

Review

Exploring the Potential Antioxidant, Anti-Inflammatory, and Anticancer Properties of *Careya arborea*: A Promising Underutilized Source of Natural Therapeutics

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Simple Summary

Native to South and Southeast Asia, *Careya arborea* is often referred to as wild guava. The name “wild guava” is derived from the appearance of its fruit, due to being round, green, and bearing a close resemblance to guavas. The young fruit is edible and is traditionally consumed for its sour taste in various regional diets, including in Sri Lanka. However, it is considered an underutilized fruit in Sri Lanka. This species holds significant value in traditional medicine systems. Various parts of the tree, including the leaves, bark, and fruit, are used to treat a wide range of ailments, such as pain, coughs, skin diseases, and gastrointestinal disorders. Scientific investigations have further supported these traditional uses. Despite its potential for medicinal use, it emphasizes the necessity of conservation measures to shield it from overexploitation and habitat degradation. It is advised that more research be conducted to fully examine its therapeutic potential in clinical settings.



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Abstract

Careya arborea, commonly known as wild guava, is a deciduous tree native to Asia, including Sri Lanka. Traditionally used to treat various ailments such as skin diseases, tumors, gastrointestinal disorders, and inflammation, it is valued for its notable astringent properties. Rich in phytochemicals, including phenolics, terpenes, sterols, tannins, and saponins, *Careya arborea* exhibits potent antioxidant, anti-inflammatory, and anticancer activities. Its anticancer effects are primarily attributed to the induction of apoptosis and the inhibition of cancer cell proliferation, with several extracts such as chloroform, ethyl acetate, and methanol demonstrating selective cytotoxicity against cancer cell lines. The high phenolic content of *Careya arborea* underpins its antioxidant potential, which plays a crucial role in mitigating oxidative stress and associated inflammatory conditions. Despite its medicinal potential, *Careya arborea* remains an underutilized plant in Sri Lanka. Greater attention should be given to promoting its use in both traditional and modern healthcare systems to harness its therapeutic benefits. Given its therapeutic potential, sustainable harvesting and conservation efforts are essential to protect this plant from overexploitation and habitat loss. Taking all these factors into account, this review emphasizes *Careya arborea*'s potential as a source of natural therapeutic agent, highlighting the importance of further research and conservation to unlock its full medicinal value for clinical applications.

Keywords: *Careya arborea*; antioxidant; anticancer; anti-inflammatory; conservation; sustainability

1. Introduction—Biological Profile of *Careya arborea*

Medicinal plants, which are the foundation of traditional medicine, have drawn significant attention in recent years due to their potential in pharmacological research. In many developing countries, the majority of the population relies on traditional medicine for primary healthcare. The value of these medicinal plants as sources of novel therapeutic compounds and lead molecules for drug development has been recognized. Consequently, there is a growing trend to evaluate medicinal plants for bioactive compounds to support further pharmacological investigations. Extensive use of medications has led to multidrug resistance, prompting the search for novel drugs from medicinal plants [1,2].

Careya arborea, is a deciduous tree widely distributed across Asia, including Sri Lanka, where it thrives in moist regions, particularly in exposed Patana fields at elevations of up to 5000 feet. Beyond Sri Lanka, it is also found in other Asian countries such as India, Afghanistan, Malaysia, and Indochina. In Sinhalese, the tree is known as ‘Kahata’, and in Tamil, ‘Ayma/Karekku/Kumbi’. *Careya arborea* is referred to as Wild Guava, Patana Oak, or Ceylon Oak in English, while its common English name is ‘Wild Guava’ due to the tree’s widespread presence in Indian forests and grasslands, coupled with its guava-like characteristics [3,4]. Despite its ecological presence, it remains an underutilized plant in Sri Lanka, though it holds significant importance due to its potential medicinal, ecological, and ethnobotanical value.

Taxonomically, *Careya arborea* belongs to the Lecythidaceae family, a group of tropical trees comprising approximately 20 genera and 450 species. While many members of this family are found in the humid tropics of South America, several genera, including *Careya*, are found in tropical Asia and parts of Africa [5]. *Careya arborea* is a medium-sized tree that typically grows to a height of 15–20 m. It is characterized by its thick, rough bark and prominent young branches bearing large leaves. Its cylindrical trunk with bark has a flaky, fissured nature with a dark gray color [6]. This tree is also known for its widespread growth and astringent gum within its stem [3,7].

The leaves of this tree are simple, arranged spirally at the tips of twigs, and occasionally form clusters. Normally, the leaves are 15–22 cm in length and 7–12 cm in width, broadly obovate, with a tapering base, toothed edges, and small, deciduous stipules [8]. The flowers of *Careya arborea* are large, bisexual, and regular, with pale green petals and pink filaments. They grow in an upright raceme structure with a diameter of 9–10 cm. Each flower consists of four distinct sepals and four petals, along with numerous stamens that are annular and connate at the base. Typically, the blooming season for this plant is between November and March [5,7]. Primarily, propagation of *Careya arborea* occurs through the seeds, and its fruit has a large drupe with a berry-like structure and is edible. They are normally 6.2–7.5 cm in length, globular, green, glabrous, and feature a waxy outer coating. The fruit is capped with persistent calyx segments. The flesh contains numerous seeds embedded within it, which can be mildly toxic [7,9] (Figure 1).



