CHAPTER VI
CONCLUSION

By using the intravital fluorescent and electron microscopic studies,the antioxidant effects of vitamin C on endothelial dysfunction and on ultrastructural changes of cerebral microcirculation in STZ were examined. The followings are the conclusions of our findings.

1. In all three monitoring time point (12, 24 and 36 wks.), the levels of plasma vitamin C in STZ-rats were significantly decreased ($p<0.01$). Plasma vitamin C level were significantly normalized to control values after the supplementation of vitamin C.

2. Vitamin C could decreased blood glucose in 36 wks STZ-vit C rats significantly as to compared to STZ-rats (STZ-rats = 398.12 ± 17.12 mg/dl, STZ-vit C rats =317.28 ± 29.58 mg/dl).

3. In 24 and 36 wks after STZ injections, hypercholesterolemia and hypertriglyceridemia were significantly occurred in STZ-rats (24 wks : STZ-rats = 114.80 ± 78.46 mg/dl., 36 wks : STZ-rats = 154.17 ± 37.09 mg/dl.). However, the supplementation of vitamin C could normalize those abnormalities of plasma cholesterol and triglyceride (24 wks:STZ-vit C = 71.00 ± 15.47 mg/dl , 36 wks :STZ-vit C = 53.56 ± 8.13 mg/dl).

4. MAP of STZ-vit C rats were significantly decreased as compared to those values of STZ-rats (12 wks: STZ-rats = 128.28 ± 2.64 to 103.74 ± 7.85 ($p<0.01$), 24 wks :STZ-rats = 128.41 ± 6.31 to 110.82 ± 1.30 ($P<0.05$) and 36 wks: STZ- rats = 125.72 ± 3.21 to 111.00 ± 3.09 ($p<0.01$)).

5. For all three monitoring time points, the cerebral arteriolar flow rate was significantly decreased only in 36 wks (0.40 ± 0.04 nl/sec)

compared with control (1.99 ± 0.10 nl/sec)($p<0.01$).But,STZ-vit C, arteriolar flow rate was significantly increased as compared to those values of STZ- rats (STZ-rats = 0.40 ± 0.04 nl/sec, STZ-vit C = 1.92 ± 0.09 nl/sec).

6. Using intravital fluorescent microscopic study, the significant increase in leukocytes adhesion to the endothelial lining of postcapillary venules (diameter = 10-50 μm) was observed in STZ-rats compared with CON-rats for all three monitoring time.The greatest increase was observed in 36 wks:STZ-rats (STZ-rats = 4.63 ± 0.33 cell/100μm,CON-rats = 0.62 ± 0.16 cell/100μm. Interestingly, these leukocytes adhesion were almost entirely prevented by vitamin C supplementation for all three monitoring time points (12 wks; STZ-rats: 3.77 ± 0.29, STZ-vit C rats: 1.18 ± 0.36 / 24 wks: STZ-rats = 3.74 ± 0.28, STZ-vit C rats = 0.468 ± 0.21 / 36 wks; STZ-rats: 4.63 ± 0.33, STZ-vit C rats: 0.19 ± 0.18 cells/100μm).

7. Using intravital fluorescent microscopy, the responses of endothelium-dependent vasodilation to Ach and ADP of cerebral arterioles were examined and presented as percent changes of vascular diameter from the baseline (20-30μm). The impairment of endothelial dependent vasodilation was observed in STZ-rats, and more severe impairment was occurred in 36 wks:STZ-rats.(responses to Ach = 34.63 ± 2.81 in STZ-rats, 63.68 ± 14.47 % changes from baseline). The supplementation of vitamin C, could significantly prevent these endothelium-dependent vasodilation to Ach and ADP. Whereas the endothelium-independent vasodilator responses to NTG was not altered in any groups. From these results it can demonstrated that the abnormal vascular function is presented only at endothelial cells, not on vascular smooth muscle cells.

8. Finally, the electronmicroscopic examination demonstrated that the thickness of small arterioles and capillary basement membrane in STZ-rats were significantly increase than those of CON-rats (capillary; 12 wks; STZ-rats= 0.133 ± 0.062 , 12 wks:CON-rats= 0.058 ± 0.003;$p<0.01$ / 36wks; STZ-rats=0.161 ± 0.010 , in CON-rats=0.073±0.004 .). Interestingly,vitamin C supplementation could prevent these diabetic ultrastructural changes.