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Potential Effects of Myrmecodia Pendants (Ant Nests) on Healing Bone Injuries

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Abstract

Myrmecodia pendens is a medical plant that can have a healing effect on bone injuries. Bone injuries can occur due to many things, including injuries due to infection, non-infection, degeneration and neoplasms. Bones are the most important part of the body for the human body because the decreased bone function will affect human activities. Therefore better bone healing is needed. This review article aims to study and analyze the role of Myrmecodia pendens in the bone wound healing process. Several studies show that Myrmecodia pendens contain flavonoids, vitamins, terpenoid saponins, quones, and glycosides, as well as anti-inflammatory substances. These ingredients are markers in the healing process. Myrmecodia pendens has been proven to speed up the healing process. The conclusion shows that Myrmecodia pendens is a medicinal plant that can speed up the healing process of bone injuries.

Keywords: Myrmecodia pendens; bone repair.

INTRODUCTION

Myrmecodia pendants, also known as "ant nests", are epiphytic plants that live on wood or tree bark. This plant has long been known in Southeast Asia for its various benefits, including bone health. Scientific studies show that the consumption of Myrmecodia pendants extract can help reduce the risk of osteoporosis, increase bone mineral density, and speed up the healing of bone fractures. These potential benefits make Myrmecodia pendant an interesting bone health supplement to study further. Ant nests (AMyrmecodia pendans) are epiphytic plants from the Hydnophytinae (Rubiceae) tribe, which are known as natural medicines and have antioxidant potential. It is believed to be able to heal wounds from several diseases, including bone wounds. Recent research shows that Myrmecodia pendants contain compounds that have the potential to have a positive effect on bone health. These compounds, such as polyphenols and flavonoids, are thought to help increase bone formation and strengthen bone structure.

There are two types of species; Myrmecoda pendens and Myrmecodia tuberosa Pl. Myrmecodia pendants contain bioactive components such as phenolics which include flavonoids, phenylpropanoids, tannins and tocopherols. These antioxidants are contained in almost all parts of this plant, from the stem, twigs to the skin. The active compounds contained in ant nests are flavonoids which have antibacterial, anti-inflammatory and antioxidant properties (3). Literature about this plant still needs to be improved, especially the features of the healing process. Therefore, the author wants to discuss the ability of this medicinal plant in the bone healing process with the aim of providing literature for researchers and readers to know about Myrmecodia pendans in the process of healing bone injuries.

METHODS AND MATERIALS

This article was written using a literature review method. We will discuss several studies related to bone wound healing.

DISCUSSION

Ant nests are part of the family Rubiaceae, Myrmecodia, Anthorrhiza, Hydnophytum, Myrmephytum, and Squamellaria (Riyanti et al., 2019a) There are five genera belonging to the Rubiaceae family which have tubers and are home to ants (Achmad et al., 2019a) (Widyawati, Pase, et al., 2020a). The Myrmecodia genus is the second most abundant genus in the world, after the Hydnophytum genera (8-D23_2850_Lilies_Anggarwati_Astuti_Indonesia, nd-a). It is estimated that the number of species in the

Myrmecodia genera is 26 species (Widyawati, Pase, et al., 2020b)(Soviati et al., 2020a)(Sudiono et al., 2020a).

Ant nests usually stick to their host plants to survive (Sudarmin et al., 2022a). The growth of ant nests is very dependent on the host plant (33-D23_2910_Lusi_Epsilawati_Indonesia, nd-a). The smoother the plant stem, the more difficult it is to find the plant. There will be no Ant Nests found on Slippery stem plants (Moatar et al., 2020a). On the other hand, you will find Ant Nests if the plant stems are rough (Moatar et al., 2020a) (Widyawati, Aron Pase, et al., 2020a)

In ethnobotanical practice, ant nests have been used for spiritual and ritual purposes(Binartha et al., 2020a). Some indigenous peoples believe that ant nests have magical or spiritual powers that can be used in healing or protective ceremonies. Anthills are often associated with courage, resilience and cooperation in these cultures (Dirgantara et al., 2022a; Sudiono et al., 2020b; Zeth et al., 2021a).

Myrmecodia pendant can be found mainly in tropical and subtropical areas in Southeast Asia and Australia such as in Indonesia (including Papua, Kalimantan, Java, Sulawesi, Sumatra)(317-1336-2-PB, nd-a) Papua New Guinea (Gde Agung Krishna Pemayun et al., 2021), Philippines (Roslizawaty et al., 2023), Cambodia(Young et al., 2020), Malaysia (including Peninsular Malaysia, Sabah and Sarawak on the island of Borneo), Australia (including Queensland and the Northern Territory) and the Solomon Islands (Gde Agung Krishna Pemayun et al., 2021).

