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APPENDICES

Table 3. Compound of Physiological solution (mM).

Chemical	Physiological solution		
	Kreb Henseleit	Ca^{2+}-Free Kreb Henseleit	Potassium Depolarizing
NaCl	119	119	27
KCl	4.7	4.7	100
$CaCl_2$	2.5	-	-
$MgSO_4$	1.0	1.0	-
KH_2PO_4	1.2	1.2	14.0
D-glucose	11.1	11.1	10
EDTA	-	0.1	-
$MgCl_2$	-	-	0.54
$NaHCO_3$	-	25	14

Table 4. Concentration-dependent relaxant effects of GSH in denude and intact rat aortic rings. The tissues were precontracted with PE (1 μM) prior to cumulative addition of GSH. L-valine was also used in place of GSH as a control

Cumulative conc. of GSH	Endothelium - intact		Endothelium - denude	
	L - valine	GSH	L - valine	GSH
2 mM	0	38.42±7.48	0	18.53±7.37*
4 mM	0	72.81±6.63	0	41.76±12.94*
6 mM	0	85.34±5.37	0	83.91±13.82
8 mM	0	90.73±3.23	0	138.42±12.49*

Data are mean ± S.E.M. of 6 separated experiments performed in preparations obtained from different animals.

*$P<0.05$ showed significant difference between intact and denude preparation on the pretreatment of GSH.

Table 5. Effects of various inhibitors [ibuprofen (IBU, 10 μM), propranolol (PP, 10 μM), atropine (ATR, 10 μM), L-NAME (10 μM), methylene blue (MB, 10 μM), glibenclamide (GLIBEN, 10 μM)] on the GSH-induced relaxation in intact rat aortic rings. The tissues were preincubated with each inhibitor for 30 min prior to addition of PE (1 μM). When the PE-induced contraction reached to maximum and sustainable stage, GSH (5 mM) was added to induce relaxation.

inhibitors	% relaxation	
	no inhibitor	with inhibitor
ibuprofen	78.41±5.27	90.67±2.91
propranolol	68.29±7.61	74.82±5.13
atropine	73.14±4.83	85.14±4.84
L - NAME	80.46±9.48	32.23±4.23*
MB	75.57±9.76	26.73±4.27*
glibenclamide	78.39±3.91	59.49±4.31*

Data are mean ± S.E.M. of 6 separated experiments performed in preparations obtained from different animals.

*$P<0.05$ showed significant difference from control group (no inhibitor).

Table 6. Concentration-dependent relaxant effects of GSH (3, 5 and 7 mM) obtained in the presence and in the absence of extracellular Ca^{2+} intact rat aorta. GSH-induced relaxation were calculated as the percentage of maximum contraction caused by PE (1 μM) under each condition.

Cumulative conc. of GSH	% relaxation	
	KHS	Ca^{2+}-free KHS with EGTA
3 mM	39.75±3.28	15.0±5.19*
5 mM	51.57±5.42	35.71±4.96*
7 mM	89.25±3.78	59.25±5.43*

Data are mean ± S.E.M. of 6 separated experiments performed in preparations obtained from different animals.

*P<0.05 showed significant difference from control group in normal KHS.

Table 7. Concentration-dependent relaxant effects of GSH (3, 5 and 7 mM) obtained in the presence and in the absence of intracellular Ca^{2+} intact rat aorta. The tissues were precontracted with PE (1 μM).

Cumulative conc. of GSH	% relaxation	
	no BAPTA - AM	BAPTA - AM
3 mM	48.33±4.22	46.33±5.82
5 mM	75.33±4.78	73.16±6.15
7 mM	87.66±3.84	84.16±4.83

Data are mean ± S.E.M. of 6 separated experiments performed in preparations obtained from different animals.

*P<0.05 showed significant difference from control group (not pretreatment with BAPTA-AM).