Figure 1. *Careya arborea*, (a) mature tree (b) leaves (c) fruit (d) flower.

2. Role in Traditional Medicine

Since the dawn of history, early humans from India, Egypt, China, and other parts of the world have utilized different plants and plant-derived remedies to treat numerous illnesses and health conditions. Traditional medicine literature contains references to approximately 25,000 herbal formulations. Furthermore, according to modern pharmaceutical reports, at least 25% of currently available pharmaceuticals are derived from plants, while many other synthetic drugs are based upon prototype chemicals initially isolated from plants [10,11]. When it comes to the plant *Careya arborea* it also possesses a rich phytochemical content with significant pharmaceutical properties [12].

Careya arborea has been traditionally used to manage many human health conditions in various countries. Especially the stem of the plant bears a notable potential in treating tumors, bronchitis, and epileptic fits. The bark of the plant has been used as a remedy in traditional medical systems for diarrhea, and dysentery with bloody stools [13,14]. Additionally, the bark has been reported to possess antipyretic properties [15,16]. In traditional practices, hot water extracts of the bark were used by postpartum women for bathing to alleviate jaundice [17]. For the treatment of hemorrhoids, bark powder mixed with honey [18], or a decoction prepared by boiling 50 g of bark in water and consuming a glass daily on an empty stomach for seven consecutive days, has been traditionally recommended [19]. Bark powder mixed with cow milk is ingested to alleviate dysentery [20], while a paste made from fresh bark is applied to scorpion stings. The bark is also traditionally used in the treatment of intestinal sores, bedsores, and in managing vata and kapha imbalances in Ayurvedic medicine [21]. The juice from the bark is applied internally for ear pain relief, and it is also employed as a leech repellent [13].

Reports have also shown that the leaves of *Careya arborea* are applied to treat ulcers, and its pulp is commonly used as a poultice to accelerate the healing of wounds. The leaves and flowers are applied as a paste to cure various skin diseases and rashes [22]. Moreover, a paste made from its flowers, combined with fruits of *Terminalia chebula* and *Emblica officinalis*, prepared with ghee, is consumed on an empty stomach to address infertility [18]. To alleviate cough and cold, the plant's persistent calyx, flowers, and fresh bark juice are given [7]. The fruits are more widely utilized as a traditional medicine than as a food item. However, it is generally considered safe to consume [18], and in certain areas of Sri Lanka, people use the fruit as a vegetable. Additionally, the root of *Indigofera cassioides* mixed with *Careya arborea* juice is often utilized for treating blood dysentery [23]. According to the traditional medicine practice of Sri Lanka, this tree is mostly used for ulcers, coughs, skin diseases, and genito-uterine diseases. The paste, made with flowers and juice of fresh bark, and honey, is known as a treatment for coughs and colds [24]. According to the traditional medicine practice of Sri Lanka, this tree is mostly used for ulcers, coughs, skin diseases, and genito-uterine diseases (Table 1).

Table 1. Medicinal Properties of *Careya arborea*.

Treated Pathologies	Plant Part	References
Tumors, bronchitis, epileptic fits, diarrhea, dysentery (bloody stools), ear pain, hemorrhoids, intestinal sores, bedsores, vata and kapha imbalances (Ayurvedic), jaundice (bathing postpartum women), coughs and colds, scorpion stings, leech repellent	Bark/Stem	[7,17]
Ulcers, wounds (poultice), skin diseases, rashes	Leaves	[22]
Skin diseases, rashes, infertility (paste with <i>Terminalia chebula</i> and <i>Emblica officinalis</i> with ghee, consumed on an empty stomach), coughs and cold (with persistent calyx and bark juice)	Flowers	[18]

Table 1. Cont.

Treated Pathologies	Plant Part	References
Wound healing (poultice), coughs and colds, infertility (combined with flowers as above)	Fruits/Pulp	[8,18,22]
Tuberculosis, skeletal fractures, blood dysentery (when mixed with <i>Indigofera cassioides</i> juice)	Root	[6,25]

3. Phytochemical Composition and Bioactive Compounds

The phytochemistry of *Careya arborea* reveals a considerable pharmacological potential resulting from its wide range of bioactive compounds. Almost every part of the plant, including flowers, fruits, seeds, leaves, and stem bark, is rich in unique compounds that are crucial for its medicinal applications. Generally, tannins can be found abundantly in the aerial parts of the plant [26]. Flowers contain triterpenoids, steroids, and tannins [27]. Several phenolic compounds have been isolated from methanol, n-hexane, ethyl acetate, and dichloromethane extracts of *Careya arborea* fruits, including gallic acid, 3,4-dihydroxybenzoic acid, quercetin 3-O-glucopyranoside, and kaempferol 3-O-glucopyranoside [28]. These compounds are known to have high antioxidant and anti-inflammatory activity [29,30]. The seeds of *Careya arborea* have been reported to contain α -spinasterone, which is known to have anti-inflammatory and cytotoxic potential [5]. Additionally, the seeds also contain Barringtonenol C, which is known to be a rare triterpenoid saponin that is shown to possess antileishmanial and anti-inflammatory activities [31].

