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# Health perks of litchi seed: A systematic review

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**Abstract**
Litchi fruit has been grown commercially throughout tropical and subtropical regions of the world for its sweet, juicy, and nutritious arils, litchi fruit is a member of the *Sapindaceae* family. Litchi seeds are discarded as waste when litchi fruit is processed into jellies, wine, and squash. The phytochemicals (flavonoids), carbohydrates (starch), oil (high unsaturated fatty acids), and proteins (bioactive peptides) found in seeds are surprisingly extensive. There were five different kinds of polar solvents used to extract the seeds. The evaluation involved the use of five extracts: water extract (WE), methanol extract (ME), 50% methanol extract (50% ME), ethanol extract (EE), and 50% methanol extract (50% EE). Evaluation of antityrosinase activity, antioxidant capacity, and total phenolic content. Litchi seed can be an affordable medical food that also functions as a natural alternative treatment for type-2 diabetes. Litchi seeds have an oblong to concave form, measuring 1-3 cm in length and 0.6-1.2 cm in width. They have a dark brown or chocolate colour. For the food businesses, the enormous quantity of seeds used in the preparation of litchi presents an unsolvable challenge. In Chinese medicine, seeds have traditionally been utilized to treat pathogenic cold, discharge stagnant humor, and relieve pain associated with orchitis, neuralgia and testicular swelling, hernias, and stomach pain. As a result, litchi seeds may be employed as an active component in many pharmaceutical and culinary compositions. A good supply of proteins (4.93%), crude fibres (24.5%), oil content (3.2%), starch polysaccharides (40.7%), and minerals (magnesium: 0.28%, calcium: 0.21%, phosphorus: 0.11%) is litchi seed. A newer source of starch for culinary applications is litchi seeds. The development of litchi seeds as a novel and potential ingredient for its numerous culinary and other application is also clarified by this thorough systematic review.

**Keywords:** Pharmaceutical, *Sapindaceae* family, food waste

## Introduction
Growing widely from tropical to subtropical regions of the world, litchi (*Litchi chinensis*), one of the major fruit crops, is a member of the sapberry family (*Sapindaceae*).Despite the fact that water makes up 76-71% of the fruit, litchi is a superfruit due to the presence of bioactive compounds (phenolics/antioxidants), minerals (P, Fe, Ca), vitamins (thiamine, niacin, riboflavin, vitamin C), sugars (glucose, fructose, sucrose), fats, protein, and flavoring agents (limonene, geraniol, neral) (Pareek, 2016) [1].Customers have come to embrace it bit by bit, and it is now quite well-liked on the global market. The fruit has multiple uses, including direct consumption and the production of juice, vinegar, jelly, and wine (Alves *et al*., 2011; Saxena *et al*., 2011) [2, 3]. Processing method improvements have decreased post-harvest losses of litchi while simultaneously creating new job opportunities and raising farmer incomes. In addition, the current generation of litchi waste, which includes seeds (10–20% depending on variety) and pericarp (15%), has created serious issues for the processing companies' ability to make profits as well as the environment. (Bhushan *et al*., 2015, 2019; Pandey & Sharma, 1989) [4, 5, 6].
Litchi seeds are rectangular to concave in shape, measuring 1-3 cm long and 0.6-1.2 cm wide. They have a dark brown or chocolate color. The predicted overall production of litchi worldwide is ~2.7 million tons, with the potential to yield up to ~0.54 million tons of the seeds annually (Chen & Huang, 2012) [7]. For the food businesses, this enormous volume of seeds during the litchi preparation is an unsolvable issue. Chinese medicine has long utilized seeds to treat pathogenic cold, relieve stagnant humor, and ease the discomfort of orchitis, nerve pain, testicular swelling, hernias, and stomach aches (Guo *et al*., 2017; Zhu *et al*., 2019) [8, 9].

Litchi seeds' nutritional profile (polysaccharides, lipids, protein, minerals, and fibers) and phytochemical profile (described in section 2) make them a promising choice for functional food formulations. The use of litchi seeds in food is still in its early stages, and extracts are being studied for their potential health benefits.

