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MARINE-DERIVED COMPOUNDS FOR WOUND HEALING AND TISSUE REPAIR

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Abstract
Natural product medicine was outstanding in traditional and modern system of medicine throughout recent decades. The study primarily evaluates the wound healing activity and healing of infected wounds by V. arborea fractions from literature and traditional form alone. Screening required appropriate and laboratory model conforming to the 3Rs principle of animal experimentation. Accordingly, a novel, adult zebrafish excision wound model was developed to screen for both activities alone and simultaneously when wounds were infected with microbe (under compromised conditions). In recent times, there is again a renaissance for screening of herbal extracts for the discovery of safer and more efficient drugs. The assessment of the active ingredients and mode of action of different aquatic medicinal plants is now underway. For the purpose of managing and treating wounds, certain medicinal plants and herbs that have been shown to be beneficial in the healing process were selected. They are slow healing wounds and wound management has been one of the challenging tasks in some conditions.
Keywords: Marine, Derived Compounds, Wound Healing, Tissue Repair.

1. INTRODUCTION

Skin is an essential tissue which controls body temperature, inhibits loss of water, electrolyte and other body constituents. It prevents the invasion of microorganism and foreign material from the environment and shields against radiation caused by UV light. There is a third subcutaneous layer under the dermis and it is chiefly composed of adipocytes [1]. But all these activities and integrity of skin tissue is lost due to wounds due to physical or chemical or immunological reasons[2]. Therefore, it is a must to look after skin and to maintain it in its shape and smoothness by healing the wound as soon as possible. Wounds are defined by the Wound Healing Society as physical trauma that results in a skin opening or disruption, which disrupts the normal structure and function of the skin [13]. They cause the epithelium to discontinue, either with or without the underlying connective tissue being lost. This includes damage to the underlying tissues or organs brought on by surgery, blows, cuts, chemicals, heat or cold, pressure, friction or shear strain, or illness. Microorganism penetrates the wound on exposure to air, thus causing contamination of the wound and eventually infection development. Wound may be caused due to physical, chemical, microbial agents, thermal or immunological tissue injury [3]. In order to achieve anatomical continuity and wound function, the general idea behind maximum wound healing is to minimize tissue damage while maintaining enough tissue perfusion and oxygenation, optimal nourishment for the tissue, and a moist wound environment. Skin wound healing is the result of a series of biological processes that begin with wound closure and proceed in a specific order to repair and restructure the damaged tissue. As much as there has been

extensive development in the pharmacy sector, drugs capable of inducing wound repair processes are still yet to reach the market.

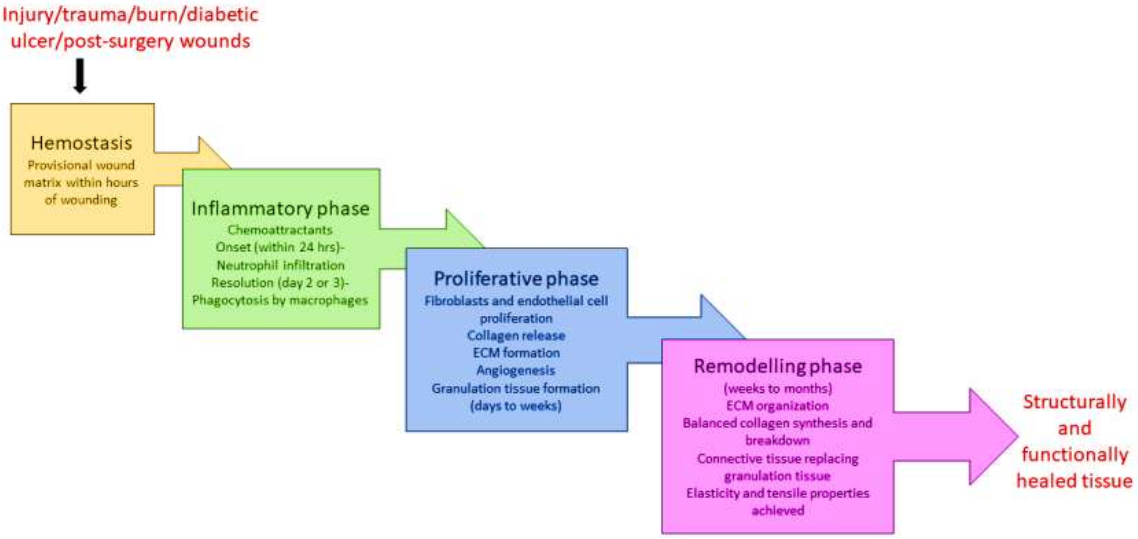


Fig. 1.1 Phases of wound healing

Besides that, due to costly therapy of high expense and unwanted side effect availability, another very important matter is the chronic wound care [4]. There is a shared awareness that reactive oxygen species (ROS) hinder wound healing because they have negative effects on cells and tissues. Synthetic absorbable biomaterials are subjected to degradation through ROS.