Ethnopharmacologically, ant nests have been used as medicine by the rural communities of Papua, including as a cure for inflammation, strengthening the body's immunity. (Putra et al., 2020a), and overcome muscle pain(Plant et al., 2021). Local people use tuber powder (hypocotyl)(Daulay et al., 2022a) (Briliannita et al., 2020)Ant nests as a brewed drink like tea [7]. One of its main properties is to help treat various types of tumours and cancer (Imaniar et al., nd-a)such as brain cancer, breast cancer, nose cancer (Moatar et al., 2020a), liver cancer, lung cancer, colon cancer, uterine cancer(Moatar et al., 2020b), skin cancer, prostate cancer (Elisabeta MOATAR et al., 2021a, 2021b), and leukaemia (Ayuningtyas et al., 2021a)(Elisabeta MOATAR et al., 2021a, 2021b; Moatar et al., 2020b, 2020a).

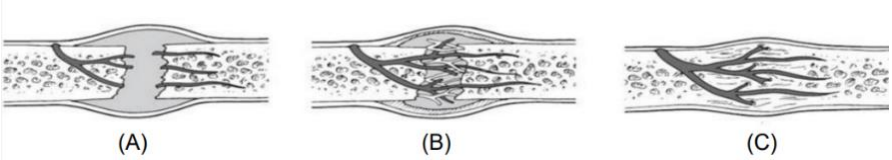
Myrmecodia Pendant interacts with ants, where the ants make tunnels in the floor of the tubers as nests and they create colonies (Suprijono & Hesti Wulan, 2022a). In the end, a natural chemical reaction occurs between the compounds released by the ants and the substances contained in the plant itself(Daulay et al., 2022b; Rabil et al., 2021a). The content of this chemical compound comes from the flavonoid group (Pongoh et al., 2022a)(Apriyanti et al., 2020a) and tannins (Binartha et al., 2020b). Flavonoids act as antibiotics and antivirals and are also used to treat and prevent several diseases, such as asthma and cataracts(Rabil et al., 2021b), diabetes, rheumatism, migraine(Kuswandani et al., 2021a), haemorrhoids, periodontitis and cancer (Suprijono & Hesti Wulan, 2022b). Myrmecodia pendans also contains antioxidant compounds (Bago, nd-a), vitamins, minerals and formic acid (Widyawati, Aron Pase, et al., 2020b). Ant antioxidants play a role in colony formation (Manurung et al., 2023a)and protect ant eggs from microorganisms

Figure 1. Myrmecodia Pendant (Ant Nest)(Widyawati, Aron Pase, et al., 2020b).

The bone healing process - for example a fracture, in principle results in the formation of new bone in a short time with minimal complications(Mohd Zuhri et al., 2020). The recorded healing rate is delayed in approximately 5-10% of cases. Complications causing delayed healing were reported in approximately 18.5% of cases(317-1336-2-PB, nd-b). The presence of biological stimuli can also influence the acceleration of bone wound healing (Tarman et al., nd. Biological stimulation can significantly accelerate wound healing by stimulating activators and accelerating cell formation (5073-Article Text-15632-1-10-20211116, nd-a; Epsilawati et al., 2019). The healing process for wounds in bones is the same as the healing process for other tissues.(5073-Article Text-15632-1-10-20211116, nd-b)

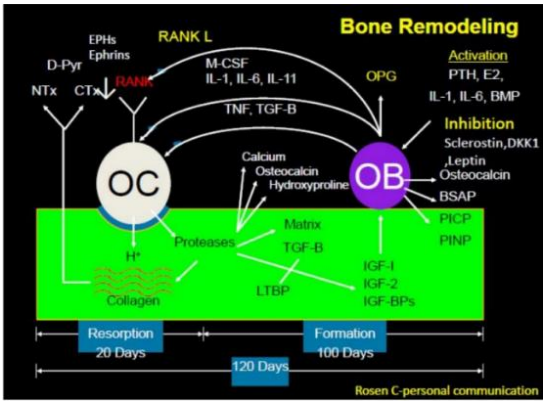
The healing process consists of 3 stages. The first phase is the inflammatory phase, this phase begins when an injury occurs and damage to the blood vessels occurs, thus inducing the formation of a hematoma and releasing inflammatory mediators. (Simaremare et al., 2021a). The result of this phase is bone callus formation. This phase lasts 5-7 days. The next stage is the reparative stage. This stage lasts 4-40 days after the first trauma (Pongoh et al., 2022b). In this phase, the callus develops, and its growth reaches 40% of the healing process (Merdana et al., 2021a). The formed hematoma and callus change into a mature callus structure caused by the growth of mediators (Kuswandani et al., 2021b), protein and calcium so that the callus can be seen

