CHAPTER I. INTRODUCTION

1.1 Background

WHO recommended daily fat intake for adults is less than 30% with no more than 10% of saturated fat and 1% of trans-fat. Excessive fat consumption, equivalent to or more than 30% of total calories, is considered to be a High-Fat Diet (HFD). The Western diet is often characterized as an HFD due to its low fiber and high saturated fats and trans fats. Red and processed meat, as well as dairy products like butter, heavy cream, and cheese, contain saturated fat, whereas trans fats are present in processed meals such as baked goods and fried dishes (Demaria et al., 2023). WHO Indonesia (2024) discovered that 11 out of 130 (8.46%) samples had high levels of Trans Fatty Acid (TFA) (over the WHO's recommended 2 g/100g total fat guideline). Products that are often consumed, like biscuits, wafers, cakes, pastries, and street food like roti maryam and martabak, have been found to have high amounts of TFA. Baking ingredients like shortening and "margarine and butter" combination were also discovered to contain high concentrations of TFA. Dietary behaviour plays a critical role in the development of neurological diseases. Studies have found that HFD can negatively impact cognitive and brain function in animal models (Sal-Sarria et al., 2024). Overloading mitochondria with excess fatty acids can elevate the production of free radicals as a byproduct of energy and steers oxidative stress (San-Millán, 2023). Wang et al. (2020) found that an HFD led to increased oxidative stress and biochemical changes in the hippocampus, a brain region crucial for learning and memory, and more conspicuous with longer exposure.

The exploration of potential therapeutic approaches that have minimal side effects and are relatively inexpensive become an urgent need in reducing cognitive impairment associated with an HFD. Antioxidants can counteract free radicals that cause oxidative stress by donating electrons to them without becoming unstable themselves. A study discovered curcumin and flavonoids from the *curcuma* genus have strong antioxidant, anti-inflammatory, and neuroprotective properties (Panknin et al., 2023). The growing interest in natural products and the resurgence of herbal medicines have prompted scientific investigations into the therapeutic potential of certain herbs like curcumin, the primary bioactive compound found in the rhizome of the turmeric plant.

Gas Chromatography-Mass Spectrometry (GC-MS) analysis of the ethanol extract from *Curcuma sumatrana* rhizomes revealed 21 bioactive compounds, mostly containing sesquiterpenoid compounds, including 7 that may have neuroprotective properties. In a study, Monosodium Glutamate (MSG) administration in mice treated with the ethanol extract of *C. sumatrana* rhizomes was able to maintain cognitive function, prevent degeneration of hippocampal cells, and significantly suppress the accumulation of Malondialdehyde (MDA) (Nawawi, 2021). The effects of *C. Sumatrana* on UC-mice induced by piroxicam could prevent colon shortening, improve the histological condition of the colon, especially preventing thickening of the tunica muscularis, maintain epithelial integrity and goblet cell quantity, and could suppress the number of leukocytes (Rahman, 2024). Administration of *C. sumatrana* extract to the livers of mice fed an HFD showed a decrease in cell degeneration, steatosis, central vein width, and MDA and SGPT (Serum Glutamic Pyruvic Transaminase) levels. The decrease in SGPT levels could be prevented

by the presence of artemisinin, that inhibiting Nuclear Factor-kappa B (NF-κB) activation, inflammatory cytokine expression, and induction of nitric oxide synthase (Annisa, 2024).

Artemisinin has anti-tumor and anti-inflammatory effects and can protect against autoimmune and brain diseases like Alzheimer Disease (AD). Its derivative, artemether, helps in the AD mouse model by reducing harmful changes in the brain. Artemether reduced learning and memory deficits in 3xTg-AD mice, blocked glial activation and cortical neuronal death, regulated oxidative stress by increasing Superoxide Dismutase (SOD) production and decreasing lipid peroxidation, and decreased tau protein phosphorylation and Aβ (amyloid-beta) accumulation. Furthermore, in 3xTg-AD mice, artemether caused the AMPK/GSK3β pathway to become phosphorylated, activating Nuclear factor erythroid 2-related factor 2 (Nrf2) and raising the amount of the antioxidant protein HO-1. These actions most likely generated the anti-inflammatory and antioxidant properties that gave artemether its neuroprotective benefit (Li *et al.*, 2019). Despite the scarcity of existing research on *C. sumatrana* as an herbal remedy, there's a potential for this endemic turmeric, *C. Sumatrana*, to protect brain structure and function to be developed. Modern scientific research has validated the effectiveness of many herbal remedies. The combination of traditional knowledge with scientific methodologies ensures the efficacy and safety of herbal medicines. Therefore, further investigation into the neuroprotective effects of this native plant in HFD-induced mice is necessary.

1.2 Problem Formation

Based on the background above, the problem formulation studied in this research are:

1. What is the effect of *C. sumatrana* extract on cognitive function in HFD-fed mice?
2. What is the effect of *C. sumatrana* extract on MDA level as a marker of oxidative stress in the brain tissue of HFD-fed mice?
3. What is the effect of *C. sumatrana* extract on the histopathology of the brain of HFD-fed mice?

1.3 Research Objectives

The objectives of this research to be accomplished are:

1. To determine the effect of *C. sumatrana* extract on cognitive performance in HFD-fed mice
2. To determine the effect of *C. sumatrana* extract on MDA level as a marker of oxidative stress in the brain of HFD-fed mice
3. To determine the effect of *C. sumatrana* extract on the histopathology of the brain of HFD-fed mice.

1.4 Research Benefits

The findings of this study are intended to provide information about the advantages of wild sumatran turmeric extract in ameliorating brain damage, enhancing cognitive function, and suppressing oxidative stress caused by a high-fat diet (HFD).