According to the phytochemical profile of *Careya arborea* leaves, the ethanolic extract has revealed maslinic acid and 2 α -hydroxyursolic acid [5]. For instance, maslinic acid has exhibited anticancer activity in HT-29 colon cancer cells by arresting the cell cycle at the G0/G1 phase and diminishing the S phase [32]. Additionally, 2 α -hydroxyursolic acid has been shown to exert anti-diabetic effects by inhibiting enzymes such as α -amylase and α -glucosidase, which facilitate carbohydrate absorption, while also improving insulin sensitivity and glucose uptake [33]. Further, taraxerol, taraxerol acetate, ellagic acid, Flavonoids, Lignans, Saponins, Triterpenes, Valepotriates, quercetin, and β -sitosterol-like compounds have been extracted from the leaves [12,31]. Another study has revealed the presence of phytochemicals such as β -amyrin, β -sitosterol, and taraxerol in *Careya arborea* leaves [34]. For instance, ellagic acid and quercetin have been shown to have antioxidant activity [35], while both taraxerol, taraxerol acetate have been shown to have antioxidant and anti-inflammatory activities. Furthermore, both β -amyrin and β -sitosterol have been shown to exhibit antioxidant activity and also moderate to strong in vitro anticancer effects across a variety of cancer cell lines [36]. The stem bark of *Careya arborea* is also rich in phytochemicals such as terpenes, sterols, tannins, and saponins [5,12,37]. Moreover, the *Careya arborea* roots have been reported to contain around ten major phytochemicals, including alkaloid, steroid, tannin, flavonoid, terpenoid, saponin, phenol, sterol, cardiac glycoside, and carbohydrate [6,38], which also show many bioactivities such as antioxidant, anticancer, antimicrobial, and anti-inflammatory activities [39].

4. Antioxidant Potential of *Careya arborea*

Reactive oxygen species (ROS) such as hydrogen peroxide, singlet oxygen, superoxide anion radicals, hydroxyl radicals, and reactive nitrogen species (RNS) are the major factors responsible for inducing oxidative and nitrosative damage to cellular components, including lipids, proteins, and nucleic acids. They are produced in the body during normal physiological processes like lipid auto-oxidation. Such damages are linked to the develop-

ment of various degenerative health conditions, including cancer, aging, arteriosclerosis, and rheumatism [40].

Antioxidants are specific compounds that help to protect cells from the harm caused by free radicals. By effectively scavenging these unstable molecules, antioxidants play a crucial role in preventing and repairing oxidative stress-induced cellular damage. Compounds such as lycopene, beta-carotene, and vitamins C, E, and A can be identified as common antioxidants [41]. Among antioxidants, those derived from plants have received significant attention due to their wide availability, biocompatibility, and potential health-promoting properties. Plant-based antioxidants often include a diverse range of bioactive phytochemicals such as flavonoids, phenolic acids, tannins, and alkaloids, which not only combat oxidative stress but also contribute to anti-inflammatory, anticancer, and cardioprotective effects. Moreover, natural antioxidants from plants are generally considered safer and more sustainable than their synthetic counterparts. This has led to a growing trend in exploring medicinal plants as promising sources of natural antioxidants [42,43]. Therefore, as an effective and accessible strategy to mitigate oxidative stress and its associated health complications, these plant-derived antioxidants can be incorporated into standard therapeutic approaches and preventive health measures.

Numerous research efforts have been directed towards evaluating the antioxidant potential of *Careya arborea* as well. A study assessed the antioxidative activity of the methanol extract from the stem bark of *Careya arborea* (MECA) using a method involving ammonium thiocyanate, which measures peroxide levels during the early stages of lipid oxidation. The antioxidant activity of MECA was due to its ability to reduce hydroperoxides while inactivating free radicals and chelating metal ions, which may result from its phytochemical profile, including flavonoids and biflavones. According to their results, MECA demonstrated concentration-dependent antioxidant activity at concentrations of 50, 100, 250, and 500 µg/mL, inhibiting lipid peroxidation of the linoleic acid system by 64.53%, 69.27%, 73.04%, and 79.93%, respectively. Notably, with 500 µg/mL of MECA, 79.93% of inhibition was achieved, and that inhibition was comparable to that of α-tocopherol at the same concentration (80.73%). α-Tocopherol is the most biologically active form of Vitamin E. The IC₅₀ (half-maximal inhibitory concentration) value for lipid peroxidation inhibition, 36.58 µg/mL, indicated a significant antioxidative potential. According to the results, it can be suggested that MECA has effectively reduced hydroperoxides and scavenges free radicals, proving its potent antioxidant activity, and the results were comparable to a well-established standard [44]. However, the study did not isolate or quantify the individual phytoconstituents responsible, limiting mechanistic understanding.

Another study demonstrated that the methanol extract and two crude extracts of *Careya arborea* bark exhibited high in vitro antioxidant activity. Among them, the methanol extract, which had the lowest IC₅₀ value, showed the highest potency. Lower IC₅₀ values ranging from 6.25 to 7.90 µg/mL showed that the extracts were particularly effective against the 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) free radicals, and further, a significant scavenging activity with IC₅₀ values of 7.42 µg/mL, 14.12 µg/mL and 10.72 µg/mL against 2,2-diphenyl-1-picrylhydrazyl (DPPH), Hydrogen peroxide (H₂O₂), and nitric oxide (NO), was observed with the methanol extracts. In this study, the ABTS assay appeared more sensitive than DPPH, likely due to its ability to react with both hydrophilic and lipophilic antioxidants, whereas DPPH primarily detects lipophilic radical scavenging [45]. Overall, after analyzing the study results, the active extracts were found to be more potent compared to the standard butylated hydroxyl anisole (BHA) in the same assays, which is a noteworthy finding [42]. The fact that the extracts outperformed a synthetic antioxidant suggests therapeutic promise, though further validation is required before clinical relevance can be established.

