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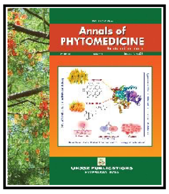

Review Article : Open Access

Exploring the nutritional value and therapeutic potential of Guava (*Psidium guajava* L.) seeds and leaves: Bioactive compounds and their industrial applications

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Abstract

Guava is a highly nutritious fruit rich in vitamins, minerals and fibre, enabling it to thrive in various soil conditions, making it economically significant. Peels and seeds are the primary by-products produced by the processing sector, of which seeds contain significant amounts of dietary fibre, protein, lipids, essential vitamins and minerals. The leaves of guava plants were explored for their curative properties, which are associated with antidiabetic, antidiarrheal, anticancer, lipid-lowering, and antimicrobial effects. The current review provides an in-depth discussion on medicinal uses and phytochemicals present in guava leaves as well as in seeds, including essential nutrients, polysaccharides, amino acids and secondary metabolites. Further, various bioactivities of the guava seed and leaf concentratesare addressed as well. Considering the presence of phytoconstituents, the industrial applications of guava seed and leaves such as functional food additives due to their nutrient content and incorporation in different food systems like herbal teas, jellies, beverages, chocolates and act as potential dietary supplement to livestockare discussed. The fermented guava seeds and dried leaves serve as biofilm agents aiding in food preservation, while the seed oil provides biosurfactants with environmental benefits. The findings of this review suggest that guava seeds and leaves, rich in bioactive compounds, hold significant potential as versatile ingredients in the development of functional foods, biopolymer films, and moisture-absorbing materials. Their incorporation can enhance the nutritional value, antioxidant capacity, and antimicrobial properties of the final products.

1. Introduction

Guava (*Psidium guajava* L.) often referred to as the"Apple of tropics" belongs to thefamily Myrtaceae, which comprises about 140 genera and 3800 to 5650 species (Rajan and Hudedamani, 2019). It is mainly grown in tropical and semitropical regions of the world, specifically South America, Asia, followed by Australia (Singh and Tyagi, 2017). The crop has originated from Tropical America, the arearanging from Mexico to Peru, and it is currently grown in over 60 nations worldwide and its worldwide production is estimated to be around 40 million tons. India is the world's biggest guava producer, followed by China and Kenya (Angulo-López *et al*., 2021). Mexico ranks fifth in the world with a production of 302,718 tons per year, and an increase is expected due to a 5% increase in the harvested area; 4% of total production is exported, primarily to the United States and Canada. Tamil Nadu is one of the leading guava cultivating state. The crop has a great commercial value and in recent years it has gained a considerable importance due to its profitable trade and export earnings. It accounts around 1, 14,557 Hectares, more than 9, 51,411 metric tonnes. The major guava producing districts in Tamil Nadu include Villupuram, Salem, Tiruvannamalai, Krishnagiri, Dindigul, and Namakkal (Santhi *et al*., 2020). Guava is referred to be one of the intricate, highly nutritive, and monetarily beneficial crops. The fruit is also referred tothe "Poor man's apple" since it is a rich of source of vitamins A and B and is highly abundant in vitamin C (Kumari *et al*., 2020; Lakshmi *et al*., 2022).

Owing to its hardy nature, it can be grown even under neglected conditions. Recently, it has gained momentum due to its adaptability to a wide range of soil conditions, especially problematic soils such as saline, alkaline, and even clayey soils (Sahu *et al*., 2025). Three flowering seasons, *viz*. Ambe bahar, Mrig bahar, and Hatti or Hastha bahar have been reported in the peninsular regions of India (Jain *et al*., 2025). Guava fruits have great market potential due to their delicious taste, aroma, and sweet flavour, with a fine balance of acid, sugar, and pectin. It can be canned, preserved, or made into jam, jelly, and nectar (Kumari *et al*., 2017). Fruits and vegetable processing industries eliminate peel, pulp, and seed as residues which are highly nutritious with economic potential (Esparza *et al*., 2020). Guava

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seeds have been utilizedrelying on their dietary attributes. In addition to a diverse range of diverse range of metabolic and biological activities, Guava seeds are an idealresource of an array of health promoting compounds, such assugars, protein, fats, electrolytes, organic compounds, secondary metabolites, along with roughage (Kumar *et al*., 2022). Leaves and seeds of guava can make potential raw materials for the food and pharmaceutical industries, owing to the highly beneficial bioactive compounds present in them.

In several nations, the radicle, foliage, periderm, twigs, and berries from the guava tree were traditionally usedfor the treatment of various illnesses. Guava leaves and bark shreds are also considered to be waste while harvesting operations under commercial planting systems. Guava leaves have great potential due to their antispasmodic, cough relief, immunomodulatory, antidiarrheic, antihypertension, antihyperlipidaemic, and antihyperglycemic properties (Huynh *et al*., 2025). The application of extract from guava leaves as a substitute for conventional pharmaceuticals has also been documented in studies conducted on animal models.This study intends to address the multitude of nutritious and bioactive molecules, deciphering the molecular mechanisms of their pharmacological and therapeutic potential as well as their commercial applications to generate income from Guava seeds and leaves.

2. Nutritional profile

Guava seeds are around 6-12 % of fruit weight, which accounts for 30% of waste products from processing, own numerous health benefits and industrial properties (Sari Darmasiwi *et al*., 2018).The principal constituents in guava seeds include 11.7% fibre,7.6% lipids, 6.1% protein, and 1.20 % carbohydrates and other compounds including vitamins, minerals, and antinutritional factors (Barbalho *et al*., 2012). Among vitamins, guava seeds include high concentration of ascorbic acid followed by tocopherol, thiamine, along with riboflavin. Studies revealed that 85 g of guava seeds, either with fruit or in processed form, corresponds to all of the recommended per day consumption of vitamin C (about 90 g) (Haleem, 2016). With minimum amount of Zn, Fe, Mn, *etc*., it is composed of vital minerals ranging from K, Na, P, Ca, and Mg (El Anany, 2015).

Understanding the importance of sustainable usage of seeds and other fruit residues, it also comprises substantial quantities of antinutrients (Udousoro *et al*., 2013). The dehydrated seeds contain about 325.67 mg/100 g of tannins, 273.63 mg/100 g phytic acid, 43.77 (TIU-trypsin inhibitor unit /mg) trypsin inhibitors, and 6.93 mg per hundred g of oxalates accordingly (Thiyagarajan *et al*., 2024). They exist in notable quantities compared to other fruit parts, minimizing nutritional valuethrough the precipitation of minerals and the fermentation process. Strategies should be followed to reduce these antinutritional factors, such as dry heating, roasting, extrusion, autoclaving, infrared, and oil extraction for further processing act as effective alternatives, conferring stability.

