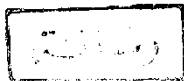


Dr. Ahmed Abdel Salam
Mohamed Ibrahim Ahmed Ibrahim
Dr. Elsayed Kamel Soliman

**BRONCHODILATOR EFFECT OF GLYCOPYRROLATE
IN EXPERIMENTAL ANIMALS**

A Thesis Submitted In Partial Fulfillment Of The M.Sc. Degree
Pharmacology

By



Hala Salah Abdel Kawy

M.B., B.Ch.

Demonstrator of Pharmacology

59956

619.9

H.S

Supervised by

Prof. Dr. El Sayed Kamel Soliman

Prof. of Pharmacology

Faculty of Medicine- Ain Shams University

Dr. Elsayed Kamel Soliman

Prof. Dr. Gaber Abdel-Sabour

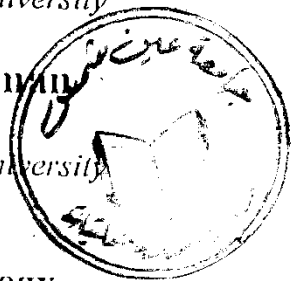
Prof. of Pharmacology

Faculty of Medicine- Ain Shams University

Dr. Alaa El-Din M. Soliman

Lecturer of Pharmacology

Faculty of Medicine- Ain Shams University



**Department of Pharmacology
Faculty of Medicine- Ain Shams University**

1998



بسم الله الرحمن الرحيم

قالوا سبحانك لا علم لنا إلا ما علمتنا
إنك أنت العظيم الحكيم.

صمدق الله العظيم

(سورة البقرة الآية ٣٢)

Acknowledgment

It is a great pleasure to express my sincere thanks and gratitude to **PROF. DR. EL SAYED KAMEL SOLIMAN**, Prof. of Pharmacology, Faculty of Medicine, Ain Shams University, for his consistent supervision, continuous enthusiastic encouragement and valuable advice that made this work possible.

I am greatly indebted to **PROF. DR. GABER ABDEL-SABOUR**, Prof. of Pharmacology, Faculty of Medicine, Ain Shams University, for his unlimited encouragement and his valuable comments and guidance.

I am also obliged to **DR. ALAA EL-DIN M. SOLIMAN**, Lecturer of Pharmacology, Faculty of Medicine, Ain Shams University for his guidance and his continuous everlasting help.

I would like to extend my gratitude to all members and colleagues of Pharmacology Department, Ain Shams University.

HALA SALAH

CONTENTS

	Page
♦ Introduction -----	1
♦ Aim of the Work -----	14
♦ Material and methods and statistical analysis -----	17
♦ Results -----	31
♦ Discussion -----	132
♦ Summary and conclusion -----	155
♦ References -----	164
♦ Arabic summary. -----	

LIST OF FIGURES

	Page
<i>Fig. (1):</i> Chemical structure of glycopyrrolate -----	17
<i>Fig. (2):</i> Chemical structure of ipratropium bromide -----	17
<i>Fig. (3):</i> Chemical structure of salbutamol -----	18
<i>Fig. (4):</i> Chemical structure of histamine -----	18
<i>Fig. (5):</i> Chemical structure of acetyl choline -----	19
<i>Fig.(6a):</i> Effect of glycopyrrolate in cumulative gradual increasing I.V. doses on acetyl choline induced increase in airway resistance in unsensitized urethanized guinea pig.-----	35
<i>Fig.(6b):</i> Effect of glycopyrrolate in cumulative gradual increasing I.V. doses of acetyl choline induced by bradycardia in unsensitized urethanized guinea pig.	36
<i>Fig.(7a):</i> Effect of ipratropium bromide in cumulative gradual increasing I.V. doses on acetyl choline induced increase in airway resistance in unsensitized urethanized guinea pig. -----	37
<i>Fig.(7b):</i> Effect of ipratropium bromide in cumulative gradual increasing I.V doses on acetyl choline induced bradycardia in unsensitized urethanized guinea pigs.-----	38
<i>Fig. (8):</i> Effect of salbutamol in cumulative gradual increasing I.V. doses on acetyl choline increase in airway resistance in unsensitized urethanized guinea pigs -----	39
<i>Fig. (9):</i> Cumulative concentration response curve for glycopyrrolate, ipratropium bromide and salbutamol on acetyl choline induced increase in airway resistance in unsensitized urethanized guinea pigs. -----	44

