

ผลของสารสกัดกะทกรกต่ออัตราการเต้นและแรงบีบตัวของหัวใจห้องบนที่แยกจากกายหนูขาว

นางสาว สาลินี ศิโรตม

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาเภสัชศาสตรมหาบัณฑิต

สาขาวิชาเภสัชวิทยา ภาควิชาเภสัชวิทยา

คณะเภสัชศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย

ปีการศึกษา 2550

ลิขสิทธิ์ของจุฬาลงกรณ์มหาวิทยาลัย

CHRONOTROPIC AND INOTROPIC EFFECTS OF *PASSIFLORA FOETIDA* EXTRACTS
ON RAT ISOLATED ATRIA

Miss Salinee Sirodom

A Thesis Submitted in Partial Fulfillment of the Requirements
for the Degree of Master of Science in Pharmacy Program in Pharmacology

Department of Pharmacology

Faculty of Pharmaceutical Sciences

Chulalongkorn University

Academic Year 2007

Copyright of Chulalongkorn University

501831

Thesis Title CHRONOTROPIC AND INOTROPIC EFFECTS OF *PASSIFLORA*
 FOETIDDA EXTRACTS ON RAT ISOLATED ATRIA
By Miss Salinee Sirodom
Field of Study Pharmacology
Thesis Advisor Assistant Professor Suree Jianmongkol, Ph.D.
Thesis Co-advisor Associate Professor Prasan Dhumma-upakorn, Ph.D.

Accepted by the Faculty of Pharmaceutical Science, Chulalongkorn University in
Partial Fulfillment of the Requirements for the Master 's Degree

.....*Pornpen Pramyothin*.....Dean of the Faculty of
Pharmaceutical Sciences
(Associate Professor Pornpen Pramyothin, Ph.D.)

THESIS COMMITTEE

.....*Siriporn Foongwithaya*.....Chairman
(Associate Professor Siriporn Foongwithaya, M.Sc.)

.....*Suree Jianmongkol*..... Thesis Advisor
(Assistant Professor Suree Jianmongkol, Ph.D.)

.....*Prasan Dhumma-upakorn*..... Thesis Co-advisor
(Associate Professor Prasan Dhumma-upakorn, Ph.D.)

.....*Withaya Janthasoot*..... Member
(Assistant Professor Withaya Janthasoot, M.Sc.)

.....*Thongchai Sooksawate*..... Member
(Associate Professor Thongchai Sooksawate, Ph.D.)

สาลินี ศิโรตม : ผลของสารสกัดกะทกรกต่ออัตราการเต้นและแรงบีบตัวของหัวใจห้องบนที่แยก
จากกายหนูขาว. (CHRONOTROPIC AND INOTROPIC EFFECTS OF *PASSIFLORA*
FOETIDA EXTRACTS ON RAT ISOLATED ATRIA) อ. ที่ปรึกษา: ผศ. ดร. สุรีย์ เจียรณ์
มงคล. อ. ที่ปรึกษาร่วม: รศ. ดร. ประสาน ธรรมอุปกรณ์, 122 หน้า.

กะทกรกเป็นพืชสมุนไพรไทยที่มีการใช้มานาน จากการศึกษา พบว่าสารสกัดกะทกรกมีฤทธิ์ด้านการ
ซึมเศร้าในแบบจำลองการซึมเศร้าในหนูถีบจักร ยังไม่ทราบถึงกลไกในการต้านฤทธิ์ซึมเศร้าที่แน่ชัด แต่จาก
การศึกษาการจับกับ receptor พบว่าสารสกัดกะทกรกสามารถจับกับ dopamine และ serotonin receptor ได้

