CHAPTER 1

INTRODUCTION

1.1 Background

Diabetes is the fifth leading cause of death worldwide, with a prevalence of 463 million people and an anticipated increase to 548 million by 2025 (Wu et al., 2021). Type 1 diabetes and type 2 diabetes are different kinds of diseases. Five to ten percent of all cases of diabetes are diabetes mellitus type 1 (T1DM), an autoimmune disease brought on by β-cells in the pancreatic islets (Campos et al., 2020). More than 90% of cases of diabetes mellitus are type 2 diabetes (T2DM), with insulin resistance and β-cell dysfunction as its leading causes. (Sameer, Banday, & Nissar, 2020). T2DM is a high cause of mortality in adults aged 50 to 74 (Wu et al., 2021). However, complications from diabetes, such as diabetic foot ulcers (DFU), are fatal. The risk is over three times higher than diabetics without ulcers (Mazlina, 2011).

DFU is characterized by chronic conditions of open wounds that do not heal and can lead to amputations. Therefore, it is crucial to have proper treatment for chronic wounds. However, present treatments for hastening up the healing of diabetes patients' wounds, particularly DFU, are insufficient to fully recover foot ulcers (Glover et al., 2021). Recently, a study has shown that hydrogels could serve better effects as wound dressings for DFU (Motley et al., 2015). Biocellulose (BC) is categorized as hydrogels that have been used as a wound dressing. It is a biocompatible extracellular polymer that is generated and exuded by some bacteria (Cherng et al., 2021). BC has a fibrillar structure and high porosity, enabling BC to absorb and adsorb active chemicals effectively. Additionally, it can improve cellular adhesion, cell proliferation, migration, and differentiation when utilized as a membrane. This fastens the process of re-epithelialization, leading to faster wound healing (de Amorim et al., 2022).

To enhance wound healing, BC can be combined with keratin which has a role in keratinocyte organization and integrity in the epithelium (Konop et al., 2021). As Poranki et al. (2014) mentioned, thermal wounds treated with keratin in keratose hydrogel showed significant wound closure compared to the control. Furthermore, diabetic wound healing has a prolonged inflammation stage, leading to more extended periods of healing and higher chances of bacterial infection (Burgess et al., 2021). In chronic leg ulcers, it is usually associated with bacterial infection; the most common agents isolate are *S. aureus* and *P. aeruginosa* (Serra et al., 2015). Thus, it is vital to have supportive properties in an antibacterial treatment.

Green tamanu (GT) oil is derived from the *Calophyllum inophyllum* tree that has been used in health-related topics as its components support wound healing activity. According to Kumar, A., & Garg, Y. (2020), *Calophyllum inophyllum* was found to have significant antibacterial effects on *S. aureu*s and *P. aeruginosa* by inhibiting the growth rate (Kumar & Garg, 2020). On the other hand, Callophilolide (CP) is the active ingredient of GT that supports it as an anti-inflammatory. Previous studies mentioned that GT has potential anti-inflammatory, which is shown in high inhibition against enzymes that promote inflammation in-vitro (Cassien et al., 2021). Since diabetic wound healing has a prolonged inflammation stage, GT would support the treatment by acting as an anti-inflammatory and antibacterial agent, hence accelerating the healing process.

In this research, keratin, which can accelerate wound closure, was combined with GT due to its antibacterial and anti-inflammatory properties. Combining keratin and GT as the wound dressing would be expected to enhance the efficacy of wound healing. The keratin was applied in the form of keratin-immersed biocellulose (KBC) with BC derived from Komagataeibacter intermedius.

1.2 Objective

The objective of this project is to investigate the effectiveness of green *Calophyllum inophyllum L.* (Tamanu) oil, Keratin, and Biocellulose (KBC) in promoting wound healing in diabetic-induced rabbits and to evaluate the in-vivo antimicrobial properties of green tamanu oil in wound dressing.

1.3 Hypothesis

The hypothesis of this study are:

- The application of KBC and GT to the wound on diabetic-induced rabbit will accelerate wound closure compared to the control
- The microbial count in the wound on diabetic-induced rabbit treated with KBC and GT has lower numbers compared to the control