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RESEARCH ARTICLE

A Review on *Nephelium lappaceum* L.

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ABSTRACT:

Nephelium lappaceum L. (Family- Sapindaceae), popularly known as 'Rambutan', is an evergreen tree, native to Malaysia but grown in other parts of the world. The plant has been used as traditional medicine for centuries especially as a remedy for diabetes and high blood pressure. Further, the fruits always remained as a potential source of minerals and other nutrients. A thorough literature survey revealed that the plant possesses several biological activities such as antidiabetic, analgesic, antiinflammatory, immunomodulatory, antioxidant, anticancer, antimicrobial and antiviral activities against dengue virus. This paper outlines an updated review on this important plant focusing on the traditional uses, phytochemistry and pharmacological aspects that would assist researchers to search scientific information in the future.

KEYWORDS: *Nephelium lappaceum* L., Traditional uses, Phytochemistry, Bioactivity, Miscellaneous study.

INTRODUCTION:

Plants have always remained as the major source of medication for preventive, curative, or protective purposes since time immemorial[1]. They are included in several traditional systems of medicine including Ayurveda, Siddha, Homoeopathy and Chinese medicines and their history of use is believed to be as old as human civilization. Several plant based medicines have afforded promising bioactive compounds that retained their usefulness in the modern drug therapy.

Nephelium lappaceum L. (Family- Sapindaceae), popularly known as 'Rambutan', is an evergreen tree about 10-12 m tall with grayish brown branches[2-4]. Because of presence of numerous hairy protuberances on the fruit, the word rambutan has been derived from the Malay word '*rambut'* which means "hair".

The tree is native to Malaysia but grown in other parts of the world[5]. The leaves glossy green and compound. Inflorescences many branched, flowers are yellowish-green to white, small sized and occur in large bunches, petalless, with mild sweet scent, dioecious (male and female flowers on separate trees) or bisexual, rich in nectar, attract bees[6].Each flower holds six to eight stamens. The superior ovary possess one to two lobes with a single style. The tree flowers twice a year[6]. Fruits are edible, oval to spherical drupe, leathery skin with flexible hairy spines, mature from green to red. Aril white, fleshy, edible and sweet and surrounds single large seed[5-8].

Despite its long tradition of use, the comprehensive literature review on this plant is still lacking. Thus, in this paper we present an updated review on this important plant focusing on the traditional uses, phytochemistry and pharmacological aspects that would assist researchers to search scientific information in the future.

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

TRADITIONAL USES:
N. lappaceum has been used as traditional medicine for centuries especially as a remedy for diabetes and high blood pressure[9]. The fruit is believed to be stomachic, astringent, anthelmintic and believed to be a good remedy to treat diarrhea and dysentery. The leaves are used in poultices for treating headache[10]. Dried fruit rind is sometimes used as an ingredient in manufacture of soap. The roots, leaves and bark are used in the manufacturing of dyes. In Malaysia, the decoction of the roots are used in while bark is used as an astringent for tongue diseases[11].

PHYTOCHEMISTRY:
Several studies have been conducted for chemical analysis and structural determination of phytoconstituents present in *N. lappaceum*. The major constituent reported is "geraniin" from the rind of *N. lappaceum* which exhibited significant therapeutic activity to safely mitigate obesity induced metabolic dysfunction. Geraniin is also found to be effective against dengue virus type-2 (DENV-2).

