

CHAPTER IV

Results

I. General observation of STZ-rats, Nicardipine treated STZ-rats and Nicardipine combined with Cilazapril treated STZ-rats.

The streptozotocin treated rat was used as an experimental model of diabetes mellitus in this study. The objective of this part of the work was to investigate the effects of nicardipine on the diabetic model and the effects of nicardipine combined with cilazapril on the diabetic model with respect to plasma glucose. The results showed in Table 4.1 indicated that all three groups (8, 16, 20 weeks) of six STZ-rats, six STZ-N rats and six STZ-NC rats were severe hyperglycemia. There was no significantly difference of plasma glucose among these three groups. The body weights of STZ-rats, STZ-N rats and STZ-NC rats were significantly decreased as compared to those of the age-match controls. However, the ratio of heart weight per 100 grams body weight in 16 and 20 weeks of STZ-rat groups, STZ-N rat groups and STZ-NC rat groups were significantly higher than those of control groups.

II. Studies of cardiovascular functions in STZ-rats, nicardipine-treated STZ-rats and nicardipine combined with cilazapril-treated STZ-rats.

Cardiovascular functions including heart rate (HR), mean arterial pressure (MAP), aortic flow rate (AFR), coronary flow rate (CFR), left ventricular isotonic contraction (LVIC) and arterial wall thickness were determined for all three different age groups (8, 16, 20 weeks) of six controls, six STZ - N rats and six STZ - NC rats as summarized in Tables 4.3-4.10. Means and standard deviations of all these assessed cardiovascular parameters were also demonstrated graphically as showed in Figures 4.1 - 4.14.

Heart rate of treated and control rats were summarized in the Table 4.4. In eight weeks after treatment, the heart rate of the treated rats were slower than those of control rats. However, the STZ - N rats showed their heart rates were much lower than the others. In the same manner, the sixteen weeks treatments showed that all STZ-treatments have their heart rates lower than those of the controls. However at twenty week experimental period, there were no difference between the STZ-rats and the controls.

In Table 4.5, the mean arterial pressure showed that at eight weeks of experimental period, mean arterial pressure of STZ-rats, STZ-N rats and STZ-NC rats were significantly less than those of the controls. Moreover, mean arterial pressure of nicardipine treated rats lower than those of the STZ-rats at the same experimental periods. In sixteen weeks

of experiments mean arterial pressure of STZ-N rats and STZ-NC rats were significantly lower than those of the control and the STZ-rats. In addition, the mean arterial pressure of STZ-NC rats group were the lowest in the same age groups. Furthermore, at twenty weeks it was found that mean arterial pressure of STZ-NC rats group were significantly less than those of the others. The systolic blood pressure and diastolic blood pressure were showed in Tables 4.6 - 4.7. The results indicated that both systolic blood pressure and diastolic blood pressure were concomitant with the results of mean arterial pressure.

Aortic flow rate of all three different age groups (8, 16, 20 weeks) of six control rats, STZ-rats, nicardipine treated STZ-rats and nicardipine combined cilazapril treated STZ-rats were not different except that the group of 16-week STZ-rats that had a decrease of aortic flow rate as compared to another groups.

Table 4.9 showed the coronary flow rate of treated and control rats. At eight weeks, coronary flow rate of STZ-rats, nicardipine treated STZ-rats and nicardipine combined with cilazapril treated STZ-rats group were not different as compared to the control rats with the same age. In 16 weeks experiment, coronary flow rate of STZ-rats and nicardipine treated STZ-rats were not different as compared to control group, with the exception of STZ-rats. STZ-treated rats which seem to have their flow rates less than those of the other groups of treatments. However, the flow rate of STZ-NC rats was significantly higher than STZ-rats.

Moreover, at twenty weeks results showed coronary flow of STZ-rat group was significant less than those of controls. Interestingly, STZ-N rats and of STZ-NC rats. The coronary flow rates of were significantly higher than STZ - rats.

Left ventricular isotonic contraction (LVIC, gm/100 gm of heart weight) were showed in Table 4.10. At eight weeks, the results of LVIC showed that there was no significant different among the three groups of STZ - rats, nicardipine treated STZ - rats and nicardipine combined cilazapril treated STZ - rats and also with those of controls. However, the results of sixteen and twenty week experimental period, showed the decrease of LVIC in STZ - rat groups as compared to those of the controls. Interestingly, at 16 and 20 weeks, there were no significant different of LVIC between the groups of nicardipine treated STZ - rat and nicardipine combined with cilazapril treated STZ - rat as compared to those of the control groups.

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III Studies of morphological examinations of hearts of STZ-rats, nicardipine treated STZ-rats and nicardipine combined treated STZ-rats

The results of morphological studies were showed in Figures 4.15-4.26. The thickness of cross - section of heart specimens were obtained from three controls, three STZ - rats, three STZ-N rats and three STZ - NC rats from each aged groups (8, 16, 20 weeks). In addition, the thickness of left ventricular wall, right ventricular wall and interventricular septal wall were measured randomly by the micrometer of light microscope 400 x - objective. Means and standard deviation of these wall thickness values were calculated and summarized in Table 4.11 - 4.13.

For the morphological studies of arterial wall thickness were showed in Figures 4.27-4.34 and Table 4.14. The thickness of cross - section of arterial wall were obtained from controls, STZ-rats, STZ- N rats and STZ- NC rats from each aged groups.

The results of these morphological examinations showed in Tables 4.11-4.14 demonstrated that :

1. At the eight and twenty weeks of experimental period, the results indicated that left ventricular wall of STZ - rats were thicker than those of controls as well as STZ - N rats and STZ - NC rats. However, the results were not consistent for those groups at sixteen weeks. Since the left ventricular wall of STZ-rats and STZ- N rats were thicker than control and STZ- NC rats as showed in Figures 4.15-4.26 and Tables 4.11-4.13.

2. At eight and twenty weeks of experimental period, the right ventricular wall thickness of STZ - rats and STZ - treated rats were not significantly different from the control groups($p < 0.05$). However, the results from sixteen weeks studies showed that the right ventricular wall of STZ - rats and STZ - N rats were thicker than controls and STZ-NC rats as graphically demonstrated in Figures 4.15-4.26 and Tables 4.11-4.13.

3. The results of interventricular septum wall thickness indicated that at eight weeks there was no significantly different between the treated and control rats. At sixteen weeks, the interventricular septum wall thickness of STZ - rats was thicker than the other groups. But at twenty weeks the interventricular septum

wall thickness of STZ - rats and STZ - N rats were thicker than those of controls and STZ- NC rats.

4. At sixteen weeks, the arterial wall thickness of STZ-rats were significantly thicker than those of controls, STZ- N rats and STZ- NC rats. Whereas at twenty weeks, the arterial wall thickness of STZ-rats were no significantly difference from those of controls, STZ- N rats and STZ- NC rats. ($p < 0.05$).



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Table 4.1 Plasma glucose (mg/dl) of 8-20 weeks of controls, STZ-rats, nicardipine treated STZ-rats, nicardipine combined with cilazapril treated STZ-rats

Groups	Plasma glucose (mg/dl)		
	8 weeks	16 weeks	20 weeks
Controls (n = 6)	104.67±19.46	99±15.11	99.5±13.37
STZ-rats (n = 6)	499.33±23.52*	490.33±47.54*	457±27.36*
Nicardipine treated STZ-rats (n = 6)	514 ± 100.26 ^{NS} *	477±35.65 ^{NS} *	480.83±39.21 ^{NS} *
Nicardipine combined with cilazapril treated STZ-rats (n = 6)	526.33±97.17 ^{NS} *	487±63.69 ^{NS} *	441.33±40.411 ^{NS} *

NS = non significant difference as compared to STZ-rat ($p < 0.05$).

* Statistical difference as compared to control ($p < 0.01$).

Table 4.2 Body weight (BW, gm) of 8 - 20 weeks of controls, STZ - rats, nicardipine treated STZ - rats, nicardipine combined with cilazapril treated STZ - rats.

Groups	Body weight (BW, gm)		
	8 weeks	16 weeks	20 weeks
Controls (n = 6)	347.00 ± 40.02	456.00 ± 39.81	409.16 ± 19.92
STZ-rats (n = 6)	229.83 ± 30.20*	266.45 ± 33.91*	325.63 ± 51.58*
Nicardipine treated STZ-rats (n = 6)	250.00 ± 28.04 ^{NS} *	255.76 ± 21.75 ^{NS} *	316.33 ± 22.64 ^{NS} *
Nicardipine combined with cilazapril treated STZ-rats (n = 6)	270.00 ± 35.38 ^{NS} *	235.50 ± 23.15 ^{NS} *	325.00 ± 18.23 ^{NS} *

NS = non significant difference as compared to STZ-rat (p<0.05).

* Statistical difference as compared to control (p<0.01).

Table 4.3 Ratio of heart weight per 100 grams body weight
8-20 weeks of controls, STZ-rats, nicardipine treated
STZ-rats, nicardipine combined with cilazapril treated STZ-rats.

Groups	Ratio of heart weight per 100 grams body weight		
	8 weeks	16 weeks	20 weeks
Controls (n = 6)	0.32 ± 0.03	0.26 ± 0.01	0.27 ± 0.01
STZ-rats (n = 6)	0.40 ± 0.12	0.45 ± 0.08 [#]	0.50 ± 0.04 [#]
Nicardipine treated STZ-rats (n = 6)	0.36 ± 0.02 ^{NS}	0.36 ± 0.03 ^{##} [#]	0.36 ± 0.02 ^{NS} [#]
Nicardipine combined with cilazapril treated STZ-rats (n = 6)	0.38 ± 0.03 ^{NS}	0.38 ± 0.05 ^{##} [#]	0.35 ± 0.01 ^{NS} [#]

Statistical difference as compared to control (p<0.05).

Statistical difference as compared to STZ-rat (p<0.05).

NS = non significant difference as compared to STZ-rat (p<0.05).

Table 4.4 Heart rate (beats/min) of 8-20 weeks of controls, STZ-rats, nicardipine treated STZ-rats, and nicardipine combined with cilazapril treated STZ-rats.

Groups	Heart rate (beats/min)		
	8 weeks	16 weeks	20 weeks
Controls (n = 6)	362.50 ± 36.02	375.00 ± 26.83	333.33 ± 39.70
STZ-rats (n = 6)	320.00 ± 39.87 [#]	295.00 ± 48.06 [#]	320.83 ± 19.08
Nicardipine treated STZ-rats (n = 6)	270.66 ± 17.22 ^{##}	295.00 ± 18.16 [#]	332.50 ± 40.71 ^{NS}
Nicardipine combined with cilazapril treated STZ-rats (n = 6)	325.00 ± 39.87 [#]	262.50 ± 32.51 [#]	334.66 ± 56.75 ^{NS}

Statistical difference as compared to control (p<0.05).

Statistical difference as compared to STZ-rat (p<0.05).

NS = non significant difference as compared to STZ-rat (p<0.05).

Table 4.5 Mean arterial pressure (mmHg) from common carotid artery of 8-20 weeks of controls, STZ-rats, nicardipine treated STZ-rats, and nicardipine combined with cilazapril treated STZ-rats.

