



Study of Pharmacological Activities and Chemical Content of Rambutan (*Nephelium Lappaceum* L.) Fruit Peel Extract: A Systematic Review

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Abstract. Indonesia has various types of plants that are efficacious as medicine. One of them is rambutan whose peel has medicinal properties. However, rambutan peel has not been widely used by most people. In recent years, there have been many studies that have tested the effectiveness of rambutan peel on health. Rambutan belongs to the Sapindaceae family that grows in tropical and subtropical climates. The method used in this systematic review is a literature study obtained from online search databases with a time span between 2008–2021. The databases used are Google Scholar, Science Direct, PubMed, and Researchgate. The selected studies have gone through selection and assessment to get the best references. Pharmacological activities such as antioxidant, antibacterial, antiviral, antiosteoporosis, anti-inflammatory, antihyperglycemic, antihypercholesterolemic and anticancer activities have been proven to be contained in rambutan peel extract after going through the testing process. The contents of rambutan peel extract are geraniin, ellagic acid, quercetin, rutin, corilagin, ethyl gallate and epigallocatechin-3-gallate with the largest constituent compound is geraniin. Geraniin compounds are proven to be effective in most of their activities such as antioxidant, antihyperglycemic, anti-viral, and anti-inflammatory. This article provides an overview of the pharmacological activity and chemical content in rambutan peel extract which is expected to be continued by researchers in the future.

Keywords: Pharmacological Activities · Chemical Content · Rambutan Fruit Peel · Systematic Review

1 Introduction

Rambutan is a plant that is easy to grow in tropical to subtropical climates with almost 2000 sub-species. Rambutan is categorized into 3 (three) varieties, namely *Nephelium lappaceum* var. Pale, var. *Lappaceum* and var. *Xanthiodes* [1]. Rambutan belongs to the ‘lerak-lerakan’ or sapindaceae group. Rambutan consists of the following parts: 27.4% total weight, 13.2% peel, 11.7% fruit, 2.53% seeds and 1.60% seed coat [2]. *Nephelium lappaceum* L is an evergreen tree with a height of 10-12 m with grayish-brown branches.

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The name rambutan comes from the Malay language which means 'rambut' because of the many hairy bumps on the peel of the fruit [3]. Rambutan is a tree native to Malaysia which is a plant originating from Southeast Asia [4].

Each part of the rambutan plant has its own benefits and properties. Rambutan fruit also has an antioxidant content of 71.5% through an antioxidant capacity test which is equivalent to ascorbic acid [1]. A study stated that rambutan leaves also have antihyperglycemic activity which is indicated by a decrease in blood glucose levels in rats. Rambutan leaves have not been fully explored, but because their properties have been identified, they can be explored further [6]. Rambutan fruit seeds can be toxic when fresh and can be consumed when the fruit is dried or roasted. Rambutan seed fat can be used as food and cosmetic ingredients [2]. The immature seeds have narcotic properties and exhibit analgesic effects that can lead to coma and death [7]. The potential utilization of rambutan seed fat has been reported to be used as bioenergy [2]. The bitter taste of the seeds is thought to be due to the alkaloid content. In addition, the methanol extract of rambutan fruit seeds also contains polyphenols, flavonoids, saponins, and tannins.

Based on HPLC test, rambutan peel contains geraniin, corilagin, rutin, ellagic acid and quercetin compounds. Rambutan fruit peel has potential as an antihyperglycemic agent [10]. Treatment on rat for 2 (two) weeks, showed that the ethanol extract of rambutan peel had activity in lowering blood glucose in alloxan-induced rat [11]. Antioxidant activity in the ethyl acetate fraction showed higher activity than vitamin E with an IC₅₀ value of 4.29 g/mL, while vitamin E was 8.48 g/m [12]. Traditionally, rambutan peel has been used as a medicine for diabetes and high blood pressure [13].

The peel is the dominant part of the rambutan fruit. The use of rambutan peel as a medicinal ingredient is still lacking. In recent years, many researchers have conducted research on the compound content and pharmacological activity of rambutan peel. These studies have not been documented in a scientific paper that can facilitate the search for pharmacological activity and the complete content of rambutan peel extract compounds. Therefore, a systematic review was conducted to determine the pharmacological activity and content of compounds in rambutan peel. This method was chosen because of the selection of selected journals in advance so that it can improve the quality of systematic reviews and can be used as a reference for further research.