Augustin and Chua[12] conducted the proximate analysis of the seeds of three rambutan clones (R4y R7 and R169) and reported that the seeds contain protein (11.9-14.1%), crude fat (37.1-38.9%), crude fibre (2.8-6.6%) and ash (2.6-2.9%). The major fatty acids in the seed fat were also reported. Ong et al[13]isolated and characterized odorous principles in the fruit through GC-MS using ethyl acetate and freon as the solvents and reported 20 most potent odorants, such as β-damascenone, (E)-4,5-epoxy-(E)-2-decenal, vanillin, (E)-2-nonenal, phenylacetic acid, cinnamic acid, ethyl 2-methylbutyrate and delta-decalactone. Based on the calculated odor activity values, β-damascenone, ethyl 2-methylbutyrate, 2,6-nonadienal, (E)-2-nonenal and nonanal were identified to be the major compounds that contribute aroma to the fruits. Ragasaet al[14] reported two diastereomeric monoterpene lactones, butenolidesiphonodin and kaempferol 3-O-beta-D-glucopyranoside-7-O-alpha-L-rhamnopyranoside in the seeds of *N. lappaceum*.

In a study, Thitilertdecha et al[15]reported isolation of ellagic acid, corilagin and geraniin from the peels and reported their antioxidant activities. The results indicated geraniin as the major constituent and exhibited much greater antioxidant activities. Harahap et al[16] reported that the seeds contain fat (38.9%), protein (12.4%) and carbohydrate (48%) respectively. The chemical properties of seed oil were acid value (0.37%), iodine value (37.64%) and saponification value 157.07%. Oleic acid (40.45%) and arachidic acid (36.36%) were the major fatty acids. The seed oil contains arachidoyl-dioleoylglycerol as the major component (49.84%).

Presence ofhederagenin 3-*O*-(3-*O*-acetyl-*β*-D-xylopyranosyl)-(1→3)-*α*-L-arabinopyranoside, together with hederagenin, hederagenin 3-*O*-(4-*O*-acetyl-*α*-L-arabinopyranosyl)-(1→3)-*α*-L-rhamnopyranosyl-(1→2)-*α*-L-arabinopyranoside, hederagenin 3-*O*-*α*-L-arabinopyranosyl-(1→3)-*α*-L-rhamnopyranosyl-(1→2)-*α*-L-arabinopyranoside, hederagenin 3-*O*-*β*-D-glucopyranosyl-(1→3)-*α*-L-rhamnopyranosyl-(1→4)-*β*-D-xylopyranoside are reported from the hull of *N.lappaceum*[17].

Physicochemical properties of seed fat revealed presence of almost equal proportion of saturated (49.1%) and unsaturated (50.9%) fatty acids. Oleic (42.0%) and arachidic (34.3%) acids were found to be the most prevailing fatty acids in the seed fat along with small amounts of palmitic (4.6%), stearic (8.0%), gadoleic (5.9%), behenic (2.1%), linoleic (2.2%), palmitoleic (0.7%), erucic (0.1%) and myristic (0.1%) acids. The study further revealed that the fat was comprised of some unknown triacylglycerols (TAG) with higher carbon numbers. z-Nose analysis revealed presence of good amounts of volatile components[18]. In another study, Lourithet al[19] studied the extractive yields and fatty acid compositions of seed fat under different extraction conditions using n-hexane as the solvent and confirmed presence of oleic and arachidic acids as the major fatty acids (31.08 ± 0.75% and 28.65 ± 0.72%) followed by gondoic, palmitic, stearic, isooleic, behenic, linoleic and palmitoleic acids. The physicochemical properties of the fat such as acid (4.35 ± 0.00 mg KOH/g), iodine (44.17 ± 0.30 g I2/100 g), peroxide (1.00 ± 0.00 g/g), saponification (246.73 ± 0.10 mg KOH/g) and unsaponified (0.10 ± 0.00%) values were reported. The moisture content of the fat was found to be 1.77 ± 0.12% with a melting point of 46.05 ± 0.05°C.