Groups	Mean arterial pressure (mmHg)		
	8 weeks	16 weeks	20 weeks
Controls (n = 6)	101.38 ± 6.18	92.49 ± 17.56	96.04 ± 19.49
STZ-rats (n = 6)	86.38 ± 31.68	108.05 ± 3.85	113.05 ± 17.84
Nicardipine treated STZ-rats (n = 6)	54.71 ± 20.66 [#] ^{##}	82.72 ± 21.50 ^{##}	102.49 ± 19.11 ^{NS}
Nicardipine combined with cilazapril treated STZ-rats (n = 6)	61.0 ± 21.47 ^{NS} [#]	44.99 ± 12.15 ^{##} [#]	76.94 ± 19.36 ^{##} [#]

Statistical difference as compared to control (p<0.05).

Statistical difference as compared to STZ-rat (p<0.05).

NS = non significant difference as compared to STZ-rat (p<0.05).

Table 4.6 Systolic blood pressure (mmHg) from common carotid artery of 8-20 weeks of controls, STZ-rats, nicardipine treated STZ-rats, and nicardipine combined with cilazapril treated STZ-rats.

Groups	Systolic blood pressure (mmHg)		
	8 weeks	16 weeks	20 weeks
Controls (n = 6)	115.83 ± 6.64	107.50 ± 16.04	112.50 ± 22.74
STZ-rats (n = 6)	105.83 ± 31.84	129.16 ± 9.70 [#]	134.16 ± 19.08
Nicardipine treated STZ-rats (n = 6)	80.00 ± 19.74 [#]	97.50 ± 26.22 ^{##}	122.50 ± 28.06 ^{NS}
Nicardipine combined with cilazapril treated STZ-rats (n = 6)	75.8 ± 25.18 ^{##}	65.00 ± 12.24 ^{+##}	94.16 ± 20.83 ^{##}

Statistical difference as compared to control (p<0.05).

Statistical difference as compared to STZ-rat (p<0.05).

NS = non significant difference as compared to STZ-rat (p<0.05).

+ Statistical difference as compare to nicardipine treated STZ-rat (p<0.05)

Table 4.7 Diastolic blood pressure (mmHg) from common carotid artery of 8-20 weeks of controls, STZ-rats, nicardipine treated STZ-rats, and nicardipine combined with cilazapril treated STZ-rats.

Groups	Diastolic blood pressure (mmHg)		
	8 weeks	16 weeks	20 weeks
Controls (n = 6)	94.16 ± 6.64	85.00 ± 18.97	88.33 ± 16.93
STZ-rats (n = 6)	76.66 ± 31.72	103.33 ± 9.30	110.83 ± 19.60
Nicardipine treated STZ-rats (n = 6)	47.50 ± 18.37 ^{##}	68.33 ± 25.23 ^{##}	90.83 ± 26.34 ^{NS}
Nicardipine combined with cilazapril treated STZ-rats (n = 6)	49.16 ± 23.11 ^{##}	34.16 ± 13.19 ^{+,##}	71.66 ± 22.94 ^{##}

Statistical difference as compared to control (p<0.05).

Statistical difference as compared to STZ-rat (p<0.05).

NS = non significant difference as compared to STZ-rat (p<0.05).

+ Statistical difference as compare to nicardipine treated STZ-rat (p<0.05)

Table 4.8 Aortic flow rate (ml/min) of 8-20 weeks of controls, STZ-rats, nicardipine treated STZ-rats, nicardipine combined with cilazapril treated STZ-rats.

Groups	Aortic flow rate (ml/min)		
	8 weeks	16 weeks	20 weeks
Controls (n = 6)	64.5 ± 0.26	68.1 ± 0.39	64.0 ± 1.04
STZ-rats (n = 6)	62.3 ± 0.38	56.8 ± 1.26 [#]	55.5 ± 1.10
Nicardipine treated STZ-rats (n = 6)	64.0 ± 0.31 ^{NS}	64.8 ± 0.42 ^{NS}	60.1 ± 0.54 ^{NS}
Nicardipine combined with cilazapril treated STZ-rats (n = 6)	65.8 ± 0.20 ^{NS}	65.3 ± 0.24 ^{NS}	64.1 ± 0.18 ^{NS}

Statistical difference as compared to control (p<0.05).

Statistical difference as compared to STZ-rat (p<0.05).

NS = non significant difference as compared to STZ-rat (p<0.05).

Table 4.9 Coronary flow rate (ml/min) of 8-20 weeks of controls, STZ-rats, nicardipine treated STZ-rats, and nicardipine combined with cilazapril treated STZ-rats.

Groups	Coronary flow rate (ml/min)		
	8 weeks	16 weeks	20 weeks
Controls (n = 6)	5.70 ± 1.56	4.83 ± 1.29	6.53 ± 1.39
STZ-rats (n = 6)	4.45 ± 1.04	3.41 ± 1.22	3.31 ± 0.81*
Nicardipine treated STZ-rats (n = 6)	5.76 ± 0.75 ^{NS}	4.46 ± 0.76 ^{NS}	6.50 ± 1.22**
Nicardipine combined with cilazapril treated STZ-rats (n = 6)	5.53 ± 0.81 ^{NS}	5.78 ± 1.37**	5.25 ± 1.17**

NS = non significant difference as compared to STZ-rats (p<0.05).

* Statistical difference as compared to control (p<0.01).

** Statistical difference as compared to STZ-rat (p<0.01).

Table 4.10 Left ventricular isotonic contraction (LVIC, gm/100 gm of heart weight) of 8-20 weeks of controls, STZ-rats, nicardipine treated STZ-rats, and nicardipine combined with cilazapril treated STZ-rats.

Groups	Left ventricular isotonic contraction (LVIC, gm/100 gm of heart weight)		
	8 weeks	16 weeks	20 weeks
Controls (n = 6)	401.08 ± 157.63	461.92 ± 80.01	433.75 ± 74.21
STZ-rats (n = 6)	436.94 ± 147.81	182.51 ± 71.32*	162.38 ± 124.73*
Nicardipine treated STZ-rats (n = 6)	448.11 ± 131.59 ^{NS}	447.34 ± 122.58**	408.81 ± 82.27**
Nicardipine combined with cilazapril treated STZ-rats (n = 6)	434.51 ± 98.34 ^{NS}	450.79 ± 118.52**	443.02 ± 109.09**

NS = non significant difference as compared to STZ-rat (p<0.05).

* Statistical difference as compared to control (p<0.01).

** Statistical difference as compared to STZ-rat (p<0.01).

Table 4.11 Sizes of left and right ventricular wall and interventricular septum wall (um) of 8 weeks of controls, STZ-rat, nicardipine treated STZ-rats, and nicardipine combined with cilazapril treated STZ-rats.

	Sizes of left and right ventricular wall and interventricular septum wall (um) of 8 week rats		
	Left ventricular wall (LV)	Right ventricular wall (RV)	Interventricular septum wall (IVS)
Controls (n = 3)	2166.66 ± 175.09	958.33 ± 144.42	1673.33 ± 155.34
STZ-rats (n = 3)	2510.00 ± 131.14 [#]	1056.66 ± 81.29	1893.33 ± 363.53
Nicardipine treated STZ-rats (n = 3)	2175.00 ± 171.97 ^{##}	976.66 ± 129.06 ^{NS}	1858.33 ± 285.36 ^{NS}
Nicardipine combined with cilazapril treated STZ-rats (n = 3)	2186.66 ± 132.50 ^{##}	835.00 ± 98.48 ^{NS}	1411.66 ± 171.48 ^{NS}

Statistical difference as compared to control (p<0.05).

Statistical difference as compared to STZ-rat (p<0.05).

NS = non significant difference as compared to STZ-rat (p<0.05).

Table 4.12 Sizes of left and right ventricular wall and interventricular septum wall (um) of 16 weeks of controls, STZ-rats, nicardipine treated STZ-rats, and nicardipine combined with cilazapril treated STZ-rats.

	Sizes of left and right ventricular wall and interventricular septum wall (um) of 16 weeks		
	Left ventricular wall (LV)	Right ventricular wall (RV)	Interventricular septum wall(IVS)
Controls (n = 3)	2211.00 ± 243.13	860.00 ± 35.00	1559.00 ± 27.55
STZ-rats (n = 3)	2648.33 ± 141.09 [#]	991.66 ± 25.65 [*]	2053.33 ± 140.02 [#]
Nicardipine treated STZ-rats (n = 3)	2273.3333 ± 253.2456 ^{NS}	953.3333 ± 22.5462 [#]	1875.0000 ± 130.2881 ^{NS}
Nicardipine combined with cilazapril treated STZ-rats (n = 3)	2218.33 ± 165.40 ^{###}	875.00 ± 62.45 ^{+ **}	1818.33 ± 105.63 ^{NS}

Statistical difference as compared to control (p<0.05).

Statistical difference as compared to STZ-rat (p<0.05)

NS = non significant difference as compared to STZ-rat (p<0.05).

+ Statistical difference as compared to nicardipine treated STZ-rat (p<0.05).

* Statistical difference as compared to control (p<0.01).

** Statistical difference as compared to STZ-rat (p<0.01).

Table 4.13 Sizes of left and right ventricular wall and interventricular septum wall (um) of 20 weeks of controls, STZ-rats, nicardipine treated STZ-rats, and nicardipine combined with cilazapril treated STZ-rats.

	Sizes of left and right ventricular wall and interventricular septum wall (um) of 20 week rats		
	Left ventricular wall (LV)	Right ventricular wall (RV)	Interventricular septum wall (IVS)
Controls (n = 3)	2355.00 ± 140.00	970.00 ± 133.32	1960.00 ± 221.97
STZ-rats (n = 3)	3130.00 ± 330.45*	1075.00 ± 25.00	2371.66 ± 201.01#
Nicardipine treated STZ-rats (n = 3)	2620.33 ± 67.41##	910.00 ± 104.76 ^{NS}	2213.33 ± 50.58 ^{NS}
Nicardipine combined with cilazapril treated STZ-rats (n = 3)	2488.33 ± 92.91**	991.66 ± 187.63 ^{NS}	1893.33 ± 129.06##

Statistical difference as compared to control (p<0.05).

Statistical difference as compared to STZ-rat (p<0.05)

NS = non significant difference as compared to STZ-rat (p<0.05).

* Statistical difference as compared to control (p<0.01).

** Statistical difference as compared to STZ-rat (p<0.01).

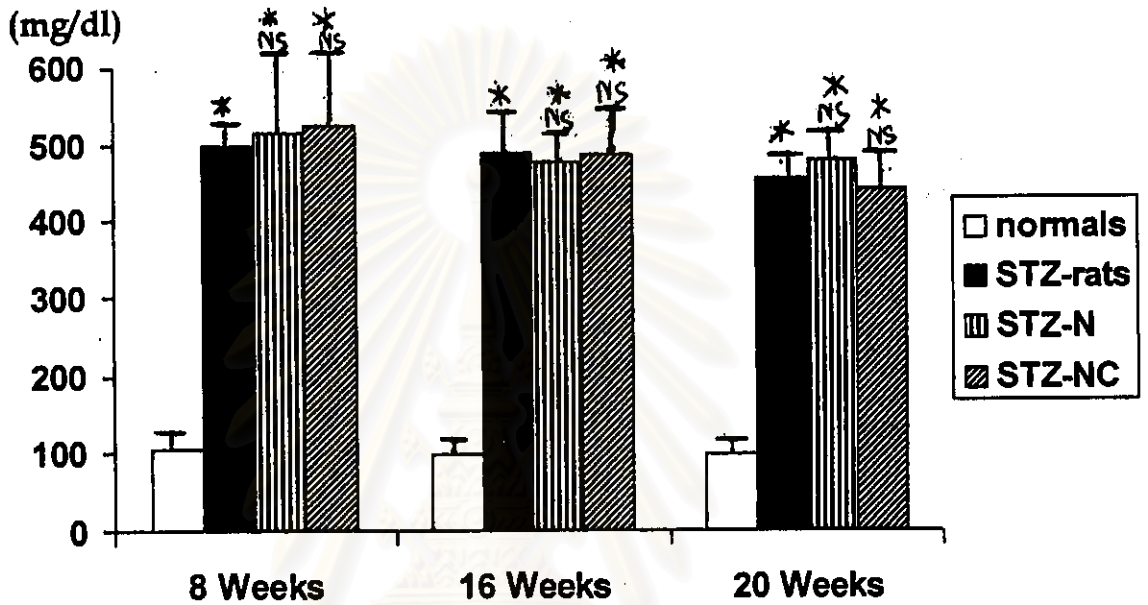
Table 4.14 Area of arterial wall thickening (μm^2) from 16 - 20 weeks of controls, STZ - rats, nicardipine treated STZ rats and nicardipine combined with cilazapril treated STZ rats.

