CHAPTER I

INTRODUCTION AND AIMS

The cobra is a reptilian in family Elapidae. Among the venoms of cobra, those of *Naja naja*, *N. n. atra*, *N. haje*, *N. nigricollis* and *Hemachatus haemacatus* have been most extensively studied. *Naja naja kaouthia*, one of poisonous snake which can be found throughout Thailand. It is well established that in most animals species, the main cause of death due to cobra venom poisoning is respiratory paralysis. Intravenous injection of this venom has been shown to be cause of cardiac arrest (Lee, 1979).

Cobra venom contains several pharmacological active polypeptides such as neurotoxins, phospholipase A and cardiotoxins (Meldrum, 1965; Lee, 1972; Yang, 1974). The most lethal component in cobra venom is the curaremimetic postsynaptic neurotoxin. Cardiotoxin, when contaminated with phospholipase A, cause a lysis of red blood cells (Condrea et al., 1964; Klibansky et al., 1968; Vogt et al., 1970). The lethality of cardiotoxin is, however, generally much lower than that of the neurotoxin. The toxicity of the cardiotoxin is closely related to marked permeability of the membranes of a variety of cell types which occur in the case of cardiac arrest (Lee, 1972).

The various actions of cobra venoms are probably a consequence of different components that have specific activities. The hemolysin and the crude cobra venom have been shown to be cause of irregular heart beats when it was applied to toad heart in situ (Sarkar et al., 1942). The venom could produce systolic arrest (Elliot, 1905; Cushny and Yagi, 1918; Epstein, 1930). In the absence of calcium ions in perfusion fluid, the cardiac muscle has been shown to become less sensitive to the venom, which produce stoppage of beat without signs of systolic contracture (Gottdenker and Wachstein, 1940). Cardiotoxin also caused systolic cardiac arrest in the absence of

external calcium ions, indicating a direct action on cardiac muscle (Sarkar, 1951). Cobra venom caused contraction of skeletal muscles. This action lost if the cell membrane was removed and the primary site of action was the membrane but was not directly on the contractile filaments (Sarkar, 1951). Recent work has suggested that after the cardiotoxin binds to the membrane, it caused depolarization which leaded to calcium influx and/ or release of calcium from the sarcoplasmic reticulum; and the toxin formed membrane pores which allow extracellular calcium to enter the muscle and caused contracture (Harvey et al., 1982). Cardiotoxic fraction from cobra venom has been found to inhibit Na^+-K^+ ATPase activity of membrane fragments of various cells (Zaheer et al., 1975). It was suggested that cardiotoxin bound to membrane lipids that were associated with the ATPase enzyme and, thereby, blocked the sodium pump. The consequent intracellular accumulation of ions would lead to osmotic lysis (Tu, 1991). Each of these possibilities leads to examine several possible mechanisms of action of the venom and its cardiotoxic fraction.

The studies in isolated rat heart have shown that low dose of crude venom from *Naja naja kaouthia* produced mild increase in heart rate but higher doses produced reduction on both rate and force of contraction (Prayoonsri Khowean, 1990). However, these effects have not been done by using cardiotoxic fraction, the component in cobra venom. It is well-known that changes in cardiovascular system will affect the normal function of organs. Changes in cardiovascular system by the effect of cobra venom which may affect to the kidney function have not been elucidated. Thus, the purpose of the present study was undertaken to clarify possible effects of crude venom and cardiotoxic fraction from *Naja naja kaouthia* on renal function and general circulation. Whether changes of bodily function by the effect of envenomation relate to an elevation of intracellular calcium, verapamil, a calcium channel blocker was used in the present experiment.