Indian Journal of Traditional Knowledge
Vol 21(1), January 2022, pp 29-39

Phyto-chemistry and therapeutic potential of litchi (*Litchi chinensis* Sonn.): An age-old ingredient in traditional medicine

Hidayatullah Mir[a,*] & Nusrat Perveen[b]

[a]Bihar Agricultural University, Sabour Bhagalpur, Bihar 813 210, India

[b]ICAR-Indian Agricultural Research Insitute, Pusa, New Delhi 110 012, India

E-mail: hidayatmay14@yahoo.co.in

Received 26 August 2019; revised 13 November 2021

The litchi (*Litchi chinensis* Sonn.), long been used in traditional medicine, has been endowed by nature with myriad biological properties that makes it a potential crop for healing various sufferings of mankind. Different bioactive compounds like flavonoids and anthocyanins have been reported from pulp as well as the non-edible tissues such as seed, pericarp, flowers and leaves which possess strong free radical scavenging activities and can be used as anti-cancerous and anti-inflammation agents. Potential role of litchi seed extracts in preventing type 2-diabetes has been suggested in recent studies. Some components identified from litchi seeds are claimed to possess anti-cancer properties mainly against lung, liver, pulmonary and cervical cancer. Leaf extracts of litchi possess significant anti-inflammatory, analgesic and anti-pyretic activities. An innovative formulation, oligonol-L, derived from fruits of litchi is reported to possess chemo-preventive and chemo-protective potential against photo-injuries such as skin photo-ageing and cancer. Thus, it could be implied that litchi tree is studded with more blissful properties than hitherto conceded. However, intensive research is paramount to unveil the exact mechanism of action of the active components in order to exploit the therapeutic and preventive potentials of this crop. The main objective of this review is to provide comprehensive information on the pharmacological activities of litchi reported till date and suggest future investigations required to exploit the nutraceutical properties of this potential plant.

Keywords: *Litchi chinensis*, Medicinal, Nutraceutical, Pharmacology, Traditional medicine

IPC Code: Int Cl.[22]: A61K 36/00, A61K 36/77, A61K 45/00

Unequivocally enthroned as the most important subtropical evergreen fruit tree, litchi botanically known as *Litchi chinensis* Sonn., is a member of family Sapindaceae and sub-family Nephaleae. It has been cultivated for its high-quality fruit from even before 1766 BC[1]. Litchi fruit surpasses many other fruits in terms of quality, flavor and colour that are attractive enough to appeal the eyes of its beholder. Owing to its nutritional value and excellent taste it is reputed as the king of fruits in China[2]. Major litchi growing countries are China, India, Taiwan, Vietnam and Thailand. Litchi was introduced in India during 18th century and India is now the 2nd largest producer after China. Main states growing litchi in India include Bihar, West Bengal, Tripura, Uttarakhand, Uttar Pradesh and Punjab[3]. Shahi litchi of Bihar has received the geographical indication by the India Patent Office in year 2018, which gives a state or a geographical region an exclusive claim over a product based on its geographical origin, reputation and quality. In different parts of world different pronunciations like litchi, lichee, lychee, laichi, lici and so on are used, however, in India it is invariably known as litchi. The edible part of fruit is a juicy translucent aril which can be eaten either fresh or processed into wine, juice, jelly and vinegar. Anthocyanins are responsible for the bright red pericarp of litchi fruit. In many cultivars of litchi, Cyanidin-3-O-rutinoside is the principal anthocyanin pigment contributing about 67% to >95% of total anthocyanins followed by Cyanidin-3-O-glucoside, malvidin-3-O-glucoside and peonidin-3-O-rutinoside[4]. Anthocyanin pigments have a wide range of properties including antioxidant, anti-inflammatory, antimicrobial and anti-carcinogenic activity[5]. Traditionally the fruit has also been used to cure stomach ulcers, obesity and diabetes, relieve coughing, to kill intestinal worms as well as possess analgesic action[6]. Seeds of litchi contain abundant amount fatty acids, polyphenols, flavonoids, sterols, saponins and volatile constituents[7]. The potential of litchi seeds and fruits to restrict the proliferation of cancerous cells has been revealed by recent medical reports[8,9]. High number of flavonoids present in litchi

*Corresponding author

seeds make it highly effective against breast cancer. The flavonoid glycoside compounds litchioside D, kaempferol 7-O-neohesperidoside and taxifolin 4'-O-β-d-glucopyranoside extracted from litchi seeds exhibited *in vitro* anti-tumour activity against LAC, Hep-G2, A549 and HeLa cell lines in the 3-(4,5-dimethylthiazol-2-yl) 2,5-diphenyltetrazolium bromide (MTT) colorimetric assay[10]. A litchi extract rich in flavanol, oligonol is reported to convert proanthocyanidins (a high molecular weight compound) into proanthocyanidins (a low molecular weight compound), thus enhancing their bioavailability[11]. Oligonol-L (formulation containing catechin-type oligomeric polyphenols), derived from fruits of litchi possesses chemo-preventive and chemo-protective potential against photo-injuries such as skin photo-ageing and photo-carcinogenesis. This could be attributed to its potential of inhibiting UV-B induced expression of COX-2, various upstream kinases and NQO-1[12]. COX-2 is a rate-limiting enzyme responsible for the biosynthesis of prostaglandins and has a role to play in UV-B induced skin carcinogenesis[13]. Several chemical compounds such as anthocyanins, flavonoids, triterpenes, tannin and sterol have been isolated from both edible and non-edible parts of litchi fruits. The knowledge of these compounds is highly important for the researchers to tap the potential of this pharmacologically important crop. However, systemic reviews concerning the bioactive compounds, preventive and therapeutic potentials of litchi are meagre[14]. This review is aimed at providing comprehensive information about pharmacological activities and the chemical constituents of litchi reported until now and to suggest future investigations required to exploit the nutraceutical properties of this potential plant.

Nutritional composition

Pulp recovery of litchi is 50-70% with average fruit weight of 16-35 g. Litchi is rich source of fibres and carbohydrates with lower protein and lipid content (Table 1). Presence of higher content of micronutrients including vitamins (B1, B2, B3, B6, E, K and C), total carotenoids (571.4 μg beta-carotene equivalent/100 g), polyphenol (178.0 mg gallic acid equivalent/ 100 g), flavanoid (53.3 mg quercetin equivalent/ 100 g), minerals etc., make litchi one of the best functional foods that can be used to promote health and ensure nutritional security of the litchi producing countries including India. Apart from the edible part, litchi seeds which are discarded as waste have also been reported to be of excellent nutritive value along with potent anti-oxidant activity[15]. Litchi seeds are devoid of gums, mucilage and naphthoquinones and contain large numbers of medicinally active secondary metabolites like glycosides, inulin, alkaloids, carbohydrates, triterpenoids, protein, fixed oils, amino acid, fats, steroids, flavonoids and phenolic group. In addition, these are rich source of protein (6.126%), carbohydrate (81.098%), fat (0.891%) and crude fiber (4.327%) with a nutritive value of 356.917 Kcal/100 g of seeds[15].

Nutritive value of fresh litchi fruits adopted from the National Nutrient Database for Standard Reference (United States Department of Agriculture, Washington, DC, USA) has been provided in Table 1.