Groups	Area of arterial wall thickness per surface area of vascular wall (μm^2)	
	16 weeks	20 weeks
Controls (n = 3)	0.4737 \pm 0.1187	0.4212 \pm 0.0376
STZ-rats (n = 3)	0.6870 \pm 0.0293 [#]	0.6097 \pm 0.0906
Nicardipine treated STZ-rats (n = 3)	0.4771 \pm 0.0238 ^{##}	0.4803 \pm 0.1814 ^{NS}
Nicardipine combined with cilazapril treated STZ-rats (n = 3)	0.4913 \pm 0.0226 ^{##}	0.4307 \pm 0.1256 ^{NS}

Statistical difference as compared to control (P < 0.05).

Statistical difference as compared to STZ - rat (P < 0.05).

NS non significant difference as compared to STZ - rat (P < 0.05).



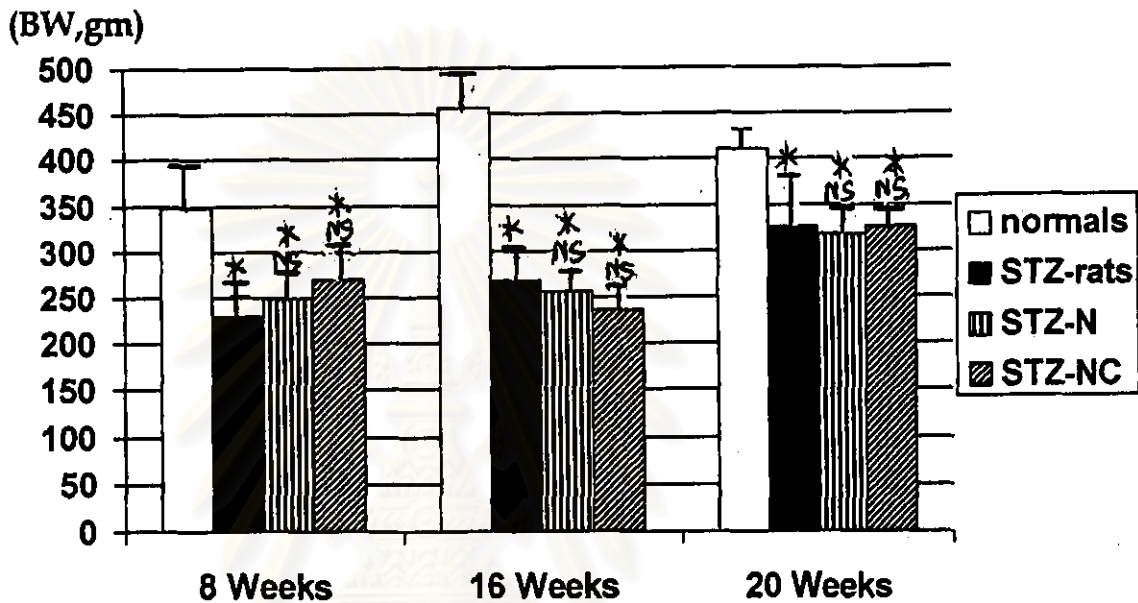
Values are mean \pm SD ; n = 6 rats.

Figure 4.1 Plasma glucose (mg/dl) of controls, STZ - rats, nicardipine treated STZ - rats (STZ -N) and nicardipine combined with cilazapril treated STZ - rats (STZ-NC) at 8, 16 and 20 weeks.

Values are mean \pm SD ; n = 6 rats.

* = Statistical difference as compared to control ($p < 0.01$).

NS = non significant difference as compared to STZ - rat ($P < 0.05$).



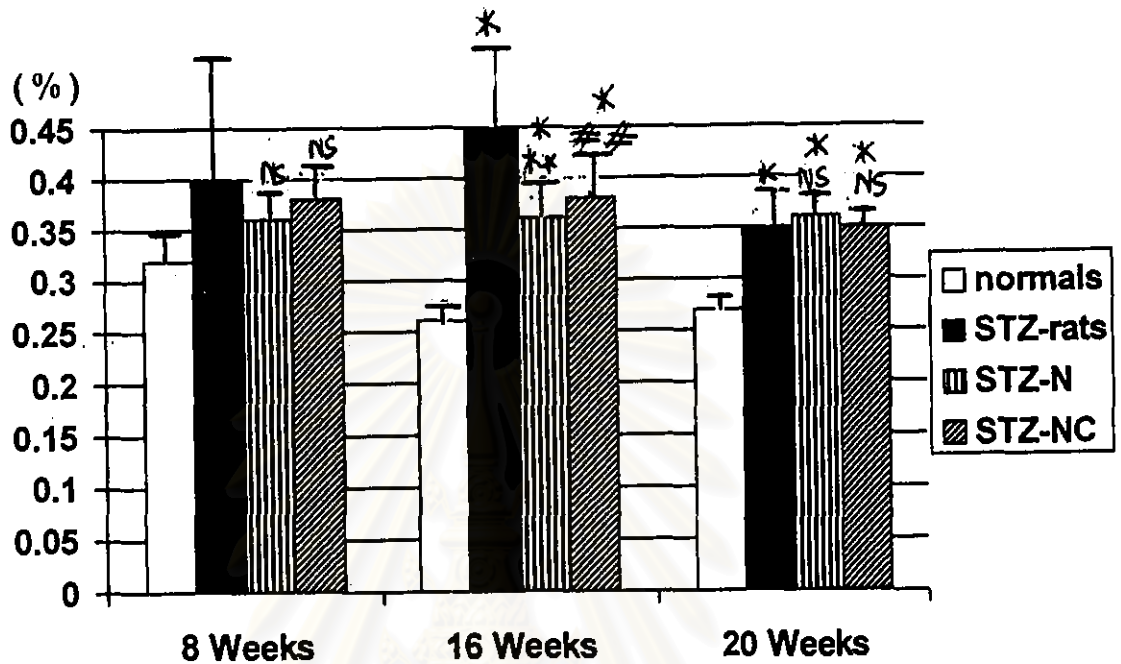
Values are mean \pm SD ; n = 6 rats.

Figure 4.2 Body weight (Bw, gm) of controls, STZ - rats nicardipine treated STZ - rats (STZ - N) and nicardipine combined with cilazapril treated STZ - rats (STZ - NC) at 8, 16 and 20 weeks.

Values are mean \pm SD ; n = 6 rats.

* = Statistical difference as compared to control (p < 0.01).

NS = non significant difference as compared to STZ - rat (P < 0.05).



Values are mean \pm SD ; n = 6 rats.

Figure 4.3 Ratio of heart weight per 100 grams body weight (%) of controls, STZ - rats, nicardipine treated STZ - rats (STZ - N) and nicardipine combined with cilazapril treated STZ - rats (STZ - NC) at 8, 16 and 20 weeks.

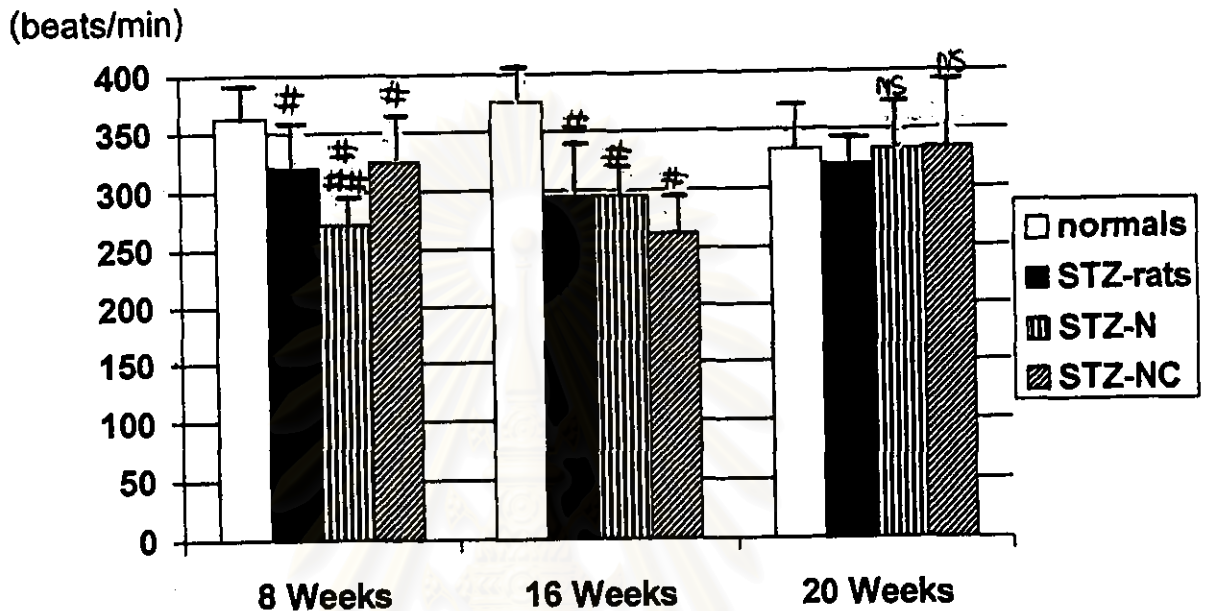
Values are mean \pm SD; n = 6 rats.

= Statistical difference as compared to STZ - rat ($p < 0.05$).

* = Statistical difference as compared to control ($P < 0.01$).

** = Statistical difference as compared to STZ - rat ($p < 0.01$).

NS = non significant difference as compared to STZ - rat ($P < 0.05$).



Values are mean \pm SD ; n = 6 rats.