Table 8. Potentiative effects of GSH on vasorelaxation-induced by Ach. Experiments were performed in endothelium-intact rat aortic rings.

Cumulative conc. of Ach	% relaxation	
	no GSH	GSH
0.01 μM	3.67±2.49	20.17±6.43*
0.1 μM	8.83±2.86	27.83±6.82*
1 μM	27.16±4.51	42.83±6.76*
10 μM	43.84±7.81	56.17±8.48*
100 μM	51.0±9.08	62.07±10.06*

Data are mean ± S.E.M. of 6 separated experiments performed in preparations obtained from different animals.

*P<0.05 showed significant difference from control group (not pretreatment with GSH).

Table 9. Potentiative effects of GSH on vasorelaxation-induced by SNP. Experiments were performed in endothelium-intact rat aortic rings

Cumulative conc. of SNP	% relaxation	
	no GSH	GSH
0.1 μM	25.75±3.68	26.25±6.59
1 μM	47.75±4.51	53.25±7.94
0.01 μM	73.75±5.72	75.75±4.34
0.1 μM	91.5±6.81	91.25±4.69
1 μM	95.25±3.63	96.01±5.72

Data are mean ± S.E.M. of 6 separated experiments performed in preparations obtained from different animals.

*P<0.05 showed significant difference from control group (not pretreatment with GSH).

Table 10. Endothelium-independent vasorelaxant effects of GSH. The tissues were precontracted with PE (1 μM), KCl (60 mM) and BayK8644 (1 μM) followed by cumulative addition of GSH and NAC (5 mM).

Cumulative conc. of GSH	PE		KCl		Bay k 8644	
	L-valine	GSH	L-valine	NAC	L-valine	GSH
2 mM	0	18.62±2.91	0	5.97±2.42	0	11.29±2.37
4 mM	0	41.61±4.86*	0	13.03±12.34	0	46.83±5.82*
6 mM	0	84.37±7.42*	0	21.33±13.58	0	78.65±6.42*
8 mM	0	13.84±10.72*	0	98.08±12.42*	0	94.32±4.31*

Data are mean ± S.E.M. of 6-8 separated experiments performed in preparations obtained from different animals.

*$P<0.05$ showed significant difference from control group (the relaxation of L-valine).

Table 11. Endothelium-independent vasorelaxant effect of NAC. The tissues were precontracted with PE (1 μM) and KCl (60 mM) followed by cumulative addition of GSH and NAC (5 mM).

Cumulative conc. of GSH	PE		KCl	
	L-valine	NAC	L-valine	NAC
2 mM	0	7.58±1.35	0	8.22±1.37
4 mM	0	25.35±6.31	0	13.68±4.38
6 mM	0	83.98±12.42*	0	43.97±9.3*
8 mM	0	147.0±13.0*	0	92.87±9.82*

Data are mean ± S.E.M. of 6-8 separated experiments performed in preparations obtained from different animals.

*$P<0.05$ showed significant difference from control group (the relaxation of L-valine).

Table 12. Effects of various inhibitors [ibuprofen (IBU, 10 μM), propranolol (PP, 10 μM), atropine (ATR, 10 μM), L-NAME (10 μM), methylene blue (MB, 10 μM), glibenclamide (GLIBEN, 10 μM)] on the GSH-induced relaxation in denude rat aortic rings. The tissues were preincubated with each inhibitor for 30 min prior to addition of PE (1 μM). When the PE-induced contraction reached to maximum and sustainable stage, GSH (5 mM) was added to induce relaxation.

inhibitor	% relaxation	
	no inhibitor	with inhibitor
ibuprofen	20.15±3.12	25.83±5.21
propranolol	23.84±3.47	24.21±3.86
atropine	19.63±2.23	25.47±2.93
L - NAME	22.48±4.08	21.54±3.24
MB	24.33±4.61	22.18±4.88
glibenclamide	27.92±4.23	16.42±2.36*

Data are mean ± S.E.M. of 6 separated experiments performed in preparations obtained from different animals.

