UNIVERSITI TEKNOLOGI MARA

CARBOXYMETHYLCELLULOSE SCAFFOLDS FOR TREATMENT OF PARTIAL THICKNESS BURN WOUND - THE ASPECTS OF WOUND MOIST REGULATION, BACTERIAL BURDEN CONTROL AND TOCOTRIENOL THERAPEUTIC

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AUTHOR'S DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulation of Universiti Teknologi MARA. It is original and is the result of my own work, unless otherwise indicated or acknowledged as referenced work. This topic has not been submitted to any other academic institution or non-academic institution for any other degree or qualification.

I, hereby, acknowledge that I have been supplied with the Academic Rules and Regulations for Post Graduate, Universiti Teknologi MARA, regulating the conduct of my study and research.

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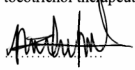
Signature of Student	:	
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ABSTRACT

Sodium carboxymethylcellulose (SCMC) is widely used in the design of wound dressing owing to its high water bonding capacity, good compatibility with skin and mucous membrane, biocompatibility and abundant availability at a low cost. This study aims to design drug-free (low (LV), medium (MV) and high molecular weight (HV)) SCMC scaffolds and promote their ability to promote partial thickness burn wound healing via wound moist regulation and microbial burden control. In addition, SCMC scaffolds of distinct wound healing ability is incorporated with γ-tocotrienol as antioxidant therapeutic and has its wound healing property assessed against pure tocopherol and tocotrienol. SCMC scaffolds were prepared by means of solvent evaporation technique and their physicochemical properties namely, in vitro erosion, moisture affinity, morphology, tensile strength, polymer molecular weight and carboxymethyl substitution were investigated against partial thickness burn wound. The transepidermal water loss (TEWL) from wound of rats treated by control > HV scaffold > LV – MV scaffold. HV scaffold possessed the highest tensile strength of all matrices and was resistant to erosion in simulated wound fluid. In spite of constituting small nanopores, it afforded a substantial TEWL than MV and LV scaffolds from wound across an intact matrix through its low moisture affinity characteristics. HV scaffold was also found to protect moisture loss with minimal accumulation at wound bed thus promoted reepithelialisation process. Transepidermal water movement wound healing by scaffolds was governed by SCMC molecular weight instead of its carboxymethyl substitution degree or matrix pore size distribution. In infected partial thickness wound, *in vitro* polymer characteristics, microstructure, gelling, bioadhesiveness, microbial inhibitory, *in vivo* microbe-colonized wound healing, microbe removal and infection control properties were examined against Gram positive *Staphylococcus aureus* and Gram negative *Pseudomonas aeruginosa. P. aeruginosa* was removed via gelling action of LV scaffold which encapsulated microbes possibly with the binding aid of their extracellular by-product. *S. aureus* was removed via HV scaffolds ability to crease into multiple tight folds to accommodate the microbes under compression and retarded its growth. SCMC scaffolds promoted healing via physical attachment and removal from wound bed which was generally aided via high polymeric carboxymethyl substitution degree and subseqeuent increased of bioadhesive property of the scaffolds. The HV-PVP scaffolds served as the vehicle of γ-tocotrienol. The vitamin incorporation was characterised by drug content of 91.238 ± 0.137 %. The instantaneous vitamin release from the carrier may affect the initial wound healing process as bi-mechanisms of modulating the transepidermal water loss contributed by the HV-PVP carrier and antioxidant activity of γ-tocotrienol. The used of HV-PVP scaffold as the carrier for γ-tocotrienol deemed to optimize its delivery to the wounded area and showed promising outcome in wound healing process.

TABLE OF CONTENTS

CHAPTER ONE
INTRODUCTION

1.1 OVERVIEW

1.1.1 Wound

Wound is defined as an injury with disruption of the normal continuity of the body structures [1]. There are several types of wounds: contused wound, incised wound, lacerated wound, open wound, penetrating wound, perforating wound, puncture wound and burn wound. Wounds can be classified as chronic as well as acute wounds. The causes of wound injury include: 1) physical agents such as trauma, extremes of temperatures, radiation and electric shock and 2) chemical agents such as asbestos, carbon monoxide and insecticides [2].

Acute wound refers to injury which occurs secondary to surgery or trauma in an individual [3]. It is characterised by a fast healing rate with complete recovery of the injury. Chronic wound is affected by factors which bring about disruption to the normal, controlled inflammatory phase or cellular proliferative phase of an injury that may delay the healing process [3, 4]. It can be defined as a loss in tissue integrity produced through frequent recurrence and/or over an extended duration. Pressure ulcer, diabetic ulcer, lower leg ulcer, vascular ulcer, post-operative open wound, and entero-cutaneous fistulae are the common examples of chronic wounds [5]. These types of wound are approached differently in terms of treatment to optimise the healing process.

1.1.2 Wound Healing

Wound is characterized by skin losses its physical integrity thus exposing the tissue to the immediate environment with an excessive loss of water [4, 6, 7]. Wound healing is a prompt response that preserves and maintains the integrity of an organ suffering tissue loss. It is a dynamic process which encompasses three overlapping phases namely inflammation, proliferation and remodeling (Figure 1.1). These sequential phases originate from the interaction and responses of cells in parallel with