Litchi in traditional medicine

Since the dawn of human civilization, different plants have been utilized by mankind for their therapeutic value and use of these natural agents in traditional medicine paved way for the isolation of many modern drugs. Traditional medicines include Unani, Ayurveda, Siddha and Chinese medicine system and have been playing a major role in primary health care of around 80% of the world's population in developing countries according to the World Health

Table 1 — Nutritional compositional of litchi edible part (*Source: USDA, National Nutrient Database for Standard Reference, 2018*)

Nutrient	Value per 100 g	Nutrient	Value per 100 g
Major Components		Minerals	
Water	81.76 g	Calcium, Ca	5 mg
Energy	66 kcal	Iron, Fes	0.31 mg
Protein	0.83 g	Magnesium, Mg	10 mg
Total lipid (fat)	0.44 g	Phosphorus, P	31mg
Carbohydrate, by difference	16.53 g	Potassium, K	171 mg
Fiber, total dietary	1.3 g	Sodium, Na	1 mg
Sugars, total	15.23 g	Zinc, Zn	0.07
		Vitamins	
Vitamin C, total ascorbic acid	71.5 mg	Folate, DFE	14 μg
Thiamin	0.011 mg	Vitamin K (Phylloquinone)	0.4 μg
Riboflavin	0.065 mg	**Lipids**	
Niacin	0.603 mg	Fatty acids, total saturated	0.099 g
Vitamin B6	0.1 mg	Fatty acids, total monounsaturated	0.12 g
Vitamin E (alpha-tocopherol)	0.07 mg	Fatty acids, total polyunsaturated	0.132 g

Organization[16]. Herbal medicines are obtained from the plants in the form of phytochemicals i.e., chemicals from plants that has effect on health, however, are not essential nutrients. China is supposed to have been growing litchi for more than 2300 years and it is being used in Chinese culture for the treatment of ailments like diabetes, obesity, stomach ulcers, cough, testicular swellings, epigastric and neuralgic pains and killing intestinal worms[17-19]. Decoctions prepared from bark, flowers and roots are used for throat gargle to alleviate various ailments of the throat while poultices made of leaves are effective in curing skin diseases[20]. Seeds have been utilized in Malay Peninsula for treating hernia, intestinal troubles, ulcers, neuralgic disorders, orchitis and lumbago[21]. In addition to China medicinal uses of litchi is also prevalent in other countries like India, Vietnam and Taiwan. The cooling effect of litchi and its potential role in curing various disorders related to digestive, excretory and reproductive system has been emphasized in Ayurveda. In India, tea prepared by litchi seed powder is said to be useful in relieving intestinal infections and alleviating neuralgic pain and inflammation of nerve which is attributed to its astringent action[22,23] and unripe fruits are given to children suffering from small pox[24]. Litchi fruits serve as an excellent thirst quencher during summer and is also used in Vietnam and Taiwan as a tonic for brain, liver and heart[25,26].

Phyto-chemical constituents

Pharmacological studies have been done in litchi since a long time indicating it to be a rich source of different groups of plant secondary metabolites. Analgesics, anti-inflammatory and antipyretic activity of petroleum ether extract of litchi leaves has been reported[27]. Recently, the hydro-alcoholic extract of litchi seed and fruit pericarp was observed to possess antioxidant, anti-inflammatory and anti-microbial activities[28]. Works done in the past few years have resulted in the isolation of large number of compounds from various parts of the litchi plants like leaves, seed pericarp and pulp. Major compounds in leaves include (-)-epicatechin, procyanidin A2 and procyanidin B2[18]. Terpenoids present in litchi leaves are mainly α-copaene (0.7-1.0%), α-bergamotene (1.0-1.3%), α-humulene (2.2-4.1%), α-sesquiphellandrene (7.2-13.6%), transcaryophyllene (12.2-33.4%) and zingiberene (38.6-66.3%)[29]. Malvidin glycoside, Leucocyanidin, saponins and cyanidin glycoside are the major chemical constituents of seeds[30]. While, 5-HMF, benzyl alcohol, hydrobenzoin and (+) – catechin are predominant in fruits[31]. Arabinogalactan, a health-promoting food component, is the main water-soluble polysaccharide present in litchi pulp having a molecular weight of 2.4×106 Da[32] apart from this, the presence of (–)-epicatechin, (–)-gallocatechin, propelargonidin, procyanidin and prodelphinidin have also been reported[33]. Mature and premature LFP contains considerable number of phenolic compounds and flavonoids[34], while condensed tannins (polymeric pro-anthocyanidins), epicatechin and procyanidin A2 with high anti-oxidant and anti-cancerous activities are the major components of fresh LFP extract[35]. The pharmacological properties of litchi pericarp are attributed to the presence of compounds like bis-(8-epicatochinyl) methane, 5-2-(2-hydroxy-5- (methoxy carbonyl) phenoxy) benzoic acid, butylated hydroxy toluene, dehydrodiepicatechin A, epicatechin, methyl shikimate, isolariciresinol, ethyl shikimate, kaempferol, proanthocyanidin A1, A2, rutin, methyl 3,4-dihydroxy benzoate and stigmasterol[36]. Gong *et al.*[37] for the first-time isolated complex A/B type epicatechin trimers and B-type (Litchitannin B1 and B2) from aqueous extract of litchi pericarp responsible for high antioxidant and anticancer activity. Some of the important biologically active compounds reported from different parts of litchi have been provided in Table 2.

Biological activities

Antioxidant properties

Antioxidant is a molecule which is capable of inhibiting the oxidation of any other molecule. They may be natural or synthetic compounds. Ascorbic acid, flavonoids, tocopherols are the natural compounds widely known for their antioxidant properties. Antioxidants find a prominent place as the major ingredients in dietary supplements with a purpose of supporting health and preventing deadly ailments such as inflammation, cancer, cataracts, cardiovascular diseases, neurodegenerative disorders and even altitude sickness[38]. Litchi fruit possesses strong antioxidant properties owing to the presence of notable amount of polyphenol (178.0 mg gallic acid equivalent/ 100 g) and flavanoid (53.3 mg quercetin equivalent/ 100 g)[39]. In litchi seeds, total phenolic content and ferric reducing antioxidant power was found to be highest for ethanolic macerate i.e., 33.657 mg GAE/100 gm dw and 707.929 µM/mL, FRAP value =1.808 respectively[15]. Fifteen compounds were isolated from 95% ethanol extract of litchi seeds eleven of which viz., 2, 5 dihydroxy-hexanoic acid,