*$P<0.05$ showed significant difference from control group (no inhibitor).

Table 13. The effects of GSH (5 mM) on the contraction-induced by PE (0.001–10 μM) in intact and denude rat aortic ring.

Cumulative conc.	Endothelium - intact		Endothelium - denude	
of PE	no	GSH	no	GSH
0.001 μM	40.23±4.34	31.82±8.41	14.03±3.13	2.13±2.49#
0.01 μM	61.87±4.82	46.14±6.42*	28.4±4.24	7.28±3.83#
0.1 μM	85.91±2.81	65.13±4.39*	62.35±2.34	30.15±2.67#
1 μM	97.82±1.95	82.41±2.86*	89.12±1.92	63.46±4.39#
10 μM	100	90.76±1.94*	100	76.92±3.42#

Data are mean ± S.E.M. of 6 separated experiments performed in preparations obtained from different animals.

*P<0.05 showed significant difference from control group of denude preparation (D).

# P<0.05 showed significant difference from control group of intact preparation (I).

Table 14. The effects of NAC (5 mM) on the contraction-induced by PE (0.001–10 μM) in intact and denude rat aortic ring.

Cumulative conc. of PE	Endothelium - intact		Endothelium - denude	
	no	NAC pretreatment	no	NAC pretreatment
0.001 μM	48.63±4.34	10.54±9.72*	14.25±3.38	4.34±2.37
0.01 μM	61.47±4.25	16.67±8.43*	28.18±4.24	9.31±2.21#
0.1 μM	85.71±2.18	46±9.18*	62.92±2.67	42.48±4.93#
1 μM	97.82±1.84	70±8.98*	85.65±1.91	74.57±4.48#
10 μM	100	83±9.58*	100	86.29±3.31#

Data are mean ± S.E.M. of 6 separated experiments performed in preparations obtained from different animals.

*P<0.05 showed significant difference from control group of denude preparation (D).

# P<0.05 showed significant difference from control group of intact preparation (I).

Table 15. The effects of GSH at concentration 5 and 8 mM on the contraction induced by PE (0.001–10 μM) in denude rat aortic ring.

Cumulative conc. of PE	control	GSH 5 mM	GSH 8 mM
0.001 μM	57.31±2.95	31.46±8.16*	37.85±10.29
0.01 μM	71.83±3.34	46.34±6.37*	47.32±9.67
0.1 μM	81.49±3.49	65.73±4.45*	55.27±9.46
1 μM	95.82±1.78	82.91±2.39*	71.81±6.89#
10 μM	100	90.39±1.78*	76.87±6.26#

Data are mean ± S.E.M. of 6 separated experiments performed in preparations obtained from different animals.

*P<0.05 showed significant difference from control group.

# P<0.05 showed significant difference from the effect of GSH (5 mM)

Table 16. The effects of NAC at concentration 5 and 8 mM on the contraction induced by PE (0.001–10 μM) in denude rat aortic ring.

Cumulative conc. of PE	control	NAC 5 mM	NAC 8 mM
0.001 μM	48.76±6.15	10.88±10.18*	23.46±1.13
0.01 μM	61.88±5.24	16.76±8.85*	30.76±3.04
0.1 μM	85.91±1.57	46.49±9.69*	31.05±6.83
1 μM	97.39±1.97	70.86±8.81*	49.15±3.28#
10 μM	100	83.47±9.78*	67.82±2.34#

Data are mean ± S.E.M. of 6 separated experiments performed in preparations obtained from different animals.

*P<0.05 showed significant difference from control group.

# P<0.05 showed significant difference from the effect of GSH (5 mM)

Table 17. Comparative inhibitory effects of various sulfhydryl containing compounds on the contraction of endothelium denude rat aorta. The equiconcentration of GSH, NAC, homocysteine and captopril (at 5 mM) were incubated with the aortic tissues 5 minutes prior to addition of PE to provoke the contraction.