BIOACTIVITY:
Toxicity studies:
N. lappaceum has a long history of human use and considered to be safe with no information of toxicity. The acute toxicity and liver function effects of crude extract from the fruit rind of rambutan in rats revealed no

toxicity at doses up to 5g/kg and there were no clinical signs of abnormality[20]. In another study, the acute and sub-chronic toxicity of the ethanol extract of rambutan rind was assessed in rats. The extract was administered orally at 50, 200, 1000 or 2000 mg/kg as single dose for 14 days. The sub-chronic toxicity studies were performed at 500 and 2000 mg/kg, p. o. of the extract for 28 days. Results of the study revealed no mortality or any sign of adverse effects in rats. There was no difference in relative organ weights and the levels of serum urea, creatinine, *alkaline phosphatase* (ALP), aspartate aminotransferase (AST) and total protein. Histological observations in the liver and kidney revealed normal architecture[21]. Rajasekaran et al[22] reported the acute toxicity of the methanol extract of the seeds (raw, boiled and roasted) and concluded that all three extracts were safe up to 2,500 mg/kg dose. The acute and sub-chronic toxicity studies of the hydroethanolic extract of rambutan rind revealed that LD_{50} was greater than 5000 mg/kg, p.o. In sub-chronic study, no mortality was observed up to 1000 mg/kg/day, p.o. for a period of 30 days but the mortality rate was 12.5% at 2000 mg/kg/day dose. Significant decrease in body weight and food consumption was noticed in both acute and sub-chronic toxicity studies. The level of serum triglycerides remained unchanged in acute toxicity study but showed a significant decrease in the sub-chronic toxicity study. However, plasma levels of AST and ALT remained unchanged in both studies[23].

Antidiabetic activity:

The ethnomedical use of *N. lappaceum* as an antidiabetic plant drug has been validated in several experimental studies. Palanisamyet al[24] reported the antidiabetic activity of the rind extracts. The extracts were effective in inhibiting alpha glucosidase and alpha amylase. In addition, the geraniin-enriched ethanolic extracts inhibited aldol reductase, the key enzyme in the polyol pathway and prevented formation of advanced glycation end-products up to the extent of 43%.

The aqueous extract of the seeds possessed hypoglycaemic activity[25]. In a study, Thinkratoket al[26] reported the α-amylase and α-glucosidase inhibition activities of the ethanol extract of the rambutan rind. The extract showed potent inhibitory effects on both α-amylase and α-glucosidase activities *in vitro* suggesting that rambutan rind is useful in the treatment of type 2 diabetes mellitus.Chung et al[27] isolated geraniin from the rind of *N. lappaceum* through HPLC followed by its evaluation in ameliorating diet-induced metabolic syndrome in rats. A four-week *in vivo* geraniin treatment at 50 mg/kg exhibited significant therapeutic potential to safely mitigate obesity-induced metabolic dysfunction.

Soenget al.[28] reported the antioxidant and hypoglycaemic activities of the ethanol extract of the seeds and its fractions in n-hexane, ethyl acetate, butanol and water. The antioxidant activity was determined by DPPH radical scavenging activity and using superoxide dismutase value. The hypoglycemic activity was estimated by inhibition of α-glucosidase activity. The results of the study revealed highest SOD activity with ethyl acetate and aqueous fractions (3.3771 and 3.0374 µg/ml respectively). However, DPPH assay showed low DPPH scavenging activity. All test samples showed promising α-glucosidase inhibition activity. Muhtadi et al[29] studied the antidiabetic activity of the ethanol extract of the fruit peels in alloxan induced diabetic rats and reported significant reduction in the blood glucose levels in alloxanized rats by the extract. In another experiment, Soenget al[30] reported the inhibitory potential of the ethanol (70%) extract and its hexane, ethyl acetate, butanol and water fractions of the seeds on glucose-6-phosphate dehydrogenase, α-glucosidase and triglyceride activities in 3T3-L1 cell line (pre-adipocytes). Results of the study revealed lowest cytotoxic activity with seed extract and hexane fraction. The seed extract was most active to lower G6PDH, α-glucosidase and TG level at the dose of 50 µg/ml.

Subramaniamet al[31] studied the antidiabetic effects of the ethanol extract from the rind of *N. lappaceum* in a high fat-induced diabetic rat model. The extract was tested at concentrations of 500 and 2000 mg for 28 days. Results of the study revealed that the rind extract possess anti-hyperglycaemic activity without any major toxic effects in high-fat diet induced diabetic rats.

