CHAPTER I

INTRODUCTION

Cobra (Naja) is a common snake throughout Asia and Africa, and cobra bite is a major cause of snake bite mortality and morbidity in Thailand. It was responsible for 25% of the 4,850 cases of snake bites reported in Thailand during a 5 year period with a case fatality of 6.5% (1).

Cobra venom is known to contain several pharmacologically active components. The most toxic fractions have been shown to be neurotoxins. Other constituents such as membrane toxins and some of the enzymes certainly contribute to the overall toxicity of the venom (2).

Neurotoxin, a curare-like postsynaptic toxin, is a potent neuromuscular blocking agent. It was shown to block neuromuscular transmission by acting on acetylcholine receptor at the motor end plate of skeletal myoneural junction (3,4,5,6), resulting in flaccid paralysis. Death in most animals is due to peripheral paralysis of respiratory muscles (2).

Membrane toxins are a group of toxins which increase the permeability of various membranes. The toxins included in this group are cardiotoxin, cytotoxin and direct lytic factor (DLF), etc. (7).

Very few pharmacokinetic studies with cobra venom have been reported. Tseng et al.in 1968 (8) studied the absorption and distribution of Formosan cobra (Naja naja atra) venom and found that crude cobra venom as well as cardiotoxin were absorbed very slowly from the injection site following a subcutaneous injection, while neurotoxin was absorbed much faster. After intravenous injection in rabbits, the plasma levels of cardiotoxin and crude venom declined much faster than that of neurotoxin. Most of the cardiotoxin and crude venom were distributed in the kidney, liver and lung while neurotoxin accumulated mostly in the kidney. The toxins were excreted in the urine (8,9). Nevertheless, there has not been any report of the pharmacokinetics of Thai cobra venom of which the amount of neurotoxin is higher than that of other cobra venoms (10).

Since cobra bites may result in serious respiratory paralysis and death, a prompt and proper management of cobra bites is required. Antivenine has been shown to be the most effective therapeutic agent in reversing the systemic poisoning in most snake bite victims although hypersensitivity reactions may occur. Other modes of treatment have been employed, and at Chulalongkorn Hospital, artificial respiration together with other supportive measures were used successfully instead of the antivenine (11). No significant difference in mortality rate was observed between the antivenine and non-antivenine treated groups. Moreover, the non-antivenine treated regimen was claimed to be beneficial in avoiding serum sickness as well as the cost in treating such complications. Nevertheless, it demands

sophisticated equipment and setups such as a respirator and well-trained personnel in an intensive care unit.

Since the use of specific antivenine is still a controversial issue in the treatment of cobra bites in Thailand, it is essential to investigate the basic pharmacokinetics of cobra venom in envenomed victims and its modification by antivenine administration. This might provide a better understanding on the action of Thai cobra venom and establish the grounds for the proper management of the Thai cobra bite. However, such a study in man is affected by several variables such as the quantity of envenoming, the time between bite and treatment, etc. Therefore, it was selected that this problem be studied on experimental animals instead of patients.

The present work was undertaken in order to study the kinetics of Thai cobra venom in rabbits and the effects of antivenine on cobra venom levels and survival. Antivenine were administered at different times after venom injection and the enzyme-linked immunosorbent assay (double-antibody sandwich method) was developed for the detection and quantitation of cobra venom in this study.