A study conducted in Sri Lanka evaluated the antioxidant potential of several wild fruits, including *Careya arborea*. Hexane, ethyl acetate, and aqueous fractions were prepared from crude methanolic extracts and assessed for antioxidant activity using the DPPH radical scavenging assay and the ferric reducing antioxidant power (FRAP) assay. Among the fractions, the ethyl acetate and aqueous extracts of *Careya arborea* exhibited the highest DPPH radical scavenging activity. It should be noted that, while the DPPH assay measures the ability of the extracts to scavenge free radicals, the FRAP assay evaluates their reducing power, reflecting complementary aspects of antioxidant activity. Together, both assays provide a comprehensive assessment of their overall antioxidant potential [45]. Further, *Careya arborea* demonstrated the highest total phenolic content (TPC) across all extracts among the fruits tested, with the crude methanolic extract recording a TPC value of 231.26 ± 3.16 mg gallic acid equivalents (GAE)/g [43].

Another study evaluating the antioxidant properties of *Careya arborea* root reported that the methanol extract showed strong radical scavenging in the ABTS assay ($IC_{50} = 20.55 \pm 0.66$ μ g/mL), whereas the DPPH IC_{50} was much higher (305.48 ± 4.59 μ g/mL), indicating moderate activity in this assay. The total antioxidant capacity was 225.34 ± 2.30 μ g/mL, supporting the extract's overall antioxidant potential. The ethyl acetate extract also exhibited notable activity, with low ABTS IC_{50} (21.41 ± 0.60 μ g/mL) but higher DPPH IC_{50} (348.62 ± 3.35 μ g/mL) and total antioxidant capacity of 173.86 ± 3.65 μ g/mL, again highlighting assay-dependent variability. Successive methanol and chloroform extracts showed moderate activity, with ABTS IC_{50} values of 33.95 ± 0.78 μ g/mL and 68.56 ± 1.23 μ g/mL, and total antioxidant capacities of 173.86 ± 3.65 μ g/mL and 137.16 ± 3.34 μ g/mL, respectively, demonstrating the influence of extraction solvent on antioxidant potential [46].

While *Careya arborea* demonstrates robust antioxidant potential, it should be noted that the results are highly assay and solvent-dependent. ABTS consistently indicated stronger activity than DPPH, emphasizing the importance of using multiple complementary assays. Although high phenolic content appears correlated with activity, direct links between individual phytoconstituents and observed effects remain underexplored. Furthermore, most studies are limited to in vitro models; thus, in vivo efficacy, bioavailability, and pharmacokinetics of the active compounds require further investigation to substantiate their therapeutic relevance. An overall diagram of the potential antioxidant activity of *Careya arborea* is provided below as a visual summary of the findings (Figure 2).

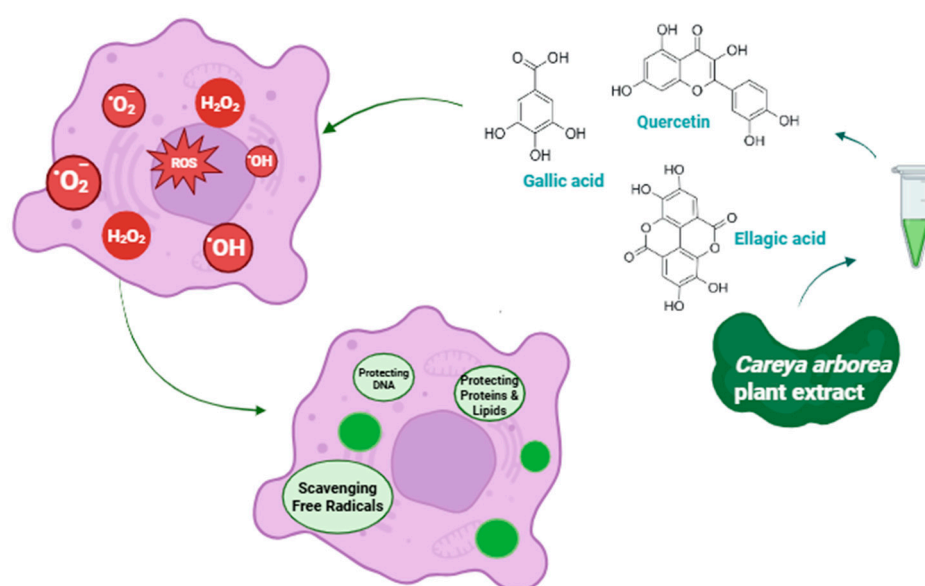


Figure 2. Antioxidant activity of *Careya arborea* plant extracts.

5. Anti-Inflammatory Potential of *Careya arborea*

Inflammation is an essential biological process in the human body that serves as a defense mechanism against infections and injuries. Mainly, two types of inflammatory conditions can be identified. Acute inflammation is a short-term condition that is characterized by its rapid onset, short duration, and localized responses due to the accumulation of fluid, plasma proteins, and leukocytes at the site of infection. During this process, cytokines and chemokines, which act as soluble mediators, are released from injured vascular endothelial cells and leukocytes to regulate and maintain the inflammatory response [47].

