

CHAPTER I

INTRODUCTION

Recently, several alternative medicines such as natural products and herbs become popular for treatment of illness either in conjunction with or in place of westernized medicines. Several herbs have been claimed for their health benefits and treatment of disease for a long time. Hence, it is unsurprisingly that herbs become center of interest in drug discovery research for their therapeutic efficacy, toxicity and drug interaction.

Passiflora foetida Linn. is a Thai herbal plant known as "Katokrok", in the Genus *Passiflora*, Family Passifloraceae (the Passion flower family). *Passiflora* plants have been used extensively as traditional medicines in several countries. For example, *Passiflora edulis* has been used as a sedative, diuretic, anthelmintic, anti-diarrhea, stimulant, and also in the treatment of hypertension, menopausal symptoms and colic of infants in South America (Chopra et al., 1956; Kirtikar and Basu, 1975). *Passiflora incarnata* is a popular traditional European remedy for insomnia, anxiety and has been used as a sedative tea in North America (Bergner, 1995). Leaf of *P. foetida* has been used to treat hysteria and insomnia in Nigeria (Nwosu, 1999). Recently, it has been shown that *P. foetida* extracts possessed potential antidepressant actions in the *in vivo* model of depression (Wijagkanalan, 2005). Although the mechanisms of actions were

not yet known, the receptor binding studies revealed that these extracts were able to bind to the dopaminergic and serotonergic receptors (Wijagkanalan, 2005).

The major phytoconstituents of the *Passiflora* species are flavonoids, glycosides, alkaloids, phenolic compounds and volatile constituents (Dhawan et al., 2004). As known, most of the flavonoid compounds have a wide range of pharmacological actions including vasodilation and cardiogenic effects (Formica and Regelson, 2000). It has been reported that quercetin, kaempferol and apigenin had a positive inotropic effect on guinea-pig papillary muscle (Itoigawa et al., 1999). It has been reported that flavonoid found in *P. foetida* included apigenin and kaempferol (Dhawan et al., 2004). Hence, it is likely that these extracts may possess intrinsic activities on the cardiovascular systems. However, there are no reports explaining the effects of *P. foetida* extracts on the heart.

The antidepressive effect of *P. foetida* extracts suggested their action on mice brain (Wijagkanalan, 2005). Unfortunately, the antidepressive effects often associate with cardiovascular problems with differential degrees. For example, tricyclic antidepressants (TCAs) have been known for its cardiovascular side effects including orthostatic hypotension, slow cardiac conduction, antiarrhythmic activity, and increased heart rate (Roose et al., 1999). Selective serotonin reuptake inhibitors (SSRIs) have been relatively less cardiovascular adverse effects than TCAs (Glassman, 1998). The effects of SSRIs on the cardiovascular system include first-degree atrioventricular block, prolonged QTc interval, and orthostatic hypotension (Rodriquez et al., 2001). In addition, activation of cardiac serotonin receptors results in positive chronotropic and

inotropic effects (Katzung, 2004). Because of the extract of *P. foetida* was able to bind to the dopaminergic and serotonergic receptor (Wijagkanalan, 2005), it is possible that these extracts activate serotonin receptor and affect cardiac functions.

Hence, this study aimed to study the potential pharmacological effects and safety profiles of *P. foetida* on the heart. In addition, the study would investigate the mechanisms of inotropic and chronotropic effects of *P. foetida* extracts, using the model of isolated rat atria. The results from this study would be beneficial for better understanding of pharmacological actions of *P. foetida* extracts which may be attributed to the therapeutic potential and side effects.

Hypothesis

Extracts of *Passiflora foetida* have the chronotropic and inotropic effects on rat isolated atria. The extracts may exert its cardiac effects via activation of adrenergic receptor and serotonergic receptor.

Objectives

1. To determine the chronotropic and inotropic effects of *P. foetida* extracts on isolated rat atria
2. To investigate the involvement of adrenoreceptor and serotonin receptors on the mechanisms of action of *P. foetida* extracts

Expected benefit and applications

This study further provides pharmacological knowledge and mechanisms of action of *P. foetida* extracts on rate and force of cardiac muscle contraction. The evaluation of chronotropic and inotropic effects as well as the potential mechanisms of *P. foetida* extracts on the isolated rat atria will further reveal its side effect to the heart and solidify the knowledge foundation for Thai herbal research development.