ในการศึกษานี้ มีวัตถุประสงค์เพื่อศึกษาผลของการออกฤทธิ์ของสารสกัดกะทกรกต่ออัตราการเต้นและแรง
บีบตัวของหัวใจโดยใช้แบบจำลองหัวใจห้องบนที่แยกออกจากกายหนูขาว (250 – 300 กรัม) จากผลการทดลอง
พบว่าสารสกัดกะทกรก PF003-2 (100 µg/ml) มีผลลดแรงบีบตัวของหัวใจห้องบนซ้ายและขวาในช่วงแรก หลังจากนั้น
นั้นจะเพิ่มแรงบีบตัวของหัวใจห้องบนซ้ายอย่างมีนัยสำคัญทางสถิติ เท่ากับ $8.76 \pm 4.01\%$ และ $19.22 \pm 4.95\%$ ใน
เวลา 3 นาทีและ 15 นาที ตามลำดับ ($p < 0.05$, $n = 6$). PF003-2 ไม่มีผลต่ออัตราการเต้นของหัวใจห้องบนขวาอย่างมี
นัยสำคัญทางสถิติ ในทางตรงกันข้าม สารสกัด PF003-(3-5) มีผลลดอัตราการเต้นของหัวใจห้องบนขวาอย่างมี
นัยสำคัญทางสถิติ เท่ากับ 9.61 ± 1.53 และ $14.87 \pm 1.17\%$ ในนาทีที่ 3 และ 15 นาที ($p < 0.05$) ผลเพิ่มแรงบีบตัว
ของหัวใจห้องบนซ้ายของ PF003-2 ยับยั้งได้ไม่สมบูรณ์และมีนัยสำคัญทางสถิติ ($p < 0.05$) ด้วย propranolol (10
µM) และ ketanserin และ ยับยั้งฤทธิ์ในการเพิ่มแรงบีบตัวของ PF003-2 ได้อย่างสมบูรณ์และมีนัยสำคัญทางสถิติ
เมื่อให้ propranolol (10 µM) ร่วมกับ ketanserin (10 µM) ($p < 0.05$, $n = 5$) ทั้งนี้การออกฤทธิ์ของ PF003-2 ไม่
เกี่ยวข้องกับการหลั่งของ Ca^{2+} จาก SR และการยับยั้งการเก็บกลับของ NE และ serotonin ที่ปลายประสาทด้วย

จากการศึกษา สามารถสรุปได้ว่า สารสกัดกะทกรกในแต่ละ fraction มีฤทธิ์ต่อหัวใจแตกต่างกัน PF003-
(3-5) มีผลต่อ pace maker activity ผลในการเพิ่มแรงบีบตัวของหัวใจห้องบนของ PF003-2 ไม่ได้เกิดจากการกระตุ้น
ให้เกิดการหลั่งของ Ca^{2+} จาก SR ภายในเซลล์ และไม่เกี่ยวข้องกับการยับยั้งการเก็บกลับของ NE และ serotonin
อาจจะได้ว่า PF003-2 ออกฤทธิ์ในลักษณะของการตอบสนองสองทาง (biphasic response) ต่อหัวใจห้องบนที่
แยกจากหนูขาว นอกจากนี้ ผลในการเพิ่มแรงบีบตัวของหัวใจของ PF003-2 อาจจะเกิดจากการไปกระตุ้นที่ β -
adrenoceptor และ serotonin receptor ได้

ภาควิชาเภสัชวิทยา.....ลายมือชื่อนิสิต..... *สาลินี ศิโรตม*
สาขาวิชาเภสัชวิทยา.....ลายมือชื่ออาจารย์ที่ปรึกษา..... *สุรีย์ เจียรณ์*
ปีการศึกษา 2550.....ลายมือชื่ออาจารย์ที่ปรึกษาร่วม..... *ประสาน ธรรมอุปกรณ์*

487 66119 33 : MAJOR PHARMACOLOGY

KEY WORD: INOTROPIC EFFECT / CHRONOTROPIC EFFECT / PASSIFLORA FOETIDA / ISOLATED ATRIA

SALINEE SIRODOM : CHRONOTROPIC AND INOTROPIC EFFECTS OF *PASSIFLORA FOETIDA* EXTRACTS ON RAT ISOLATED ATRIA. THESIS ADVISOR: ASST. PROFESSOR SUREE JIANMONGKOL, Ph.D., THESIS COADVISOR: ASSOC. PROFESSOR PRASAN DHUMMA-UPAKORN, Ph.D. , 122 pp.

