Trends in Food Science & Technology 85 (2019) 201–210

Contents lists available at ScienceDirect

Trends in Food Science & Technology

journal homepage: www.elsevier.com/locate/tifs

Review

Rambutan(*Nephelium lappaceum* L.):Nutritional and functional properties

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ARTICLE INFO

Keywords:
Nephelium lappaceum L.
Biological properties
Nutritional
Anti-nutritional aspects
Bioactive compounds

ABSTRACT

Background: The rambutan (*Nephelium lappaceum* L) is an exotic fruit native to the Southeast Asia and currently cultivated in different tropical areas, among them in southern México. It is characterized by its nutritionals and functionals properties and has been relevant for its commercialization and acceptance in different countries and Mexico represents one of the main producers and exporter of rambutan in the world.

Scope and approach: In this review, we summarize information about of the bioactive compounds present in the rambutan fruit, together with the nutritionals properties that it presents as a functional food, with a focus on its by-products (pulp, seed and peel). The rambutan fruit contains important bioactive compounds, mainly the peel has a high content of antioxidants which are of interest in the food, cosmetic and pharmaceutical industries.

Key findings and conclusions: Extracts of rambutan fruit, mainly from the peel, have been shown to possess phytochemical compounds that exhibit antioxidant, antimicrobial, antidiabetic, antiviral, anti-inflammatory, anti-hypoglycemic and anti-proliferative effects in various *in vitro* and *in vivo* tests. However, it is necessary to further analyze the nutritional and functional potential of this fruit, the therapeutic mechanisms involved and to develop its industrial process as a functional or nutraceutical food product.

1. Introduction

The rambutan (*Nephelium lappaceum* L.) is a tropical fruit that belongs to the Sapindaceae family; it is a fruit, originally from Malaysia, whose name is derived from the Malay word ¨*Rambut*¨, meaning ¨*Hair*¨, concerning the soft thorns that cover the fruit surface. Rambutan fruit is ovoid with a red (or yellow) pericarp. It is covered with soft thorns varying in color from yellow to red or green (Akhtar, Ismail, & Shaari, 2017; Arenas et al., 2010; Li, Zeng, & Shao, 2018). The tree is of medium height with evergreen leaves that grow from 12 to 20 m. Its leaves measure 5–15 cm wide and 10–30 cm long. The fruit is 3–6 cm long and 3–4 cm wide. The seed is bright brown and measures 2–3 cm long (Suganthi & Marry Josephine, 2016).

Currently, the rambutan fruit is grown in Malaysia, Thailand, Indonesia, and India; in the Americas, production is centered in the countries of the humid tropics: Colombia, Ecuador, Honduras, Costa Rica, Trinidad and Tobago, Cuba and Mexico (Castillo-Vera, López-Guillén, & Sandoval-Esquivez, 2017). The rambutan varieties originating from Malaysia and Indonesia were introduced into Mexico during the 1950s. In the state of Chiapas, many varieties were introduced, but they have been cultivated with the passage of time into varieties such as R-104, RI-133, RI-148, RI-115, R-134, R-161, R-170, R-3, R-156, R-160, and R-162 (Caballero-Pérez et al., 2011; Fraire, 2001, p. 41; Núñez, 2006). In Mexico, rambutan plantations have been established in other states such as Oaxaca, Tabasco, Guerrero, Colima, San Luis Potosí, Nayarit and Michoacán, with vegetal materials obtained from the Soconusco region of Chiapas (Arenas, 2010).

In Mexico, the rambutan was reproduced by seeds with good genetic selections, obtaining excellent production and quality for marketing (Peréz & Pohlan, 2004). Given its acceptance in the regional and national markets, the rambutan is an economic option for the diversification of fruit crops in Chiapas, México, mainly in the coffee growing areas located at altitudes between 100 and 1000 m above sea level, with average temperatures of 28 °C, precipitation of 4000 mm and 75% relative humidity during spring and summer (Fraire, 1999, p. 34). The growing interest in this crop has caused an increase in new plantations in the area of Soconusco in the state of Chiapas (Joo-Pérez et al., 2017). The national production in Mexico of this exotic fruit is concentrated in six municipalities of the state of Chiapas: Cacahoatán, Tapachula, Frontera Hidalgo, Metapa de Domínguez, Huehuetán, and Tuzantán;

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https://doi.org/10.1016/j.tifs.2019.01.018
Received 25 September 2018; Received in revised form 29 November 2018; Accepted 22 January 2019
Available online 29 January 2019
0924-2244/

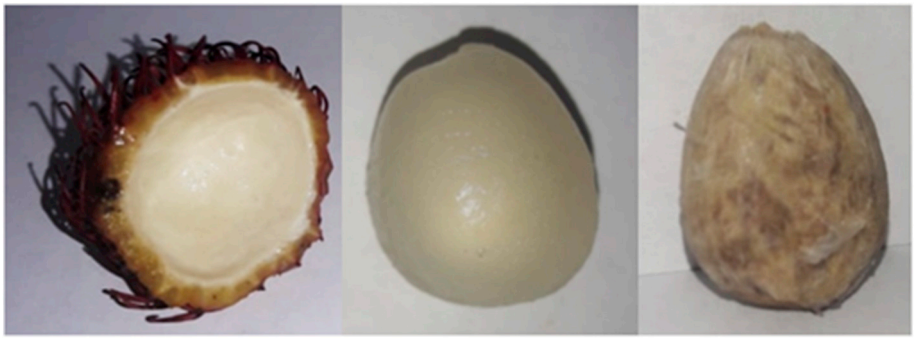

Fig. 1. Rambutan: (a) Peel (b) pulp (c) seed.

Table 1
Weight and percentage of the constituent portions proposed by Solís-Fuentes et al., 2010 in rambutanfruit.

Fruit Portion	Weight (g)	%
Whole Fruit	27.4 (± 2.2)	100
Peel	13.2 (± 1.8)	45.7 (± 3.2)
Pulp	11.7 (± 0.6)	44.8 (± 2.5)
Seed	2.53 (± 0.22)	9.5 (± 0.7)
Embryo	1.60 (± 0.21)	6.1 (± 0.6)

although production levels are estimated as a sown area of 835.96 ha with a production of 8730.27 tons valued at 1 million dollars, there exist backyard plantations and unregistered commercial orchards that could increase the official records. For export, the rambutan must weigh a minimum of 30 g and demonstrate a sweetness of 18% in the Brix degree scale; however, the rambutan of Chiapas reach 22° Brix, making them superior in terms of sweetness (Avendaño-Arrazate, Moreno-Pérez, Martínez- Damián, Cruz-Alvarez, & Vargas-Madríz, 2018; SAGARPA 2016).