2 Methods

Systematic reviews provide more comprehensive and accurate information when compared to traditional literature [14]. There are 3 steps used in writing a systematic review, namely search study, data collection and study selection, and risk of bias study. After conducting a quality assessment, the studies obtained are summarized in a systematic review.

2.1 Search Study

The search strategy is an important part of a systematic review so that it can present complete data, easy to understand and can be repeated by other authors [15]. Study sources

Table 1. Study Search Keywords

NO.	KEYWORDS
1	("Compound" OR "Content Compound") AND ("Nephelium lappaceum L rind" OR "Nephelium lappaceum L peel")
2	("Compound" OR "Content Compound") AND ("Rambutan Rind" OR "Rambutan peel")
3	("Chemistry" OR "Chemistry Compound") AND ("Nephelium lappaceum L rind" OR "Nephelium lappaceum L peel")
4	("Pharmacology activity" OR "Pharmacology Properties") AND ("Nephelium lappaceum L rind")
5	("Pharmacology" OR "Pharmacology activity") AND ("Nephelium lappaceum L rind" OR "Nephelium lappaceum L peel")
6	("Pharmacology" OR "Pharmacology activity") AND ("Rambutan Rind" OR "Rambutan peel")
7	("Isolation" OR "Isolation of Compound") AND ("Nephelium lappaceum L rind" OR "Nephelium lappaceum L peel")
8	("Isolation" OR "Isolation of Compound") AND ("Rambutan Rind" OR "Rambutan peel")

were obtained by downloading online on search databases such as Google Scholar, Science Direct, PubMed, Researchgate and bibliographic lists of obtained journals. The selection of journals was based on several inclusion criteria, namely the search year 2008 to 2021 with Indonesian and English language journals.

The keywords used in the study search are as follows (Table 1).

2.2 Data Collection and Study Selection

These criteria need to be carried out to ensure that the selected studies are systematic and impartial [16]. Eligibility criteria include inclusion and exclusion criteria that are used as a reference to limit the research to be sought.

2.3 Study Risk of Bias

The risk study is carried out by conducting an assessment by at least 2 (two) reviewers in each domain using assessment points containing questions about the completeness of the study by assessing low risk, high risk or unclear criteria to be assessed.

3 Result and Discussion

Journals obtained and passed the checking were 145 journals. Title duplication screening got 119 ago on abstract and content screening. A total of 17 journals were assessed for quality assessments which were assessed for completeness of data from each journal. In this systematic review written from 17 journals obtained through the selection that has been made. Journals are obtained based on quality assessment (Fig. 1).

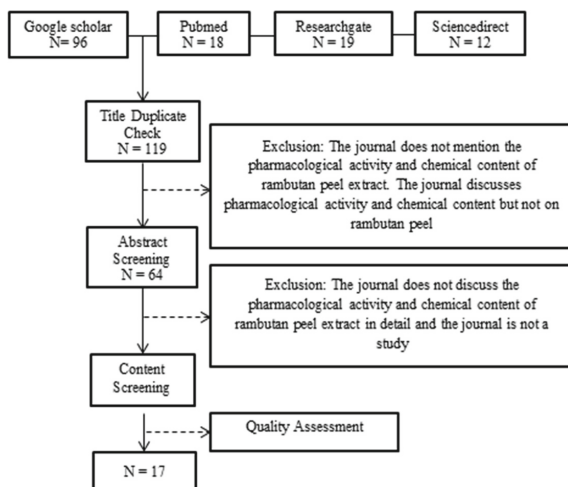


Fig. 1. Step of Journals Selection

Table 2. Content Compound of Rambutan Peel Extract

Compounds	Reference
Quersetin	[9, 10, 19]
Geraniin	[9, 10, 19, 20]
Ethyl Gallate	[9]
Epigallocatechin-3-galate	[9]
Corilagin	[9, 19]
Rutin	[9]
Ellagic acid	[9]
Gallic acid	[19]

3.1 Chemical Content of Ethanol Extract of Rambutan Fruit Peel

Rambutan fruit peel contains flavonoids, tannins and saponins. Phenol content is the largest content in the test response under conditions of extraction temperature, ultrasonic power, extraction time and controlled solid-liquid ratio, which is 552.64 ± 1.57 mg GAE/100 g [17]. Meanwhile, the total phenol and flavonoid content with ethanol solvent was stated to be higher at the total phenol content at 244.00 ± 4.34 mg GAE/g [18].

