A review: extraction, phytochemicals, and biological activities of rambutan (Nephelium lappaceum L) peel extract

Zhang Tingting a,1, Zhou Xiuli b,1, Wang Kun a, Sun Liping a, Zhuang Yongliang a,⇑

a Faculty of Food Science and Engineering, Kunming University of Science and Technology, No. 727 South Jingming Road, Kunming, Yunnan 650500, China
b Department of Cardiology, The First People’s Hospital of Yunnan, No.157 Jinbi Road, Kunming, Yunnan 650034, China

ABSTRACT

Rambutan (Nephelium lappaceum L.) peels are produced during application process. Drying methods of rambutan peel, including open sun, oven, oven vacuum, and freeze-drying, have been describes in this study. The extraction technologies of dried rambutan peels were reviewed, such as maceration and hot extraction, microwave-assisted extraction, ultrasonic-assisted extraction, and supercritical fluid extraction. The phytochemicals of rambutan peel extracts were analyzed, and the puriﬁcation and stability of geraniin was reviewed. Rambutan peel extracts exhibit wide bioactivities in vitro and in vivo, and these bioactivities depend chief on the phenolic contents and proﬁles in the different extracts. The safety of rambutan peel extracts was analyzed. In addition, rambutan peel extracts could be used as important components to make different products, which are potentially applied in food, medicine, and cosmetic. However, the extracts efﬁciency must be further increased using some emerging technologies. Furthermore, the bioactive mechanism and bioavailability of the extract in human system should be further evaluated.

1. Introduction

Rambutan (Nephelium lappaceum L.), which belongs to the family of Sapindaceae, is an important tropical commercial fruit in Southeast Asia, Australia, South America, and African countries. In recent years, rambutan is gaining increasing attention and widely acceptance due to its sweet, juicy and exotic appearance. The color of rambutan ranges from green, red to yellow to orange yellow, and the normal size is approximately 3–4 cm in diameter and 3–6 cm in length (Muhamed et al., 2019). The rambutan fruit is composed of peel, pulp, seed, and embryo, which account for 45.7%, 44.8%, 9.5%, and 6.1% of the total dry weight, respectively (Jahurul et al., 2020). Rambutan is often used for fresh consumption and industrially processed into jams, juices, canned fruit, jellies, marmalades, and spreads. These processing forms produce a large amount of peel and seed by-products (Mahmood et al., 2018; Rakariyatham et al., 2020). Therefore, taking advantage of these by-products in industrial applications is very important.

In recent years, many studies have reported on rambutan peels. The chemical composition of rambutan peel is cellulose, hemicellulose, and lignin, in which the cellulose content is 24.28%, the hemicellulose content is 11.62%, and the lignin content is 35.34% (Hernández-Andrade et al., 2019). In addition, some mineral contents in the rambutan peels were reported in previous studies. Meanwhile, many studies revealed that rambutan peel contains a high content of phenolics (Hernández et al., 2019). Phenolics are well known to be important secondary metabolites that determine the sensory and nutritional quality of plant products. Phenolics play various roles in the overall sensory appearance of food, ranging from color to taste and mouthfeel properties, and they might also indirectly impact aroma perception. Moreover, phenolics can contribute to health benefits related to the dietary ingestion of plant products (Macedo et al., 2021). Previous studies showed that rambutan peel extracts have anti-inﬂammatory, antioxidant, antimicrobial, antibacterial, anti-osteoporosis (OP), antiphotoaging, antiproliferative, antihyperglycemic, and antidiabetic activities. The bioactivities of rambutan peel extracts depend mainly on their phenolic contents and compositions. Furthermore, many factors can affect the phenolics and their bioactivities of rambutan peels from different sources, including cultivars, climate, harvest, soil, and extractive process. Numerous studies exhibited that rambutan peels from different localities have different phenolic contents and compositions, leading to different bioactivities.
bioactivities (Hernández-Hernández et al., 2019; Jahurul et al., 2020). In this review, the drying and extract methods of rambutan peels will be described. In particular, phytochemicals especially ingredient content and type of phenolics in rambutan peels will be illustrated. Finally, the different bioactivities of different rambutan peel extracts will be presented. The overview is shown in Figure 1. This study will provide theoretical basis and technical support for the utilization of rambutan peels.

2. Drying method

Previous studies have shown that the selection of drying method and its parameters could influence the chemical and biological activities, because differences in chemical contents and compositions were observed in the same material with different drying methods (Vidinamo et al., 2020). Open sun, oven, oven vacuum, and freeze-drying methods have been used in the drying process of rambutan peel, as shown in Table 1.
Table 1. Drying and extract method in rambutan peels.

| Methods                        | Drying method                  | Solvent            | Process                        | Results            | References               |
|--------------------------------|--------------------------------|--------------------|--------------------------------|--------------------|--------------------------|
| Maceration and hot extraction | open sun drying for 2–4 days    | hydroethanolic (85%) | room temperature 7 days        | 18%                | Thinkratok et al. (2014) |
|                                | oven-dried at 65 °C for 24 h    | methanol (80%)     | 0.5 g in 15 mL. 15 min         | 310 mg GAE/g dw    | Phuong et al. (2020a)    |
|                                | oven-dried at 50 °C until complete dryness | ethanol:water (1:2) | boiled 10 min                   | /                 | Yuvakkumar et al. (2015) |
|                                | oven-dried at 65 °C for 24 h    | methanol (80%) ethanol (50%) water | 1:30 (w/v) 30 °C 20 min | 17.11 g GAE/100 g dm | Phuong et al. (2020a)    |
|                                | oven-dried at 65 °C for 24 h    | methanol (80%) ethanol (50%) water | 1:30 (w/v) 30 °C 20 min | 17.11 g GAE/100 g dm | Phuong et al. (2020a)    |
|                                | oven-dried at 40 °C and dry blending | water ethanol | 1:10 (w/v) 40 °C 24 h | 13.2% 17.8% | Palanisamy et al. (2008) |
|                                | oven-dried at 40 °C and milling process | water ethanol | 1:10 (w/v) 40 °C 24 h | 23.4% 33.2% | Go et al. (2020) |
|                                | oven-dried at 60 °C for 48 h    | ethanol            | 1:10 (w/v) room temperature 24 h | 41.6% | Subramaniam et al. (2012) |
|                                | oven-dried at 60 °C for 48 h    | water              | 20 g in 100 mL 60 °C 30 min    | 58.2% | Hernández et al. (2017) |
|                                | oven-dried at 60 °C for 48 h    | HCl (10 g/L) NaOH (10 g/L) water ethanol (96%) hydroethanolic (600 g/L) | 1g in 10 mL boiling 10 min, | 189 mg GAE/g DW 258 mg GAE/g DW 235 mg GAE/g DW 233 mg GAE/g DW 315 mg GAE/g DW | Monrroy et al. (2020) |
|                                | oven-dried at 60 °C for 48 h    | ethanol            | 1:15 (w/v) room temperature 24 h | 24.06% | Perera et al. (2012) |
|                                | oven-dried at 60 °C for 48 h    | ethanol (95%)      | 1:10 (w/v) 24 h 26% | 26% | Moorthy et al. (2019) |
|                                | oven-dried at 45 °C             | ethanol (80%)      | 1:10 (w/v) 2 h 20% | 20% | Go et al. (2020) |
| Fresh oven-dried at 45 °C for 24 h | aqueous ethanol (80%) | 1:10 (w/v) 2 h 50 °C | 304.52 mg GAE/g DW decreased 10.52% | 26% | Boyano-orozco et al. (2020) |
| oven-dried at 65 °C for 24 h    | MeOH (80%)                      | 0.5 g in 15 mL ice 15 min | 12.68 g/100 g | 21.36% | Sekar et al. (2014) |
| oven-dried at 30–40 °C          | petroleum ether ethyl acetate chloroform methanol | 18–20 h | 1.31% 1.09% 1.87% 21.36% | Chaiwarit et al. (2021) |
| oven-dried at 45 ± 2 °C for 24 h | water ethanol 95% water-ethanol (40:60) | room temperature 18 h 1g in 20 mL. | 26.68% 26.92% 34.92% | Chaiwarit et al. (2021) |
| lyophilized                     | ethanol                         | 48 h               | 151.00 mg/g | 2.06% | Mota et al. (2020) |
| lyophilized                     | water                           | room temperature overnight | 402 mg/g DW | 25.1% | Thitilertdecha et al. (2008) |
| lyophilized                     | successively ether methanol water | /                 | 2.8% | 2.06% | Thitilertdecha et al. (2010) |

(continued on next page)
Open sun drying is the oldest, most popular, cheapest, and free method for the drying of plant, especially in the tropics and subtropics. However, the slow drying rate of open sun drying results in product exposure to environmental pollution, time consumption, and weather dependence. Open sun drying of different plants usually takes few hours, even to few days, and it is affected by the product characteristics and drying conditions, including physical structure, humidity, temperature, and air velocity. Thinkratok et al. (2014) reported that the rambutan peel was dried at room temperature for 2–4 days. Li, Sun, and Zhuang (2021) studied the drying of rambutan peel at open sun condition, which was dried for 5 days.

Oven drying is a low-temperature convection or forced air oven, which is mainly used in laboratory environment. An oven is an independent device with a heat source, a fan for circulation, and multiple trays for drying various foods at one time. As shown in Table 1, rambutan peel drying was investigated using an oven drier at different temperatures from 30 °C to 65 °C in previous studies. Li et al. (2021) compared different oven temperatures of 40 °C, 60 °C and 80 °C and found that the dry time of these temperatures were 31, 25, and 20 h, respectively. In this study, the total phenolic contents at 40 °C, 60 °C and 80 °C were 227.87, 241.83 and 185.83 mg/g, respectively, which showed that different dry temperatures had an obvious effect on the yield of phenolics from rambutan peel.

Freeze drying is a dehydration process in which a solvent or suspension is crystallized at a low temperature, and then ice crystal sublimates from solid state to vapor state. During the freeze-drying process, under the conditions of low temperature and lack of oxygen, the material is cooled to a frozen state, and the frozen water is removed by sublimation, which makes the dried raw materials maintain high biological, chemical and physical properties, and reduces the amount of bioactive compounds. Different freeze-drying technique and conditions could affect ice formation and morphology of dehydrated matrices (Harnkarnsujarit et al., 2015), leading to the yield of phenolics from the rambutan peel. Mota, Morte, Silva and Chinalia (2020), Phuong et al. (2020c), Li et al. (2021), and Thitilertdecha et al. (2010) used freeze drying to prepare rambutan peel. Phuong et al. (2020c) and Li et al. (2021) compared oven drying and freeze drying of rambutan peels. Phuong et al. (2020c) reported that the yield of phenolic contents using freeze drying was 30 g GAE/100 g dry weight (dw), which was higher than that of oven-dried rambutan peel (17 g GAE/100 g dw). Li et al. found that the total phenolic content of freeze drying was 278.33 mg/g dw, which was significantly higher than those of oven drying. These results showed that freeze drying could obtain a higher retention of bioactive components and bioactivities, which was in accordance with previous conclusions (Harnkarnsujarit and Charoenrein, 2011; Siol et al., 2022).