Wide range of bioactive substances with nutritional advantages may be found in guava leaves (Sriram *et al*., 2023). Polysaccharides comprise long polymer chains, each unit made of mono-saccharides (Luo *et al*., 2019). Proteins are composed of amino acids as the structural units and have practical applications in growth, development, enzyme regulation, and plant defence signalling mechanisms. It has roughly 82.47 per cent ash, 0.62 per cent lipids, 18.53 % amino acids, 12.74 % starch, 103 mg/100 g of vitamin C, and 1717 mg of gallic acid equivalent /g polyphenols (Shabbir *et al*., 2020). Guava leaf extract is a good source of active elements, including Ca, K, Na, Fe, B, Mg, Mn, vitamin C, in addition to vitamin B (Thomas *et al*., 2017). Intake of guava leaves in processed form minimizes the risk of deficiency-related disorders such as hypocalcaemia, hypophosphatemia, and osteoporosis.

3. Phytoconstituents

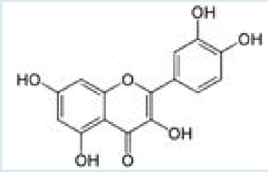
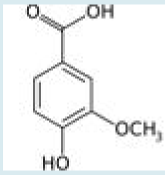
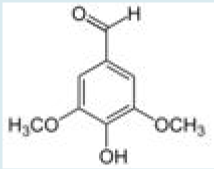
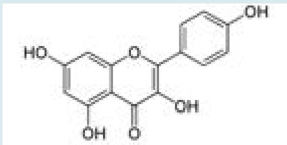
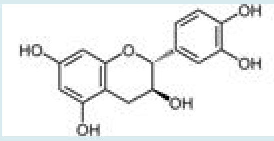
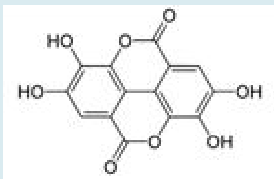
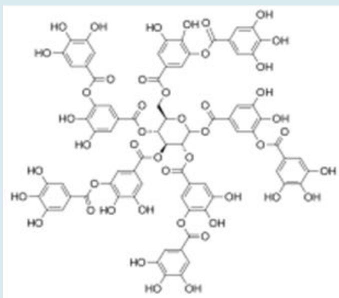
Various bioactive compounds wereanalysedfrom seeds of guava notably antioxidants such as vitamin C alongside dietaryfibre (soluble and insoluble form), carotenoids, flavonoids (monomeric flavanols, flavanols, bioflavonoids, neoflavanoids), tocopherols (γ-tocopherol, β-sitosterol) and other phenolic compounds (vanillic acid, vanillin), tannins, saponin and lipid compounds (Liu *et al*., 2018).

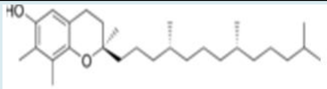
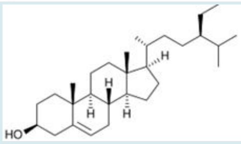
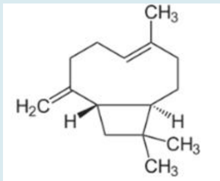
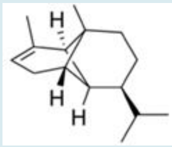
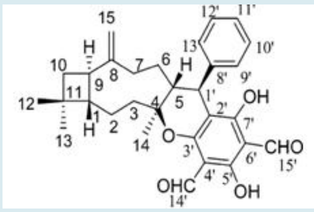
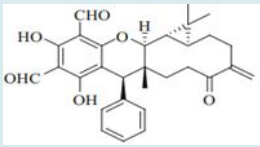
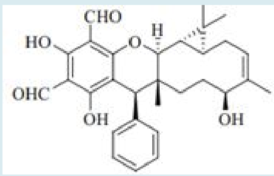
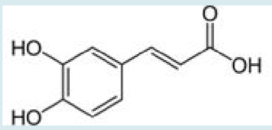
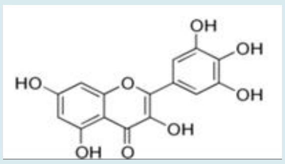
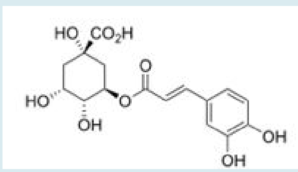
Phytoconstituents derived from guava seeds are available in the form of seed oil and are extracted using different organic solvents such as acetone, methanol, petroleum ether, n-hexane, and ethanol (Prommaban *et al*., 2019). Soxhlet extraction, solvent extraction, superficial extraction, microwave-assisted extraction, and ultrasound-assisted extractionare the methods generally followed to isolate phytochemical compounds (Narvaez-Cuenca *et al*., 2020). It was demonstrated that seed oil extract obtained using petroleum ether from solvent extraction offers 78.4% linoleic acid, 29.2 mg of tocopherols, and 92.3 mg of phenolic compounds per 100 grams (Malacrida and Jorge, 2013). Despite some limitations, organic solvents are not used for extraction owing to their noxious effects on well-beingandthe ecosystem. However, organic solvents, including ethyl alcohol, supercritical carbon dioxide, and ethyl acetate, might serve as eco-friendly solutions to recover guava seed oil (Lavenburg *et al*., 2021).

4. Therapeutic potential

As already discussed,guava seeds contains an immense amount of proteins (glutelin), polysac-charides, lipids, dietary fibre, vitamins, minerals, *etc*. (Kapoor *et al*., 2020; Ling and Chang, 2017). These compounds are dual action in nature exhibit metabolic activities and biological functions, and can reduce health risk factors. Guava seeds are stated to have antioxidant, antimicrobial, neuroprotective, and immunomodulatory effects (Da Silva Lima *et al*., 2019). Essential oils include trans-caryophyllene and eucalyptol, which correspond to a significant portion of guava leaves (Hassan *et al*., 2020). A diverse set of secondary metabolites had been identified such as phenol carboxylic acids, vitamin P, sugar derivatives, amine-like Substances, and sapogenin glycosides. Two new benzophenone galloyl glycosides, called as guavinoside A and B, one quercetin galloyl glycoside referred asguavinoside C, and five quercetin glycosides,were identified from guava leaf extracts (Li *et al*., 2020). The guava leaf extract in water comprises pyrogallol-5-carboxylic acid ,3,4-dihydroxycinnamic acid, 5-O-caffeoylquinic acid, cianidanol, epicatechol and epigallocatechin-3-gallate (Liu *et al*., 2014).The resulting nutraceuticals are estimated as well analysed using solid-state nuclear magnetic resonance (NMR) spectroscopy. The following sections put forward an extensive overview of these Phytoconstituents and their effects.

