DEVELOPMENT OF NOVEL AND ENVIRONMENTALLY FRIENDLY BIO-ACTIVE DERMAL DRUG DELIVERY WOUND PATCH FOR WOUND HEALING

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UNIVERSITI SAINS MALAYSIA

2023

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by

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Thesis submitted in fulfilment of the requirements for the degree of Master of Science

September 2023

ACKNOWLEDGEMENT

It is a genuine pleasure to express my deep sense of thanks and gratitude to God and my heavenly angel mom, Mrs. Yogeswari who have granted me all the grace and strength to complete this research successfully. Next, I would like to express my appreciation to my supervisor, Associate Professor Dr. Sasidharan Sreenivasan who has allowed me to conduct my research work under his supervision. I also like to thank my co-supervisor, Associate Professor Dr Nadras Othman from the School of Materials and Mineral Resources Engineering, Universiti Sains Malaysia for her constant support. Besides that, my appreciation goes to Institute for Research in Molecular Medicine (INFORMM), Universiti Sains Malaysia (USM) for allowing me to conduct my postgraduate studies here. I would also like to acknowledge the financial assistance of USM by awarding me the Graduate Assistant Scheme (GRA), which financially supported me throughout my master's degree. I owe a deep sense of gratitude to my father, Pirem Sunder, and my siblings, Shanthiny, Tarishinie, Visihnu, and Arkash Cheti for their never-ending love, support, and encouragement. Finally, I would like to pay my gratitude to all my friends for constantly supporting and encouraging me especially Ruvanesh. I'm incredibly grateful for him, who stood by to support me throughout the whole journey with his constant love and motivation. Without you, I would not have been able to thrive in my master's programme or balance my research with everything else.

SHARMINY PIREM SUNDER

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LIST OF SYMBOLS

%	Percent
<	Less than
>	Greater than
µL	Microlitre
µm	Micrometre
℃	Degree Celsius
cP	Centipoise
g	Gram
ha	Hectare
mL	Millilitre
n	Sample size of a particular group
p	Statistical probability of the hypothesis
sec	Seconds
µg	Microgram
HC	heavy chain

LIST OF ABBREVIATIONS

ACF	Aberrant crypt foci
ADP	Adenosine 5´ diphosphates
Agro-waste	Agricultural waste
ANOVA	Analysis of Variance
ATP	Adenosine Triphosphate
BOD	Biological oxygen demand
C. albicans	*Candida albicans*
C. hirsutus	*Cocculus hirsutus*
CFU	Colony forming unit
CRAMP	Cathelicidin-related antimicrobial peptide
D	Diameter
E. guineensis	*Elaeis guineensis*
ECM	Extracellular matrix
EPCs	Endothelial progenitor cells
FAO	Food and Agriculture Organization
GelMA	Gelatin methacryloyl
h	Hour
IL	Interleukin
kg	Kilogram
m	Molecular mass
M	Molar
mg	Milligram

Mha	Millihectare
MIROS	Malaysian Institute of Road Safety Research
mL	Millilitre
MTT	3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-tetrazolium bromide
NIH	National Institute of Health
OD	Optical density
PBS	Phosphate-buffered saline
PDGF	Platelet Derived Growth Factors
PQQ	pyrroloquinoline quinone
PVA	Polyvinyl alcohol
PVADH	PVA dehydrogenase
ROS	Reactive Oxygen Species
RT	Room temperature
S. aureus	*Staphylococcus aureus*
S.D	Standard deviation
Sec	Seconds
SEM	Scanning Electron Microscopy
SPSS	Statistical Package for The Social Sciences
SSI	Surgical site infection
TGF	Transforming growth factor
TNF	Tumor necrosis factor
TSB	Tryptic soy broth
USA	United States of America
USM	Universiti Sains Malaysia
UV	Ultraviolet

v/v	Volume per volume
w	Weight
WHO	World Health Organization
WRI	World Resources Institute