Passiflora foetida is a Thai herbal plant. It has been reported that *P. foetida* extract possessed potential antidepressant actions in the *in vivo* model of depression, mice swimming test. Although the mechanisms of actions were not yet known, the receptor binding studies revealed that *P. foetida* extracts were able to bind to dopamine and serotonin receptors.

This study aims to investigate the mechanisms of inotropic and chronotropic effects produced by *P. foetida* extracts, using the model of isolated rat atria (250 – 300 g). The results showed that *P. foetida* extracts, subfraction PF003-2 (100 µg/ml) had transiently depressed contractile force on both left and right atria, followed by significant increasing the force of contraction by $8.76 \pm 4.01\%$ and $19.22 \pm 4.95\%$ at 3min and 15 min, respectively ($p < 0.05$, $n = 6$). PF003-2 had no significant chronotropic effect on right atria. PF003-(3-5), by contrast, showed significant negative chronotropic effect to right atria by 9.61 ± 1.53 and $14.87 \pm 1.17\%$ ($p < 0.05$) in 3 min and 15 min. The positive inotropic effect of PF003-2 was significantly partially inhibited by propranolol (10 µM) and ketanserin (10 µM) and was completely inhibited by pretreatment of propranolol (10 µM) and ketanserin (10 µM) together ($p < 0.05$, $n = 5$). PF003-2 possessed intrinsic inotropic activity which did not relate to Ca^{2+} release from SR and inhibition effect to reuptake of NE and serotonin

In conclusion, the results in this study suggested that each of PF extracts were different in their inotropic and chronotropic action on the isolated rat atria. It has been suggested that PF003-(3-5) had potential effects on pace maker activity. Positive inotropic effect of PF003-2 was not related to a release of Ca^{2+} from SR and an inhibition of NE and serotonin reuptake. It is possible that PF003-2 may have biphasic activity on isolated rat atria. In addition, PF003-2 may exerted its positive inotropic effect via activation on β -adrenoceptor and serotonin receptor.

Department Pharmacology.....Student's signature.....*Salinee Sirodom*
 Field of study Pharmacology.....Advisor's signature.....*Suree Jianmongkol*
 Academic year 2007.....Co-advisor's signature.....*Prasan Dhumma-upakorn*

ACKNOWLEDGMENTS

The present study was carried out in the Department of Pharmacology, Faculty of Pharmaceutical Sciences, Chulalongkorn University.

I wish to express my sincere gratitude to my advisor, Assistant Professor Dr. Suree Jianmongkol, and my co-advisor, Associate Professor Dr. Prasan Dhumma-upakorn, for their valuable advices and guidances, criticism, encouragement, and numerous discussions during my dissertation work.

I am greatly indebted to Associate Professor Dr. Ruti Suttisri, Department of Pharmaceutical Botany, Faculty of Pharmaceutical Science, Chulalongkorn University, for providing the *Passiflora foetida* extracts used in this study.

I express my special thanks to the personals of Department of Pharmacology, Faculty of Pharmaceutical Sciences, Chulalongkorn University, for friendship during my dissertation works.

Finally, I thank my family and my friends for their understanding and optimism that have been vital for the finishing of this work.

Contents

	PAGE
Abstract (Thai).....	iv
Abstract (English).....	v
Acknowledgements.....	vi
Contents.....	vii
List of tables.....	ix
List of figures.....	xiii
List of abbreviations.....	xxi
Chapter	
I Introduction.....	1
II Literature review.....	5
Pharmacological effects of <i>Passiflora</i>	5
<i>Passiflora foetida</i> Linn.....	7
Effects of antidepressant on the heart.....	9
Regulation of cardiac function.....	10
III Materials and Methods	
Laboratory Animals.....	21
Experimental instruments.....	21
Drugs and Chemicals.....	22
Experimental methods.....	22

