CHAPTER I
INTRODUCTION

Peptic ulcer diseases, which are characterized by a presence of sores or holes in the lining of the stomach or duodenum, are commonly found all over the world (Sonnenberg and Everhart, 1996). The diseases were reported in all regions in Thailand but have never been accurately assessed. During 1981 and 1988, the hospitalization rate for peptic ulcer cases throughout the country remained fairly constant at around 0.1% of total population (Wilairatana *et al*., 1991). To date, although the cases decline, the diseases are still important because of death from gastric bleeding in some cases. Moreover, some studies indicated that chronic ulceration or prolonged inflammation may develop gastric cancer (Correa, 1996; Suzuki *et al*., 2006). The diseases are influenced by an imbalance of damaging factors and host mucosal defense. A number of factors were reported to cause peptic ulcer including hyperacidity, *Helicobacter pylori* infection, non-steroidal anti-inflammatory drugs, smoking and genetic factors (Richardson, 1985; Marshall and Warren, 1984). In particular, *H. pylori* infection has been detected nearly 100% in patients with duodenal ulcer, and usually found in gastric ulcer patients. However, these damaging factors are unable to destroy the gastric mucosa where the mucosal defense properly functions.

Many mucosal defense mechanisms against the deleterious substances in gastrointestinal tract were proposed such as glutathione (GSH), glutathione S-transferases (GSTs) and glutathione peroxidase (GPx) (Sinning *et al*., 1993). GSTs are enzymes that play an important role in phase II in cellular defense against various electrophilic compounds by inactivating the compounds for further elimination out of the cell (Habig *et al*., 1974). Human GSTs can be classified into six classes; namely, alpha, mu, pi, theta, sigma and omega (Mannervik *et al*., 1985; Hayes and Pulford, 1995; Armstrong, 1997; Hayes and McLellan, 1999; Sheehan *et al*., 2001; Board *et al*., 2000). Particular interest has been focused on the GST pi (GSTP) class because of its significant over-expression in many human tumor tissues. In gastrointestinal tissues, the GSTP is the major GST expressed in the stomach (Hoensch *et al*., 2002). Some studies indicated that the risk of gastric cancer increased when expression of GSTP was low or absent in combination with *H. pylori* infection. This difference in

GSTP activity was thought to be the result of polymorphisms in the *GSTP* gene (Hayes and Pulford, 1995; Ali-Osman *et al*., 1997)

In dyspeptic patients, gastroduodenal endoscopic examination revealed different lesions of the biopsied specimens, taken from greater curvature of the antrum close to the pyloric ring, and they can be simply grouped into ulcer and non-ulcer. The causes of gastric ulcer can be explained by the imbalance of the damaging factors and the host mucosal defense as mentioned above. However, the reason of no ulcer in a number of patients is not clear and has never been explained. Since GSTP polymorphism influences the enzyme activity level and a change in the enzyme activity might lead to the ulceration via an alteration of the gastric mucosal defense, it is anticipated that the presence or absence of ulcer in dyspeptic patients may associate with individuals' variation in *GSTP* gene. Therefore, it was hypothesized that the GSTP genotype from patients with peptic ulcer may be different from the genotype of patients with no ulcer.