PEMBANGUNAN TAMPALAN LUKA BIOAKTIF PENGHANTARAN UBAT YANG NOVEL DAN MESRA ALAM UNTUK PENYEMBUHAN LUKA

ABSTRAK

Pembalut luka atau pembalut luka berubat yang berfungsi dengan baik dalam penyembuhan luka dan tidak membahayakan alam sekitar adalah sangat penting. Pembalut luka kulit sintetik yang boleh didapati di pasaran pada hari ini tidak boleh terbiodegradasi secara semulajadi dan menimbulkan isu alam sekitar yang ketara. Dengan itu, penggunaan sisa pertanian untuk membuat pembalut luka kulit yang boleh terbiodegradasi dan sekaligus mengurangkan masalah alam sekitar adalah idea yang baik. Tumbuhan *Elaeis guineensis* dilaporkan dalam literatur yang mempunyai keupayaan yang baik dalam aktiviti penyembuhan luka dan biasanya ditinggalkan sebagai sisa pertanian di kawasan perladangan. Oleh itu, kajian ini dijalankan untuk membangunkan pembalut luka bio-aktif yang mampu bertindak sebagai penghantar untuk ubat dan mesra alam yang mengandungi ekstrak *E. guineensis* untuk penyembuhan luka. Daun *E. guineensis* diekstrak dengan menggunakan teknik pengekstrakan maserasi yang menghasilkan ekstrak berwarna perang gelap. Seterusnya, ekstrak daun *E. guineensis* dicampur dengan PVA untuk membangunkan pembalut luka kulit yang boleh terbiodegradasi secara semulajadi. Beberapa sifat fizikokimia telah dinilai dan dilaporkan, seperti rupa, berat purata, ketebalan, kandungan lembapan, kelikatan dan pH. Pembalut luka kulit yang dibangunkan mempunyai ketebalan purata 0.020 mm dan berat 3.87 mg dengan kandungan lembapan 17.61%. Tambahan, nilai pH pembalut luka kulit yang dibangunkan ialah 6.97, dengan nilai kelikatan 2.56 cp. Keputusan ini menunjukkan bahawa pembalut luka kulit yang dibangunkan adalah sangat sesuai dan selamat untuk digunakan sebagai agen penyembuhan luka. Akhir sekali, kajian biodegradasi pembalut luka kulit yang dibangunkan dengan atau tanpa bahan tambahan semula jadi ekstrak daun *E. guineensis* yang telah dijalankan selama 25 hari menunjukkan perbezaan yang ketara dari segi saiz, berat, dan pemerhatian morfologi permukaan berasaskan Mikroskop Elektron Imbasan (SEM). Pengurangan ketara dari segi saiz dan berat pembalut luka kulit dibangunkan dengan ekstrak daun *E. guineensis* membuktikan bahawa pengadunan ekstrak daun *E. guineensis* dengan PVA dapat mempercepatkan kadar biodegradasi pembalut luka dermal yang dicipta. Akhir sekali, aktiviti antibakteria pembalut luka kulit yang dicipta dengan atau tanpa ekstrak daun *E. guineensis* terhadap *Staphylococcus aureus* yang dilakukan menggunakan kaedah Colony-forming unit (CFU) membuktikan bahawa penambahan ekstrak daun *E. guineensis* pada tampalan luka meningkatkan aktiviti antibakteria terhadap mikrob jangkitan luka. Kesimpulannya, kajian ini berjaya membangunkan pembalut luka kulit bioaktif terbiodegradasi daripada ekstrak sisa pertanian daun *E. guineensis* untuk digunakan sebagai pembalut ubat serta aplikasi penyembuhan luka pada masa hadapan.

DEVELOPMENT OF NOVEL AND ENVIRONMENTALLY FRIENDLY BIO-ACTIVE DERMAL DRUG DELIVERY WOUND PATCH FOR WOUND HEALING

ABSTRACT

Having a wound-healing dermal patch or medicated dressings that work well in wound healing and doesn't harm the environment is crucial. The commercially available synthetic dermal patches, plasters, and wound dressings in the market today are non-biodegradable, posing significant environmental issues. As a result, it is a great idea to reuse agro-waste to make a biodegradable dermal wound patch and, eventually, reduce environmental problems. *Elaeis guineensis* plant was reported with good wound healing activity in the literature and is commonly left as agro-waste at plantation areas. Therefore, this study was conducted to develop an environmentally friendly bio-active dermal drug-delivery wound patch containing *E. guineensis* for wound healing. The *E. guineensis* leaf was extracted using methanol by maceration extraction techniques, which yielded a dark brown paste-like crude extract. Subsequently, *E. guineensis* leaf extract was blended with polyvinyl alcohol (PVA) to develop a biodegradable dermal wound patch. Several physicochemical properties were evaluated and reported, such as appearance, average weight, thickness, moisture content, viscosity, and pH. The developed dermal wound patch had an average thickness of 0.020 mm and a weight of 3.87 mg with 17.61% of moisture content. The pH of the prepared dermal wound patch solution was 6.97, with a viscosity value of 2.56 cp. These results showed that the developed dermal wound patch is an appropriate and safe candidate to be utilized as a wound-healing agent. Finally, the biodegradation evaluation of the created dermal wound patches blended with and without natural additives of *E. guineensis* leaf extract for 25 days resulted in significant variances in the size, weight, and Scanning Electron Microscopy (SEM) based surface morphology observation. The apparent reduction of size and weight of the dermal wound patch made with *E. guineensis* leaf extract proved that blending *E. guineensis* leaf extract with PVA could fasten the degradation rate of the developed dermal wound patch. Finally, the antibacterial activity of the developed dermal wound patch made with or without *E. guineensis* leaf extract against *S. aureus* that was performed using the Colony-forming unit (CFU) method proved that the additionof *E. guineensis* leaf extract to the wound patch increased the PVA patch’s antibacterial activities against the wound infection microbe. In conclusion, this study successfully developed a biodegradable bioactive dermal wound patch from agro-waste of *E. guineensis* leaf extract to utilize in future medicated dressings and as well as wound healing applications.