Test compounds	The contraction of PE single dose at conc. (μM)			
	0.01	0.1	1	10
control	101.32±2.64	98.94±4.52	104.15±9.31	105.31±2.97
L - valine	88.34±9.41	86.72±4.79	104.33±9.15	107.14±11.12
GSH	8.58±5.47*	75.98±9.17*	75.54±2.61	112.41±4.36
NAC	14.38±8.71*	73.34±9.16*	104.81±10.03	114.74±11.07
homocysteine	29.41±5.42*	65.66±8.14*	94.51±1.89	108.23±5.72
captropril	65.29±10.45*	87.81±4.39*	96.47±1.86	116.87±6.96

Data are mean ± S.E.M. of 6 separated experiments performed in preparations obtained from different animals.

*$P<0.05$ showed significant difference from control group.

Table 18. Effects of GSH or NAC on the aortic contraction induced by serotonin (5-HT) (1 μM), histamine (His) (1 μM), phenylephrine (PE) (1 μM) KCl (60 mM) tetraethylammonium (TEA) (1 mM) and phorbal ester (PMA) (1 μM), Endothelium-denude aortic rings were treated with GSH (5 mM) 5 min prior to addition of contractants.

contractants	control	GSH (5 mM)	NAC (5 mM)
5 -HT (1 μM)	100	64.24±5.31*	69.43±7.13*
histamine (1 μM)	100	47.23±13.26*	39.72±11.21*
PE (1 μM)	100	95.71±2.71	102.45±9.41
TEA (1 mM)	100	94.38±11.52	98.14±3.92
KCl (60 mM)	100	96.51±6.95	106.6±5.34
PMA (1 μM)	100	103.14±8.18	-

Data are mean ± S.E.M. of 6 separated experiments performed preparations obtained from different animals.

*P<0.05 showed significant difference from control group.

Table 19. Comparative effects of certain sulfhydryl containing compounds and L-valine on the endothelium-independent contraction induced by PE or caffeine in Ca^{2+}-free medium.

Test compounds	The contraction in Ca^{2+}-free medium induce by	
	PE	Caffeine
control	94.31±10.03	-
L - valine	93.87±9.51	92.89±10.13
GSH	34.43±4.47*	101.42±9.42
NAC	55.14±4.91*	88.92±12.03
homocysteine	68.5±6.39*	-
captropril	43.66±8.07*	-

Data are mean ± S.E.M. of 6 separated experiments performed in preparations obtained from different animals. *$P<0.05$ showed significant difference from L-valine group.

Table 20. The inhibitory effect of L-valine, GSH and NAC against contraction induced by $CaCl_2$. The endothelium-denude aortic ring were suspended in high K^+, Ca^{2+}-free condition, followed by cumulative addition of $CaCl_2$ cumulatively. Either L-valine, GSH or NAC (5 mM) were added 5 min prior to $CaCl_2$ treatment.

Cumulative conc. of $CaCl_2$	L – valine	NAC	Conc. of GSH		
			2 mM	5 mM	8 mM
0.003 mM	4.67±2.83	2.33±2.39	2.84±1.43	1.83±1.41	0 ±2.84
0.015 mM	15.6±8.76	4.67±2.53	5.36±1.78	6.5±2.79	0 ±3.02
0.03 mM	27.2±8.42	9.5±3.46*	19.93±1.52	10.33±5.76*	1.32±4.38*
0.15 mM	47.54±6.84	18.5±4.38*	37.83±3.47	19.00±7.46*	5.43±25.61*
0.3 mM	64.4±4.82	27.67±4.67*	49.32±6.71	26.67±8.73*	13.41±5.53*
0.5 mM	77.8±3.18	39.5±6.42*	68.29±6.93	30.17±9.43*	19.86±6.78*
3 mM	88.0±3.63	48.17±9.68*	78.81±4.82	46.17±10.02*	25.49±8.19*
15 mM	100	51.0±10.37*	95.76±5.42	44.17±9.18*	30.27±7.28*

Data are mean ± S.E.M. of 6 separated experiments performed in preparations obtained from different animals.

