CHAPTER I

INTRODUCTION AND AIMS

It is widely accepted that acute renal failure due to Viperine snake bite (*Vipera russelli siamensis*) is most common and one of the causes of death in patients who have been bitten (Chugh *et al.*, 1975; 1984; Chugh and Sakhuja, 1980; Sitprija and Boonpucknavig, 1979). It is also the one of the important health problems in the rural areas of Thailand (Trisnananda, 1979). The Russell's viper venom contains the elements of C, H, N, S, O and organic components of lipid, carbohydrate, amino acid, nucleoside, nucleotide, organic phosphate compounds (Ganguly and Malkana, 1936; Iwanana and Suzuki, 1979). The venom also consists of various proteolytic enzymes including several isoenzymes of phospholipase A_2, kininogenase, phosphodiesterase, amino acid esterase, proteinase, peptidase, α-amino acid oxidase, hyaluronidase, 5' nucleotidase, deoxyribonuclease (Iwanaga and Suzuki, 1979). The rest contains of many substances that remain unpurify. The factor X activating enzyme, proteinase, in Russell's viper venom, is well known as a potent activated factor relevant to the clotting system and also could be used for differentiation of bleeding tendency from factor VII or factor X deficiency (Macfarlane, 1961; 1967). The properties of venom are powerful coagulation (Aung-Khin, 1977; 1978), vasculotoxic (Varagunam and Panabokke, 1970; Shastry *et al.*, 1977), hematotoxic (Mahasandana *et al.*, 1980), and direct cytotoxic (Chugh *et al.*, 1975; Sitprija

and Boonpucknavig, 1979). These toxins have been shown to cause the release of various autacoids, e.g. histamine, prostaglandins, kinin, 5-hydroxytryptamin, slow reacting substance (Rothchild and Rothchild 1979). Recently, the Russell's viper venom was separated by means of Sephadex G-75 column chromatography into five fractions and phospholipase A_2 activity was concentrated in fraction II and III (Huang and Lee, 1984). Pharmacological properties of phospholipase A_2 from snake venom was shown to have a variety of actions, for example : hypotension (Ho and Lee, 1981), neurotoxicity (Lee and Ho, 1982), local capillary damage (Fearn *et al.*, 1964), tissue necrosis (Suzuki and Iwanaga, 1970), and anticoagulant (Boffa *et al.*, 1982). The releasing autacoids probably have some effects on several organ system (Huang, 1984a; 1984b). The changes in kidney function, including the release of some autacoids such as prostaglandins and kinin have been reported (Freeman, 1984). The persistent renal vasoconstriction is also shown after envenomation (Tungthanathanich, 1983). The effects of various enzymes from venom are complex actions. The factor X activating enzyme could convert autoprothrombin C (factor X) to activated factor X which occur rapidly (Macfarlane, 1967) and was due to DIC (disseminated intravascular coagulation) in patients (Chugh *et al.*, 1975).

The pathogenesis of acute renal faillure after envenomation remains obscure. Pathophysiological changes in human victims can be done by only observations in the hospital. Renal hemodynamic studies in the patients during the period of renal failure have shown a decrease in renal cortical blood flow (Sitprija and Boonpucknavig, 1979). Several contributing factors are considered as being

responsible for the development of renal failure include hypotension (Sitprija and Boonpucknavig, 1979), intravascular coagulation (Aung-Khin, 1977; Chugh *et al.*, 1977) intravascular hemolysis (Condrea, 1979), hemoglobinuria (Reid, 1968; Peiris *et al.*, 1969), arteritis (Sitprija *et al.*, 1974), glomerular lesions and nephrotoxicity (Sitprija and Boonpucknavig, 1979). Scattered reports concerning the renal lesions include tubular necrosis (Chugh *et al.*, 1975; Sarangi *et al.*, 1980), cortical necrosis (Oram *et al.*, 1963), hemorrhagic glomerulonephritis (Sitprija and Boonpucknavig, 1980), arteritis (Sitprija *et al.*, 1974), hemorrhagic interstitial nephritis (Sitprija *et al.*, 1982), mesangial proliferation (Sitprija and Boonpucknavig, 1977) have been pointed out. The basis for current understanding of the role of venom can be defined mainly from the experimental model. Previous reports indicated that Russell's viper venom 0.1 mg/kg bw. in dog was given intravenously showed a depression in cardiovascular and renal functions (Tungthanathanich, 1983). It is interesting that the decrement of renal functions persisted while the cardiovascular changes have been recovered. No evidence is available so far to indicate if the changes in kidney functions are due to direct toxic action of the venom by toxin or if it occur indirectly as a consequent of cardiovascular change or in combinations. In the past decade, the effect of *Agkistrodon piscivorus* venom enhanced the activity of alkaline phosphatase and leucine amino-peptidase in urine of rats (Raab and Kaiser, 1966). The other evidence from the study on crotoxin attributed the renal tubular lesions partly to the effect of lysocithin formed by the activity of phospholipase A_2 (Hadler and Brazil, 1966). The results of renal

pathological changes are also due to hemorrhage resulting from consumptive coagulopathy (Aung-Khin, 1978; Chugh *et al.*, 1977), vasculitis (Varagunam and Panabokke, 1980) and direct nephrotoxicity (Sitprija and Boonpucknavig, 1979).

The present investigation aims to elucidate the direct effect of Russell's viper venom on renal hemodynamics with relation to renal morphological changes following intrarenal infusion of venom.