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CHAPTER 1

INTRODUCTION

1.1 Overview and rationale of the study

Elaeis guineensis is an edible oleaginous plant known as African oil palm or macaw-fat (García, 2016). Oil palm plantations have been expanding dramatically which explains its high productivity, mainly in Southeast Asia, which has the potential to serve as a major economical profitable plant. Following the drop in rubber prices, increased demand for palm oil eventually led to the growth of oil palm plantations where, the development of new plantations on previously forested land, and as well as the replacement of old rubber plantations (Shevade & Loboda, 2019). At present, according to Malaysian Palm Oil Council, Malaysia is greatly known throughout the world as the second largest producer and exporter of palm oil products in the world, producing about 17.73 million tons of palm oil and 2.13 million tons of palm kernel oil (Ferdous Alam *et al*., 2015). Oil palms are now grown throughout the humid tropical lowlands (Lim *et al*., 2011) accounting for about 18.1 Mha in 43 countries, especially in Indonesia, 17.1 Mha and in Malaysia, 4.6 Mha (Murphy *et al*., 2021). The edible oil and fat industries include 17 different types of oils and fats that fall under the categories of vegetable oils and animal fats. The production of edible oils and fats worldwide rose by over 176% over 26 years, from 84.6 million tonnes (Mt) in 1992/93 to 233.3 Mt in 2018/19, as shown in Figure 1.1. That equals a 5.7 Mt annual increase on average (Khor *et al*., 2021). The latest generated plantation map predicts that Peninsular Malaysia had 5.5 Mha under plantations in 2014 and huge industrial-sized plantation covering 2,631,070 ha with 89% (2,335,260 ha) under oil palm cultivation (Figure 1.2) (Shevade & Loboda, 2019).

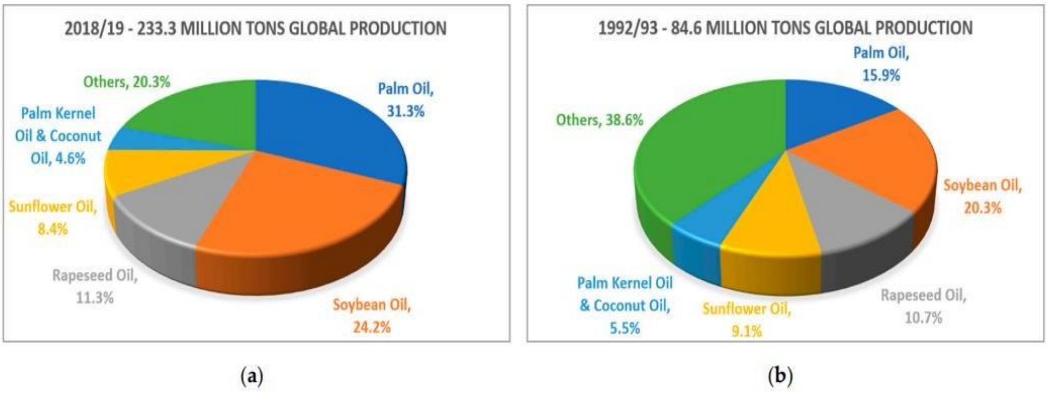

Figure 1.1: Market shares of 17 edible oils and fats produced worldwide in (a) 2018-2019 and (b) 1992-1993

Source: Khor *et al*., 2021.

