

Ramania (*Bouea Macrophylla Griffith*) extract as a wound healing agent: A Literature Review

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ABSTRACT

Background: The bibliometric analysis of Traumatic Dental Injury (TDI) prevalence worldwide between 1999-2018 ranged from 6%-59%, while the 2018 RISKESDAS data on the proportion of soft tissue injuries after traffic accidents was 20.1%. WHO has encouraged its members to expand the use of traditional complementary medicine in order to further investigate about alternative therapies development based on traditional medicine, one of which is the use of herbal medicines for wound healing, systemic diseases and even cancer treatment because of its high efficacy and safety, as well as minimal side effect. This proves the equivalent ability of traditional medicine to modern therapy. *Bouea macrophylla* Griffith has potential as a wound healing agent through anti-inflammatory and antioxidant mechanisms. This study aims to obtain a theoretical basis for *Ramania* leaf extract (*Bouea macrophylla* Griffith) effect on the wound healing process in soft tissue. **Methods:** Studies from 2010 to 2020 were collected from PubMed, Google Scholar, Web of Science databases using the keywords of *Bouea macrophylla*, *Bouea+macrophylla+Griffith+Wound+Healing*. The search results in a total of 56 articles and 5 selected literatures which were included to be reviewed. **Results:** *Ramania* (*Bouea macrophylla* Griffith) is proven to accelerate wound healing process because it possesses anti-inflammatory and antioxidant properties. The plant contains flavonoids, phenolics, triterpenoids, steroids, saponins, alkaloids and tannins. Flavonoids have antioxidant properties that may accelerate wound curing process by deactivating and defeating the harmful impact of free radicals. **Conclusion:** *Ramania* (*Bouea macrophylla* Griffith) has been shown to have potential to accelerate wound healing process.

Keyword: Herbal medicine, *Bouea Macrophylla* Griffith, Wound Curing.

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Introduction

Traumatic dental injury (TDI) is an injury caused by an impact on the hard and soft tissue of the oral cavity. This incident was more of an accident and happened suddenly. Based on the literature, 25% of TDIs occur in school-age children and 33% experience trauma in the permanent dentition phase [1]. The prevalence of Traumatic Dental Injury (TDI) worldwide using bibliometric analysis between 1999-2018 is ranging from 6%-59%, while data from RISKESDAS 2018 on the proportion of soft tissue injury after traffic accident is 20.1% [2,3]. The TDI classification most often used in dental practice consists of 6 categories, namely no traumatic dental injury, treated traumatic dental injury, enamel fracture, enamel-dentin fracture, pulp injury and missing tooth due to the traumatic dental injury [4]. Treatment of TDI tends to be expensive and difficult because the trauma that occurs often

involves a large amount of tissue, and requires a long follow-up time. One of the treatments for TDI in soft tissue often uses drugs, such as antibiotics, in addition to the necessary surgery [1,5].

The goal of soft tissue wound healing treatment is to stop bleeding, clean the wound area of foreign objects, dead cells, and bacteria in the healing process. The wound healing process is affected by many factors, including the type of medication used. Wound healing medications can be used with a variety of different types and types, one of which is the use of herbal medications. Herbal therapy is a low cost medicinal solution, an ingredient that is relatively easy to find and does not cause harmful side effects due to the use of natural ingredients [6].

WHO has encouraged its members to expand the use of traditional complementary medicine in order to further study the development of alternative therapies based on traditional medicine, one of which

is the use of herbal medicines for wound healing processes, systemic diseases and even cancer treatment because of its high efficacy and safety, as well as minimum side effect. This proves the ability of traditional medicine to be equivalent to modern medicine so that many health experts are interested in using and developing traditional medicine as an alternative therapy. One of the plants that can be used as medicinal plants is *Ramania* (*Bouea macrophylla* Griff) [6-8].

The *Ramania* plant grows in Southeast Asia, especially in Thailand, Malaysia, and Indonesia. As an archipelagic country, this plant is spread across almost all regions of Indonesia, such as Aceh, North Sumatra, Riau, West Sumatra, Jambi, Banka Belitung, Lampung, Banten, West Java, West Kalimantan, South Kalimantan, Ambon and Maluku. This plant belongs to the buia genus and the family Anacardiaceae. In the leaves, there are secondary metabolites such as flavonoids, steroids, phenols, and terpenoids. Flavonoids are useful as antioxidants, antibiotics, antimicrobials, and anti-inflammatories. *Ramania* leaves contain 167.06 g/mg of flavonoid compounds, and the IC50 value of *ramania* leaf extract is 35.808 g/mg [8-10].

Utilization of *Ramania* leaves will be very useful, especially for the management of TDI in soft tissues. Therefore, it is necessary to study the literature on the efficacy of *Ramania* leaves as a wound healing drug.

Methods

The literature study in this article was started from searching databases such as PubMed, Google Scholar, Scopus, Web of Science with the keywords *Bouea macrophylla*, *Bouea+ macrophylla +Griffith+ Wound+ Healing* Then the articles were re-selected based on several criteria, namely the suitability of the article for the purpose of a literature review, articles describing the ingredients of *Ramania*, and the results of using *Ramania* extract in experimental animals. from 2010-2020. From the search results, a total of 56 articles and 5 selected literatures were found for review. The selected literature was used Indonesian and English.

Results

The first article aims to compare the total flavonoid content in *Ramania* stems and leaves with the maceration method. The average value of flavonoids in the stem extract of *Ramania* was lower than that in the leaves, namely 11.14 g/mg and 17.15 g/mg, respectively. There were significant differences between the two groups based on independent t-test results.