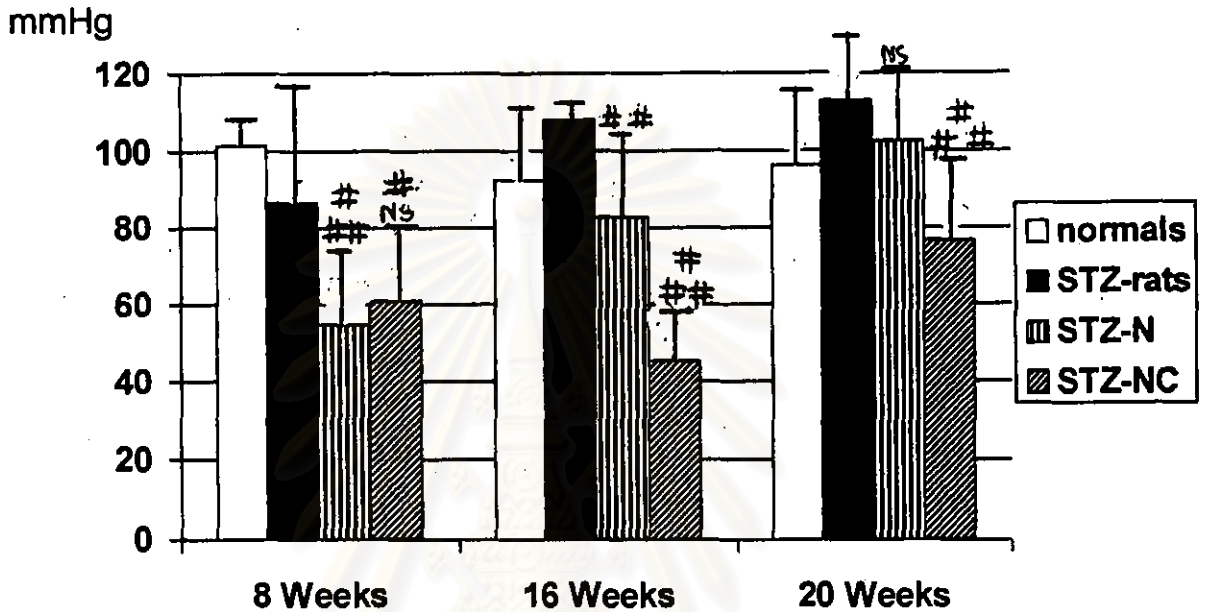
Figure 4.4 Heart rate (beats, min) of controls, STZ - rats, nicardipine treated STZ - rats (STZ - N) and nicardipine combined with cilazapril treated STZ - rats (STZ - NC) at 8, 16 and 20 weeks.

Values are mean \pm SD; n = 6 rats.

= Statistical difference as compared to control ($P < 0.05$).

= Statistical difference as compared to STZ - rat ($p < 0.05$).

NS = non significant difference as compared to STZ - rat ($P < 0.05$).



Values are mean \pm SD ; n = 6 rats.

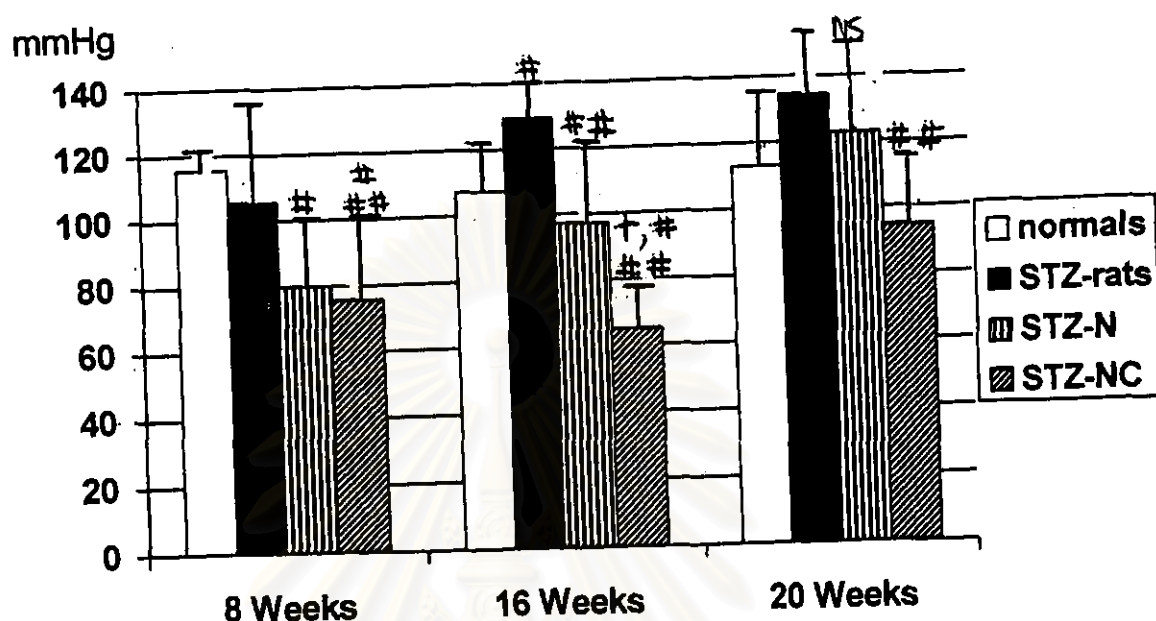
Figure 4.5 Mean arterial pressure (mmHg) of controls, STZ - rats, nicardipine treated STZ - rats (STZ - N) and nicardipine combined with cilazapril treated STZ - rats (STZ - NC) at 8, 16 and 20 weeks.

Values are mean \pm SD; n=6 rats.

= Statistical difference as compared to control (P < 0.05).

= Statistical difference as compared to STZ - rat (p < 0.05).

NS = non significant difference as compared to STZ - rat (P < 0.05).

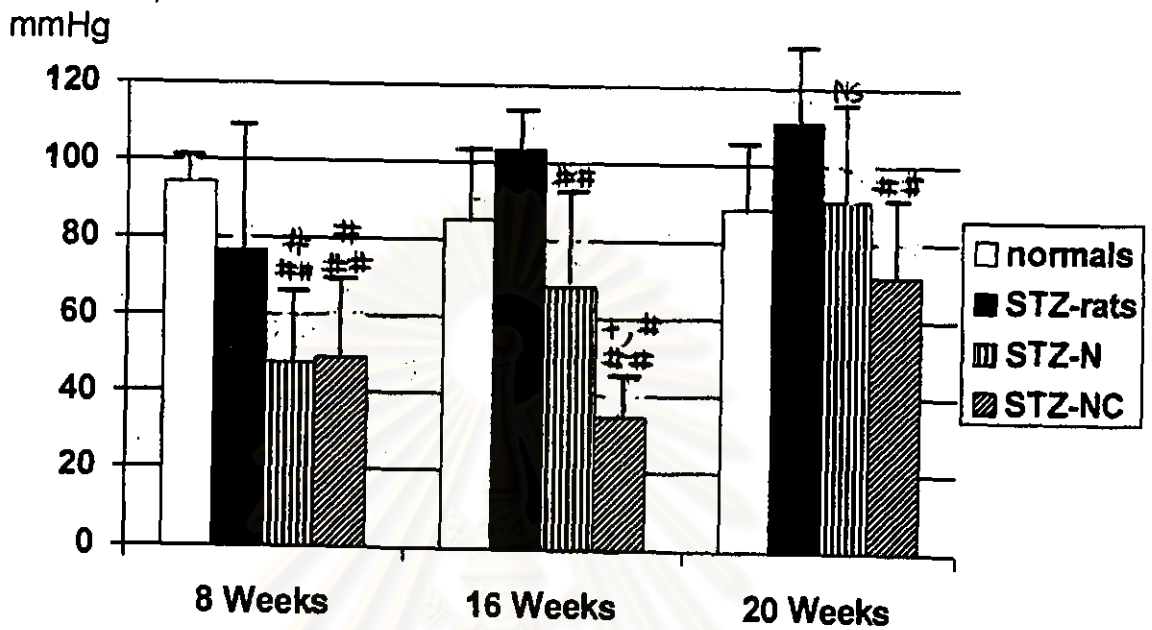


Values are mean \pm SD ; n = 6 rats.

Figure 4.6 Systolic blood pressure (mg Hg) of controls, STZ - rats, nicardipine treated STZ - rats (STZ - N) and nicardipine combined with cilazapril treated STZ - rats (STZ - NC) at 8, 16 and 20 weeks.

Values are mean \pm SD; n = 6 rats.

- # = Statistical difference as compared to control ($P < 0.05$).
- ## = Statistical difference as compared to STZ - rat ($p < 0.05$).
- + = Statistical difference as compared to nicardipine treated STZ - rat ($p < 0.05$).
- NS = non significant difference as compared to STZ - rat ($P < 0.05$).

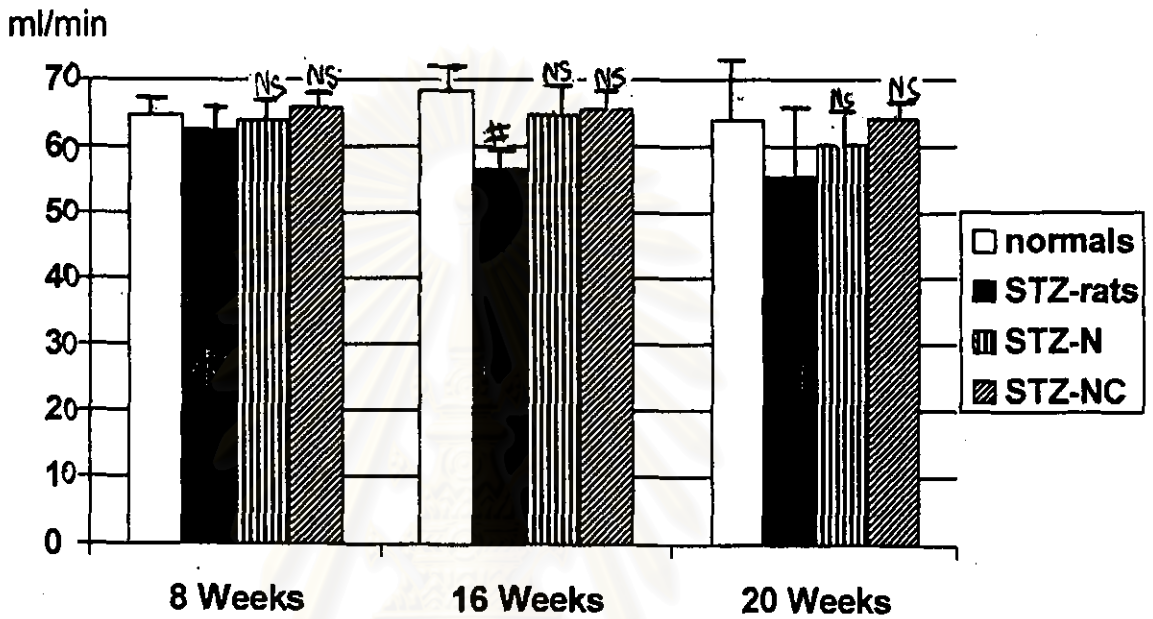


Values are mean \pm SD ; n = 6 rats.

Figure 4.7 Diastolic blood pressure (mmHg) of controls, STZ - rats, nicardipine treated STZ - rats (STZ - N) and nicardipine combined with cilazapril treated STZ - rats (STZ - NC) at 8, 16 and 20 weeks.

Values are mean \pm SD; n = 6 rats.

- # = Statistical difference as compared to control (P < 0.05).
- ## = Statistical difference as compared to STZ - rat (p < 0.05).
- + = Statistical difference as compared to nicardipine treated STZ - rat (p < 0.05).