radiographically(Azzahra Attamimi & Indah Permata Yuda, 2022a; Rumpun et al., 2021a)The final stage is the remodelling stage. This phase covers approximately 70% of healing time, occurring within 1-2 years(Manurung et al., 2023b). The characteristic of this phase is that there is a continuous process of bone formation and resorption. The result is the formation of new tissue(Khairiah et al., 2019; Rizqiana et al., 2023).

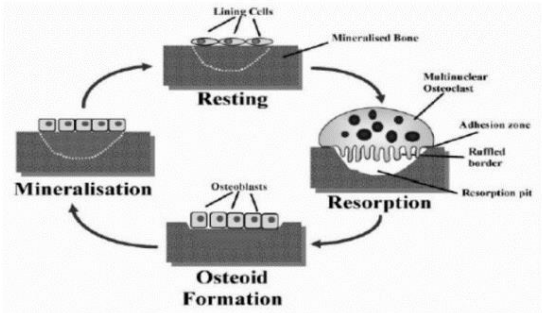


Figures 2. (a) Shows the healing process in the bone from the inflammatory phase where new blood vessels, hematoma and smooth callus form. (b) Reparative phase where growth and development of calcium-rich reparative calluses occurs. (c) Lastly is the resorption phase where the bone matrix is formed, where processes in the form of resorption and apposition occur(Mohd Zuhri et al., 2020)

Bone is an active tissue that will undergo continuous remodeling physiologically(Sudarmin et al., 2022b). This remodelling process consists of two aspects, namely the formation of osteoblasts and bone resorption by osteoclast activity (8-D23_2850_Lilies_Anggarwati_Astuti_Indonesia, nd-b). This renewal process lasts throughout life, allowing for the formation of new bone during calcium homeostasis (Apriliani et al., 2020a)still sufficient for this activity. This activity is achieved and regulated by the multiple actions of systemic hormones and local mediators (Alawiyah Al Attas et al., 2023a; Simaremare et al., 2021b).



Figures 3. Biochemical processes of bone remodeling. Describes the 120 day healing process where several mediators are actively involved in the process(5073-Article Text-15632-1-10-20211116, nd-c).



Figures 4. The process of bone remodeling is described as a continuous process, where bone formation and resorption processes continue to occur(Adhelina et al., 2017a)

The bone remodelling cycle begins with the recruitment of osteoclast precursor cells, which will then turn into osteoclasts. Adult osteoclasts will synthesize proteolytic enzymes, which are responsible for digesting the collagen matrix (Martati & Ciptadi, 2020a). This bone resorption is the first stage of the remodeling cycle. Osteocytes to see the bone remodelling process(Rachmi et al., 2021a), usually by checking for signs of bone remodelling. Examples of biochemical markers of bone remodelling, such as in the bone resorption process, are hydroxyproline or various collagen cross-links(Merdana et al., 2021b)and telopeptides, while markers of bone formation are propeptides of type I collagen (Bago, nd-b), osteocalcin (OC) and alkaline phosphatase (AP)(Sigit, nd). This phase lasts a very long time and is under the control of the apoptotic effect carried out by osteoclasts(Priyanti et al., 2023; Ramadhan et al., 2018).

The next phase of the remodelling cycle is where preosteoblasts from mesenchymal stem cells in the bone marrow become mature osteoblasts (Putra et al., 2020b),which then synthesizes bone matrix, especially type I collagen(Zeth et al., 2021b)and regulates the mineralization of newly formed bone(Rachmi et al., 2021b).Some mature osteoblasts mineralize and turn into Biomarkers of bone formation and resorption, reflecting the overall activity of osteoblasts and osteoclasts in bone. (Adhelina et al., 2017b). These markers can also be used as markers of growth and healing (Ant Nest Nest Extract Nanoparticles Preparation, nd).

Table 1. Biochemical markers for bone formation (Mohd Zuhri et al., 2020)(Apriliani et al., 2020b)(Dirgantara et al., 2022b).