Contents

viii

	PAGE
IV Results.....	30
V Discussions and Conclusions.....	92
References.....	97
Appendices.....	106
Curriculum vitae.....	122

List of tables

	PAGE
Table 1 Summary of characterized 5-HT receptors, with selected agonist/ antagonist agents.....	21
Table 2 Chemical compound for Krebs-Henseleit Solution (mM/L).....	107
Table 3 Effects of DMSO (0.25 % V/V) on rate and force of contraction on isolated left and right atria	108
Table 4 Effects of PF002-(1-4) (100 μ g/ml) on rate and force of contraction on isolated left and right atria.....	108
Table 5 Effects of PF002-(5-6) (100 μ g/ml) on rate and force of contraction on isolated left and right atria.....	109
Table 6 Effects of PF002-7 (100 μ g/ml) on rate and force of contraction on isolated left and right atria.....	109
Table 7 Effects of PF003-1 (100 μ g/ml) on rate and force of contraction on isolated left and right atria.....	110
Table 8 Effects of PF003-2 (100 μ g/ml) on rate and force of contraction on isolated left and right atria.....	110
Table 9 Effects of PF003-(3-5) (100 μ g/ml) on rate and force of contraction on isolated left and right atria.....	111
Table 10 Effects of NE (0.1 μ M) on rate and force of contraction on isolated left and right atria.....	111

List of tables

	PAGE
Table 11 Effects of propranolol (10 μM) on rate and force of contraction on isolated left and right atria.....	112
Table 12 Effects of NE (0.1 μM) in the presence of propranolol (10 μM) on rate and force of contraction on isolated left and right atria.....	112
Table 13 Effects of PF003-2 (100 $\mu\text{g/ml}$) in the presence of propranolol (10 μM) on rate and force of contraction on isolated left and right atria.....	113
Table 14 Effects of serotonin (1 μM) on rate and force of contraction on isolated left and right atria.....	113
Table 15 Effects of ketanserin (10 μM) on rate and force of contraction on isolated left and right atria.....	114
Table 16 Effects of serotonin (10 μM) in the presence of ketanserin (10 μM) on isolated rate and force of contraction of left and right atria.....	114
Table 17 Effects of PF003-2 (100 $\mu\text{g/ml}$) in the presence of ketanserin (10 μM) on isolated rate and force of contraction of left and right atria.....	115
Table 18 Effects of PF003-2 (100 $\mu\text{g/ml}$) in the presence of propranolol (10 μM) and ketanserin (10 μM) on rate and force of contraction on isolated left and right atria.....	115
Table 19 Effect of caffeine (10 mM) and PF003-2 (100 $\mu\text{g/ml}$) on the relationships between the T_i / T_{ss} and the rest interval of range 10 to 300 seconds.....	116

List of tables

	PAGE
Table 20 Effects of tyramine (10 μM) on rate and force of contraction on isolated left and right atria.....	117
Table 21 Effects of tyramine (10 μM) on rate and force of contraction on isolated left and right atria in rat pretreated with reserpine (5 mg/kg. i.p. for 5 days).....	117
Table 22 Effects of PF003-2 (100 $\mu\text{g/ml}$) on rate and force of contraction on isolated left and right atria in rat pretreated with reserpine (5 mg/kg. i.p. for 5 days).....	118
Table 23 Effects of NE (0.1 μM) on rate and force of contraction on isolated left and right atria in 5 min.....	118
Table 24 Effects of NE (0.1 μM) on rate and force of contraction on isolated left and right atria (5 min) in the presence of amitriptyline (10 μM).....	119
Table 25 Effects of NE (0.1 μM) on rate and force of contraction on isolated left and right atria (5 min) in the presence of PF003-2 (100 $\mu\text{g/ml}$).....	119
Table 26 Effects of serotonin (1 μM) on rate and force of contraction on isolated left and right atria (5 min).....	120
Table 27 Effects of fluoxetine (1 μM) on rate and force of contraction on isolated left and right atria (5 min).....	120