The rambutan is constituted by the following parts: 27.4% total weight, 13.2% peel, 11.7% pulp, 2.53% seed and 1.60% embryo, as shown in Fig. 1 (Solís-Fuentes, Camey-Ortíz, Hernández-Medel, Pérez-Mendoza, & Durán-de-Bazúa, 2010). Additionally, it is appreciated for its refreshing flavor and exotic appearance (Ong et al., 1998). This fruit is consumed in the following forms: fresh, processed, stuffed with a piece of pineapple and canned in syrup (Sirisompong, Jirapakkul, & Klinkesorn, 2011). Additionally, in countries such as Malaysia and Thailand, juices, jellies and jams are obtained from this fruit (Morton, 1987). In Mexico, it is consumed in liquor, canned, as juice and in chocolate form—based on the seeds.

However, these processed forms produce a significant amount of peel and seed waste; for this reason, it is crucial tore use these wastes in industrial applications (Santana-Méridas, González-Coloma, & Sánchez-Vioque, 2012).

In this present review, we analyze and discuss the benefits of this fruit in terms of its nutritional composition and its functional properties, including an appreciation of the byproducts of rambutan. The studies carried out with this fruit, in which they have been considered of high added value, have estimated the recovery reach of these by-products and their potential use in the area of health for advances in medicine, food, cosmetics and pharmaceuticals due to their richness of bioactive compounds. Therefore, the use of rambutan fruit in future industrial foods, pharmaceuticals, and cosmetic applications can be considered.

1.1. Taxonomy

Scientific classification of *Nephelium lappaceum* L. taken from Sukmandari, Dash, Jusof, & Hanafi, 2017

Kingdom: Plantae
Subkingdom: Tracheobionta
Super Division: Spermatophyta
Division: Magnoliophyta
Class: Magnoliopsida
Subclass: Rosidae
Order: Sapindales
Family: Sapindaceae.
Genus: *Nephelium* L.
Species: *Nephelium lappaceum* L.

2. Nutritional properties

Rambutan fruit has a weight average formed by all of its parts (pulp, peel, and seed) (Solís-Fuentes et al., 2010), and the percentages by weight of each part of this fruit (*Nephelium lappaceum* L.*)* are presented in Table 1.

2.1. Seed

Several studies have been carried out on the physicochemical properties of the rambutan seed, which has an average weight of 6.1% of the entire fruit. It was determined by a proximal analysis of rambutan seed that, on average, the seeds consist of 34.4% humidity content, 1.2% ash, 7.8% protein, 11.6% crude fiber, 46% carbohydrates, and 33.4% fat on a dry basis. All these values were obtained under chemical analysis of the rambutan seed, where the samples were dehydrated and evaluated following the official techniques of analysis (Horwitzs, 1995). Additionally, it was determined that the main fatty acids in an average rambutan seed are 40.3% oleic, 34.5% arachidonic, 6.1% palmitic, 7.1% stearic, 6.3% gondoic, 2.9% behenic, and 1.5% palmitoleic, among 50.7% saturated fatty acids and 48.1% monounsaturated fatty acids. The fat from rambutan seed (FRS) was extracted using a Soxhlet apparatus and hexane, which was previously purified by distillation. Finally, in this study, all of the following were determined: fat refraction index (1.468 at 40 °C), saponification index (186 mg KOH/g fat), acidity index (3.95 mg KOH/g fat) and iodine index (47.0 cg I/g fat) with the Kaufman method (Solís-Fuentes et al., 2010). Serida et al. (2012) reported the physicochemical and nutrient properties of the remaining 38.9% content of rambutan seed oil and performed a proximal analysis to determine the content of proteins (12.4%), carbohydrates (48%), ash (2.26%) and moisture (3.31%). The chemical properties of the seed oil were also analyzed, obtaining free fatty acids (0.37%), iodine value (37.64%) and the saponification value (157.07%). The main fatty acids in rambutan seed oil were oleic acid (40.45%) and arachidonic acid (36.36%). The values obtained from the physicochemical analysis of rambutan seed oil were according to the Association of Official Analytical Chemists. The percentages of free fatty acids (FFAs) were calculated using lauric acid as a factor. The iodine and saponification values were determined with AOAC Official Methods 993.20,1997 and 920,160,1999. The nutrient composition of

rambutan was analyzed for protein with the micro Kjedahl method, and moisture content, total ash and fat were determined by the methods of the AOAC (1990); carbohydrates were analyzed with the method of Pearson (1976). Another study conducted by Chai, Adzahan, Karim, Rukayadi, and Ghazali (2019a) used rambutan seed to produce a powder very similar to cocoa and analyzed the physicochemical properties of the rambutan seeds of different roasting and fermentation conditions; in addition to a cytotoxicity study, as a result, it was found that rambutan seed powder contains volatile compounds and colors very similar to cocoa powder. Meanwhile, the toxicity assay (brine shrimp lethality) proved not to be toxic. The contents of crude fat in roasted seeds were low in comparison to the control (without roasting). The fatty acid composition of roasted rambutan seed fat revealed that oleic acid (38.21–41.66%) and linoleic acid (27.06–31.62%) were the main fatty acids. In addition, they reported the triacylglycerol profile (TAG) of rambutan seed powder fat where no significant differences of TAG profile were found in any roasting condition. The study of raw fat was determined using the official method (AOAC, 1984). To determine the composition of fatty acids, the method of Cocks and van Rede (1966) was used, and the TAG profile was determined with high-performance liquid chromatography (HPLC).

Rambutan seeds can be used as an alternative for future food industry applications due to their high content of nutritional compounds such as carbohydrates, proteins, mucilage, and oil, among others. Therefore, this utilization can avail the wastes of this fruit for various applications (Mahmood, Fazilah, Yang, Sulaiman, & Kamilah, 2018a).

Below, some reports on the proximal analysis of rambutan seed (*Nephelium lappaceum* L.) are shown in Table 2.

2.2. Pulp

The pulp of rambutan is consumed fresh, and water is the largest component of the fruit (Fraire, 2001, p. 41). Watson (1984) determined the chemical composition of the rambutan fruit on the basis of 100 g pulp: water content (83 g), caloric value (63 cal), proteins (0.8 g), carbohydrates (14.5 g), calcium (25 mg), vitamin C (20–45 mg) and iron (3 mg).

