

Potential Combination of Wuluh Starfruit (*Averrhoa bilimbi* L.) and Clove (*Syzygium aromaticum*) Extract Gel for Incision Wound Healing

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ABSTRACT

Background: Incision wounds are usually caused by an incision in the skin and underlying tissue by a sharp, sterile or non-sterile instrument. The potential use of herbal ingredients as medicine is believed to have the advantage of minimal side effects. Supported by Indonesia's geographical conditions, which have a tropical climate with fertile nature and have many TOGA (Family Medicinal Plants), even plants which are cooking spices such as starfruit (*Averrhoa bilimbi* L.) and cloves (*Syzygium aromaticum*) have the potential to be used as an antibacterial and anti-inflammation agent on incision wound. **Method:** A Literature review by taking information from 23 journals and 1 textbook. Journals were obtained from the search engines Google Scholar and PubMed NCBI. The data and information obtained are processed to support the research objectives. **Result:** Infection of the incision wound can be caused by exposure to bacteria from instruments and non-sterile materials that touch the wound. Phenolic compounds in the extract of wuluh starfruit (*Averrhoa bilimbi* L.) and cloves (*Syzygium aromaticum*) act as antibacterial agents and anti-inflammatory agent that reduce levels of inflammatory mediator cytokines, namely IL-1 β , IL-6, TNF- α significantly. The high water content in the gel assists in tissue granulation and epithelialization in moist conditions. **Conclusion:** Combination of wuluh starfruit (*Averrhoa bilimbi* L.) and clove (*Syzygium aromaticum*) extract gel have the potential to heal incision wounds

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1. INTRODUCTION

A wound is defined as a break in the continuity of the skin or mucosa due to physical damage, thermal damage, or medical conditions or procedures. A cut is typically caused by an incision in the skin and underlying tissue by a sharp instrument such as a shard of glass, a scalpel, a knife, or a sheet of metal. The wound edges are clearly defined, elongated, and the corners can be brought together [1]. A 2018 retrospective analysis of medical service recipients identified that 8.2 million people experienced wounds with or without infection [2]. The phases of wound healing are divided into hemostasis, inflammation, proliferation, maturation, and remodeling [3].

The skin plays a role in protecting and regulating the body's internal environment from harmful external substances. Numerous efforts and innovations have been made in designing and synthesizing wound dressing materials with antimicrobial effects and good wound closure capabilities. To address the shortcomings of traditional wound dressings such as gauze, bandages, and plasters, hydrogel dressings can be used, which have been extensively studied for their exceptional performance in maintaining wound moisture, enabling complete wound closure in a short time [3].

The potential use of herbal ingredients as medicines is believed to have the advantage of minimal side effects. Herbal-based medicines in wound care management offer benefits such as disinfection and the ability to provide a favorable environment for the wound healing process [4]. Herbal ingredients are more affordable, and Indonesia's tropical climate, fertile natural resources, and abundant TOGA (Family Medicinal Plants) are also beneficial. Even plants that are primarily used as cooking spices, such as starfruit (*Averrhoa bilimbi* L.) and cloves (*Syzygium aromaticum*), have the potential to be used as antibacterial agents for cuts.

Cloves (*Syzygium aromaticum*) are one of the most valuable medicinal plants, used by people worldwide for centuries. This plant is commercialized by drying its flower buds, which are used as a spice or seasoning in various formulations by the food and even pharmaceutical industries [5].

Starfruit (*Averrhoa bilimbi* L.) is primarily cultivated for medicinal purposes in many tropical and subtropical countries worldwide. A literature survey on this plant indicates that starfruit fruit is used as an antimicrobial agent [6]. Both plant extracts have the potential to be used as wound remedies if processed properly.

Traditional medicine has been recognized as beneficial in supporting modern medical systems. Even in the current era of globalization, technological developments and the use of medicinal plants in Indonesia are growing rapidly.

2. METHOD

A literature review was conducted, drawing on 23 journals and one textbook. Journals were obtained from the search engines Google Scholar and NCBI's PubMed. The data and information obtained were processed to support the research objectives.