*$P<0.05$ showed significant difference from L-valine group.

Table 21. Inhibitory effects of GSH and homocysteine (5 mM) contraction induced by addition of $CaCl_2$ (1 mM) in the presence of various contractants in Ca^{2+}-free KHS. Various contractants include PE (1 μM), 5-HT (1 μM), KCl (30 mM) and Bay K8644 (10 μM).

Contractant	control	GSH	homocysteine
PE	100.50±2.31	84.21±6.79*	86.81±3.58*
5 - HT	105.82±6.84	74.29±6.47*	83.73±4.37*
KCl	101.23±6.35	78.31±8.43*	95.27±2.98*
Bay K8644	103.15±4.32	60.15±7.39*	87.34±3.77*

Data are mean ± S.E.M. of 6-8 separated experiments performed in preparations obtained from different animals.

*P<0.05 showed significant difference from control group.

Table 22. Effects of GSH on spontaneous contraction of Ca^{2+}-depleted aortic ring upon addition of Ca^{2+} into medium.

Contractant	L - valine	GSH
PE	101.83±6.84	68.5±7.97*

Data are mean ± S.E.M. of 6 separated experiments performed in preparations obtained from different animals.

*P<0.05 showed significant difference from control group (L-valine).

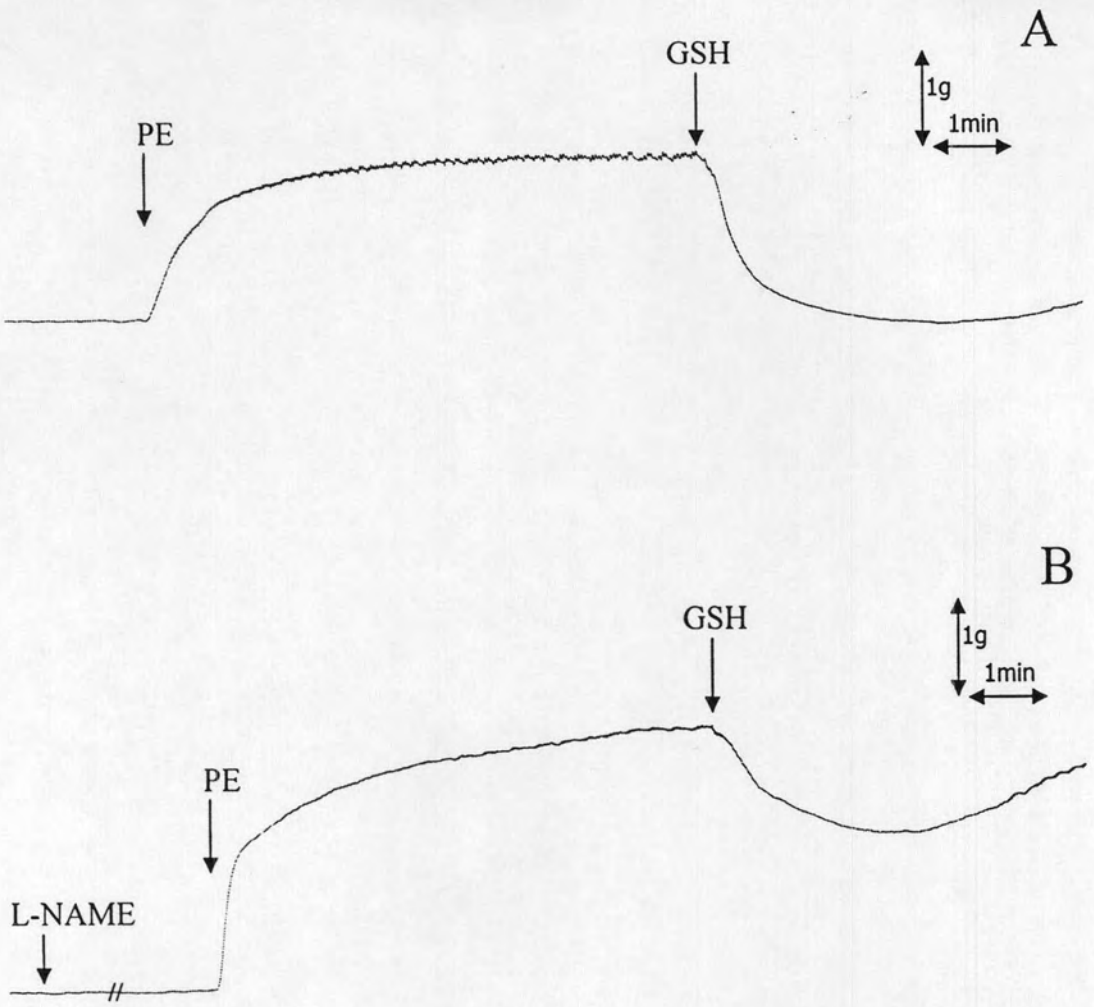

Fig. 34 The representative tracing of the relaxation induced by GSH (5 mM) on endothelium-intact rat aortic rings which were preincubated in the absence (A) or presence (B) of L-NAME (10 μM) for 30 minutes prior to addition of PE (1 μM) and GSH (5 mM).