Furthermore, a variety of pharmaceutical and food formulations may employ litchi seeds as an active ingredient. Litchi seed is rich source of starch polysaccharides (40.7%), proteins (4.93%), crude fibres (24.5%), oil content (3.2%) and minerals (Magnesium: 0.28%; Calcium: 0.21%; Phosphorus: 0.11%) (Anwar, Mahmood, Mehmood, & Aladedunye, 2014; Koul & Singh, 2017) [10. 11]. Litchi seed is an emerging alternative to starch for food applications since it is an unconventional source and is more readily available as industrial waste. According to Jaiswal & Kumar (2015) [12], starch has a better purity when separated and exhibits superior thermal stability, water holding capacity (WHC), and structural morphology. This suggests that the food sector may use it. Lichi seed's fatty acid composition showed the presence of palmitic acid (12%), linoleic acid (27%), linolenic acid (11%), and cyclo propanoic acid (42%) (Ding, 1999). Researchers have discovered that the crude saponins and sterol derivatives present in litchi seeds play a part in membrane dynamics and other biological activities (Koul&Singh, 2017) [11]. The proteins derived from litchi seeds contain all the essential amino acids. However, two unique amino acids called α-methylenecyclopropyl glycine (α-MCPG) and hypoglycin A (HGA) limit the use of litchi seeds in food because they have a hypoglycemic effect on humans(Ding,1999) [13].Extracts from litchi seeds have shown a variety of bioactivities, including anti-inflammatory, anti-hyperlipidemia, anti-inflammatory, anti-diabetic, anti-diabetic, anti-microbial, and anticancer (liver, colorectal, lung, and nasal cavity malignancies)(Guo *et al*., 2017) [8]. The remarkable composition of polysaccharides, antioxidants, fatty acids, and protein found in litchi seeds makes them a good option for use in the creation of functional meals. For instance, by preventing lipid peroxidation and adipogenesis, the watery extract of litchi seeds functions as a natural addition and improves the safety and quality of meat paste (Qi, Huang, Huang, Wang, & Wei, 2015) [14].

This review highlights nutritional and phytochemical esteem of the litchi seeds with an aim to improve its utilization as pharmaceutical uses in health cures. Further, the biological activities of litchi seed extract (LSE) and application of litchi seed as a functional ingredient in the foods will be comprehensively discussed.

## The scenery of lychee seeds

Ancient Chinese medicine recognized the amazing therapeutic properties of lychee seed, which is the mature, dry seed of *Litchi chinensis* Sonn. The lychee seed has a pleasant, sweet flavor and the potential to be a useful thirst-quencher. Several Chinese-patented medications, include Jinlida granule (Tian *et al*., 2018) and Jiangtangtongmai pills (Su *et al*., 2017), which were authorized by the Chinese Food and Drug Administration, were utilized in clinical settings to treat diabetes.

## Pharmacology

### Improving Insulin Resistance

One of the main factors contributing to the development of type 2 diabetes mellitus is insulin resistance (IR), a pathological state characterized by the inability of insulin to induce glucose elimination (Brown and Walker, 2016) [17]. While the exact pathophysiology of insulin resistance (IR) in diabetes mellitus remains unclear, recent theories suggest that endoplasmic reticulum stress, mitochondrial dysfunction, oxidative stress, inflammatory response, and insulin receptor mutations could be the underlying processes (Yaribeygi *et al*., 2019) [18]. An intragastric injection of a lychee seed water extractant significantly reduced hyperinsulinemia and increased insulin sensitivity in the glucose tolerance test (Guo *et al*., 2003a) [19]. The lychee seed extract group's insulin resistance index was much lower than that of the control group, which gradually raised the insulin sensitivity index (Man *et al*., 2016) [20]. Studies conducted *in vitro* have verified that the active ingredients in lychee semen can considerably lower the mRNA expression of glucose regulatory protein 78, which is involved in endoplasmic reticulum stress and unfolded protein response (UPR) activation (Liao *et al*., 2014; Li *et al*., 2015). By decreasing the levels of TNF-α, hyper-leptinemia, and FFA (free fatty acid) in diabetic rats, lychee seed extracts may enhance insulin sensitivity (Guo *et al*.,2004) [3].

### Anti-cancer properties

Cancer is a prevalent and major cause of death and illness worldwide, with an estimated 9.6 million deaths from the disease in 2018 (WHO, 2018). A growing body of pharmacological research indicates that Litchi seed extracts can prevent the growth of metastatic tumors and may have anticancer properties (Hsu *et al*., 2012; Emanuele *et al*., 2018) [25, 26]. Both *in vitro* and *in vivo*, litchi seeds showed anti-prostate cancer capabilities, with flavonoid chemicals being the most prevalent chemical component (Guo *et al*., 2017) [8]. Many data from investigations on human and animal cell lines have demonstrated that using litchi seeds or their therapeutic components exhibits the anti-tumor activities towards various cancers by influencing the proliferation, apoptosis, autophagy, metastasis, chemo-therapy and radiation therapy sensitivity, stemness, metabolism, angiogen- esis, and immunity via multiple targeting (Wang, 2011) [27], lung (Chung *et al*., 2017) [28], and colorectal cancer (Emanuele *et al*., 2018) [26].

### Antioxidant activities

Living creatures rely heavily on oxygen for their energy metabolism. Oxygen-derived free radicals can cause a variety of lifestyle issues, including as diabetes, cardiovascular disease, neurological disorders, respiratory diseases, and cancer. Litchi seeds contain physiologically active components such as flavonoids, phenolics, and oligosaccharides, which can be used as a natural antioxidant to maintain health (Xu *et al*., 2011) [30], *In vitro* and *in vivo* studies support this claim (Prasad *et al*., 2009) [31]. According to Emanuele *et al*. (2018) [26], litchi seeds contain significant levels of ascorbic acid and β-carotene, which can be used as a natural source of antioxidants (PCA) (Queiroz, Abreu, Oliveira, Ramos, & Fraguas, ´ 2015) [32]. Litchi seeds contain a variety of bioactive chemicals, including four methyl jasmonate analogs, one lignanoside, and 15

flavonoids. The lignanoside and flavonoids show significant antioxidant potential (Dong, Huang, Wang, & He, 2019) [14].