Table 2 — List of biologically active compounds isolated from *L. chinensis*

Compound	Plant parts	Reference
Polysaccharide		
Arabinogalactan	Pulp	32
Flavan-3-ols		
Phenolics	Leaves,	17, 54
(–)-Epicatechin	pericarp, pulp, seeds	
Litchitannin B1 and B2, complex A/B type Epicatechin trimers	Pericarp	37
(+)-Catechin	Pulp	17
Proanthocyanidins		
proanthocyanidin A1, A2	Pericarp	36
Procyanidin A2, Procyanidin B2	Leaves	17, 54
Proanthocyanidin B2	Leaves	17
Propelargonidin, Procyanidin, Prodelphinidin	Pulp	27
Anthocyanins		
Cyanidin-3-glucoside, Cyanidin-3-rutinoside, Malvidin-3-glucoside	Pericarp	4
Phenolics		
Protocatechuic acid	Seeds	40
Coumaric acid	Seeds	40
Gentisic acid	Flowers	41
Fatty Acids		
Methyl dihydrosterculate	Seeds	40
Terpenoids		
Other compounds		
Litchiol A and Litchiol B	Seeds	40
Sesquipinsapol B, Sesquimarocanol B	Leaves	55
Benzyl alcohol	Fruits	31
Hydrobenzoin	Fruits	31

scopoletincoumaric acid, protocatechuic acid, 2α, 3α-epoxy-5,7,3',4'-tetrahydroxyflavan-(4β-8-catechin), pterodontriol D-6-O-β-D-glucopyranoside, naringin, narirutin, pinocembrin-7-rutinoside, dihydrocharcone-4'-O-β-D-glucopyranoside and pinocembrin-7-neohesperidoside were priorly known[40]. Four newly isolated compounds included, 2-α,3α-epoxy-5,7,3', 4'-tetrahydroxyflavan-(4β-8-catechin), 2β,3β-epoxy-5,7,3'4' tetrahydroxyflavan-(4α-8-epicatechin), litchiol A and litchiol B. Further, among the fifteen compounds, protocatechuic acid, 2α,3α-epoxy-5,7,3',4'-tetrahydroxyflavan-(4β-8)-catechin), 2α,3α-epoxy-5,7,3',4'-tetrahydroxyflavan-(4β-8) epicatechin and 2β,3β-epoxy-5,7,3',4'-tetrahydroxyflavan-(4α-8) epicatechin exhibited moderate antioxidant activity[40].

Three water-soluble polysaccharide fractions (LFP) viz., LFP1, LFP2 and LFP3 were isolated from litchi pulp out of which LFP3 exhibited strongest antioxidant activity attributed to scavenging of superoxide and hydroxyl radicals[41]. Gentisic acid and epicatechin are the major phenolic acid and flavonoid respectively present in the LFWEs. LFWEs decreased the accumulation of serum lipids and liver lipids in hamsters fed with fat rich diet and increased the hepatic anti-oxidative capacities. Furthermore, it was found to decrease liver damage/inflammatory indices, CRP levels and MMP-9 activities corresponding to the slighter liver damage[42]. CRP produced in liver as a response to inflammation, act as a blood test marker for swelling in the body. MMPs are a family of enzymes which are responsible for remodeling of extracellular matrix proteins. They play significant role in inflammation, arthritis, cardiovascular diseases, fibrosis and cancer. The anti-oxidant property along with anti-inflammatory effect of LFWEs was responsible for its protective effect on liver damage of hamsters fed with fat rich diet[42]. The antioxidant activities of litchi pericarp are attributed to the presence of high levels of total phenolics and flavonoids in it. Phenolic compounds are described to have an inhibitory effect on angiotensin I-converting enzyme (ACE) which regulates blood pressure by facilitating conversion of angiotensin-I to angiotensin-II, which is a potent vasoconstrictor and also helps in the degradation of the vasodilator bradykinin leading to hypertension[43-46]. Litchi pericarp is reported to contain large amount of bioactive phenolic compounds in free as well as bound form[47]. High concentrations of phenolic compounds were obtained from litchi pericarp extracts using pectinase, β-glucosidase and tannase and it was reported that the enzyme assisted produced extract showed increased ferric reducing antioxidant capacity, angiotensin I-converting enzyme inhibition ability and DPPH radical scavenging activity[48]. Moreover, the absence of anti-nutritional factors in the pericarp makes it a potential ingredient in the development of functional foods and pharmaceutical products to treat hypertension[28,48].

Anti-cancerous properties

Today cancer has become one of the most dreaded diseases of mankind, cure of which is coveted for years. It is largely considered as a preventable disease, as its cure is generally difficult once it takes over the body. Polyphenolic compounds have ortho-diphenolic structure which gives them high oxidative capacity and hence, the plants rich in these compounds possess antioxidant properties. Supplements with antioxidant properties are anticipated to decrease the risk

of breast cancer[49] and consuming food and beverages rich in polyphenols (e.g., anthocyanins, flavones and catechins) might lower the incidence of cancers[50]. Extracts of various parts of litchi like leaves and seeds exhibit a strong bioactivity against cancer cells. Anticancer activity of LFP extract against human breast cancer was reported by Wang *et al.*[8]. A strong repressive effect on the growth of both ER positive and negative breast cancer cells *in vitro* and ER negative breast cancer *in vivo* suggests the potential use of LFP in the discovery of anticancer drugs[8]. Epicatechin, proanthocyanidin B2, proanthocyanidin B4 have also been extracted from litchi pericarp tissues and are expected to play a significant role in preventing breast cancer[51]. The cell growth of EAC of mice and S180 sarcoma both under in vivo and *in vitro* condition was found to be significantly inhibited by litchi medicated serum[52], as well as the HepG2 human liver cancer, inducing cell apoptosis[53]. Among 6 flavonoids, including epicatechin, luteolin, kaempferol 3-O-a-rhamnoside, procyanidin, A2 kaempferol 3-O-b-glucoside and rutin isolated from ethanolic extract of litchi leaf, procyanidin A2 exhibited highest anticancer activities against human hepatoma HepG2 and human cervical carcinoma Hela cells. However, against human lung cancer A549 and human breast cancer MCF-7 cells, it exhibited poor activity[54]. Three sesquilignans viz., sesquipinsapol B, ehletianol C and sesquimarocanol B, purified from litchi leaf exhibited effective *in vitro* cytotoxicities against human cancer cells HepG2 and Hela[55]. Sesquipinsapol B and sesquimarocanol B had strong cytotoxic activity against nasopharynx carcinoma cells CNE1 and CNE2, respectively[56]. Litchi stone is reported to possess anti-tyrosinase activity and (–)-epicatechin, (–)-epicatechin-3-gallate, proanthocyanidin B2, gallic acid extracted from litchi seeds were found to significantly inhibit tyrosinase activity[7]. Litchtocotrienols A-G and macrolitchtocotrienol A isolated from leaves of litchi exhibited minor cytotoxicity against HepG2 and AGS cells lines under *in vitro* conditions[56]. A significant decrease in the viability and growth of prostate cancer PC3, DU145, RM1 and C4-2B cells was observed for NLS in a dose-dependent manner[57]. NLS induces cell apoptosis and cell cycle G1/S phase arrest by inactivating Akt signaling pathway associated with activation of mitochondrial caspase-dependent apoptotic cascades, up-regulation of CDK inhibitors p21 and p27 and inhibition of correlated cyclin/CDK network. Thus, NLS can prove to be a potential source for developing a safer alternative therapy for treating prostate cancer[57]. Thiesen *et al.*[58] demonstrated the potential use of litchi leaf extract as an alternative to synthetic filters for photo chemo protection against UVA and UVB radiation to avoid skin cancer and other harmful effects of UV radiations. Based on the findings of a preliminary *in vitro* assay, the authors claimed that the extract is photo-safe and protects the Red Blood Cell membrane against oxidative damage by decreasing the formation of ROS without evoking any irritant effect[58]. Anti-cancerous properties of two novel compounds, B-type (Litchitannin B1 and B2) and complex A/B type epicatechin trimers extracted from aqueous litchi pericarp was observed recently by Gong *et al.*[37]. They reported a higher cytotoxicity of these compounds on the proliferation of human lung adenocarcinoma cells (A549) than Litchi anthocyanins[37]. High doses (200 and 400 µg mL^{-1}) of aqueous extract of litchi seed were found to inhibit the proliferation of normal mammary cells (MCF10A) as well as inhibited epithelial mesenchymal transition (EMT), invasion and migration in breast cancer cells depending upon concentration and time[59].

