CHAPTER 1
INTRODUCTION

1.1 Background of Research

Alcohol is no stranger when it comes to humans. Alcohol consumption has increased enormously within the years (Das and Vasudevan, 2006). For the past decade or so, the history of alcohol intake by humans has been recorded (O'Shea, 2010). Alcoholism is a continuous and universal problem among humans (Weor, 2010). In the past, alcoholic beverages were used universally by humans for their medical, antiseptic and analgesic properties.

The increase of alcohol abuse over the years has also caused an increase in liver diseases. The extent of liver damages secondary to alcohol consumption are immeasurable which can include acute alcohol hepatitis, Alcoholic Liver Disease (ALD), cirrhosis and hepatocellular carcinoma (Mann, 2003).

The liver is known to modulate chemical levels in the blood and eliminate products such as bile. Blood that exits the stomach and intestines flows through the liver. The liver then processes the blood into forms that are simpler to use by the rest of the body and also nontoxic by breaking down, balancing, creating nutrients and metabolizing drugs.

Alcohol is highly abused by humans and can be very harmful for the organs of the body. The effects of excessive alcohol intake can cause damage on more than one organ in the body. The vital target of injury is the liver that acts as the primarysite of alcohol metabolism (Karinch *et al*., 2008). Alcoholic Liver Disease

(ALD) is the number one liver disease worldwide and is caused by chronic excessive ethanolintake (Pari *et al*., 2007).

Alcohol toxicity is a frequent result of morbidity globally in the current generation (WHO, 2011). The regularity of ALD all over the world corresponds to the amount of alcohol ingested by humans. The highest intake of alcohol and regularity of the disease is in eastern Europe, southern Europe and United Kingdom (WHO, 2011).

About a quarter of the Europe's population ingests a dangerously high volume of alcohol. There was a definitive rise in the alcohol intake between the years 1950 till1984 in Japan. It is linked to the increase in cirrhosis morbidity and mortality (Parrish*et al*., 1991).

The intake of ethanol for a long period of time can instigate oxidative stress inthe liver because of the imbalance between the prooxidant and antioxidant systems (Nordmann *et al*., 1992). The vulnerability of the liver to ethanol toxicity can stimulatealcoholic liver disease (Lieber, 2000).

The histologic manifestation of the liver injury in chronic ethanol abuse may progress from steatosis to focal inflammation, focal necrosis, fibrosis and also cirrhosis, which can result in alcoholic liver disease (Zakhari, 2007).

Coconut oil can be obtained from the tree (*Cocos nucifera* L.), family Aracaceae(palm family). Everything from the coconut palm is beneficial, with an exceptional economical value (Bruce, 2004). Coconut oil or copra oil is a consumable oil obtained from the kernel of mature coconuts that comes from the coconut palm (Kumar, 1997). Virgin Coconut Oil (VCO) in its authentic form of

coconut oil is said to be colorless and free from rancidity. Virgin Coconut Oil (VCO) is rich in naturalantioxidants, and vitamin E which can hinder peroxidation reactions. The odor of fresh coconut can differ from mild to intense depending on the extraction method used (Marina *et al*., 2009). After coconut oil was discovered it has been used worldwide for various reasons such as for its medical use, food ingredients and also as functional food (Ghazali, 2009).

Virgin Coconut Oil is made up of Medium Chain Triglycerides (MCT) which isdifferent compared to animal fats that is made up of long chain saturated fatty acids (Bezard *et al*., 1971). Medium Chain Fatty Acids (MCFA) are different from long chainfatty acids because it is helpful in protecting the body from heart disease. It is also stated that MCFA decreases the possibility of heart disease and atherosclerosis (Conrado, 2003).

Virgin Coconut Oil (VCO) is becoming popular because of the health benefits given its phenolic acids and flavonoid contents (Srivastava *et al*., 2016). Stated by a phytochemical analysis, the important phenolics in VCO are p-coumaric and ferulic acids (Illam *et al*., 2017).

It is discovered that VCO reduces oxidative stress, dyslipidemia and inflammation of organs in animal models through its antioxidant activities (Hamsi *et al*., 2015).

1.2 Problem Statement

Based on the problems stated in my introduction, the problem that can be formulated is : Can Virgin Coconut Oil (VCO) repair the histopathology of the liver in mice (*Mus musculus*) induced by alcohol?

1.3 Theoretical Basis

Ethanol is a small particle that is soluble in both water and lipids, as a result it pervades all the tissue of the body and crucial functions. Ethanol influences practically all the organs of the body therefore, immoderate intake of ethanol can lead to various diseases such as gastrointestinal, neurological, cardiovascular diseases and also malignant tumor (Mandayam *et al*., 2004).

The capacity of intake and the sequence of drinking, particularly large intakes of alcohol can dictate the weight of the disease. There are also other components suchas genetic susceptibility and dietary intolerance that may be co – factors in alcohol induced damage (Norberg *et al*., 2003).

The vital targets for ethanol toxicity are the liver, brain, heart, skeletal muscles and exocrine pancreas. Oxidative damage to mitochondrial proteins, phospholipids (cardiolipin) and mitochondrial DNA (mtDNA) in the liver is caused by acute and chronic ethanol intoxication (Fromenty *et al*., 1995). In mice, oxidative degradation and reduction of hepatic mtDNA is caused by acute intragastric ethanol administration(Mansouri *et al.,* 1999).