Markers	Home Network	Sample Analysis	Analysis Method
Total Alkaline Phosphatase (ALP); specific for bone formation only in patients who do not have liver or bile duct disease (Primasari et al., 2112).	Bones, liver	Serum	Colometry
Bone alkaline phosphatase (B-ALP); ct-specific osteoblast production; some procedures show cross-reactivity with hepatic ALP isoen-enzyme	Bone	Serum	Colometry, electrophoresis, precipitation, IRMA, EIA
Osteocalcin (OC, BGP); certain osteoblast products; there are several reactive forms in the blood; some can nastati during bone resorption	Bones, platelets	Serum	RIA, ELISA, IRMA, ECLIA
C-terminal propeptide of type I procollagen (PICP); specific proliferating osteoblast and fibroblast products (Azzahra Attamimi & Indah Permata Yuda, 2022b).	Bones, skin, soft tissue	Serum	RIA, ELISA
N-terminal propeptide of type I procollagen (PINP); specific proliferating osteoblast and fibroblast products; some are included in the framework matrix	Bones, skin	Serum	RIA, ELISA

IRMA-immunoradiometric assay: EIA-enzyme immunoassay: RIA-radio immuno assay: ELISA-enzyme-linked immunosorbent assay: ECLIA-electrochemiluminiscence immunoassay(5073-Article Text-15632-1-10-20211116, nd-a)

Table 2. Biochemical markers for bone formation(Epsilawati et al., 2019)(Hidajat et al., 2018)(33-D23_2910_Lusi_Epsilawati_Indonesia, nd-b).

Markers	Home Network	Sample Analysis	Analysis Method
Hydroxyproline, total and dialyzable (OH-Pro, OHP); specific for all fibrillar collagen and some collagen proteins, including Ciq and elastin; present in newly synthesized and mature collagen	Bones, skin, cartilage, soft tissue	Urine	Colometry, HPLC
Pyridinoline (PYD, Pyr); high concentration of cartilage and bone collagen: absent in skin; only found in mature collagen	Bones, tendons, cartilage	Urine	HPLC, ELISA
Deoxypyrindoline (DPD, d-Pyr); high concentrations are only found in bone collagen: and found in cartilage or skin; only found in mature collagen	Bone, dentin	Urine	HPLC, ELISA
Cross-linked C-terminal telopeptide of type I collagen (ICTP); high proportion of bone collagen in type I collagen; some may come from newly synthesized collagen	Bones, skin	Serum	RIA
Cross-linked C-terminal telopeptide of type I collagen (fragments alpha-CTX, beta-CTX); in type I collagen; possibly a high proportion of bone collagen	All tissues containing type I collagen	Urine, Serum	ELISA, RIA, ECLIA
Cross-linked N-terminal telopeptide of type I collagen (NTX fragments); in type I collagen; most of the bones	All tissues containing type I collagen	Urine (alpha/beta), Serum (beta)	ELISA, RIA, ICMA
Hydroxylysine-glycosides (Hyl-Glyc); collagen and collagen protein; glucogalactosyl-hydroxylysine is highly abundant in soft tissue collagen and Ctq; galactosyl-OHLys is highly represented in bone collagen	Bone, skin, soft tissue, serum complement	Urine	HPLC, ELISA
Bone sialoprotein (BSP); synthesized by active osteoblasts and located in the extracellular bone matrix; appears to express osteoclast activity	Bone, dentin, hypertrophic cartilage	Serum	RIA, ELISA
tartaric-resistant acid phosphatase (TR-ACP); osteoclasts, platelets, erythrocytes	Bones, blood	Plasma/Serum	Colometry, RIA, ELISA
Free gamma carboxygastamine acid (GLA); produced from bone proteins (e.g. osteocalcin, matrix protein Gla) and from coagulation factors	Blood, bones	Serum/Urine	HPLC

HPLC-high performance liquid chromatography; ELISA - enzyme-linked immunosorbent assay; RIA - radio immuno assay, ECLIA-electrochemiluminiscence immunoassay; ICMA - immunochemiluminometric assay(Hidayat et al., 2020)

Research regarding the content of Myrmecodia pendans has been studied for several years, especially in relation to health or the prevention and treatment of certain diseases (Soviati et al., 2020b). However, research related to bone healing is still rare. To find out whether Myrmecodia pendans has an effect, researchers have studied and studied the basic addition and decomposition of certain biochemicals (Alawiyah Al Attas et al., 2023b).