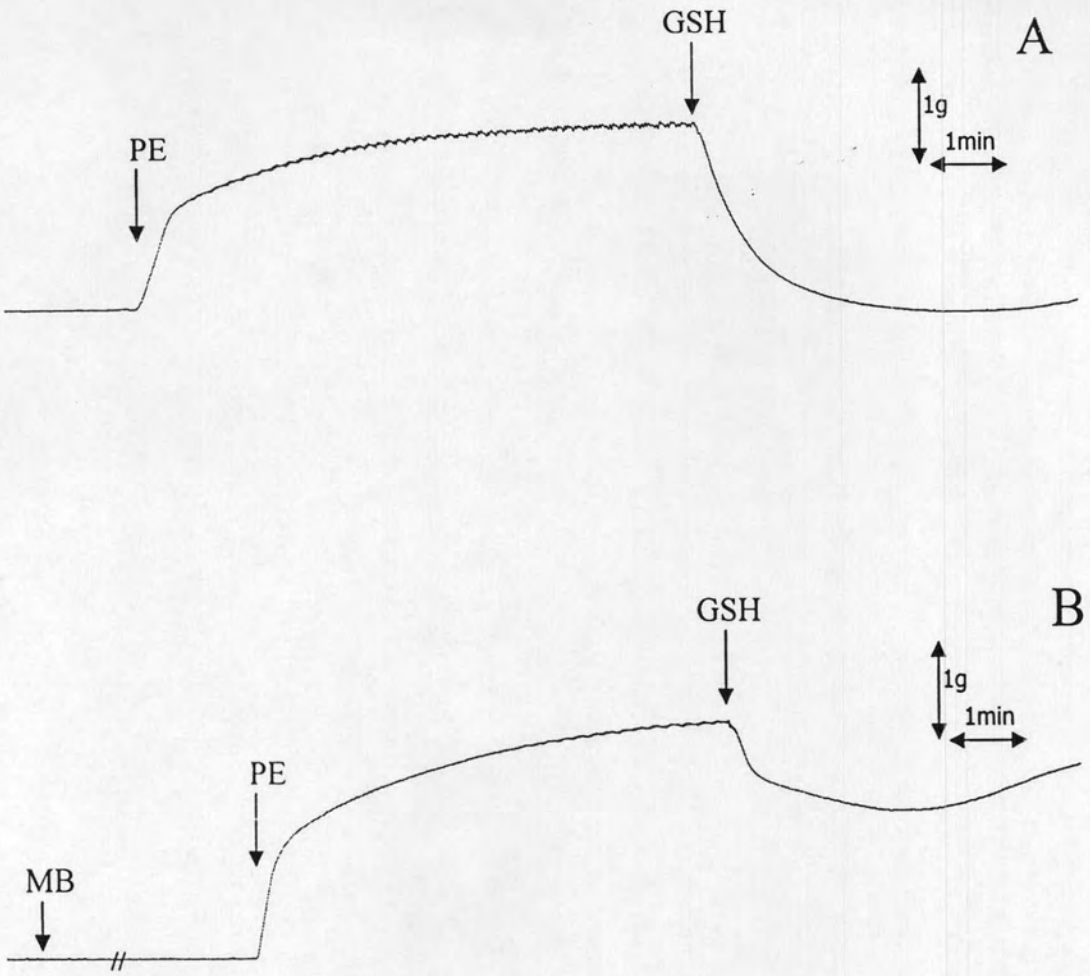

Fig. 35 The representative tracing of the relaxation induced by GSH (5 mM) on endothelium-intact rat aortic rings which were preincubated in the absence (A) or presence (B) of methylene blue (10 μM) for 30 minutes prior to addition of PE (1 μM) and GSH (5 mM).