### 3. Extractions of rambutan peels and their phytochemicals

#### 3.1. Extraction method

The extract rate of each bioactive compound from plant is widely known to depend on the type of extract method applied (Lucia et al., 2020). Therefore, the extraction process of phenolic compounds from plant is the most crucial step in any related research (Garcia-Salas et al., 2010; Gallego et al., 2019). The common factors mainly influencing the extraction processes are substrate properties of the materials, the type of solvent used, extract temperature and time, liquid–solid ratio, and sample particle size (Minh et al., 2020).

The type of extract solvent is one of the most important factors affecting the extract efficiency of bioactive compounds. Solvent polarity plays a significant role in improving the solubility of the phenolics (Garcia-Salas et al., 2010). Solvents with different concentrations and polarities have been applied to extract phenolics from rambutan peels. As shown in Table 1, the extract solvents of rambutan peel mainly include water, ethanol, and methanol with different concentrations. In addition, the usage of hydroethanol, hydrochloric acid, and sodium hydroxide as...
extract solvent was reported, in which hydroethanol allowed for the extraction of both polar and semipolar compounds. Phuong et al. (2020a, b,c) revealed that the total phenolic content extracted from rambutan peel was 310 mg gallic acid equivalents (GAE)/g when using 80% of methanol. Subramaniam, Radhakrishnan, Chakravarthi, Palanisamy and Haleagraraha (2015) obtained a 41.1% yield of ethanolic (1:10, w/v) extract from rambutan peel. Palanisamy, Ming, Masilamani, Subramaniam, Teng and Radhakrishnan (2008) compared the phenolic yields with extracting solution of water and ethanol (1:10, w/v) concentration and discovered that the extract with ethanol displayed a higher yield. Phuong et al. (2020a,b,c) used 80% methanol, 50% ethanol, and water as extract solvents to obtain rambutan peel extracts, and the yields of total phenolics were 17.11, 12.25, and 9.17 g GAE/100 g, respectively. Monirroy, Araiz and Garcia (2020) researched the effect of 10 g/L hydrochloric acid, 10 g/L sodium hydroxide, water, 96% ethanol, and 600 g/L ethyl alcohol as extract solvents on the yield of phenolics from rambutan peel, and the yields were 189, 258, 235, 233, and 315 mg GAE/g, respectively. Gusman and Tsi (2015) studied the effect of ethanol with different concentrations (0%, 40%, 60%, 80%, and 95%) on the yield of total phenolics of rambutan peel. The results showed ethanol concentration significantly affected the yield of total phenolics, and 40% of ethanol markedly demonstrated the highest extraction efficiency. Chaiwarit et al. (2021) compared the effect of water, 95% ethanol, and 60% ethanol on the phenolic extract yield of rambutan peel, and the yields were 26.68%, 26.92%, and 34.92%, respectively. Sun et al. (2012) utilized three different solvents, namely, deionized water, 60% ethanol, and 60% methanol, to extract the phenolics of rambutan peel, and the result showed the ethanol extract had significantly higher soluble phenolic contents than the water and methanol extracts. The above literature reports showed that the differences in phenolic yield could be explained by the difference in solvent polarity. The polarity of each type of phenolics is determined by the difference in carbon skeleton and the type and quantity of substituents. The different solvents have different polarities, and the polarities of common solvents were water > methanol > ethanol > acetone. The different solvents can selectively extract different hydrophobic or hydrophilic phenolics from rambutan peel, thus highlighting the importance of studying and determining the optimal extract solvent for each sample type. However, rambutan peels from different sources in the process of phenolic extract have different requirements for solvent polarity, which may be related to the forms, compositions and contents of phenolics in the different rambutan peel.

Except for the difference in extract solvent, the extract temperature, time, and liquid-to-solid ratio also differed in the extraction process of rambutan peel. As shown in Table 1, the extract temperature ranged from room temperature to boiling, the time ranged from 3 min to 36 h, and the liquid-to-solid ratio ranged from 2:1 to 30:1 according to the previous extract data of rambutan peel. These extraction processes need to be optimized to increase the yield of extract. Response surface method (RSM) is a statistical tool for experimental modelling, which is often used to optimize the extraction process of bioactive compound. RSM can reduce the experimental runs, optimize the experimental processes, and check the interaction between the extract factors without reducing its quality (Box et al. 1978). Therefore, RSM could give the best value of the process factors to achieve maximum extraction or good response. Boyano-Orozco et al. (2020), Maran et al. (2017), and Sun et al. (2012) optimized the extract condition of rambutan peel by using the RSM design.

Previous studies showed that the extract methods of rambutan peel included conventional and new extraction techniques. The conventional extraction method is maceration and hot extraction, including reflux, shaking, blending, and stirring. Previous studies mostly chose conventional extraction method to prepare rambutan peel extract. However, maceration and hot extraction usually takes a long time and consumes many solvents, resulting in low efficiency/yield and quality. In recent years, the demand for new extract technologies, including microwave-assisted extraction (MAE), ultrasonic-assisted extraction (UAE), and supercritical fluid extraction (SFE), have been used to obtain the extract of rambutan peels. The potential implementations of these techniques improve extract yield, especially the extract of phenolics from rambutan peel.

MAE is identified to be a potential alternative to conventional extract method. MAE is a process that uses microwave energy to heat solvent in contact with the materials and isolate the bioactive compounds from the materials into the solvent. The microwave energy is transferred by molecular interactions through the mechanisms of dipolar rotation and ion conduction. Sun et al. (2012) extracted the soluble phenolic compounds in rambutan peel by using MAE with ethanol as solvent, and the operating parameters of MAE were optimized by RSM. The optimum extract conditions were 80.85% ethanol concentration, 58.39 s extract time, and 24.51:1 liquid-to-solid ratio. Under these conditions, the soluble phenolic yield was 213.76 mg GAE/g DW. Chaiwarit et al. (2021) researched the influence of MAE and maceration method with water, 95% ethanol, and 60% ethanol in obtaining bioactive compounds from rambutan peel. The MAE process operated at a frequency of 2450 MHz at 200 W showed higher efficiency than maceration; shortened the extract time from 18 h to only 3 min; and increased the yields in water and 95% ethanol by 5.13% and 2.08%, respectively. However, the yield in 60% ethanol between MAE and maceration had no significant difference.

UAE is a potential extract method that has the advantage of being economical and efficient, with shorter extract time. UAE uses ultrasonic bath with different solvent concentrations, liquid-to-solid ratios, times, temperatures, and ultrasonic frequencies. These factors may vary and need to be optimized in accordance with the type of materials. The phenolics obtained from rambutan peel by UAE is an emerging interest. The optimal conditions, including the type of solvents and their concentration, time, and the temperature for extracting phenolics from rambutan peel by using UAE method were explored by Phuong et al. (2020a,b,c). Methanol solution (80%) was found to be beneficial to improve the extraction yields of phenolics due to its polarity and the minimization of the amount of solvent. UAE significantly increased the phenolic yield of rambutan peel by 15% compared with methanolic extraction. Finally, an UAE extraction procedure obtained 55–64 g of frozen powder from 1 kg of fresh rambutan peel, and the total phenolic content in this powder was 250–300 mg GAE/g. Monirroy et al. (2020) studied the extracts of rambutan peel by using different solvents via UAE. The extracts of 1 g of dry rambutan peel were obtained by UAE or boiling for 10 min, with solvents varying from 10 g/L sodium hydroxide NaOH, 10 g/L hydrochloric acid, 96% ethanol, and 600 g/L ethyl alcohol to aqueous solutions. The phenolic contents in the extracts obtained by UAE ranged from 208 mg/g to 340 mg GAE/g, while the extracts obtained by boiling ranged from 189 mg GAE/g to 315 mg GAE/g. The phenolic yields obtained by UAE with sodium hydroxide, hydrochloric acid, hydroethanol, and aqueous solution were significantly higher than those obtained by boiling. However, the phenolic content of ethanolic extract in UAE decreased compared with that in boiling. Méndez-Flores et al.(2018) obtained rambutan peel extract by UAE, and the best extract conditions were mass/volume ratio of 1:7, extraction time of 10 min, and 10% ethanol/water. In this condition, the total phenolic content was 487.67 mg GAE/g. Maran et al. (2017) obtained bioactive compounds from rambutan peel by UAE accompanied with RSM. The optimal conditions of all the process factors were ultrasound power of 20 W, extract temperature of 50 ºC, solid-to-liquid ratio of 1:18.6 g/mL, and extract time of 20 min. Under these conditions, the phenolic yield was 552.64 mg GAE/g. Moreover, Gusman et al. (2015) investigated the optimal ultrasound and extract conditions of freeze-dried rambutan peels (approximately 150 g) in Taiwan. This study indicated that liquid-to-solid ratio, solvent concentration, duration, and the method of extraction significantly influenced the recovery of phenolic extracts. The optimal liquid-to-solid ratio was 15:1 when using 40% ethanol, and the extract time was 12 h for conventional extract but only 2 min for UAE. In addition, UAE for 2 min resulted in a higher phenolics recovery than with conventional extract for 12 h, suggesting that UAE could be more effective than conventional method for extracting phenolics from rambutan peel. In addition, it was found that...
the combination of MAE and UAE technologies showed high potential to extract phenolics. Estrada-Gil et al. (2022) researched the Mexican rambutan peel and found that the yield of MAE/UAE hybrid extraction was an average of 156.96 mg of GAE/g of dry rambutan peel for the hydroxylable phenolics content, followed by UAE and MAE with 21.32 and 9.48 mg of GAE/g of dry rambutan peel, respectively. Compared with previous studies, the yield of phenolics in rambutan peel was low. However, the study indicated that the MAE-UAE combined technology resulted in a high extraction yield of phenolics, compared to the yields obtained by a single extraction technology.

SFE has become an effective method to separate bioactive compounds. The extraction of phenolics by SFE refers to the process of using supercritical fluid to extract bioactive compounds from solid or liquid substances under the condition of higher than the critical pressure and temperature of the fluid. When the fluid pressure is above its critical pressure, the density of the fluid increases and the solubility of the bioactive compounds increases rapidly. When the fluid pressure falls below the critical pressure, the solubility of the bioactive compounds in the fluid decreases rapidly and then precipitates out of the fluid. The separation of phenolics by SFE has been widely studied throughout the last two decades (Katarynya et al., 2018). Palanisamy et al. (2008) obtained rambutan peel phenolics by SFE. The rambutan peel powder was placed in an extraction vessel, and CO₂ was passed through the vessel at a flow rate of 300 bar and a temperature of 50 °C for 2 h. The gas flow rate was set at 30 g/min. The soluble fraction was collected in liquid CO₂ precipitated at the end of the run. The product obtained was a completely pure extract without liquid organic solvents. Ethanol was used to flush the lines. The obtained yield of the ethanolic extract of rambutan peel by SFE was 17.8%, and the extract had a high phenolic purity of 762 mg GAE/g extract.