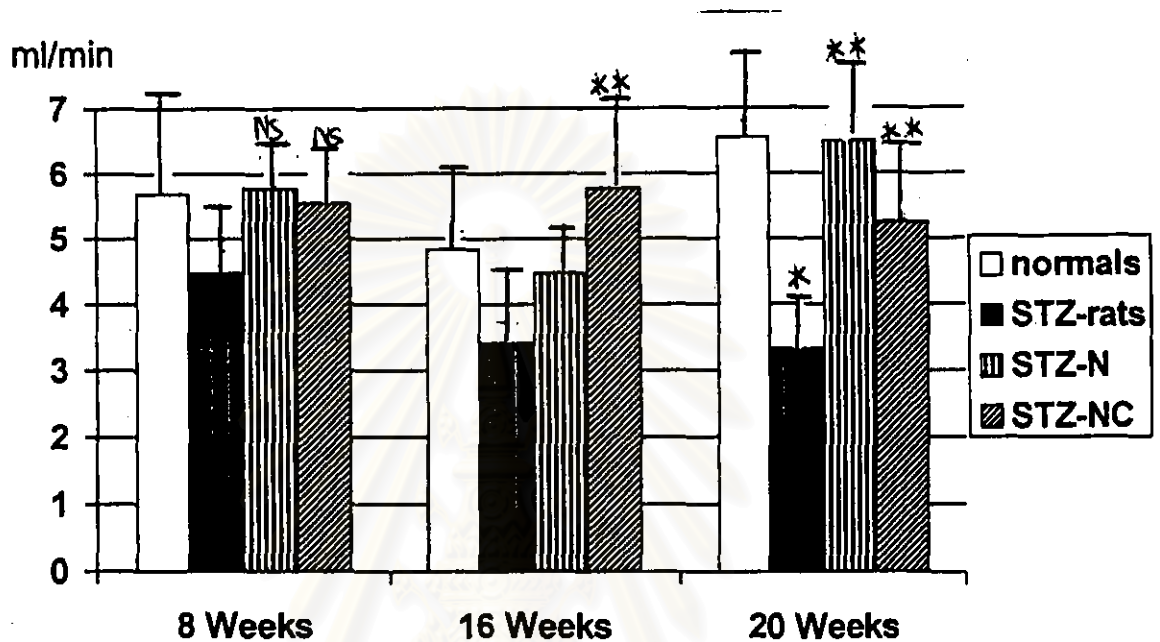
Values are mean \pm SD ; n = 6 rats.

Figure 4.8 Aortic flow rate (ml/min) of controls, STZ - rats, nicardipine treated STZ - rats (STZ -N) and nicardipine combined with cilazapril treated STZ - rats (STZ -NC) at 8, 16 and 20 weeks.

Values are mean \pm SD; n = 6 rats.

= Statistical difference as compared to control (P < 0.05).

NS = non significant difference as compared to STZ - rat (P < 0.05).



Values are mean \pm SD ; n = 6 rats.

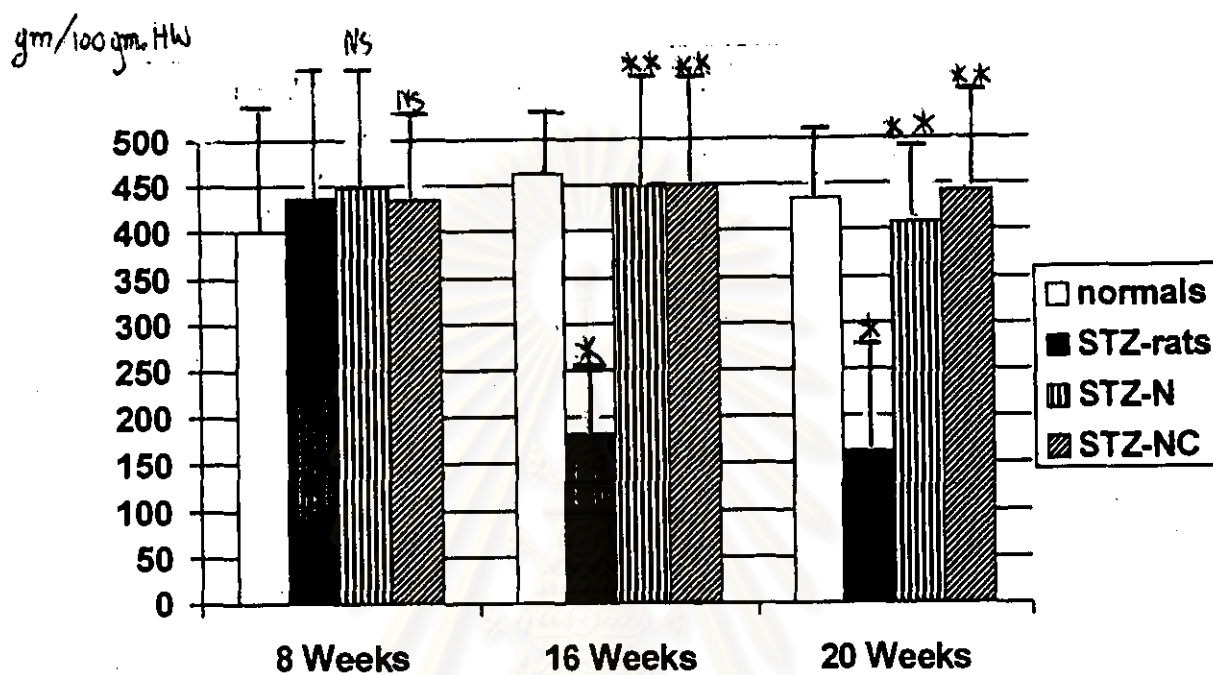
Figure 4.9 Caronary flow rate (ml/min) of controls, STZ - rats, nicardipine treated STZ - rats (STZ -N) and nicardipine combined with cilazapril treated STZ - rats (STZ - NC) at 8, 16 and 20 weeks.

Values are mean \pm SD; n=6 rats.

* = Statistical difference as compared to control (P < 0.01).

** = Statistical difference as compared to STZ - rats (P < 0.01).

NS = non significant difference as compared to STZ - rat (P < 0.05).



Values are mean \pm SD ; n = 6 rats.

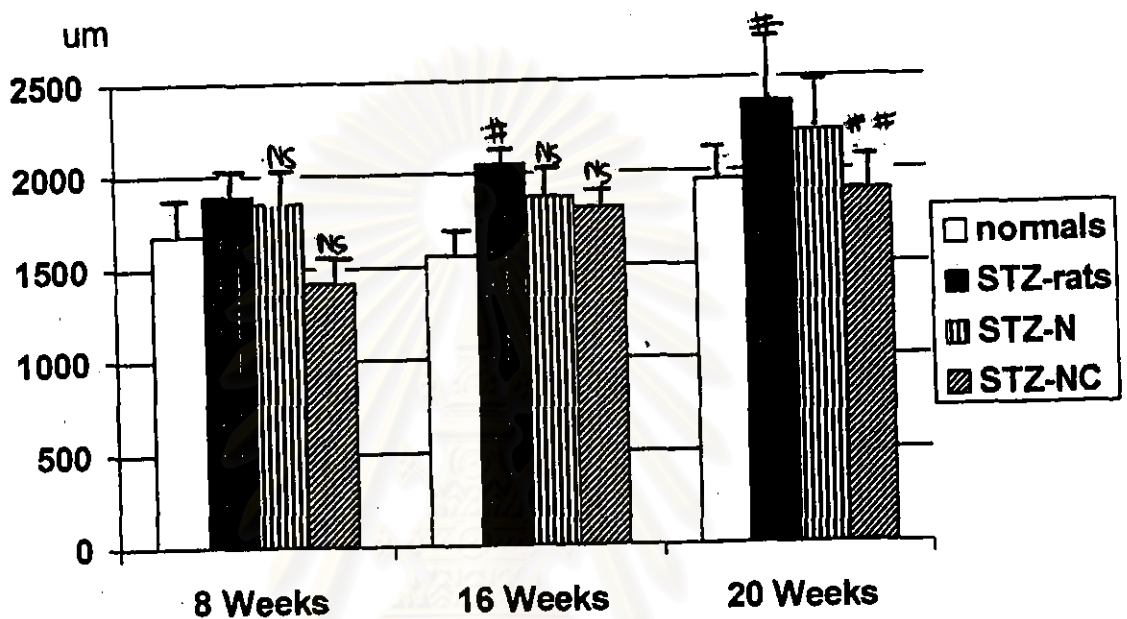
Figure 4.10 Left ventricular isotonic contraction (gm/ 100 gm of heart weight) of controls STZ - rats, nicardipine treated STZ - rats (STZ -N) and nicardipine combined with cilazapril treated STZ - rats (STZ - NC) at 8, 16 and 20 weeks.

Values are mean \pm SD ; n = 6 rats

= Statistical difference as compared to control (P < 0.01).

** = Statistical difference as compared to STZ - rats (P < 0.01).

NS = non significant difference as compared to STZ - rat (P < 0.05).



Values are mean \pm SD ; n = 3 rats.

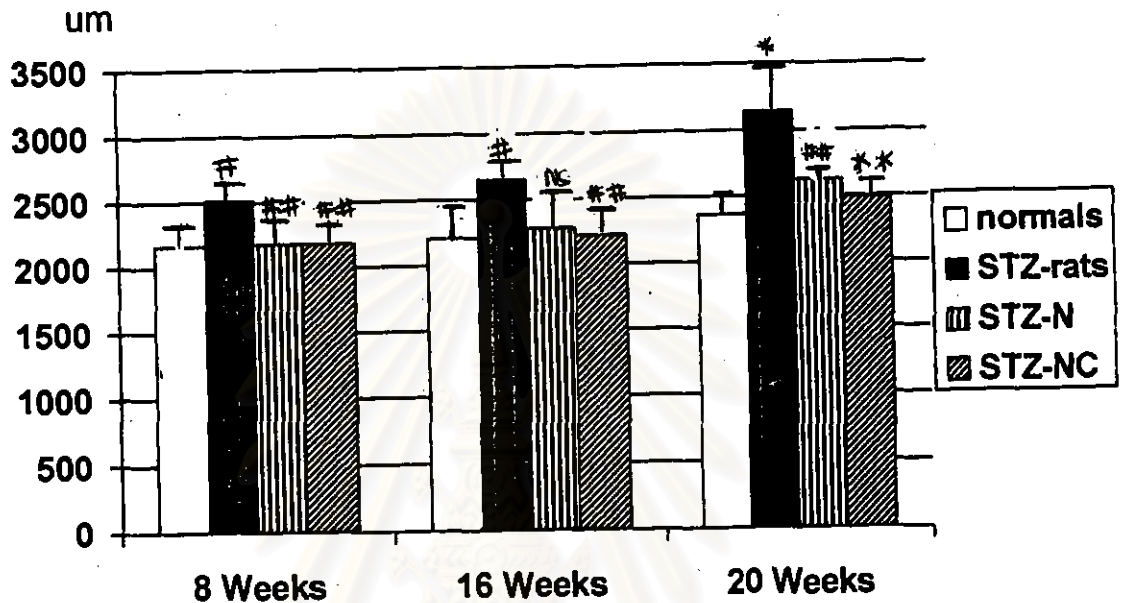
Figure 4.11 Size of interventricular septum wall (μm) of controls, STZ - rats, nicardipine treated STZ - rat (STZ-N) and nicardipine combined with cilazapril treated STZ - rats (STZ-NC) at 8, 16 and 20 weeks.

Values are mean \pm SD ; n = 3 rats.

= Statistical difference as compared to control ($P < 0.05$).

= Statistical difference as compared to STZ - rat ($P < 0.05$).

NS = non significant difference as compared to STZ - rat ($P < 0.05$).



Values are mean \pm SD ; n = 3 rats.

