I. INTRODUCTION

1.1. Background

Hypertension is one of the most important public health problem which challenges the worldwide because of its high frequency and concomitant risks of cardiovascular and kidney disease. It has been identified as a leading risk factor for mortality and was ranked third as a cause of disability (Manimunda, 2010). According to Basic Health Research (2013), the highest proportionality causes of death in Indonesia is the in-contagious disease such as cardiovascular disorders (26.4%) including hypertension (6.8%) and stroke (15.4%).

The potential harmful effects of hypertension can be prevented or even reduced if it is detected early enough (American college of Physician, 2008). All patients with pre-hypertension and hypertension should be prescribed lifestyle modifications (Dipiro, 2008). However, controlling patient blood pressure through antihypertensive agents approach still remains the major action in managing the cases of hypertension (Sever and Messerli, 2011).

Those are several drugs introduced to reduce blood pressure such as calcium channel blockers (CCBs), the alpha blockers, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), and direct renin inhibitors (DRIs) (Sever and Messerli, 2011). Even if the patient had been obedient to their therapy regiments, the blood pressure control by the drug was achieved in only 31% of the patients (Kearney, 2004) and (Di Piro, 2008).

Since the pathologic conditions vary among patients, including in hypertension disease, a pathological approach therapy is needed to increase its effectiveness (Food and Drug Association, 2014). Therefore, the use of different models of hypertension will bring the benefit to differentiate the response produced by each condition to the treatment given.

All hypotensive agents can produce side effects occasionally with serious consequences (Freis, 2006). A dramatic increase of blood glucose caused by a long consumption of Calcium channel blockers had introduced by Goodman and Gilman (2006) on human subjects. Angiotensin II receptor blockers had been reported to abrupt reduction in renal function and hyperkalemia (British Hypertension Society, 2008). Cough is more prevalent in patients on ACEIs. When used during pregnancy, the DRI can injure or be fatal to the developing fetus (Agency for Healthcare Research and Quality, 2011). In addition, a discovery for a safer and more effective drugs is still being conducted even though there has been a massive increase in the number and variety of medications available (World Health Organization, 2008).

Scopoletin is one of the most important phenolic compounds which had been isolated from several sources, such as *Scopolia japonica* Maxim., *Scopolica carniolica* Jacq., *Atropa belladonna* L, *Convolvuss cammonia* L., *Erycibeobtusifolia*, *Aster tataricus, Foeniculum vulgare, Morinda citrifolia* and *Cassava* sp and etc, which are available in abundant amount in Indonesia (Nelson, 2005).

Scopoletin displayed a moderate antioxidant activity (Lemos *et al*,. 2006), vasorelaxant (Iizuka *et al.*, 2007) and hypotensive (Guantai and Addae, 2007) in-vitro. It has also been claimed to reduce blood pressure through a vasodilation and/or might have an

ACE inhibitory effects. It is reported to exhibit an activity to inhibit the hydrolysis of acetylcholine esterase that is responsible for muscle and organ relaxations (Kumar& Rajeev, 2010).

In order to promote the effectiveness of hypertension therapy, a series of experimental models of hypertension have been developed (Dornas and Silva, 2011). The use of relevant models to mimic human cardiovascular disease may offer useful information by allowing an understanding of the cause and progression of the disease status as well as potential therapeutic interventions (Badyal *et al*., 2003).

This research project will provide an overview role of scopoletin on several models of hypertension. By these models, the overview will propose a specific activity of scopoletin to treat hypertension.

1.2. Research questions

As the backgrounds aforementioned above, these following questions are appeared:

1. Is scopoletin effective to reduce the blood pressure in vivo?
2. In which model of hypertension where scopoletin is more effective to reduce the blood pressure?

1.3. Objectives

The objectives of this study are:

1. To determine the effectiveness of scopoletin in reducing the blood pressure on different models of hypertension
2. To investigate the kind of hypertension model(s) where scopoletin is more effective to reduce the blood pressure.

1.4. Hypothesis

Based upon the objectives above, the following hypothesis are arised:

1. Scopoletin is effective on different models of hypertension.
2. Scopoletin will be more effective in certain model of hypertension.


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