Anti-diabetic properties

With the changes in lifestyle characterized by changed food habits, less physical work etc., diabetes has emerged as an epidemic disease in the past few years affecting a major portion of the population. In various studies conducted so far, it has been proved that the fruits rich in phenolic compounds are highly effective against diabetes. Diabetes is characterized by hyperglycemia which results in an overload of cellular glucose in the kidneys, which in turn results in mitochondrial dysfunction and subsequently renal injury[60]. LSE is reported to contain different types of pinocembrin glycosides and catechin-rich compounds, which are attributed to its hypoglycemic roles in preventing T2D progression[61]. Treatment of STZ/high fat diet induced diabetic rats with LSE resulted in their protection against kidney, pancreas and liver damage by improving insulin resistance and glucose tolerance. Furthermore, it also improved lipid and glucose metabolism and repressed the apoptosis-induced inflammation and hepatic damage for protecting the body against diabetic exacerbation[61]. These results confirm that LSE can be a potential agent for the prevention of early stage T2D.

LSE caused a decline in the levels of urinary glucose thus, inducing an early recovery from renal injury and resulted in protection of kidney morphology and mass in diabetic rat. APLC showed

better hypoglycemic activity in normal rats as compared to standard gliclazide, further, the treatment of STZ induced diabetic rats with APLC resulted in significant reduction in the elevated plasma glucose levels[62]. The hypoglycemic and anti-hyperglycemic activity of APLC against STZ induced diabetic rats can be attributed to the presence of high levels of anthocyanins and polyphenols in the aqueous pericarp extract of litchi[62]. Intake of oligonol, a low-molecular-weight polyphenol obtained from litchi which is derived as a product of oligomerization of polyphenols, improved insulin resistance which often precedes type-2 diabetes[63]. Oligonol derived from green tea and litchi extract has also been reported to exhibit antioxidative and hypolipidaemic activities on hepatic damage and renal damage in type 2 diabetic mice[64]. Litchi pulp is rich in phenolics and the varieties with high high procyanidin or (-)-epicatechin content could be a great choice as hypoglycemic food[65]. Oligonol was found to be safe for human consumption in a clinical study involving rats where the safety of oligonol was determined using acute and sub-chronic studies and genotoxicity assays[66]. Oligonol administered to female and male rats at the rate of 2000 mg/kg body weight, did not cause any adverse effect in single dose acute study and the gain in body weight as well as food consumption remained within normal range and hence the LD_{50} was found to be greater than 2000 mg/kg body weight. Further, the micronucleus assay in mice, demonstrated that oligonol did not induce any micronuclei or suppress bone marrow, thus confirming that it does not cause any chromosome aberrations[66].

Anti-obesity property

Obesity has become a nagging problem particularly in the developed countries in the past few decades. Change in the food habit like increased consumption of more energy-dense that includes high-fat or sugar foods may be considered as the potential cause of the increasing obesity levels[67]. It is a known fact that high-fat diets results in a significant increase in the body and liver weights, which invariably leads to problems like obesity, hyperlipidemia and fatty liver[67]. Natural polyphenols are claimed to lower down lipid absorption in intestine or else promote lipid catabolism in the body, ultimately leading to decline in level of serum lipids[67]. As demonstrated by an *in vitro* study, naturally-occurring polyphenols possess lipase inhibitory activities[68] and litchi being a rich source of polyphenols is a blatant answer for problems like obesity. Oligonol present in litchi fruit has been found to be effective in decreasing body weight, abdominal circumference, and visceral fat volume[42]. High fat/cholesterol diet fed hamsters, when made to drink polyphenol rich litchi-flower solution, a significant decrease in serum and hepatic lipids (cholesterol and triglyceride) was observed[42]. Litchi-flower-water extract (LFWE) contains many phytochemicals namely phenols, flavonoids and tannins. Yang *et al.*[67] reported that drinking LFWE lowers the serum lipids and peroxidation and also amends the serum cholesterol profile as well as total antioxidant capacity in high fat/cholesterol diet fed hamsters. A higher fecal lipid excretion is reported to be highly associated with lower serum lipid level, which in turn alleviates the hepatic lipid accumulation[69]. Thus, it can be anticipated that increased fecal lipid and bile acid excretions of hamsters drinking LFWE is associated with the lipid-lowering effect of LFWE[67]. LFWE is reported to up regulate LDL receptor, which in turn results in clearing of serum cholesterol and PPAR-alpha, this further leads to increased β-oxidation of fatty acids and down regulate fatty acid synthase, eventually decreasing lipogenesis[42].

Anti-microbial properties

Being rich in different types of secondary metabolites including terpenoids, tannins, alkaloids and flavonoids, plants are found to exert *in vitro* antimicrobial property[70]. In plants, antimicrobial proteins and peptides are discovered mostly in seeds, where they accumulate in higher levels and can also function as storage proteins[71]. These antimicrobial peptides are now considered as good antifungal substances and occasionally show antibacterial activities *in vitro*[72]. The bark extracts of litchi are reported to possess bioactive compounds exhibiting antibacterial and antioxidant activities[73]. The aqueous-methanolic extract of litchi bark exhibited maximum growth inhibition against *Bacillus subtilis,* among six different bacterial strains namely, *Micrococcus luteus, Proteus mirabilis, Bacillus licheniformis, Salmonella typhimorium Nocardia asteroids* and *Bacillus subtilis* used in the study[73]. Bhat and Al-daihan[74] reported that the aqueous seed extracts of *L. chinensis* showed moderate antibacterial activity against *Streptococcus pyogenes, Staphylococcus aureus, Bacilllus subtillis, Pseudomonas aeruginosa* and *Escherichia coli* among which the highest inhibitory activity was against *Streptococcus pyogenes.* Amongst procyanidin A2,

luteolin, (–)-epicatechin and quercetin-3-O-rutinoside isolated from extract of litchi leaves only luteolin was reported to possess strong antimicrobial activity towards *S. aureus, E. coli, S. dysenteriae, Salmonella* and *B. thuringiensis* while the remaining could exhibit only a moderate activity[55]. In a recent study, largest zone of inhibition for gram positive *Staphylococcus aureus* using aqueous extracts of litchi seeds and highest zone of clearance for *Klebsiella pneumoniae* by methanolic extract of the litchi pericarp was reported by Mutha *et al.*[28]. The effectiveness of plant extracts against both Gram-negative and Gram-positive bacteria indicates the presence of broad-spectrum antimicrobial components[28].