Table 1: Chemical structures of phytochemicals recognized in guava seeds and leaves

Classification	Phytoconstituents	Molecular structure	References
		Guava seeds	
Phenols	Quercetin		El-Sattar *et al.* (2020)
	Vanillic acid		Liu *et al.* (2018)
	Syringaldehyde		NarvaezCuenca *et al.* (2020)
Flavonoid	Kaempferol		Taha *et al.* (2019)
	Catechin		Chen *et al.* (2015)
Tannins	Ellagic acid		Haleem (2016)
	Tannic acid		Thiyagarajan *et al.* (2024)

Tocopherols	γ- tocopherol		Prommaban *et al.* (2020)
	β- sitosterol		Prommaban *et al.* (2020)
		Guava leaves	
Sesquiterpene	β-Caryophyllene		Hassan *et al.* (2020)
	Copaene		Chintagunta *et al.* (2019)
Monoterpenes	Guajadial		Huang*et al.* (2019)
	Psidiguajadiol		Zhang *et al.* (2022)
	Psiguadiol		Hou *et al.* (2019)
Phenols	Caffeic acid		Liu *et al.* (2014)
	Myricetin		Lorena *et al.* (2021)
	Chlorogenic acid		Wang *et al.* (2017)

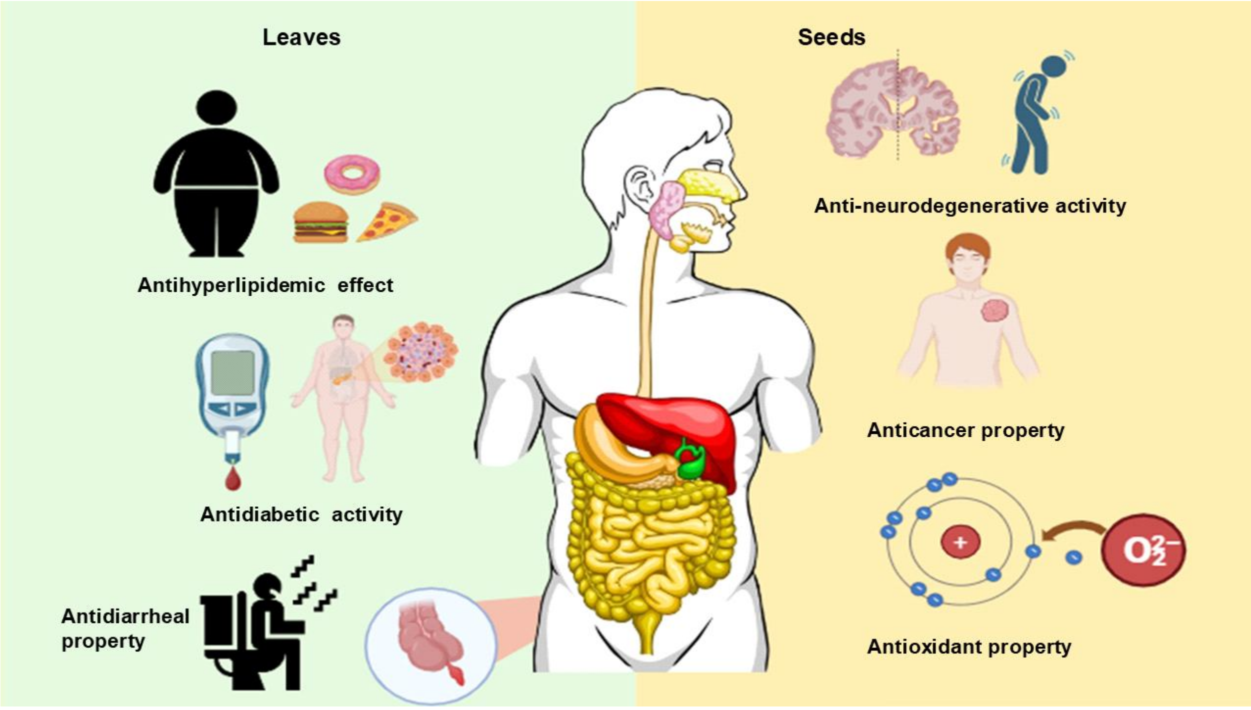


Figure 1: Pharmacological effects of Guava leaves and seeds (created in Biorender.com).

4.1 Antioxidant property

Oxygen is an indispensablecomponent for living beings, which contributes a crucial part in the respiration process and energy generation. However, Serious illnesses result in inflammatory processes, neurological disorders, hemochromatosis, respiratory problems, and acquired immune deficiency syndrome, which generate free radicals during respiration (Patlevic *et al*., 2016). The occurrence of reactive oxygen species (ROS) brings about oxidative damage, which retards the innate antibody system.The use of synthetic antioxidants inhibits free radical production, modifying human biological functions with a decrease in oxidative stress. Phenols are proven to have antioxidant properties, inhibiting cellular damage (Shahidi and Zhong, 2015). The guava seeds are rich in phenolic compounds of around 973.8 mg/100 g, including 4-hydroxy cinnamic acid, salicylic acid and 3,3',4',5,7-pentahydroxyflavone, which are primary phenolic compounds comprising hydrogen atom donating, reducing, singlet oxygen scavenging properties (El Sattar *et al*., 2020).

Phytoconstituents from guava seeds contains glucocyanidin, rhamnolutein, catechin, 3,4,5-trihydroxybenzoic acid, homogenistic acid, and norizalpin in revealed properties against cellular damage and cancer incidence (Chen *et al*., 2015). Lipids, polyphenols, in addition to phytosteroids of guava seeds macerated using the Soxhlet extraction method, serving as guava seed oil, reduce the serum phospholipid levels and oxidative stress, exhibiting antioxidant properties (Prommaban *et al*., 2020). It has been stated that metabolites produced during the fermentation of seeds with *Lactobacillus* might contain antioxidant properties because of inhibition of ROS generation and protection against lipid peroxidation (De Oliveira *et al*., 2020). Overall, the findings reveal that seeds have greater free radical scavenging ability than fruit pulp, with an emphasis on the recovery of fruit leftovers to develop as functional food ingredients.

Gallate, meletin, rhamnolutein, ellagic acid, methoxy cinnamic acid, isoquinoline, and corilaginoline are reported to be the predominant constituents in guava leaves liable to antioxidant properties (Taha *et al*., 2019). The free radical scavenging ability of concentrates from guava leaves was correlated with its phenolic concentration, of quenched free radical production, since bound phenols were insoluble. Yeast and bacterial strains were used to co-ferment guava leaves with anticipation of inhibiting autoxidation with presence of polyphenol constituents (Wang *et al*., 2017). Polysaccharides present in guava leaves havea protective effect against oxidative stress triggered by H_2O_2, impeding ROS generation, decreasing lipid peroxidation and cell death (Kim *et al.* 2016).