<i>Fig.(10):</i>	Effect of glycopyrrolate in cumulative gradual increasing I.V. doses on histamine induced increase in airway resistance in unsensitized urethanized guinea pigs. -----	47
<i>Fig.(11):</i>	Effect of ipratropium bromide in cumulative gradual increasing I.V. doses on histamine induced increase in airway resistance in unsensitized urethanized guinea pigs. -----	48
<i>Fig.(12):</i>	Effect of salbutamol in cumulative gradual increasing I.V. doses on histamine induced increase in airway resistance in unsensitized urethanized guinea pigs. -----	49
<i>Fig.(13):</i>	Cumulative concentration response curve for glycopyrrolate, ipratropium bromide and salbutamol on histamine induced increase in airway resistance in unsensitized urethanized guinea pigs.-	54
<i>Fig.(14):</i>	Effect of glycopyrrolate in cumulative gradual increasing I.V. doses on acetyl choline induced increase in airway resistance in ovalbumin sensitized urethanized guinea pigs. -----	57
<i>Fig.(15):</i>	Effect of ipratropium bromide in gradualal increasing I.V. doses on acetyl choline induced increase in airway resistance in ovalbumin sensitized urethanized guinea pigs.-----	58
<i>Fig.(16):</i>	Effect of salbutamol in cumulative gradual increasing I.V. doses on acetyl choline induced increase in airway resistance in ovalbumin sensitized urethanized guinea pigs.-----	59
<i>Fig.(17):</i>	Cumulative concentration response curve for glycopyrrolate, ipratropium bromide and salbutamol on acetyl choline induced increase in airway resistance in ovalbumin sensitized urethanized guinea pigs. -----	64

<i>Fig.(18):</i>	Effect of glycopyrrolate in cumulative gradual increasing I.V. doses on histamine induced increase in airway resistance in ovalbumin sensitized urethanized guinea pigs.-----	67
<i>Fig.(19):</i>	Effect of ipratropium bromide in cumulative gradual increasing I.V. doses on histamine induced increase in airway resistance in ovalbumin sensitized urethanized guinea pigs.-----	68
<i>Fig.(20):</i>	Effect of salbutamol in cumulative gradual increasing I.V. doses on histamine induced increase in airway resistance in ovalbumin sensitized urethanized guinea pigs.-----	69
<i>Fig.(21):</i>	Cumulative concentration response curve for glycopyrrolate, ipratropium bromide and salbutamol on histamine induced increase in airway resistance in ovalbumin sensitized urethanized guinea pigs. -----	74
<i>Fig.(22):</i>	Effect of glycopyrrolate in cumulative gradual increasing doses on precontraction induced by submaximal dose of acetyl choline in isolated guinea pigs tracheal spiral strips. -----	79
<i>Fig.(23):</i>	Effect of ipratropium bromide in cumulative gradual increasing doses on precontraction induced by submaximal dose of acetyl choline in isolated guinea pigs tracheal spiral strips.-----	80
<i>Fig.(24):</i>	Effect of salbutamol in cumulative gradual increasing doses on precontraction induced by submaximal dose of acetyl choline in isolated guinea pigs tracheal spiral strips.-----	81
<i>Fig.(25):</i>	Cumulative concentration response curve for glycopyrrolate, ipratropium bromide and salbutamol on precontraction induced by submaximal dose of acetyl choline in isolated guinea pigs tracheal spiral strips. -----	86