3. RESULTS AND DISCUSSION

The skin consists of several layers that support each other, starting with the outermost epidermis, dermis, and hypodermis [1]. The skin is the largest organ in the human body and can be said to be a multifunctional organ, with functions such as protection, touch, thermoregulation of body temperature, synthesis of vitamin D, and excretion of both salt and water [1]. This is in line with the journal published by [7], which states that the skin plays a role as an organ of thermoregulation, sensory, and metabolic processes, as well as a protective function against xenobiotics, ultraviolet light, and microbes. Therefore, it can be concluded that the skin is a multilayered organ that plays a role in sensory functions, excretion, temperature regulation, and protection from external dangers, which will be disrupted if the skin layer is opened by a cut.

A cut is a wound caused by a sharp object. Cuts usually occur due to incisions in the skin and underlying tissue by sharp tools or objects such as broken glass, scalpels, knives, or zinc sheets. A cut is characterized by clearly defined, elongated edges, and the corners of the wound can be brought together [1]. Cuts can occur both intentionally and unintentionally, therefore, there are sterile cuts, such as those from surgical procedures, and non-sterile cuts, such as those caused by kitchen knives. Cuts are very common in everyday life, most of which are non-sterile, and can lead to complications such as infection. Therefore, there is an urgency for rapid and appropriate treatment and care to prevent infection.

According to Janis & Harrison (2016), the phases of wound healing are divided into hemostasis, inflammation, proliferation, maturation, and remodeling. In the hemostasis phase, a platelet thrombus acts as a temporary plug, useful for reducing blood flow from the wound [1]. Furthermore, a journal article written by Golebiewska (2015) [8] states that in the inflammatory phase, platelets become activated when the continuity of the endothelial layer is broken and the subendothelial matrix is released, or if inflammation occurs. Platelet activation is followed by an influx of inflammatory cells within the first 1 to 2 days, initiated by leukocytes, neutrophils, and monocytes. Fibroblasts and endothelial cells then settle on the fibrin framework formed by platelet activation. Neutrophils, followed by monocytes, are rapidly activated into macrophages in the tissue. These cells are responsible for further tissue debridement and release additional cytokines and growth factors that promote fibroblast proliferation, angiogenesis, and keratinocyte migration. The presence of these substances is crucial and vital in the wound healing process [3]. This is followed by a proliferation process that occurs due to a

combination of several processes, namely epithelialization, angiogenesis or vascular formation, tissue granulation formation, and collagen deposition [1]. This is followed by a wound maturation process that requires reorganization through the deposition of new collagen, glycosaminoglycans, and proteoglycans. The strength of a healed wound is determined by the quality and quantity of collagen [3].

The inflammatory phase can be prolonged if bacteria and debris are not removed. This can cause further tissue damage and delay the onset of the proliferative phase, increasing the risk of the wound becoming chronic [9]. Therefore, antibacterial agents are needed to support white blood cell function to prevent the inflammatory phase from prolonging and allow the body to quickly initiate the proliferation, maturation, and remodeling phases of the cut wound.

Cloves (*Syzygium aromaticum*) are known to be a major source of flavonoid compounds, namely quercetin and kaempferol, as well as phenolic acids such as ferulic acid, caffeic acid, ellagic acid, and salicylic acid [10]. The antibacterial activity of cloves (*Syzygium aromaticum*) occurs through an oxidative mechanism by disrupting redox homeostasis and the formation of microorganisms by inhibiting the redox cycle, which produces superoxide radical anions and hydrogen peroxide, which cause oxidative stress in bacteria and disrupt bacterial membrane formation (Ajiboye, 2016). Previous research has shown that clove flower bud extract (*Syzygium aromaticum*) extracted in 80% ethanol exhibits antibacterial properties against *Bacillus* and *Serratia marcescens* bacterial isolates [10]. However, the dosage should be considered, as the World Health Organization (WHO) stipulates that the acceptable daily oral dose of cloves for humans is 2.5 mg/kg body weight [10]. Therefore, clove flower bud extract (*Syzygium aromaticum*) has the potential to be a herbal antibacterial agent in the treatment of cuts.