4.2 Anticancer activity

Cancer is a multifaceted health ailment in response to various extrinsic and intrinsic factors that contribute to the abnormal synthesis of ROS. According to the World Health Organization, cancer is one of the most prevalent causes for mortality worldwide (Chanu and Singh, 2022; Didkowska and Koczkodaj, 2022). The significant cytotoxic effects in humans lead to an imbalance between antioxidants and ROS. The presence of singlet unpaired electrons and radicals trigger ROS generation, resulting in disruptions in metabolic activity, mitochondrial dysfunction, peroxisome activity, and oncogenic processes (Ganesh and Massague, 2021). This can lead to single nucleotide polymorphism, genotoxicity and reorganisation, DNA-protein crosslinks, as well as DNA repair, along with lipid peroxidation that compromises cell membrane integrity and promotes tumour development. The production of oxidases, cyclooxygenases, lipases, lipoxygenases, and thymidine phosphorylase affects immune cells. The detrimental effects of radiation and chemotherapy, alongside the advancement of multidrug efficacy, highlight the need for non-toxic and safe treatment options for cancer patients (Mokhtari *et al.*, 2017).

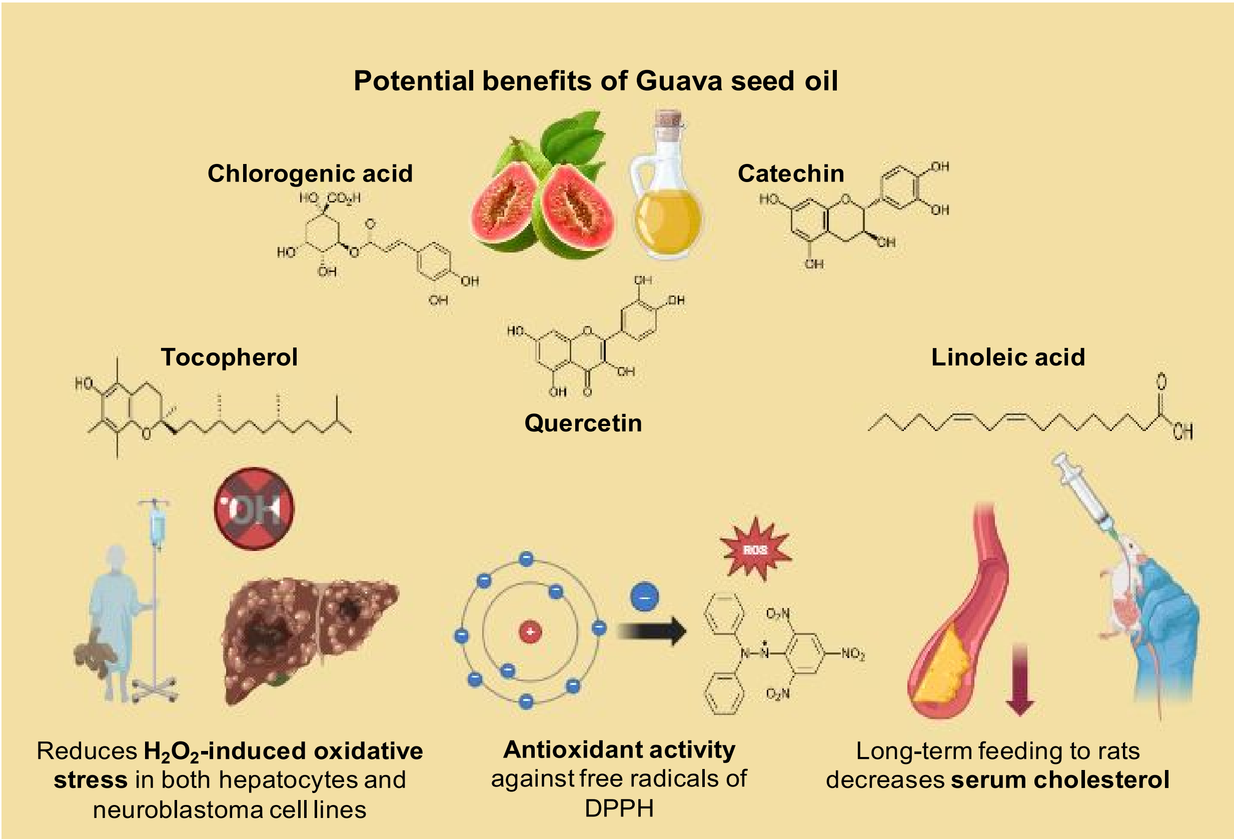


Figure 2: Bioactive compounds present in Guava seed oil (created in Biorender.com).

The immunomodulatory function of guava seed extract in the context of cytokine secretion ratio wasused to study its impactin inhibiting the growth of prostate cancer (PC-3) and breast cancer (MCF-7) cells, increasing the efficiency of the immune system recognising the existence of splenocytes and macrophages (Lin and Lin, 2017). Further research was done, and it was identified that modification of apoptotic proteins (Bcl-2 and Fas) had direct action on cancer cells, and cytokine secretion profiles had indirect action. The proportion of Bax (proapoptotic) and Bcl-2 (Antiapoptotic), decides the action of cancer cells. The gene expression of Fas mRNA belonging to the death receptor family also leads to apoptosis of cancer cells (Lin and Lin, 2020c).

The concentrated extract of guava seed oil from n-hexane comprises lipophilic compounds such as linoleic acids, tocotrienols, tocopherols, and phenolics that suppress K-562 cellular multiplication in a dose-modulated way with 50 per cent of inhibitory concentration (IC_{50}) ranges of 155 and 137 µg/ml measured 24 and 48 h later (Prommaban *et al.*, 2019). The semi-purified fractions of ethyl acetate extract containing phenolics was evaluated with the colorimetric analysis and exhibited a superior cytotoxic effect against hepatocellular carcinoma with the dosage around 200 µg/ml, with an IC_{50} of 75.5 µg/ml (Mahmoud *et al.*, 2024). The phytoconstituents possessing anticancer properties such as monoterpenoids, triterpenoids, sesquiterpenoids, astringents, psiguadials, volatile oil compounds, flavonoids, benzophenone glycosides, and miscellaneous quinones (Jiang *et al.*, 2020). The study has reported that Psiguadial D restricts human hepatoma cells (Hep G2) and protein tyrosine phosphatase (PTP 1B). The antitumor effects of guava leaves showed that compounds such as terpenoids and flavonoids regulate the immune system, and suppress signal transfer mechanism, adhesion of tumour cells, and angiogenesis, inhibiting the outbreak of cells (Biswas *et al.*, 2019). Angiogenesis refers to the process of the formation of blood vessels from previously established ones related to the growth of tumour cells. Prolonged angiogenesis leads to the growth of tumour cells and means of cellular waste disposal (Correa and Couto, 2016).

