CHAPTER VII
CONCLUSION

This study demonstrates the involvement of autophagy and apoptosis during caffeine potentiated METH-induced neurotoxicity in an *in vitro* model, which represented the combination effect of METH and caffeine in Ya-Ba tablet. We confirm that caffeine enhance METH-induced toxicity in neurons by cell viability assay. The induction of apoptosis, as seen by activation of caspase3 and increase of autophagic flux, as shown by the reduction of p-mTOR, p-4EPb1, and LC3II expression was found in cells after combined treated of caffeine with METH. Inhibition of autophagy in two drug combination treatment significantly reduced cell viability suggesting the protective role of autophagy on caffeine potentiated METH toxicity. Taken together, this finding reveals the dual roles of caffeine in potentiating METH-induced neurotoxicity. First caffeine potentiates METH-induced neurotoxicity by induction of apoptosis cell death. Second, caffeine plays protective role by increasing autophagic flux that can antagonize apoptotic cell death. However, further study to elucidate the involvement of other pathways those play roles in apoptosis and autophagy is necessary.