Additionally, the determined nutrients of rambutan pulp are reported in Table 3, where N was the most abundant macronutrient in the fruit (77–87 mg), followed by K (63–81 mg), Ca (22–31 mg), P (11–13 mg), Mg (9–13 mg) and S (4–6 mg). The most abundant micronutrient in the fruit was Mn (0.26–0.38 mg), followed by Fe (0.16–0.23 mg), B (0.12–0.16 mg), Zn (0.09–0.11 mg) and Cu (0.08–0.10 mg) (Vargas, 2003).

The fat content in the pulp is lower compared to the rambutan seed (Issara, Zzaman, & Yang, 2014). Fila, Itam, and Johnson (2013) determined the proximal composition of fresh rambutan (*Nephelium lappaceum*) based on (g/100 g), with a humidity content of (78.46), ash (0.60), crude protein (0.66), crude fiber (0.38), fat (0.24), CHO (19.66), and caloric value (83.44 K/Cals).

Table 2
Proximal analysis proposed by Wahini et al. (2018) in rambutan seed.

No.	Composition of Rambutan nutritional substances	%
1	Ash content	1.70
2	Water	14.20
3	Carbohydrate	64.19
4	Lipid	6.01
5	Protein	11.38
6	Fiber	2.51
7	Vitamin B	0.33
8	Mineral (Ca—Fe—P)	62.50

2.3. Peel

The mineral content of the rambutan peel was determined and reported by Hernández et al. (2017) as Cu (0.070), Mn (0.14), Fe (0.29), Zn (0.080), Mg (0.15), K (0.57), Na (0.04), and Ca (0.51); the composition of rambutan peel was obtained in mg/L dry rambutan peel.

The rambutan peel also exhibits a chemical composition of fiber as cellulose, hemicellulose, and lignin; reported values included cellulose content of 24.28 ± 2.30 (% w/w), hemicellulose at 11.62 ± 2.31(% w/w) and lignin at 35.34 ± 2.05 (% w/w) (Oliveira, Santos, Paula, Gonçalves, & José, 2016).

Furthermore, it has been reported that rambutan peel has a high content of phenolic compounds and antioxidant activity (Okonogi, Duangrat, Anuchpreeda, Tachakittirungrod, & Chowwanapoonpohn, 2007; Palanisamy et al., 2008). Therefore, it has been shown that it is a potential source of antioxidants for food products, cosmetics, and pharmaceuticals due to its antioxidant activity content and nontoxic capacity for normal cells (Palanisamy et al., 2008).

Compared to rambutan seed extracts, the peel contains a greater amount of antioxidant compounds; these are mainly polyphenolic compounds known for their biological activities and include geraniin, corilagin, and ellagic acid, a group of ellagitannins that are present in the rambutan peel, and among them the major compound is geraniin. Some reports on the identification of bioactive compounds are listed in Table 4 (Akhtar et al., 2017; Thitilertdecha, Teerawutgulrag, & Rakariyatham, 2008; Yoswathana & Eshtiaghi, 2013). Thitilertdecha, Teerawutgulrag, Kilburn, and Rakariyatham (2010) reported that these compounds may be obtained by a methanolic extraction method, while Hernández et al. (2017) performed extractions with ethanol and reported that rambutan peel contained the same compounds: geraniin, corilagin and ellagic acid.

On the other hand, it should be noted that the content of polyphenols in the peel depends on cultivation and fruit stage development (Kondo, Tsuda, Muto, & Ueda, 2002; Škerget et al., 2005). However, some factors have been studied such as type of solvent, pH, temperature, solvent-to-solid ratio, particle size and extraction technique, which contribute to the efficacy of polyphenol extraction (Herrero, Cifuentes, & Ibañez, 2006; Kronholm, Hartonen, & Riekkola, 2007).

Geraniin belongs to the ellagitannins, which are a group of hydrolyzable tannins that hydrolyze to form corilagin and gallic acid (Okuda, Yoshida, & Hatano, 1995). It has been shown that geraniin, together with its hydrolyzed products, possesses a variety of biological properties, including antioxidant, antimicrobial, anti-inflammatory, anti-hyperglycemic, antidiarrheal, anesthetic and anticarcinogenic activities (Cheng, Ton, & Kadir, 2016). Therefore, it has been suggested that rambutan peel is a promising source of natural antioxidants for the food, cosmetic and pharmaceutical industries.

3. Biological properties in seed

3.1. Antioxidant activity

The antioxidant activity has also been analyzed in rambutan seed. Luma, Tajul, and Fered Saadoon (2015) reported the phenolic compound content in rambutan seed extract, obtaining a value of 40.49 ± 0.01 mg of GA/100 g total polyphenols in rambutan seed extract. Then, a mixture of cocoa butter and rambutan seed extract was made in which antioxidant activity DPPH (diphenyl-1-picrylhydrazyl scavenging) was measured with a value of 60.16 ± 0.23 μmol trolox/100 g fat. The study recommends up to 40% of rambutan seed fat as a substitute for cocoa butter. Fidrianny, Fikayuniar, and Insanu (2015) also reported the antioxidant activity of four varieties of rambutan, Lebakbulus, Rajah, Rapiah, and Binjai, through the DPPH and ABTS (2,2′-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid)) assays, and the ethanol and ethyl acetate extract from the four varieties showed high antioxidant potentials. Thitilertdecha et al. (2008) evaluated the

Table 3
Content of minerals in rambutan pulp.

Minerals in Rambutan pulp (mg) in dry base						
Macronutrients	**N**	**K**	**Ca**	**P**	**Mg**	**S**
	77–87	63–81	22–31	11–13	9–13	4–6
Micronutrients	**Mn**	**Fe**	**B**	**Zn**	**Cu**	
	0.26–0.38	0.16–0.23	0.12–0.16	0.09–0.11	0.08–0.10	

antioxidant activity of rambutan seed and peel extracts through FRAP (ferric reducing antioxidant power), free radical removal, linoleic peroxidation and β-carotene bleaching tests. The peel extracts exhibited a higher antioxidant activity compared to the seed extracts in all of the tested assays ($P < 0.05$). Chunglok, Utaipan, Somchit, Lertcanawanichakul, and Sudjaroen (2014) reported the antioxidant capacity of rambutan seed extracts by dry weight (DW) using the ABTS and DPPH assays (Trolox equivalent antioxidant), and the results obtained were 172.09 ± 9.28 mg/g DW and 383.38 ± 10.03 mg/g DW, respectively.