In summary, the extraction yields of different literatures are very different, which may be caused by different cultivated varieties of rambutan, determination methods of phenolics contents and calculation methods of phenolics yields. Generally, compared with traditional extract technologies, the new extract technologies significantly improved the extraction of phenolics from rambutan peel. Meanwhile, the new extract technologies could realize automation, shorten the extraction time, and reduce organic solvent consumption. MAE can effectively release phenolics because of the heat irradiation, which is produced through the vibration of the water molecules in the medium, but high temperatures can result in a degradation of phenolics when exposed to long time. The non-heating characteristic of UAE makes it more convenient to apply than MAE. According to the previous studies, the UAE extraction technology takes the shortest time and has the highest efficiency of extracting phenolics. However, considering the ultrasonic action area and attenuation, the diameter of extraction equipment should not be too large, which may affect the processing capacity of rambutan peel. In a word, different extraction technologies with optimal condition can achieve the best extraction results. In the process of optimizing extraction, the advantages and disadvantages of different extraction technologies should be fully considered.

3.2. Phytochemicals

Phytochemicals, especially phenolics, in plants are thought to be the major bioactive compounds, having potential bioactivities on health. Phytochemicals are classified in accordance with their chemical structure, from simple structures, such as phenolic acids, to highly polymerized structures, such as tannins. These phytochemicals from plants are currently divided into hydroxycinnamic and hydroxybenzoic acid derivatives, flavones, flavonols, flavanols, and anthocyanins (Tsong et al., 2021). Many previous studies reported the phytochemicals of rambutan peel extracts from different regions in the world.

According to the investigation of Thitilertdecha et al. (2010) the three main fractions of phenolics extracted from rambutan peel were identified as ellagic acid, corilagin, and geraniin. In addition, 53.5 mg of ellagic acid, 71.9 mg of corilagin, and 568.0 mg of geraniin were gained from 1 g of methanolic extract, and the sum of these three fractions was 693.4 mg/g extract. Nguyen et al. (2019) analyzed two fractions of rambutan peel extract, including soluble and bound fractions. The phenolics of the two fractions were identified using UPLC-QTOF-MS/MS. The main phenolics were ellagic acid, geraniin, and galloylshikimic acid in the soluble fraction, while ellagic acid, gallic acid, and quercetin hexoside were found in the bound fraction. In addition, 13 compounds extracted from rambutan peel through HPLC/ESI/MS method were found by Hernandez et al. (2017), including apigenin, apigenin arabinoside glucoside, bre-vifolin carboxylic acid, castalagin/vescalagin, corilagin, geraniin, p-coumaroyl glucose, vanillic acid, ellagic acid, ellagic acid pentoside, galloyl-bis-HHDP-hexoside, hexoside, pelar-gonidin, and vitisin A. The main compounds were identified in accordance with peak area, including ellagic acid, corilagin, and geraniin. Besides the ingredients mentioned above, six other ingredients of phenolics from rambutan peel were explored, including gallic acid, isorhamnetin 3-O-glucoside-7-O-rhamnoside, gallic acid 3-O-galactate, galloyl-HHDP-hexoside, pedunculagin, and thefлавин 3,5-O-digallate.

The ingredient content and type of phenolics had otherwise when extracted with different solvents through different methods. A study by Phuong et al. (2020c) showed that the main phenolics in methanolic extract were geraniin, ellagic acid, quercetin, rutin, and corilagin. Among them, geraniin had the highest content with two isomers (397 mg/g), followed by ellagic acid and quercetin at 177 and 167 mg/g, respectively. The main phenolic types in the water extract were same as those in the methanolic extract, but the content was less, in which quercetin demonstrated the highest content (186 mg/g), followed by ellagic acid and geraniin (155 mg/g and 137 mg/g, respectively). This study showed that the effect of solvents on the phenolics of rambutan peel extract was obvious. Asghar et al. (2021) prepared rambutan peel extracts by using different solvents in the order of their increasing polarity viz as follows: chloroform < ethyl acetate < acetone < ethanol < methanol < water. Chemical profiles were analyzed by HPLC and LC-MS. Only three compounds were identified by HPLC in the ethyl acetate extract, namely, malic acid, vitamin C, and chlorogenic acid. Three more were found in the acetone extract, including epigallocatechin gallate, catechin hydrate, and quercetin. Furthermore, 54 and 44 compounds were revealed in ethyl acetate and acetone extracts by LC-MS analysis.

Thitilertdecha and Rakarirayatham (2011) reported the accumulation of phenolics at different growth stages of two rambutan cultivar (Rongrien and Sereechompoo) peels. During fruit maturation, the accumulation of phenolics in the rambutan peel of Rongrien and Sereechompoo cultivars continuously improved, until reaching a maximum of 1653 and 733 mg/fruit when rambutans were harvested at 112 and 98 days after full bloom, respectively. Geraniin, corilagin, and ellagic acid were found in the peels of both cultivars. They were quantified, and the major component was found to be geraniin. The accumulation of geraniin, corilagin, and ellagic acid in the peels increased and reached the maximum at the harvest stage. In particular, the contents of geraniin could reach 1011 and 444 mg/fruit for Rongrien and Sereechompoo cultivars, respectively.

In the previous studies, the phenolics of rambutan peel were analyzed (Sun et al., 2012). Three fractions, including free, soluble conjugate, and insoluble-bound phenolics, were obtained by alkaline hydrolysis, and their contents were 185.12, 27.98, and 9.37 mg GAE/g dry weight, respectively. The soluble extract was obtained by ethanol solvent, and 51 compounds were identified in the extract by using UPLC-Q-Orbitrap-MS². This extract was purified by NKA-9 resin adsorption technology, and the purification processes increased the total phenolic purity from 579.72 mg GAE/g extract to 877.11 mg GAE/g extract (Zhuang et al., 2017b). The purification process also removed citric acid, quinic acid, ferulic acid hexoside, apigenin glucoside, and kaempferol hexoside. Thirty-nine compounds were identified from the purified extract, including one simple phenolic acid, one flavone, five hydroxyzable tannins, five hydroxybenzoic acids, six ellagic acids and conjugates, 10...
flavonoids, and 11 flavonols. Geraniin was semi-quantified by gallic acid via UPLC-Q-Orbitrap-MS² and showed 122.18 mg/g extract, which was the highest among all identified phenolics. Corilagin was quantified using its standard being 7.56 mg/g dry weight. Furthermore, UPLC-QQQ-MS was applied to accurately quantify the contents of geraniin and corilagin by their respective standards (Li et al., 2018). The contents of corilagin and geraniin were 7.87 and 140.02 mg/g, respectively. The contents of corilagin quantified using UPLC-Q-Orbitrap-MS² and UPLC-QQQ-MS by its standard had no significant difference. However, the content of geraniin was higher than that of UPLC-QQQ-MS quantified by the standard, compared to the semi-quantitative results of UPLC-Q-Orbitrap-MS² by gallic acid.

According to above reports, the phytochemicals of different rambutan peel extracts are mainly ellagitannins, including geraniin, corilagin, and ellagic acid. However, the phenolic profiles of rambutan peels are diverse due to the differences in cultivars, cultivable soil, and methods for extract and analysis.

### 3.3. Purification of geraniin

Geraniin, as a kind of ellagitannin, has attracted much attention (Cheng et al., 2017; Perera et al., 2015). Geraniin was found to be the major constituent of rambutan peel extracts. Thus, rambutan peel could be used as a potential source of geraniin. Large-scale purification of geraniin from rambutan peel extracts should be completed to obtain geraniin with relatively high purity to meet the requirement of geraniin quantity for industrial application.

Zhuang et al. (2017b) purified crude rambutan peel extract using different resins. NKA-9 resin was chosen to dynamically purify the rambutan peel extract due to good adsorption ability and desorption ratio. The content of geraniin was from 88.32 mg/g extract to 122.18 mg/g extract.

Palanisamy et al. (2011) focused on obtaining geraniin from the ethanolic extract of rambutan peel. Five g of ethanolic extract, obtained from 16.7 g rambutan peel, was first separated on a RP-18 glass column to yield 3 g of yellowish fraction. One g of this fraction was used in subsequent purification on a preparative HPLC. Geraniin was further obtained with 20% acetonitrile. Finally, geraniin with high purity was obtained. Another purification method was reported by Perera et al. (2012). A total of 362 g of crude ethanolic extract was obtained from a weight of 1506 g of dried rambutan peel, and the yield was 24.06%. The crude extract was subjected to reverse-phase C18 chromatography in 20 g batches to isolate geraniin, and geraniin was eluted with acetonitrile-water (10:90) solvent system. The water fraction containing geraniin was crystallized, and the geraniin purified by crystallization was 2.23 g. The total yield of geraniin from the crude extract was 11.15%, and the yield of geraniin from rambutan peel was 2.68%. HPLC analysis of purified geraniin showed that geraniin had a high purity of 97.80%. A minor impurity identified as corilagin constituted 2.20%.

The previous study reported a rapid separation and purification method for geraniin from rambutan peel extract (Li et al., 2021). The content of geraniin in freeze-dried rambutan peel was 12.67% (w/w). The extract was purified by medium-pressure liquid chromatography and preparative HPLC. Finally, geraniin with a purity of 95.63% and a yield of 6.00% was obtained. The purity of geraniin was slightly lower than that in the study of Perera et al. (2012), but the yield of geraniin had an obvious improvement.

### 3.4. Change in geraniin

Geraniin, which is rich in rambutan peel extract, is unstable and could easily produce a series of homologous derivatives under the effect of various factors, including alkali, temperature, light, enzymes, microorganisms, and gut bacteria (Espín et al., 2007). The changes in geraniin in previous studies are shown in Figure 2.

The stability of geraniin was significantly affected by thermal treatment. Li et al. (2021) studied that the mass concentration of geraniin reduced from 304.48 μg/mL to 252.31 μg/mL after treatment at 60 °C for 10 h, and the percentage of degradation loss was 17.13%. During the first 2 h of heating at 100 °C, geraniin was rapidly degraded, and the percentage of degradation loss was 73.97%. After heating at 100 °C for 10 h, no geraniin was detected. The thermal degradation products of geraniin belonged to phenolics, and seven compounds were mainly identified using UPLC-Q-Orbitrap-MS², including gallic acid, corilagin, hexahydroxybiphthalic acid, brevifolin carboxylic acid, galloyl-bis-HHDP-glucose, ellagic acid, and brevifolin. Several studies showed that ellagitannins are not intactly absorbed; however, they could be metabolized by the intestinal flora. As an ellagitannin, the initial metabolism of geraniin begins in the stomach, where geraniin is hydrolyzed to free ellagitannins, and a small percentage of geraniin was further metabolized by gut bacteria into smaller...
metabolites, such as tetrahydroxy-uro lithin D, trihydroxy-uro lithin C, dihydroxy-uro lithin A, and monohydroxy-uro lithin B, which are absorbed into the circulation due to their increased lipophilicity (Perera et al., 2015).

4. Biological activity

In this section, some studies on the bioactivities of different rambutan peel extracts, including antioxidant, antimicrobial, antihyperglycemic, antidiabetic, inhibitory skin aging, anti-OP, anti-inflammatory, and antiproliferative activities, in various tests in vitro and in vivo were reviewed, as shown in Table 2.

4.1. Antioxidant activity

Antioxidant activity is widely known to scavenge free radicals, maintain redox balance and metal chelating activity, inhibit enzymatic and non-enzymatic activities, and then regulate oxidant stress. Due to the existence of multiple oxidation mechanisms, no single determination method could accurately reflect the total antioxidant capacity of rambutan peel extracts. Therefore, several antioxidant activity indicators were simultaneously measured after a rambutan peel extract was obtained in previous reports. In addition, rambutan peel extracts could be applied as food preservative due to their antioxidant activities.