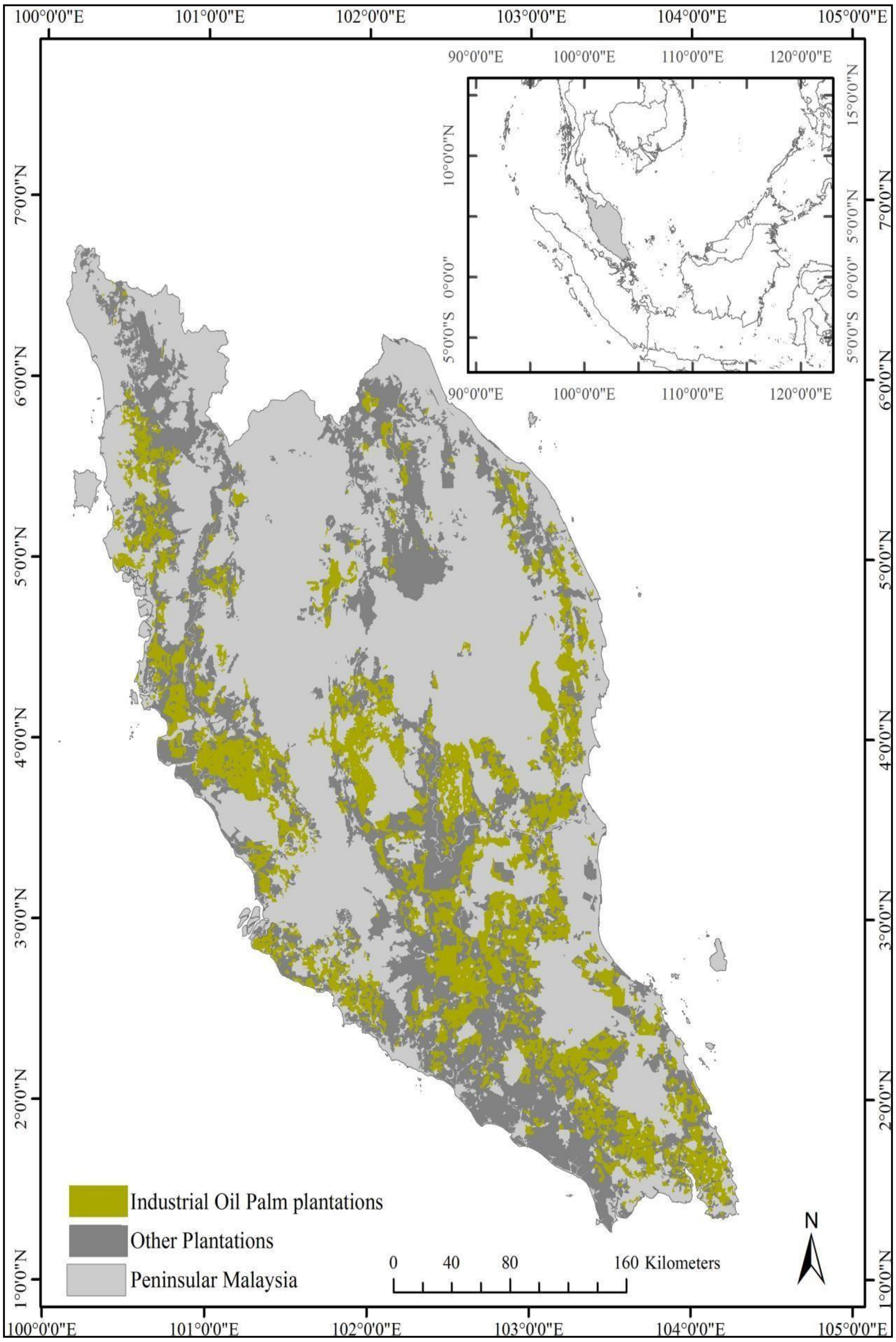

Figure 1.2: Peninsular Malaysia with industrial oil palm plantations and otherplantations from World Resources Institute (WRI)

Source: Shevade & Loboda, 2019.

Research states that domestic palm oil production is expected to increase by about 55% to 25 million tons in the year 2035. The demand for palm oil is mainly for food consumption, industrial non-food uses, and biodiesel, and it is estimated to rise to 1.4 million tons in 2035 (Gan & Li, 2014). Together with the expansion of plantation area of oil palm, significant problems arise when the amount of waste produced during agro-industrial activities also increases and it is reported that approximately 85.5% of agro-waste in Malaysia comes from the oil palm industry andpalm oil mills (Faridah *et al.*, 2018). Hence, the expansion of oilpalm plantations has generated a large amount of agro-waste such as empty fruit bunches, shells, kernels, fronds, and leaves (Faridah *et al.*, 2018) that eventually created problems in replanting operations and led to tremendous environmental concerns. For instance, untreated effluent from the oil palm mill that produces from the oil extraction, washing, and cleaning-up processes are being discharged into water streams and this action deteriorates the environment (Singh *et al.*, 2015). Improper handling of the agro-waste or likely known as residue from oil palm processing may lead to environmental and health concerns, as it can contribute to eutrophication, pollution, and any other type of disturbances for both aquatic and terrestrial life (Maluin *et al.*, 2020). There is an effective possible action to reduce agro-waste from oil palm plantations which are by converting the agro-waste into a useful product.

Understanding factors that are causing bad effects on the environment and health is thus important to identify the way to prevent them before it's too late. One of the agro- waste from *E. guineensis* is the leaf that could be converted into a useful product rather than just leaving it on a plantation area that consequently led to immense environmental problems According to a study done by Sasidharan *et al.* (2010), *E. guineensis* leaf extract was applied on *Candida albicans* infected wound in the rat model that resulted on reduced microbial count and significantly accelerates the period of wound healing, thus supporting the traditional use of *E. guineensis* leaf. Moreover, a previous study on '*in vitro* and *in vivo*' also depicts that the *E. guineensis* leaf extract exhibits outstanding antimicrobial activity against both bacteria and fungi, especially against the yeast *C. albicans* (*in vitro* and *in vivo*) and *S. aureus* (*in vitro*), which are the most abundant species affecting wounds (Chong *et al*., 2008; Rajoo *et al*., 2010; Vijayarathna *et al.*, 2012). Next, another study was conducted to determine the wound healing activity of *E. guineensis* leaf extract in the *S. aureus* infected rat model, it demonstrates that the leaf extract possesses good wound healing activity in the *S. aureus* infected wound model in rats by retarding the *S. aureus* bacterial growth (Rajoo *et al*., 2010). Furthermore, the toxicity of *E. guineensis* leaf methanol extract against brine shrimp (*Artermia salina*) and mice for toxicity was also tested and both tests verified that *E. guineensis* leaf was non-toxic and safe for commercial applications (Syahmi *et al*., 2010).

Moreover, another study on the antioxidant and hepatoprotective activity of methanolic extracts of *E. guineensis* leaf firmly reported that *E. guineensis* leaf possesses good *in vitro* antioxidant activity and *in vivo* hepatoprotective measures against paracetamol-induced liver damage in mice. The investigation proved that this activity's possible mechanism might be due to the free radical-scavenging and antioxidant activities which is mainly because of the presence of polyphenols in the leaf extract (Sasidharan *et al*., 2009). Since *E. guineensis* leaf is rich in polyphenols, another study was done to investigate the effectiveness of natural antioxidant acquired from oil palm leaves as an aging retardant in natural rubber vulcanizates and the findings depicts that *E. guineensis* leaf can be a favorable multifunctional additive in polymer processing technology (Anandhan *et al*., 2011; Shuhaimi *et al*., 2014). Therefore, the development of a novel bioactive drug-delivery wound patch from *E. guineensis* leaf extract, which is rich with various biological activities and natural polymer improver properties is one of the most intensely persuaded goals of us.