3.2. Antibacterial activity

The antibacterial activity of the aqueous extracts of *Litchi chinensis* and *Nephelium lappaceum* seeds was determined. Both aqueous extracts exhibited moderate inhibition against pathogenic, Gram-positive strains such as *Staphylococcus aureus, Streptococcus pyogenes* and *Bacillus subtilis* and Gram-negative strains such as *Escherichia coli* and *Pseudomonas aeruginosa*. The highest inhibitory activity was that of *Litchi chinensis* (15 ± 0.55 mm) against *S. pyogenes* (Bhat & Al-daihan, 2014). Rajasekaran et al., 2012 studied the methanolic extract of rambutan seed (raw, boiled and roasted). The antibacterial activity was tested against two pathogenic strains, Gram-positive and Gram-negative, with the plaque diffusion assay and underwent a test of minimum inhibitory concentration (MIC); the results reported that *Staphylococcus epidermidis* was the most sensitive strain to methanolic extracts from raw and boiled seed (MIC 40 mg/mL).

3.3. Antidiabetic activity

Soeng, Evacuasiany, Widowati, and Fauziah (2015) reported that rambutan seed extract exhibited a high content of α-glucosidase inhibitory activity, with an IC_{50} value of 9.92 μg/mL relevant to hypoglycemic activity. Additionally, it was shown that the rambutan seed extract and the hexane fraction have an inhibitory potential against G6PDH and α-glucosidase as well as the TG level in 3T3-L1 cell lines at a dose of 50 μg/mL. Another study, based on a rambutan seed infusion, had an effect in reducing the blood glucose level and the body weight of mice induced with alloxan tetrahydrate. This infusion was administered to mice with a dose of 3.12 g/kg.bw of infusion of rambutan seed (Rahayu, Zakir, & Keban, 2013). Additionally, the antidiabetic potential of rambutan seed powder (peeled and unpeeled) was determined using the *in vitro* mechanism of yeast glucose uptake (*Saccharomyces cerevisiae*). The rambutan seed powder was shown to improve glucose uptake at a concentration of 25 mg/mL (Cruz, Rao Avupati, & Azizullah, 2017).

3.4. Antiproliferative activity

Chunglok et al. (2014) reported the antiproliferative activity of methanolic extracts from the seeds and peels of three tropical fruits: rambutan (*Nephelium lappaceum* L.), litchi (*Litchi Chinensis Sonn.*) and tamarind (*Tamarindus indica* L.). The antiproliferative activity was studied in human mouth carcinoma cells (CLS-354). The MTT reduction assay and Annexin V-FITC/PI staining were carried out for cytotoxicity and induction of apoptosis, but the rambutan seed extract did not exhibit toxicity to human carcinoma cells (CLS- 354) or PBMC.

3.5. Anti-inflammatory activity

One study demonstrated the analgesic and anti-inflammatory activity of methanol extract from rambutan seeds. The extract exhibited high analgesic and anti-inflammatory activities of 51.27% and 58.86% (Morshed, Dash, Ripa, Foyzun, & Mohd, 2014). Additionally, the anti-nociceptive activity of methanolic extracts from raw, boiled and roasted seeds was studied using the Eddy hot plate method. The results showed that the anti-nociceptive activity exhibited by crude methanol seed extract was superior to that of boiled methanol seed extracts. The extracts of roasted methanol seed showed no activity (Rajasekaran et al., 2012).

Table 4
Identification of the main phytochemicals compounds present in rambutan peel.

ID	Compounds	Molecular Weight (g/mol)	Group	References
1	Corilagin	634	**Ellagitannin**	(Thirtiledecha et al., 2010; Hernádez et al., 2017; Zhuang, Y. et al., 2017; Méndez et al., 2017)
2	Ellagic acid	302		(Thirtiledecha et al., 2010; Hernádez et al., 2017 Zhuang, Y. et al., 2017; Méndez-Floreset al.,2017; Sun, Zhang, & Zhuang, 2012.)
3	Geraniin	952		(Palanisamy, Ling, Manaharan, & Appleton, 2011; Hernádez et al., 2017; Zhuang, Y. et al., 2017; Perera, Appleton, Hwee, Elendran, & Palanisamy, 2012; Thirtiledecha et al., 2010; Méndez-Flores, Hernández-Almaza, Sáenz-Galindo, & Ascacio-Valdes, 2017; Palanisamy et al., 2011)
4	Ellagic acid pentoside	433		Hernádez et al. (2017)
5	Brevifolin carboxylic acid	291		Hernádez et al. (2017)
6	Catechin	289	**Flavonoids**	(Zhuang, Y. et al., 2017; Sun et al., 2012.)
7	Rutin	609		(Zhuang, Y. et al., 2017; Sun et al., 2012.)
8	Apigenin	269		Hernádez et al. (2017)
9	Protocatechuic acid	153	**Hydroxybenzoic acid**	(Zhuang, Y. et al., 2017; Sun et al., 2012.)
10	Syringic acid	197		(Zhuang, Y. et al., 2017; Sun et al., 2012.)
11	Caffeic acid	180	**Hydroxycinnamic acid**	Sun et al. (2012)
12	Chlorogenic acid	354		Sun et al. (2012)

3.6. Antiviral activity

The inhibition activity of reverse transcriptase with rambutan seed was evaluated using 22.5 kDa trypsin reverse transcriptase inhibitors with trypsin inhibitory activity and α-chymotrypsin. The rambutan seed showed good medicinal potential; furthermore, the inhibition activity of HIV-1 reverse transcriptase was evaluated. The results exhibited a successful inhibition of the reverse transcriptase, obtaining an IC_{50} of 0.73 μM (Fang & Ng, 2015).

4. Biological properties in pulp

4.1. Antioxidant and anti-inflammatory activity

The antioxidant activity of the rambutan pulp extract was evaluated by Chingsuwanrote, Muangnoi, Parengam, and Tuntipopipat (2016) with the DPPH assay, in which a relatively low result was observed. Additionally, Palanisamy et al. (2008) noted that rambutan pulp extract showed weak antioxidant activity with the ABTS and DPPH assays compared to those obtained from the peel.

The anti-inflammatory activity was determined with ethanolic extracts of the pulp of two varieties of rambutan, Rongrien and Sichompu (Chingsuwanrote et al., 2016). The ethanolic extract of both varieties inhibited the secretion of TNF-α, but not IL-8, due to the antioxidant activity of the active compounds present in all parts of the rambutan fruit.