List of tables

PAGE

Table 28 Effects of serotonin (1 μM) on rate and force of contraction on isolated left and right atria (5 min) in the presence of fluoxetine (1 μM).....	121
Table 29 Effects of serotonin (1 μM) on rate and force of contraction on isolated left and right atria (5 min) in the presence of PF003-2 (100 $\mu\text{g/ml}$).....	121

List of figures

	PAGE
Figure 1 <i>Passiflora foetida</i> Linn. or in Thai name, "Katokrok").....	7
Figure 2 Cardiac myofilaments.....	13
Figure 3 Mechanism of cardiac contraction mediated through beta-adrenergic receptor	14
Figure 4 Diagram of a noradrenergic axonal terminal showing the release and re-uptake of norepinephrine	18
Figure 5 The activation of NE and ACh on cardiaomyocyte	19
Figure 6 Diagram shows the release and reuptake of serotonin.....	19
Figure 7 Preparation of isolated rat atria.....	24
Figure 8 An example of rest-state contraction in papillary muscle.....	27
Figure 9 Chronotropic and inotropic response on the left and right atria before treating.....	36
Figure 10 Chronotropic and inotropic response on the left and right atria in the presence of DMSO (0.25% V/V).....	37
Figure 11 Inotropic response on the left atria in the presence of DMSO (0.25% V/V).....	38
Figure 12 Chronotropic and inotropic response on the right atria in the presence of DMSO (0.25% V/V).....	39

List of figures

	PAGE
Figure 13 Chronotropic and inotropic response on the left and right atria in the presence of PF002-(1-4) (100 $\mu\text{g/ml}$).....	40
Figure 14 Chronotropic and inotropic response on the left and right atria in the presence of PF002-(5-6) (100 $\mu\text{g/ml}$).....	41
Figure 15 Chronotropic and inotropic response on the left and right atria in the presence of PF002-7 (100 $\mu\text{g/ml}$).....	42
Figure 16 Chronotropic and inotropic response on the left and right atria in the presence of PF003-1 (100 $\mu\text{g/ml}$).....	43
Figure 17 Chronotropic and inotropic response on the left and right atria in the presence of PF003-2 (100 $\mu\text{g/ml}$).....	44
Figure 18 Chronotropic and inotropic response on the left and right atria in the presence of PF003-(3-5) (100 $\mu\text{g/ml}$).....	45
Figure 19 The inotropic response on the left atria in the presence of PF extract ; PF002-(1-4), PF002-(5-6) and PF002-7 100 $\mu\text{g/ml}$	46
Figure 20 The inotropic response on the left atria in the presence of PF extract ; PF003-1, PF003-2 and PF003-(3-5) 100 $\mu\text{g/ml}$	47
Figure 21 The inotropic response on the right atria in the presence of PF extract ; PF002-(1-4), PF002-(5-6) and PF002-7 100 $\mu\text{g/ml}$	48

List of figures

	PAGE
Figure 22 The chronotropic and inotropic reponse on the right atria in the presence of PF extract ; PF003-1, PF003-2 and PF003-(3-5) 100 $\mu\text{g/ml}$	49
Figure 23 The chronotropic reponse on the right atria in the presence of PF extract ; PF002-(1-4), PF002-(5-6) and PF002-7 100 $\mu\text{g/ml}$	50
Figure 24 The chronotropic response on the right atria in the presence of PF extract ; PF003-1, PF003-2 and PF003-(3-5) 100 $\mu\text{g/ml}$	51
Figure 25 Chronotropic and inotropic response on the left and right atria in the presence of propranolol (10 μM).....	52
Figure 26 Chronotropic and inotropic response on the left and right atria in the presence of NE (0.1 μM).....	53
Figure 27 Chronotropic and inotropic response of NE (1 μM) on the left and right atria in the presence of propranolol (10 μM).....	54
Figure 28 Chronotropic and inotropic response of PF003-2 (100 $\mu\text{g/ml}$) on the left and right atria in the presence of propranolol (10 μM).....	55
Figure 29 The chronotropic and inotropic reponse of (A) NE (0.1 μM) and (B) propranolol (10 μM).....	56