Based on today's medical field technology, dermal patch technology is frequently used to deliver drugs and medications penetrating the skin without any needles (Toshkhani *et al*., 2013). Transdermal systems are an advisable procedure for delivering drugs or medications over the skin of patients as its convenient and pain- free compared to the delivery of medication like oral, topical, intravenous, and intramuscular that will be painful for the patient (Tanwar & Jambheshwar, 2016). Moreover, the advancements in dermal patch (wound- dressing product) technology have proven to be the fastest, easiest, safest, and most economical way to heal an infected wound (Anandhan *et al*., 2011; Sen, 2019).

Presently, the synthetic dermal patches, plasters, and wound dressings in the market are non-biodegradable, leading to tremendous environmental problems. So, incorporating agro-waste such as oil palm leaf with wound patches is believed to increase the biodegradability of the wound patch, which eventually decreases the ecological issue. Hence, various studies are being conducted using natural polymer from agro-waste to develop a complete biodegradable dermal wound patch. For example, a dermal wound patch was produced using aqueous extract and mucilage of *Cocculus hirsutus* and by cross-linking with Polyvinyl alcohol (PVA), which is one of the most readily biodegradable vinyl polymers. It was reported that complete biodegradation of the dermal film was observed within 25 days in sandy soil, black loamy, and red soil (Nilani *et al*., 2010). When considering the biodegradability of PVA, it is important to note that PVA is indeed a biodegradable polymer as it can be broken down by microorganisms in the environment. The biodegradation of PVA primarily occurs through the action of specific enzymes produced by microorganisms, such as bacteria and fungi, which can hydrolyze the polymer chains of PVA. The biodegradability of PVA also depends on several factors, including the specific characteristics of the PVA polymer, environmental conditions, and the presence of appropriate microorganisms capable of degrading it. Factors such as the degree of polymerization, the presence of cross-linking agents, and the chemical structure of PVA can also influence its biodegradation rate (Wu *et al*., 2019). Thus, the inclusion of natural polymers derived from agro-waste, such as oil palm leaf or plant extracts, in combination with PVA can enhance the biodegradability of wound patches and contribute to decreasing the ecological issues associated with non-biodegradable synthetic patches. The use of intentionally degradable polymers in today's technology has been brought into prominence with innovations in drug delivery systems. For instance, in this study, PVA is used to develop a novel bioactive dermal drug-delivery wound patch with *E. guineensis* leaf as natural polymer improver properties.

1.2 Problem statement

The most recent retrospective analysis of the Medicare 5% dataset for 2014 that examined wounds from all categories, including acute and chronic wounds, pointed out that about 8.2 million Medicare beneficiaries had at least one type of wound or infection (Nussbaum *et al*., 2018). Furthermore, Medicare spending estimates for all wound types ranged from $28.1 billion to $96.8 billion, and it was reported that the most expensive treatments were for surgical wounds ($11.7, $13.1, and $38.3 billion), followed by diabetic foot ulcers ($6.2, $6.9, and $18.7 billion). The highest cost approximate for the service site was for hospital outpatients ($9.9–$35.8 billion), followed by hospital inpatients ($5.0–$24.3 billion). The 2018 market research report predicted that the global wound-closure products market would exceed $15 billion by 2022. In 2024, it is estimated that the advanced wound care market targeting surgical wounds and chronic ulcers is expected to exceed $22 billion (Shuhaimi *et al*., 2014). Wound restoration is a difficult and tightly regulated physiological process involving homeostasis, inflammation, proliferation, and tissue remodelling. There is a significant demand for wound care products in the world's largest wound dressing markets which is the United States and Europe (Sen, 2019). Therefore, the development of an environmentally friendly, naturally derived, smart novel bioactive dermal drug-delivery wound patch could reduce healthcare costs. In addition, this will also benefit society as the cost of the treatment will be less and more affordable.

Besides that, more attention is paid to pollution caused by non-biodegradable synthetic polymers, which has resulted in worldwide concern about biodegradable substances. Nature itself can inspire the development of fully biodegradable materials, presenting enhanced bioactive potentialities and sustainability via medicinal plants. Medicinal plants typically promote wound healing by initiating skin cell proliferation and differentiation with extra benefits, such as antimicrobial activities against the infected wound. Furthermore, PVA is cross-linked with the *E. guineensis* leaf extract in this study to enable the developed wound patch readily biodegradable. Thus, the use of degradable PVA polymers filled with *E. guineensis* leaf extract to develop novel bioactive dermal drug-delivery wound patches has been brought into prominence with drug-delivery innovations systems.

1.3 Research Objectives

1.3.1 General objective

The current study was conducted to develop novel and environmentally friendly agro-waste of *Elaies guineensis* leaf extract-based bioactive dermal wound patch for wound healing.

1.3.2 Specific objectives

I. To develop the *Elaies guineensis* leaf extract-based bioactive dermal wound patch.

II. To evaluate the physicochemical properties of the developed *Elaies guineensis* leaf extract-based bioactive dermal wound patch.