Phytoingredients such as β-caryophyllene, flavonoids (apigenin), and tocopherols present in guava leaves has been identified to possesscell growth inhibition properties against human colon carcinoma cell strains, CaCo2, HT-29, and SW-480. The β-caryophyllene contributes to its synergistic effect with HIF-1α, influencing metabolic functions and biochemical pathways related to oxygen deprivation, the dissemination of tumours, and negatively impacting cancer-mediated angiogenesis (Lok *et al.*, 2020). HIF-1α is also associated with the transcription of vascular endothelial growth factor (VEGF) alongside β-caryophyllene, indicating anticolorectal cancer properties. Researchers have reported that guajadial compounds present in guava leaves alleviate cancer disorders through their significant effects on estrogen receptors, triggering apoptosis by mitigating DNA replication and restricting cells in the G1 phase (Huang *et al*., 2019). Phytoconstituents such as prunol, prunetol, apigenol and biflavonoids found in guava leaves exhibit prominent effects by inhibiting cyclin-dependent kinases (CDK-2,6), cholecalciferol receptor, scatter factor receptor, transmembrane receptor, progesterone receptor, glitazone reverse insulin resistance receptor and T-cell growth factor. These compounds are responsible for tumour hypertrophy, angiogenesis, tumour adhesion, and the depletion of the extracellular matrix.

4.3 Antimicrobial activity

Several plant defence mechanisms are exhibited, either localized or systemic resistance to confer the incidence of pathogens, *i.e.,* viruses, bacteria, fungi, and mycoplasma-like organisms.The frequency of systemic microbial infections and their epidemiological rates, such as bacteraemia, pyelonephritis, spinal fever, pneumonitis, and stomach inflammation, significantly affect the entire human system, leading to global mortality (Ahmed *et al*., 2024). Microorganisms include *Staphylococcus, Shigella, Salmonella, Bacillus, Clostridium,* and *Pseudomonas* are causes of pathogenicity for food poisoning worldwide. The biochemical and genetic pathways involve the upregulation of differentially expressed genes, pathogenesis related PR-proteins, hypersensitive response, and induction of systemic-induced resistance (Hughes and Andersson, 2017). Establishing multi-drug notified to resolve the constraints of multi-drug resistance (Adamczak *et al*., 2019; Rossiter *et al*., 2017). Phytoconstituents derived from natural resources demonstrate their accountable antimicrobial properties by restricting microbial cell wall development, impeding biofilm formation, suppressing activity of DNA replication and transcription activity, and subjugation of bacterial toxin synthesis (Mickymaray, 2019).

The phenolic compounds extracted using ethanol and acetone solvents from guava seed meal exhibited antimicrobial activity with the highest inhibition zone against five bacterial strains (Anand *et al*., 2019).The polyphenol compounds produced from seed meal were known to interact with the cellular membranes of bacteriaand were frequently associated with the hydrophobic nature of biologically active substances. AMPs (antimicrobial peptides) are defined as small chainlinked amino acids constituting the primary innate plant defence mechanism through functions of cationicity and amphipathicity. It involves several mechanisms such as ionic disequilibrium, permeability changes, and lipid bilayer destabilization (Huan *et al*., 2020). As a biotechnological tool for combating ailments in humans, the recombinant Pg-AMP 1 isolated from guava seeds shows inhibitory efficacy against a range of Gram-negative bacteria (*Escherichia coli, Klebsiella pneumoniae,* and *Pseudomonas aeruginosa*) and Gram-positive bacteria (*Staphylococcus aureus, epidermidis*) (Tavares *et al*., 2012).

Antimicrobial agents are found in the aromatic oils partitioned from guava leaves were effective against *P. aeruginosa, Streptococcus faecalis, Escherichia coli, S. aureus,* and *Bacillus subtillis* (Ullah *et al*., 2020). The occurrence of additional phytochemicals, such as phenolic compounds, flavonoids, isoprenoids, glycosomes, and steroidal glycoalkaloids, exerts a significant effect against microbial infections. The fermented guava leaf extract produced by ESI/MS was analysed and reported the include of 3,4,5-trihydroxybenzoic acid, 3-caffeoylquinic acid, fenicularin, rutoside, isoquercetin, sophoretin, robigenin, and flavonols. These substancescan limit ergosterol and glucosamine, which act as indicators for fungal cell growth (Das and Goswami, 2019). Other phenolic compounds, such as hydro-soluble tannins isolated in guava leaves observed to possess antiseptic properties that own the mode of action, including holding back the substratum, disrupting oxidative phosphorylation, and external cell matrix enzyme alleviation (Jayakumari *et al*., 2023). The decoction of guava leaves prepared at various concentrations has been reported to possess a hindering impact on microbial colonization and conjugation of bacterial toxins on epithelial cells, modifying the inflammatory response with higher amounts of antioxidants (Almulaiky *et al*., 2018). The silver nanoparticles synthesized from guava leaf extract exhibit prominent antimicrobial activity against DPPH and ABTS radicals cations (Bose and Chatterjee, 2016).

4.4 Antidiabetic activity

Amidst the widespread systemic diseases, diabetes mellitus is reported to be universal owing to either elevated blood serum glucose levels or excessive glucose production, *i.e.,* hyperglycaemia, which is insufficient production of insulin by the pancreas or disruption in hormonal functions (Ashwini and Mahalingam, 2020). The condition is demarcated as minimal discharge of insulin (type 1 diabetes) and incapability of cells to respond to insulin released (type 2 diabetes). The IDF reported that about 451 million people were recorded to be diabetic patients. Around 5 million deaths have been reported, and by 2045, the worldwide population is projected to grow by 693 million individuals (Cho *et al*., 2018). This chronic disorder accounts for the third major reason for the death rate worldwide, following heart disease and cancer. Manufacturing drugs such as acarbose might develop harmful side effects; in contrast, it restricts enzyme activity, including α-amylase and α-glucosidase, compared to other treatments (Iid *et al*., 2020; Zhong *et al*., 2019). The roughage content of guava seeds demonstrates antidiabetic activity combined with guava pulp and wheat flour (El Din and Yassen, 1997; Kaushik, 2019). Guaijaverin and avicularin flavonoid compounds extracted from guava leaves represent significant ability in fixing pancreatic β-cells and morphological characteristics of liver cells in diabetes affected mice. The guaijaverin shows repressed action on the blood glucose level and dipeptidyl peptidase, regulating homeostasis, wherein avicularin restricted intercellular fat conglomeration by inhibiting glucose intake *via* GLUT-4 under laboratory-based conditions.The study reported that guava leaf polysaccharides extracted using an ultrasound-assisted extraction method exert a strong inhibiting effect on α-glucosidase, around 99.54% with the dosage of 100 micrograms per mlameliorates diabetes incidence (Luo *et al*., 2018). Guava leaf polysaccharides were attributable to their exceptional decline in overall cholesterol, fatty acids, malonaldehyde content, digested serum protein, fasting blood glucose, and creatinine levels, along with increased antioxidant enzyme activity under *in vitro* conditions. Another group of scientists reported polysaccharides from guava leaf extracts for their antidiabetic property in streptozotocin-stimulated diabetic mice in addition to calorific diet (Luo *et al*., 2019).