4.1.1. In-vitro model

Palanisamy et al. (2008) illustrated that the rambutan peel ethanolic extract has a good scavenging free radical activity, comparable to that of vitamin C and much higher than that of grape seed. This study was the first to demonstrate that the ethanolic extract from rambutan peel had high phenolic content, low prooxidant capacity, and good antioxidant activity. The phenolic content of this extract was 762 mg GAE/g, and the IC₅₀ values of Galvinoxyl and ABTs-scavenging activities were 1.7 and 1.7 μg/mL, respectively. In a study by Monroy et al. (2020), the rambutan peel extract exhibited high antioxidant activity with high inhibitory ABTS⁺ radical cations and DPPH radical activities. The antioxidant activity of rambutan peel extract is higher than those reported about apples, grapes, kiwis, plums, broccoli, garlic, peppers, and spinach. Nguyen et al. (2019) reported the antioxidant activities of two rambutan peel extracts (soluble and bound phenolic extracts), including inhibitory DPPH and ABTS⁺ radicals and FRAP values. The scavenging DPPH activities of the soluble and bound phenolic extracts were 46.38 and 30.87 μg TE/100 g, respectively, while their inhibitory ABTS⁺ activities were 54.09 and 42.95 g TE/100 g. In addition, FRAP values at 66.05 and 27.63 μg Fe²⁺/100 g were found in the soluble and bound phenolic extracts, respectively. More antioxidant activity indicators were established by Sun et al. (2012), who prepared free, soluble conjugate, and insoluble-bound fractions by alkaline hydrolysis, and the antioxidant activities of the three fractions were evaluated in five model systems in vitro, including DPPH-scavenging activity, reducing power, lipid peroxidation inhibition activity, OH⁻ scavenging activity, and nitrite-scavenging activity. The results showed that the free fraction had higher antioxidant activities than the soluble conjugate and insoluble-bound fractions. The IC₅₀ values of the free fraction were 4.21, 3.55, 85.53, 19.12, and 17.06 μg/mL in five model systems. Li et al. (2018) reported that rambutan peel extract had good Fe²⁺ and Cu²⁺ chelating capacities, with EC₅₀ values of 0.80 and 13.0 mg/mL, respectively. Meanwhile, the extract obviously inhibited the production of hydroxyl radical, with an IC₅₀ of 62.4 μg/mL. Impressively, the effect of this extract on AAPH-induced DNA damage was explored in this study, and the extract effectively inhibited radical-induced plasmin DNA strand breakage. In addition, this extract showed a protective effect on H₂O₂-induced oxidative damage in HepG2 cells (Zhuang et al., 2017a). It could reduce the intracellular level of ROS, increase SOD activity in HepG2 cells, improve oxidative stress defense, and then inhibit cell apoptosis. Thitilertdecha et al. (2010) evaluated the antioxidant activities of rambutan peel extracts obtained using ether, methanolic, and aqueous solvents, respectively. Several potential antioxidant indicators, including free-radical scavenging activity, reducing power, linoleic peroxidation, and β-carotene bleaching, were evaluated. The methanolic fraction had the highest antioxidant activity, as evidenced by the IC₅₀ of DPPH inhibition being 4.94 μg/mL higher than that in ascorbic acid and BHT. Sekar et al. (2014) reported the inhibitory effects of different rambutan peel extracts on DPPH radical and tyrosinase, and the IC₅₀ of tyrosinase inhibitory activities were 38.88 and 51.44 μg/mL, respectively. According to above studies, different rambutan peel extracts had different in vitro antioxidant activities, which were depend chiefly on their phenolic contents and profiles.

4.1.2. In-vivo model

The previous study reported that the rambutan peel ethanolic extract has a protective effect on D-gal-induced aging in mice (Zhuang et al., 2017a,b). This extract decreased D-gal-induced oxidative stress in mice by regulating the levels of T-AOC, SOD, GSH-Px, and MDA in serum, liver, and kidney. In addition, this extract significantly reduced histopathological changes in the liver and kidney of D-gal-induced mice. It also had protective effect against lipid peroxidation and accumulation of the liver in obese male Wistar rats, as observed by Setyawati et al. (2015). The research showed that the extract with the dose of 15 and 30 mg/kg bw significantly decreased MDA levels and did not significantly down-regulate the expression of PPARs. Interestingly, rambutan peel extract has the ability to protect the erythrocytes and hemoglobin of rats exposed to cigarette smoke, as reported by Lisdiana et al. (2017). Cigarette smoke is an exogenous free radical, which could damage the structure and function of erythrocyte membrane. The rambutan peel extract could maintain and improve the number of erythrocytes and hemoglobin in the rat blood exposed to cigarette smoke.

4.1.3. Food system

Apart from the in-vitro and in-vivo antioxidant activities of rambutan peel extract, the protection effect of the extract on oil by inhibiting lipid oxidative was determined. Phuong et al. (2020b) evaluated the effect of rambutan peel on the oxidative stability of soybean oil stored at 4 °C and 30 °C in the dark and light and deep fried with potatoes at 160 °C. The oil mixed with the extract at 1000 μg GAE/g could effectively delay the reaction of oxidation during storage in comparison with the oil without the extract. During frying, the extract could delay the lipid oxidation of oil. The contents of thiobarbituric acid reactive substances of potatoes fried in oil with the extract were much lower than those without the extract. Therefore, rambutan peel extract has good antioxidant effects, and it could effectively inhibit lipid oxidation in oil during storage and deep frying. Furthermore, Mei et al. (2014) reported the effect of rambutan peel extract on the stability of sunflower oil. The crude extract of rambutan peel was purified using silica-packed open column chromatography by increasing the polarity of solvents (ethyl acetate, chloroform, and methanol), and the three subfractions were obtained. One subfraction with a concentration of 300 μg/g was found to have better effect for 2 years of storage period at ambient temperature, comparable with that of tocopherol and BHA. These results indicated that the rambutan peel extract could be a potential source of antioxidants for the stability of sunflower oil.

4.2. Antimicrobial and antibacterial activities

Rambutan peel extracts have been found to have a wide range of activity against bacteria and microbes. Thitilertdecha et al. (2008) reported the antibacterial activity of different rambutan peel extracts with different solvents (ether, methanol, and aqueous solvent) against eight bacteria, including Escherichia coli (E. coli), Klebsiella pneumoniae (K. pneumonia), Salmonella typhi (S. typhi), Pseudomonas aeruginosa (P. aeruginosa), Vibrio cholerae (V. cholera), Staphylococcus aureus (S. aureus), Enterococcus faecalis (E. faecalis), and Staphylococcus
Table 2. Biological activities of rambutan peel extracts.

| Activity | In vitro | In situ/real food | In vivo | Results and mechanisms | References |
|----------|----------|------------------|---------|-------------------------|------------|
| Antioxidant activities | DPPH•, ABTs | ABTs, DPPH•, FRAP | | Single electron transfer mechanism | Monroy et al. (2020) |
| | Reducing power, DPPH•, OH•, Lipid peroxidation inhibition, Nitrite-scavenging ability | | | The range of IC50 values of DPPH•: 1.7–90.91 μg/mL. The range of IC50 values of ABTs: 0.76–57.94 μg/mL. | Monroy et al. (2020) |
| | DPPH•, Reducing power, Linoleic peroxidation, β-carotene bleaching | DPPH•, Tyrosinase activity | | | |
| | ABTs, FRAP | ABTs, FRAP, Superoxide anions, Reducing power, Limited cell death | | | |
| Lipid peroxidation | | | | | |
| H2O2-induced HepG2 cells | | | Cell viability | | |
| | | | Inhibitory apoptosis of cell | | |
| | | | Inhibitory ROS generation in cell | | |
| | | | | Zhuang et al. (2017a) |
| D-gal-induced aging mice | | | T-AOC, MDA, SOD, GSH-Px activities in serum, liver and kidney | | |
| | | | Histopathological changes of liver and kidney | | |
| | | | Palanisamy et al. (2008) |
| DPPH•-induced confluent cell death, Splenocytes | | | Reducing the activation of the apoptotic pathway | | |
| | | | Increase the levels of physiological antioxidants in the cell | | |
| | | | | Palanisamy et al. (2008) |
| | | | High-fat-diet induced obese male Wistar rats | | |
| | | | Inhibitory peroxidation in liver | | |
| | | | Decreased MDA content | | |
| | | | Expression of PPARγ | | |
| | | | | Setyawan et al. (2015) |
| | | | Cigarette smoke rats | | |
| | | | Increased number of red blood cells | | |
| | | | Increased hemoglobin levels | | |
| | | | | Lidiana, Dewi (2017) |
| | | | Soybean oil stored at 4 and 30 °C in the dark and light | | |
| | | | Inhibiting lipid oxidative | | |
| | | | | Phuong et al. (2020b) |
| | | | Deep fried with potatoes at 160 °C | | |
| Sunflower oil at 60 °C for 24 days | | | Peroxide value, p-anisidine value, Thioarbituric acid reactive substances, iodine value, Free fatty acids | | |
| | | | | Mei et al. (2014) |

