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Potential Pharmacological Effects of Candlenut Seeds (*Aleurites moluccana*): a Literature Review

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Abstract

Background: Traditional medicine is used by 88% of people in the world and 31.4% of Indonesian people. The source of traditional medicine that has been used for generations especially comes from plants. Candlenut (*Aleurites moluccana*) is a plant that is widely known, both as a food supplement and as an ingredient in traditional medicine. **Objectives:** This study aims to examine the potential pharmacological effects of candlenut seeds and leaves on rat models. **Methods:** Data was collected based on experimental research articles related to the effects of candlenuts on rat models obtained from PubMed, Google Scholar, and ScienceDirect which met the inclusion and exclusion criteria. The keywords used in the article search were candlenut (*Aleurites moluccana*), therapeutic effect, and *Rattus norvegicus*. **Key findings:** The research results show that candlenut seed extract can reduce plasma glucose, plasma lipoprotein, AST, GGT, and hypersensitivity reactions, candlenut leaf extract can trigger re-reendothelialization in type 2 DM patients, reduce pancreatic malondialdehyde levels, and serum triglycerides, candlenut seed oil can also be useful to stimulate hair growth. **Conclusions:** Candlenuts have several pharmacological effects on rat (*Rattus norvegicus*) models including anti-inflammatory, hair growth, triggering re-reendothelialization, and reducing body weight, blood glucose, lipoproteins, triglycerides, and malondialdehyde.

Keywords: *Aleurites moluccana*, Pharmacological effect, *Rattus norvegicus*

Introduction

Traditional medicine is used by about 88% of people in the world, such as herbal medicines, acupuncture, acupressure, and yoga. In Indonesia, according to the 2018 Basic Health Research report, it was recorded that 31.4% of people used traditional health services. Traditional medicine is a health service that has gone through a long history regarding knowledge, skills, beliefs, and experience to care for people's health, both physical and mental health. Meanwhile, Herbal medicine is a treatment method using active ingredients derived from plant parts such as leaves, roots or flowers which have an influence on the body [1,2].

In general, herbal medicine is used by the public to treat disease and is rarely used for preventive purposes or as a promotive health effort. Herbal treatment is usually done as an initial treatment before using conventional treatment. Some of the reasons that people most often give why herbal medicine is an option for treatment include knowledge about the benefits of herbal medicine, family traditions, and dissatisfaction with conventional medicine. Even though herbal medicines are used to treat diseases, there are still many people who are not aware of the potentially dangerous risks of herbal medicines [3].

One of the natural ingredients that is widely used in Indonesia is candlenut (*Aleurites moluccana*). Candlenut is a plant that grows widely and is spread across Southeast Asia, Polynesia, South Asia, and Brazil. Almost all parts of the candlenut plant can be used and have been believed for generations to provide medicinal effects, be it the leaves, bark, or seeds. Candlenut contains *flavonoids, polyphenols, vitamins, folate, protein, carbohydrates, tannins, alkaloids, saponins, steroids* and *terpenoids*. Candlenuts are believed to be useful for accelerating hair growth, healing skin wounds, relieving diarrhea and asthma, and increasing analgesic effects [4].

Candlenuts have been used by several countries, both for cooking spices and for traditional medicine. In Japan, the stems of the candlenut plant are used to treat tumors. In Indonesia, candlenut stems are also used to treat bloody diarrhea and dysentery. In Malaysia, ground candlenut pulp is widely used to treat fever, wounds, headaches, and swollen joints. Other parts of the candlenut plant that can be used include leaves and oil. Crushed candlenut leaves are widely used to treat stomach ulcers, asthma, and hepatitis. Candlenut oil is widely used for hair care, laxative and worm eradication [5]. Apart from having several benefits, candlenuts are also easy to find, especially in Indonesia. Candlenut trees grow easily in both dry and wet climates at heights between 0-800 meters above sea level [6,7].

This research aims to examine further the potential pharmacological effects of candlenuts, especially in

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preparations taken from the leaves and seeds. This information is very important for the development of candlenuts as a traditional medicinal ingredient. Candlenut has great potential to be developed as a traditional medicine considering its abundant availability and has been widely used in the lives of the people of Indonesia and also other countries.

Materials and Methods

This research is a systematic review of the literature on the Google scholar, PubMed, and ScienceDirect databases. Article searches were carried out based on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) [8]. The strategy used to search for literature uses the PICO framework to help determine inclusion and exclusion criteria of a problem or population to be analyzed. The intervention in question is an action taken or a management action for an individual case as well as a presentation about the management. Comparison: management that was used as a comparison [9]. Outcome means results or outcomes obtained in research. PICO in this study includes Population (P), namely Rats (*Rattus norvegicus*), Intervention, namely the administration of *Aleurites moluccana* both extract and oil preparations, Comparators (C) none, and Outcome (O) in the form of pharmacological effects. The inclusion criteria for this research include: (1) Articles with an experimental research design; (2) Original articles from primary sources; (3) Research articles published within the last 10 years (2013-2023); (4) Full-text articles in English, (5) Full-text articles in Indonesian; (6) Articles with research samples that do not use a comparison or placebo (7) Articles that examine candlenut extract or oil products. Meanwhile, the exclusion criteria for this research include: (1) the same articles (duplicate articles) and (2) articles that do not have a complete structure.