4.5 Anti-inflammatory property

Guava seedsoffers abundant supply of polysaccharides, are known to acquire immunomodulatory and anti-inflammatory activities (Barbosa and de Carvalho Junior, 2021; Yin Miao *et al*., 2019). Inflammation comprises of diverse set of interactions between soluble factors (cytokines) and cells present in any tissue due to traumatic, infectious, toxic, or anti-immune injuries. Polysaccharides activate immune cells to proliferate white blood cells including macrophages by phagocytosis (Sindhu *et al*., 2021). A Study demonstrated categorizing polycarbohydrates present in guava seeds into 3 conjugated protein components such as GSF 1, GSF 2, and GSF 3. Among these compounds, GSF 3 highlighted dominant effect by suppressing inflammation and modulates immune system (Lin and Lin, 2020a). The polyphenols present in seeds isolated using ethanol-water repressed the maturation of carcinoma cell strains, which further decreased cytokinin secretion ratio profiles (Lin and Lin, 2020c).

4.6 Antidiarrhea activity

The major reasons for mortality of infants between ages 0 and 5 has been reported as diarrhoea. It also affects another age group of people, weakening metabolic activities and homeostasis (Morris *et al*., 2011). The majority of pharmaceutical firms are engaged in the creation of novel medications that have the potential to treat this illness. There is a growing focus on recognizing and assessing biologically active substances from plant sources to bypass the complications linked to synthetic medications include costiveness, intestinal occlusion, broncho constriction, and nausea (Gupta and Birdi, 2015).

A water-based extract from guava leaves having dosage around 52-410 mg was consumed and reported to reduce diarrheal infection, decrease intestinal peristalsis, and tardy removal of excrement (Ojewole *et al*., 2008). The leaf extracts from guava at different concentrations possess significant antidiarrheal properties with minimal discharge of intestinal fluid and dampness of faeces. Based on the different animal models and human patients, it was conferred that guava leaves have potential health benefits against diarrheal infections(Mazumdar *et al*., 2015).

4.7 Antihyperlipidaemic property

Guava leaves possess antidiabetic properties, producing substantial effects with reduced glycemia levels and glucose homeostasis (Beidokhti *et al*., 2020). The drop in blood sugar content promotes the intake of glucose resilience, which is crucial to avoid weight loss due to impaired carbohydrate metabolism. The ethanol extract derived from guava leaves were supplemented in the eating regimens of rabbits resulting in major decrease of serum triglyceride levels and LDL cholesterol, lowering HDL cholesterol levels (Olaniyan, 2017). Other reports conclude that leaf extracts have improved the enzymatic activity of glucokinase and G6Pase with declined insulin levels and other hormonal functions being regulated (Vinayagam *et al*., 2018).

Leaf extracts are also stated to alleviate insulin resistance through PI3/Akt signalling function in the type 2 diabetes mouse model with the concentration of 5 mg per kilogram of weight. The compounds have significantly affected the metabolic abnormalities in obese rats and have critically reduced glycemia and insulin resistance without changing weight (Yang *et al*., 2020). It significantly restored endothelial malfunction by replenishing Endothelium-Derived Hyperpolarizing Factor (EDHF) and nitric oxide-mediated vasodilation in aortic rings. Polysaccharides present in guava leaves had restricted steatotic liver disease and low-grade systemic inflammation in adipocytes, which also demonstrates hepatoprotective effects (Díaz-de-Cerio *et al*., 2017; Li *et al*., 2022). Guava leaf polysaccharides supplemented intocalorific diet had attenuated fat storage and visceral obesity, decreasing serum cholesterol and triglycerides (Tella *et al*. 2019).

4.8 Antineurodegenerative property

Cognitive maladies such as dementiaand Parkinsonism are regarded as prevalent neurocytological ailments in the world. Oxidative stress caused by ROS generation, protein buildup in neurons, dysfunction in ubiquitin conjugation or post-translational modifications, the inadequate proportions of chemical messengers in the synaptic gap, disintegration or injury to thebrain are the determinants of nervous system-related disorders (Hua *et al*., 2015; Sharifi-Rad *et al*., 2020).

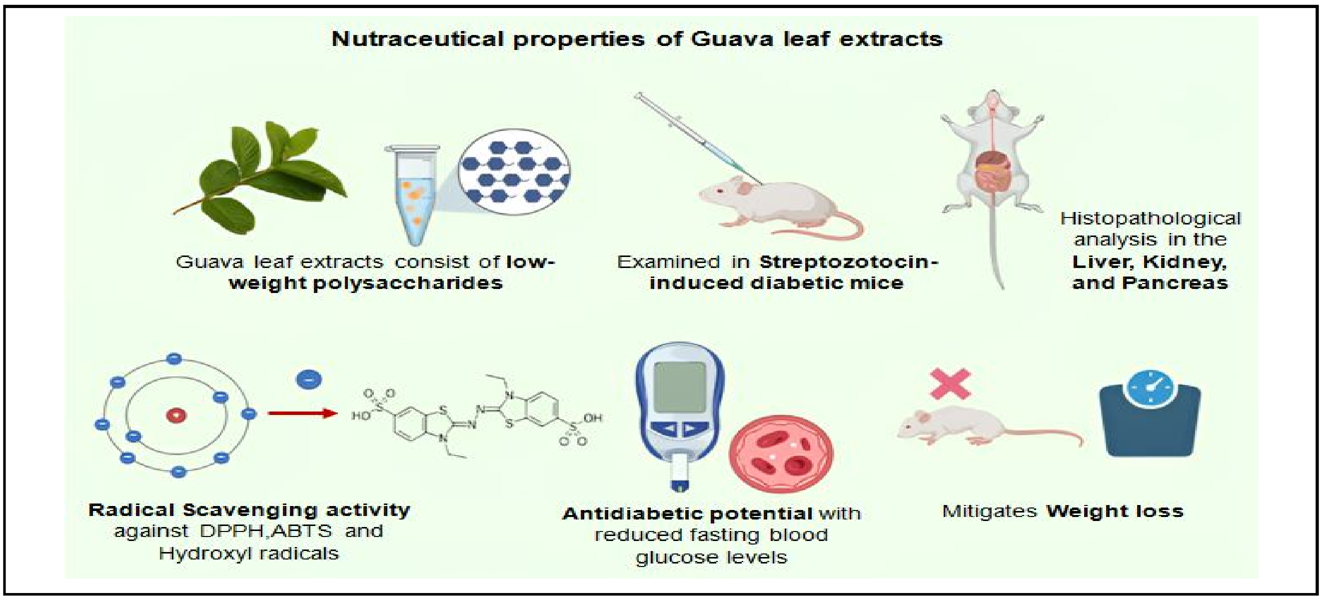


Figure 3: Therapeutic effects of Guava leaf extracts administered in diabetic mouse model (created in Biorender.com)