<i>Fig.(26):</i>	Effect of glycopyrrolate in cumulative gradual increasing doses on precontraction induced by submaximal dose of histamine in isolated guinea pigs tracheal spiral strips.-----	89
<i>Fig.(27):</i>	Effect of ipratropium bromide in cumulative gradual increasing doses on precontraction induced by submaximal dose of histamine in isolated guinea pigs tracheal spiral strips.-----	90
<i>Fig.(28):</i>	Effect of salbutamol in cumulative gradual increasing doses on precontraction induced by submaximal dose of histamine in isolated guinea pigs tracheal spiral strips.-----	91
<i>Fig.(29):</i>	Cumulative concentration response curve for glycopyrrolate, ipratropium bromide and salbutamol on precontraction induced by submaximal dose of histamine in isolated guinea pigs tracheal spiral strips. -----	96
<i>Fig.(30):</i>	Combined effect of glycopyrrolate in cumulative gradual increasing doses and salbutamol single dose on precontraction induced by submaximal dose of acetyl choline in isolated guinea pigs tracheal spiral strips. -----	98
<i>Fig.(31):</i>	Combined effect of ipratropium bromide in cumulative gradual increasing doses and salbutamol single dose on precontraction induced by submaximal dose of acetyl choline in isolated guinea pigs tracheal spiral strips. -----	101
<i>Fig.(32):</i>	Cumulative concentration response cure for glycopyrrolate and ipratropium bromide with salbutamol single dose on precontraction induced by submaximal dose of acetyl choline in isolated guinea pigs tracheal spiral strips. -----	103

<i>Fig.(33):</i> Combined effect of glycopyrrolate in cumulative gradual increasing doses and salbutamol single dose on precontraction induced by histamine in isolated guinea pigs tracheal spiral strips. -----	105
<i>Fig.(34):</i> Combined effect of ipratropium bromide in cumulative gradual increasing doses and salbutamol single dose on precontraction induced by histamine in isolated guinea pigs tracheal spiral strips. -----	108
<i>Fig.(35):</i> Cumulative concentration response for glycopyrrolate and ipratropium bromide with salbutamol single dose on precontraction induced by submaximal dose of histamine in isolated guinea pigs tracheal spiral strips. -----	110
<i>Fig.(36):</i> Effect of glycopyrrolate in cumulative gradual increasing doses on neuromuscular transmission in rat phrenic nerve diaphragm preparation (direct stimulation). -----	115
<i>Fig.(37):</i> Effect of ipratropium bromide in cumulative gradual increasing doses on neuromuscular transmission in rat phrenic nerve diaphragm preparation (direct stimulation). -----	116
<i>Fig.(38):</i> Effect of glycopyrrolate in cumulative increasing gradual doses on neuromuscular transmission in rat phrenic nerve diaphragm preparation (indirect stimulation). -----	117
<i>Fig. (39)</i> Effect of ipratropium bromide in cumulative gradual increasing doses on neuromuscular transmission in rat phrenic nerve diaphragm preparation (indirect stimulation). -----	118
<i>Fig.(40):</i> Effect of glycopyrrolate in cumulative gradual increasing doses on neuromuscular transmission in rat phrenic nerve diaphragm preparation (high frequency). -----	119

<i>Fig.(41):</i>	Effect of ipratropium bromide on neuromuscular transmission in rat phrenic nerve diaphragm preparation (high frequency). -----	120
<i>Fig.(42):</i>	Effect of glycopyrrolate on neuromuscular transmission in rat phrenic nerve diaphragm preparation (tetanic contraction). -----	121
<i>Fig.(43):</i>	Effect of ipratropium bromide on neuromuscular transmission in rat phrenic nerve diaphragm preparation (tetanic contraction). -----	122
<i>Fig.(44):</i>	Effect of glycopyrrolate on the rate and amplitude of heart beats in isolated rabbit auricle pretreated with acetyl choline. -----	128
<i>Fig.(45):</i>	Effect of ipratropium bromide on the rate and amplitude of heart beats in isolated rabbit auricle pretreated with acetyl choline. -----	129