The pathogenesis of ethanol is caused by many factors. In early stages there areevents that may happen for example mitochondrial damage, Reactive Oxygen Species (ROS) generation and steatosis that can be the direct outcome of ethanol

metabolism, which also happens to be a characteristic of acute and chronic alcohol exposure (Lieber,2004).

The development of ALD varies depending on several factors which may include the dose, time span and type of alcohol consumption, drinking patterns, gender and ethnicity (Bellentani *et al*., 1997). Other factors may also include genetics, the variation in immunological and metabolic responses, nutritional status, smoking and obesity (Nath *et al*., 2009).

The excretion of ethanol includes three enzyme systems inside the liver. The first enzyme is cytosolic Alcohol Dehydrogenase (ADH), the second enzyme is catalyses reversible oxidation of ethanol to acetaldehyde, and the third enzyme is Cytochrome P450-2E1 (CYP2E1). However, the third enzyme plays a small role in theexcretion of ethanol (Chrostek *et al*., 2005).

Oxidative stress is known to be a damaging process caused by a disproportion among the excessive development of Reactive Oxygen Species (ROS) and limited antioxidant defense (Circu, 2010). An overflow of ROS accumulation enhances cell death by causing oxidative damage to cellular macromolecules involving lipids, proteins and also DNA (Valko *et al*., 2007). The rise in damage generated by ROS is said to decide the cell fate by instigating cell cycle arrest and apoptosis (Kuo *et al*., 2007).

Alcoholic liver damage is commonly linked to tissue necrosis and also infiltration of neutrophils as well as other inflammatory cells. It is shown in studies of isolated hepatocytes that TNF - α causes a varied pattern of cell death which is identified by using a Fluorescence – Activated Cell Sorter (FACS) with

the help of fluorescence markers for apoptosis and necrosis (Pastorino *et al*., 2000). Discarding of tissue from unwanted or damaged cells is a defense mechanism from an apoptosis reaction (Leist *et al*., 1997).

Virgin Coconut Oil that is derived through a wet process comes from coconut milk under controlled temperature may obtain more beneficial effects compared to copra oil considering it retains almost all of its beneficial components. Virgin CoconutOil is known to lower total cholesterol, triglycerides, phospholipids, Low Density Lipoprotein (LDL) and Very Low Density Lipoprotein (VLDL) cholesterol and elevates high density lipoprotein (HDL) cholesterol in serums and tissues in comparison to copra oil (Nevin *et al*., 2004).

In addition, proper allocation of VCO is said to elevate antioxidant enzymes and decrease lipid peroxidation content (Nevin *et al*., 2006). Virgin Coconut Oil (VCO) is also known to have an exceptional antithrombotic effect compared to copra oil (Nevin *et al*., 2008). In contrast to other vegetable oils, VCO is said to have a high concentration of MCFA in the form of Medium Chain Triglycerides (MCT). It is also high in Saturated Fatty Acids (SFA), for example lauric acid (Assuncao *et al*., 2009).

In the liver, MCT is primarily metabolized by β-oxidation. During this process, carnitine palmitoyl transferase enzyme is not needed for intra-mitochondrial fatty acidtransport and results in MCT being metabolized quicker. Furthermore, acetyl-CoA molecules that are formed during the oxidation process are ideally metabolized to ketone bodies (Ooyama *et al*., 2009). It is stated that Virgin Coconut Oil (VCO) has antimicrobial, anti-inflammatory, anticancer and

hepatoprotective properties (Hery *et al*., 2008). Diets containing Virgin Coconut Oil VCO is said to have useful results on the lipid metabolism by decreasing lipogenesis and boosting the rate of fatty acid catabolism in rats (Arunima *et al*., 2012).

Virgin Coconut Oil (VCO) is known for its potent natural phenolic antioxidants(Marina *et al*., 2009). Virgin Coconut Oil (VCO) has beneficial health reactions towards oxidative stress-related disorders (Nevin *et al*., 2006) which correlate with polyphenolsfound in the oil itself (Marina *et al*., 2009).

1.4 Aim of Research

To examine the histopathology on the liver of an alcohol induced male mice (*Musmusculus*) and determine whether VCO can repair the histopathology of the liver in a male mice (*Mus musculus*) induced by alcohol.

1.5 Outcome of Research

1. To give the public knowledge of coconut oil used as a pre - treatment on an alcohol induced liver of a mice.
2. From the outcome of this research we will know the accurate amount of coconut oil as a pre – treatment that prevents excessive damage from happening to the liver of a mice.
3. To create a thesis that creates knowledge for other vets or people in the histopathological department of vet medicine that there are possibilities in manufacturing virgin coconut oil as a herbal and organic antidote towards damaged liver due to alcohol consumption.

1.5.1 Theoretical Benefits

This research is expected to show the benefits of Virgin Coconut Oil (VCO) on the histopathology on the liver of an alcohol induced male mice (*Mus musculus*).

1.5.2 Practical Benefits

It is hoped that the results of this study will show the effects of VCO on the histopathology in the liver of an alcohol induced male mice (*Mus musculus*).

1.6 Hypothesis

The hypothesis of this research is VCO can repair the histopathology of the liverin mice (*Mus musculus*) induced by alcohol.