List of figures

	PAGE
Figure 30 The inotropic reponse of NE (10 μM) on left atria in the presence of propranolol (10 μM).....	57
Figure 31 The inotropic and chronotropic reponse of NE (10 μM) on right atria in the presence of propranolol (10 μM).....	58
Figure 32 The inotropic reponse of PF003-2 (100 $\mu\text{g/ml}$) on the left atria in the presence of propranolol (10 μM).....	59
Figure 33 The inotropic reponse of PF003-2 (100 $\mu\text{g/ml}$) on the left atria in the presence of propranolol (10 μM).....	60
Figure 34 Chronotropic and inotropic response on the right atria in the presence of serotonin (1 μM).....	61
Figure 35 Chronotropic and inotropic response on the left and right atria in the presence of ketanserin (10 μM).....	62
Figure 36 Chronotropic and inotropic response of serotonin (10 μM) on the left and right atria in the presence of ketanserin (1 μM).....	63
Figure 37 Chronotropic and inotropic response of PF003-2 (100 $\mu\text{g/ml}$) on the left and right atria in the presence of ketanserin (10 μM).....	64
Figure 38 The chronotropic and inotropic response of (A) serotonin (1 μM) and (B) ketanserin (10 μM) on the left and right atria.....	65

List of figures

	PAGE
Figure 39 The inotropic response of serotonin (1 μM) on left atria in the presence of ketanserin (10 μM).....	66
Figure 40 The chronotropic and inotropic response of serotonin (1 μM) on right atria in the presence of ketanserin (10 μM).....	67
Figure 41 The inotropic response of PF003-2 (100 $\mu\text{g/ml}$) on the left atria in the presence of ketanserin (10 μM).....	68
Figure 42 The inotropic response of PF003-2 (100 $\mu\text{g/ml}$) on the left atria in the presence of ketanserin (10 μM).....	69
Figure 43 The chronotropic and inotropic response of PF003-2 (100 $\mu\text{g/ml}$) on the right atria in the presence of propranolol (10 μM) and ketanserin (10 μM).....	70
Figure 44 The inotropic response of PF003-2 (100 $\mu\text{g/ml}$) on the left atria in the presence of propranolol(10 μM) and ketanserin (10 μM).....	71
Figure 45 The inotropic and chronotropic response of PF003-2 (100 $\mu\text{g/ml}$) on the left atria in the presence of propranolol(10 μM) and ketanserin (10 μM).....	72

List of figures

	PAGE
Figure 46 A representative example on inotropic response of (A) control, (B) Caffeine and (C) PF003-2 on the rest interval of the range 10 to 300 seconds on left atria.....	73
Figure 47 Effect of caffeine on the relationships between the T_i / T_{ss} and the rest interval of range 10 to 300 seconds.....	74
Figure 48 Effect of PF003-2 on the relationships between the T_i / T_{ss} and the rest interval of range 10 to 300 seconds.....	74
Figure 49 Chronotropic and inotropic response on the left and right atria in the presence of tyramine (10 μM).....	75
Figure 50 Chronotropic and inotropic response of tyramine (10 μM) on the left and right atria in rats pretreated with reserpine (5 mg/kg, i.p. for 2 days).....	76
Figure 51 Chronotropic and inotropic response of PF003-2 (100 $\mu\text{g/ml}$) on the left and right atria in rats pretreated with reserpine (5 mg/kg, i.p. for 2 days).....	77
Figure 52 The chronotropic and inotropic response of tyramine (10 μM) on the left and right atria in normal rat.....	78
Figure 53 The chronotropic and inotropic response of tyramine (10 μM) on (A) left and (B) right atria in reserpinized rat (5 mg/kg, i.p. for 2 days).....	79