**Neuroprotection**

Neurodegenerative illnesses cause irreversible neuron loss and protein deposition in the brain and peripheral organs, resulting in altered physiochemical properties (Kovacs, 2018) [34]. Litchi seeds play a significant function in neuroprotection, according to pharmacological research. An *in vivo* investigation suggested litchi seed saponins (LSS)inhibiting apoptosis improves cognitive performance and reduces neuronal damage in the hippocampus of AD rats (Rattus norvegicus) by decreasing caspase-3 mRNA expression, Bax protein expression, and increasing Bcl-2 protein expression (Wang *et al*., 2017a) [16].

**Efforts to reduce obesity and cholesterol**

Obesity is a significant epidemiologic concern in both developed and developing countries. Hyperlipidemia is a medical disorder that can lead to obesity and other related problems. It is characterized by elevated levels of triacylglycerols, total cholesterol, and LDL, as well as decreased HDL (Chen *et al*., 2014) [36]. Litchi seeds' potential to reduce lipid levels in high-fat rat models is due to their high unsaturated fatty acid profile and saponin content (Guo *et al*., 2003) [19].

Litchi seed protein inhibited pancreatic lipase across a pH range of 3 to 8, with a maximum activity of 59% at pH 8. Minimum at pH 3 (23%). In 3T3-L1 preadipocyte cells, aqueous LSE (200 μ g/mL) helps prevent obesity by inhibiting adipogenesis-related genes like CCAAT/enhancer binding proteins α (C/EBP α), C/EBP β, C/EBP δ, peroxisome proliferator-activated receptors (PPARγ), and Krüppel-like factor 9 (KLF9) (Qi *et al*., 2015) [14]. Almeida *et al*. (2018) [37] found that adding litchi seed flour to a high-calorie meal reduced visceral adipose tissue mass and helped maintain body weight.

**Kidney protective influence**

Diabetic kidney disease (DKD), a severe microvascular consequence of diabetes, is the leading cause of end-stage renal failure and the biggest predictor of mortality in diabetic patients(Reidy *et al*., 2014; Thomas *et al*., 2016) [38, 39].Strict glycemic management significantly lowers DKD morbidity, indicating that metabolic abnormalities caused by hyperglycemia, particularly alterations in energy use and mitochondrial damage, play a crucial role in disease progression(Reidy *et al*., 2014) [38]. Lychee seed saponin can reduce blood glucose levels and improve kidney damage in diabetic nephropathy model rats by suppressing inflammatory factors and reducing inflammation in renal tissue (Qin,2017) [40].

**Security of Food and Regulations**

Litchi seeds contain high levels of cyclopropanoic fatty acids, including dihydrosterculic acid (cis-9, l0-methyleneoctadecanoic acid) (41-60%), and 2-hexyl-cyclopropaneoctanoic acid (cis-7,8-methylenehexadecanoic acid) (2.3-4%) (Gontier *et al*., 2000; Ahmad *et al*., 2017; Jie & Chan, 1977).Litchi seeds contain varied concentrations of MCPG and hypoglycin A (HGA), which are important indicators for assessing their safety as a nutraceutical source. Gray and Fowden discovered MCPG, a powerful hypoglycemic amino acid, from litchi kernel in 1962.MCPG metabolizes to MCPF-CoA, a hazardous molecule that disrupts fatty acid β-oxidation and has hypoglycemic properties(Ding, 1999) [13].Litchi seeds contain toxic amino acids that inhibit gluconeogenesis and fatty acid β-oxidation, resulting in hypoglycemia in animal models and rendering them unsuitable for human intake (Spencer & Palmer, Sander, Terhardt, Sander, & Janzen). Optimize the percentage of litchi seeds as a health ingredient in food or pharmaceutical formulations based on the levels of MCPG and HGA.

Excessive amounts of litchi seed or aril may be hazardous to humans. HGA has a maximum tolerant dose (MTD) of 1.5 mg/kg for rats weighing 230 g and 0.22 mg/kg for humans weighing 60 kg. Consumption of more than 13.2 mg of HGA may result in acute toxic encephalopathy. However, no estimates for MCPG are available at this time (Blake, Bennink, & Jackson, Yang).

**Conclusion**

This review focuses on the safety, health advantages, and nutritional makeup of litchi seed. The review also demonstrated that the litchi fruit's seed remnants likewise have a superior composition of bioactive polysaccharides, peptides, and PCs, with a higher concentration of healthy unsaturated fatty acids.

It is clear that multidisciplinary research intervention has made it easier to turn waste litchi seed into a nutritious product for the pharmaceutical sector. Furthermore, not enough information is available regarding the different chemicals from litchi seeds' bioavailability in the human body. There are a few things to think about when conducting lychee seed research in this area.

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