CHAPTER VI

CONCLUSION

Experimental results of the present study suggested following conclusions:

1. The TD_{50} of THF and GBL as considered from the loss of righting reflex test were 15.18 mmol/kg (95% CI, 11.88–19.39 mmol/kg) and 4.60 mmol/kg (95% CI, 3.25-6.51 mmol/kg), respectively. The TD_{50} of THF and GBL as considered from the failure in rotarod test were 7.00 mmol/kg (95% CI, 5.22-9.40 mmol/kg), and 0.85 mmol/kg (95% CI, 0.52-1.38 mmol/kg), respectively.

2. The LD_{50} of THF for intracerebroventricular injection was 79.28 μmol/mice (95% CI, 45.87-137.05 μmol/mice).

3. THF and GBL had depressant effects on locomotor activity, but the pattern of effects on locomotor activity at low doses of THF and GBL was different. At THF doses of 3, 5, and 10 mmol/kg, i.p., locomotor activity was reduced and different from that of saline for the entire 150-min test period. At GBL doses of 1 , 3, and 5 mmol/kg, locomotor activity was reduced and was different from that of saline for the first 60 min of testing with 1 and 3 mmol/kg and for the first 80 min of testing with 5 mmol/kg, and then activity was returned to baseline. At GBL dose of 10 mmol/kg, locomotor activity was reduced for the entire 150-min test period.

4. In the open-field and elevated plus maze test, THF (0.1 and 0.3 mmol/kg, i.p.), and GBL (0.1 and 0.3 mmol/kg, i.p.) did not demonstrate any anxiolytic properties.

5. Deficits in spatial learning and long term memory retrieval were observed at doses of 1 and 3 mmol/kg, i.p. THF and at a dose of 1 mmol/kg GBL, with repeated administration. There were no effects of THF and GBL at the doses of 0.1 and 0.3 mmol/kg on working memory in Y-maze test.

6. THF and GBL, at doses of 0.1 and 0.3 mmol/kg, i.p. did not demonstrate any antidepressant effects in the open-space swimming model.

7. Chronic treatment with THF (10 mmol/kg, i.p. and challenged with THF 15 mmol/kg, i.p.) showed marked tolerance on the sedative-hypnotic effects.

8. THF (3 and 5 mmol/kg, i.p.) and GBL (0.5 and 1 mmol/kg, i.p.) did not have reinforcing properties, since the place preference score and differences in time spent in white compartment (between preconditioning and postconditioning in the conditioned place preference test) were not different when compared to the control mice.

9. Effects of THF on impairment of motor function in the rotarod test could be antagonized for a short duration by CGP 35348, a $GABA_B$ receptor antagonist. It is suggestive that the mechanism of THF-induced motor impairment may involve $GABA_B$ receptors.