## CHAPTER IV

## RESULT

## I. Studies of plasma glucose and body weight in STZ and STZ- C1 and

 STZ-C8The streptozotocin treated/rat was used as an experimental model of diabetes mellitus in these studies. The objective of these part of work was to investigate the effect of cilazapril on the diaberic model with respect to plasma glucose level to body weight. The results showed in table 4.1 indicated that at the experimental period of 8 and 20 weeks, there was no significantly different of STZ-rats and both cilazapril treated groups. In table 4.2 , the body weights of all groups of STZ-rats and cilazapril- treated STZ-rats, were significantly decreased as compare to their $a_{\sigma} \mathrm{e}$ matched controls.

## II. Studies of cardiovascular functions in STZ-rats and cilazapril-  <br> Cardiovascular functions including CAP, HR, AFR, and LVIC were detemined for all groups at the experimental periods of 8 ani 20 weeks. Means and standard deviations of all these parameters were summarized in table 4.3-4.9 and

 were also demonstrated graphically in Fig. 4.3-4.9.1)Results in table 4.3-4.5 and Fig. 4.3-4.5 indicated that MAP, SBP, and DBP of STZ-rats were significantly increase as compared to the controls at both experimental monitored periods ( 8 and 20 weeks). Interestingly, the results also indicated that the dose of $0.01 \mathrm{mg} / \mathrm{kg} . B W . /$ day had no effect on this diabetic hypertension in both groups of STZ-C1 and STZ-C8. In other words, it was
confirmed the previous result in Table 3.1 that this dose of $0.01 \mathrm{mg} / \mathrm{kg}$. BW/day cilazapril was an non-antihypertensive dose. Moreover, the results indicated that cilazapril with antihypertensive doses (both 1 and $10 \mathrm{mg} / \mathrm{kg}$. BW/day) could be used to prevent or treat the diabetic hypertension. Since diabetic hypertension was significantly occured in both 8 and 20 weeks of experimental periods.
2) Results in table 4.6 and Fig. 4.6 indicated that heart rates were significantly slower than the age match controls at both experimental monitored periods (8 and 20 weeks). But, the results indicated that only the dose of $10 \mathrm{mg} / \mathrm{kg}$. BW/day in both groups of STZ-C1 and STZ-C8 could improve the heart rates at 20 weeks of experimental period.
3) The same as the result of heart rates determination, aortic flow. rates at both experimental monitored periods were significantly decreased as compare to the age matched controls as showed in table 4.7 and Fig. 4.7. The results also indicated that the doses of cilazapril $0.01,1$, and $10 \mathrm{mg} / \mathrm{kg}$. BW/day in both groups of STZ-C1 and STZ-C8 could improve aortic flow rates significantly in both 8 and 20 weeks of experimental periods.
4) Results in table 4.8 and Fig. 4.8 indicated that coronary flow rate of STZrats were significantly increased as compared to the controls at both experimental monitored periods ( 8 and 20 week). Moreover, the results indicated that cilazapril $0.01,1$, and $910 \mathrm{mg} / \mathrm{kg}$. BW/day in both groups of STZ-C1 and STZ-C8 could improve coronary flow rate in 8 and 20 \%eeks of experimental periods.
5) The results showed in table 4.9 and Fig. 4.9 demonstrated that the values of left ventricular isotonic contraction (LVIC) were normalized by divided by heart weight ( g ) of STZ-rats became significantly less than the age matched controls at both exrerimental monitored periods ( 8 and 20 week). Interestingly, the results also indicated that cilazapril could increase the values of LVIC in both groups of STZC 1 and STZ-C8.
6) The $R$ value ratios of heart weight per 100 gram body weights in table 4.10 and Fig. 4.10 indicated that hearts of STZ-rats have become hypertrophy as compared to the age matched controls. That are concomitant with the results of LVIC, and cilazapril seemed to attenuate this abnormallity.