The content of compounds in rambutan peel extract such as quercetin, geraniin, ethyl gallate, and epigallocatechin-3-galate which has the potential as antihyperglycemic because it contains strong antioxidants. Rambutan peel extract also contains corilagin, rutin, ellagic acid [9], and gallic acid [19]. Geraniin compound was identified as the main component of rambutan peel [20] (Table 2).

Table 3. Pharmacological Activities of Rambutan Peel Extract

Pharmacological Activity	Test for Activity	References
Antioxidant	free radical scavenging activity	[22]
	Correlation Analysis	[18]
Antibacterial	Ethanol, methanol. Chloroform and water of <i>Salmonella typhi</i> , <i>Vibrio cholera</i> , <i>Enterococcus faecalis</i> , <i>Staphylococcus epidermidis</i> , <i>Pseudomonas aeruginosa</i> , <i>Bacillus cereus</i> <i>Proteus vulgaricus</i> , <i>Bacillus subtilis</i> , <i>Streptococcus pyogenes</i> , <i>Staphylococcus aureus</i> , <i>Escherichia coli</i>	[9]
Antiviral	Inhibition of DENV-2	[23]
Anti-osteoporosis	RANKL cell induced	[24]
Anti-inflammatory	Free Radical and metal chelating activity	[25]
Antihyperglykemia	Inhibitor activity of alpha and beta glukosidase	[22]
Anti hipercholesterolemia	Test of rat induced cholesterol	[11]
Anti Cancer	Antiproliferative effect on cell line MDA-MB0231 and cell line MG-63	[21]

Based on the research [9] it is known that the content of phenolic compounds in rambutan peel extract consist of 5 types, which are geraniin, corilagin, rutin, ellagic acid and quersetin. Geraniin is the largest constituent of rambutan peel with a content of 397.28 ± 6.74 mg/g and the smallest is corilagin with a content of 3.81 ± 1.89 mg/g [9].

Extraction of rambutan peel with methanol yield 25.5% higher than other solvents and the extract obtained was relatively more polar with the highest content of polyphenolic compounds [21]. Extraction of rambutan peel with methanol yield 25.5% higher than other solvents and the extract obtained was relatively more polar with the highest content of polyphenolic compounds [21].

3.2 Pharmacological Activity of Ethanol Extract of Rambutan Fruit Peel

The chemical content of rambutan peel has several pharmacological activities. Among the activities of rambutan peel can be used as the development of new drugs from medicinal plants. The pharmacological activities of rambutan peel extract include antioxidants, antibacterial, antiviral, antiosteoporosis, anti-inflammatory, antihyperglycemic, anthohypercholesterolemic and anti-cancer activities (Table 3).

3.2.1 Antioxidant

Measurement of antioxidant capacity can be done by testing the activity of free radical scavengers. The free radical scavenging activity of rambutan peel is comparable to that of geraniin [22]. Because the largest compound that makes up the peel of the rambutan

fruit is geraniin. Antioxidants can stabilize free radicals that can cause oxidative cell damage.

The highest DPPH value was extracted with ethanol solvent compared to water solvent. The free radical scavenging activity of DPPH has an IC₅₀ value of 24.99 g/mL for the ethanol extract and 144.59 g/mL for the aqueous extract. Correlation analysis between phenolic content and DPPH showed a linear correlation ($p < 0.01$) [18].

3.2.2 Antibacterial

Rambutan fruit peel has potential against several bacteria. Ethanol extract has activity against *Salmonella typhi* bacteria. Water, ether and methanol extracts showed activity against *Vibrio cholera*, *Enterococcus faecalis*, *Staphylococcus epidermidis* and *Pseudomonas aeruginosa* bacteria. Then the chloroform extract had activity against *Bacillus cereus* and *Proteus vulgaricus* bacteria. When compared with the seeds of rambutan fruit which only has activity on *Bacillus subtilis*, *Streptococcus pyogenes*, *S. aureus*, *P. aeruginosa* and *Escherichia Coli* bacteria [9].

The main phenolic compounds such as geraniin, ellagic acid, quercetin, rutin, and chorilagin contained in the methanol extract of rambutan peel showed inhibitory activity against bacteria with different concentrations and incubation times [9].

3.2.3 Antiviral

The compound that affects the inhibition of DENV-2 is geraniin. It was concluded that geraniin compounds could inhibit the action of DENV-2 by influencing the virus or by binding to viral receptors that were involved in viral penetration into cells but did not involve cellular receptors. Geraniin works extracellularly so that it can increase interaction with virions or virus particles. This interaction can reduce the infectivity of DENV-2 [23].

