CHAPTER I

INTRODUCTION

The rationale for the study

Tobacco smoking and tobacco addiction are major worldwide health problems involved with health and economic impact on society [1, 2]. The leading causes of death from smoking are cardiovascular diseases, chronic obstructive pulmonary disease and lung cancer [3, 4], making it necessary to develop strategies for reducing tobacco consumption and treating nicotine dependence. Nicotine is considered to be the primary component of tobacco smoke that causes tobacco dependence [5]. Successful smoking cessation is difficult because physiological and psychological dependence and withdrawal symptoms will be developed after long-term smoking. Currently available smoking cessation agents (i.e., nicotine replacement therapy, bupropion and varenicline) have limited efficacy and relapse rate has been reported to be high, revealing a continuing need for development of alternative, and more efficacious smoking cessation pharmacotherapies [6, 7].

Vernonia cinerea Less. is an annual plant that has been reported to have many medicinal properties. Different parts of the plant have different therapeutic values. The plant has been used for analgesic [8, 9], antipyretic [8, 9], anti-inflammation [8, 10-12], treatment malaria fever [13], antibacterial [14, 15], and cancer treatment [16]. In recent studies, *V. cinerea* extracts (VE) showed efficacy in reduction of smoking rate and supplementation with VE provided benefit related to reduced smoking rate in smokers [17, 18]. However, the mechanism of action of VE in smoking cessation is not well understood. Thus, this study will provide information of the effect of VE and possible mechanism of VE on nicotine withdrawal symptoms for further studies of development of therapeutic agent for smoking cessation.

Hypothesis of the study

VE will be able to attenuate nicotine withdrawal symptoms in mice and the involved mechanism of VE will be related to alterations of nicotinic and muscarinic receptor activities in mouse brain.

Objectives of the study

1. To investigate the effect of VE on nicotine withdrawal symptoms in mice.
2. To determine the affinity of VE on nicotinic and muscarinic receptors.
3. To determine the effect of VE on nicotinic and muscarinic receptors expression in mouse brain.

Expected output of the study

The possible mechanism of action of VE in reduction of withdrawal symptoms involved with nicotinic and muscarinic receptors.

Expected outcome of the study

The result of this study could be fundamental information for further studies of VE as therapeutic agent for smoking cessation.