CHAPTER V

CONCLUSION

In order to evaluate the antidepressant activity of CU 763-14-07 and CU 763-14-10, the behavioral despair test (Forced swimming test), the locomotor activity test and the rotarod test were chosen. In addition, monoamine levels in the rat brain measured by HPLC were investigated in subchronic treatment (7 days, intraperitoneally). Amitriptyline and pargyline, standard antidepressant drugs, were used as positive controls in this study.

Forced swimming (behavioral despair) test is a behavioral animal model that is one of the most widely used screening tests for antidepressant drugs. It is simple, short, and cheap to perform. This model is sensitive to many antidepressant agents. The combination with other tests, such as motor activity and rotarod test, allows specific assessment of antidepressant activity.

In an animal model of behavioral despair test, the treatment of experimental animals with a nonselective MAO Inhibitor, pargyline, and a tricyclic antidepressant, amitriptyline, produced significant decreases in the immobility time. These standard antidepressants were used as positive controls to check the validity of the experimental protocols.

The present study showed a degree of antidepressant activity of CU 763-14-07 and CU 763-14-10, both test substances produced significant decreases in immobility time in the forced swimming test at certain doses (10 mg/kg and 20 mg/kg for CU 763-14-07 and 20 mg/kg for CU 763-14-10). CU 763-14-07 and CU 763-14-10 did not increase the motor activity of mice. On the other hand, they suppressed motor activity especially at higher doses. These results suggested that, firstly, the improved performance of animals was not due to the increased motor activity and, secondly, the

ineffectiveness of these two substances at higher doses might be due to the interaction of antidepressant activity with decreased motor activity. Furthermore, in rotarod test, both of the test compounds did not induce motor incoordination or muscle relaxation. These findings implied the CNS depressant activity of CU 763-14-07 and CU 763-14-10 found at higher doses might lead to compromised motor activity but they were not associated with deficits in psychomotor control such as motor incoordination or muscle relaxation.

The study of monoamine neurotransmitter levels in the rat brain revealed that CU 763-14-07 administration induced only a significant increase in NE levels whereas CU 763-14-10 significantly increased NE, DA and 5-HT levels in the rat brain. These changes in CNS monoamine levels are in accordance with the hypothesis that increased monoamine neurotransmitter activity in the brain might play a role in the antidepressant activity of CU 763-14-07 and CU 763-14-10.

In conclusion, these results demonstrated that CU 763-14-07 and CU 763-14-10 displayed a certain degree of antidepressant activity in the primary screening tests. Therefore, they may be potential candidates for drug development as antidepressants. However, further studies are required to elaborate their mechanism, efficacy and safety.