CHAPTER I

INTRODUCTION

1.1 Background

Thymus vulgaris possesses a lot of active ingredients including thymol, carvacol and flavonoids. The main chemicals of thyme are essential oils such as borneol, carvacol, linalool and thymol, the bitter flavor, tannin, saponin and triterpenic acids *(Shabnum et al., 2011*). It shows that constituents such as thymol and carvacrol in *Thymus vulgaris* have some effects on the immune response *(F. C. Fachini-Queiroz, et al., 2012).* Medicinal plants and their extracts have been used traditionally worldwide both to treat and prevent some accute diseases such as inflammatory and cardiovascular diseases, arthritis, diabetes, and other diseases *(Juhás et al., 2008).* T. *vulgaris* which is found to be a perennial plant originating from, Africa, central and southern Europe and Asia is commonly used due to those two functions *(Rustaiyan et al., 2000; Braga et al., 2006)*. T. *vulgaris* extracts are famous in alternative medicine because of their activities such as antitussive, antiasthmatic, antiseptic, bronchodilator, antispasmodic, antiviral, antibacterial and antifungal *(Marino et al., 1999; Pina-Vaz et al., 2004)*. In addition, T. *vulgaris* extracts are proved to have anticarcinogenic compounds *(Arcila-Lozano et al., 2004)* and the immunomodulation properties *(Bukovska et al., 2007; Ocaña and Reglero, 2012).* Additionally, T. *vulgaris* is referred by many researchers for its polyphenol and flavonoid, its potential to be antioxidant, scavengers of free radical, antiplatelet, vasorelaxant, antithrombin, antihylperlipidemic, anti-inflammatory and anti-diabetic contents *(Miura et al., 2002; Vigo et al., 2004; Nekeety et al., 2011).*

There are a lot of drugs and chemicals that can improve different immune response aspects. Immunopotentiation can be created by enhancing the level of immune response that develops the response intensity rate and extension or development of response to other non-immunogenic components *(Rofaiil et al., 2007).* Typhoid fever is one of the emerging diseases in developing countries not to mention Indonesia. This disease is caused by *Salmonella* sp. This has been the cause of people being hospitalized. This disease can cause a fatal multisystemic disease as it spurs the intestinal bleeding and perforation. Moreover, it can even lead to complications like hepatitis, meningitis, nephritis, myocarditis, bronchitis, pneumonia, osteomyelitis, and mumps. *Salmonella* sp includes *Salmonela Typhimurium*. There were an estimation of 94 million Salmonella sp cases of gastroenteritis which caused approximately 150 thousands people died every year worldwide by WHO research

from 2001 to 2005. *Salmonella typhimurium* causes the serious problems after S*. Enteritidis*. In Africa, *Salmonella enteritidis* represented just over qquarter and *Salmonella typhimurium* represented quarter from the total isolates. Moreover, in Asia, Europe and Latin America, *Salmonella entiritidis* was often isolated by as much as 38%, 87% and 31% simultabously). As much as 29% of *Salmonella typhimurium* is the most frequent reported cases which then was followed by *Salmonella enteritidis* North America, (WHO et al., 2003).

Research on typhoid fever disease can be done using animal models such as mice, as *Salmonella typhimurium* in mice causes systemic infections and the diseases are similar to those seen in humans who are infected by *S.Typhimurium* (Mittru¨cker *et al*., 2000; Ugrinovic *et al*., 2003).

Chronic gastroenteritis because of S. typhimurium is an essential case that threatens the immune system of people compromised in the West, and is fatal for children and the elderly in developing countries. The estimation of 1.3 billion cases every year causes approximately 3 million people die in the world. Thus, studies of mice infected naturally which then develop symptoms of a disease which has similarity to that examined in human beings are very important (Ozkaya et al., 2011). Moreover, the cause of invasive sickness in rats is closely similar to the case in human suffering from Typhoid fever. There is intravenous inoculation of bacteria residing in the intracellular compartment of spleen and liver. In early stages of infection, salmonella is restricted, and grows mainly in PMN and macrophages (Khana et al., 2009). Additionally, some experiment results showed that microphiles and neutrophils are essential for the host to survive when it gives the initial reaction to Salmonella infections (Alun et al.,2002).

The bacterium ability to attach, attack and persist in the cells of the host becomes important in the Salmonella infection pathogenesis. In infections which is systemic, macrophages are a niche for the proliferation of the bacteria in host organisms. S.Typhimurium is characterized and the frequency at which these bacteria collide is important for infection efficiency. Invasion of salmonella intestinal macrophages, through a mechanism which depends on survival, replication, phagocytosis, and spread in the host organism including, liver (Achouri et al., 2014).

IL12 stimulates TH1 (CD4-specific antigen) cells to release IFN-γ which in turn induce NK cells to produce IFN-γ (Murphy et al., 2012) specifically needed to activate macrophage. Macrophage and natural killer cells are able to produce many

different cytokines and are primarily for the host to survive during the major response to Salmonella infection (Lapaqueet al., 2009).

1.2 Research Problem

The main problem which underlies this study says "Is there any effect of *thymus vulgaris* extract as an anti-inflammatory activity in mice infected with S. *typhimurium*?" Problems in this area can be formulated as the following research questions:

1) Does *Thymus vulgaris* extract increase blood IL-12 in mice infected by *S. typhimurium*?

2) Does *Thymus vulgaris* extract decrease bacterial colonies in the liver of mice infected by *S. typhimurium*?

1.3 Research Objective

1.3.1 General Objective

This research was conducted with the general objective to prove the benefits of *Thymus vulgaris* extract as an anti inflammatory agent in mice infected with *S. typhimurium.*

1.3.2 Specific Objective

According to the research questions, the following specific objectives are drawn as follows:

1) To prove the effect of the *Thymus vulgaris* extract to increase blood IL-12 of mice infected with *S. typhimurium.*

2) To prove the effect of the *Thymus vulgaris* extract to decrease the bacterial colonies in the Liver in mice infected with. *S. typhimurium.*

1.4. Significance of Research

1.4.1 Theoretical benefits

1) This study supports the interests of further research on the benefits of extract of *Thymus vulgaris* especially in infectious diseases.

2) It is also adds knowledge expansion, especially about the benefits of *Thymus vulgaris* as an immunomodulator and antibactrial agent

1.4.2 Practical benefits

1) Practically, the result of *Thymus vulgaris* study is beneficial to be widely used an adjunct to the herbal (phototherapy), immunomodulation and anti bactarial medicine after clinical trial.