The selected articles are original articles containing an abstract, introduction, methods, results, and discussion with an experimental study research design. The article search strategy uses an online database using keywords including Candlenut (*Aleurites moluccana*), therapeutic effect, Rattus norvegicus. Researchers use "AND" as a Boolean operator. The use of the boolean operator "AND" aims to combine different concepts and aspects as search keywords so the documents to be obtained can more specific.

The process of selecting articles and assessing quality starts from initial selection based on the suitability of the titles, followed by reading the summary and finally reading the entire contents of the article. Publications related to the selected articles as well as the bibliographies of the selected articles were also examined. The research results are arranged in the form of tables and narratives that explain the potential pharmacological effects of candlenuts based on the results of research that has been conducted and published.

Results and Discussion

The results of articles search using keywords in the Google Scholar, PubMed, and ScienceDirect databases obtained 139 articles (138 articles from Google Scholar, 1 article from PubMed, and no articles found in ScienceDirect). The article selection process is explained in Figure 1. Seven identical or duplicate articles were removed and 125 articles were excluded because the article title did not match the research topic, was not an experimental study, and had an incomplete structure. Then, the entire full-text of each article was read and so, obtain 7 articles that met the specified inclusion and exclusion criteria.

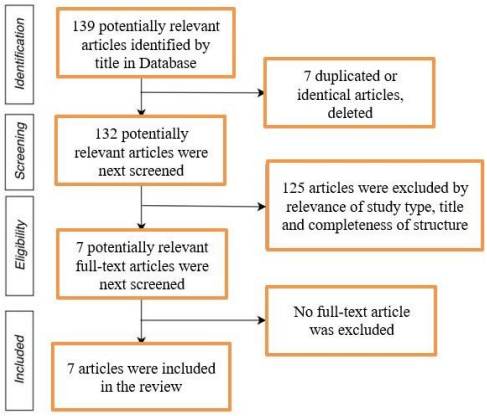

Figure 1 Flow Chart of the article selection

The effect of *Aleurites moluccana* on Rheumatoid Arthritis (RA)

Based on research by Quintão et al., (2019), administration of candlenut extract (*Aleurites moluccana*) to RA model mice induced with Complete Freund Adjuvant (CFA) had an effect in strengthening anti-hypersensitivity and anti-inflammatory activity. *Aleurites moluccana* can provide effects similar to the effects of the drug dexamethasone and the isolated compound *2"-O-rhamnosyl swertisin*. Administration of *Aleurites moluccana* significantly reduced mechanical hypersensitivity in the ipsilateral and contralateral hind paws of CFA-injected rats and reduced edema in the paws. In addition, *Aleurites moluccana* extract was also effective in repairing CFA-induced joint damage in RA mice. The anti-hypersensitivity and edema reduction effects provided by A. moluccana are in line with the anti-inflammatory effects that have been studied previously [10].

The effect of *Aleurites moluccana* on hair growth

Research conducted by Miftahurahma et al., (2023) shows that *Aleurites moluccana* oil can stimulate hair growth. The group given *Aleurites moluccana* oil showed faster hair growth compared to controls at an application frequency of three times a day but was not significantly different compared to those applied once and twice a day. Some of the compounds contained in *Aleurites moluccana* oil that have the potential to influence hair growth include: flavonoids, saponins, polyphenols, linoleic acid, linolenic acid, and oleic acid [11].

The flavonoids in *Aleurites moluccana* also have a mechanism to damage bacterial cell walls so they have bactericidal activity. *Saponin* compounds can form foam which can cleanse the scalp of dirt and saponin has counter-irritant properties which can increase hair growth due to increased peripheral blood circulation. *Aleurites moluccana* oil contains polyphenols and oleic acid which are useful as antioxidants which cause relaxation of blood vessels in the hair follicle area, thereby accelerating hair

Tabel 1 Studies Characteristic

Authors, years	Study design, subject	Dosage Form	Result
Rosa, et al., 2022	Experimental, Obesity Rat models	Leaf extract	Reduces glucose, lipoprotein, AST and GGT in the blood plasm
Nugraheny et al., 2018	Experimental, High-Fat Diet/Streptozotocin- Induced Rats models	Leaf extract	Induces re- endothelialization
Quintao, et al. 2019	Experimental, Rheumatoid Arthritis Rats models	Leaf extract	reduces hypersensitivity
Pratiwi, et al. *2016*	Experimental, Type 2 DM Rats models	Leaf extract	reduces serum Malondialdehyde (MDA) levels
Puspitasari,2016	Experimental, Type 2 DM Rats models	Leaf extract	reduces serum Malondialdehyde (MDA) levels
Maulida, K. H.; Mardhiyyah, K; Nurdiana, 2016	Experimental, Type 2 DM Rats models	Leaf extract	reduce serum triglyceride levels
Miftahurahma, N. M. L; Andriyanto ; Manalu, W; Ilyas, A. Z. 2023	Experimental, Rats	Oil	stimulates hair growth

growth and slowing hair loss, *Aleurites moluccana* oil also contains high levels of l*inolenic* and *linoleic acids*, this content is believed to build hair and skin tissue [11].