2. REVIEW OF LITERATURE

Screening of new wound healing drugs is done in models based on the type of wounds. Wound models can be used for testing healing potential of novel drugs, to expose pre-known agents of wound healing mechanism of action and for measuring efficacy of wound healing potential of reference agents[5]. In vivo models like human, rodents, rabbit and porcine models though desirable violate 3Rs' principle, i.e., replacement, reduction and refinements in animal use. The use of superior mammalian animals replaced by inferior models like the fish, was stressed. Accordingly, we attempted to develop a Danio rerio (Zebrafish) derived wound or infected wound to study the kinetics of healing in the presence of phytocompounds [11].

Free-radical-scavenging enzymes (FRSE), a cytoprotective enzymatic category of enzymes, are essential for reducing, deactivating, and eliminating ROS as well as controlling the wound-healing process. Acute response-induced inflammation causes neutrophils to coordinate their infiltration into the wound site[12]. As part of their regular "respiratory burst" activity, these cells generate free radicals. Additionally, non-phagocytic cells connected to the wound produce free radicals via the non-phagocytic NAD (P) H oxidase pathway. As a result, reactive species with nitrogen and oxygen centers, as well as their derivatives, are abundant near the wound site[10]. Lipid peroxidation, DNA strand breaking, and enzyme inactivation are all caused by the radicals' induction of oxidative stress. These include enzymes that scavenge free radicals[7]. Given evidence of oxidants' involvement in the pathophysiology of numerous illnesses, antioxidants may have therapeutic value in treating various conditions[15]. Applying substances with free radical-scavenging properties topically to patients has been shown to greatly speed up wound healing processes and shield tissues from oxidative damage [14].

3. MATERIALS AND METHODS

Another name for a contusion is a bruise. The underlying tissues and blood vessels are damaged, while the skin on top is normally unharmed due to forceful trauma. Bleeding from tiny arteries into tissues causes the color shift. When red blood cells are stuck in tissue gaps, they lose oxygen and turn black[6]. Because blood circulates towards the body's surface, bruises can also form behind deeper tissues, such as bone injuries, and not be apparent for a while. A hemorrhage occurs when blood accumulates in a small area of tissue. A hemorrhage's tightly packed blood can exert pressure on surrounding tissues, perhaps resulting in pain and nerve compression. There is a chance that a hemorrhage could become infected, necessitating the operative evacuation of others [9].

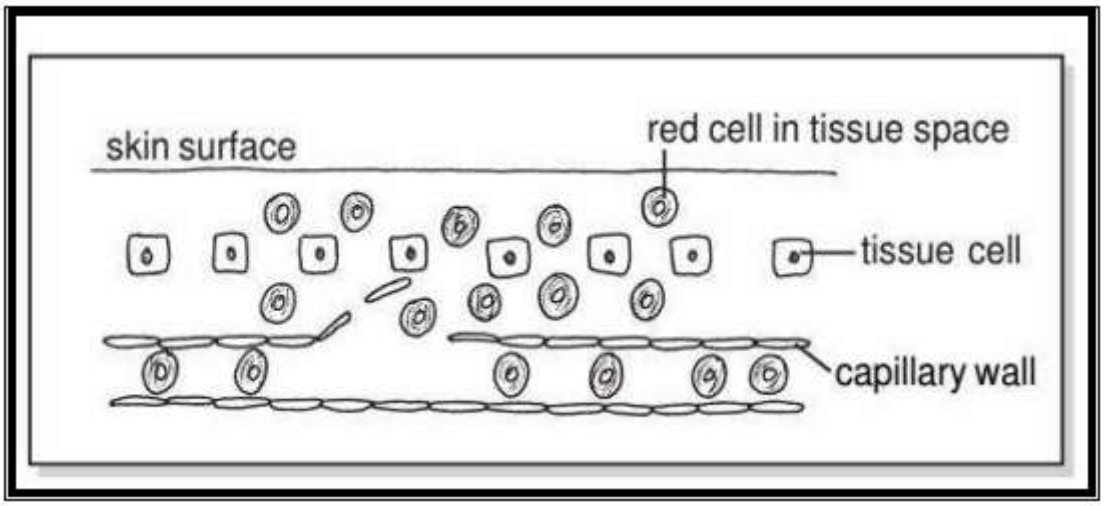
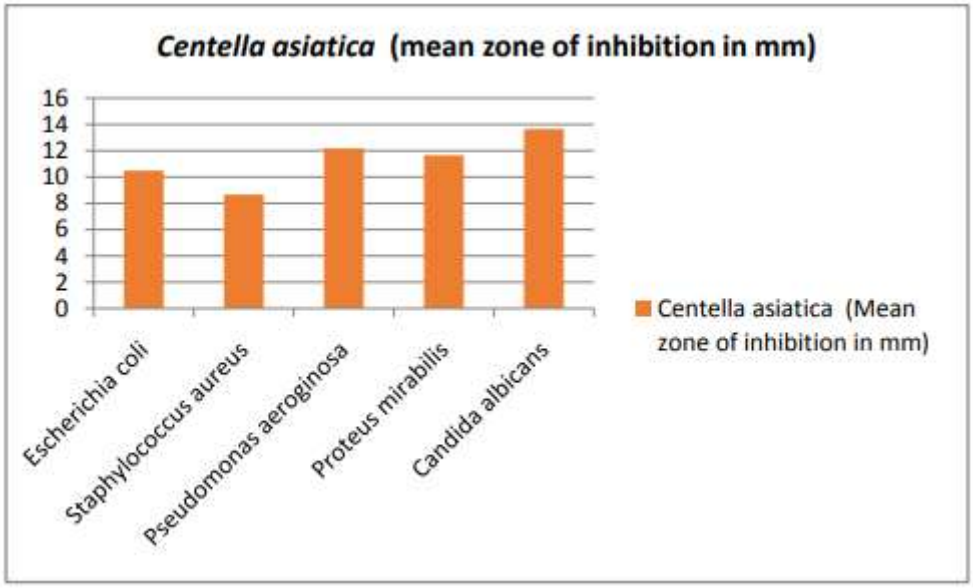