Muhtadiet al[32] reported the antidiabetic and antihypercholesterolemia activities of the ethanol extracts of the fruit peels of *N. lappaceum* and *Durio zibethinus*. The antidiabetic activity was studied on alloxan induced diabetic rats and the antihypercholesterolemia activity was assessed by estimating cholesterol gained by the animals when fed with high-fat diet. The results of the study indicated that *N. lappaceum* and *D. zibethinus* peel extracts possess significant antidiabetic and antihypercholesterolemia activities at doses of 125 to 500 mg/kg respectively.

Analgesic and Anti-inflammatory activity:

The ethanol extract of the rind is reported to possess protective effects of against collagen induced arthritis in rats at dose levels of 100 and 200 mg/kg, p.o. The results of the study demonstrated significant reduction in arthritis induced changes in body weight and paw edema. A significant reduction in the C-reactive protein and histopathological changes were also noticed in the treatment groups[33].Rajasekaran et al[22] reported the antinociceptive activity of the methanol extracts of raw, boiled and roasted seeds using Eddy's hot plate method.

The results demonstrated superior anti-nociceptive activity by the raw seeds than the boiled ones. On the other hand, the roasted seed extract did not show any activity. In another study, Morshedet al[33] reported the analgesic and anti-inflammatory activity of the methanol extract of the seeds. The extract exhibited potent analgesic and anti-inflammatory activities.

CNS depressant activity:
The methanol extract of the raw and boiled seeds significantly reduced the locomotor activity in a dose dependent manner in rats[21]. As a continuation to this work, Morshed et al[33] reported the CNS depressant activity of methanol extract of the seeds using hole cross and open field models. The results showed 88.09% and 85.94% suppression of locomotor activity with 500 mg/kg of the extract when compared with diazepam (1mg/kg) that revealed 92.85% and 92.77% of suppression of locomotor activity.

Antidiarrhoeal activity:
The methanol extract of the seeds are reported to possess significant antidiarrhoeal activity of when tested using castor oil induced diarrhoeal model in rats. The extract exhibited significant inhibition of fecal dropping compared to loperamide[34].

Cardiovascular activity:
Srisawat et al[35] reported the acute effects of ethanol extract of rambutan bark on cardiovascular and respiratory responses in rats. The results demonstrated prolonged cardiovascular response (increases in MABP, systolic blood pressure and heart rate).

Antimicrobial activity:
Several studies have been carried out in the past validating the antimicrobial potential of *N. lappaceum*. Mohamed et al[36] reported the antimicrobial activity of the petroleum ether, chloroform and ethanol extracts of peel of *N. lappaceum* against *Staphylococcus aureus, Bacillus subtilis, Bacillus cereus, Lactobacillus bulgaricus, Escherichia coli, Proteus vulgaricus, Pseudomonas aeruginosa, Salmonella typhi, Saccharomyces cerevisiae, Candida lypolytica, Rhizopusspp., Aspergillus niger* and *Chlamydomucorspp*. The results revealed that the extracts are active against all tested bacteria except *P. aeruginosa*. The extract also showed activity against *C. lypolytica*. In another study, Thitilertdecha et al[37] reported the antibacterial activities of various extracts of the seeds and peel of *N. lappaceum*. All peel extracts exhibited potential antibacterial activity against *P. aeruginosa*, *Vibrio cholerae*, *Enterococcus faecalis*, *S. aureus* and *Staphylococcus epidermidis* except *E. coli*, *Klebsiella pneumonia* and *S. typhi*. The most sensitive strain, *S. epidermidis*, was inhibited by the methanol extract (MIC 2.0 mg/mL).Tadtong et al[38] studied the antimicrobial activity of the methanol extract of the peels of *N. lappaceum* against *S. aureus*, MRSA and *Streptococcus mutans, E. coli* and *Candida albicans*. The test results revealed positive zone of inhibition against *S. aureus*, MRSA and *S. mutans,* whereas no activity was noticed against *E. coli* and *C.albicans*. Rajasekaranet al[22] reported that the antibacterial activity of the methanol extracts of raw and boiled seeds are effective against *S. epidermidis*.