(continued on next page)
| Activity                          | In vitro | In situ/real food | In vivo        | Results and mechanisms                                                                                                                                                                                                 | References                      |
|----------------------------------|----------|-------------------|----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------|
| **Antimicrobial activities**     |          |                   |                |                                                                                                                                                                                                                        |                                 |
| Five of Gram-negative            |          |                   |                | Methanol is the better solvent for more consistent extraction of antimicrobial substances compared to the other solvents                                                                                                 | Thitierdecha et al. (2008)      |
| Three of Gram-positive           |          |                   |                |                                                                                                                                                                                                                        |                                 |
| S. aureus, MRSA, S. mutans, E. coli, C. albicans |          |                   |                | Phenolic compounds                                                                                              | Tadtong et al. (2011)           |
| MRSA                             |          |                   |                |                                                                                                                                                                                                                        |                                 |
| S. pyogenes, S. aureus, E. coli, P. aeruginosa |          |                   |                | Potent phytochemicals quantitatively and not in qualitatively in the methanolic extracts Yellow rambutan peels higher than red rambutan peels in antimicrobial activities | Sekar et al. (2014)             |
| B. subtilis, P. aeruginosa, MRSA, K. pneumonia, S. pyogenes, S. enterica |          |                   |                | A library of potentially bioactive compounds Computationally inhibiting the ATP-binding domain of the chaperone, DnaK of P. aeruginosa and MRSA                                                                 | Asghar et al. (2021)            |
| Six of Gram-negative             |          |                   |                | Bind to membranes of bacteria Disrupt membrane integrity The loss of barrier function The partial hydrophobicity of bioactive compounds                                                                                 |                                 |
| Three of Gram-positive           |          |                   |                |                                                                                                                                                                                                                        |                                 |
| Raw chicken breast fish          |          |                   |                | Phenolic groups interacted and bound to protein Microbial growth inhibition. Higher concentration in the in situ test compared to the in vitro test                                                                 | Phuong et al. (2020a)           |
| **Antihyperglycemic and antidiabetic activities** |          |                   |                |                                                                                                                                                                                                                        |                                 |
| α-glucosidase                    |          |                   |                | The ability of different extracts to inhibit α-amylase however was not as pronounced, where only the ethanolic extract displayed activity. Correlated strongly to its high phenolic content | Palanisamy et al. (2011)        |
| α-amylase aldol reductase         |          |                   |                | Purified extract showed stronger bioactivity than crude extract, which might be due to their differences in phenolic profiles                                                                                           | Palanisamy et al. (2011)        |
| AGEs inhibition                   |          |                   |                |                                                                                                                                                                                                                        |                                 |
| α-glucosidase                    |          |                   |                |                                                                                                                                                                                                                        |                                 |
| α-amylase aldol reductase         |          |                   |                |                                                                                                                                                                                                                        |                                 |
| AGEs inhibition                   |          |                   |                |                                                                                                                                                                                                                        |                                 |
| the formation of amadori products, dicarbonyl compounds and AGEs |          |                   |                |                                                                                                                                                                                                                        |                                 |
| α-glucosidase                    |          |                   |                |                                                                                                                                                                                                                        |                                 |
| α-amylase                        |          |                   |                |                                                                                                                                                                                                                        |                                 |
| High-fat diet in combination with streptozotocin and nicotinamide inject |          |                   |                | ALT, ALP, TG, TC, LDL, HDL, Creatinine, Plasma insulin, blood glucose level and improve insulin levels. Pancreas histology, kidney and liver function                                                                  |                                 |
| High-fat diet combined streptozotocin induced mice |          |                   |                | CRE, GSP, TG, TC in serum TP, GC, SOD, GSH-PX, MDA in liver Histopathological of liver, pancreas and kidney PAS and TGF-β1 staining of kidney                                                                 | Ma et al. (2017)                |
| High-fat diet rats               |          |                   |                | Hypertension Impaired glucose and lipid metabolism Ectopic fat deposition Expression of mitochondrial genes                                                                                                       | Chen et al. (2020)              |
| metabolic risks by diet mimicking metabolic syndrome |          |                   |                | Body weights, White adipose tissue deposits, Organ weights, Triacylglycerol, Biomarkers of renal and liver dysfunction, Insulin resistance, Decreased insulin sensitivity, Percentage of beta-cell function | Chung et al. (2014)             |
| Alloxan induced-diabetic Rats     |          |                   |                | Blood glucose level Cholesterol level                                                                                                                                  | Muhtadi et al. (2015)           |
| **Antiphotaging activities**     | solar protect factor |          |                   | Electron delocalization Lone pairs of electrons and double bonds of molecules                                                                                                         | Mota et al. (2020)              |
| UV-induced hairless mice          |          |                   |                | Increase collagen and HA Decrease inflammatory cytokines Phosphorylation of MAPK Histopathological                                                                        | Xiao et al. (2019)              |
| elastase inhibitory              |          |                   |                |                                                                                                                                                                                                                        |                                 |
| collagenase inhibition           |          |                   |                |                                                                                                                                                                                                                        |                                 |
| human skin fibroblasts            |          |                   |                | MMP-2 level                                                                                                                                  | Lourith et al. (2017)           |

(continued on next page)
| Activity                                      | In vitro                                                                 | In situ or real food                                                                 |
|----------------------------------------------|--------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
| Anti-inflammatory activities                  | In vitro Anti-inflammatory responses on RAW 264.7 cells model             |                                                                                     |
| Anti-infective activities                     | LPS-induced RAW 264.7 cell model                                         |                                                                                     |
| Antiproliferative activities                  | Human macrophage cell F2, human monocytic leukemia cell 2, and MCF-7 cells |                                                                                     |
| Antitumoral activity                          |Anti-tumoral activity on human macrophage cell F2, human monocytic leukemia cell 2, and MCF-7 cells |                                                                                     |

### 4.3. Antihyperglycemic and antidiabetic activities

Diabetes mellitus is a global problem that has a major effect on health, the quality of life, life expectancy, and the healthcare system. One current method to treat diabetes is to inhibit carbohydrate hydrolyzing enzymes, such as α-glucosidase and α-amylase, in the digestive tract to decrease postprandial hyperglycemia by retarding the absorption of glucose. Another method is to inhibit the key enzymes in the polyol pathway, including aldose reductase, which could effectively inhibit the formation of advanced glycosylation end products (AGEs). Rambutan peel extracts could inhibit the activities of several digestive enzymes and decrease the formation of AGEs.

First, the antidiabetic activities of rambutan peel extracts were evaluated in *vivo*. U.D. Palanisamy et al. (2011) showed that the rambutan extract could inhibit the growth of *P. aeruginosa* and MRSA. In addition, some studies indicated that rambutan peel extract could inhibit the growth of *E. coli* and *Candida albicans*. This finding was similar to the report of Sekar et al. (2014). This extract showed good antimicrobial activity against *S. aureus* and MRSA, and the diameters of the inhibitory zone were >10 mm. In addition, the MIC of the extract against *S. aureus* and MRSA were 2 and 0.4 mg/mL, respectively. Asghar et al. (2021) studied the antibacterial activity of products extracted from yellow rambutan peel with different solvents against six pathogens, including *B. subtilis*, *P. aeruginosa*, MRSA, *K. pneumonia*, *S. pyogenes*, and *S. enterica*. Compared with the extracts obtained using other solvents (chloroform, methanol, ethanol, and water), those obtained using ethyl acetate and acetone showed significant antibacterial activity towards all tested strains. Furthermore, this study reported that the extract computationally inhibited the ATP-binding domain of chaperone, the DnaK of *E. coli*, and MRSA, and the diameters of the inhibition zone were >10 mm.

These previous studies showed that rambutan peel extracts has good inhibitory Gram-positive bacterial activity and no activity against Gram-negative bacteria. Moreover, the high potency as antibacterial agent against MRSA was identified.

Furthermore, Phuong et al. (2020a) studied the antimicrobial activity of methanolic extract from rambutan peel against some Gram-positive and -negative bacteria, and this extract was applied in real food due to its antimicrobial activity. The results showed that the extract had potential inhibitory effect against *E. coli*, *V. parahaemolyticus*, *V. campbellii*, *P. aeruginosa*, *V. anguillarum*, *S. enteritidis*, *S. aureus*, *C. albicans*, and *L. monocyctogenes in vitro*. Although food matrices are partially protected against bacteria, the extract inhibited *S. enteritidis* in raw chicken breast for 14 days at 4 °C in *in-situ* tests. The extract reduced *V. parahaemolyticus* by 1.5 log CFU/g in fish during 10 days of cold storage. Moreover, the antimicrobial activity of rambutan peel extract (RPE) can be enhanced by mixing with cinnamon essential oil (CEO), especially when the ratio RPE and CEO was 5:5, the synergist effect against Gram-positive bacteria and Gram-negative bacterial reached the best. The mixture of RPE and CEO is a potential natural antibacterial compound and could be used in food packaging film for prolonging the shelf life of fresh meat and meat products (Khanoomkon et al., 2022).
peel ethanolic extract could inhibit the carbohydrate hydrolyzing enzymes, and the IC_{50} values of inhibitory α-glucosidase and α-amylase activities were 2.7 and 70.8 μg/mL, respectively. In addition, the extract could inhibit α-lactalbumin, and the IC_{50} value was 0.04 μg/mL. The maximum inhibitory activity of the extract for AGE formation was found at the incubation time of 7 days, 43% for rambutan peel ethanolic extract and 38% for green tea. The rambutan peel extract had higher AGE inhibition activity than green tea. Moreover, U. Palanisamy et al. (2011) further evaluated the hypoglycemic activity of geraniin rapidly purified from the extract. The results showed that the purified extract possessed higher hypoglycemic activity, with the IC_{50} values of inhibitory α-glucosidase and α-amylase activities being 0.92 and 0.93 μg/mL, respectively. Zhuang et al. (2020c) also checked the inhibitory activity of the glycation of crude and purified extracts in vitro. Both exhibited good performance, including the formation of amadori products, dicarbonyl compounds, and AGEs. The purified extract showed stronger bioactivity than the crude extract, possibly due to their differences in phenolic profiles. At a concentration of 10 μg/mL, the inhibitory effects of crude and purified extracts on AGE formation were 32.52% and 44.07%, respectively.

Then, the antidiabetic activities were detected in vivo. Ma et al. (2017) evaluated the antidiabetic activity of rambutan peel extract by using a type II diabetic mouse model induced by streptozotocin combined with high-fat diet. The results indicated that the extract regulated the body weight and decreased the fasting blood glucose level in diabetic mice. The extract obviously decreased the serum levels of total cholesterol, creatinine, glycated serum protein, and triglyceride of diabetic mice in a dose dependent manner. The glycogen content in liver was also regulated. In addition, the extract further increased the activity of SOD and GSH-Px in diabetic mice and decreased lipid peroxidation. Histological analysis indicated that the extract could protect the tissue structure of the kidney, liver, and pancreas. Finally, the extract reduced the renal mesangial index and suppressed the expression of TGF-β in diabetic mice. The potential ability of the peel extract in regulating hyperglycemia in diabetes in vitro and in vivo was studied by Subramaniam et al. (2015). The IC_{50} values of the extract on the inhibitory activities of α-glucosidase and α-amylase were 6.44 and 93.35 μg/mL, respectively, similar to the report published by Palanisamy et al. The in-vivo antidiabetic effects of rambutan peel extract were further evaluated in a high-fat-induced diabetic rat model. The results showed that the rambutan peel extract could reduce the blood glucose level and improve the insulin levels of diabetic rat. Pancreatic histology also showed that rambutan peel extract has healthy pancreas morphology. The activity of the extract was comparable to that of metformin. In addition, Muhtadi et al. (2015) explored the antidiabetic and anti-hypercholesterolemic activities of rambutan peel ethanolic extract, with successive doses of 125, 250, and 500 mg/kg body weight (bw). This study indicated that the extract possessed antidiabetic and anti-hypercholesterolemic activities at doses of 125–500 mg/kg bw. The blood glucose and cholesterol levels in a dose of 500 mg/kg bw decreased by 61.76% and 60.75%, respectively. The anti-hypercholesterolemic activity of rambutan peel extract was higher than that of cholestyramine.

Lastly, Chung, Ton, Gurtu and Palanisamy (2014) reported that geraniin, which was obtained from rambutan peel, could improve metabolic risks by diet-minicking metabolic syndrome. This study was the first to show that an orally available geraniin could safely improve many negative pathological sequel of metabolic syndrome. Geraniin at 50 mg/kg bw showed significant therapeutic potential, and it could safely alleviate obesity-induced metabolic dysfunction, including body weights, white adipose tissue depot, organ weights, triglyceride, biomarkers of renal and liver dysfunction, insulin resistance, and decreased insulin sensitivity and percentage of beta-cell function. Chen et al. (2020) studied the metabolic effects and possible mechanism of geraniin from rambutan peel in rats with metabolic syndrome induced by high-fat diet. The result showed that geraniin could improve multiple metabolic abnormalities, such as hypertension, impaired glucose and lipid metabolism, and ectopic fat deposition in the visceral fat and liver. Geraniin was found to be comparable to metformin. This finding was similar to the report of Subramaniam et al. (2015). Transcriptomic results showed that geraniin had a profound effect on liver expression. Lipid and steroid metabolic processes were also regulated by geraniin. According to differential transcriptomes, geraniin significantly regulated the expression of mitochondrial genes, which may potentially affect the activity of mitochondria.