III. To study the biodegradability of the developed *Elaies guineensis* leaf extract-based bioactive dermal wound patch.

CHAPTER 2

LITERATURE REVIEW

2.1 Skin structure

The skin is the largest organ of the body, with a total area of about 20 square feet, made up of water, protein, fats, and minerals. It plays a major role in providing an airtight, watertight, and flexible barrier separating the internal organs of the body from the external environment (Rousselle *et al*., 2019). Generally, skin acts as a protection for the body from microbes and the elements as well as modulating body temperature under various thermal conditions. The human skin is divided into two apparent layers: epidermis and dermis, with the hypodermis or subcutaneous layer, which is not part of the skin, but comprised of the skin structure since it attaches to the dermis by collagen and elastic fibers (Oguntala *et al*., 2021) as shown in Figure 2.1.

The thickness of every layer of the skin depends on the body region and is categorized based on the thickness of the epidermal and dermal layers. The most outer layer of the skin is the epidermis. Epidermis is a superficial layer of stratified squamous epithelium without any blood vessels, composed mainly of keratinocytes (95%) and dendritic cells (5%) (Gilaberte *et al*., 2016). It is divided into four layers based on keratinocyte morphology and the degree of differentiation into cornified cells which are called Stratum basal, Stratum spinosum, Stratum granulosum, and Stratum corneum (Hollingshead *et al*., 2021). Epidermis acts as a physical and chemical barrier between the interior body and the exterior environment (Nafisi & Maibach, 2018).

The dermis underlies the epidermis and consists of highly vascularized and innervated connective tissue that aids the epidermis and the skin appendages

(Aspinall *et al*., 2020). The dermis has connective tissue, blood vessels, oil and sweat glands, nerves, hair follicles, and other structures. It is composed of two layers, a thin upper layer called as papillary dermis and a thick lower layer called as reticular dermis (Carroll, 2007). The papillary dermis is formed by elastic fiber and fine collagen fibers where this layer is rich in blood vessels, macrophages, mast cells, and other inflammatory cells. It is found in thicker epidermis regions like the foot pads and nasal plate. Beneath the papillary dermis is the reticular dermis where this layer is made up of coarse collagen fibers and elastic fibers. This layer also consists ofadipocytes, melanocytes, mast cells, nerve fibers, and small blood vessels (Aspinall *et al*., 2020). The main role of the dermis is to support the epidermis and the nerve endings in the dermis as it can detect touch, temperature, pressure, and pain stimuli. Besides that, with the presence of sweat glands in the dermis, we can produce sweat in response to certain weather, such as heat and stress. The evaporation of sweat off the skin is crucial to our self to balance homeostasis by cooling down our body. Hair follicles that underlie the dermis are important in producing hairs around the body. The presence of hair on the skin will help in regulating body temperature, protection from injury, and enhancement of sensation (Nafisi & Maibach, 2018).

The hypodermis or subcutaneous tissue is the innermost layer of skin and is composed of lipocytes. The subcutaneous tissue is composed of lobules of adipocytes separated by fibrous septa which are formed from collagen and blood vessels. The vast number of fibers from the dermis extending into the subcutaneous layer leads to a stronger connection between these two sections (Lai-Cheong & McGrath, 2017). In short, skin is the frontier with the exterior environment and is naturally exposed to a variety of chemical, physical, and biological agents, which is called an exposome (Schalka, 2021). The skin is capable to cooperate with other tissues to maintain the whole system of the body through the production of cytokines, neurotransmitters, hormones, and their receptors (Zmijewski & Slominski, 2011).

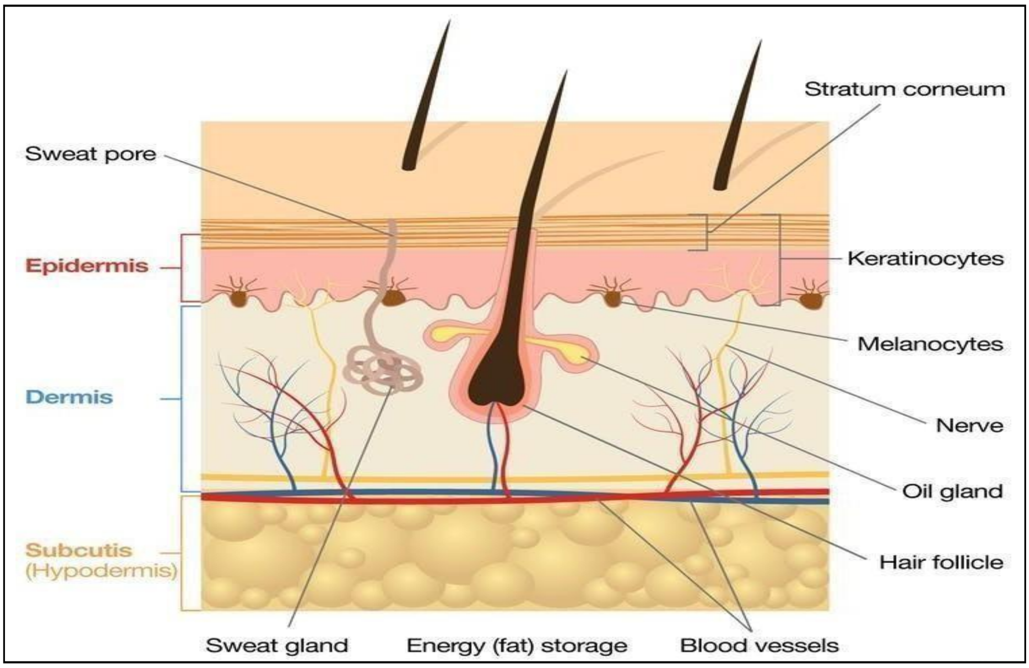

Figure 2.1: The skin layers
Source: Boer *et al*., 2016.