The aqueous extract of the whole fruit, outer skin and fruit sap of *N. lappaceum* were studied for possible antimicrobial activity against *S. aureus, Salmonella pneumonia, Clostridium diphtheria, B. cereus, Clostridium tetani, E. coli, S. typhi, Aeromonashydrophila, K. pneumonia, P.aeruginosa* and fungal pathogens such as *A.niger, A. fumigatus, C.albicans, Phytophthora infestants* and *Trichophyton rubrum*. The fruit sap showed less activity against *P. aeruginosa*. The whole fruit extract showed a high inhibitory action against *A. hydrophila* and minimum effect on *S. aureus*. The skin extract registered a maximum activity against *P. aeruginosa* and minimum activity against *C. tetani*. All the test samples registered good antifungal activity against test organisms[39].Another study confirmed that the aqueous extract of the seeds possess antibacterial activity against *S. aureus*, *Streptococcus pyogenes*, *Bacillus subtillis*, *E. coli* and *P. aeruginosa*[40].

In a comparative antibacterial study, Sekaret al[41]reported the antibacterial activities of the methanol extracts of the peels of red and yellow varieties of *N. lappaceum* against *S. pyogenes, S. aureus, E. coli* and *P. aeruginosa*. The extract of the yellow variety showed more potency against *S. pyogenes* and *S. aureus* than the red variety. However, there was no zone of inhibition against *E. coli* and *P. aeruginosa* respectively.

Antiviral activity:
The antiviral activity of geraniin isolated from the rind of *N. lappaceum* was tested against dengue virus type-2 (DENV-2) using plaque reduction assay. The stage of DENV-2 replication cycle where geraniin impose its inhibitory action was also determined through the time-of-addition assay. Through this assay, it was shown that geraniin exhibits its inhibitory potential on DENV-2 at the early stage of DENV-2 life cycle, which primarily involves the envelope (E) protein. Docking study showed that geraniin interacts with this major protein. In conclusion, geraniin from the rind of *N. lappaceum* possesses antiviral activity against DENV-2 through the mechanism of inhibiting viral attachment, most probably by binding to the E protein, hence disrupting the infection process[42].

Larvicidal activity:
The larvicidal activity of the ethanol extract of *N. lappaceum* along with three other Philippine plant species, *Citrus microcarpa*, *Chromolaena odorata* and *Jasminum sambac* against third in star larvae of dengue mosquito, *Aedes aegypti* was reported by Dumaoalet al[43]. The results of the study revealed statistically significant relationship ($p<0.05$) between concentration of the extracts of four plants and mortality rate.

Antioxidant activity:
Reactive oxygen species (ROS) are essential for the supply of energy, chemical signaling and detoxification and their concentration in the body is controlled under the influence of several endogenous enzymes such as catalase, superoxide dismutase and glutathione peroxidase. However, their over production due to unfavorable conditions cause damage to the biomolecules. *N. lappaceum* is believed to be a potential source of antioxidants and therefore, several studies have been reported in the literature.

Thitilertdecha et al[34] reported the phenolic contents and antioxidant and antibacterial activities of various extracts of the seeds and peel of *N. lappaceum*. The results revealed higher amount of phenolic contents in the methanol extract of peels and demonstrated potential antioxidant activities than the seed extracts in including reducing power, β-carotene bleaching, linoleic peroxidation and free radical scavenging activities. The antioxidant activity of the ethanol extract of the fruits using ABTS assay is reported by Tachakittirungrod et al[44]. The results indicated significant antioxidant activity of the extract.Another study revealed presence of high phenolic content, low pro-oxidant capacity and strong antioxidant activity of the rind of *N. lappaceum*[45].

