Chapter 1

Introduction

1.1. Background

Wound is a common injury of the body easily neglected as a minor problem. However, chronic wounds fail through the normal wound-healing process in an orderly and timely manner (Frykberg & Banks, 2015), whereas surgical wounds heal at an average of 6 weeks or more depending on the complexity of the medical condition (Ireton, Unger & Rohrich, 2013). It is evident that not all wounds are superficial thus, further exploration on the use of wound dressings in order to hasten healing time especially wounds with a long healing period.

A common treatment for wound injuries is iodine. Iodine has been used throughout the years due to its broad spectrum, anti-inflammatory activities, low cytotoxicity, and antiseptic properties (Bigliardi et al., 2017). However, iodine-intolerant people are not able to take amounts of iodine higher than the needs of the body. Thus, as an alternative, natural plant usage in wound healing is researched. There are several treatments available for wound injuries, one of which involves the use of curcumin.

Curcumin (CUR) is one of the most commonly studied compounds as it is a prominent constituent of *Curcuma longa* which makes up to 77% of its composition (Kumari et al., 2022) and has been traditionally used as a wound healing agent. Cheppudira et al. (2013) have presented research on the effect of CUR on severe burn wounds in addition to its analgesic and anti-inflammatory effects. In addition, Purohit et al. (2013), observed faster *in vivo* wound healing results in *Curcuma longa* ethanolic extract as compared to standard povidone-iodine. This showed that CUR exhibited the potential to be used as an active ingredient to assist wound healing and can be incorporated into a delivery system for wound care application. However, due to its poor bioavailability, low water solubility, rapid metabolism, and low stability in alkaline mediums, there is a need to increase the wound healing efficiency of CUR as a wound dressing. The development of CUR as a wound dressing can be further enhanced with the combination of a broad-spectrum antibiotic to increase bacterial resistance such as levofloxacin.

Levofloxacin (LEVO) is a water-soluble fluoroquinolone-class drug with higher effectiveness against gram-positive bacteria than most drugs (Podder & Sadiq, 2022). As a wound dressing application, LEVO has been widely reported as an antibacterial drug within polymeric drug delivery systems (Siafaka et al., 2016). Due to increased side effects, LEVO is not used as frequently. However, severe side effects such as those affecting the gastrointestinal tract and central nervous system can be avoided with the use of LEVO in topical applications (Peng et al., 2022). Topical applications such as wound dressings are essential for wound injuries as it blocks potential infection while accelerating wound healing.

As a component that makes up the wound dressing, polymers such as cellulose, chitosan, alginate, gelatin, polycaprolactone (PCL), zein, and fibrin are essential. Among these polymers, ethyl cellulose (ethocel), a derivative of cellulose, is a biodegradable semi-natural polymer widely used in polymeric formulations due to its stability to heat, light, water, oxygen, and chemicals (Wasilewska & Winnicka, 2019; Horvat et al., 2022). In addition, ethocel has good tensile strength and flexibility which is a main advantage for wound dressings that require strong yet elastic properties (Tudoroiu et al., 2022; Sheokand et al., 2023). Another potential polymer is the amphiphilic zein protein with high biodegradability and biocompatibility (Jing et al., 2018). Zein showed anti-oxidative and anti-microbial properties which could further prevent infection of the wound (Akhmetova et al., 2020). Moreover, both ethocel and zein are not as expensive compared to most polymers, thus, would increase cost-efficiency and will be compared for wound healing efficiency.

Several studies have researched drug-loaded wound dressings in several different forms such as hydrogels, films, bandages, nanofibers, patches, and liposomes (Alven, Nqoro & Aderibigbe, 2020). However, recent research in 3D printing to produce wound dressings has been increasing. 3D-printed wound dressings have several advantages such as personalized dressing, multi-delivery of drugs, and high reliability (Tsegay, Elsherif & Butt, 2022). In addition, the use of the semi-solid extrusion (SSE) technique, or robocasting, for 3D printing is able to emphasize the advantages of 3D printing without the need of preparing a filament.

Several researchers have explored the use of SSE 3D printing. However, previous studies utilizing SSE 3D printing to produce dressings with CUR and LEVO have not been researched. Hence in this study, ethocel and zein are utilized as polymers to make CUR- and LEVO-loaded dressing to hasten wound healing and prevent infection.

1.2. Objective

The objective of this study is to compare ethocel and zein as potential polymers for CUR- and LEVO-loaded 3D-printed wound dressing in terms of their physicochemical and mechanical characteristics as well as drug release properties.

1.3. Hypothesis

1. Wound dressing fabricated from ethocel would have superior physicochemical and mechanical characteristics compared to zein
2. Wound dressing fabricated from zein would have higher and faster drug release compared to dressing fabricated from ethocel