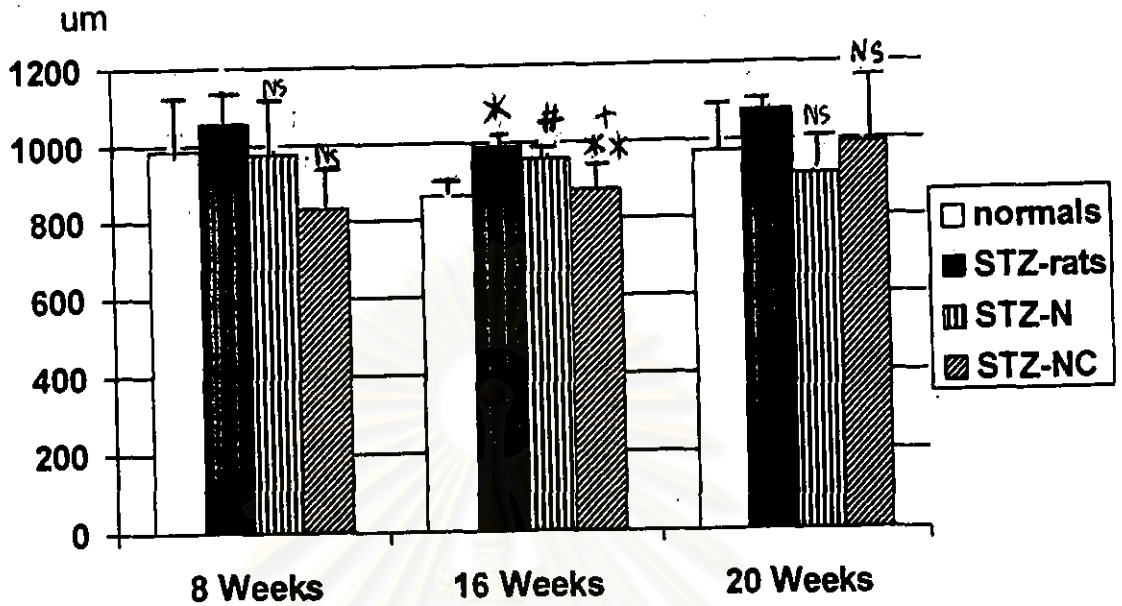
Figure 4.12 Size of left ventricular wall (μm) of control , STZ - rats, nicardipine treated STZ - rats (STZ -N) and nicardipine combined with cilazapril treated STZ - rats (STZ - NC) at 8, 16 and 20 weeks.

Values are mean \pm SD ; n = 3 rats

= Statistical difference as compared to control (P < 0.05).

= Statistical difference as compared to STZ - rat (P < 0.05).

NS = non significant difference as compared to STZ - rat (P < 0.05).



Values are mean \pm SD ; n = 3 rats.

Figure 4.13 Size of right ventricular wall (μm) of control, STZ - rats, nicardipine treated STZ - rats (STZ - N) and nicardipine combined with cilazapril treated STZ - rats (STZ - NC) at 8, 16 and 20 weeks.

Values are mean \pm SD ; n = 3 rats

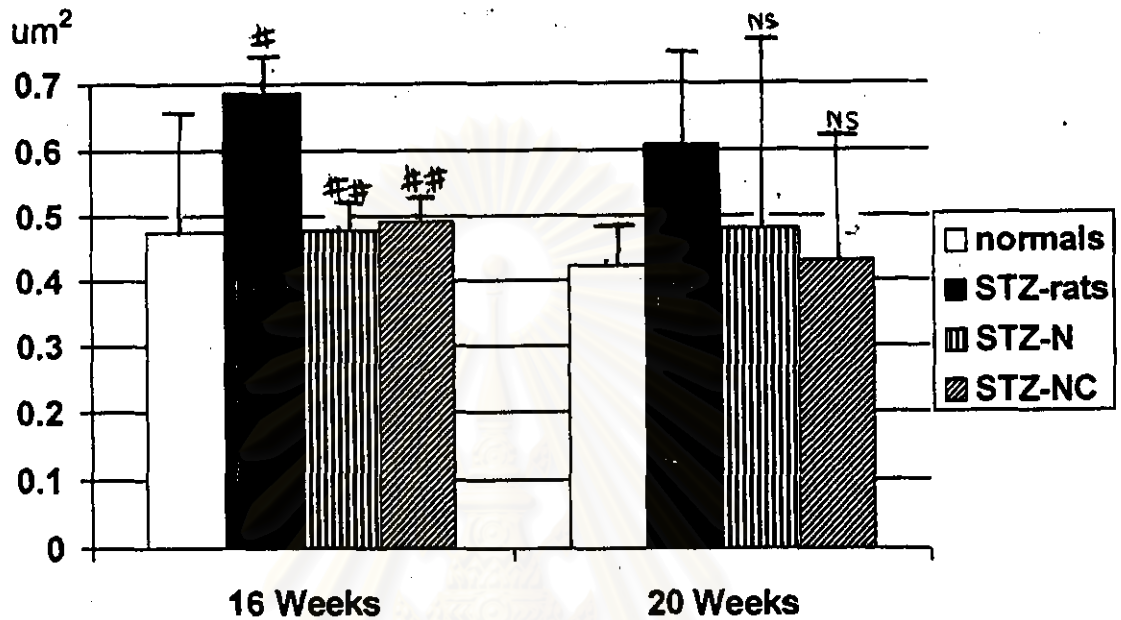
= Statistical difference as compared to control ($P < 0.05$).

* = Statistical difference as compared to control ($P < 0.01$).

** = Statistical difference as compared to STZ - rat ($P < 0.01$).

+ = Statistical difference as compared to nicardipine treated STZ - rat ($P < 0.05$).

NS = non significant difference as compared to STZ - rat ($P < 0.05$).



Values are mean \pm SD ; n = 3 rats.

Figure 4.14 Area of arterial wall thickness per surface area of ventricular wall (μm^2) of control, STZ - rats, nicardipine treated STZ - rats (STZ - N) and nicardipine combined with cilazapril treated STZ - rats (STZ - NC) at 16 and 20 weeks.

Values are mean \pm SD ; n = 3 rats

= Statistical difference as compared to control ($P < 0.05$).

= Statistical difference as compared to STZ - rat ($P < 0.05$).

NS = non Significant difference as compared to STZ - rat ($P < 0.05$).

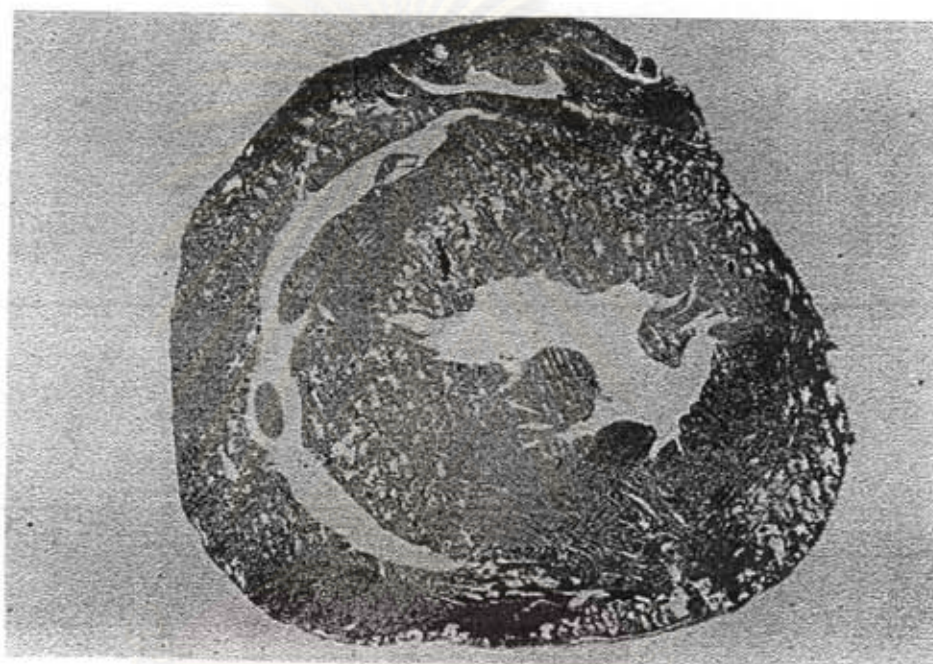


Figure 4.15 The cross - section of 8 - week control heart showed left ventricle (LV), right ventricle (RV) and interventricular septum (IVS) .

(Eosin & Hematoxylin x 40)



Figure 4.16 The cross - section of 16 - week control heart showed left ventricle (LV), right ventricle (RV) and interventricular septum (IVS) .

(Eosin & Hematoxylin x 40)

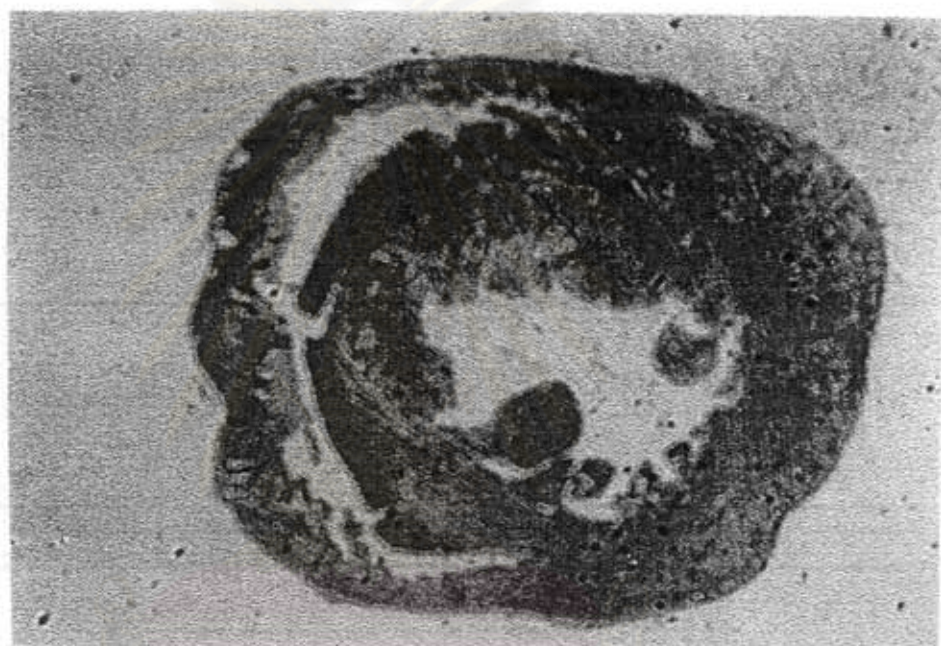


Figure 4.17 The cross - section of 20 - week control heart showed left ventricle (LV), right ventricle (RV) and interventricular septum (IVS) .

