

_		
Table (1): 44		
Showing the effect of amlodipine in different levels on the		
mean arterial blood pressure of sodium pentobarbital		
anaesthetized dogs (30 mg/kg)		
Table (2): 50		
Showing the effect of nifedipine in 3 dose		
levels on the mean arterial blood pressure of sodium		
pentobarbital anaesthetized dogs (30 mg/kg)		
Table (3): 69		
Showing the effect of amlodipine in different dose levels		
on the contractility of the isolated perfused toad's heart		
measured as cm height.		
Table (4): 74		
Showing the effect of nifedipine in 4 doses levels on the		
isolated perfused toad's heart measured as cm height.		
Table (5): 77		
Showing the effect of amlodipine in different dose levels		
on myocardial contractility of the isolated perfused rabbit's		
heart measured as cm height.		
Table (6): 83		
Showing the effect of nifedipine in several dose levels on		
the contractility of the isolated perfused rabbit's heart		
measured as cm height.		
Table (7): 86		
Showing the effect of amlodipine in several dose levels on		
the coronary flow rate of the isolated perfused rabbit's		
heart as measured by ml/minute.		
Table (8): 87		
Showing the effect of nifedipine in several dose levels on		
the coronary flow rate of the isolated perfused rabbit's		
heart as measured by ml/minute.		
Table (9): 89		
Showing the effect of amlodipine in different dose levels		
on the phenylephrine induced contraction of the isolated		
aortic strip preparation of the rabbit measured as gm		
tension		

Table (10):

92

Showing the effect of nifedipine in different dose levels on the phenylephrine induced contraction of the isolated aortic strip preparation of the rabbit measured as gm tension.

Table (11):

95

Showing the effect of amlodipine in different dose levels on the flow rate of the isolated perfused rat's hind-limb measured as ml/min.

Table (12):

96

Showing the effect of nifedipine in different dose levels on the flow rate of the isolated perfused rat's hind-limb measured as ml/min.

Table (13):

98

Showing the effect of amlodipine in different dose levels on the histamine induced contraction of the isolated perfused tracheal spiral of the guinea pig measured as gm tension.

Table (14):

101

Showing the effect of nifedipine in different dose levels on the histamine induced contraction of the isolated perfused tracheal spiral of the guinea pig measured as gm tension.



List of Figures

Page

Fig. (1A):

45

The effect of amlodipine I.V. in graded doses ranging (1.25-40 mg) on the mean arterial blood pressure (in mmHg) of anaesthetized dogs under spontaneous respiration.

Fig. (1B):

47

Showing the site of action of amlodipine on the arterial blood pressure of anaesthetized dogs under spontaneous respiration.

Fig. (1C):

48

Continue site of action of amlodipine on arterial blood pressure of anaesthetized dogs under spontaneous respiration.

Fig. (2):

51

Effect of graded doses of (1.86-7.46 mg) of nifedipine on the arterial blood pressure of anaesthetized dogs under spontaneous respiration.

Fig. (3):

54

Effect of amlodipine (0.135-0.27 mg/kg) on ECG of sodium pentobarbital anaesthetized dogs.

Fig. (4):

55

Effect of nifedipine (0.27-0.54 mg/kg) on ECG of sodium pentobarbital anaesthetized dogs.

Fig. (5):

57

Curative effect of amlodipine (0.27 mg/kg) against epinephrine-induced dysrhythmias in sodium pentobarbital anaesthetized dogs.

Fig._.(6): 58

Prophylactic effect of amlodipine 0.27 mg/kg against epinephrine-induced dysrhythmias in sodium pentobarbital anaesthetized dogs.

Fig. (7): 60

Curative effect of nifedipine (0.54 mg/kg) on epinephrine-induced dysrhythmia in sodium pentobarbital anaesthetized dogs.

Fig. (8): 61

Prophylactic effect of nifedipine (0.54 mg/kg) against epinephrine-induced dysrhythmias in sodium pentobarbital anaesthetized dogs.

Fig. (9): 63

Curative effect of amlodipine (0.27 mg/kg) against ouabaininduced dysrhythmias in sodium pentobarbital anaesthetized dogs.

Fig. (10): 64

Prophylactic effect of amlodipine (0.27 mg/kg) against ouabain-induced dysrhythmias in sodium pentobarbital anaesthetized dogs.

Fig. (11): 66

Curative effect of nifedipine (0.54 mg/kg) against ouabain-induced dysrhythmias in sodium pentobarbital anaesthetized dogs (30 mg/kg).

Fig. (12): 67

Prophylactic effect of nifedipine (0.54 mg/kg) against ouabain (120 µg/kg) induced dysrhythmias in sodium pentobarbital anaesthetized dogs (30 mg/kg).

Fig. (13A): 70

Effect of amlodipine (20-160 ng/5 ml cannula) on isolated perfused toad's heart.