List of figures

	PAGE
Figure 54 The chronotropic and inotropic response of PF003-2 (100 $\mu\text{g/ml}$) on (A) left and (B) right atria in reserpinized rat (5 mg/kg, i.p. for 2 days).....	80
Figure 55 The chronotropic and inotropic response of NE (0.1 μM) and NE (0.1 μM) in presence of amitriptyline (10 μM) on the left and right atria.....	81
Figure 56 The chronotropic and inotropic response of NE (0.1 μM) and NE (0.1 μM) in presence of PF003-2 (100 $\mu\text{g/ml}$) on the left and right atria.....	82
Figure 57 The chronotropic and inotropic response of NE (0.1 μM) on the left and right atria.....	83
Figure 58 The chronotropic and inotropic response of NE (0.1 μM) and NE (0.1 μM) in presence of amitriptyline (10 μM) on (A) left and (B) right atria.....	84
Figure 59 The chronotropic and inotropic response of NE (0.1 μM) and NE (0.1 μM) in presence of PF003-2 (100 $\mu\text{g/ml}$) on (A) left and (B) right atria.....	85

List of figures

	PAGE
Figure 60 The chronotropic and inotropic response of serotonin (1 μM), fluoxetine (1 μM) and serotonin (1 μM) in presence of fluoxetine (1 μM) on the left and right atria.....	86
Figure 61 The chronotropic and inotropic response of serotonin (1 μM), fluoxetine (1 μM) and serotonin (1 μM) in presence of PF003-2 (100 $\mu\text{g/ml}$) on the left and right atria.....	87
Figure 62 The chronotropic and inotropic re2ponse of serotonin (1 μM) on the left and right atria.....	88
Figure 63 The chronotropic and inotropic response of fluoxetine (1 μM) on the left and right atria.....	89
Figure 64 The chronotropic and inotropic response of serotonin (1 μM) and serotonin (1 μM) in presence of fluoxetine (10 μM) on (A) left and (B) right atria.....	90
Figure 65 The chronotropic and inotropic reponse of serotonin (1 μM) and serotonin (1 μM) in presence of PF003-2 (100 $\mu\text{g/ml}$) on (A) left and (B) right atria.....	91

List of Abbreviations

ACh	=	acetylcholine
ADP	=	Adenosine diphosphate
ATP	=	Adenosine triphosphate
AV	=	Arterioventricular
BMP	=	beat per minute
Ca ²⁺	=	calcium ion
CaCl ₂	=	Calcium chloride
CGRP	=	Calcitonin-gene related peptide
CHD	=	Coronary heart disease
CO ₂	=	Carbondioxide
CNS	=	Central Nervous System
DMSO	=	dimethyl sulfoxide
Hz	=	Hertz
K ⁺	=	Potassium ion
KCl	=	potassium chloride
KH ₂ PO ₄	=	Potassium dibasic phosphate
Kg	=	kilogram
KHS	=	Krebs-Henseleit solution
L	=	litre
M	=	molar
MgSO ₄	=	Magnesium sulfate
Min	=	minute
MW	=	molecular weight
mg	=	milligram
ml	=	milliliter
mM	=	millimolar
ms	=	millisecond
μg	=	microgram

n	=	number of experiments
Na ⁺	=	sodium ion
NaCl	=	Sodium chloride
NaHCO ₃	=	Sodium bicarbonate
NE	=	norepinephrine
PNS	=	Parasympathetic Nervous System
P-value	=	probability value
PF	=	<i>Passiflora foetida</i>
RSC	=	Rested-State Contraction
SA	=	sinoatrial
SEM	=	standard error of mean
SNS	=	Sympathetic Nervous System
SR	=	sarcoplasmic reticulum
SSRI	=	Selective Serotonin Reuptake Inhibitor
T _{ss}	=	the steady state tension
T _i	=	an initial tension
TN	=	Troponin
TN-C	=	Troponin-C
TN-I	=	Troponin-I
β	=	beta
μ	=	micro
°C	=	degree of Celsius
v/v	=	volume by volume
V	=	Volt
%	=	percent
5-HT	=	5-Hydroxytryptamine (serotonin)