CHAPTER V
CONCLUSION

By using three experimental protocols including *in vivo* whole body model, dorsal skindfold chamber model, and isolated perfused rat heart model, the pharmacological effects of AM on cardiovascular functions were investigated. The parameters representing the cardiovscular functions were monitored as follows: mean arterial pressure (MAP), heart rate (HR), arteriolar diameters, cardiac contractility (dP/dT), and coronary blood flow (CBF). The overall experimental results could be concluded following :-

1). *In vivo* whole body model, the iv injection of 1nmol/kg BW of AM caused the significant decrease in MAP by 29.9±3.3 mmHg ($p<0.001$). There was no significant change in HR during this 10 minute hypotensive interval in this model.

2). By using dorsal skindfold chamber model , the topical application of 10^{-7} M of AM for 3 minute significantly increased in arteriolar diameters (4.8±1.3% for the second order arterioles and 14.2±3.6% for the third order arterioles) The arterioles with the diameter of 30-40 μm were significantly increased more than the arterioles with the diameter of 50-60 μm.

3). Using the isolated perfused rat heart model, the cardiac contractility was significantly decreased by bolus injection of 20 μg AM (-3.72±1.14%; $p<0.05$). Concomitantly, the positive chronotropic effect of AM was also observed. Heart rate was significantly increased (+9.48±1.35%; $p<0.01$).

4). In isolated perfused rat heart model, the results also indicated that the bolus injection of AM were significantly increased CBF (+18.93±

0.63%; $p<0.001$).

5). After endothelial degradation by Triton X-100, the slightly but significantly relaxing response to AM was observed (+4.64±1.50% in endothelium-damage; +15.70±0.91% in endothelium-intact). The result implied that AM-induced coronary vasodilation are mediated via both endothelium-dependent and endothelium-independent mechanisms.

6). Using L-NNA, the NO synthase (eNOS and iNOS) inhibitor, the result indicated that the mechanism of AM on coronary vasodilation is endothelium-dependent and assesses through EDRF (NO) (CBF increase by 14.90±1.22% in AM+L-NNA group; by 18.93±1.42% in AM alone group).

7). Using glibenclamide, K_{ATP} channels blocker, the result indicated that the mechanism of AM on coronary vasodilation is also mediated via K_{ATP} channels(CBF increase by 5.46±0.67% in AM+glibenclamide group; by 18.93±1.42% in AM alone group). Since specific receptors for AM and K_{ATP} channels have been identified in endothelial cells as well as in vascular smooth muscle cells, AM may activate K_{ATP} channels on both endothelial cells and vascular smooth muscle cells resulting in the coronary vasodilation.