5. Biological properties in peel

5.1. Antioxidant activity

The antioxidant activity is considered very important because it plays a crucial role in mediating free radicals and reactive oxygen species (ROS), which are considered harmful to human health (Croft, 1999; Halliwell, 1996). Therefore, several studies on rambutan peel have been reported as a potential source of antioxidants.

Thitilertdecha et al. (2010) reported that the antioxidant activity of methanolic extract of *N. lappaceum* peel was greater than the BHT (butylated hydroxytoluene) and that the lipid peroxidation activity (77–186 times) and DPPH (42–87 times) results were greater than the BHT control; it is worth mentioning that the DPPH and ABTS assays were expressed as IC_{50} (g/ml) values of the methanolic extracts of rambutan peel. Another study conducted by Palanisamy et al. (2008) showed a high phenolic content in rambutan peel, low pro-oxidant capacity, and a strong antioxidant activity. Mistriyani, Riyanto, and Rohman (2018) reported the study of two varieties of rambutan (Aceh and Binjai) extractions made by maceration using methanol as a solvent; the fractions were obtained by using petroleum ether, chloroform and ethyl acetate, wherein the ethyl acetate fraction exhibited the highest anti-radical activity as shown by using ABTS, with IC_{50} values of 3.10 μg/mL and 0.77 μg/mL for Aceh and Binjai, respectively; the FRAP assay also revealed that the fraction of ethyl acetate had the highest values of 1424.897 ± 28.56 μg/mg. A similar work realized by Rohman, Riyanto, Mistriyani, and Endro Nugr (2016) with methanolic extracts using the same Binjai variety cultivar of rambutan as in Mistriyani et al. (2018) revealed high antioxidant activities. The fraction of ethyl acetate showed stronger antioxidant activity among the samples evaluated, with IC_{50} values of 2.66 μg/mL (cultivar: Aceh) and 2.62 μg/mL (cultivar: Binjai). The ethyl acetate fraction also showed high contents of phenolic and flavonoid compounds of 37.72 ± 4.52 g of gallic acid equivalent (GAE)/100 (Aceh) and 32.40 ± 2.37 g of GAE/100 g (Binjai).

Additionally, anthocyanins were extracted from rambutan peel with 80% ethanol and 1% acetic acid. The extracts were purified, and the total content of anthocyanin was evaluated, obtaining 181.3 mg/100 g. The extracts were stable under low pH conditions (1 and 3), but the anthocyanin extracts were shown to degrade at a higher temperature. In addition, isolated anthocyanins showed antioxidant activity for FRAP, lipid peroxidation, and DPPH assays (Sun et al., 2011).

The antioxidant activity of rambutan peel and seed was exhibited using the DPPH assay (Manaf, Bakar, Khalili, & Kabiru, 2016). The rambutan peel showed higher yields of 29.97 ± 2.69 and 22.1 ± 1.89% with respect to the seed for the aqueous and ethanol extracts, respectively. However, the DPPH assay for the ethanolic and aqueous extracts showed a higher antioxidant activity in rambutan peel than the seed, obtaining 95.73% ± 1.63 and 80.25 ± 3.15% with IC_{50}values of 24.99 ± 2.82 μg and 144.59 ± 1.36 μg, respectively. Hernández et al. (2017) determined ABTS (38.24 mg/mL) and FRAP (0.203 GAE/mL). The antioxidant activity was also evaluated with ethanolic extracts of several selected tropical fruits: rambutan, banana, mangosteen, and longan; the rambutan peel extract showed the highest antioxidant activity (77.21 ± 0.17%) compared to longan (73.24 ± 0.11%), mangosteen (46.97 ± 0.29%) and banana (41.65 ± 0.22%) (Nor Helya, Lau Sin, & Rubiatul Adawiah, 2016).

5.2. Antibacterial activity

Studies have been carried out on the use of extracts of fruit wastes as natural antimicrobial agents, and the fruit of rambutan is no exception; however, most of its antimicrobial potential lies within the peel. Thitilertdecha et al. (2008) performed a study with extracts of rambutan peel and seed, evaluating eight strains of pathogenic bacteria: *Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Salmonella typhi, Vibrio cholerae, Enterococcus faecalis, Staphylococcus aureus* and *Staphylococcus epidermidis*. The extracts of rambutan peel showed a higher antibacterial activity compared to the seed against the strains *Pseudomonas aeruginosa, Vibrio cholerae*, *Enterococcus faecalis*, *Staphylococcus aureus* and *Staphylococcus epidermidis*, but no antibacterial activity was found against *E. coli*, *K. pneumoniae*, and *S. Typhi*.

Therefore, another study showed that rambutan peel extracts have a maximum antimicrobial activity against *P. aeruginosa* (7.2 ± 0.1 mm) and a minimal activity against *C. tetani* (3.6 ± 0.1 mm), as reported by Malini and Maheshkumar (2013). Two varieties of red and yellow rambutan peel were also compared, and the methanolic extract of the yellow rambutan peels showed more activity than the red rambutan peels against *Streptococcus pyogenes* and *Staphylococcus aureus* by obtaining an inhibition zone of 7–10 mm and 5–12 mm, respectively, in different concentrations. However, both extracts showed no inhibition against *Escherichia coli* and *Pseudomonas aeruginosa* (Sekar et al., 2014). Similarly, Tadtong et al. (2011) exhibited the antimicrobial activities of rambutan peel extract (*Nephelium lappaceum* L.), obtaining antibacterial activity against *Staphylococcus aureus* ATCC6538, methicillin-resistant *Staphylococcus aureus* (MRSA) DMST20645 and *Streptococcus mutans* ATCC25175T, but no antibacterial activity was found against Gram-negative strains *Escherichia coli* ATCC25922 and *Candida albicans* ATCC10231. The minimum inhibitory concentration (MIC) against *S. aureus* ATCC6538 and MRSA DMST20645 was 2 and 0.4 mg/mL, respectively, which coincides with Thitilertdecha et al. (2008) and Sekar et al. (2014), who found no antimicrobial activity against Gram-negative strains of *E. coli, K. pneumoniae, Pseudomonas aeruginosa, Candida albicans* and *S. typhi*.

