Chapter I

Introduction

It has been known that a low potassium diet intake results in an increase in potassium reabsorption by the distal nephron and of renal conservation at this time (Imbert-Teboul et al., 1987). During potassium defeciency, the morphological and physiological changes of intercalated cells have been observed. These effects cause the increasing of K-ATPase activity (Malnic, 1964; Linas et al., 1979), and also the reabsorption of potassium is increased. However, the molecular basis for active potassium reabsorption in kidney cells remains unknown.

Potassium reabsorption and hydrogen ion secretion have been shown to link functionally which is supported by the fact that acidosis is accompanied with alterations of luminal membranes of intercalated cells (Hagege et al., 1974). The similar result was also observed during potassium-depletion (Sachs et al., 1982).

H-K ATPase has been first described in frog gastric microsomes and more recently it has been found in the mammalian colon. (Ganser and Forte, 1973; Lee et al., 1974) This enzyme is involved in the gastric acid secretion (Gustin and Goodman, 1981). It has been proposed that H-K ATPase may be a candidate for potassium reabsorption in the renal distal tubule because this electroneutral pump exchanges potassium againt hydrogen ion and thus would also account, at least in part, for

proton secretion prevailing in the collecting tubule. (Sachs et al. 1982) Furthermore, the kidney K-ATPase displays similar kinetic and pharmacological properties as H-K ATPase previously observed in gastric (Ganser and Forte, 1973) and intestinal mucosa (Gustin and Goodman, 1981), and is therefore probably functional similar to it.

Several data have been suggested that H-K ATPase inhibitor, omeprazole, has a unique mechanism of action within the parietal cell where it inhibits H-K ATPase in secretory membranes. (Larsson et al., 1984; Wallmark, 1986). It is a potent inhibitor of gastric acid secretion in several animal models, such as in dog (Larsson et al., 1983) and man (Lind et al., 1983). The previous study has suggested that the collecting duct possess ouabian-insensitive, omeprazole-sensitive K-ATPase activity (Doucet and Marsy, 1987). Therefore, whether or not H-K ATPase activity is present in the mammalian nephron, particularly in those distal nephron segments where active potassium ion reabsorption is observed, is still opened to question. It has been reported that given omeprazole orally in normokalemic condition has not affect to urinary electrolyte output and urine pH (Howden and Reid, 1984). Therefore, the hypokalemic animals in the present experiment were performed. In this condition, H-K ATPase activity in the distal nephron was suspected to be more activated.

The present study is performed to determine the effect of omeprazole, gastric H-K ATPase inhibitor, can affect on the acid excretion in the kidneys of hypokalemic dogs and whether the mechanisms of potassium ion reabsorption and hydrogen ion secretion in dog kidneys are related to the activity of H-K ATPase.