CHAPTER 1

INTRODUCTION

According to WHO, diabetes mellitus (DM) is a metabolic condition where the body is unable to produce or even recognize insulin, making the sugar level in the blood increase (Sapra & Bhandari, 2021). Diabetic foot ulcers are the most common complications in persons with poorly controlled diabetes (DM). This syndrome can be caused by inadequate glycemic control, underlying neuropathy, a slow and progressive circulation disorder (PVD), or terrible foot care. Also, this can happen when the areas are exposed to repeated trauma. In some cases, people with severe diabetic foot ulcers have to undergo lower leg amputation to prevent further infection, commonly by *Staphylococcus.* Around the world, 9.1 to 26.1 million suffer from diabetic foot ulcers. Usually, people at any age are commonly suffering from diabetes mellitus (DM), but the prevalence increased among people at the age of 45 and above. The frequency of diabetic foot ulcers is expected to rise as the rate of recently diagnosed diabetics rises year after year (Oliver & Mutluoglu, 2021). There is also a condition before people develop diabetes called prediabetes. Prediabetic condition defined as having a blood glucose level above the normal threshold but not high enough to be diagnosed as a diabetes. This condition is at a high-risk state of developing diabetes with a rate of 5% to 10% conversion every year. Some studies revealed that change of lifestyle give a significant impact to reduce the chance of conversion from prediabetic condition to diabetes for about 40% to 70%, and others mentioned that the use of pharmacotherapy such as metformin is efficient to improve the condition while other drugs can result in adverse effects in some patients (Bansal, 2015). Hence, in this experiment, the matrix of bacteria cellulose and tamanu oil as dressing are investigated to promote wound healing in diabetic-induced mice.

Because wound dressings act as a barrier, it is critical to create appropriate dressings. The best dressings encourage healing while causing the least amount of discomfort to patients. They also need to be able to eliminate unwanted exudate, enhance autolytic debris, and retain sufficient moisture for

healing simultaneously. In order to speed healing and reduce the danger of infection, wound dressings should have a specific way to apply, be flexible, stable, have barrier properties, be biodegradable, have the right viscosity, and be easy to remove. Looking at the specialty a wound dressing should have, therefore, adequate materials are needed (Zheng, Li, Luo & Wang, 2020).

Bacterial cellulose (BC) or biocellulose is a kind of cellulose generated by bacteria from the secretion of polysaccharides derived from carbon sources. It's made up of lignin and hemicellulose-free membranes that have a high elastic modulus and tensile strength when wet (Moraes et al., 2016). This nanostructured cellulose offers excellent biocompatibility and biodegradability, as well as superior physicochemical and mechanical characteristics, it also has higher purity making it available to be used directly (Portela, Leal, Almeida & Sobral, 2019), easier extraction as well as a 3D structure that resembles an extracellular matrix than plant-based cellulose. Furthermore, BC has the potential to be used in a variety of disciplines, including medication delivery, bioprinting, implants, and artificial organs (Zheng, Li, Luo & Wang, 2020). Like any other material, BC also has its drawbacks, one of them is that BC lacks antibacterial properties (Esa et al., 2014), hence Tamanu Oil will come in place.

Calophyllum inophyllum L. or usually called Tamanu is a type of tree that grows mainly along the seashore of Polynesia and Melanesia (Léguillier et al., 2015). Tamanu's leaves, fruits, skin as well as oil extracted from the nuts have been widely used as a traditional medicine up until now and mainly for topical wound applications (Raharivelomanana et al., 2018). The oil of Tamanu is used to treat wounds and relieve neuropathy associated with leprosy as well as other skin-associated diseases (Léguillier et al., 2015). Tamanu Oil contains callophyllolide (CP) that has proven to be able to produce pro-inflammatory cytokine (IL-1β, IL-6, and TNF-α) as well as intensify the anti-inflammatory cytokines (IL-10) production. It also has the ability as an antibacterial agent and increases the regeneration of fibroblast and keratinocytes. Tamanu oils come in four different colors: black, light green, yellowish, and dark-deep-rich green and in this experiment, deep green oil will be utilized in this experiment.

Mice will be utilized as an organism in this experiment to assess the efficiency of the hydrogel matrix since they are more cost-effective and easier to handle than rabbits since rabbits are more fragile and more prone to get sick. The Bacteria cellulose hydrogel in this study will be generated and extracted from *Komagataeibacter intermedius* cultured in MRS medium, and Tamanu oil will be procured. The mice will subsequently be injured and treated with the hydrogel matrix after being induced to develop a diabetic-like organism.

1.1. Objectives

To extract and characterize biocellulose and tamanu oil, to assess the antibacterial activity of biocellulose/tamanu oil against *S. aureus*, as well as producing BC hydrogels with adequate physico mechanical characteristics to be utilized as a dressing, the goal of this study was to see how the dressings affected wound healing in diabetic-induced mice.

1.2 Hypothesis

The hypothesis of this experiment is that the biocellulose-tamanu hydrogel matrix is able to induce wound healing and prevent any infections due to the antimicrobial activity of the tamanu oil