2.2 Wounds

Wounds can be defined as an injury that breaks in the continuity of any bodily tissues or on the skin, where this includes cuts, scrapes, scratches, and punctured skin (Järbrink *et al*., 2017). Within this general definition, many subdivisions on the reason for wounds underlie such as wounds that occur due to accidents, surgery, sutures, and stitches. According to The Malaysian Institute of Road Safety Research (MIROS), it is stated that the number of cases involving injuries due to accidents on the road in 2019 was 15,044 while in 2020 was 17,236 cases. MIROS pointed out that the increment of cases of about 2,192 cases from 2019 to 2020 involving injuries due to accidents on the road is one of the issues that must be taken seriously.

Besides that, the surgical wound usually occurs due to improper handling of the wound during the surgery which eventually could lead to infections in a few areas of the skin at the area where the incision is made, beneath the incision in muscles and tissues surrounding muscles and infections in other parts of the body involved in the surgery (Ban *et al*., 2017). Surgical site infection (SSI) is the most common complication affecting 40% of patients in a year worldwide. This is very sad as it will eventually increase a patient's risk of morbidity and mortality and can lead to tremendous economic consequences (Ban *et al*., 2017).

The wound is usually classified into two elements which are open wounds and closed wounds. An open wound is an injury involving an external or internal break in body tissue, usually involving the skin. There are four major types of open wounds which are abrasion, avulsion, laceration, and puncture.

Abrasion (Figure 2.2) can be described as superficial injuries on the skin by a traumatic removal, detachment, or disruption of the epidermis that is mainly caused by friction (Leite *et al*., 2020). When the skin collides tangentially with a rough or hard surface, a lateral rubbing action scrapes off the outer layer of the skin, keratinized parts, exposing the more sensitive layers like denuded corium which will be initially covered with serosanguineous fluid (Ishii, 1968). Therefore, abrasions do not result in bleeding, but the injury will appear wet due to the fluid. Then, after a short time, the tissue fluid will eventually dry out and forms a brownish scab. Normally, if the lesion did not reach the dermis, it can heal within several days without scarring. Another type of abrasion is caused by a vertical impact on the skin called pressure or crushing abrasion where in this case, the imprint of the causative object can be reflected by the shape of the skin injury (Leite *et al*., 2020).

Figure 2.2: Abrasion injury
Source: Leite *et al*., 2020

Examples of abrasion injuries are scraped knees or road rashes. A researcher reported that soft tissue injuries like abrasion injuries are the major common type of injury to all motorcyclists involved in crashes but it's not life-threatening. In most cases, abrasion injury will only result in slight pain. However, it can also lead to serious health implications such as infections and scarring (Meredith *et al*., 2015) because the break in the skin enables the germs easily to travel from the external environment to inside the skin (Pollak & Saukko, 2013). It is very important to clean the wound by rinsing it with water, then flushing it with a sterile solution to remove any debris on the wound. Mostly, a scab will be formed as a natural bandage. The action of picking the scab must be avoided as it can delay the period of healing (Meredith *et al*., 2015).

The second type of open wound is avulsion. An avulsion is a type of wound caused by a tearing force in which, a portion of skin and underlying tissue will be partially or completely torn away (Sorg *et al*., 2017). Avulsion is one of the ugliest injuries where they are much more than simple lacerations but lesser than full amputations. Despite being called as avulsion injury, this can also be called as degloving injury. Degloving can be described as an avulsion that encloses an extremity and causes the layers of tissue to pull away no matter where the injury is; fingers, feet, and hands (Sakai *et al*., 2017). The most common causes of skin avulsions are explosions, animal bites, industrial equipment malfunctions, and motor vehicle accidents. This type of injury often causes unstoppable bleeding as the injury might damage all three layers of skin, epidermis, dermis, and hypodermis. Besides that, due to the force of the injury, the damages can completely dislodge those body parts *(Sorg et al*., 2017). This type of wound cannot be closely stitched because the tissues might be missing

(Rahimizadeh & Javadi, 2020). This injury typically needs professional medical attention, especially if the wounds are very large as it can lead toexcessive bleeding and a higher potential for infections. Based on research done by Yao*et al*. (2019), avulsion usually takes a longer period to heal depending on the extent of the injuries and always needs surgical interventions to heal properly, thus cannot be treated appropriately without a professional. Large area skin avulsion injuries, mainly those caused by motor vehicle accidents or machine injuries, frequently come with secondary skin necrosis, uncovered wound, fracture malunion or non-union, scar contracture deformation, amputation, and even may lead to high morbidity and even mortality, if the injury is handled inappropriately (Chen & Liu, 2016). Clinical treatment of degloving injuries remains significant because surgeons themselves need to face serious difficulties in wound coverage, and infections and to deal with the combined fractures and injuries of the blood vessels, nerves, and tendons (Chen & Liu, 2016). Figure 2.3 shows an example of ring avulsion injury.