4.4. Inhibitory skin aging

Ultraviolet (UV) irradiation is a crucial factor causing skin photoaging. UV irradiation can produce reactive oxygen species (ROS), and excessive UV irradiation can accelerate the production of proinflammation cytokines. ROS and proinflammation cytokines could induce the formation of MMPs, increase MMP contents and activities, and then decrease the formation of collagen in skin. Two methods are often used to protect skin from UV irradiation. One method is to absorb UV irradiation and minimize exposure to radiation; the other is to increase the reduce power in skin. Many reports have shown that rambutan peel extract has two actions for antiphotoaging.

Mota et al. (2020) found that rambutan peel extract could be used as a natural additive to enhance the sun protection factor (SPF) of final product. Rambutan peel extract could absorb UBV radiation between the ranges of 290 and 320 nm. Adding 1% concentration of rambutan extract could improve SPF from 0.4 to 11.2 and further increase it to 26.3 when 7.5% of ethylhexyl methoxyccinnamate (EHMC) was added. The increase in SPF is due to the synergistic effect between the phenolics of the rambutan peels and the EHMC. In addition, sunscreen formulation containing 1.00% rambutan peel extract showed the potential to minimize the risk of toxicity of synthetic agent and reduce the production cost of sunscreen by 45%. Meanwhile, the utility of rambutan peel extract in skin-aging treatments was reported by Lourith et al. (2017). The elastase inhibitory activity of rambutan peel extract was 31.08% at a tested concentration of 0.25 mg/mL, and the collagenase inhibitory activity was 53.99% at a tested concentration of 0.125 mg/mL. Rambutan peel extract was found to be safe to human skin fibroblasts, and the safe concentration was 0.01 mg/mL. In addition, it inhibited MMP-2 by 23.11% at 0.01 mg/mL.

Furthermore, Xiao et al. (2019) studied the protective effects of rambutan peel extract and/or peptide LSGYP and the additive effect of both on skin photoaging in UV-induced hairless mice. The results indicated that the extract and/or LSGYP had protective effect on photoaging skin. The extract showed positive effects on the regulation of oxidant stress (antioxidant enzyme activities and glutathione and malondialdehyde contents), inflammatory cytokine levels (IL-1α, TNF-α, and IL-6 levels) and MMP levels (MMP-1, MMP-3, and MMP-9). The histological changes revealed that the extract and LSGYP had good protective effect on skin tissue and endogenous collagen. Furthermore, the extract and LSGYP produced an additive effect on skin photoaging in UV-induced mice.

4.5. Anti-OP

OP is a usual bone disease, which is characterized by low bone density, proneness to bone fragility, and high risk of fracture. According to the report of World Health Organization, with global population aging, about 62% of men and 72% of women over the age of 50 are predicted to suffer from OP or osteopenia by 2022. Zhuang et al. (2020) evaluated the effect of rambutan peel extract on OP by using two models, RANKL-induced RAW264.7 cells and retinoid-acid-induced osteoporotic rats. RAW264.7 cells could be differentiated into osteoclasts by using RANKL. Different concentrations (0.5, 1.0, 2.5, and 5.0 μg/mL) of rambutan peel extract had no significant effect on cell viability. The extract reduced the number of TRAP-positive cells significantly in a dose-dependent manner. In addition, the extract treatment decreased the total TRAP activity in RANKL-stimulated RAW264.7 cells. The extract treatment also significantly improved calcium loss in
retinoid-acid-induced osteoporotic rats. The level of serum phosphorus in OP rats was increased, and the levels of total alkaline phosphatase and osteocalcin in serum of OP rats were further decreased. In addition, the extract increased the qualities of the femur and tibia of osteoporotic rats to some extent, such as bone length, bone mineral density, bone maximum load, trabecula relative bone density, and cortical bone area ratio. Histological changes showed that the extract could effectively improve the bone microstructure of OP rats by regulating the trabecular bone separation and cortical bone thickness.

4.6. Anti-inflammatory properties

The anti-inflammatory property of rambutan peel extract was tested in an LPS-induced RAW 264.7 cell model. In this model, NO was over-produced and the iNOS level increased obviously. The excessive NO involves a number of events, including the reactions of oxidative stress and inflammation. The production of NO may be derived from the modulation of iNOS. Rambutan peel extract significantly inhibited the NO production and regulated the levels of iNOS mRNA in LPS-induced RAW 264.7 cells, and the activities increased in a dose-dependent manner (Li et al., 2018).

Rambutan peel extract also showed positive influence on rheumatoid arthritis, a chronic inflammatory disease that mainly targets the synovial tissue, cartilage, and subchondral bone. The effect of rambutan peel extract on collagen-induced arthritis (CIA) in dark agouti rats was studied by Kumar et al. (2012). CIA rats were given 100 and 200 mg/kg of rambutan peel extract orally from day 25 to day 50. The extract significantly inhibited the physiological, biochemical, and histopathological changes during arthritis rats. In addition, rambutan peel extract could significantly reduce the body weight and paw edema induced by arthritis and reduced the C-reactive protein. After treatment with rambutan extract, the histopathological changes caused by arthritis were significantly regulated. Furthermore, the effect of rambutan extract on the levels of MMP-13 and TIMP-1 was in a dose-dependent manner.

4.7. Antiproliferative activities

Research revealed that rambutan peel extracts possess antiproliferative activities on human cell lines KB, Caco-2 cells, MDA-MB-231, HeLa human cervical adenocarcinoma, and MG-63 human osteosarcoma cells (Khaizil Emlyia et al., 2013; Khonkarn et al., 2010). The yellow cultivar showed slightly better effect than the red cultivar on MDA-MB-231 and MG-63 cells, with IC_{50} values of 5.42 and 6.97 μg/mL, respectively. However, a higher concentration (≥49.5 μg/mL) of both extracts was needed to decrease the HeLa cell viability. In addition, Ling et al. (2010) reported the anti-proliferative activities of 13 plants native to Malaysia, including rambutan, and the methanolic and aqueous extracts of rambutan peel with doses of 50 and 100 μg/mL had no cytotoxic effects on 4T1 cells and 3T3 cells.

4.8. Other pharmacological properties

The antihypercholesterolemic activity of rambutan peel extract was evaluated by Suciati et al. (2020). Some main compounds from rambutan peel extract were analyzed as squalene synthase inhibitors by using simulation molecular docking. The docking results indicated that geraniin, corilagin, and ellagic acid could bind with squalene synthase active site and form stable bonds. Geraniin had the lowest binding free energy. In addition, ADMET results revealed that 75% of geraniin, corilagin, and ellagic acid compounds could be absorbed by human digestion. They were well distributed and did not cause liver toxicity. The antihypertensive activity of rambutan peel extract was also reported (Looi et al., 2020). In-vitro studies showed that the geraniin from rambutan peel extract could inhibit ACE. In-silico molecular docking showed that geraniin could form a series of hydrogen and hydrophobic interactions with the active site of ACE and inhibit ACE activity. Furthermore, geraniin could decrease systolic blood pressure in a high-fat diet-induced obese Sprague–Dawley rats. In addition, blood pressure reduction in SHR was reported after oral consumption and intravenous administration of geraniin.

The effect of geraniin, extracted from rambutan peel extract, on dengue virus type-2 (DENV-2) was evaluated by Ahmad et al. (2017). The results showed that geraniin inhibited DENV-2 plaque formation, with an IC_{50} of 1.75 μM. Geraniin decreased viral infectivity and inhibited DENV-2 from attaching to the cells, but it had a slight effect on its penetration. Geraniin was discovered to had high effective at the early stage of DENV-2 infection. According to the molecular docking result, geraniin could interact with DENV E protein at the DIII region, while geraniin was bound to rE-DIII with high affinity.

5. Application

According to previous studies, phenolics have good bioactivities. Therefore, phenolics could be used as important components to make different products. These products have extensive applications in food, medicine, and cosmetic industry (Khumkomgool et al., 2020). Recently, some reports showed that rambutan peel extract, as an active material, could be made into biofilms, creams, and micro-encapsulations.

Go and Song (2020) reported new citrus Junos Pomace cectin (CJP) films combined with different concentrations of rambutan peel extract. These films were able to block out light by reducing light transmittance. In addition, with the dose of the extract increased, the antioxidant activities of the CJP films increased. In addition, the previous study of the authors showed that rambutan peel extract combined with pachyrhizus starch (PS) could be added into tilapia skin collagen (TSC) to improve the thermal stability of TSC films. TSC film containing 10% PS and 0.5% of the extract showed the highest tensile strength. The incorporation of extract and PS improved the thermal stability of TSC films (Zhuang et al., 2019).

Yun et al. (2021) found that incorporation of rambutan peel extract (RPE) enhanced the light, water vapor and oxygen barrier abilities, mechanical property, and antioxidant and antimicrobial activities of Chitosan (CS) films. The structural, physical and functional properties of the films were greatly influenced by the addition amount of RPE. CS film with 5% RPE had the highest barrier, mechanical, antioxidant and anti-microbial properties. Moreover, pork wrapped with CS film containing 5% of RPE presented the lowest total volatile basic nitrogen level, thiobarbituric acid reactive substance value, total viable count and the best sensory attributes on the 8th day. The results suggested the potential of CS film containing 5% of RPE as an active packaging material in pork preservation.

Chollakup et al. (2020) reported the blending of cassava starch and whey protein isolate films incorporated with cinnamon oil and rambutan peel extract. The effects of native starch, acetylated starch, cinnamon oil, and rambutan peel extract on the film characteristics and antioxidant and antibacterial activities were evaluated. Hydrogen bonding and hydrophobic interaction were observed among protein, starch, and polyphenols. Active compounds reduced water vapor permeability according to the starch types controlling the dispersion of cinnamon oil. Starch promoted the release of phenolics and scavenging radical activities in water and 50% ethanol. In vitro and in real food, the antibacterial activity of the blend films differed, which depended on the release of phenolics and food components, respectively.

Rambutan peel extract was used to prepare an antiaging cream by Sekar et al. (2017), due to its antioxidant and antiaging properties. The amount of the extract in the cream was 3% (w/w). The cream was o/w type of emulsion, and the pH was in the range of 4.90–5.20. The physico-chemical parameters of this cream, including homogeneity, appearance, odor, spreadability, after feel, type of smear, removal, microbial limit test, and stability, were determined. The results revealed that the formulation of antiaging creams is consistent with the quality of their components, hence useful for consumers. In addition, the cream did not cause redness, edema, inflammation, and irritation in irritancy studies.
indicating that it is safe to be used on the skin and has tremendous potential for cosmetic market development.

