CHAPTER 1 INTRODUCTION

1.1 Background

Endosulfan is a pesticide belonging to the organochlorine group of pesticides, under the cyclodiene subgroup. Introduced in the 1950's, it emerged as a leading chemical used against a broadspectrum of insects and mites in agriculture and allied sectors. It acts as contact and stomach poison and has a slight fumigant action. It is used in vegetables, fruits, paddy, cotton, cashew, tea, coffee, tobacco and timber crops. It is also used as a wood preservative and to control tse-tse flies and termites (Hermann, 2003). It is not recommended for household use. Intentional misuse of endosulfan for killing fish and snails has also been reported (EJF, 2002). Endosulfan was also reported as used deliberately as a method of removing unwanted fish from lakes before restoring (Hermann, 2003).

Various investigations have been conducted in various countries to understand the status of organochlorine pesticides contamination in foodstuffs and its exposure to human (Rahmawati, 2013). The U.S. Environmental Protection Agency (EPA) identifies the most serious hazardous waste sites in the nation. U.S. EPA then includes these sites the National Priorities List (NPL) and targets them for federal clean up activities. U.S. EPA has found endosulfan in at least 176 of the 1.699 current or former NPL sites. The total number of NPL sites evaluated for endosulfan is not known. But the possibility remains that as more sites are evaluated, the number of sites at which endosulfan is found may increase. EPA has initiated action to end the use of endosulfan because it can pose unacceptable

health risks to farmworkers and wildlife and can persist in the environment (Jessilynn *et al*., 2013).

Endosulfan exhibits toxicity towards mammalian and other organisms and act as a one of the main cause of poisoning in humans in many countries as reported by Wesseling *et al*. (2005). Two cattle died acutely after being sprayed for lice control with a cyclodiene organochlorine insecticide, endosulfan. Three other cattle became acutely ill, but survived after symptomatic therapy and removal of the insecticide from their skin and prevention of enterohepatic circulation (Kelch and Kerr, 1997). Clinical signs of acute exposure to endosulfan include salivation, hyperactivity, respiratory distress, diarrhea, tremors, hunching and convulsions (WHO, 2004).

Research about effect of endosulfan mostly been done in brain, liver, and kidney, but research about endosulfan in lung is limited maybe because of endosulfan is not highly volatile with the result that reputed that lung is not exposed. The truth is lung can be exposed via peroral starts from gaster, intestine, vena porta hepatica, liver, vena hepatica, vena cava posterior, heart, as far as lung through pulmonary artery. They are broad spectrum insecticides. They are nerve poisons but specific action is unknown. They seem to work on CNS (Radey and Sinha, 2010). Endosulfan arrived in lung through GABA receptor which is located in lung (Nili *et al*., 2008). The existence of toxic material in lung may caused hemodynamic disorder as following congestion and hemorrhage because of endosulfan was caught in a blood vessel, emphysema and inflammation because inflammation is a local immune respons in the body and this might be the reasons

of the infiltrated neutrofil and macrophages in lung which is causing emphysema as well as the imbalance between protease-antiprotease and oxidant-antioxidant. As we know that lung is one of the most important respiratory organ. Once it is exposed to endosulfan, it might be harmful for animals.

Based on the background above the research untitled the effect of endosulfan on histopathological changes of *Mus musculus* lung will be conducted.

1.2 Statement of Problem

Does endosulfan cause pathological changes of *Mus musculus* lung which is exposed to endosulfan?

1.3 Theoretical Base

In pure form endosulfan exists as colourless crystals. But the technical product is brownish crystals with slight odour of sulphur dioxide. Technically endosulfan is a mixture of two isomers: α endosulfan and β endosulfan in the ratio 7:3. Technical grade endosulfan contains 94% alpha endosulfan and beta-endosulfan and other related compounds like endosulfan alcohol, endosulfan ether and endosulfan sulfate (Harikrishnan and Usha, 2004). It is also found in the environment due to oxidation by biotransformation. It is a known gamma amino butyric acid (GABA) antagonist, similar to other organochlorine compounds (Gupta, 1976; Seth *et al*., 1986). GABA is a major inhibitory neurotransmitter in the central nervous system. This amino acid binds to its receptor and stimulates the flux of chloride ions, causing the reduction of neuronal membrane electrical

activity followed by inhibition of neurons. Acute exposure to endosulfan stimulates CNS resulting in lack of coordination, gagging, vomiting, diarrhea, agitation, convulsions and loss of consciousness. Apart from CNS, it has been shown to affect renal, hepatic, respiratory, reproductive and immune systems in mammals (Singh and Pandey, 1989; Lo, 1995; Rawat *et al*., 2002; Srikanth and Seth, 1990; Kiran and Varma, 1988; Pistl *et al*., 2001; Choudhary and Joshi, 2003; Banerjee *et al*., 2001).

Generally, cell or tissue respons injury by means of 3 stages, (1) adaptation, (2) degeneration or intracellular and extracellular accumulation and (3) cell death (Arimbi *et al*., 2013). When the cell is exposed to an injurious agent or stress, a sequence of events follows that is loosely termed cell injury. Cell injury is reversible up to a certain point. If the stimulus persists or is severe enough from the beginning, the cell reaches a point of no return and suffers irreversible cell injury and ultimately cell death. Cell death is the ultimate result of cell injury (Cobb *et al*., 1996).

Mechanism of toxic chemical injury to the cell through two ways, whether substances will directly bind to molecules/cell organelle components resulting in permeability rise and energy transport dependents hampered or non active chemical substances must be changed to reactive toxic metabolites afterwards work on target cell (Cobb *et al*., 1996).

Their acute toxic effects in animals are principally due to hyperexcitation in the nervous system and death is frequently ascribed to respiratory failure after the disruption of nervous system function (Coats, 1990). Hemorrhages in all part of

the system can be seen (Mor and Ozmen, 2003; Hatipoglu *et al*., 2009). Lungs are commonly affected especially in acute poisoning (Mor and Ozmen, 2003). Acute lethal or near-lethal doses have resulted in congestion in the lungs, liver, kidneys, stomach, and intestines. According to one study, acute intoxication with endosulfan involves two stages: gastrointestinal symptoms, tonic-clonic convulsions, respiratory depression, metabolic acidosis, and hyperglycemia and hemodynamic instability appear within 4 hours of ingestion. Pulmonary edema and pulmonary aspiration, consumption coagulopathy with decreased platelets, elevated serum transaminases, and persistent hemodynamic instability can develop subsequently (Jessilynn *et al*., 2013). Lungs are generally edematous and hemorrhagic (Mor and Ozmen, 2003; Hatipoglu *et al*., 2009; Fazekas, *et al*., 2010).

1.4 Aims of Research

The aim of this research is to prove the effect of endosulfan causing congestion, hemorrhage, emphysema, and inflammation on *Mus musculus* lung through histopathology assessment with hematoxylin eosin staining.

1.5 Outcomes of Research

1. To provide an overview and understanding about the toxic effect of endosulfan
2. To provide an overview and understanding to the public about the risk factors of using endosulfan
3. This study may also useful as references or comparison for subsequent researches especially for the development of scientific research

1.6 Hypothesis

Endosulfan does effect pathological changes of *Mus musculus* lung which is exposed to endosulfan.