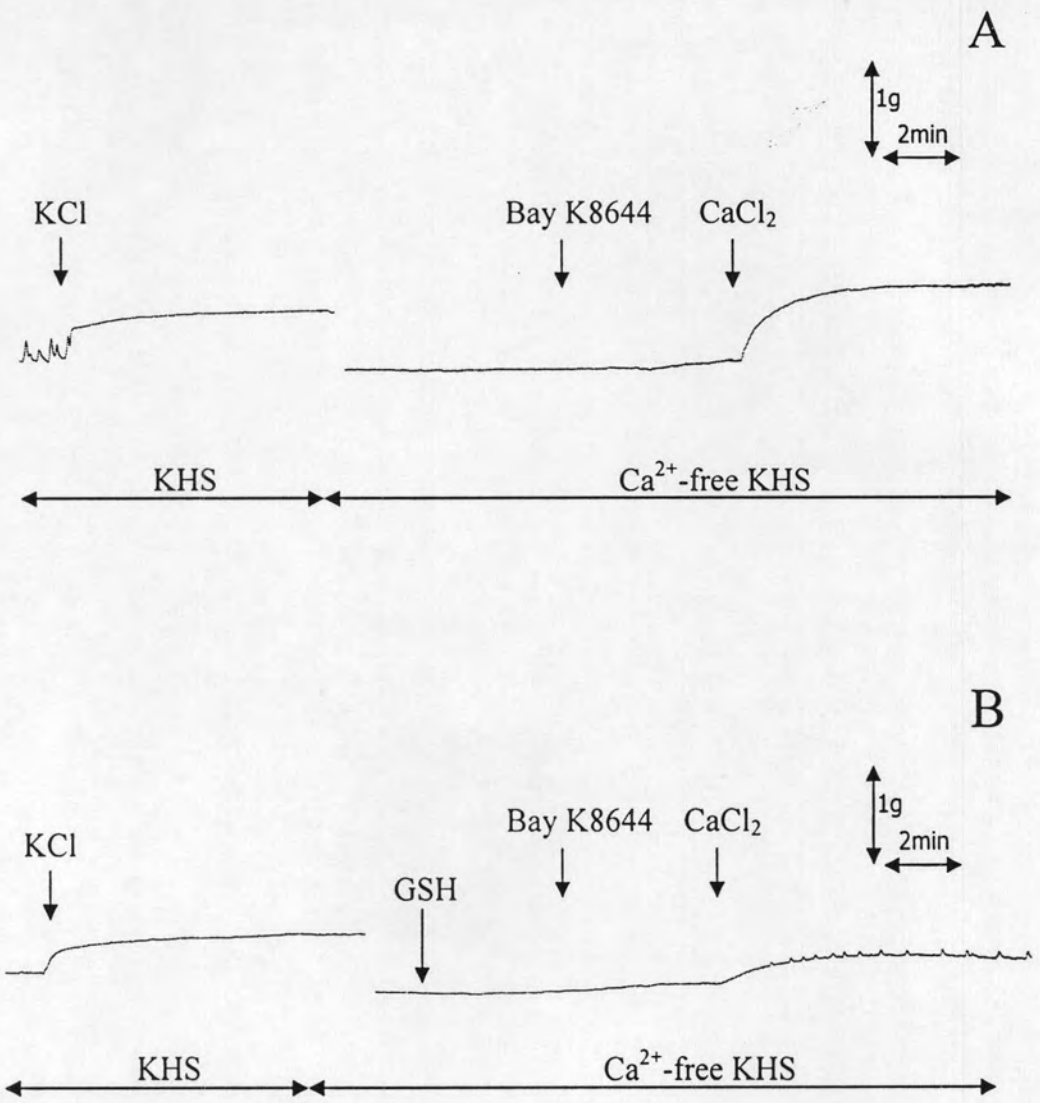

Fig. 36 The representative tracing showing the agonist induced contraction followed by addition of $CaCl_2$ in Ca^{2+}-free condition. The contraction in Ca^{2+}-free condition were observed after adding $CaCl_2$ (1 mM) in to medium. GSH (5 mM) were absence (A) and presence (B) with aortic tissues for 5 min before addition of Bay K8644.

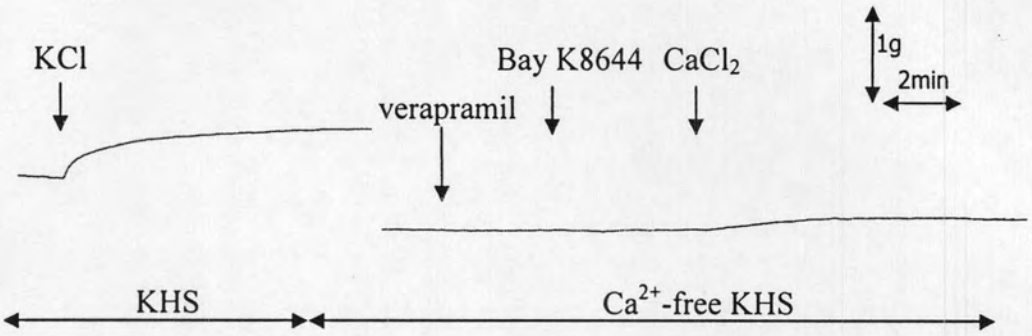

Fig.37 The representative tracing showing the agonist induced contraction followed by addition of $CaCl_2$ in Ca^{2+} free condition. The contraction in Ca^{2+}-free condition were observed after adding $CaCl_2$ (1 mM) in to medium. Verapramil (10 μM) was preincubated with aortic tissues for 5 min before addition of 5-HT or KCl.

VITAE

Miss Nattaya Chaothanaphat was born in July 15, 1975, Chonburi, Thailand. She graduated with a Bachelor of Science in Pharmacy in 1998 form Faculty of Pharmaceutical Sciences, Huachiew Chalermprakiet University, Thailand. She also graduated with a degree of Master of Science in Pharmacy in 2000 form Faculty of Pharmaceutical Science of Chulalongkorn University, Thailand. After graduation, she worked in Huachiew Chalermprakiet University, Thailand, for three year. In 2003, she started for the degree of Docter of Science in Philosophy Program in Biopharmaceutical Science form Faculty of Pharmaceutical Science of Chulalongkorn University, Thailand.