The effect of *Aleurites moluccana* on - reendothelialization

Candlenut leaf extract (*Aleurites moluccana*) has various ingredients, one of which is the flavonoid swertisin. The flavonoid swertisin in candlenut oil is known to have several pharmacological effects including hypoglycemic, wound healing and anti-inflammatory. The result of research conducted by Nugraheny et al. (2019) found that candlenut leaf extract can increase the ability of reendothelialization in people with type 2 diabetes mellitus [12].

There were endothelial dysfunction and impaired neovascularization in mice models of type 2 diabetes mellitus that also in line with the research of Ambasta et al. (2017). This study assessed the increase in reendothelialization through two mechanisms, namely increasing the number of late endothelial progenitor cells (EPC) using the marker CD34+/CD133- and counting the number of endothelium cells in the tail artery using hematoxylin eosin (HE) staining. Based on research, it was found that doses of 200mg/kgbw and 400mg/kgbw could increase late EPC in peripheral blood circulation, while doses of 100mg/kgbw, 200mg/kgbw, and 400mg/kgbw could increase rat tail artery endothelial cells. This ability is thought to come from the flavonoid swersetin which has hypoglycemic, anti-inflammatory, and wound healing activities [13,14].

Potential Effects of Aleurites moluccana as anti-hypercholesterolemia

The results of research conducted by Rosa et al. (2022) show that giving candlenut extract (*Aleurites moluccana*) to obese Wistar rats for 28 days can reduce body weight, blood glucose and lipoproteins. *Aleurites moluccana* seeds contain *linolelaidic* and *palmitoleic acids. Linolelaidic acid* inhibits gene expression in lipogenesis through binding to PPAR-α (*peroxisome proliferator-activated receptors*) and triggers transcription of genes involved in lipid oxidation. In addition, palmitoleic acid stimulates insulin in muscles and reduces hepatic steatosis. *Aleurites moluccana* seeds also contain α- and *β-amyrenone* which are associated with the inhibition of enzymes related to the absorption of fats and carbohydrates [15].

The effect of Aleurites moluccana on Type II Diabetes Mellitus.

Enzymatically, glucose will undergo autooxidation and will produce OH. Non-enzymatically, a reaction will occur between glucose and non-enzymatic proteins to produce advanced glycation end products (AGEs) precursors. In the sorbitol pathway, there will be a release of superoxide in the mitochondria. These three pathways will produce free radicals which disrupt insulin production in the pancreas and increase oxidative stress levels. Increased oxidative stress will damage the integrity of cell membranes coated with unsaturated fatty acids and will cause increased levels of lipid peroxidation metabolites, namely MDA, which is used as a marker of oxidative stress due to increased levels of free radicals. The decrease in MDA levels when administering candlenut extract indicates a decrease in free radical levels so that it will influence reducing insulin production disorders in the pancreas [16,17].

Another study was conducted by Maulid et al. (2016) on type 2 diabetes mellitus rat models. The results of which showed that administration of candlenut (*Aleurites moluccana*) leaf extract could reduce serum triglyceride levels with a greater reduction than the positive control group. The larger the dose given, the greater the decrease in serum triglyceride levels that occurs [18]. This happens because the flavonoid compound swertisin in candlenut leaf extract (*Aleurites moluccana*) has a very strong inhibitory effect on the activity of the *α-glucosidase*

enzyme. This enzyme has a role in carbohydrate metabolism which releases *α-glucose*, causing an increase in blood glucose levels after eating. Inhibition of the *α-glucosidase* enzyme causes a delay in carbohydrate absorption in the intestine and will slow the increase in blood glucose levels. Normal blood glucose levels will prevent excessive formation of triglycerides [19,20].

Conclusion

The results of this study can be concluded that Aleurites moluccana has an anti-hypersensitivity effect on Rheumatoid Arthritis model mice, can stimulate hair growth in rats models, increasing the ability to re-reendothelize in type-2 diabetes mellitus rats models, has an anti-hypercholesterolemia effect, and anti-diabetes type 2 effect in obesity rats models. This research shows that *Aleurites moluccana* has many benefits as a herbal medicine. However, to be able to use it in treatment, more comprehensive research is still needed, including complete toxicity tests, dosage formulation and dosage determination, so that it can be used as a reference for the use of this herb in health services.

Supplementary Material

None

Author Contributions

SAB : Conceptualization, Methodology, Writing-Original Draft. **IKN** : Data Curation, Formal Analysis, Visualization. **SENA** : Supervision, Funding Acquisition, Writing- Review & Editing. **DLS** : Supervision, Writing- Review & Editing. **AS** : Supervision, Writing- Review & Editing. **SMA** : Supervision, Writing- Review & Editing. **DCT** : Supervision, Writing- Review & Editing. **ES** : Supervision, Writing- Review & Editing.

Conflict of Interest

The authors have no financial conflicts of interest to declare.

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