Other biological activities possessed by litchi

In addition to afore mentioned properties, *Litchi chinensis* possess plethora of biological activities, some of which have already been revealed and yet others remain an important field of future research. The by-products of litchi possess antioxidant, anti-hyperlipidemic, anti-inflammatory, anti-hyperglycemic, hepatic and cardioprotective activities. Hydro-alcoholic extract of litchi leaves were also reported to possess strong anti-inflammatory and analgesic activity[75]. *In vitro* immunomodulatory assay of a novel polysaccharide (LCP50W), having a molecular weight of 4.72×10^4 Da, isolated from litchi pulp has been reported to promote the growth of mouse splenocytes and enhance the cytotoxicity of natural killer cells[76]. It boosted the secretion of Th1 cytokine IFN-γ whilst inhibited the secretion of Th2 cytokine IL-4. Furthermore, an enhanced expression of T-bet inhibition of the zinc-finger transcription factor, GATA-3 expression was also reported[76]. Two important bioactivities of polysaccharides are their Immuno-modulation capability and improvement of gastrointestinal micro environment[76]. High pancreatic lipase inhibitory activity of litchi seed protein has also been reported[77]

Glucans are reported to improve the lymphocyte proliferation along with decrease in the ulcer severity scores in oral human studies[78]. LFE showed collagen and ADP-induced platelet aggregation in rat platelet-rich plasma along with significantly prolonging coagulation times and increasing fibrinolytic activity[79]. Litchi-flower-water extracts (LFWEs) showed protective effects against liver damage of high fat diet fed hamsters that can be accounted for the anti-oxidative and anti-inflammatory activities of LFWEs[11]. Hepato-protective effects of $CHCl_3$ and MeOH extracts of litchi leaf has been shown on paracetamol-induced liver damage in wister albino rats wherein the MeOH extract was more effective than $CHCl_3$ extract when compared to silymarin[80]. Silymarin is a flavonoid complex containing silybin, silydianin and silychristin derived from the milk thistle plant (*Silybum marianum*). It is popular for its use as liver protectant and decongestant. The hepato-protective properties of aqueous extracts of litchi fruit pulps can be attributed to their anti-apoptotic and antioxidant effects in comparison to silymarin[26]. Phenolic compounds are known for their inhibitory effect on ACE[43,45]. ACE regulates blood pressure by facilitating the conversion of angiotensin-I to angiotensin-II which is a potent vasoconstrictor and in the degradation of the vasodilator bradykinin which results in hypertension[44,46]. Kessy *et al.*[48] reported enhanced recovery as well as biotransformation of phenolic compounds with improved ACE-inhibition capacity and antioxidant on treatment of litchi pericarps by β-glucosidase, pectinase and tannase suggesting that enzyme-assisted extraction could produce ingredients that will be promising in the development of pharmaceutical products and functional foods against hypertension. Polyphenol rich litchi seed extract was reported to significantly decrease systolic blood pressure and alleviate hypertension-induced renal damage[81].

Anti-nutritional compounds in litchi

Litchi is a plant with medicinal value having both its edible and in-edible parts being rich in bioactive compounds. It cannot be denied that in addition to the health promoting factors, fruits can also contain various anti-nutritional compounds which can interfere with nutrient-absorption, digestion and can be toxic depending upon the amount in which it is consumed. Thus, using a particular plant part fraction for pharmacological purpose cannot be recommended without first determining the toxicological effects that its chronic and sub-chronic consumption can cause. Results of acute toxicity studies showed that an intra-peritoneal litchi leave extract up to a concentration of 1.0 g/kg was non-toxic[5]. An inexplicably intense neurologic illness affecting children of young age has been reported recently in Muzaffarpur district of Bihar (popular litchi producing region of India), Vietnam and Bangladesh which is characterized by low blood sugar, seizures and encephalopathy[82]. In India, the exposure to MCPG, a toxin found in litchi seeds, was hypothesized to be the reason that might

have caused AES in some children[82]. On the other hand, the investigations in Vietnam and Bangladesh focused basically on the prospect that the pesticides sprayed in the orchards of litchi might be the cause of this illness[82]. However, Bandyopadhyay *et al.*[83] reported the epidemiological investigation of the AES outbreak in Malda District of West Bengal, India which claimed 34 deaths among the 72 AES patients admitted and for the first time conveyed that the evidence collected indicate a viral etiology. Endorsing the findings of Bandyopadhyay *et al.*[77], these allegations were also overruled by Nath *et al.*[84] who proposed that the consumption of litchi fruit and the resulting hypoglycemia might have enhanced AES, although, it cannot be considered as actually being the sole causal factor thus, obviating any claim that AES might have been occurring solely due to consumption of litchi fruits

Litchi peel, pulp and seeds (both in fresh and processed forms) and were evaluated for the levels of nitrate, oxalic acid, inhibitory activities of lipase and phenolic compounds, trypsin and alpha-amylase[85]. The results confirmed that the anti-nutritional factors like nitrate, phenolic compounds and trypsin inhibitor, lipase and alpha-amylase present in litchi fractions do not exceed the amount that can preclude their uses in fresh or dried form. Thus, they can be used in the development of new products as well as in food enrichment[85]. Oxalic acid which is one of the potent anti-nutritional factors that cannot be metabolized by humans and is involved in the formation of Calcium oxalate that comprise about 75% of the kidney stone, was not detected in any of the litchi fractions[85].

Brief information on different phyto-chemicals present in litchi and their pharmacological potential has been provided in Table 3.

Table 3 — List of biologically active compounds isolated from *L. chinensis* and their pharmacological properties.

Compound	Biological activity	Reference
Phenolics	Antioxidant, cytotoxicity, antiviral, antimicrobial, anticancer, anti-tyrosinase activity	17, 37, 54, 51
Flavan-3-ols		
(–)-Epicatechin		
(+)-Catechin	Antioxidant	31
Proanthocyanidins		
Proanthocyanidin A1, A2	Pericarp	36
Procyanidin A2	Antioxidant, antimicrobial, antiviral, anticancer (against human hepatoma HepG2 and human cervical carcinoma Hela cells	17,54
Proanthocyanidin B2, B4	Antioxidant, Anticancer (against breast cancer)	30,51
Phenolics		
Protocatechuic acid, Coumaric acid	Antioxidant	40
Gentisic acid	Antioxidant	42
Other compounds		
Litchiol A and Litchiol B	Antioxidant	40
Sesquipinsapol B, Sesquimarocanol B	Antioxidant, Cytotoxicity	55
tannins, and saponins	anti-inflammatory and analgesic	30
Luteolin	Antimicrobial	55
Litchitannin B1 and B2, complex A/B type Epicatechin trimers	Anticancer and Antioxidant	37
Oligonol	Hypolipidaemic and antioxidative	64

Conclusion

Litchi (*Litchi chinensis* Sonn.) has been known to the human civilization for several centuries. Its significance in various cultures, both for consumption as a delicious fruit as well as for treating various ailments of mankind is blatant, with China being one of the pioneer nations to recognize the nutraceutical properties of this crop as evident from the account of traditional Chinese medicine. However, until now, litchi remains an inexhaustible source for research as far as its pharmacological activities are concerned. There is a long way to go before we can exploit this wonder of nature and intensive research is indeed a paramount to identify various other bioactive compounds present and to unveil their mode of action thus enabling them to be utilized for developing novel pharmaceutical products.

