

CHAPTER VI

CONCLUSION

1. In a long term memory-related behavior study, *C. comosa* hexane extract (CHE) could improve the spatial reference memory on the OVX rats, whose memory was found to be impaired at the 67th day after the OVX surgery. This effect of CHE is similar to that estradiol did. OVX slightly impaired the spatial memory on the rat in a short-term Morris water maze study while CHE and estradiol treatment augment the OVX effect. OVX did not affect the working memory on the rat.

2. CHE selectively affected the hippocampal estrogen receptor alpha mRNA concentration on the OVX rats, while estradiol affecting both ER alpha and beta. However, CHE did not affect the ER level in the ovary intact rats.

3. A 3D-reconstruction method had been developed to study the brain morphology. The method provided a 3 dimensional vision for inspecting the brain and its internal structures. Volume of each reconstructed structure could be measured. By using this method, the hippocampal volumes were compared between the groups in the long-term behaviors test. CHE and estradiol increased the proportional hippocampal volumes to the body weight while the absolute volume was related to the animal body weight. CHE and estradiol also increased the proportional neuron densities in CA1 and CA3 areas.

4. CHE could affect the antioxidant enzyme (SOD, GPx, CAT) activities in the rat brains with the oxidative stress induced by ethanol. CHE could act against the enzyme activity in the specific brain regions (i.e. GPx in hippocampus), but the effects was augmented by the ethanol (i.e. SOD in cerebellum) and the synergic effects of CHE and ethanol (i.e. catalase in cerebellum) were observed.

5. Pharmacokinetics study of the CHE provided the *in vivo* exposure screening results for identify the compounds which were absorbed from the gastric-intestinal track. The pharmacokinetic parameter of these absorbed compounds, such as the bioavailability, systematic clearance time, distribution in the brain and uterus and biological levels, provided the information to design the more delicate experiments in the active compounds screening and further studies.

Conclusively, the hypothesis that *C. comosa* hexane extract could exert the similar effect to the estrogen on the memory of OVX rat was proved in the memory-related behaviors study, estrogen receptor mRNA quantification study and brain morphology study. The CHE could also affect the antioxidant enzyme activities in the rat brain with or without ethanol-induced oxidative stress. All these evidence support that CHE has a high potential to be the substitute for estrogen replacement therapy to against the cognitive degeneration on the postmenopausal women. Pharmacokinetics study in the animal provides the options for selecting the compounds for further studies.