Chapter I

Introduction and Aims

The kidneys are held to be critical organs during snakebite. Patients bitten by Russell's viper have variable clinical syndromes and acute renal failure is one of the causes of death (Aung-Khin, 1978 ; Sarange et al., 1980). Many papers reported about the effects of Russell's viper venom on the renal function, but the mechanisms responsible for development of acute renal failure following envenomation are still unclear, for example alteration of systemic circulation and the direct nephrotoxic effect of the venom.

The early reports have been shown that the venom causes renal dysfunction by the effect on vascular system that changes the renal hemodynamics (Chugh et al., 1975 ; Jeyarajah,1984). However there was no correlation between the severity of renal failure and coagulopathies (Shastry et al., 1977) and acute renal failure has been noted in some cases of Russell's viper bite without hypotension (Sitprija and Boonpucknavig, 1977). The venom affected general cardiovascular for a short period, then general circulation returned to normal within two days while renal dysfunction still persisted (Tungthanathanich, 1983 ; Tongvonchai, 1984). The local vasoconstriction occurred in the kidney after envenomation which has been suggested to be mediated through renin-angiotensin system activation (Chaiyabutr, 1985). In the isolated perfused rat kidney, the venom produced a dose dependent fall in inulin clearance and rise in fractional excretion of sodium, demonstrated the direct nephrotoxicity of

the venom (Ratcliffe and Pukrittayakamee, 1985). Changes of peritubular transmembrane potential were recorded in the triturus proximal tubular cell during envenomation. The results were compared with actions of 2-4 dinitrophenol (DNP) on the depolarization of cell membrane and were discussed in the role of the venom on the mechanism of transport of ions across the cell membrane (Chaiyabutr et al., 1985). It has been known that the transport of sodium ion in the renal tubular cell is active transport. Adenosine triphosphate (ATP) which is produced mainly by oxidative phosphorylation in mitochondria is generally used as the energy source. The specific binding sites with very high affinity for thyroid hormone have been reported on the inner membrane of rat liver mitochondria, direct effects of thyroid hormones to increase oxygen consumption when added in vitro to isolated rat liver mitochondria and to increase ATP formation have also been reported (Oppenheimer, 1979)

The treatment with thyroid hormone has been reported to enhance recovery from toxic acute renal failure (Siegel et al., 1984 ; Cronin and Newman, 1985) and ischemic acute renal failure in rat (gaudio et al., 1984). Rats, which are induced acute renal failure by mercuric chloride, treated with thyroxine had an accelerated reversal of the defect in several enzymes including alkaline phosphatase and Na-K ATPase (Schulte-Wissermanh et al., 1977). Thyroid hormone not only increase Na-K ATPase activity, but also increase the number of Na-K ATPase units in the renal cortex. (Lo et al., 1976 ; Lo and Edelman, 1976). This hormone is also known to augment protein synthesis and stimulate glucose and amino acid uptake by epithelial cells (Segal and Ingbar, 1979 ; Segal and Ingbar, 1980).

The studies on the relationship between the role of thyroid hormone and the effect of Russell's viper venom on renal functions have not been assessed before. The present investigation aims to study whether changes in renal function either hyperthyroid or hypothyroid rats is affected by Russell's viper venom.