Secondary metabolites, comprising the major class of compounds, including cinnamic acids, terpenoids, and nitrogen-containing bases, exhibit neuroprotective activity (Reshi *et al*., 2023). It has been reported that guava seeds have no direct effect on neuropsychological functions and appear to be a rich source of potential phytoconstituents such as polyphenols modifying cell signalling pathways to confer immunity against neurodegenerative effects (Liu *et al*., 2018). A study by mentioned that antioxidants such as phenolic compounds (chlorogenic acid, quinic acid, and hydrolysable tannins), plant stanols and triglycerides quantified from guava seed oil safeguard the cells against hydrogen peroxide-induced radical damage and describe neuronal protection. Further studies need to be undertaken laboratory (with multitude of neurons and neurovascular units) and within living organisms (using animal models) to untangle the practicality and biological mechanisms of guava seed derivatives in cerebroprotection (Prommaban *et al*., 2020).

5. Industrial applications

Accounting for the necessity of fruit residue waste management from processing industries, measures are taken to recover guava seeds and leaves for economic use in the form of food and other industries. Feasible products synthesized from guava seeds are discussed in the following sections.

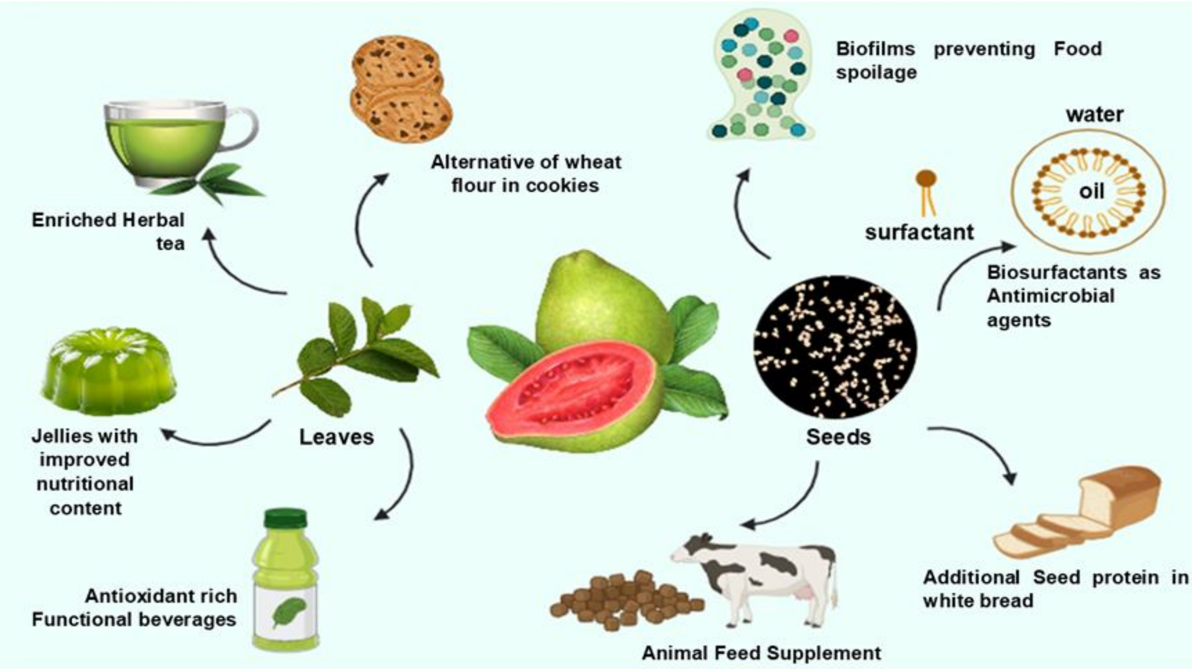


Figure 4: Industrial applications of Guava seeds and leaves (created in Biorender.com).

5.1 Dietary supplement ingredient

Guava seeds are excellent providers of proteins, including amino acids, polyunsaturated fatty acids, and fibre, and are mainly used in confectionery items. Guava seed flour plays an effective substitute for whole wheat flour in the cookies production (ElDin and Yassen, 1997). Wheat flour infused in guava seed flour, had a prominent effect on external parameters of cookies such as magnitude, broadness, and density (Ayo and Johnson, 2018). Regarding the nutritional profile, the iron content of cookies is increased with a reduction in total carbohydrate content. The potentiality of guava seed flour to generate antimicrobial compounds against *Staphylococcus aureus*, upholding *Weissella confusa* and underscoring capabilityin production of synbiotic foods and maintaining food perishability (Serna-Cock *et al*., 2013).The inclusion of guava seed protein isolate by milling process into wheat flour supplies additional protein content in white bread (Perez-Rocha *et al*., 2015).

The demand for herbal tea consumption and its production is rising, offering health benefits as well as economic profits (Akila *et al*., 2018). Given that guava leaves are rich in phytoconstituents, there is a need to incorporate these plant based compounds into the diet (Liu *et al*., 2023). Different processing methods, including standard drying, hot water blanching, along with stem blanching, were employed to standardize herbal tea preparation. It was found that the stem blanching method resulted in the highest retention of phenols, antioxidants, and significant amounts of flavonoids and tannins. This preparation method gained overall acceptance due to its flavour, aroma, and appeal (Thangaraj *et al*., 2021). Incorporating guava leaves into foodstuffs such as jelly provides unique and innovative way to introduce new flavours, enhancing nutritional content. Studies have shown that guava leaf enriched jelly contains significant amounts of sugars, amino acids, ascorbic acid, and niacin compared to control treatments. The texture was not adversely impacted by the addition of guava leaves, but the antioxidant levels increased with compounds such as quercetin and gallocatechin (Sampath Kumar *et al*., 2021).