This is related to the second article comparing the extraction method of *Ramania* leaves to the total flavonoid value. There were 4 extraction methods used, namely ethanol maceration, ethanol soxhletation, n-hexane maceration, and n-hexane soxelation method. The results showed that the highest total flavonoid value was *Ramania* leaf extract using ethanol maceration method (167.06 gs/mgs). Meanwhile, the lowest was the n-hexane soxhelation method (35.3 gs/mgs). The results of T-Tests showed significant differences between each group.

The content of flavonoids in *ramania* extract affects its efficacy in wound healing. In the following article, it was concluded that the administration of 15% *ramania* leaf extract could increase the density of collagen fibers in subcutaneous wounds on the backs of wistar rats with an average value of $1,934 \pm 0.026$ on the seventh day and $1,117 \pm 0.006$ on the fourteenth day.

In addition, the antioxidant properties of *Ramania* were proven by the application of the extract on mice that had been irradiated with

ultraviolet B-light. Here, *Ramania* extract was shown to have anti-photo-aging and moisturizing properties by activating cornified envelope proteins and filaggrin-processing enzymes. Another benefit of *Ramania* extract is as an ingredient to increase radiosensitivity to radiation for cancer treatment. Pre-treatment with *Ramania* seed extract before irradiation could increase the radiosensitivity of breast cancer cell lines with increased sensitization ratio (SER).

Discussion

Traumatic dental injury (TDI) is an injury caused by an impact on the hard and soft tissue of the oral cavity. One of the treatments for soft tissue TDI often involves the use of supportive medications, such as antibiotics, to support surgical procedures [1]. The goal of a soft tissue wound healing treatment approach is to stop bleeding, cleanse the wound area of foreign objects, dead cells, and bacteria for the healing process. The wound healing process is a complex process influenced by many factors, including the type of drug used. One source of alternative medicine is derived from nature. Herbal therapy is a medical solution with a low price, materials that are relatively easy to find, and have no harmful side effects because they use natural ingredients [6].

WHO recommends expanding the use of herbal medicine, one of which is for wound healing, systemic diseases and even cancer treatment because of its high efficacy and safety, as well as minimal side effects. With the fact that the efficacy of traditional medicine is equivalent to modern medicine, this has become the basis for developing natural ingredients as a source of medicinal ingredients.

One of the ingredients in this herbal plant is flavonoids. Flavonoids play an important role as antioxidants that help the wound healing process. Function of flavonoids as exogenous antioxidants are capture free radicals and activate Nrf2 in inflammatory phase, to maintain balance between oxidants and antioxidants in the body [8].

To see the source of the optimal total flavonoid content, it was proven in a study that compared the total flavonoid content of *Ramania* stems and leaves with the maceration method. The results of the average value of flavonoids in *Ramania* leaf extract were higher than the leaves, which were 11.14 g/mg and 17.15 g/mg, respectively. This can be the basis for taking leaves as a source of herbal medicinal ingredients [11]. Flavonoids, which function as antioxidants, are obtained from the *Ramania* plant through an extraction process. There are 4 extraction methods used, namely ethanol maceration method, ethanol soxletation, n-hexane maceration and n-hexane soxation method. Based on the research in the article, the highest total flavonoid content was *Ramania* leaf extract with ethanol maceration method (167.06 gs/mgs). While the lowest is the n-hexane soxhelation method (35.3 gs/mgs). From these results, the best method that can be used to extract flavonoids is the ethanol maceration method [6].

The content of flavonoids in *ramania* extract affects its efficacy in wound healing. In the following article, it was concluded that the administration of 15% *ramania* leaf extract could increase the density of collagen fibers in subcutaneous wounds on the back of wistar rats with an average value of 1.934 ± 0.026 on the seventh day and 1.117 ± 0.006 on the fourteenth day. In the proliferative phase, the number of fibroblasts increases, which is affected by the number of macrophages. This happens because the flavonoid content has an important role in activating macrophages. As the number of macrophages increases, the secretion of TGF-B increases. TGF-b has a function to trigger the proliferation and migration of fibroblasts [8].

The antioxidant properties of *Ramania* were also proven by the application of extracts on mice that had been irradiated with ultraviolet B-light. The breakdown of filaggrin by caspase-14 produced by NMF is an important moisture-producing process. *Ramania* extract stimulated the expression of filaggrin and caspase-14 in UV-B irradiated mice. Prolargin is reduced to filaggrin by the enzymes matriptase and prostatic. Proteins that play a role in increasing enzyme levels were induced by *ramania* extract [12].

Another benefit of *Ramania* extract is as an ingredient to increase radiosensitivity to radiation for the treatment of cancer. Pre-treatment with *Ramania* seed extract before irradiation could increase radiosensitivity of breast cancer cell lines with an increase in sensitivity ratio (SER). The possible molecular mechanism to explain the action of *Ramania* seed extract is the suppression of the phosphorylation of ERK1/2, AKT and JNK [13].

Conclusion

It can be resolved due to the antioxidant properties of the flavonoid active principles, the excerpt of the *ramania* plant has an impact on wound healing process, it is capable of producing moisture that supports the wound healing process and increases the radiosensitivity effect about cancer radiation treatment methods.

What is known about the topic?

One of the secondary metabolites contained in *Ramania* extract is a flavonoid which is believed to have antioxidant and anti-inflammatory properties so that it can be used to accelerate wound healing.

What does this study add to the literature?

With the available evidence, we will continue our research on *Ramania* extract as the basis for developing traditional medicinal plants.

What are the implications of the results?

Flavonoids in *ramania* extract affects its efficacy in wound healing, being able to create moisture that supports the wound healing and increase density of collagen fiber in subcutaneous wounds.

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