(Eosin & Hematoxylin x 40)



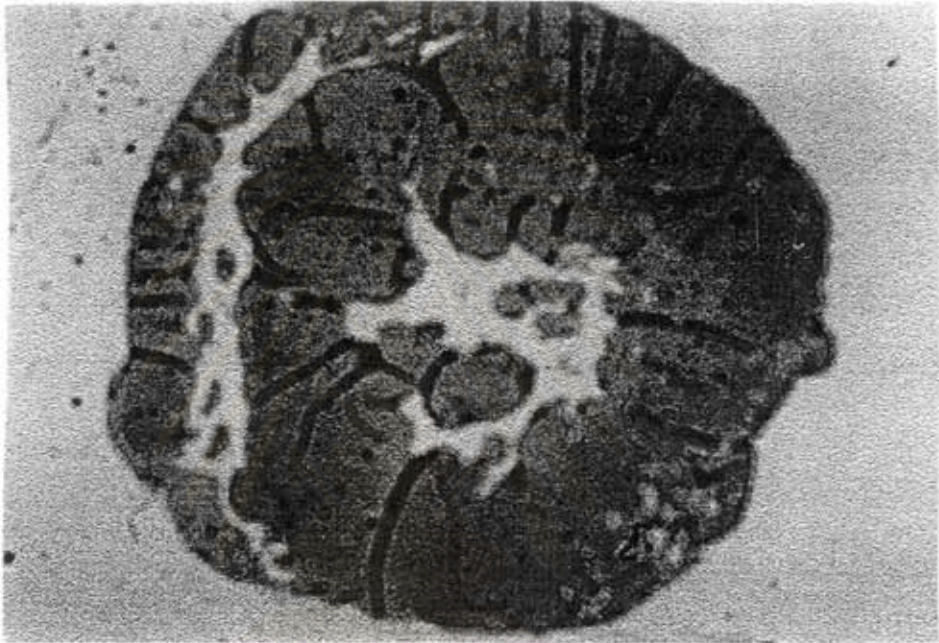
Figure 4.18 The cross - section of 8 - week STZ - rat heart showed left ventricle (LV) , right ventricle (RV) and interventricular septum (IVS) .

(Eosin & Hematoxylin x 40)



Figure 4.19 The cross - section of 16 - week STZ - rat heart showed left ventricle (LV) , right ventricle (RV) and interventricular septum (IVS) .

(Eosin & Hematoxylin x 40)



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Figure 4.20 The cross - section of 20 - week STZ - rat heart showed left ventricle (LV) ,right ventricle (RV) and interventricular septum (IVS) .

(Eosin & Hematoxylin x 40)



Figure 4.21 The cross - section of 8 - week STZ - N rat heart showed left ventricle (LV) , right ventricle (RV) and interventricular septum (IVS) .

(Eosin & Hematoxylin x 40)

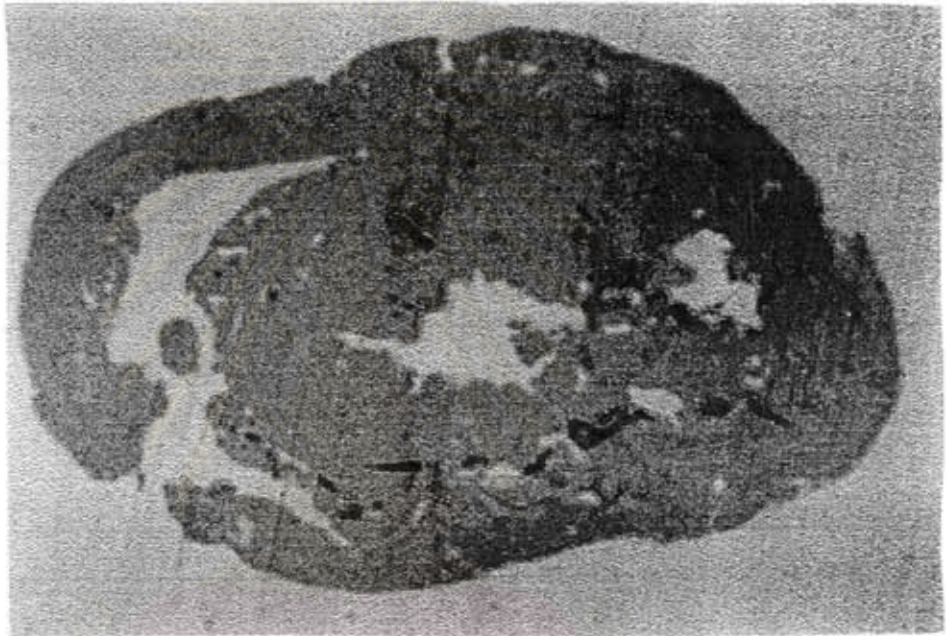


Figure 4.22 The cross - section of 16 - week STZ - N rat heart showed left ventricle (LV) , right ventricle (RV) and interventricular septum (IVS) .

(Eosin & Hematoxylin x 40)

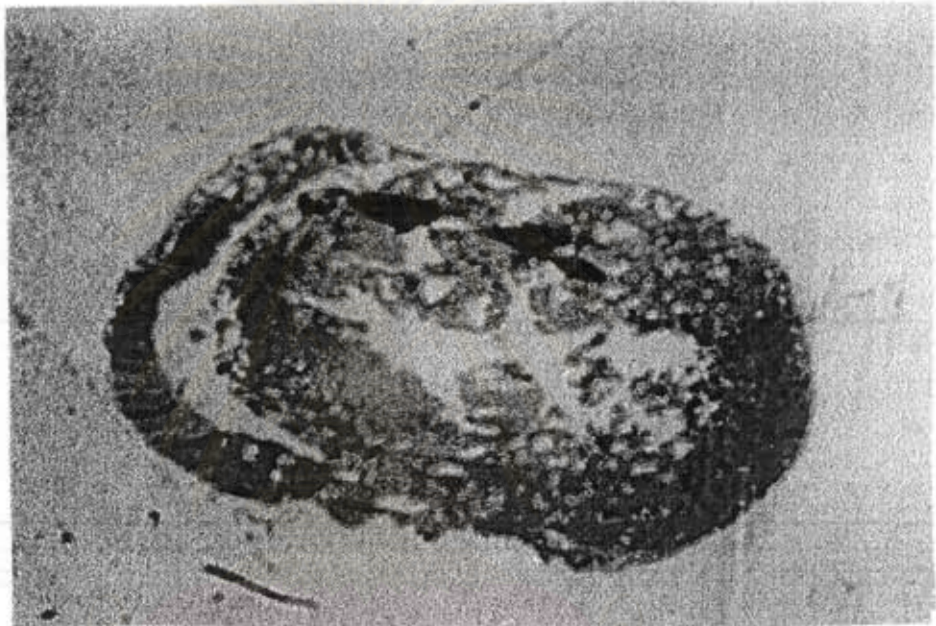


Figure 4.23 The cross - section of 20 - week STZ - N rat heart showed left ventricle (LV) , right ventricle (RV) and interventricular septum (IVS) .

(Eosin & Hematoxylin x 40)

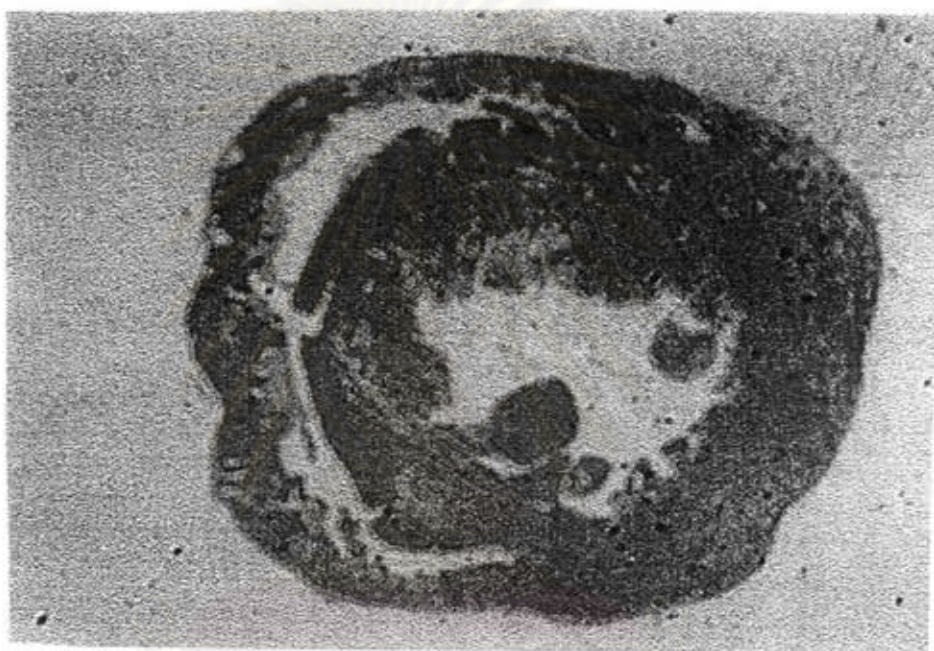


Figure 4.24 The cross - section of 8 - week STZ - NC rat heart showed left ventricle (LV) , right ventricle (RV) and interventricular septum (IVS).

(Eosin & Hematoxylin x 40)

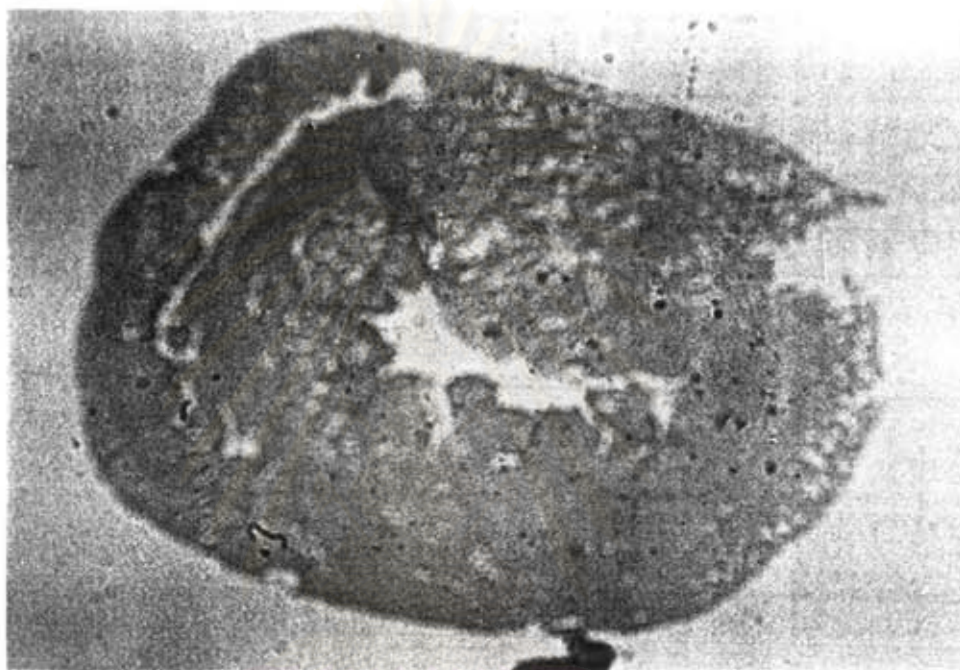
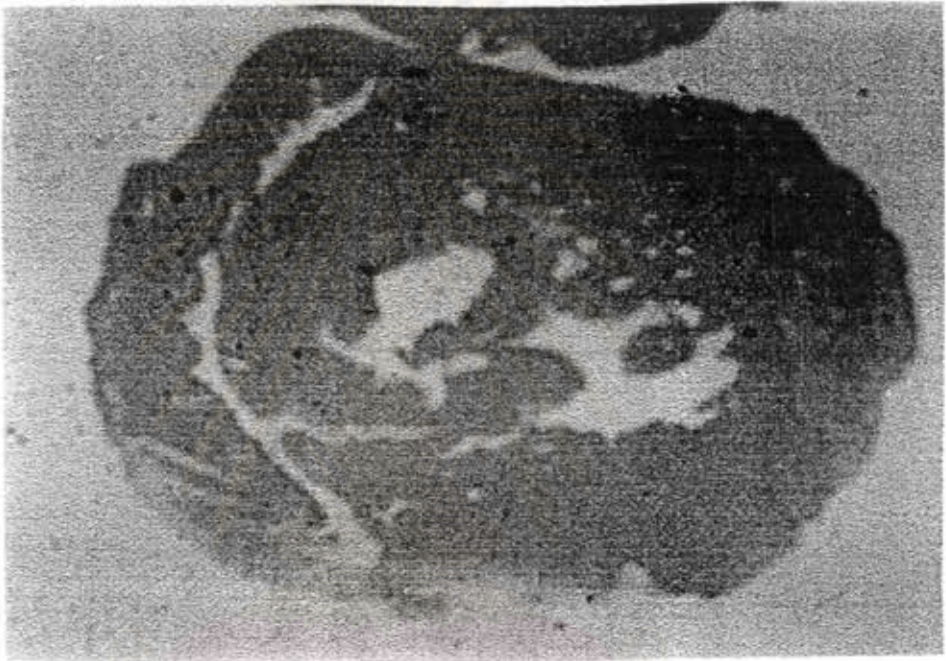


Figure 4.25 The cross - section of 16 - week STZ - NC rat heart showed left ventricle (LV) , right ventricle (RV) and interventricular septum (IVS).

