

I. INTRODUCTION

Background

Diabetes Mellitus is a degenerative ailment this is classified as a worldwide epidemic. These diseases are among the top 4 contributors to mortality after heart disease, cancer, and chronic respiratory diseases (Rafsanjani, 2020). The International Diabetes Federation estimates that 463 million adults between the ages of 20 and 79 are now dealing with diabetes. According to projections, the total population will reach 578 million (10.2 %) in 2030 and 700 million (10.9 %) in 2045 (IDF, 2019). Diabetes mellitus can be brought on by several circumstances, including an unhealthy lifestyle, indifference to weight due to lack of exercise activity, advancing age, and having a history of the disease that parents pass down to their children. Other organs may also be affected by diabetes complications, like hypoglycemia, ketoacidosis, and diabetic neuropathy (Kallinikou *et al.*, 2019).

Somatic neuropathy and autonomic neuropathy are the two main subtypes of diabetic neuropathy. Numbness, burning, and tingling, particularly in the toes, soles of the feet, and lower legs, are symptoms of somatic neuropathy. Unlike autonomic neuropathy, which does not manifest symptoms until a late stage. Cardiovascular, gastrointestinal, urogenital, metabolic, and pupillary dysfunction are just a few of the organs whose function is affected by diabetic autonomic neuropathy. Cardiovascular autonomic neuropathy raises a diabetes patient's risk of passing away. In this instance, early autonomic neuropathy diagnosis and treatment are crucial for persons with diabetes mellitus (Tsfaye, 2010).

Controlling metabolic glucose levels has been utilized as a treatment for diabetic neuropathy. In addition, drugs such as N-methyl-D-aspartate receptor antagonists (NMDAR), reactive oxygen species (ROS) inhibitors, aldose reductase inhibitors, PKC inhibitors, serotonin-norepinephrine reuptake inhibitors (SNRIs), and anticonvulsants. Hallucinations, sleepiness, and memory loss are side effects. Coupled with the high cost of treatment, poor pharmacokinetics, and drug resistance, there is a shift in drug use from synthesized to natural-based drugs (Arora *et al.*, 2021).

Since the beginning of time, several kinds of spices have been discovered by typically utilized as cooking spices. Many also have other properties, which make them used as medicines. An illustration is the andaliman fruit (*Z. acanthopodium*). The results of research by Wijaya *et al.*, (2018) that andaliman has the potential as an antioxidant andaliman fruit is rich in oil containing alkaloids and saturated fat. Other biological activities found in the genus *Zanthoxylum* are analgesic, antinociceptive, antibiotic, anti-inflammatory, hepatoprotective, antiplasmodial, antiproliferative, anthelmintic, antiviral, antifungal, and immunostimulant (Purba and Sinaga, 2017). Andaliman can also use as a food preservative.

Triterpenoids, which can be utilized as a diabetic treatment in some medicinal plants, are present in the seeds of *Z. acanthopodium*, according to Saragih and Arsita (2019). Research findings by Manurung *et al.*, (2021) that demonstrate diabetic wound healing in FGF expression exhibit that the components in the nano herbal haramonting and andaliman encourage cell division and proliferation to produce wound tissue. With the consideration that andaliman fruit has many good

health benefits, andaliman is strongly suspected of being able to prevent diabetic neuropathy and can be developed as a raw material for herbal-based drugs. So that the need for research on the effects of *Zanthoxylum acanthopodium* fruit extract on alloxan-induced diabetic neuropathy is one of the efforts to explore potential natural medicinal materials.

Formulation of the Problem

Based on the above background, the formulation of the problems studied in this study are:

1. What are the bioactive compounds in andaliman fruit extract that has potential as anti-diabetic neuropathy?
2. How is the effect of andaliman fruit extract on sensation of the paws function and on balance disorders due to diabetic neuropathy in mice?
3. How is the effect of andaliman fruit extract on the accumulation of Malondialdehyde (MDA) in the tissues of the central nervous system area due to diabetic neuropathy in mice?
4. How is the effect of andaliman fruit extract on purkinje cells damage of cerebellum in diabetic neuropathic mice?

The Objective of Research

The objectives to be achieved from this research are:

1. To determine the bioactive compounds in andaliman fruit extract that has potential as anti-diabetic neuropathy.
2. To determine the effect andaliman fruit extract on sensation of the paws function and on balance disorders due to diabetic neuropathy in mice.

3. To determine the effect andaliman fruit extract for the accumulation of Malondialdehyde (MDA) in the tissue area of the central nervous system due to diabetic neuropathy in mice.
4. To determine the effect andaliman fruit extract on purkinje cells of cerebellum in diabetic neuropathic mice.

The Benefits of Research

The results of this study are expected to be used as a source of information for the public regarding the efficacy of andaliman fruit extract in preventing diabetic neuropathy and free radicals.

