CHAPTER 1

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder and is characterized by high blood glucose levels. Worldwide, the number of patients is rapidly growing with an increase in obesity and aging in the general population. Diabetes mellitus is categorized into two types. Type 1 insulin dependent diabetes does not have the physical ability to produce insulin. Therefore, all of patients require synthetic insulin, which is delivered by regular injections, or by an insulin pump. Type 2 non- insulin dependent diabetes, on the other hand, can produce insulin, however, not in sufficient enough amounts to meet their body's insulin need. The best way to control postprandial plasma glucose levels is with medication in combination with dietary restriction and an exercise program. Diabetes drugs commonly use in treatments are sulfonylureas, biguanides, alpha-glucosidase inhibitors, thiazolidinediones and meglitinides. However, some of these drugs can have negative side effects at higher dose (Ohmura *et al*., 1998; Mudaliar and Henry, 2001) and not suitable for use during pregnancy (Larner, 1985.; Valiathan, 1998). Therefore, search for safe and more effective agents has continued to be an important area of active research. Since ancient times, diabetes has been treated orally with several medicinal plants or their extracts based on folklore medicine. These herbal remedies are apparently effective, produce minimal or no side effects in clinical experience and are of relatively low costs in compared to diabetes drug treatments. Furthermore, after the recommendation made by WHO on diabetes mellitus, investigations on hypoglycemic agents from medicinal plants have become more important (WHO, 1980). The therapeutic approach to decrease postprandial hyperglycemia is to retard adsorption of glucose through inhibition of carbohydrate hydrolyzing enzymes, such as α-amylase in the digestive organs.

Alpha-amylase (1,4-α-D-glucan-glucanohydrolase, EC3.2.1.1) catalyzes the hydrolysis of α-1, 4-glucan bonds in starch, maltodextrins and maltooligosaccharides. This enzyme is present in animals, plants, bacteria and fungi. In humans the digestion of starch involves several stages. Initially, partial digestion by the salivary amylase results in the degradation of the polymeric substrate into shorter oligomers. Later on in the gut these are further hydrolyzed by pancreatic α-amylase into maltose, maltotriose and small maltooligosaccharides. Therefore, α-amylase from both sites have been considered as a target for postprandial hyperglycemia through mild inhibition of the enzymatic to decrease meal-derived glucose adsorption (Yoon and Robyt, 2003).

Plant α-amylase inhibitors (AI) are classified into two major groups: proteinaceous and nonproteinaceous α-amylase inhibitor. The proteinaceous α-amylase inhibitor are found in cereals and legumes, such as common beans (*Phaseolus valgalis*) (Gibbs and Alli, 1998; Lee *et al*., 2002), wheat (*Triticum aestivum*) (Franco *et al*., 2000), barley *(Hordeum vulgareum)* (Abe *et al*., 1993), and corn seeds (Figueira *et al*., 2003). Wheat α-amylase inhibitor (>4 mg/ml) can reduces α-amylase activity more than 90% inhibition without affecting other enzyme that can digest starch in duodenum (Choudhury *et al*., 1996). The nonproteinaceous α-amylase inhibitor contains diverse type of organic compound such as acarbose (Kim *et al*., 2002), acarbose analogues (Yoon and Robyt, 2003), Hibicus acid 6-methyl ester (Hansawasdi *et al*., 2000). Other than, phenolic compound such as tannin (Kandra *et al*., 2004), luteolin and flavonoid (Kim *et al*., 2000) can inhibit α-amylase activity from saliva and pancreatic, respectively.

Several starch dependent insect-pests utilize α-amylases for carbohydrate metabolism, releasing mixture of oligosaccharides for energy production. Due to their importance, different forms of α-amylases can be found in a unique insect species, to guarantee the digestive process efficiency. Otherwise, as these insects are totally dependent on α-amylases for their survival, these enzymes are good target candidates for bio-insecticides by using α-amylase inhibitors (Franco *et al*., 2002). Alpha-amylases inhibitors play a key role in plant defense toward pests and pathogens, which cause severe damages to field crops and stored grains. As these inhibitors could show different specificities against α-amylases from different sources (Franco *et al*., 2000), inhibitors with a wide specificity spectrum are strongly favored for insect control (Franco *et al*., 2002; Chrispeels *et al*., 1998).

Sataw (*Parkia speciosa* Hassk.) is a leguminous plant belonging to Mimoceae family. Local people believed that its edible seeds could control diabetes. Jamaluddin, *et al*. (1995) found that stigmast-4-en-3-one from green pericarp of *P. speciosa* reduced a significant glucose level in blood of alloxan-induced diabetic rats. An amylase inhibitor activity of green pericarp crude extract of *P. speciosa* has been also reported (Taugbodhitham, 2000). In order to discover the usefulness of the green pericarps of *P. speciosa* for diabetes remedy and the scientific explaination for the local believe, four objective of the study were created.

Objectives

1. Evaluation of the level of α-amylase inhibitor in fresh green pericarps of *P*arkia *speciosa* Hassk.
2. Purification and biochemical characterization of the purified amylase inhibitor.
3. Study on its possible roles in reduction of blood glucose level *in vitro via* luminal enzymes involve in postprandial hyperglycemia *i.e*. α-amylase, α-glucosidase and sucrase.
4. Study on potential application of the inhibitor on pest control .