(Eosin & Hematoxylin x 40)



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Figure 4.26 The cross - section of 20 - week STZ - NC rat heart showed left ventricle (LV) , right ventricle (RV) and interventricular septum (IVS).

(Eosin & Hematoxylin x 40)



Figure 4.22. The cross - section of 16 - week STZ - N rat heart showed left ventricle (LV) , right ventricle (RV) and interventricular septum (IVS) .

(Eosin & Hematoxylin x 40)



Figure 4.28 Lightphoto micrograph of intramural coronary artery from left ventricular myocardium of 20 - week control heart.

(Elastic x 400)



Figure 4.29 Lightphoto micrograph of intramural coronary artery from left ventricular myocardium of 16-week STZ-rat heart. (Elastic x 400)

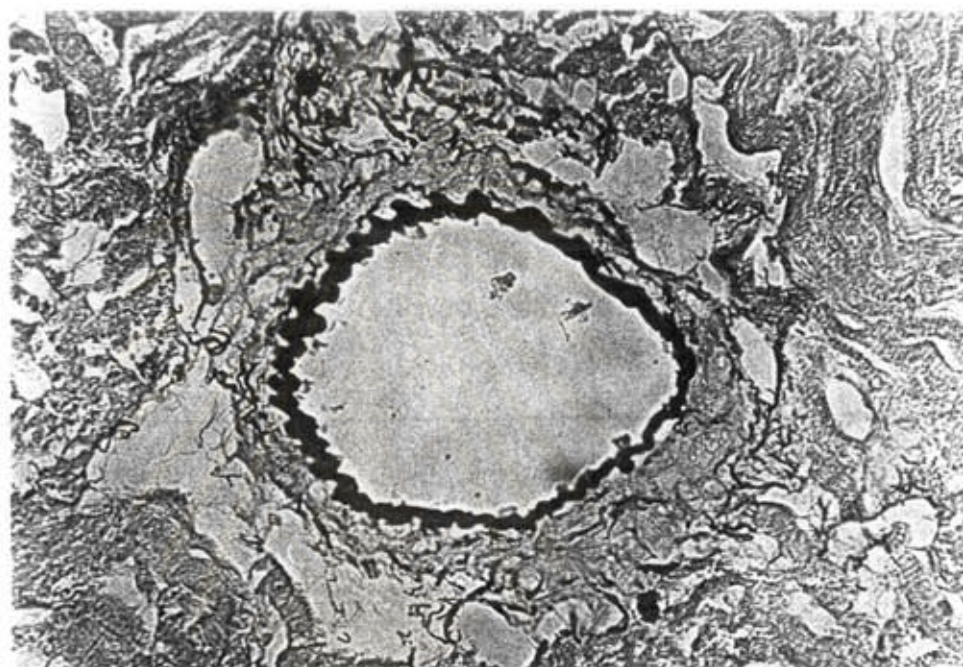


Figure 4.30 Lightphoto micrograph of intramural coronary artery from left ventricular myocardium of 20 - week STZ-rat heart. (Elastic x 400)

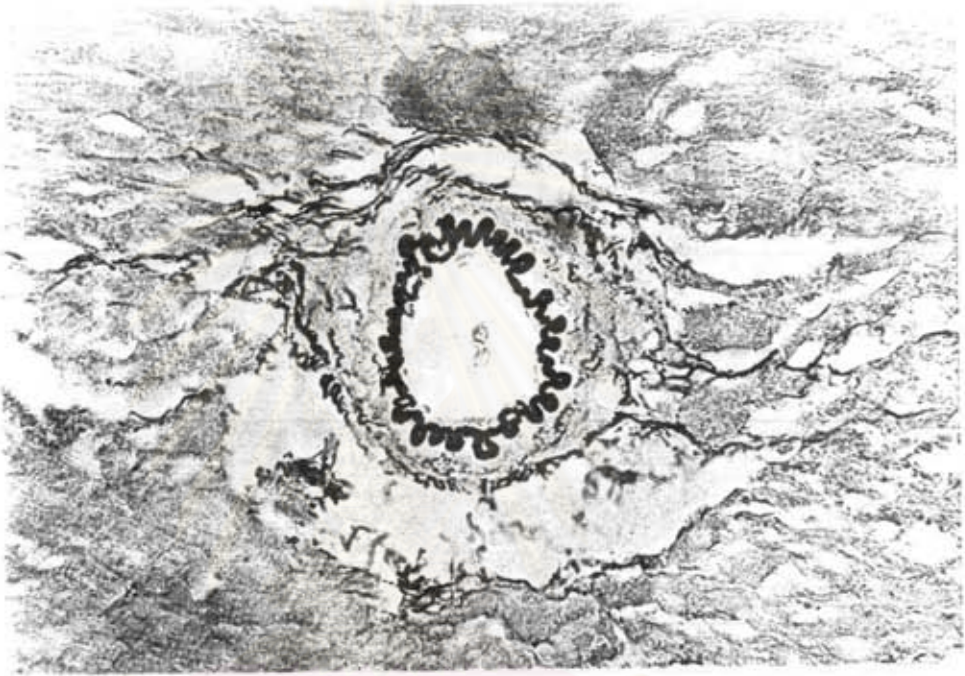


Figure 4.31 Lightphoto micrograph of intramural coronary artery from left ventricular myocardium of 16 - week STZ - N rat heart. (Elastic x 400)

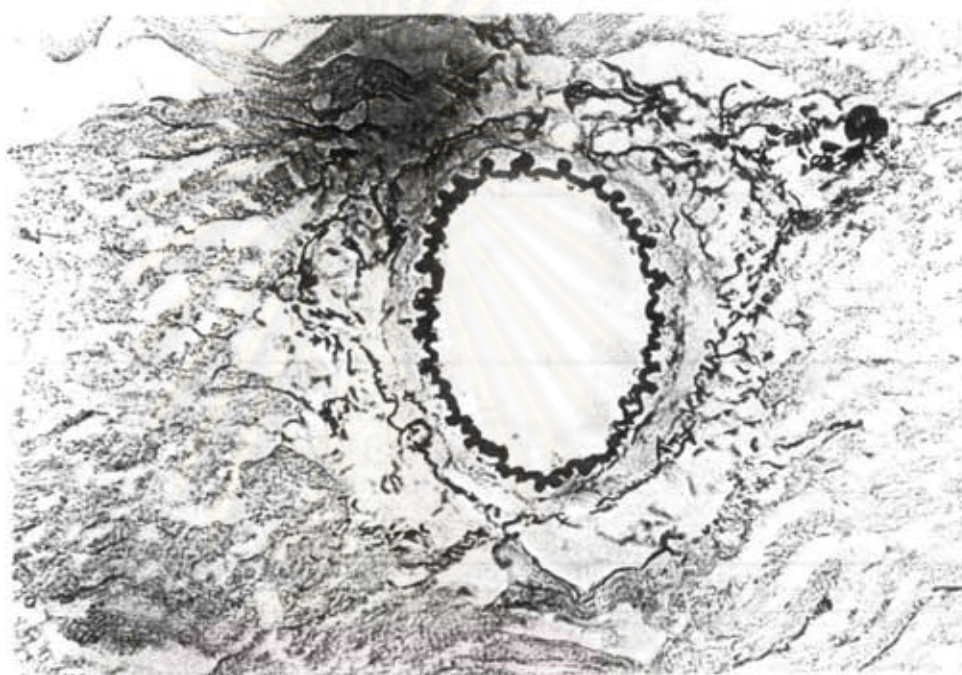


Figure 4.32 Lightphoto micrograph of intramural coronary artery from left ventricular myocardium of 20 - week STZ - N rat heart. (Elastic x 400)



Figure 4.33 Lightphoto micrograph of intramural coronary artery from left ventricular myocardium of 16 - week STZ - NC rat heart. (Elastic x 400)

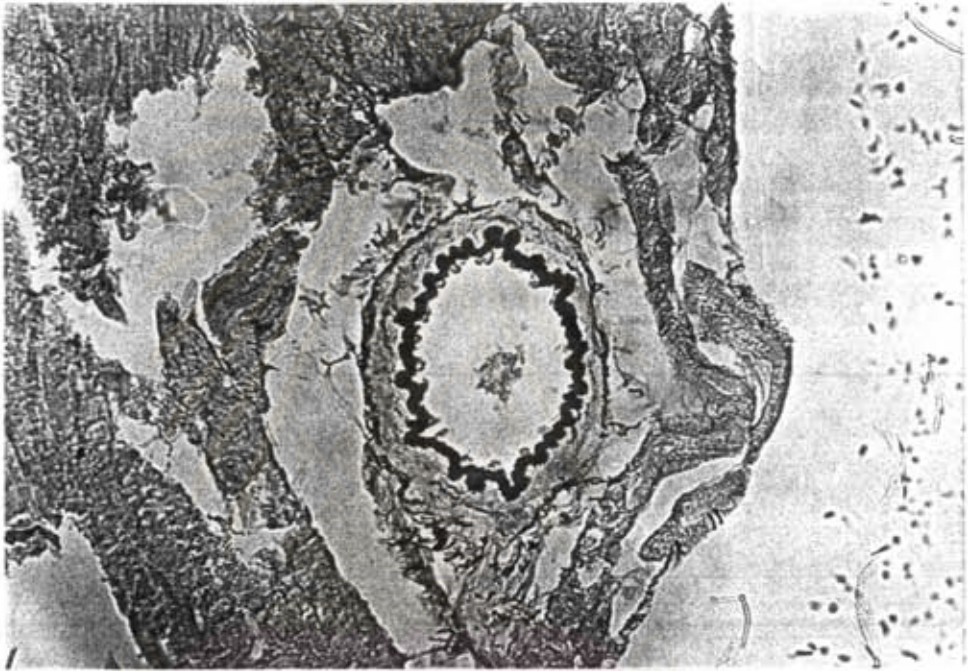


Figure 4.34 Lightphoto micrograph of intramural coronary artery from left ventricular myocardium of 20 - week STZ - NC rat heart. (Elastic x 400)