Figure 1: Structure of contusion

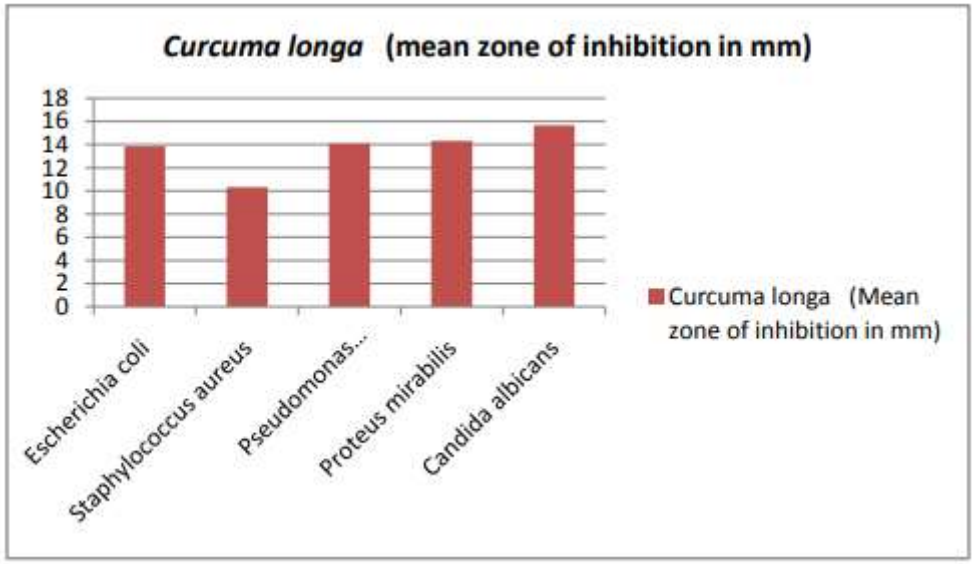
A few of the basic causes of this condition are infection, breakdown of components of extracellular matrix (ECM) by microbial enzymes, comorbidity and cytokine stimulus-induced pathologic metabolic state. This inflammation if not controlled leads to further breakdown of tissue components resulting in shattering of naturally occurring growth factor and receptor signals. The resident cells of the wound bed undergo senescence and are not allowed to proceed into the proliferative phase. In addition, the generation of reactive oxygen species (ROS) components induces further ECM injury and the oxidative stress contributes to the DNA damage-induced cell cycle arrest such that the wound fails to heal. The master controller of this vicious cycle of events is uncontrolled inflammation. Control of wound inflammation is essential to enable the tissue to undergo the natural sequence of proliferative and remodelling phases under controlled conditions. As opposed to the other inflammatory conditions, the wound healing process is initiated by a healthy inflammatory phase that is absolutely essential to make the wound microenvironment healthy eliminating the microbes and damaged tissue, presenting the appropriate cytokine and growth factor balance for subsequent events (Fig. 1). This stage is also known to peak at the first 24 hours of a wound and then heal naturally as a result of changing phenotypes of the infiltrated inflammatory cells. This healing is crucial for the onset of the other stages of actual healing.