Ling et al[46] reported the antioxidant activity total phenolic content, elemental composition and cytotoxity activities of the aqueous and ethanolic extracts from thirteen Malaysian plants including *N. lappaceum*. The results of the study demonstrated strong correlation of antioxidant activity with the total phenolic content and thus better activity of the ethanol extract compared to the aqueous extracts with no cytotoxicity. As a continuation to this work, Khonkarn et al[47] reported the antioxidant activity and cytotoxicity activity of the fruit peel extract of rambutan together with mangosteen and coconut against human cell lines. The results of the study revealed that the ethyl acetate fraction of rambutan peel possessed highest polyphenolic content and revealed better antioxidant activity. In another experiment, Sikderet al[48] reported the antioxidant, cytotoxic, thrombolytic and membrane stabilizing activities of the methanol extracts of leaves of *N. lappaceum*, *Pandanus foetidus*, *Ludwigia repens* and the whole plant of *Adiantum philippens* using DPPH radical scavenging activity. The study indicated highest free radical scavenging activity for *N. lappaccam*. On the other hand, the methanol extracts of *A. philippens* and *P. foetidus* demonstrated significant brine shrimp lethality. Weak thrombolytic activity was observed for the test samples.

Sun et al[49] isolated anthocyanins from the pericarp using 80% ethanol and 1% acetic acid and reported the antioxidant activity of the isolated anthocyanins using assays of reducing power, lipid peroxidation and DPPH, superoxide anion and hydroxyl radicals. The results demonstrated the antioxidant activity of the anthocyanins.

Nurhudaet al[50] studied the effect of water and steam blanching on browning enzymes and antioxidant activities of peel extracts. The study included determination of residual peroxidase (POD) and polyphenoloxidase (PPO) activities, free radical scavenging activity, total polyphenol content and peel extract colour. The results demonstrated significant reduction of water and steam blanching POD and PPO activities without causing significant difference in the total phenolic contents and the antioxidant capacity. Fidriannyet al[51]reported the antioxidant activities of seed extracts of four varieties of rambutan using DPPH and ABTS methods. The correlation of total flavonoid content, total phenolic content and total carotenoid content was analyzed by Pearson's method. The results of the study revealed very strong antioxidant activity of the ethyl acetate and ethanol seed extracts of all four varieties. Various peel extracts of four varieties rambutan were tested for antioxidant activities using DPPH and FRAP assays and their correlation between total flavonoid, phenolic, and carotenoid contents were studied in different extracts of rambutan peels with DPPH antioxidant activities and Ferric Reducing Ability of Power (FRAP) capacities. The DPPH scavenging activities in different peel extracts from the four varieties showed linear result with FRAP capacities[52].Setyawatiet al[53] reported the effect of rambutan peel extract on lipid peroxidation and accumulation in the liver of obese rats through measurement of MDA levels and PPARγ expression studies. The results showed significant decrease in MDA levels but decreasing of *PPAR*γ expression was not significant. In another study, Samuagamet al[54] reported *in vivo* antioxidant potentials of rambutan peel extract and effects on liver enzymes in rats. The antioxidant activity was evaluated using liver enzymatic and non-enzymatic systems. The results of the study demonstrated significant increase ($p<0.05$) in superoxide dismutase, glutathione reductase, catalase and lipid peroxidation levels. Fidrianny et al[55] reported the antioxidant activity of different of *N. lappaceum* leaves using DPPH and ABTS methods and correlated