This is supported by research on the antibacterial activity of ethanol extract of starfruit (*Averrhoa bilimbi* L.), which is rich in phytochemicals such as flavonoids, phenols, and saponins [11]. The phenolic compounds in starfruit (*Averrhoa bilimbi* L.) function as antibacterial agents by damaging the bacterial cytoplasmic membrane, which causes the release of important metabolites contained in the bacterial cytoplasm. It has been reported that ethanol extraction (80%) from starfruit (*Averrhoa bilimbi* L.) can inhibit *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, *Salmonella typhimurium* ATCC 14028, *Staphylococcus aureus* ATCC 25923, *Vibrio parahaemolyticus* ATCC 17802 (Prastiyanto, 2020). The ethanol extract of starfruit (*Averrhoa bilimbi* L.) showed an inhibition zone ranging from 10-14.5mm against all strains in the inhibition test (Prastiyanto, 2020). Then, in a study conducted by Suluvoy in 2017 on the inflammatory phase, the inflammatory cytokine mediators IL-1 β , IL-6, and TNF- α significantly decreased in the starfruit (*Averrhoa bilimbi* L.) extract treatment group. However, the dosage should be considered because the LD50 of starfruit (*Averrhoa bilimbi* L.) extract is more than 5000 mg/kg/BW in Wistar rats, but no research has shown the LD50 of starfruit (*Averrhoa bilimbi* L.) extract in humans (Suluvoy, 2017). It can be said that starfruit (*Averrhoa bilimbi* L.) extract has the potential as an antibacterial and anti-inflammatory agent in the wound healing process. The findings above demonstrate that the two herbal extracts (cloves and starfruit) have antibacterial and anti-inflammatory effects that support the wound healing process, particularly in preventing a prolonged inflammatory phase that could prolong wound healing.

Hydrogel preparations were chosen for the treatment of cuts due to their hydrophilic structure and demonstrated exceptional potential for absorbing wound exudate and allowing oxygen diffusion to accelerate wound healing. Hydrogels can serve as a medium for delivering antibacterial agents [12]. Although conventional gel preparations are considered adequate and widely used for wound healing, with advances in technology, hydrogels are considered superior due to their numerous advantages. Hydrogel wound dressings are made using a physical cross-linking method, which is non-toxic and simpler than chemical cross-linking [13]. However, hydrogels still have drawbacks, such as their insufficient rigidity, and their limited hydrophilic characteristics, making them difficult to use as a sole ingredient in wound dressings. Many researchers have demonstrated that combining the main hydrogel raw material, PVA (Polyvinyl alcohol), with chitosan through cross-linking can significantly improve its mechanical and absorption properties [14].

Therefore, the hydrogel combination of starfruit (*Averrhoa bilimbi* L.) and clove (*Syzygium aromaticum*) extracts will become a herbal-based medicinal preparation capable of providing effective. Thus, a hydrogel combination of starfruit (*Averrhoa bilimbi* L.) and clove (*Syzygium aromaticum*) extracts will be a herbal-based medicinal preparation capable of providing antibacterial effects and maintaining a moist environment around the wound, making it suitable for the wound healing process.

Chitosan is a natural polymer with drainage properties and the prevention of exudate formation. Chitosan acts as a grafting substrate in the wound healing process. Gas circulation in chitosan-based gels is considered beneficial for the wound healing process [15].

The chemical properties of chitosan allow gel formation in acidic media. Chitosan-based hydrogels act as water absorbers at the site of swelling. Tissue healing occurs well in water-based media, making chitosan an excellent wound dressing material [15].

4. CONCLUSION

A gel combination of starfruit (*Averrhoa bilimbi* L.) and clove (*Syzygium aromaticum*) extracts has the potential to heal cuts.

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