However, when the inflammation becomes persistent, it becomes chronic inflammation, a state often associated with long-term tissue damage, and with time, it can lead to various chronic diseases, including diabetes, autoimmune conditions, neurological diseases, cardiovascular diseases, and cancer [48,49]. Extensive research over the past two decades has emphasized the importance of controlling inflammatory conditions by suppressing inflammation and inhibiting inflammatory biomarkers [50]. Given this context, plants have traditionally been used to manage inflammation. In Sri Lanka, traditional medical systems such as Ayurveda and the indigenous system (Deshiya Chikitsa) have long employed a wide range of medicinal plants to treat inflammatory conditions and related disorders. *Careya arborea*, has also depicted considerable promise in this regard [51]. Preliminary research performed in this field has shown that the bioactive compounds of this plant can modulate the inflammatory responses by targeting specific biomarkers engaged in the inflammatory process.

The anti-inflammatory potential of the methanol extract of *Careya arborea* (CAME) was evaluated in Wistar albino rats using carrageenan-induced paw edema. Oral administration of CAME at 100 and 200 mg/kg significantly reduced paw edema by 48.87% and 65.53%, respectively ($p < 0.001$), compared to the reference drug indomethacin (10 mg/kg). Biochemical analyses revealed that CAME mitigated inflammation-associated increases in malondialdehyde, C-reactive protein, NO, and myeloperoxidase levels. Histological assessments further demonstrated suppressed serum levels of TNF- α and IL-1 β , supporting the observed anti-inflammatory effects. HPTLC profiling of CAME identified quercetin (0.177%) and betulinic acid (3.14%), compounds likely contributing to its pharmacological activity. While these results indicate a dose-dependent anti-inflammatory effect, the relative potency compared to standard drugs and the mechanistic contribution of individual phytoconstituents warrant further investigation [51].

The anti-inflammatory activity of the methanol extract of *Careya arborea* (MECA) was evaluated in both acute and chronic inflammation models. Acute inflammation was assessed using carrageenan-, dextran-, histamine-, and serotonin-induced paw edema in mice, while chronic inflammation was evaluated via a cotton pellet-induced granuloma model. MECA exhibited significant ($p < 0.05$), dose-dependent inhibition of paw edema across all acute models, with inhibition rates increasing from 50 to 200 mg/kg body weight, comparable to the standard drug indomethacin. In the chronic model, MECA (200 mg/kg) demonstrated an antiproliferative effect of 45.26%, relative to 57.76% for indomethacin (10 mg/kg), indicating moderate efficacy. These findings suggest that MECA possesses broad-spectrum anti-inflammatory activity; however, this study showed that its potency is lower than conventional drugs, and the specific contribution of individual phytoconstituents remains to be elucidated [52].

In an earlier study, a methanolic extract of *Careya arborea* stem bark was assessed and exhibited notable anti-inflammatory activity. Building on this foundation a group of researchers conducted a study focusing on isolating and evaluating the anti-inflammatory potential of coumaroyl lupendioic acid (CLA), a newly identified lupane-type triterpene derived from the same plant. In vitro COX-1 and COX-2 enzyme inhibition assays were

utilized to assess the inhibitory effects of the isolated compounds. COX, or cyclooxygenase, is a prostaglandin-endoperoxide synthase enzyme that plays a significant proinflammatory role in the body [53]. It exists in two isoforms, COX-1 and COX-2, in mammalian cells. Given their role in inflammation, these enzymes have become attractive targets for the development of novel anti-inflammatory agents [54,55]. In this study, six novel lupane-type triterpene derivatives were isolated from the stem bark of *Careya arborea*. Among these, CLA demonstrated COX-2 selectivity comparable to the reference drug celecoxib. In carrageenan-induced inflammation models, CLA (at both 10 and 20 mg/kg) outperformed betulinic acid, reducing inflammation by 42.6% and 66.9%, respectively, compared to 26.8% and 50.4% inhibition by betulinic acid at the same doses. Moreover, CLA effectively inhibited key proinflammatory mediators, including NO, neutrophil infiltration, prostaglandin E₂, TNF- α , IL-1 β , and IL-6. Histopathological and immunohistochemical analyses revealed that CLA preserved rat paw tissue architecture and downregulated the expression of NF- κ B, COX-2, and TNF- α , demonstrating its capacity to modulate inflammation at the molecular level. Overall, these findings highlight *Careya arborea* as a promising anti-inflammatory agent capable of acting against diverse inflammatory triggers [16]. While CLA shows potent anti-inflammatory activity and COX-2 selectivity, the data are primarily preclinical. Collectively, these studies support *Careya arborea* as a promising anti-inflammatory agent across different models and molecular targets. However, most evidence remains preclinical, with variable potency depending on extract type, dose, and assay. The relative contributions of individual phytoconstituents, pharmacokinetics, bioavailability, and potential toxicity of the active compounds, including CLA, require further investigation before clinical translation. Additionally, standardization of extracts and comparison with established drugs are necessary to assess therapeutic relevance. To encapsulate these observations, an overall diagram illustrating the potential anti-inflammatory activity of *Careya arborea* is presented below (Figure 3).