total flavonoid, phenolic and carotenoid content in the extracts. The results of the study revealed high correlation between total phenolic content in all extracts along with their significant antioxidant activity.Chingsuwanrote et al[56]studied the antioxidant and anti-inflammatory activities of the ethanol extracts of the fruit pulps of *Durio zibethinus* and *N. lappaceum* from two popular cultivars of *D. zibethinus* (Monthong and Chanee) and two popular cultivars of *N. lappaceum* (Sichompu and Rongrien). Non-differentiated U937 monocyte-like cells were pre-treated with the extracts prior to inducing oxidative stress with H_2O_2 and the antioxidant capacity was measured from the suppressive effect on ROS formation. Anti-inflammatory activity was assessed by measuring secretion of cytokines/chemokines into medium of lipopolysaccharide-induced differentiated U937 cells treated with the extracts. The results indicated more potent activity of *D. zibethinus* at suppressing ROS formation and decreasing secretion of tumor necrosis factor alpha (TNF-α) and interleukin-8 (IL-8) than *N. lappaceum* extract. *D. zibethinus* from the Monthong cultivar showed greater antioxidant and anti-inflammatory activities than Chanee cultivar. *N. lappaceum* collected from the cultivar Sichompu inhibited ROS formation but the extract from Rongrien had no significant activity. Both *N. lappaceum* cultivars inhibited secretion of TNF-α, but not IL-8 secretion. Muhtadi, et al[57]reported the antioxidant activity of *N. lappaceum* fruit peel extracts in nanoemulsion gel formulation using DPPH scavenging and Ferric thiocyanate (FTC) methods. The result revealed promising antioxidant activity of the prepared formulation.

Manafet al[58] reported the total phenolic and flavonoid contents and antioxidant activity of the aqueous and ethanol extracts of rambutan peel and seeds. Total phenolic and flavonoid contents were found to be higher in the peels than the seeds, and all extracts exhibited varying degrees of antioxidant activities. Artanti et al[59] studied the antiradical activity of the ethyl acetate fraction of the ethanol extract of *N. lappaceum* along with two other plants *Phaseolus vulgaris* and *Pleurotus ostreatus* using DPPH method and reported varying degrees of activity. The DPPH radical scavenging activity of the methanol extract, petroleum ether and ethyl acetate fractions of rambutan peel cultivar simacan and lebak bolus was reported by Permatasari et al[60]. The ethyl acetate fraction of rambutan peel cultivar lebak bolus showed maximum antiradical activity with highest phenolics and flavonoid contents, accounting of 47.71% (w/w) gallic acid equivalent and 29.59% (w/w) rutin equivalent, respectively. Rohman et al[61] evaluated the antiradical activities of methanol extract of rambutan peel and its petroleum ether, chloroform and ethyl acetate fractions from two cultivars (Aceh and Binjai). The methanol extract and its fractions revealed strong DPPH antiradical activities with maximum phenolics and flavonoid contents.

Anticancer activity:

The anticancer activity of the methanol extract of red and yellow varieties of *N. lappaceum* against breast cancer cells (MDA-MB-231), cervical cancer cells (HeLa) and osteosarcoma cancer cells (MG-63) were studied by Khaizil et al[62]. The results showed promising activity for the yellow verity against MDA-MB–231 and MG-63 with IC_{50} value 5.42±1.67 µg/ml and 6.97±1.02 µg/ml respectively. However, extracts of bothvarieties did not show any antiproliferative activity towards HeLa. Chunglok et al[63] reported antioxidant and anticancer activities of the methanol extracts from seeds and pericarps of three selected tropical fruits including *N. lappaceum*, *Litchi chinensis* and *Tamarindus indica* using ABTS and DPPH radicals scavenging methods. Total phenolic content was determined by using the Folin-Ciocalteu method. Anticancer activity was studied on human mouth carcinoma (CLS-354) cells. MTT reduction assay and Annexin V-FITC/PI staining were carried out for cytotoxicity and apoptosis induction respectively. Results of the study revealed weak activity against CLS-354 cells.