The use of rambutan peel extract as starting materials for the synthesis of AgNP using aqueous medium at room temperature has also been studied. An analysis of UV–Visible spectrum showed the formation of AgNP, and a scanning electron microscope-energy-dispersive X-ray (SEM-EDS) was used to demonstrate that the AgNP was synthesized in a uniform manner with wide particle size distribution. The synthesized AgNPs showed antibacterial activity against *Salmonella paratyphi* with 50 μL of AgNP (Lestari, 2018).

5.3. Antidiabetic activity

Recently, many investigations have been conducted for possible

applications of the rambutan peel. Lestari, Djati, Rudijanto, and Fatchiyah (2014a) and Lestari et al. (2014b) reported that rambutan peel extract is a promising herbal medicine against obesity. Therefore, several studies have shown that the rambutan peel extract has antidiabetic activity.

Ma, Guo, Sun, and Zhuang (2017) evaluated the antidiabetic activity in a mouse model of type 2 diabetes. This work showed that rambutan peel extract increased body weight and reduced fasting blood glucose levels, serum levels of total cholesterol, triglycerides, creatinine and glycosylated serum protein in diabetic mice in a dose-dependent fashion. The glycogen content in the mouse liver was recovered with the rambutan peel extract, which further increased the activity of superoxide dismutase, glutathione peroxidase and reduced lipid peroxidation in diabetic mice. Furthermore, histological analysis showed that rambutan peel extract effectively protected the tissue structure of the liver, kidney, and pancreas. Additionally, it decreased the mesangial index and inhibited the expression of TGF-β in the kidneys of diabetic mice.

A study was performed by Muhtadi, Haryoto, Sujono, and Suhendi (2016) with rambutan (*Nephelium lappaceum* L.) and durian (*Durio zibethinus Murr.*) peel extracts in diabetic rats receiving doses of 500, 250 and 125 mg/kg.bw for 11 days. The highest percentage reduction in blood glucose levels, 61.76 ± 4.26%, was shown by rambutan peel extract at a dose of 500 mg/kg.bw; the activity change was higher than that of the positive control and of durian peel extract at a dose of 500 mg/kg.bw, which reduced glucose levels by 50.19 ± 3.66%. The rambutan and durian peel extracts showed antidiabetic activities at doses from 125 to 500 mg/kg.bw.

The antidiabetic effects of rambutan peel extract were investigated in a diabetic rat model standardized with geraniin. Male Sprague Dawley rats were fed with a high-fat diet and injected with 210 mg kg^{-1} nicotinamide and 55 mg kg^{-1} of streptozotocin to induce type 2 diabetes. The diabetic rats were treated with rambutan peel extract at concentrations of 500 and 2000 mg for 28 days. Positive control rats were treated with 200 mg metformin. The yield from rambutan peel ethanolic extract was 41.1%, while the geraniin present in the extract was quantified as 33.0 ± 0.2 mg geraniin/g extract. The study showed that diabetic rats treated with 2000 mg of rambutan peel had a reduction in blood glucose levels and improved insulin levels similar to the group treated with metformin. The histology of the pancreas showed that the group treated with 2000 mg of rambutan peel had a healthy pancreatic morphology, and the treatment was comparable to the effects observed in the metformin-treated group (Subramaniam, Radhakrishnan, Chakravarthi, Palanisamy, & Haleagrahara, 2015).

5.4. Antiproliferative activity

The antiproliferative activity towards breast cancer cells (MDA-MB-231), cervical cancer cells (HeLa) and osteosarcoma cancer cells (MG-63) was determined in a study with rambutan peel extract. Two varieties of rambutan, yellow and red, were used. The *in vitro* cytotoxicity of the rambutan peel extract was compared to a normal MDCK cell line using the methylene blue test and cisplatin as a positive control. The methanolic extract of yellow rambutan peel exhibited activity against MDA-MB-231 and MG-63 with IC_{50} values of 5.42 ± 1.67 μg/mL and 6.97 ± 1.02 μg/mL, respectively. Both varieties of rambutan showed no antiproliferative activity against HeLa (Khaizil Emylia, Nik Aina, & Mohd Dasuki, 2013). The antiproliferative activity of methanolic extracts of seeds and peels of three tropical fruits, rambutan (*Nephelium lappaceum* L.), litchi (*Litchi Chinensis Sonn.*) and tamarind (*Tamarindus indica* L.) was also evaluated. The MTT reduction assay and Annexin V-FITC/PI staining were conducted for cytotoxicity analysis and induction of apoptosis. Tamarind seed extract showed cytotoxicity for human mouth carcinoma cells (CLS-354), while litchi and rambutan seed and peel had no toxicity to human mouth carcinoma cells (CLS-354) and PBMC (Chunglok et al., 2014). Khonkarn, Okonogi, Ampasavate, and Anuchapreeda (2010) evaluated the antiproliferative activity against the human cell lines KB (human epidermal carcinoma of the mouth with contaminant HeLa) and Caco-2 (human colorectal adenocarcinoma) with extracts of rambutan, mangosteen, and coconut peel. The coconut peel extract showed a cytotoxic effect on the KB cell line by the MTT assay, while rambutan and mangosteen showed no cytotoxic effects for both cells.

5.5. Anti-inflammatory activity

The phenolic compounds present in plants have been studied due to their properties of the elimination of free radicals and protection against cell deterioration, and one of the most important properties of phenolic compounds is anti-inflammatory activity. In studies performed, anti-inflammatory activity has been evaluated in the rambutan peel using RAW 264.7 cells induced by lipopolysaccharides (LPS) and rambutan peel phenolic compounds (RPP) through the expression of the inducible nitric oxide (iNOS) gene, in which concentrations of nitric oxide (NO) secretion were determined; the results showed that the RPP induced at 400 μg/mL of iNOS decreases NO content significantly, inhibiting by 40.2%, besides improving mRNA levels of inducible NO synthase in RAW 264.7 cells induced by LPS (Li, Li, Hou, Zhuang, & Sun, 2018).

The anti-inflammatory activity of two varieties of rambutan, Rongrien and Sichompu, was determined using ethanolic extracts from all parts of the fruit, in which it was demonstrated that both varieties inhibited the secretion of TNF-α but not IL-8 (Chingsuwanrote et al., 2016).

5.6. Antiviral activity

Abdul Ahmad et al. (2017) performed studies with rambutan peel and observed antiviral activity against the type 2 dengue virus (DENV-2), with an IC_{50} of 1.75 μM, by inhibiting the mechanism of viral anchoring. In addition, the studies demonstrated that the compound inhibits viral binding by binding to the E-DIII protein and interfering with the initial cell-virus interaction.