3.2.4 Anti-osteoporosis

Osteoporosis/OP rat model in vivo was incubated with retinoic acid to evaluate the ability to inhibit OP with serum biochemical indicators (serum calcium, serum phosphorus, alkaline phosphate/ALP and osteocalcin/OCN), physicochemical and histological properties. In the serum calcium and phosphorus in the positive and phenolic groups, rambutan peel was larger than in the model group. In ALP and OCN levels, rambutan peel was able to reduce 17.93% and 43.11%, respectively. These results suggest that rambutan peel can improve blood indicators related to bone metabolism in retinoic acid-induced OP rat [24].

3.2.5 Anti-inflammatory

The phenolic content of rambutan peel has been shown to have anti-inflammatory activity. The main phenolic compounds that contribute to anti-inflammatory activity are geraniin, catechins, and ellagic acid. Phenolic compounds act as anti-inflammatory by reducing the production of inflammatory mediators or through free radicals and metal chelating activity [25].

3.2.6 Antihyperglycemia

The inhibitory activity of alpha and beta glucosidase in rambutan peel extract was higher than that of geraniin with IC₅₀ values of alpha glucosidase 0.106 ± 0.080 and beta-glucosidase 7.02 ± 0.99 . Beta glucosidase is a measure of the reaction in which -glucosidase hydrolyzes p-nitrophenylb-D-glucopyranoside in the formation, as a cosmetic product [22]. The content of flavonoids such as tannins, polyphenols, quercetin, catechins and EGCG can reduce blood glucose levels in test animals by inhibiting glucose absorption so as to stimulate insulin release and indirectly by pass the antioxidant process. The decrease in blood glucose levels by geraniin is due to its ability to prevent formation [10].

3.2.7 Antihypercholesterolemia

Test the effect of lowering blood cholesterol on rambutan peel extract using 3 (three) different doses. Rambutan fruit peel extract was shown to have a strong activity in lowering cholesterol levels in the blood of rats about 60.75% stronger than the positive control. This shows that the ethanolic extract of rambutan peel is very effective as an antihypercholesterolemia with herbal medicinal ingredients [11]. There have not been many studies related to rambutan peel as an antihypercholesterolemic agent, so it is necessary to carried out ongoing research on rambutan peel as an antihypercholesterolemic agent.

3.2.8 Anti-cancer

Antiproliferative effect on cell line MDA-MB0231 and cell line MG-63 was demonstrated by rambutan peel extract after 72 hours of incubation. Yellow and red rambutan peels did not show any antiproliferative effect on HeLa cancer cells. Compounds that are thought to have anti-cancer activity are polyphenol compounds. These compounds are considered capable of neutralizing biological reactive oxygen species (ROS). ROS are species involved in anti-cancer. High ROS reduction can prevent cancer, while ROS can be reduced by synthetic antioxidants or natural antioxidants [21].

Research shows that the yellow and red rambutan peel extract samples had cytotoxic effect. A low value of IC₅₀ on MDA-MB-231 (5,42 ug/mL and 12,4 ug/mL) and MG-63 (6,97 ug/mL and 13,95 ug/mL) cell compare to MDCK cell which has higher IC₅₀ (37,15 ug/mL and 37,15 ug/mL). In addition, the antiproliferative effects also low on MDCK cells. The values of MDA-MB-231 cells and MG-63 cells showed significant anti-proliferative values with IC₅₀ values of 20 g/ml and were accepted as having anti-proliferative effects on cancer cell assays. It is necessary to test on benign cells to determine side effects on normal cells [21].

4 Conclusion

Rambutan fruit peel is a waste from rambutan fruit that is still often thrown away. However, now there are many studies that prove the efficacy and usefulness of rambutan peel as an alternative to herbal medicine. It has been proven in research that the ethanolic extract of rambutan peel has several beneficial compounds, namely quercetin,

geraniin, ethyl gallate, corilagin, ellagic acid, rutin and epigallocatechin-3-gallate. Among the compounds that have benefits as medicinal ingredients include quercetin, geraniin, ethyl gallate, and epigallocatechin-3-gallate which have the potential as antihyperglycemic and antioxidant. The pharmacological activity of the ethanolic extract of rambutan peel is as an antibacterial, antiviral, antiosteoporosis, anti-inflammatory, antihypercholesterolemic and anticancer activity. It is necessary to develop research related to the benefits of rambutan peel that can be used as medicine.

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