## III. Studies of morphological examinations of hearts of STZ-rats and cilazapriltreated STZ-rats

The cross section of heart specimens were obtained from three controls, three STZ-rats, and three cilazapril-rreated specimens at each doses ( $0.01,1$, and 10 mg ) of 20 weeks STZ-rats by using the experimental procedure as described previously in chapter III. Thickness of left ventricular wall, right ventricular wall and interventricular septum wall were measured randomly with the micrometer of light microscope with 4 X objective. Mean and standard deviation of these wall thickness values were calculated and summarized in table 4.11 and Fig. 4.11-4.14.

The results of these morphological examinations indicated that:

1) Left ventricular walls of the three hearts of STZ-rats were thicker than controls, and was not significantly different from the age matched controls.
2) Right ventricular walls and interventricular septum walls were not significantly different between STZ-rats, cilazapril treated STZ-rats and age matched controls.

## จหาลงกรณ์มหาวิทยาลัย <br> IV Study of coronary artery, arteriole, and capillary wall thickness of STZ-rats

 and cilazapril-treated STZ-rats.The cross sections of heart specimens were obtained from three controls, three STZ-rats and three cilazapril-treated STZ-rats of 8 and 20 weeks at each doses ( $0.01,1$, and 10 mg ) of 20 weeks treated rats. In this investigations, cross sectional areas of coronary artery, artericle and capillary walls were be assessed with scanning electron microscope (JSM 5300). The thickness of vascular wall was randomly
measured at 3 positions. Numerical values were reported as means and SD, and comparison between controls and STZ-rats,and between STZ-rats and cilazapriltreated STZ-rats at each dose.

The results of morphological observations indicated that:

1) At 8 weeks after induced STZ-rats, wall thickening of coronary arteries, arterioles, and capillaries of STZ-rats wete not different from controls.
2) Wall thickness of coronary eyteries, arterioles, and capillaries of STZ-rats were thicker than controls at 20 weeks after induced diabetic rats and were no significantly difference from the age matohed controls for all groups that treated with cilazapril $0.01,1$, and 10 mg day and 8 weeks after STZ-rats.

From Fig. 4.19-4.28 , the endothelial cells from scanning electron microscopy showed that the endothelial cell surface was irregular and swallen. These abnormal-looking areas of S2Z-rats was different from of controls. The endothelial cells of nondiabetic rats showed clear cell margin. The cell surface was smooth. These results indicated that treatment with cilazapril groups could improve these abnormallities.


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Table 4.1 Plasma glucose ( $\mathrm{mg} / \mathrm{dl}$ ) at 8 and 20 wks after STZ-injections of Controls, STZ-rats, and Cilazapril treated STZ-rats.


Table 4.2 Body weight (BW,g) wks of Controls, STZ-rats, and Cilazapril treated STZ-rats of 8,20 .


Table4.3 Mean arterial pressure ( mmHg ) of $8,20 \mathrm{wks}$ of Controls, STZ-rats, and Cilazapril treated STZ-rats.


Table4.4 Systolic pressure ( mmHg ) of $8,20 \mathrm{wks}$ of Controls, STZ-rats, and Cilazapril treated STZ-rats.

|  | Groups |  |
| :--- | :--- | :--- | :--- |

Table 4.5 Diastolic pressure ( mmHg ) of 8,20 weeks of Controls, STZ-rats, and Cilazapril treated STZ-rats.


Table 4.6 Heart rate of 8,20 wks of Controls, STZ-rats, and Cilazapril treated STZ-rats.

