

Chapter 1

Introduction

1.1. Background

In the last three decades, herbal medicine use has increased rapidly, with at least 80% of the people in the world taking or relying on herbal medicine as their primary medicine. Without exception, pregnant women are also among those who consume herbal medicine. The usage rate of herbal medicines depends on many factors. Around 7 to 55% of women worldwide are reported to consume herbal medicine during their pregnancy (Illamola et al., 2020; Adane et al., 2020). Especially in Indonesia, 68% of Indonesians consume herbal medicine with 40% self-medicating and around 60% of pregnant Indonesian women having taken drug supplements or herbal medicine (Rahayu et al., 2020; Purnamawati & Ariawan, 2012). The consumption of herbal medicine in pregnancy may be due to various reasons, including physiological problems, such as nausea and vomiting, where about 50 to 90% and diarrhea about 14.3% of pregnant women are affected, respectively (Soma-Pillay et al., 2016; Newman et al., 2019). Common consumption of herbal medicine by pregnant women containing ginger, ginseng, and peppermint oil used to alleviate those pregnancy side effects. However, some herbal medicines are used in practices, which are indicated for uterine stimulants and labor inducers (Illamola, et al., 2020; Mills et al., 2006).

In addition to being a major consumer of herbal medicine, Indonesia is also one the largest producers of herbal medicine in the world. According to the Embassy of the Republic of Indonesia in Brussels (2021), Indonesia ranked 19th as a herbal medicine exporter in 2019 and in 2020, the export value was reported to increase by 14.08%, making Indonesia one of the biggest producers of herbal medicine, typically for ginger and tumeric. With this increasing herbal medicine growth, Indonesia is able to compete in supplying these herbal medicines. Although herbal medicines are widely produced and used, there are limited studies on its efficacy meaning its safety remains untested and poorly or even not monitored which is still an issue since their interactions, adverse effect, contraindication and

other drug related problems may arise (Ekor et al., 2014).

Toxicity studies using animals can be done to know the safety of a medicine. In this study zebrafish embryos were used for testing teratogenicity of the herbal medicine. Zebrafish are approximately 87% genetically similar to humans (Jayasinghe & Jayawardena, 2019). In addition, they have a short life cycle and high fertility, making them a leading edge of toxicology research with the advantage of shorter research time. In comparison to a classic toxicity screening such as rodents and other mammals (dogs and rabbits), zebrafish have some advantages. While classical toxicology screening is time consuming and sometimes really expensive, as explained before zebrafish have a faster and cheaper option with enough significant data to conduct the study (Modarresi Chahardehi et al., 2020). Their nervous, cardiovascular, and digestive systems are morphologically and physiologically similar to humans. Thus with high genetic similarities, zebrafish embryo has been proposed as an alternative for assessing teratogenic effect. Furthermore, their genome has been fully sequenced, connecting the phenotypic changes in zebrafish to possible changes in the human body. Thus it is suitable for testing or screening drugs that are potentially toxic to humans. Using zebrafish also eases the visualization of the zebrafish embryo due to its transparency (Modarresi Chahardehi et al., 2020; Keshari, et al., 2016; MacRae & Peterson, 2015; Zon & Peterson, 2005). Additional advantages of utilizing zebrafish is their small size and rapid reproduction rate which can be used for large assays. Even though the administration is through the aqueous environment and low similarity on the anatomic aspect with humans, the drug's efficacy, bioavailability and toxicity can still be observed (Vaz et al., 2018).

1.2. Objective

The main objective of this research is to determine median lethal concentration (LC50), teratogenic index (TI), and to observe the morphology deformities in zebrafish embryos that are treated with marketed herbal medicines in Indonesia.

1.3. Hypothesis

The hypothesis for this project is that the herbal medicines tested show teratogenicity signs and can be categorized as harmful through LC50 calculation and lethal morphology indicators.