5.7. Anticancer activity

Recent studies have shown evidence demonstrating that reactive oxygen species (ROS) are involved in the development of cancer. However, the role of bioactive compounds represents an important consideration. Yuvakkumar, Suresh, Nathanael, Sundrarajan, and Hong (2014) and Yuvakkumar V. (2015) have shown antimicrobial activity and inhibition of cancer cells using extracts of rambutan peel (Viet, 2017).

Thirteen plants native to Malaysia, including rambutan, were also evaluated. The methanolic and aqueous extracts of rambutan peel showed no cytotoxic effects towards 4T1 cells (mouse breast cancer cells) and 3T3 cells (mouse embryonic fibroblast cells) at doses of 50 and 100 μg/mL (Ling, Radhakrishnan, Subramaniam, Cheng, & Palanisamy, 2010). In another study, *in vitro* activity against human osteosarcoma cancer cells was evaluated with ethanolic extracts of rambutan peel, which showed activity but had no effect on normal cells. However, the extract induced G2/M arrest by inhibiting the progression of the cancerous cell cycle (Hidayat, Ridhwan, & Azman, 2011). Table 5 resume the biological activities of rambutan fruit.

Table 5
Biological activitiesoframbutan fruit.

Bioactivity	Extraction	Part of the fruit	Model	Reference
Antioxidant Activity	Methanolic	Peel	DPPH, Linoleic Peroxidation.	Thitilertdecha et al. (2010)
	Aqueous, ethanolic	Peel	Peroxynitritegenerator 3-morpholinosydnonimine (SIN-1), Peroxyl radical generator 2,2′-azobis (2-amidinopropane) dihydrochloride (AAPH)	Ling, Saito, Palanisamy, Cheng, and Noguchi (2012)
	Ethanolic	Peel	ABTS, DPPH	Palanisamy et al. (2008)
	Methanolic	Peel	ABTS, FRAP	Mistriyani et al. (2018)
	Aqueous, Ethanolic	Peel	DPPH, ABTS	Palanisamy et al. (2011)
	Methanolic	Peel	DPPH	Rohmanet al. (2016)
	Aqueous, Ethanolic	Peel and Seed	DPPH	Manafet al. (2016)
	Ethanolic	Peel	ABTS, FRAP	Hernández et al. (2017)
Antibacterial Activity	Ether, Aqueous, Methanolic	Peel and Seed	*E. coli, K. pneumoniae, P. aeruginosa, S. typhi, V. cholerae, E. faecalis, S. aureus y S. epidermidis*	Thitilertdecha et al. (2008)
	Aqueous	Peel and pulp	*P. aeruginosa, C. Tetani, A. hydrophila,*	Malini and Maheshkumar (2013)
	Methanolic	Peel	*S. pyogenes* y *S. Aureus,E. Coli, P. aeruginosa*	Sekar et al. (2014)
	Methanolic	Peel	*S. aureus* ATCC6538, *S. aureus* DMST20645,*S. mutans* ATCC25175T, *E. coli* ATCC25922 y *C. albicans* ATCC10231	Tadtong et al. (2011)
	Aqueous	Seed	*S. aureus, S. Pyogenes, B. subtillis, E. coli y P. aeruginosa*	Bhat and Al-daihan (2014)
Antidiabetic Activity	Ethanolic, Acetic acid	Peel	Mouse with type 2 diabetes	Ma et al. (2017)
	Ethanolic	Peel	Diabetic rats with intraperitoneal alloxan	Muhtadiet al. (2016)
	Ethanolic	Peel	Diabetic rats	Subramaniamet et al. (2015)
	Ethanolic	Seed	G6PDH and α-glucosidase	Soenget al. (2015)
Antiproliferative Activity	Methanolic	Peel	Breast cancer cells (MDA-MB-231), cervical cancer cells (HeLa), osteosarcoma cancer cells (MG-63).	KhaizilEmyliaet al. (2013)
	Methanolic	Peeland Seed	Human mouth carcinoma cells (CLS-354), PBMC cells.	Chungloket al. (2014)
	Ethanolic	Peel	KB cells, HeLa cells, Caco-2 cells.	Khonkarnet al. (2010)
Anti-inflammatory Activity	Ethanolic	Pulp	TNF-α, IL-6, IL-8, and MCP-1	Chingsuwanroteet al. (2016)
	Ethanolic	Peel	Rats with collagen-induced arthritis (CIA)	(Kumar et al., 2012)
	Methanolic	Seed	Rats induced with acetic acid and formalin	Morshed et al. (2014)
	Methanolic	Seed	Mice induced with morphine sulfate	Rajasekaranet al. (2013)
Antiviral Activity	Ethanolic	Peel	Dengue virus type 2 (DENV-2)	Abdul Ahmad et al. (2017)
	Buffer	Seed	HIV-1 Reverse transcriptase	Fang and Ng (2015)
Anticancer Activity	Methanolic, Aqueous	Peel	4T1 (Mouse breast cancer cells), 3T3 (Mouse embryonic fibroblast cells)	Ling et al. (2010)
	Ethanolic	Peel	Cancer cells of human osteosarcoma	Hidayatet al. (2011)

6. Anti-nutritional aspects of rambutan fruit

The nutritional value and anti-nutritional content have not been given much attention, especially regarding the waste components of fruits, seeds and peels, and it is necessary to evaluate the nutritional and anti-nutritional content. Therefore, anti-nutrient contents in dry and fresh samples were evaluated in the pulp, seed, and peel of rambutan; components such as saponin, alkaloids, hydrocyanic acid, phenols, oxalate, tannins, and phytates were found in all parts of the fruit, although in very insignificant quantities ($P < 0.05$) in the anti-nutrient compounds in the different parts of the fruit, seeds and peel, so that their consumption would not affect the consumer and is recommended for both human and animal diets (Fila et al., 2012).

Chai et al. (2019b) reported the anti-nutritional content of the rambutan seed during fermentation, demonstrating that the content of free fatty acids increased by 4.3 times and the crude fat content of the seed was reduced by 22% after 10 days of fermentation. They also showed that after seven days of rambutan seed fermentation, the arachidonic acid was reduced and replaced by linoleic acid and that only 14.5% of the triacylglycerol remained in the fat of the seed at the end of the fermentation process. Additionally, the content of saponins and tannins showed a reduction after fermentation of 67% and 47%, respectively, in the seed. In addition, the solid fat index at 37 °C in the fermented seed was higher compared to the fat of the unfermented seed.