Moreover, many studies that are reported have been performed under *in vitro* conditions or in animals like mice, rats or hamsters, the metabolic pathways of whose are not exactly similar to that of humans. Thus, further clinical research is essential to explore the beneficial effects of different litchi extracts on humans. This review presents brief information on the biological activities of litchi along with litchi seeds and pericarp which are discarded by people as well as are byproducts in litchi processing industries. The exploitation of nutraceutical properties of these byproducts can be an outstanding example of waste utilization. However, before they can be used in modern medicine, verification of their safety and clinical trials is highly recommendable. It is

anticipated that this review will serve as a source of preliminary information for understanding the potential of litchi as a medicinal plant in relation to its biological properties. Nevertheless, a comprehensive understanding of action mechanism of various bioactive constituents that have been discovered in litchi and establishment of a correlation between the pharmacological activities and medicinal uses will indubitably be the thrust of future research.

Conflict of Interest

We have no conflicts of interest to disclose.

Authors' Contributions

NP conceptualized, critically reviewed the research articles and wrote the manuscript. HM revised the manuscript critically for important intellectual content and equally contributed in the preparation of Manuscript.

References

1 Menzel C M, The pattern and control of reproductive development in lychee: a review, *Sci Hortic*, 22 (4) (1984) 333-345.

2 Zhang Z W, China, the native home of litchi, In: Zhang Z W, Yuan P Y, Wang B Q, Qiu Y P & Li J S (eds) Litchi: Pictorial Narration of Cultivation, Pomology Research Institute, Guangdong Academy of Agricultural Science, China, 1997, p. 12–17.

3 Sarkar T, Nayak P & Chakraborty R, Litchi (Litchi chinensis Sonn.) products and processing technologies: An Update, *Ambient Sci*, 5 (2018) 11–16.

4 Mir H & Ahmad F, Enzymatic browning in litchi (*Litchi chinensis* Sonn.), In: *Litchi Global Perspectives*, Vishal Nath, M. Feza Ahmad, H. Mir, *et al.* (eds.), Bihar Agricultural University, Sabour, 2016, p. 1-6.

5 Faramarzi S, Pacifico S, Yadollahi A, Lettieri A, Nocera P, *et al.*, Red-fleshed apples: Old autochthonous fruits as a novel source of anthocyanin antioxidants, *Plant Food Hum Nutr*, 70 (2015) 324–330.

6 Obrosova I G, Chung S S & Kador P F, Diabetic cataracts: mechanisms and management, *Diabetes Metab Res Rev*, 26 (2010) 172–180.

7 Prasad K N, Yang B, Yang S Y, Chen Y L, Zhao M M, *et al.*, Identification of phenolic compounds and appraisal of antioxidant and antityrosinase activities from litchi (*Litchi chinensis* Sonn.) seeds, *Food Chem*, 116 (2009) 1–7.

8 Wang X, Yuan S, Wang J, Lin P, Liu G, *et al.*, Anticancer activity of litchi fruit pericarp extract against human breast cancer *in vitro* and in vivo, *Toxicol Appl Pharmacol*, 215 (2006) 168-178.

9 Xiao L Y, Zhang D, Feng Z M, Chen Y W, Zhang H, *et al.*, Studies on the antitumor effect of lychee seeds in mice, *J Tradit Chin Med*, 27 (2004) 517–518.

10 Xu X, Xie H, Hao J, Jiang Y & Wei X, Flavonoid glycosides from the seeds of *Litchi chinensis*, *J Agric Food Chem*, 59 (2011) 1205–1209.

11 Ogasawara J, Kitadate K, Nishioka H, Fujii H, Sakurai T, *et al.*, Oligonol, A new lychee fruit derived low molecular form of polyphenol, enhances lipolysisi in primary rat adipocytes through activation of the ERK1/ pathway, *Phytother Res*, 23 (2009) 1626–1633.

12 Kundu J K, Choi K S, Fujii H, Sun B & Surh Y J, Oligonol, a lychee fruit-derived low molecular weight polyphenol formulation, inhibits UV B-induced cyclooxygenase-2 expression, and induces NAD (P)H: quinine oxidoreductase-1 expression in hairless mouse skin, *J Funct Foods*, 1 (2008) 98-108.

13 An K P, Athar M, Tang X, Katiyar S K, Russo J, *et al.*, Cyclooxygenase-2 expression in murine and human nonmelanoma skin cancers: Implications for therapeutic approaches, *Photochem Photobiol*, 76 (2002) 73–80.

14 Yao P F, Gao Y, Simal-Gandara, J, Farag M A, Chen W, *et al.*, Litchi (Litchi chinensis Sonn.): A comprehensive review of phytochemistry, medicinal properties and product development, Food Func, 12 (2021) 9527-9548.

15 Shukla R K, Painuly D, Porval A & Shukla A, Proximate analysis, nutritive value, total phenolic content and antioxidant activity of *Litchi chinensis* Sonn, *Nat Prod Ind J*, 8 **(**2012**)** 361–369.

16 Gupta S K, Pharmacology and Therapeutics in the New Millennium, Narosa Publishing House, New Delhi, 2001.

17 Zhao L, Wang K, Wang K, Zhu J & Hu Z, Nutrient components, health benefits, and safety of litchi (Litchi chinensis Sonn.): a review, *Compr Rev Food Sci Food Saf*, 19 (4) (2020) 2139-2163.

18 Castellain R C, Gesser M, Tonini F, Schulte R V, Demessiano K Z, *et al.*, Chemical composition, antioxidant and antinociceptive properties of *Litchi chinensis* leaves, *J Pharm Pharmacol*, 66 (2014) 796-1807.

19 Obrosova I G, Chung S S & Kador P F, Diabetic cataracts: mechanisms and management, *Diabetes Metab Res Rev*, 26 (2010) 172–180.

20 Pandey R M & Sharma H C, The litchi ICAR. New Delhi, India, 1989 1–79.

21 Ahmad S A & Sharma S C S, Fruit & Vegetable Juice Therapy. Pustak Mahal, New Delhi, India, 2001.

22 Lim T K, Edible Medicinal and Non-Medicinal Plants. 6, Fruits. Springer Science & Business Media B V, Dordrecht, Netherlands, 2013 p. 45–58.

23 Miller L, Ayurvedic Curative Cuisine for Everyone. Lotus Press, Twin Lakes, USA, 2011 p. 79–82.

24 Parihaar R S, Bargali K & Bargali S S, Diversity and uses of ethno-medicinal plants associated with traditional agroforestry systems in Kumaun Himalaya, *Indian J Agric Sci*, 84 (12) (2014) 1470–1476.

25 Bhalla-Sarin N, Prasad U S, Kantharajah A S & Jain S M, Micropropagation of litchi (*Litchi chinensis* Sonn.), *Micropro Woody Trees Fruits*, 75 (2003) 721–731.

26 Bhoopat L, Srichairatanakool S, Kanjanapothi D, Taesotikul T, Thananchai H, *et al.*, Hepatoprotective effects of lychee (*Litchi chinensis* Sonn.): A combination of antioxidant and anti-apoptotic activities, *J Ethnopharmacol*, 136 (2011) 55–66.

27 Besra S E, Sharma R M & Gomes A, Anti-inflammatory effect of petroleum ether extract of leaves of *Litchi chinensis* Gaertn, (Sapindaceae), *J Ethnopharmacol*, 54 (1996) 1–6.