| Groups | Experimental periods |  |
| :---: | :---: | :---: |
|  | 8 weeks | 20 weeks |
| Controls $\quad(\mathrm{n}=5)$ | $387.80 \pm 17.58$ | $378.00 \pm 12.55$ |
| STZ-rats ( $\mathrm{n}=5$ | $308.00 \pm 1$ | $285.00 \pm 28.64{ }^{*}$ |
| STZ-C1 0.01 mg | 5.00 | $354.00 \pm 20.74$ |
| STZ-C1 1 mg | 5.0 | $351.00 \pm 15.17$ |
| STZ-C1 10 mg | 0 | $374.00 \pm 15.07{ }^{\text {\# }}$ |
| STZ-C8 0.01 mg ( $\mathrm{n}=5$ ) |  | $340.00 \pm 15.81$ |
| STZ-C8 $1 \mathrm{mg} \quad(\mathrm{n}=5)$ | 令均 | $348.00 \pm 17.61$ |
| STZ-C8 10 mg |  | $366.00 \pm 17.75{ }^{\text {\# }}$ |
| Statistical difference as compared to controls $(\mathrm{p}<0.05) ? \tilde{}$ |  |  |
|  |  |  |
| Statistical difference as compared to STZ-rats ( $\mathrm{p}<0.05$ ). |  |  |
|  |  |  |

Table 4.7 Aortic flow rate ( $\mathrm{ml} / \mathrm{min}$ ) of 8,20 wks of Controls, STZ-rats, and Cilazapril treated STZ-rats.


Table 4.8 Coronary flow rate ( $\mathrm{ml} / \mathrm{min}$ ) of 8,20 weeks of Controls, STZ-rats, and Cilazapril treated STZ-rats at 8 and 20 wks after STZ-injections.


Table 4.9 Left ventricular isotonic contraction (LVIC.g/g of heart weight) of Controls, STZ-rats, and Cilazapril treated STZ-rats.


Table 4.10 Ratio of heart weight per 100 g . body weight (\%) of Controls, STZ-rats, and Cilazapril treated STZ-rats.


Table4.11 Size of left and right ventricular wall and interventricular septum wall ( $\mu \mathrm{m}$ ) of 8,20 wks of Controls, STZ-rats, and Cilazapril treated STZ-rats.

*Statistical difference as compared to controls ( $\mathrm{p}<0.05$ ).
\# Statistical difference as compared to STZ-rats ( $p<0.05$ ).
\$ Non significant different as compared to control, and STZ-rats ( $p<0.05$ ).

Table 4.12 Thickness of intramural coronary artery ( $\mathrm{d}=50-70 \mu \mathrm{~m}$ ), arteriole ( $\mathrm{d}=10-20 \mu \mathrm{~m}$ ), and capillary wall ( $\mathrm{d}=5-10 \mu \mathrm{~m}$ ) from left ventricular myocardium of 8,20 weeks of Controls, STZ-rats, and Cilazapril treated STZ-rats.


* Statistical difference as compared to controls ( $p<0.05$ ).
\# Statistical difference as compared to STZ-rats ( $\mathrm{p}<0.05$ ).

Figure 4.1 Mean $\pm$ SD of plasma glucose ( $\mathrm{mg} / \mathrm{dl}$ ) of 8, 20 weeks of Controls, STZ-rats, and Cilazapril treated STZ-rats.

PLASMA GLUCOSE(mg/dl)


PLASMA GLUCOSE(mg/di)


* Statistical difference as compared to controls( $\mathrm{p}<0.05$ ).

Figure 4.2 Mean $\pm$ SD of body weight (BW,g) of 8,20 weeks of Control, STZ-rats, and Cilazapril treated STZ-rats.


* Statistical difference as compared to controls( $\mathrm{p}<0.05$ ).

Figure 4.3 Mean $\pm$ SD of mean arterial pressure ( mmHg ) of 8,20 weeks of Controls, STZ-rats, and Cilazapril treated STZ-rats.


* Statistical difference as compared to controls( $\mathrm{p}<0.05$ ).
\# Statistical difference as compared to STZ-rats( $\mathrm{p}<0.05$ ).

Figure 4.4 Mean $\pm$ SD of systolic pressure ( mmHg ) of 8,20 weeks of Controls, STZ-rats, and Cilazapril treated STZ-rats.