4. RESULT AND DISCUSSION

Wound healing and improvement in wound management measures and in compromised status are the greatest challenges to healthcare providers globally. The largest predisposing factor that transforms acute wounds into non-healing wounds is prolonged or excess inflammation. Although a series of usual conditions is responsible for impairment in healing, underlying pathologies differ with each wound [8].



(a)



(b)

Figure 2: Mean zones of inhibition

An estimated 13 million individuals worldwide have deranged healing wounds yearly, the figure of which is increasing in populations with growing ages. The non-healing wounds are silent epidemics, whose effects spread on the social, psychological and economic condition of the patient and caretaker family and health care system. In India, one has reported the prevalence of non-healing wounds to be 4.5 per 1000 and acute wounds to be 10.5 per 1000. Conversion of acute to nonhealing wounds as a result of prolonged or severe inflammation is multifactorial. Some of the causes of this condition include infection, microbial enzyme degradation of extracellular matrix (ECM) components, comorbid altered metabolic state and cytokine stimuli.

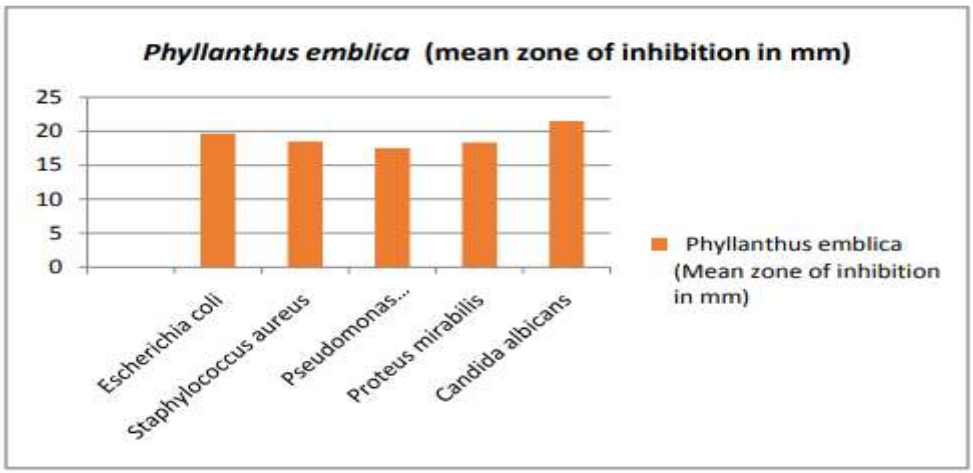


Figure 3: Mean zones of inhibition against tested pathogens

Wound healing drugs with microbicidal and modulating effects of inflammation (natural molecules being a part of them) could facilitate faster wound management by rebuilding the beneficial microenvironment so that the cellular events repertoire can unfold. The timely coordination of the above events is disrupted in chronic wounds due to one or the other reason. Delayed healing of wounds is primarily due to infection; hence, infection control would be the priority in wound care. Such injuries are treated with an aseptic technique, debridement, and anti-microbial medication. Use of natural products with anti-microbial properties would be an addition to the efficacy of microbial killing in the healing process.

5. CONCLUSION

The main purpose of the skin, the largest anatomical organ in the human body, is to serve as a barrier against chemicals, radiation, microbes, temperature, and physical forces. The epidermis and dermis are the two layers that make up skin. The avascular topmost layer, known as the basement membrane, is made up of stratified squamous epithelium and keratinocytes that are connected to the dermis by interlacing collagen fibers. The epidermis offers mechanical protection. Because the dermis includes blood vessels that supply the skin with

nutrition and oxygen, it is regarded as the intermediate layer of the skin. Fibroblast cells and two layers of connective tissue make up the majority of the dermis. The hypodermis, or subcutaneous fat, lies beneath the dermis. Although it is technically not a component of the skin, it is extremely challenging to tell the difference between the dermis and hypodermis. The dermal ECM is composed of fibrillar collagens and related proteins, while the epidermal ECM has basal lamina. Beyond cell adhesion, the skin's ECM distribution heterogeneity permits a range of cell autonomous and non-autonomous functions. As the body's outer anatomical barrier, skin is subjected to injury in the form of abrasions, ruptures, penetrating trauma etc., as it performs normal functions. The epidermal wounds heal quickly in contrast to wounds deeper in the skin where all skin layers come into play. In addition to providing protection, the skin plays two vital roles: sensation and regulation. Wounds impact the functions of the skin and might have disastrous effects in some situations.

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