CHAPTER V

DISCUSSION AND CONCLUSION

1. Severity of diabetes

Diabetes was induced by a single intraperitoneal injection of 55mg/kg body weight of Streptozotocin (STZ) in the DV and DI groups. As expected, the body weight was significantly decreased while the plasma glucose was markedly increased in the DV and DI groups when compared to the control group. There were no significant differences in these two parameters between the DV and DI groups. Therefore, the u0126 treatment did not affect the severity of diabetes, suggesting that activation of ERK does not play an important role in this aspect.

2. Abnormal motor nerve conduction velocity

MNCV was significantly decreased in the DV and DI groups in the forth week but not at the end of experiment (the seventh week) compared with the C group. The transient slowing of MNCV might be due to the recovery of the abnormality.In contrast, the previous study (Burnand et al., 2004) and (Sufyan et al., 2006) has found the MNCV deficit in the eighth week. As a result, the recovery seen in this study might be due to the technical problems. Therefore, we could not conclude that u0126 did not affect the nerve conduction velocity abnormality in diabetes. Repeated experiment in the future is needed to verify the role of ERK in nerve conduction deficit.

3. Western blot analysis

Western blot analysis showed that the level of ERK-P was significantly increased in the DV. The previous study (Fernyhough et al., 1999) and (Price et al., 2003) has found activation of ERK increased in DRG neuron from diabetic rats. In addition, the level of ERK-P in the DI was lower than that in the DV and similar to the C groups. Therefore, the ERK inhibitor u0126 can inhibit ERK activation and is an effective tool to study the role of ERK in diabetic neuropathy.

4. Morphological studies

4.1 Nerve morphometry

The results of this study showed the decreased myelin thickness including the trend toward reduced axon diameter and number of large myelinated fiber. Zemp C et al., 1981 has reported the similar findings. Structural abnormalities can explain the decreased nerve conduction velocity. Since these abnormal findings were partly reversed in the the DV and DI groups, whether ERK activation plays a role in the development of nerve pathology in diabetic rats remains to be proved. Early start and /or longer duration of the treatment should be done in the future studies.

4.2 DRG morphometry

The number of L4 DRG neurons was decreased in the DV and DI groups compared with the C group. The previous study (Motoko et al., 2002) has found the similar reduction in the number of L4 DRG neurons which might be due to apoptosis (Russel et al., 1999). Moreover, no significant difference between the DV and DI groups was found, suggesting that u0126 did not affect the loss of L4 DRG neuron in diabetic rats. In addition, areas of nucleus and nucleolus in the DV and DI groups were not different from those of the C group. Therefore, these two parameters were not altered in diabetes.

In conclusion, the ERK inhibition by u0126 confirmed with Western blot analysis did not affect severity of diabetes and DRG morphometric abnormalities. However, the effect of u0126 on slowing of MNCV could not be concluded due to the technical problems. Moreover, there was a trend toward improvement in the nerve pathology with the ERK inhibition. In order to understand the precise role of ERK activation in diabetic neuropathy, future studies with modifications of the treatment protocol must be done.