Rambutan peel extract also could serve as microencapsulation. Boyano-orozco et al. (2020) prepared the microencapsulation of rambutan peel extract through spray drying. The best spray drying encapsulating operations were as follows: inlet temperature of 160 °C, outlet temperature of 80 °C, and 10% encapsulating agent dose in the feeding solution. Under these operations, retention and encapsulation levels were higher than 85%, and the values of moisture content, water activity, and Hauser index were 3.95%, 0.25, and 1.42, respectively. The results revealed that the optimized powder of the extract had good solubility and morphological characteristics, and the microcapsule had no ruptures. Microencapsulation of rambutan peel extract could be applied to natural ingredients in food, medicine, and cosmetic industry.

6. Safety and regulation

Rambutan peel extract could be used as a natural bioactive agent due to the content, composition, and bioactivities of the phenolics. However, safety is the primary element to be considered before application. Many studies have focused on the safety of different rambutan peel extracts.

Thinkratok et al. (2014) studied the safety of rambutan peel extract by a male mouse model. Acute toxicity was evaluated by treating the rats orally with the extract at different concentrations (1000–5000 mg/kg), and the sub-chronic toxicity was evaluated by treating the rats with single doses of the extract (500, 1000, and 2000 mg/kg) daily for 30 days. Food consumption and body weight gain were obviously decreased in acute and sub-chronic toxicity analysis. In an acute toxicity study, the extract did not affect the serum levels of TG, AST, and ALT, and the LD50 value was analyzed to be higher than 5000 mg/kg. In the sub-chronic toxicity study, the extract significantly reduced the plasma TG level and blood urea nitrogen. However, the plasma AST and ALT levels were not altered, and the TC levels did not show any remarkable change. No mortality and toxicity symptoms were found up to 1000 mg/kg/day. However, the mortality rate was 12.5% with a dose of 2000 mg/kg/day.

The acute and sub-chronic toxicity of ethanol extract from rambutan peel was evaluated using Sprague–Dawley rats by Subramaniam et al. (2012). In the acute study, a single oral administration of rambutan peel extract with different doses of 50, 200, 1000 and 2000 mg/kg was used in rats for 14 days. In the sub-chronic toxicity study, the extract with two doses of 500 and 2000 mg/kg was administered to rats for 28 days. Neither mortality nor adverse effects were found in rats. No significant differences were observed in the relative organ weights and biochemical analysis. The histology of liver and kidney also showed no obvious changes. Therefore, the lethal dose of the ethanol extract of rambutan peel was higher than 2000 mg/kg. The no-observed-adverse-effect-level of the extract is thought to be up to 2000 mg/kg in rats.

The acute and sub-chronic toxicities of rambutan peel extract with higher concentrations than those in the study of Subramaniam et al. (2012) were evaluated using oral administration on Kunming mice and Sprague–Dawley rats, respectively, by Li et al. (2020). In the acute toxicity study, the LD50 of the extract was determined to be higher than 5000 mg/kg bw in vivo. In the subacute toxicity study, the extract showed no obvious adverse effect at doses of 312 and 625 mg/kg bw. However, body weight gain was significantly reduced at a dose of 2500 mg/kg bw of the extract, and the extract at doses of 1250 and 2500 mg/kg bw revealed toxicities to kidney, liver, and spleen in rats based on hemato-logical and biochemical analyses. Furthermore, the extract revealed toxicity on different tissues at 2500 mg/kg bw based on histopathological analyses.

A comprehensive acute oral toxicity of geraniin and a geraniin-enriched rambutan peel extract in Sprague–Dawley rats was reported by Moorthy et al. (2019). After a single oral dose, the LD50 values for geraniin and the extract were determined to be 2000 mg/kg bw. The hepatocytes of three rats treated with geraniin exhibited a “foamy appearance.” Therefore, the no-observed-adverse-effect level of geraniin was lower than 2000 mg/kg, while that of rambutan peel extract rich in geraniin was up to 2000 mg/kg. To sum up, the dosage of rambutan peel extract should be carefully selected to improve biological activity and reduce adverse reactions.

7. Conclusion and future perspectives

Rambutan fruit is widely accepted all over the world, and it is gradually industrialized. The intervention of multi-disciplinary research has promoted the conversion of rambutan peel waste to a healthful ingredient for industries. Rambutan peel has obviously become a good source of food functional components because of its phenolics and bioactivities. However, some challenges in the production and application of phenolics still exist, thereby limiting the rapid expansion of rambutan peel market. The following challenges should be considered in future studies:

(1) Although some efficient extraction techniques, such as MAE, UAE, and SFE, were used to prepare the rambutan peel extracts, some emerging technologies, including pulsed electric field, high voltage electrical discharge, instant controlled pressure drop, were not used for the extract of rambutan peels. These technologies may increase the extract efficiency of bioactive compounds by increasing the extract yield, shortening the extraction time, and decreasing energy consumption. Meanwhile, the extract process must be applied for application to a large scale of operation. In addition, producing phenolics with good quality and consistency at the industrial level is difficult, while stability data of phenolics during production and storage procedure are lacking.

(2) Producing rambutan peel phenolics with bioactivity and consumer acceptable taste is difficult. The beneficial effects of rambutan peel phenolics in human studies are also lacking. Meta-analysis of scientific evidence related to the health benefits of the phenolics is insufficient. Although many studies have been carried out to determine the bioactivity of phenolics in vitro, the fate of these functional molecules in the gastrointestinal tract and their absorption and bioavailability have not been fully explored. In vivo scientific evidence about the mechanism of action of pheno-lics and dose–response relationship is insufficient, and data on the bioavailability of various compounds from rambutan peel in the human system are scarce. In addition, scientific data related to the absorption, distribution, metabolism, and excretion of rambutan peel phenolics are not available. If the consumption of phenolics is greater than the recommended amount, scientific data on the risks associated with phenolics should be considered.

Declarations

Author contribution statement

All authors listed have significantly contributed to the development and the writing of this article.

Funding statement

Sun Liping was supported by National Natural Science Foundation of Yunnan Province [202101AT070084].

Professor Zhuang Yongliang was supported by National Natural Science Foundation of China [31864021].

Data availability statement

No data was used for the research described in the article.

Declaration of interest’s statement

The authors declare no conflict of interest.
Additional information

No additional information is available for this paper.

References

Ahmad, S.A.A., Palanisamy, U.D., Tejo, B.A., Chew, M.F., Tham, H.W., Hassam, S.S., 2017. Geraniin extracted from the rind of Nephelium lappaceum tends to dendrite virus type-2 envelope protein and inhibits early stage of virus replication. Virol. J. 14, 229.

Asghar, A., Tan, Y.C., Zahoor, M., Abidin, S.A.Z., Yow, Y.V., Khan, E., et al., 2021. A scaled-approach to unearth potential antibacterial components from epicarp of Malaysian Nephelium lappaceum L. Sci. Report. 11, 13859.

Box, G., Hunter, W.G., Hunter, J.S., 1978. Statistics for Experimenters. John Wiley & Sons, New York.

Boutoncier, L., Gallardo-Velazquez, T., Meza-Márquez, O.G., Osorio-Revilla, G., 2020. Microencapsulation of rambutan peel extract by spray drying. Foods 9 (7), 899.

Chowdri, T., Kangron, N., Sommarin, S.R., Rachapantup, J., Junmahasathan, T., Kumpudee-Vollrath, M., et al., 2020. Extraction of tropical fruit peels and development of HPMC Film containing the extracts as an active antibacterial packaging material. Molecules 26, 2265.

Cheng, H.S., Ton, S.H., Kadir, K.A., 2017. Ellagittannin geraniin: a review of the natural sources, biosynthesis, pharmacokinetics and biological effects. Phytochemistry Rev. 16 (1), 159–193.

Cheng, H.S., Goh, B.H., Pang, S.C.W., Mbs, M.M.A., Med, B., Ton, S.H., et al., 2020. Pleiotropic ameliorative effects of ellagittannin geraniin against metabolic syndrome induced by high-fat diet in rats. Nutrition 79–80, 110973.

Chollapuk, R., Boonpong, S., Booncha, W., Khaokhanong, N., Kongin, K., Soonthornwit, R., et al., 2020. Antioxidant and anti-bacterial activities of casava starch and whey protein blend films containing rambutan peel extract and cinnamon oil for active packaging. LWT - Food Sci. Technol. 120 (1), 109573.

Chung, A.P.Y.S., Ton, S.H., Gurtu, S., Palanisamy, U.D., 2014. Ellagittannin geraniin supplementation ameliorates metabolic risks in high-fat diet-induced obese Sprague Dawley rats. J. Funct.Foods 9, 173–182.

Espín, J.C., González-Barrón, R., Cerda, B., López-Bote, C., Rey, A.L., Tomás-Barberán, F.A., 2007. Iberian pig as a model to clarify obscure points in the bioavailability and metabolism of ellagittannin in humans. J. Agric. Food Chem. 55 (25), 10476–10485.

Estrada-Gil, L., Contreras-Espível, J.C., Flores-Gallegos, C., Zugasti-Cruz, A., Govea-Salas, M., Mata-Gómez, M.A., Rodríguez-Herrera, R., Ascacio-Valdez, J.D., 2022. Recovery of bioactive ellagitannins by ultrasound/microwave-assisted extraction from Mexican rambutan peel (Nephelium lappaceum L.). Molecules 27 (5), 1592.

Gallego, R., Bueno, M., Herrero, M., 2019. Sub- and supercritical fluid extraction of bioactive compounds from plants, food-by-products, seaweeds and microalgae-an update. Trends Anal. Chem. 116, 198–213.

García-Salas, P., Morales-Soto, A., Segura-Carretero, A., Fernández-Gutiérrez, A., 2010. Phenolic-compound-extraction systems for fruit and vegetable samples. Trends Food Sci. Technol. 21 (1), 58–64.

Go, E.J., Song, K.B., 2020. Development and characterization of citrus junos pomace peel extracts as sources for compounds with antioxidant and antiproliferative activities against human cell lines. Food Chem. Toxicol. 48 (8), 2122–2129.

Khunkomgoool, A., Saneulsutana, T., Harnkarnsujarit, N., 2020. Active meat packaging from thermoplastic cassava starch containing sappan and cinnamon herbal extracts in LIPPE blow film extrusion. Food Packag. Shelf Life 26, 100527.

Kumar, S., Chakravartti, S., Chiew, G.S., Subramaniam, T., 2012. Protective effects of Nephelium lappaceum rind extract against collagen-induced arthritis in dark agouti rats. J. Biol. Sci. 12 (7), 385–392.

Li, Y., Zhou, H., Zhong, C., Li, Z., 2018. Metal chelating, inhibitory DNA damage, and anti-inflammatory activities of phenolics from rambutan (Nephelium lappaceum) peel and the quantifications of geraniin and corilagin. Molecules 23 (9), 2263.

Li, Y., Zhang, Y., Tan, W., Sun, L., 2020. In vivo acute and subacute toxicities of phenolic extract from rambutan (Nephelium lappaceum) peels by oral administration. Food Chem. 320, 126618.

Li, Y., Sun, L., Zhang, Y., 2021. Purification and thermal stability of geraniin from Nephelium lappaceum L. Food Sci. (N.Y.) 62 (15), 44–49.

Ling, L.T., Radhakrishnan, A.K., Subramaniam, T., Cheng, H.M., Palanisamy, U.D., 2010. Assessment of antioxidant capacity and cytotoxicity of selected malaysian plants. Molecules 15 (4), 2139–2151.