7. Application and traditional use

For centuries, rambutan (*Nephelium lappaceum* L.) has been used as a traditional medicine in remedies for prevention of diabetes and high blood pressure (Suganthi & Marry Josephine, 2016). Additionally, in Malaysia, the peel of dried rambutan fruit is used for traditional medicine to treat fever, dysentery and diarrhea, upset stomach and as an anthelmintic (Mahmood et al., 2018 b). Rambutan leaves can relieve headache, while the rind can be used as an astringent, and a decoction of roots can relieve fever if consumed normally (Ragasa, de Luna, Cruz, & Rideout, 2005). The fruit also acts as a vermifuge, which helps to expulse intestinal worms (Suganthi & Marry Josephine, 2016). The rind is used as an astringent for tongue diseases (Sukmandari et al., 2017).

The applications for rambutan fruit, such as those for its seeds, are valuable for the industry because of their high content of fats and oils (oleic acid and arachidonic acid), which are used for cooking and soap making. Roots, leaves, and rinds are used for the production of dyes (Suganthi & Marry Josephine, 2016). Various patents are reported in Table 6.

8. Future trends

It has been shown that rambutan exhibits functional properties in all parts of the fruit, whether edible or inedible. It contains diverse beneficial components to human health (Abdul Rohman, 2017). However, more research is needed for the isolation and characterization of the chemical constituents responsible for the therapeutic activities attributed to the fruit, peel, and seed. Likewise, knowledge of physiological or molecular mechanisms involved in the biological and pharmacological activities is essential (Akhtar et al., 2017). In addition, more data are needed on the bioactivity and safety of the extracted compounds to project the real potential of the particular phytochemical compounds.

Table 6
Registers of some patents of rambutan fruit.

Title of the patent	Information about the patent	Part of the fruit	Date of the patent	Country
A kind of rambutan enzyme nutrient solution	The beneficial effects of the present invention are: A kind of rambutan enzyme nutrient solution, which nourishes the blood, enhances immunity and has heat-clearing and detoxification.	Whole fruit	04/20/2018	China
Yellow rice wine of fruit taste and preparation process thereof	The present invention focuses on the yellow rice wine, is a kind of wine prepared from rambutan, StenocalyxMicheli, raspberry, *Physalis peruviana*, and passion fruit.	Pulp	04/13/2018	China
Formula of rambutan and durian beverage	The invention discloses a formula of a rambutan and durian beverage. The formula comprises the following raw materials: rambutan fruit condensed juice, durian condensed juice between other compounds.	Pulp	03/09/2018	China
Extracting method of red pigment in rambutan peel	The present invention obtains a red pigment from the rambutan peel, achieving a relatively high purity of the bio-flavonoid complex while maintaining a good bioactivity.	peel	03/06/2018	China
Cosmetic pack with an effect of restoring skin elasticity	The cosmetic pack of the present invention has effects of adjusting microcirculation of blood capillary of the skin, improve the vigor of face skin cell, and improve the elasticity of the skin, and also has effects of moistening the skin.	Peel	11/07/2017	China
One kind of rambutan jam powder processing method	The present invention of rambutan jam improve the utilization of raw materials, no artificial formula is added, can change rambutan natural flavor, relieves diarrhea and is anti-inflammatory.	Pulp	10/10/2017	China
Brewing method of *Nephelium lappaceum* fruit wine	The present invention establishes a brewing method of *Nephelium lappaceum* fruit wine with a rich in fruity aroma, stable in color, mellow in taste and high in quality.	Pulp	08/18/2017	China
A sandwich lyophilized rambutan ball and preparation method thereof	The present invention discloses a sandwich lyophilized rambutan ball, this product has an effect on nutrition, a good stomach effect, suitable for anemia (physical weakness).	Peel and pulp	07/07/2017	China
A kind of *Nephelium lappaceum* and lychee soybean milk	The present invention promotes appetite, benefits spleen, nourishes brain, strengthens the body, beautifies and nourishes skin with a mixture of *Nephelium lappaceum* and lychee soybean milk.	Pulp	06/09/2017	China
Rambutan peel beer	In the present invention, the beer with rambutan peel allows obtaining a sanitary effect caused by the peel of the rambutan, while drinking beer, at the same time it provides a good deep intestinal processing.	Peel	02/22/2017	China
One kind of rambutan cake and its processing method	The present invention provides a cake of rambutan promotes digestion, stomach strengthening, and other health effects have a simple process, less investment, quick, effective and easy to implement standardized production.	Pulp	01/04/2017	China
One kind of rambutan potato chips and preparation method thereof	The present invention discloses a kind of orang Dan potato chips, maximizes the retention of the large potato itself nutritional ingredients, also has higher nutritional value, delicious fragrance, has an important role in health care.	Pulp	12/21/2016	China
One kind of canned rambutan	The present invention reveals a canned rambutan, has a rich flavor, sweet taste, without irritation, is easy to drink, can promote blood circulation, improves immunity, delays aging and cares for the skin.	Pulp	11/09/2016	China

Additionally, pharmacokinetic evaluations are required to highlight the bioavailability of particular compounds. Likewise, in most *in vitro* studies, the stability of extracted phytochemicals and conditions to maintain the cell culture before the experiment are discarded, and this could limit the results in different ways. However, this does not limit the applications in future research regarding rambutan peels and seeds used as cheaper alternatives to produce multifunctional prebiotics and drugs with minimal or no side effects (Mahmood et al., 2018b). Therefore, in this review, we highlighted the importance of the use of peel and seed waste as byproducts, since they can be used as nutraceuticals and health supplements.

9. Conclusions

The rambutan (*N. lappaceum*) fruit is produced in the southeastern region of México and South Asian countries. Chemical components of this fruit are potential alternative sources of minerals and their functional properties. This fruit has been explored for applications of biological activities because scientific studies have shown the presence of several bioactive compounds in rambutan, including ellagitannins such geraniin, ellagic acid, and corilagin, that are beneficial for human health and have been evaluated through *in vitro* and *in vivo* tests to promote their importance as mediators to counteract cancer, certain viruses, obesity, diabetes, microbial infections, cell oxidation, and inflammation. However, little is known about the mechanism of action and metabolism in clinical trials with humans to valorize their potential source and establish a final use of these compounds in pharmaceutical, cosmetic and food industry applications.

Acknowledgments

This study was funded by the Autonomous University of Coahuila, México. Cristian Hernández received financial support from CONACYT for his MSc studies.

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