28 Mutha A, Dsouza M R & Bhat V, Evaluation of pharmacological activities of seed and pericarp of *Litchi chinensis* Sonn, *Int J Eng Sci Res*, 6 (1) (2018) 2347-6532.

29 Wang Y J, Zhao D X, Gao J L & Peng Z Q, Volatile components of *Litchi chinensis* Sonn. leaf oil extracts obtained by simultaneous distillation extraction, *J Essent Oil Bear Pl,* 16 (2013) 161-165.

30 Kilari E K & Putta S, Biological and phytopharmacological descriptions of *Litchi chinensis*, *Pharmacogn Rev,* 10 (19) (2016) 60-65.

31 Zhou Y, Wang H, Yang R, Huang H, Sun Y, *et al.*, Effects of *Litchi chinensis* fruit isolates on prostaglandin E2 and nitric oxide production in J774 murine macrophage cells, *BMC Complemen Altern Med,* 12 (2012) 20–28.

32 Yang B, Prasad K N & Jiang Y, Structure identification of a polysaccharide purified from litchi (*Litchi chinensis* Sonn.) pulp, *Carbohyd Polym,* 137 (2016) 570–575.

33 Ibrahim S R M & Mohamed G A, *Litchi chinensis*: medicinal uses, phytochemistry, and pharmacology, *J Ethnopharmacol,* 174 (2015) 492–513.

34 Zheng G, Yi Z, Zhang J & Zhong D, Studies on the anti-oxidative effect of extract from mature and premature litchi pericarp, *Nat Prod Res Dev,* 15 (2003) 341.

35 Sarni-Manchado P, Le Roux E, Le Guerneve C, Lozano Y & Cheynier V, Phenolic composition of litchi fruit pericarp, *J Agric Food Chem,* 48 (2000) 5995.

36 Ma Q, Xie H, Li S, Zhang R, Zhang M, *et al.,* Flavonoids from the pericarps of *Litchi chinensis*, *J Agric Food Chem,* 62 (2014) 1073-1078.

37 Gong Y, Fang F, Zhang X, Liu B, Luo H, *et al.*, B Type and Complex A/B Type Epicatechin Trimers Isolated from Litchi pericarp Aqueous Extract Show High Antioxidant and Anticancer Activity, *Int J Mol Sci,* 19 (2018) 301; doi:10.3390/ijms19010301

38 Govindarajan R, Vijayakumar M & Pushpangadan P, Antioxidant approach to disease management and the role of 'Rasayana' herbs of Ayurveda, *J Ethnopharmacol,* 99 (2005) 165–178.

39 Septembre-Malaterre A, Stanislas G, Douraguia E & Gonthier M P, Evaluation of nutritional and antioxidant properties of the tropical fruits banana, Litchi, mango, papaya, passion fruit and pineapple cultivated in Réunion French Island, *Food Chem,* 212 (2016) 225–233.

40 Wang L, Lou G, Maa Z and Liu X, Chemical constituents with antioxidant activities from litchi (*Litchi chinensis* Sonn.) seeds, *Food Chem,* 126 (2011) 1081–1087.

41 Kong F, Zhang M, Kuang R, Yu S, Chi J, *et al.*, Antioxidant activities of different fractions of polysaccharide purified from pulp tissue of litchi (*Litchi chinensis* Sonn.), *Carbohyd Polym*, 81 (2010) 612–616

42 Chang Y, Yang D, Chiu C, Lin Y, Chen J, *et al.*, Antioxidative and anti- inflammatory effects of polyphenol-rich litchi (*Litchi chinensis* Sonn.)-flower- water extract on livers of high-fat-diet fed hamsters, *J Funct Foods*, 5 (2013) 44–52.

43 Al Shukor J N, Van Camp, G B, Gonzales D, Staljanssens K, Struijs M J, *et al.,*. Angiotensin-converting enzyme inhibitory effects by plant phenolic compounds: A study of structure activity relationships, *J Agric Food Chem,* 61 (48) (2013) 11832-11839.

44 Carey R M, The intrarenal renin-angiotensin system in hypertension, *Adv Chronic Kidney Dis,* 22 (3) (2015) 204-210.

45 Guerrero J L, Castillo, M. Quiñones, S. Garcia-Vallvé, L. Arola, G. Pujadas, *et al.* Inhibition of angiotensin-converting enzyme activity by flavonoids: Structure-activity relationship studies, *PLoS One*, 7 (11) (2012) e49493.

46 Velez J C Q, The importance of the intrarenal renin–angiotensin system, *Nat Clin Pract Nephrol,* 5 (2) (2009) 89-100.

47 Reichel M, Triani R, Wellhöfer J, Sruamsiri P, Carle R, *et al*., Vital characteristics of litchi (*Litchi chinensis* Sonn.) pericarp that define postharvest concepts for Thai cultivars, *Food Bioprocess Tech,* 6 (5) (2013) 1191-1206.

48 Kessy H N E, Wang K, Zhao L, Zhao M & Hu Z, Enrichment and biotransformation of phenolic compounds from litchi pericarps with angiotensin I- converting enzyme (ACE) inhibition activity, *LWT- Food Sci Tech,* 87 (2018) 301-309.

49 Fleischauer, A T, Simonsen N & Arab L, Antioxidant supplements and risk of breast cancer recurrence and breast cancer-related mortality among postmenopausal women, *Nutr Cancer*, 46 (2003) 15-22.

50 Nasaani I, Oh-Hara T, Feng W Y, Johnston J, Chan K, *et al.*, Blocking telomerase by dietary polyphenols is a major mechanism for limiting the growth of human cancer cells *in vitro* and in vivo, *Cancer Res,* 63 (2003) 824-830.

51 Zhao M, Yang B, Wang J, Liu Y, Yu L, *et al.*, Immunomodulatory and anticancer activities of flavonoids extracted from litchi (*Litchi chinensis* Sonn.) pericarp, *Int Immunopharmacol,* 7 (2007) 162–166.

52 Lin N, Xiao L Y & Pan J Q, Effects of semen litchi on the expressions of S180 and EAC tumor cells and Bax and Bcl-2 proteins in rats, *China Pharm,* 19 (2008) 1138–1140.

53 Xiong A H, Shen W J & Xiao L Y, Effect of semen litchi containing serum on proliferation and apoptosis of HepG2 cells, *J Chin Med Mater,* 31 (2008) 1533–1536.

54 Wen L, Wu D, Jiang Y, Prasad K N, Lin S, *et al.*, Identification of flavonoids in litchi (*Litchi chinensis* Sonn.) leaf and evaluation of anticancer activities, *J Funct Foods,* 6 (2014a) 555–563.

55 Wen L, He J, Wu D, Jiang Y, Prasad K N, *et al.*, Identification of sesquilignans in litchi (*Litchi chinensis* Sonn.) leaf and their anticancer activities, *J Funct Foods,* 8C (2014b) 26–34.

56 Lin Y, Chang J, Cheng S, Wang C, Jhan Y, *et al.*, New bioactive chromanes from *Litchi chinensis*, *J Agric Food Chem,* 63 (2015) 2472–2478.

57 Guo H, Luo H, Yuan H, Xia Y, Shu P, *et al.*, Litchi seed extracts diminish prostate cancer progression via induction of apoptosis and attenuation of EMT through Akt/GSK-3β signalling, *Sci Rep,* **7** (2017) 41656.