[^0]Figure 4.5 Mean $\pm$ SD of diastolic pressure ( mmHg ) of 8,20 weeks of Controls, STZ-rats, and Cilazapril treated STZ-rats.


[^1]Figure 4.6 Mean $\pm$ SD of heart rate(beats/min) of 8,20 weeks of Controls, STZ-rats, and Cilazapril treated STZ-rats.


* Statistical difference as compared to controls( $\mathrm{p}<0.05$ ).
\# Statistical difference as compared to STZ-rats( $\mathrm{p}<0.05$ ).

Figure 4.7 Mean $\pm$ SD of aortic flow rate $(\mathrm{ml} / \mathrm{min})$ of 8,20 weeks of Controls, STZ-rats, and Cilazapril treated STZ-rats.


* Statistical difference as compared to controls( $\mathrm{p}<0.05$ ).
\# Statistical difference as compared to STZ-rats( $\mathrm{p}<0.05$ ).

Figure 4.8 Mean $\pm$ SD of coronary flow rate $(\mathrm{ml} / \mathrm{min})$ of 8,20 weeks of Controls, STZ-rats, and Cilazapril treated STZ-rats.


* Statistical difference as compared to controls( $\mathrm{p}<0.05$ ).
\# Statistical difference as compared to STZ-rats( $\mathrm{p}<0.05$ ).

Figure 4.9 Mean $\pm$ SD of left ventricular isotonic contraction (LVIC g/g of heart weight) of 8,20 weeks of Controls, STZ-rats, and Cilazapril treated STZ-rats.

## LVIC(g/g of HW)



* Statistical difference as compared to controls( $\mathrm{p}<0.05$ ).
\# Statistical difference as compared to STZ-rats( $\mathrm{p}<0.05$ ).

Figure 4.10 Mean $\pm$ SD of ratio of heart weight per $100 \mathrm{~g} / 100 \mathrm{~g}$ body weight( $\mathrm{R}, \%$ ) of 8,20 weeks of Controls, STZ-rats, and Cilazapril treated STZ-rats.


[^2]Figure 4.11 Mean $\pm$ SD of thickness of left ventricular wall(LV), right ventricular wall(RV), and interventricular septum wall(IVS) of 8 weeks of Controls and STZ-rats.


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Figure 4.12 Mean $\pm$ SD of thickness of left ventricular wall (um) of 8,20 weeks of Controls, STZ-rats, and Cilazapril treated STZ-rats.


Q 9\% Statistical difference as compared to controls( $\mathbf{p < 0 . 0 5 ) \text { . }}$ \# Statistical difference as compared to STZ-rats( $\mathrm{p}<0.05$ ).

Figure 4.13 Mean $\pm$ SD of thickness of right ventricular wall (um) of 8, 20 weeks of Controls, STZ-rats, and Cilazapril treated STZ-rats.


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ล $98 \cap$ \$ Non significant difference as compared to controls and STZ-rats $(\mathrm{p}<0.05)$.

Figure 4.14 Mean $\pm$ SD of thickness of interventricular septum wall(um) of 8, 20 weeks of Controls, STZ-rats, and Cilazapril treated STZ-rats.


Q 98 \$ Non significant difference as compafed to controis $\frac{\rho}{\text { and } S T Z-r a t s(~} \mathbf{p}<0.05$ ).

Figure 4.15 Mean $\pm$ SD of thickness of intramural coronary artery ( $\mathrm{d}=50-70 \mathrm{um}$ ), arteriole ( $\mathrm{d}=10-20 \mathrm{um}$ ), and capillary $(\mathrm{d}=5-10 \mathrm{um}$ ) wall from left ventricular myocardium of 8 weeks of Controls and STZrats.


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Figure 4.16 Mean $\pm$ SD of thickness of intramural coronary artery wall ( $\mathrm{d}=50-70 \mathrm{um}$ ) from left ventricular myocardium of 20 weeks of Controls, STZ-rats, and Cilazapril treated STZ-rats.