Suharyanto and Bambang (2019) conducted research on experimental animals by adding liquid extract of Myrmecodia pendans which was given to several experimental mice. Some mice were given additional DMBA, which is believed to cause lung cancer. The results of the study showed that mice that were given

additional Myrmecodia pendans infusion after being suspected of suffering from lung cancer actually showed recovery with increased appetite.(Diantoro et al., 2022). This proves that sick mice can be cured. However, the results of this study cannot confirm that the infusion fluid containing Myrmecodia pendans has a healing effect because no biochemical markers were examined. The results were only seen based on changes in behaviour.(Ayuningtyas et al., 2021b). Similar research was also carried out by Nurul et al. (2020), who researched human cancer cells where cancer cells were given active ethanol extract obtained from Myrmecodia pendants (Suprijono et al., nd). The results obtained show that the ethanol compound from Myrmecodia pendans is able to reduce many cancer cells in humans (Martati & Ciptadi, 2020b). In this study, direct examination was carried out on humans, the results of which were based on histopathological examination. In contrast to the first study, the results obtained were more realistic (Suprijono et al., nd).

Research related to testing the isolation of active Myrmecodia pendants compounds has been carried out by several researchers, including÷ Hertiani et al (2023), who carried out Myrmecodia pendants phytochemical tests. In this study, an immune stimulant test was carried out, which examined the proliferation of lymphocytes and phagocytosis of macrophages given the ethanol extract of n-hexane fraction, ethyl acetate and water with concentrations of 10, 20, 50 and 100 ÿg/mL. This research provides results where the effect of macrophage phagocytosis will be higher if 50 ÿg/mL of Myrmecodia pendens extract is added.(Imaniar et al., nd-b; Suryana et al., 2024) (Scientific Journal et al., 2024)

Similar research was also conducted by Muslichah (2022). This study shows the optimal anti-inflammatory activity of 70% ethanol extract, n-hexane fractionation, the ethyl acetate fraction, compared with 70% ethanol fraction of Myrmecodia pendens (Suprijono & Hesti Wulan, 2022c).In this study, the results showed that the anti-inflammatory results in the form of a total 70% ethanol extract of Myrmecodia pendens were better and optimal when extracted in fractionated form. (Rabil et al., 2021c).

These two studies prove that administering or adding Myrmecodia pendens extract accelerates solid healing (Achmad et al., 2019b). This is evidenced by increased macrophage activity and anti-inflammatory effects.

Soeksmanto A. Subroto M. Wijaya et al. (2019) also examined Myrmecodia pendens phytochemical tests carried out on the water fraction, n-hexane fraction and ethyl acetate fraction. The fraction carried contains antibacterial effects against Streptococcus viridans (Apriyanti et al., 2020b). Similar research was also carried out by Fatriadi (2020), who showed that phytochemical tests on Myrmecodia pendens tubers were carried out using fractions: water fraction, n-hexane fraction and ethyl acetate fraction (Anggarwati Astuti et al. nd). The results of research from these two researchers prove that the phenolic, tannin, flavonoid, and terpenoid content actually has an antibacterial effect.(Rumpun et al., 2021b). These studies prove that Myrmecodia pendens can speed up the healing process by preventing the invasion of microorganisms in wounds (Anggarwati Astuti et al., nd).

Research that focuses on the healing process of new bone was carried out by Ismardianita et al. (2021). This research was conducted by examining the effect of Myrmecodia pendens extract on the healing of tooth sockets after extraction by looking at changes in the expression of Transforming Growth Factor-ÿ, Insulin-Like Growth Factors (IGFs) and changes in osteoblast and osteoclast levels. (Riyanti et al., 2019b). Based on the research results, data was obtained that Myrmecodia pendens significantly increased the levels of osteoblasts, TGF-Factor-ÿ, Growth Factor and reduced the levels of osteoclasts. (Education & Counselling, n.d.).Although there has not been much research focusing on bone healing, Myrmecodia pendens counts. It is believed to heal bone injuries (Isolation and Molecular Identification of Endophyte bacteria of Ants' Nest Plant (Myrmecodia Pendans), nd; Yulian & Ismail, nd)

CONCLUSION

The conclusion is that the ant nest plant (Myrmecodia pendens) contains phenolics, tannins, flavonoids, terpenoids and can actually act as an anti-inflammatory, and antibacterial agent. It can also has the ability to increase levels of biochemical markers in the healing process, so that Myrmecodia pendens can be used to accelerate wound healing, especially in bones, improving People's quality of life.

Conflict of Interest: There are no conflicts of interest.

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