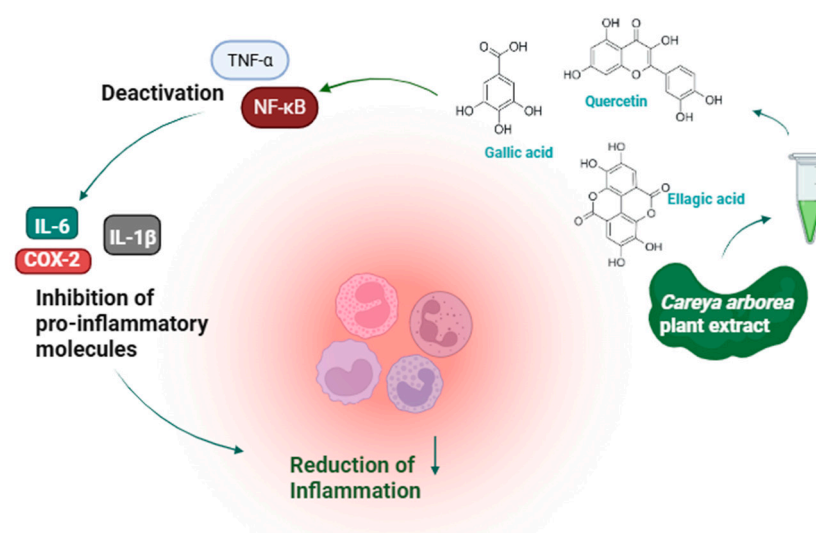


Figure 3. Anti-inflammatory activity of *Careya arborea* plant extracts.

6. Anticancer Potential of *Careya arborea*

In the modern world, cancer is a critical challenge that is harder to overcome, and a definitive and flawless cure for this disease remains elusive in today's medicine. Considering the severe side effects associated with conventional treatments, plant-based therapies have gained considerable attention in combating cancer. Nearly 60% of the current anticancer drugs have an origin from natural sources [56]. Numerous herbs have been

clinically studied and are being extensively analyzed for their phytochemical components to understand their anti-tumor effects on various cancers [57].

Among them, the plant *Careya arborea* has drawn considerable attention as a promising candidate due to its phytochemical properties, which are potentially effective against cancer. A recent study evaluated its effects against Dalton's lymphoma ascites (DLA)-induced ascitic and solid tumors in mice. Administration of the methanol extract from *Careya arborea* bark at doses of 250 and 500 mg/kg body weight for 10 days led to a significant reduction in body weight gain, packed cell volume, and viable tumor cell count compared to the DLA control group. Additionally, the extract restored hematological and biochemical parameters to near-normal levels, and repair of liver and kidney tissue damage caused by tumor inoculation further highlights the plant's potential as an anticancer agent. In vitro studies on cancer cell lines showed that the methanol extract (MECA) exhibited considerable cytotoxicity against HeLa (Cervical cancer), HEP-2 (Laryngeal carcinoma), and RD (Rhabdomyosarcoma) human cancer cell lines with average IC_{50} values of 9.4, 16.0, and <62.5 $\mu\text{g/mL}$, respectively. Importantly, against normal Vero cells (kidney cells of an African green monkey), the IC_{50} was much higher (127.2 $\mu\text{g/mL}$), indicating selective cytotoxicity toward cancer cells [58]. It should be noted that the DLA mouse model and in vitro assays provide initial insights, but they may not fully predict efficacy in humans. The variability in IC_{50} values across cell lines also indicates that the extract's potency may be cell type-dependent.

Another in vivo study using Ehrlich's Ascites Carcinoma (EAC)-bearing Swiss albino mice evaluated the anticancer potential of the methanol extract of *Careya arborea* stem bark (MECA). Following tumor inoculation, MECA was administered at doses of 50, 100, and 200 mg/kg body weight per day for 14 days, and its effects on tumor growth, mean survival time, hematological profiles, and serum and liver biochemical parameters were assessed. Treatment with MECA significantly increased the mean survival time from 18 days in untreated mice to 38 days in treated groups. Moreover, ascites volume, packed cell volume, and viable tumor cell count were markedly reduced in a dose-dependent manner. While these findings indicate that MECA can inhibit tumor progression and prolong survival in EAC-bearing mice, the study is limited to a single tumor model, which may not fully reflect human cancers [59].

As the *Careya arborea* stem bark extracts, its roots also have demonstrated anticancer potential. When the effect of the root extracts was studied using A549 (Lung carcinoma), U87 (Glioblastoma), HCT 116 (Colon cancer), MCF-7 (Breast cancer) and HeLa (Cervical cancer) human cancer cell lines, the IC_{50} values for the crude methanol extract ranged from 46.49 ± 0.4 to 54.73 ± 3.3 $\mu\text{g/mL}$, indicating its notable cytotoxicity against all the tested cancer cell lines with U87 being the most sensitive to the extract. The successive petroleum ether extract also had notable activity against all the cell lines, with IC_{50} values ranging from 48.84 ± 1.3 to 75.57 ± 1.8 $\mu\text{g/mL}$. The successive ethyl acetate extract exhibited moderate cytotoxicity, with IC_{50} values varying from 233.21 ± 2.1 to 552.11 ± 5.5 $\mu\text{g/mL}$ [46].