Lindsay, R., Fw, P.K., 2017. Effects of rambutan peel extract to the number of erythrocytes and haemoglobin in rats exposed to cigarette smoke. J. Phys. Conf. 824 (1), 012060.

Looi, D., Goh, B.H., Khan, S.U., Ahmad, N., Palanisamy, U.D., 2020. Metabolites of the ellagittannin, geraniin inhibits human ACE in vitro and in silico evidence. Int. J. Food Sci. Nutr. 1–8.

Lourth, N., Kanlayavatthanakul, M., Chakul, P., Chansriniyom, C., Bunwatcharaphanphaksan, P., 2017. In vitro and cellular activities of the selected fruits residues for skin aging treatment. An. Acad. Bras. Cirurg. 89, 577–589.

Lucía, P., Federica, M., Rita, N., Stefania, M., Luissela, V., Alessandra, N., 2020. Bioactive phenolic compounds from agri-food wastes: an update on green and sustainable extraction methodologies. Front. Nutr. 7, 60.

Ma, Z., Zhang, X., Sun, L., Zhuang, Y., 2019. Antidiabetic effects of phenolic extract from rambutan peels (Nephelium lappaceum) in high-fat diet and streptozotocin-induced diabetic mice. Nutrients 9 (8), 801.

Macrő, P.A.N., Silvano, A.H., Paixão, M.D.R., Queiroz, O.W., Araújo, P.G., Maria, P.G., 2020. Functional and nutritional properties of selected Amazon fruits: a review. Food Res. Int. 147, 101152.

Mahmood, K., Kamilah, H., Alias, A.K., Ariffin, F., 2018. Nutritional and therapeutic potentials of rambutan fruit (Nephelium lappaceum L.) and the by-products: a review. J. Food Meas. Char. 12 (3), 1556–1571.

Maran, J.P., Manikandan, S., Nivetha, C.V., Dinesh, R., 2017. Ultrasound assisted extraction of bioactive compounds from Nephelium lappaceum L. fruit peel using central composite face centered response surface design. Arab. J. Chem. 10 (S1), S30–S38.

N. lappaceum Lappaceum – Nephelium lappaceum L. (Mexican variety) husk. Asian Paci. J. Trop. Med. (12), 676–681.

Maht, P.N.N., Le, T.T., Dang, M.Q., Camp, J.V., Raes, K., 2020. Selection of extraction conditions of phenolic compounds from rambutan (Nephelium lappaceum L.) peel. Food Bioprod. Process. 222, 222–229.

Muhammad, S., Anizia, O., Garca-Salas, P., 2020. Active compound identification in extracts of N. lappaceum peel and evaluation of antioxidant capacity. J. Chem. 1, 1–14.

Moorthy, M., Khoo, J.J., Palanisamy, U.D., 2019. Acute oral toxicity of the ellagittannin geraniin and a geraniin-enriched extract from Nephelium lappaceum L. rind in Sprague Dawley rats. Helinyon 5 (8), e02337.

Momot, M.D., Morte, A.N.D.M., Silva, L.C.R.C., Chinalia, E.A., 2020. Sunscreen protection factor enhancement through supplementation with rambutan (Nephelium lappaceum L.) ethanolic extract. J. Photochem. Photobiol. B. 205, 111837.

Muhammad, S., Kurien, I., Iyer, K.S., Remzema, A., Thomas, S., 2019. Natural diversity of rambutan (Nephelium lappaceum L.) in Kerala, India. Genet. Resour. Crop Evol. 66 (5), 1073–1100.

Muhammad, S., Kurien, I., Iyer, K.S., Remzema, A., Thomas, S., 2019. Natural diversity of rambutan (Nephelium lappaceum L.) in Kerala, India. Genet. Resour. Crop Evol. 66 (5), 1073–1100.

Muhammad, S., Kurien, I., Iyer, K.S., Remzema, A., Thomas, S., 2019. Natural diversity of rambutan (Nephelium lappaceum L.) in Kerala, India. Genet. Resour. Crop Evol. 66 (5), 1073–1100.

No additional information is available for this paper.
Phuong, N.N.M., Le, T.T., Nguyen, M.V.T., Camp, J.V., Raes, K., 2020b. Antioxidant activity of rambutan (Nephelium lappaceum L.) peel extract in soybean oil during storage and deep frying. Eur. J. Lipid Sci. Technol. 122 (2), 1900214.

Phuong, N.N.M., Le, T.T., Dang, M.Q., Camp, J.V., Raes, K., 2020c. Selection of extraction conditions of phenolic compounds from rambutan (Nephelium lappaceum L.) peel. Food Bioprod. Process. 122, 222–229.

Rakariyatham, K., Zhou, D., Rakariyatham, N., Shahidi, F., 2020. Sapindaceae (Dimocarpus longan and Nephelium lappaceum) seed and peel by-products: potential sources for phenolic compounds and use as functional ingredients in food and health applications. J. Funct. Foods 67, 103846.

Rottinawati, T., Tijitraresmi, A., Wiusuputi, M.V., 2018. In vitro activity of rambutan (Nephelium lappaceum) peel extract from Indonesia to methicillin-resistant staphylococcus aureus (MRSA). Dhaka Univ. J. Pharm. Sci. 17 (2), 197–203.

Sekar, M., Jaffar, F.N.A., Zahari, N.H., Mokhtar, N., Zulkifli, N.A., Kamaruzaman, R.A., et al., 2014. Comparative evaluation of antimicrobial properties of red and yellow rambutan fruit peel extracts. An. Res. Rev. Bio. 4 (24), 3869–3874.

Sekar, M., Sivalinggam, P., Mahmad, A., 2017. Formulation and evaluation of novel antiaging cream containing rambutan fruits extract. Int. J. Pharmaceut. Sci. Res. 8 (3), 1056–1065.

Setyawati, A., Dewi, A.K., Athiillah, M.F., Lestari, U., Lestari, S.R., 2015. The effect of rambutan (Nephelium lappaceum L.) peel extract on lipid peroxidation in liver of obese rats. Int. Conf. Bio. Sci. (ICBS) 2, 326–329.

Sidol, M., Sadowska, A., Król, K., Najman, K., 2022. Bioactive and physicochemical properties of exotic fruit seed powders: mango (Mangifera indica L.) and Rambutan (Nephelium lappaceum L.) obtained by various drying methods. App. Sci.-Basel 12, 49995.

Subramaniam, S., Chakravarti, S., Palanisamy, U.D., Radhakrishnan, A., Haleaghrara, N., 2012. Acute and sub chronic oral toxicity assessment of the ethanolic extract from the rind of Nephelium lappaceum in rats. J. Pharmacol. Toxicol. 7 (8), 378–385.

Subramaniam, S., Radhakrishnan, A., Chakravarti, S., Palanisamy, U.D., Haleaghrara, N., 2015. Antihyperglycemic effects of Nephelium lappaceum rind extract in high fat-induced diabetic rats. Int. J. Pharmacol. 11 (6), 542–551.

Suciati, L., Lestari, S.R., Lukita, B., 2020. Molecular docking studies of geraniin, corilagin, and ellagic acid from rambutan (Nephelium lappaceum L.) peel extract against squalene synthase as potential anti hypercholesterolemia. AIP Conf. Proc. 2231 (1), 040040.

Sun, L., Zhang, H., Zhuang, Y., 2012. Preparation of free, soluble conjugate, and insoluble-bound phenolic compounds from peels of rambutan (Nephelium lappaceum) and evaluation of antioxidant activities in vitro. J. Food Sci. 77 (2), C198–C204.

Tadtong, S., Athikomkulchai, S., Worachanon, P., Chalongpol, P., Chaichanachaihan, P., Saratedenchai, V., 2011. Antibacterial activities of rambutan peel extract. J. Health Res. 25 (1), 36–37.

Thinkratok, A., Suwannaphrapha, P., Srisawat, R., 2014. Safety assessment of hydroethanolic rambutan rind extract: acute and sub-chronic toxicity studies. Indian J. Exp. Biol. 52 (10), 989–995.

Thitilertdecha, N., Rakariyatham, N., 2011. Phenolic content and free radical scavenging activities in rambutan during fruit maturation. Sci. Hortic. 129 (2), 247–252.

Thitilertdecha, N., Thitilertdecha, N., Rakariyatham, N., 2008. Antioxidant and antibacterial activities of Nephelium lappaceum L. extracts. LWT - Food Sci. Technol. (Lebensmittel-Wissenschaft - Technol.) 41 (10), 2029–2035.

Thitilertdecha, N., Rakariyatham, N., 2010. Identification of major phenolic compounds from Nephelium lappaceum L. and their antioxidant activities. Molecules 15 (3), 1453–1465.

Tseng, J.L., Goh, L.P.W., Gansau, J.A., How, S.E., 2021. Review of Nephelium lappaceum and Nephelium ramboutan-ake: a high potential supplement. Molecules 26, 7005.

Vidinamo, F., Fawzia, S., Karim, M.A., 2020. Effect of drying methods and storage with agro-ecological conditions on phytochemicals and antioxidant activity of fruits: a review. Crit. Rev. Food Sci. Nutr. 62, 353–361.

Xiao, J., Liu, B., Zhuang, Y., 2019. Effects of rambutan (Nephelium lappaceum) peel phenolics and Leu-Ser-Gly-Tyr-Gly-Pro on hairless mice skin photoaging induced by ultraviolet irradiation. Food Chem. Toxicol. 129, 30–37.

Yun, D., Qin, Y., Zhang, J., Zhang, M., Qian, C., Liu, J., 2021. Development of chitosan films incorporated with rambutan (Nephelium lappaceum L.) peel extract and their application in pork preservation. Int. J. Biol. Macromol. 189, 900–909.

Yuvakumar, R., Suresh, J., Saravanakumar, B., Joseph Nathanael, A., Sun Ig, H., Rajendran, V., 2015. Rambutan peel promoted biomimetic synthesis of biospired zinc oxide nanochains for biomedical applications. Spectrochim. Acta Mol. Biomol. Spectrosc. 137, 250–258.

Zhang, Y., Ma, Q., Guo, Y., Sun, L., 2017a. Protective effects of rambutan (Nephelium lappaceum) peel phenolics on H2O2-induced oxidative damages in HepG2 cells and galactose-induced aging mice. Food Chem. Toxicol. 108, 554–562.

Zhang, Y., Ma, Q., Guo, Y., Sun, L., 2017b. Purification and identification of rambutan (Nephelium lappaceum) peel phenolics with evaluation of antioxidant and antiglycation activities in vitro. Int. J. Food Sci. Technol. 52 (8), 1810–1819.

Zhang, Y., Ruan, S., Yao, H., Sun, Y., 2019. Physical properties of composite films from tilapia skin collagen with pachyrhizus starch and rambutan peel phenolics. Mar. Drugs 17 (13), 662.

Zhang, Y., Sun, X., Liu, B., Hou, H., Sun, Y., 2020. Effects of rambutan peel (Nephelium lappaceum) phenolic extract on RANKL-induced differentiation of RAW264.7 cells into osteoclasts and retinoic acid-induced osteoporosis in rats. Nutrients 12 (4), 883.