The development of a novel chocolate formulation with guava leaves has been experimented with using response surface methodology, underscored successful results with notable values of texture, colour, and flavour (Faccinetto-Beltran *et al*., 2021; Ramprasad and Kale, 2023). The chocolate had been produced with an exceptional amount of ascorbic acid of 122.3 mg/100 ml, meeting the desirable quality standards. 3-D printable cheesecake, considered to be the food of the future, was developed by incorporating guava leaves to reduce the glycaemic index (Park *et al*., 2022). The printing performance was improved in addition to significant amounts of antioxidants, total phenols, and flavonoids (Prabhakar *et al*., 2024). Guava leaves at the concentration of 10% with paneer whey, sugar had been reported to possessthe highest phenol and flavonoid content would be appropriate for creating batches of antioxidant-rich functional drinks, whereas guava leaf extract used at 3%, proven to be more acceptable in terms of pH, acidity and TSS (Shalini and Ritu, 2018).

5.2 Biofilm

Fermented guava seeds improve sugar and water content, and reduce lipid and protein levels with the decrease in antinutritional factors. They are used as food supplements since they contain five amino acids that produce metabolic fuels for the digestive system (Darmasiwi *et al*., 2018). These natural compounds are extensively applied in food preservation techniques, acting as microbial barriers against environmental stresses (Thappa *et al*., 2024). They are used in the food industry to safeguard from water, autoxidation, and rancidity.

The conventional fermentation method allows using banana leaf wrap to lead to microbial contamination (Yoshimura *et al*., 2022). Leavening the guava seeds isa key alternative to producing biodegradable films, preventing food spoilage. During fermentation of guava seed flour, microorganisms come under the genera *Lactococcus, Oenococcus, Pseudococcus, Streptococcus,* and *Lactobacillus* were grown in $CaCO_3$-infused MRS Agar, forthe generation of 2-hydroxy-propanoic acid. Withinthe 8 strains produced, J-6 and J-8 strains were superior in forming edible biofilms, where guava seeds serve as probiotics in lactic acid synthesis, extending product acceptability and durability (Darmasiwi *et al*., 2018).

5.3 Biosurfactant production

The surface-activebio compounds produced by microorganisms interact with or modify the properties of surfaces or interfaces (Manga *et al*., 2021; Patel and Kharawala, 2022). They exhibit both hydrophobic and hydrophilic characteristics playingan active role in environmental remediation, anti-inflammatory, wound healing, cleaning agents, *etc*. Guava seeds are the key source of oil content ranging from 10-15%, constituting monounsaturated fatty acids, carotenoids, tocopherols, and other volatile compounds that act as powerful antioxidants preventing cellular damage (Kapoor *et al*., 2023). Rhamnolipids, a subclass of biosurfactants is one of the components in guava seed noted for its high surface activity and biodegradability compared to chemical surfactants (Dobler *et al*., 2016). The guava seeds had evolved as a powerful substrate in the production of biosurfactants supplying an adequate carbon source for microbial growth.

Edible coatings are stated to be one of the traditional methods of overcoming the side effects of chemical coatings with harmful substances (Sharif *et al*., 2017). Bananas, carambola, and tomato coated using these biosurfactant compounds laid out a positive impact on quality parameters. Fruits treated with guava leaf extracts possess moisture content, with 7-12% weight loss retaining the nutritional value (Islam *et al*., 2018). The water dependant extract of guava leaves in the ratio of 1:6 shows antimycotic activity producing the least number of colonies (2.28 CFU/g) within three days compared to control treatments, thus extending shelf-life (Gituma and Njue, 2019).

5.4 Livestock dietary enhancement

Owing to its potential source of carbohydrates and dietary fibre, guava seeds are used in animal feeds. Germinated seeds are more effective since the mobilization of complex insoluble carbohydrates to simple sugars takes place, improving available carbohydrates/net carbs and probiotic activity (Ling and Chang, 2017). The addition of seed sources to the dietary schedules of lamps, leads to a reduction in cholesterol quantity, improving metabolic functions (Costa *et al*., 2018; Georganas *et al*., 2020). About 18 g of guava leaf meal had been supplemented to the daily diet of chickens where it had been reported with the highest feed conversion ratio and specific growth rate. In aspects of body proportion, chicks given this type of diet have high levels of protein with less fat compared to other treatments (Khan, 2023). The chicks were observed with an increase in muscle growth and reduced fat deposition suitable for a commercial viewpoint (Daing *et al*., 2020). Reports conclude that yellow strawberry guava leaves had been reported to increase the quality of eggs with high antioxidant and antimicrobial properties limiting the biochemical pathways of cyclooxygenase (COX), which comes under proinflammatory molecules (Dos Santos *et al*., 2020).

Table 2: Commercial uses of guava seeds and leaves

Products	Importance	References
	Guava seeds	
Fat replacer	Light-coloured edible oil and can be refined to a low free fatty acid content	Kumar *et al*. (2022)
Guava seed oil	Used in oil paints, lubricants, surface coatings, pharmaceuticals and cosmetics.	Kumar *et al.* (2022)
Biodiesel production	Spent coffee grounds and guava seeds were used as biomass residues to for the extraction of lipids and their application to obtain biodiesel.	Veitiade Armas *et al.* (2024)
Guava seed protein	Used as an adsorbent and as a precursor of carbon for the adsorption of acid dyes in wastewater treatment.	Elizalde Gonzalez and Hernandez Montoya (2009)

Guava leaves		
Fish feed	Weight gain, specific growth rate, performance index, food conversion ratio. protein efficiency ratio, survival rate had been improved.	Omitoyin *et al.* (2019)
Hard candy	Infused with lemongrass having high antibacterial activity against *P. aeruginosa* and *S. pyogenes* with overall acceptability.	Halim *et al.* (2022)
Cosmetic products	ethanolic extract loaded silk fibroin nanoparticles protect phenolic compounds, prolong their release times, and enhance their efficacy.	Pham *et al.* (2023)
Packaging material	Incorporated with gelatin chitosan packaging for extending meat shelf-life.	Velarde *et al.* (2025)

6. Conclusion

Guava seeds are rich in amino acids, lipids, minerals and ascorbate. Guava leaf extracts have also been extensively studied for their free radical scavenging activity, anticarcinogenic and hypoglycaemic properties, as well as other remedial attributes due to presence ofnumerous bioactive compounds. These compounds function as immunopotentiators and disease-modifying drugs for diabetes mellitus, malignant neoplasm, and digestive, neurological, and coronary heart diseases. Beyond the agro-food sector, the application of guava seeds and leaves is a new field of subject to investigation in other sectors, including the livestock, drug, and cosmetic industries. Therefore, seeds and leaves of guava, with their diverse pharmaceutical benefits, require further development for a broad spectrum of applications. Future studies need tofocus on the identification and isolation of new bioactive compounds for the development of drugs with resistance to multiple diseases.

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Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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