The stem bark extracts of this plant have also demonstrated significant anticancer potential, while the leaves have shown even more pronounced anticancer activity. As an example, the ethanolic extract of the *Careya arborea* leaves was used to investigate cell viability, migration, and its mechanism. Two human breast cancer cell lines, MCF-7 and MD-MBA-231, were assessed using the sulforhodamine B (SRB) assay. The results indicated that the leaf extract significantly suppressed cell proliferation in both cell lines after 24 and 48 h of treatment. The IC_{50} values for MCF-7 cells were 34.78 ± 1.30 $\mu\text{g/mL}$ and 18.88 ± 2.18 $\mu\text{g/mL}$, while for MD-MBA-231 cells, the values were 110.75 ± 10.66 $\mu\text{g/mL}$ and 26.28 ± 1.11 $\mu\text{g/mL}$, respectively. Notably, the extract exhibited a potent inhibitory effect on MCF-7 cells compared to MD-MBA-231 cells. As a result, subsequent experiments

focused on MCF-7 cells to further explore the drug's mechanisms of action. Phase-contrast microscopy revealed that MCF-7 cells were nearly completely eradicated after exposure to the leaf extract concentrations of 100–250 µg/mL. Additionally, the extract significantly inhibited the colony-forming ability of MCF-7 cells, with remarkably low IC₅₀ values of 3.48 ± 0.15 µg/mL. Interestingly, the concentration of the plant extract required to inhibit MCF-7 cell growth was lower than that needed to suppress cell proliferation, underscoring its potent anticancer activity [60]. Further investigations revealed that the leaf extract did not affect p21 expression, but it significantly reduced cyclin D1 expression. The p21 and cyclin D1 are proteins that promote the invasiveness of tumors while increasing metastasis. They are typically overexpressed in many human cancers, such as breast, prostate, and cervical carcinomas [61,62]. Moreover, *Careya arborea* extract was able to induce apoptosis in cancer cells by increasing the caspase 3 and cytochrome C proteins that play a crucial role in inducing apoptosis [63]. Furthermore, another parallel experiment showed that 5 µg/mL of ethanolic leaf extract reduced cell viability by 50% by triggering apoptosis in cancer cells. The extract also induced necrosis at higher concentrations (10 µg/mL), in all areas of the cancer cells, indicating its apoptosis and necrosis-inducing ability in tumor cells. In terms of cell migration, treatment with the extract significantly suppressed MCF-7 cancer cell migration and was associated with reduced expression of MMP-2 and MMP-9 proteins in the culture medium [60]. These results demonstrate that the leaf extract exerts anticancer effects through multiple mechanisms, including apoptosis induction, inhibition of cell proliferation, and suppression of migration. However, the studies are confined to in vitro models, primarily MCF-7 cells, limiting generalizability across cancer types, thus warrants further investigations.

Furthermore, the cytotoxic potential of ethyl acetate (EA-CA) and ethanol (EO-CA) extracts of *Careya arborea* leaves was evaluated in a study using the SRB assay. The extracts were tested against human cancer cell lines, including KB (Nasopharyngeal), HOP62 (Lung carcinoma), ME180 (Cervical cancer), and K562 (Leukemia) cells. As evidenced by the lowest total growth inhibition (TGI) and GI₅₀ (concentration required for 50% growth inhibition) values, the ethanol extract of *Careya arborea* had the most potent anticancer activity, with a GI₅₀ value of 43.4 µg/mL against the HOP62 cell line, and the second potent GI₅₀ value was 45.3 µg/mL against the ME180 cell line. Chromatographic studies also supported these findings by revealing that the plant's ethanol extract contains polyphenols such as gallic acid and quercetin, and their antioxidant properties are likely responsible for this cytotoxic activity [39,64]. While the ethanol extract shows promising cytotoxicity across multiple cancer cell lines, the specific contribution of individual polyphenols versus other compounds remains unclear, with no assessment of effects on normal cells.

Pancreatic cancer remains a major global health challenge due to its poor prognosis, often resulting from late-stage diagnosis and limited effectiveness of conventional treatments such as chemotherapy and radiotherapy. A group of researchers developed nanoparticles 195 ± 50 nm in size from the methanolic extract of *Careya arborea* bark to evaluate their anticancer potential against pancreatic cancer cells. In vitro, cytotoxicity assays revealed that these nanoparticles inhibited up to 60% of the MiaPaCa-2 cell proliferation (Pancreatic cancer). Furthermore, as evidenced by DNA fragmentation tests, the *Careya arborea* nanoparticles were capable of inducing apoptosis in pancreatic cancer cells, highlighting the efficacy of the nanoparticles made from *Careya arborea* bark extract against pancreatic cancer [65]. These results indicate that *Careya arborea* possesses anticancer potential, which is further enhanced through nanotechnology-based formulations.

These results demonstrate that *Careya arborea* shows multi-faceted potential anticancer activity, affecting proliferation, apoptosis, and metastasis-related pathways. However, further mechanistic studies, isolation of active compounds, in vivo validation, and toxicity

assessments are essential before therapeutic application can be considered. To consolidate these observations, an illustrative diagram of the prospective anticancer activities of *Careya arborea* is shown below (Figure 4).

