CHAPTER I

INTRODUCTION AND AIM

Ethylene glycol (EG) is an alcohol which contains a hydroxyl group on each carbon atom. It is completely dissolved in water. EG has a low freezing point and is a relatively nonvolatile liquid with a boiling point of 197 °C. Because of its properties, EG is used as an antifreeze solution or a coolant solution for internal combustion engines. The sweet taste of EG encourages consumption by dogs and cats (Bahri, 1991). After ingestion, EG is rapidly absorbed from the gastrointestinal tract and uniformly distributed to the blood and the tissues (Bachmann and Golberg, 1971). EG will be changed to toxic metabolites by the liver enzymes. The life-threatening features of EG intoxication are due to toxic metabolites of EG rather than to the parent compound itself. Common clinical signs are ataxia, muscle fasciculation, depression vomiting, and hypothermia. The toxic metabolites may enter the cerebrospinal fluid, causing ataxia and signs of drunkenness (Thrall, Grauer, and Mero, 1984; Dial et al.,1994a).

Even though EG intoxication is not the most common cause of intoxication in small animals, it has clinical toxicological significance because of the high associated mortality. The high death rate has been attributed to the delay in the presentation, diagnosis, and therapy, since the successful treatment has to be administered within four hours after ingestion. Drugs of choice for the treatment of intoxicated animals are ethanol and 4-methylpyrazole. Both of them limit the EG transformation by the competitive inhibition and allow the EG to be excreted unchanged in the urine.

The death is fundamentally due to renal failure and uremia (Sanyer, Oehme, and McGravin, 1973). EG has been shown to induce the osmotic diuresis and to

promote dehydration. Nephrotoxic metabolites of EG can be detected in the serum of intoxicated dogs as early as three hours after EG ingestion (Bahri, 1991). Changes in serum chemistry imply that renal damages are apparent from 18 to 24 hours after EG ingestion (Smith et al., 1990). Therefore, the protection of acute renal failure has not been successful in late-diagnostic animals.

The typical renal lesions of EG intoxication are congestion, the presence of tubular proteinaceous casts, and various degrees of tubular damage ranging from hydropic degeneration to necrosis with karyorrhesis, pyknotic nuclei, and disrupted tubular epithelium(Sanyer et al., 1973). The tubular ultrastructural lesions have been shown to be the cellular vacuolization, the distention of the parabasal extracellular spaces, the formation of apical cytoplasmic buds, the increase of mitochondria density and cellular rupture (Smith et al.,1990). These tubular lesions occurred as early as 5 hours after EG ingestion and they showed the most prominent at 18 to 24 hours. A similar pattern of tubular damages has been described from the experimental studies for the ischemic renal failure(Dobyan, Nagle, and Bulger, 1977), and other nephrotoxic forms of acute renal failure (Ganote, Reimer, and Jennings, 1974). The predilection of the tubular damages to injury in multiple forms may be related to their high level of metabolic activity, meanwhile numerous mitochondria of the tubular cells are susceptible to the toxic effects of the EG metabolites which result in the lack of energy for active transport and the loss of the tubular functions.

Form previous studies, few data are available on changes in general circulation, renal hemodynamics, and renal function relating to the free radical formations of intoxicated animals by EG. However, there are several reports of tubular necrosis related to the free radical formations, for example, the ischemic acute renal failure (Paller, Holidal, and Feris, 1984), the glycerol-induced acute renal failure (Guidet and Shah, 1989), and the gentamicin-induced acute renal failure (Walker and Shah, 1988).

The objectives of this experiment were, therefore, to study the general circulation and the renal circulation which are related to kidney function. and to

clarify the mechanism of tubular necrosis by measuring the kidney lipid peroxide concentration and the xanthine oxidase activity in EG intoxicated dogs.