Figure 4.17 Means $\pm$ SD of wall thickness of intramural coronary arterioles ( $\mathrm{d}=10-20 \mathrm{um}$ ) of left ventricular myocardium of Controls, STZ-rats, and Cilazapril treated STZ-rats at 20 weeks after the STZ injection.


Figure 4.18 Mean $\pm$ SD of thickness of intramural capillary wall( $\mathrm{d}=5-10 \mathrm{um}$ ) from left ventricular myocardium of 20 weeks of Controls, STZ-rats, and Cilazapril treated STZ-rats.



Figure 4.19 The cross-section of 8 week control heart showed left ventricle (LV), right venticle (RV) and intervenfficular septum (IVS).
(Eosin \& Hematoxylin $x^{4}$ )
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Figure 4.20 The cross-jection of 8 week STZ-rat heatt showed left ventricle (LV),
right ventricle (RV) and interventricular septum (IVS).
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Figure 4.21 The cross-section of 20 week control heart showed left ventricle (LV), fight ventrice (RM) and interyentricular septum(IVS). (EDsin \& Hematoxylin, x4)


Figure 4.22 The cross-section of 20 week STZ-rat heart showed left ventricle (LV), right ventricle (RV) and interventricular septum (IVS). (Eosin \& Hematoxylin x4) จุหาลงกรณมหาวิทยาลัย


Figure 4.23 The cross-section of 20 week STZ-C1 0.01 mg heart showed left vefticle (EY), tight ventricle ©RM and interventricicular septum (IVS). (Eosin \& Hematoxylin x4) จุหาลงกรณมหาวิทยาลัย


Figure 4.24 The cross-section of 20 week STZ-C1 1 mg heart showed left ventricle (LD), right ventricte (RV) and interventricuar septum (IVS).
(EOsin \& Hematoxylin x 4 )
จุหาลงกรณมหาวิทยาลัย


Figure 4.25 The cross-section of 20 week STZ-C1 10 mg heart showed left ventricle (LV), fight ventricle (RV) and interventricular septum (IVS).
(Eosin \& Hematoxylin x4)



Figure 4.26 The cross-section of 20 week STZ-C8 0.01 mg heart showed left yentricle (IV), right ventricief(RV) and interyentricular septum (IVS) (EOsin \& Hematoxylin $\times 4$ )
จุหาลงกรณมมหาวิทยาลัย


Figure 4.27 The cross-section of 20 week STZ-C8 1 mg heart showed left ventricle (LV), right yenftiole (RY) and interventricular septum (IVS). (EOSin \& Hematoxylin $x^{4}$ ) จุหาลงกรณมมหาวิทยาลัย


Figure 4.28 The cross-section of 20 week STZ-C8 10 mg heart showed left ventricle (LVPrieht qenticlef(RV) and interyentricular septym (IVS). (Eosin \& Hematoxylin x 4 )
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Figure 4.29 Scanning electron microscope showed the thickness of intramural



Figure 4.30 Scanning electron microscope showed the thickness of intramural

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Figure 4.31 Scanning electron microscope showed the thickness of intramural
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Figure 4.32 Scanning electron microscope showed the thickness of intramural



Figure 4.33 Scanning electron microscope showed the thickness of intramural 6 ㅇ coronary artery (um) from 20 week STZ-CP 0.01 mg rat. จุหาลงกรณ์มหาวิทยาลัย


Figure 4.34 Scanning electron microscope showed the thickness of intramural
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Figure 4.35 Scanning electron microscope showed the thickness of intramural

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& \text { จุหาลงกรณ์มหาวิทยาลัย }
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Figure 4.36 Scanning efectron microscope showed the thickness of intramural

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Figure 4.37 Scanning election microscope showed the thickness of intramural

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Figure 4.38 Scanning electron microscope showed the thickness of intramural

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Figure 4.39 Scanning electron microscope showed the thickness of intramural 6 -
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Figure 4.40 Scanning electron microscope showed the thickness of intramural 6 a
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Figure 4.41 Scanning electron microscope showed the thickness of intramural

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Figure 4.42 Scanning electron microscope showed the thickness of intramural $\overbrace{\text { el }}^{0}$ coronary arteriole ( $\mu \mathrm{m}$ ) from 20 week STZ-rat.