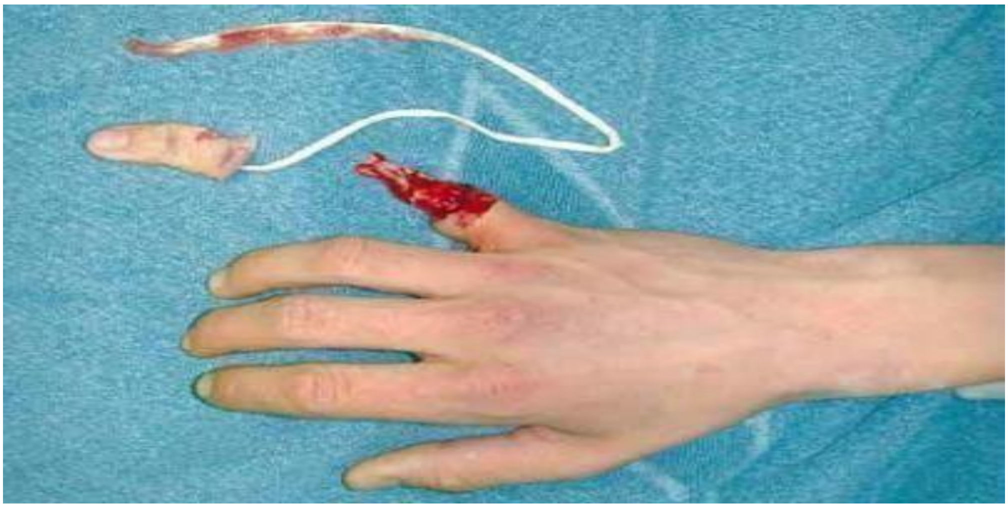

Figure 2.3: Ring avulsion

Source: Bouz *et al*., 2021

Another type of open wound is laceration which can be described as a wound, in which a deep opening of the skin and the underlying tissues will be cut or torn (Brinker *et al*., 2003). Lacerations are commonly caused by accidents, or incidents involving knives, machinery, or other sharp tools. The result of the skin hitting a sharp object or an object hitting the skin with force will cause damage to various layers of skin that eventually lead to rapid and extensive bleeding (Payne-James, 2015). Generally, the number of cases that underlies laceration wounds is the highest among young adulthoods (18 – 35 years old) when compared to adulthoods (36 – 55 years old). It is proven that the major reason why younger workers always encounter injuries like lacerations is due to lesser experience when handling new toolsor machinery that can cause cuts at their working place (Sen, 2019). In 2005 only, nearly 13.8 million people visit emergency rooms under the case of laceration care in the United States (García-Gubern *et al*., 2010) and the clinical presentation of lacerations usually varies based on location, depth, width, length, and the severity of the wound (Brinker *et al*., 2003).

Minor lacerations can be cleaned using a few different solutions such as tap water, sterile saline solution, or antiseptic solutions. Antibiotics are only required when the wound is infected because excessive use of antibiotics may lead to side effects (Sen, 2019) like digestive problems, fungal infection, and anaphylaxis. All uninfected wounds should be covered with moist gauze followed by the application of dry gauze and lastly, cover with a bandage. The step of applying wet to dry dressing is to allow the bandage to stick to the dead tissue in performing a mechanical debridement and to allow new healthy skin to grow (Sen, 2019). If the wound is being treated in less than 12 hours from the injury time, then, it can be closed by sutures or staples method. Meanwhile, for those wound that is being treated after 48 hours, they will be suspected to be infected. This type of wound should be directly rushed for medical attention as the wound must notbe closed completely (Garzotto, 2009). Figure 2.4 shows an example of a minor laceration wound on the knee.

Figure 2.4: Minor laceration wound on knee

Source: Garzotto, 2009

Next, a puncture wound is a deep wound that occurs due to sharp and pointed objects, such as nails, jagged pieces of metal or wood, glass, needles, and seashells. Although a puncture wound may appear like just a small entry of a hole and not seem serious they need treatment from healthcare providers as this type of wound can be infected easily (Lavery *et al*., 1996). This is because, dirt and germs can be carried deep into the tissue as the injury may extend into the deeper tissue layers (Garzotto, 2009). The opening of the skin might be smaller and may not bleed much but they can't be treated like how treatment for cuts is treated because these small holes in the skin can lead to disguise serious injury (García-Gubern *et al*., 2010). In some cases, the piece of objects that cause the skin to puncture might break off and remain under the skin where this incidence can lead to long-term bone infection. Research shows that deep puncture wounds of the foot are common injuries among children as they usually go barefoot everywhere, and this just heightens the risk of puncture wounds (Sen, 2019). Mostly, puncture wounds that occur due to a bite or rusty piece of metal, such as a rusty nail need prompt medical attention because it may carry bacteria or spores like *Clostridium* spp. that can cause tetanus into the skin and tissue (Payne-James, 2015). Figure 2.5 shows an example of a puncture wound on the foot.

Figure 2.5: Puncture wound on foot

Source: Payne-James, 2015