58 Thiesen, L C, Baccarin T, Fischer-Muller A F, Meyre-Silva C, Couto A G, *et al.*, Photochemoprotective effects against UVA and UVB irradiation and photosafety assessment of *Litchi chinensis* leaves extract, *J photochem photobiol,* 167 **(**2017**)** 200-207.

59 Ma Y L, Yan F, Wei W J, Deng, J, Li L, *et al.*, Litchi Seed Aqueous Extracts play a role in suppression of epithelial-mesenchymal transition, invasion and migration in breast cancer cells, *Cell Cycle,* 19 (2020) 317–325

60 Vanhorebeek I, Gunst J, Ellger B, Boussemaere M, Lerut E, *et al.*, Hyperglycemic kidney damage in an animal model of prolonged critical illness, *Kidney Int,* 76 (5) (2009) 512–520.

61 Man S, Ma J, Wang C, Li Y, Gao W, *et al.*, Chemical composition and hypoglycaemic effect of polyphenol extracts from *Litchi chinensis* seeds, *J Funct Foods,* 22 (2016) 313-324.

62 Kilari E K, Koratana R & Putta S, Effect of aqueous pericarp extract of *Litchi chinensis* on hypoglycemic and antihyperglycemic activities in normal and in streptozotocin induced diabetic rats, *Pharm Biol Eval,* 2 (1) (2015) 29-35.

63 Nishihira J, Sato-Ueshima M, Kitadate K, Wakame K & Fujii, H, Amelioration of Abdominal Obesity by Low-Molecular Weight Polyphenol (Oligonol) from Lychee, *J Funct Foods,* 1 (4) (2009) 341–348.

64 Noh J S, Park C H & Yokozawa T, Treatment with oligonol, a low-molecular polyphenol derived from lychee fruit, attenuates diabetes-induced hepatic damage through regulation of oxidative stress and lipid metabolism, *British J Nutr,* 106 (2011) 1013–1022.

65 Lv Q, Si M, Yan Y, Luo F, Hu G, *et al.*, Effects of phenolic-rich litchi (*Litchi chinensis* Sonn.) pulp extracts on glucose consumption in human HepG2 cells, *J Funct Foods,* 7 (2014) 621–629.

66 Fujii H, Nishioka H, Wakame K, Magnuson B A & Roberts A, Acute, subchronic and genotoxicity studies conducted with oligonol, an oligomerized polyphenol formulated fom lychee and green tea extracts, *Food Chem Toxicol,* 46 (2008) 3553-3562.

67 Yang S F, Tseng J K, Chang Y Y & Chen Y C, Flaxseed oil attenuates non-alcoholic fatty liver of hyperlipidemic hamsters, *J Agric Food Chem,* 57 (2009) 5078–5083.

68 Sugiyama H, Akazome Y, Shoji T, Yamaguchi A, Yasue M, *et al.*, Oligomeric procyanidins in apple polyphenol are main active components for inhibition of pancreatic lipase and triglyceride absorption, *J Agric Food Chem,* 55 (2007) 4604–4609.

69 Tzang B S, Yang S F, Fu S G, Yang H C, Sun H L, *et al.*, Effects of dietary flax seed oil on cholesterol metabolism of hamsters, *Food Chem,* 114 (2009) 1450–1455.

70 Saad S, Taher M, Susanti D, Qaralleh H & Awang A F, *In vitro* antimicrobial activity of mangrove plant *Sonneratia alba, Asian Pac J Trop Biomed,* 2 (6) (2012) 427–429.

71 Candido E S, Pinto M F, Pelegrini P B, Lima T B, Silva O N, *et al.*, Plant storage proteins with antimicrobial activity: novel insights into plant defense mechanisms, *FASEB J,* 25 (2011) 3290–3305.

72 Thevissen K, Kristensen H, Thomma B P H J, Cammue B P A & Francois I E J A, Therapeutic potential of antifungal plants and insect defensins, *Drug Discov Today,* 12 (2007) 966–972.

73 Shahwar D, Raza M A, Mughal M A S, Abbasi M A & Ahmad V U, Comparative study on the antioxidant and antimicrobial activities of stem-bark extract of *Litchi chinenesis* and its organic fractions, *J Chem Soc Pakistan,* 32 (3) (2010).

74 Bhat R S & Al-daihan S, Antimicrobial activity of *Litchi chinensis* and *Nephelium lappaceum* aqueous seed extracts against some pathogenic bacterial strains, *J King Saud Univ,* 26 (2014) 79–82.

75 Chauhan S, Kaur N, Kishore L & Singh R, Pharmacological evaluation of anti-inflammatory and analgesic potential of *Litchi chinensis* gaertn. (sonn.), *Int J Pharm Sci,* 6 (7) (2014) 116-119.

76 Jing Y, Huang L, Lv W, Tong H, Song L, *et al.*, Structural characterization of a novel polysaccharide from pulp tissues of *Litchi chinensis* and its immunomodulatory activity, *J Agric Food Chem,* 62 (2014) 902–911.

77 Mhatre S V, Bhagit A A & Yadav R P, Protenaceous pancreatic lipase inhibitor from the seed of litchi chinensis, *Food tech Biotech* 57 (2019) 113-118.

78 Koray M, Ak G, Kurklu E, Tanyeri H, Aydin F, *et al.*, The effect of beta-glucan on recurrent aphthous stomatitis, *J Altern Complement Med,* 15 (2) (2009) 111–112.

79 Sung Y Y, Yang W K & Kim H K, Antiplatelet, anticoagulant and fibrinolytic effects of *Litchi chinensis* Sonn. extract, *Mol Med Rep,* 5 (2012) 721–724.

80 Basu S, Haldar N, Bhattacharya S, Biswas S & Biswas M, Hepatoprotective activity of *Litchi chinensis* leaves against paracetamol-induced liver damage in rats, *Eur J Sci Res,* **7** (2012) 77–81.

81 Yao Y, Liu T, Yin L, Man S, Ye S, *et al.*, Polyphenol-Rich Extract from Litchi chinensis Seeds Alleviates Hypertension-Induced Renal Damage in Rats, *J Agri Food Chem,* 69 (7) (2021) 2138-2148.

82 Shrivastava A, Srikantiah P, Kumar A, Bhushan G, Goel K, *et al.*, Outbreaks of unexplained neurologic illness-Muzaffarpur, India, 2013-2014, *Morb Mortal Wkly Rep,* 64 (2015) 49–53.

83 Bandyopadhyay B, Chakraborty D, Ghosh S, Mishra R & Rahman M, Epidemiological investigation of an outbreak of acute encephalitis syndrome (AES) in Malda district of West Bengal, India, *Clin Microbio,* 4 (2015) 181. DOI: 10.4172/ 2327-5073.1000181.

84 Nath V, Sharma S & Barman K, Acute Encephalitis Syndrome and its alleged litchi (*Litchi chinensis*) connection—A review and status, *Indian J Agric Sci,* 86 (3) (2016) 283–290.

85 Queiroz E, de R, de Abreu C M P, Rocha D A, Simao A A, *et al.*, Anti-nutritional compounds in fresh and dried lychee fractions (*Litchi chinensis* Sonn.), *Afr J Agric Res* 10 (6) (2015) 499-504.