Figure 4.43 Scanning electron microscope showed the thickness of intramural
 จุหาลงกรณ์มหาวิทยาลัย


Figure 4.44 Scanning electron microscope showed the thickness of intramural coronary arterpoge (رm fromm 20 week9 STZ-C1 dmg rat. จุหาลงกรณ์มหาวิทยาลัย


Figure 4.45 Scanning electron microscope showed the thickness of intramural
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efrenarg arperidy iamofrom $20 /$ week $S T Z G 10 \mathrm{mg}$ rat จุหาลงกรณ์มหาวิทยาลัย


Figure 4.46 Scanning electron microscope showed the thickness of intramural coronary arterole (mm) from 30 week STZ.C8 0.01 mg rat. coronary artenole (min) from 20 week Siz-68 0.0 จุหาลงกรณ์มหาวิทยาลัย


Figure 4.47 Scanning electron microscope showed the thickness of intramural

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Figure 4.48 Scanning electron microscope showed the thickness of intramural
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Figure 4.49 Scanning electron microscope showed the thickness of intramural capillary (ump) from 8 week eontrol cat. $\cap ? \approx$ จุหาลงกรณ์มหาวิทยาลัย


Figure 4.50 Scanning electron microscope showed the thickness of intramural
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Figure 4.51 Scanning electron microscope showed the thickness of intramural
capillary (gum)from $2 \theta$ week control rat. $\cap ? \approx$
จุหาลงกรณ์มหาวิทยาลัย


Figure 4.52 Scanningelectron microscope showed the thickness of intramural



Figure 4.53 Scanning electron microscope showed the thickness of intramural capillary $(\mu \mathrm{m})$ from 20 week SEZ Cl 0,01 mg rat. จุหาลงกรณ์มหาวิทยาลัย


Figure 4.54 Scanning electron microscope showed the thickness of intramural capillary ( 4 m ) from 20 week STZ -Cl 1 mg rat. ศูนยวิทยทรพยากร จุหาลงกรณ์มหาวิทยาลัย


Figure 4.55 Scanning eflectron microscope showed the thickness of intramural capillary ( $\mu$ mi) from 20 week STZ-C1 10 mg rat ศูนยวีทยทรพยากร จุหาลงกรณ์มหาวิทยาลัย


Figure 4.56 Scanning electron microscope showed the thickness of intramural capillary ( $\mu \mathrm{m}$ ) from 20 week STZ-C8 0.01 mg rat. ศูนยวทยทรพยากร จุหาลงกรณ์มหาวิทยาลัย


Figure 4.57 Scanning electron microscope showed the thickness of intramural capillary ( $\mu \mathrm{m}$ from 20 week STZ-C8 1 mg rat.
ศูนยวทยยทรพยากร จุหาลงกรณ์มหาวิทยาลัย


Figure 4.58 Scanning electron microscope showed the thickness of intramural capillary ( $\mu \mathrm{m}$ ) from 20 week STZ-C8 10 mg rat. ศูนยวทยยรพยากร จุหาลงกรณ์มหาวิทยาลัย


[^0]:    * Statistical difference as compared to controls( $\mathrm{p}<0.05$ ).
    \# Statistical difference as compared to STZ-rats( $\mathrm{p}<0.05$ ).

[^1]:    * Statistical difference as compared to controls( $\mathrm{p}<0.05$ ).
    \# Statistical difference as compared to STZ-rats $(\mathrm{p}<0.05)$.

[^2]:    * Statistical difference as compared to controls( $\mathrm{p}<0.05$ ).
    \# Statistical difference as compared to STZ-rats( $\mathrm{p}<0.05$ ).

