



CHAPTER I

INTRODUCTION

Background and Rationale

Macrophages are important immune cells that function in the regulation of immune responses in various tissues of the body including lympho-haematopoietic organs, skin, gut, other portals of entry and the nervous system [1]. These cells are the key cells of innate response. They also act as antigen presenting cells to present antigenic peptides to T lymphocytes in cell-mediated immune responses. Macrophages are also effectors cells when antibodies specifically recognized antigen in humoral immune responses.

Many stimuli are able to activate macrophages to generate immune response. Examples of these stimuli are phagocytosis of microbes or foreign antigen particles, components of bacterial cell walls such as lipopolysaccharide (LPS), cytokines from activated TH1 cells and mediators of the inflammatory response. Activated macrophages are far more active than resting cells in eliminating microbes. They exhibit higher phagocytic activity and greater capacity to kill ingested microbes, increase production and secretion of inflammatory mediators, increase ability to activate T cells, and secrete various cytotoxic proteins required for eliminating viral infected cells, tumor cells, and intracellular bacteria.

Activated macrophages release a wide range of mediators such as several cytokines and pro-inflammatory cytokines, reactive oxygen species, nitric oxide and prostaglandins. These mediators involve in the inflammatory response which is a part of the innate immune response. However, chronic infection or chronic inflammation can cause the chronic release or overproduction of these mediators which are harmful to the host tissues and lead to tissue damage and chronic inflammatory diseases such as rheumatoid arthritis [2].

Anti-inflammatory agents are commonly used to reduce inflammatory cardinal signs, pain, swelling and fever, in many acute and chronic inflammatory diseases. These agents are mainly classified into 2 groups, steroidal drugs and non-steroid anti-inflammatory drugs (NSAIDs). Steroidal drugs suppress several functions of immune cells as well as macrophages. They inhibit production of several inflammatory mediators in macrophages. NSAIDs are the most widely used anti-inflammatory drugs. They inhibit cyclooxygenase 2 (COX-2) which is responsible for excess production of PGs from macrophages. There is the other group of drugs called disease modifying anti-rheumatic drugs (DMARDs) which also used to treat several autoimmune diseases that have chronic inflammation such as rheumatoid arthritis, systemic lupus erythematosus, and Crohn's disease. Some drugs in this groups are anti-proinflammatory cytokine agents, such as TNF- α and IL-1 inhibitor. There are a lot of side effects from the use of both steroidal drugs and NSAIDs. Chronic use of steroidal drugs can severe infection due to immunosuppressive effect of the drugs. The most common side effect of NSAIDs is the damage of the mucosa of the digestive tract. All of cytokine inhibitors still have high cost and have to be administered via parenteral routes. Novel anti-inflammatory agents are still needed to replace these conventional drugs.

It has been known for a long time that drugs derived from medicinal plants still make a large contribution to drug discovery. Plants are the rich sources of several clinically used drugs. Many compounds from plants have been reported to exhibit anti-inflammatory activities. Some of them are used in modern medicine as well as as alternative medicine. *Derris reticulata* Craib is a plant in Leguminosae family which has flavonoids as its major active compounds similar to other plants in genus *Derris* [3-4]. It has been used as expectorant and thirst relief. Flavonoids from several medicinal plants have been demonstrated to have a variety of biological activities including antibacterial, antiviral, antioxidant, antiulcerogenic, cytotoxic, antineoplastic, mutagenic, antihepatotoxic, antihypertensive, hypolipidemic, antiplatelet, and anti-inflammatory activities [5]. This study aimed to investigate potential anti-inflammatory activity of the ethanol extract from the stem of *D. reticulata* by investigating the effect of the ethanol

extract on phagocytic activity and the production of inflammatory mediators in activated macrophages. The results from this study may reveal benefit information of this plant in medicine. This may lead to the discovery a new medicinal plant which has compounds with anti-inflammatory activity.

Objective

To study the effect of the ethanolic extract from the stem of *Derris reticulata* on the phagocytic activity, nitric oxide production and the RNA expression of several proteins involve in inflammation in LPS-activated macrophages.

Hypothesis

The ethanolic extract from the stem of *D. reticulata* inhibits LPS-induced macrophage activation.

Keywords

Derris reticulata, activated macrophage, anti-inflammation, pro-inflammatory cytokines, pro-inflammatory mediators, phagocytosis.