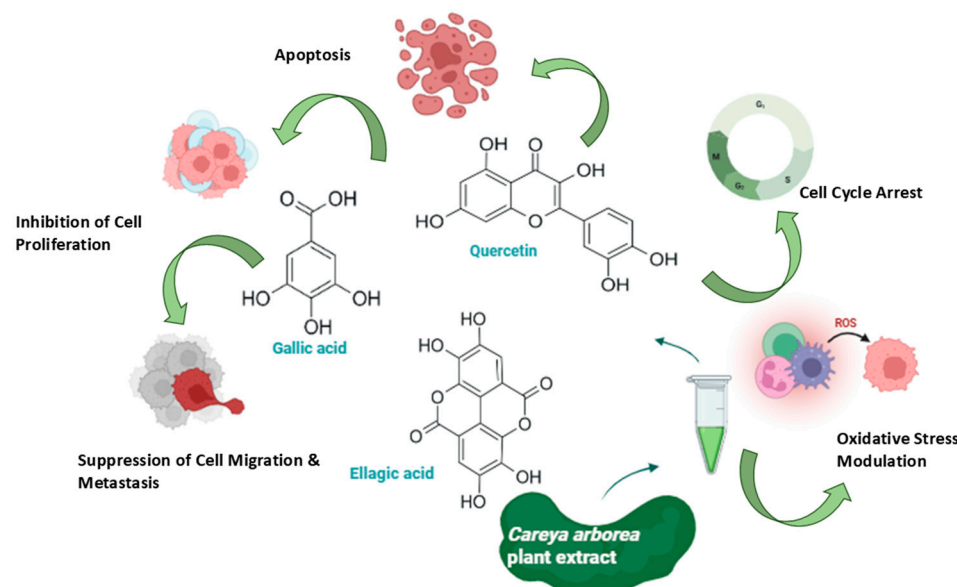


Figure 4. Anticancer activity of *Careya arborea* plant extracts.

7. Conservation and Sustainable Harvesting of *Careya arborea*

Sri Lanka's economy relies heavily on its biological resources, making it essential to closely monitor the risks faced by its native biota. The rapid growth of the human population, widespread dependence on agriculture, and excessive exploitation of timber have placed significant stress on the country's flora. Many endemic species, including medicinal plants used for millennia in traditional medical systems, are now either extinct or under threat of extinction. As a result, Sri Lanka is witnessing a loss of wild populations and a corresponding decline in genetic diversity. Although natural regeneration of these species does occur, successful establishment remains limited. In response, the government has taken measures to increase the populations of medicinal plants in their natural habitats, promote their cultivation and propagation in areas beyond their original range, and strengthen the knowledge base through education and awareness initiatives. Like many underutilized species, *Careya arborea* faces habitat degradation and pressure from unsustainable harvesting. Despite its natural regeneration capacity, poor seedling establishment hinders population recovery. Its inclusion in conservation strategies, through in situ protection, propagation, and incorporation into reforestation or agroforestry programs, is crucial to prevent genetic erosion and ensure its availability for future research and traditional use [66,67].

Conservation strategies should integrate in situ and ex situ approaches, community-based management, and modern biotechnological tools such as tissue culture and seed banking. Furthermore, linking conservation with livelihood generation, for example, through inclusion in agroforestry systems or the development of value-added herbal products, could provide long-term incentives for sustainable use. Aligning these measures with global biodiversity commitments, such as the Convention on Biological Diversity and the UN Sustainable Development Goals, would strengthen both national and international support. Finally, fostering collaboration among researchers, traditional practitioners, policymakers, and local communities is essential to safeguard this underutilized yet valuable species for future generations [68].

8. Conclusions

Careya arborea is a medicinally significant plant exhibiting a wide range of pharmacological activities, notably prospective antioxidant, anti-inflammatory, and anticancer properties. These therapeutic effects are largely attributed to its rich phytochemical composition, including flavonoids, phenolic compounds, alkaloids, and terpenoids, which position this plant as a valuable candidate in the field of drug discovery and development. As demonstrated in various studies, the plant's extracts have shown distinct capacities to neutralize free radicals, modulate inflammatory pathways, and inhibit cancer progression by influencing key cellular mechanisms. Importantly, *Careya arborea* remains an underutilized fruit plant in Sri Lanka, despite its rich medicinal and nutritional potential. Promoting consumption of its fruit as a dietary source of natural antioxidants and other health-enhancing phytochemicals could offer preventive benefits and support overall well-being. Its incorporation into functional foods or nutraceutical formulations should be explored to broaden its applications beyond traditional medicine. To advance the development of plant-based therapeutics, it is imperative to conduct robust in vitro and in vivo studies, followed by well-structured clinical trials. Moreover, integrating advanced techniques for the isolation and characterization of novel bioactive compounds, alongside strategies to improve their bioavailability, will be critical. Bridging traditional medicinal knowledge with modern pharmacological and molecular approaches will further enhance the therapeutic potential of this plant. In light of its medicinal potential, the conservation of *Careya arborea* should be prioritized through integrated strategies, including sustainable harvesting, habitat preservation, and cultivation-based interventions to ensure its long-term availability. Efforts to promote the cultivation of medicinal plants on farms should be supported through targeted education and awareness programs. Moreover, effective conservation requires not only governmental initiatives but also active collaboration among private stakeholders, local communities, and conservation bodies to ensure the species is sustainably utilized and preserved for future generations. In conclusion, the diverse pharmacological properties of *Careya arborea*, combined with its status as an underutilized fruit, underscore the importance of continued scientific investigation, not only to unlock its potential in developing accessible healthcare solutions but also to support its conservation and sustainable use.

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