Immunomodulatory activity:

Shrestha and Handral[64] reported the immunomodulatory activity of the ethanol extract from rind of N. *lappaceum* fruit including its protective effect against cyclophosphamide induced immunosuppression. The immunomodulatory activity was assessed through the humoral (haemagglutination antibody titre model), cell-mediated immunity (delayed type hypersensitivity reaction model), haematological parameters, carbon clearance assay (phagocytic index), organ index (spleen and thymus) and histopathological study of mice thymus. The results of the study indicated significant increase in the antibody titer and DTH response in response to sheep red blood cells when compared to normal control and cyclophosphamide control group. There was a prominent increase in the WBC count, spleen index, thymus index and the phagocytic index in immune suppressed group treated with ethanolic extract of *N.lappaceum*rind compared to the immune suppressed control group. The result suggested that the ethanolic extract has the potential to modulate the immune system as well has a protective effect against CP-induced immune suppression.

Miscellaneous study:

Fila et al[65] reported anti-nutrients assessment of pulp, seed and rind of *N. lappaceum*. The study revealed presence of saponins, alkaloids, hydrocyanic acid,

phenols, oxalate, tannins and phytates as anti-nutritional components but at tolerable concentrations. Yoswathana[66] reported the extraction of oil from the seeds of *N. lappaceum* by supercritical fluid extraction using carbon dioxide as the solvent, while maceration and soxhlet extraction using ethanol as the solvent. An optimization study was performed using response surface methodology. The results indicated that supercritical carbon dioxide extraction is competitive with conventional extraction in terms of shorter extracting times, higher percentage of oil yield, usage of less organic solvent and environmental friendly process. Emdadul-Haqueet al[67] extracted polyphenol oxidase from the peels of *N. lappaceum* and studied the biochemical characteristics. The results of the study revealed that polyphenol oxidase extracted from possess higher affinity towards catechol at an optimum pH of 5.9.

In an experiment, Mei et al[68] investigated the oxidative properties of sunflower oil supplemented with *N. lappaceum* extract in comparison with synthetic antioxidant under accelerated conditions. The results of the study suggested that rambutan extract could be used as an alternative source of antioxidant in the oil industry to delay lipid oxidation. Yuvakkumara et al[69] studied the biosynthesis of NiO nanocrystals using *N. lappaceum* peel extract. The prepared nanocrystals were coated on cotton fabrics and their antibacterial activity was evaluated.

Eiamwat et al[70] reported the physicochemical properties of defatted seed flour of *N. lappaceum* after alkaline treatment. The results of the study revealed that the alkali-treated flour had a significant increase in bulk density, swelling power, water adsorption capacity, emulsion capacity and stability. However, a reduction in turbidity, solubility and oil absorption capacity were also noticed. Pasting measurements of the alkali-treated flour showed significant increase in peak viscosity, breakdown, setback and final viscosity while pasting temperature was decreased. Further, the alkaline treatment decreased the least gelation concentration, but increased the apparent viscosity.

Sekar and Noordin[71] reported the formulation and evaluation of herbal shampoo containing rambutan leaves extract. The formulation containing the methanol extract of the leaves was analysed for its physicochemical properties. The results of the study revealed that the formulated shampoo possessed satisfactory conditioning performance. Further, Sekar et al[72] reported the antiaging activity of four creams containing methanol extracts of flesh and peels of *N. lappaceum* in different proportions. The results revealed significant antiaging activity of the test extracts in the formulations.

CONCLUSION:

N. lappaceum is a very popular plant in Malaysia and other South Asian countries for its edible fruits. The plant also finds its application in the traditional medicine for centuries especially as a remedy for diabetes and high blood pressure. Further, the fruits always remained as a potential source of minerals and other nutrients. A thorough literature survey revealed that the plant possesses several biological activities such as antidiabetic, analgesic, antiinflammatory, immunomodulatory, antioxidant, anticancer, antibacterial, antifungal and antiviral activities against dengue virus. The need of the hour is to explore this plant for possible biological activities in detail.

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CONFLICTS OF INTEREST:

The authors declare no conflicts of interest.

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