

**"LAKSHMANA PHALA (*Annona muricata*): ANATURAL CHEMOTHERAPY AGENT FOR CANCER TREATMENT"****Dr. Archana Rajeev^{*1}, Dr. K. Madhusudana Rao², Dr. Yamini Diwakar³, Dr. T. Leela Rani⁴**¹PG Scholar- Dr NRS Govt. Ayurveda College, Vijayawada.²Professor and HOD- Dr NRS Govt. Ayurveda College, Vijayawada.³Assistant Professor- Dr NRS Govt. Ayurveda College, Vijayawada.⁴Assistant Professor- Dr NRS Govt. Ayurveda College, Vijayawada.

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ABSTRACT

The world we live in today is plagued by the scourge of adulteration and pollution, which has led to a significant increase in cancer cases. The air we breathe, the water we drink, and the food we eat are all tainted with toxic substances that can cause irreparable harm to our health. The consequences of this are stark, with cancer emerging as a major public health concern in India. According to recent statistics, the country is witnessing a staggering rise in cancer cases, with over 1.3 million new cases diagnosed every year. The cancer burden in India is expected to increase further due to lifestyle changes, environmental pollution, and inadequate healthcare infrastructure. At this critical juncture, nourishment plays a vital role in helping patients cope with the demands of treatment. A well-balanced diet rich in essential nutrients can

help boost energy levels, support immune function, and manage side effects. Lakshman phal, also known as soursop or *Annona muricata*, is a fruit with various medicinal properties in Ayurveda. It belongs to the Annonaceae family and has been used traditionally for a very long time. This review article focuses on the potential benefits of Lakshmana phala in cancer treatment and immunity boosting, as referenced. The article discusses how Lakshmana phala's bioactive compounds may help inhibit cancer cell growth, induce apoptosis, and support the body's natural defense mechanisms, highlighting its potential as a valuable

adjunct therapy in cancer treatment.

INTRODUCTION

Globally, cancer is a leading cause of death, with an estimated 20 million new cases and 9.7 million deaths in 2022. Projections indicate a substantial increase in new cases by 2050. Cancer is a heterogeneous and multifactorial disease in which a series of genomic/molecular alterations cause the uncontrolled growth and proliferation of the cells, causing a rapid increase in tissue mass in the affected parts of the body. Under normal conditions, a cell gets signals to die and to supplant the organism with a young and healthier cell. Cancer cells grow using the body's oxygen and supplements, depriving other cells of regular supplements and growth factors.^[1]

Chemotherapy primarily works by circumventing the cancer cells from further growth and division. Cancer cells usually divide and grow at a much accelerated rate than normal cells and are physiologically possess very high endogenous stress. Therefore, the drugs can destroy them rapidly and more effectively in comparison to other surrounding cells^[1] But chemotherapy, can be a gruelling experience that leaves patients physically and emotionally drained. The harsh reality is that chemotherapy not only targets cancer cells but also affects healthy cells, leading to debilitating side effects like fatigue, weakness, and loss of energy.

Lakshmana phala is a miraculous fruit, exhibits potential as a natural chemotherapy agent by inhibiting cancer cell division and promoting nourishment to damaged tissues. Its bioactive compounds may help control tumor growth, preventing further proliferation and metastasis. By targeting cancer cells, Lakshmana phala may offer a holistic approach to cancer management, reducing the harmful effects of conventional chemotherapy. Additionally, its nourishing properties may help repair and rejuvenate damaged tissues, enhancing overall well-being and quality of life for cancer patients. As a potential adjunct therapy, Lakshmana phala's unique mechanisms of action make it an intriguing area of study in the pursuit of complementary cancer treatments.

AIM AND OBJECTIVE

1. To systematically review and analyze information on other review articles, international journals about Lakshmana phala's traditional uses, benefits, and potential therapeutic applications.
2. To explore the natural chemotherapy properties of Lakshmana phala, focusing on its

potential to inhibit cancer cell growth, induce apoptosis, and prevent metastasis, thereby assessing its efficacy as a complementary cancer treatment.

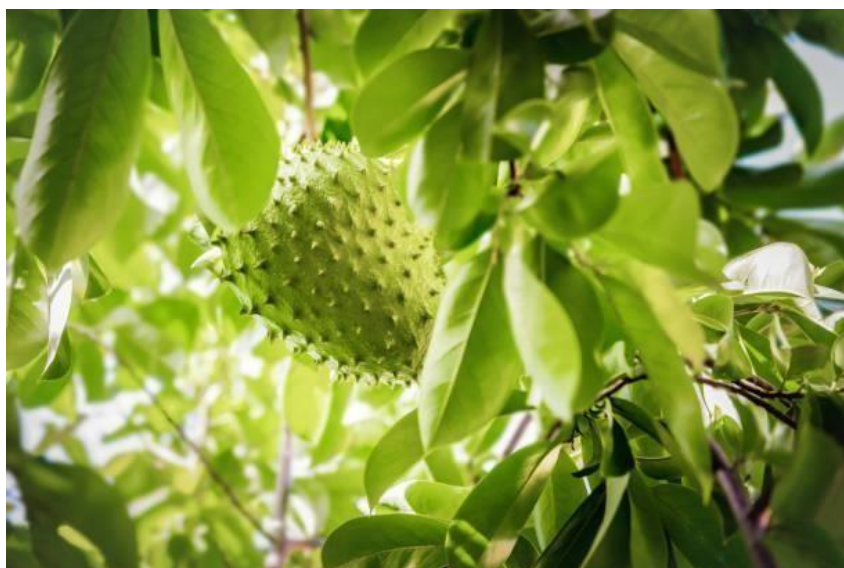
3. To elucidate the mechanisms by which Lakshmana phala's phytoconstituents control cancer.

MATERIALS AND METHODS

- A comprehensive review of other articles, was conducted to gather traditional knowledge on Lashmanaphala.
- Relevant peer-reviewed articles, journals and online databases were searched and analyzed to understand modern pharmacological perspectives on Lashmanaphala.
- The collected data from traditional knowledge and modern pharmacological analysis were critically analyzed and synthesized to draw meaningful conclusions about Lashmanaphala's potential in cancer treatment.

BOTANICAL DISCRIPTION AND DISTRIBUTION

Annona muricata is also known as soursop, graviola, guanabana, paw-paw, and sirsak. It belongs to the Annonaceae family, which has around 130 genera and 2300 species.^[2,3] Originally from the warmest tropical regions of South and North America, *A. muricata* is now found in many tropical and subtropical areas worldwide, including India, Malaysia, and Nigeria.^[4]



The bark of *Annona muricata* is greyish-brown in color and has a rough texture. The leaves of *Annona muricata* are large, glossy, dark green in color, simple, alternate, petiolate, Oblong or

elliptical in shape. The inflorescence of *Annona muricata* is solitary or in clusters of 2-3 flowers with axillary or supra-axillary. The flowers of *Annona muricata* are greenish-yellow in color in triangular in shape with 3 sepals and 6 petals. The fruit of *Annona muricata* is a syncarp, formed by the fusion of multiple ovaries. It is large, heart-shaped, and green in color which is 15-20 cm in diameter with soft, creamy pulp and numerous seeds. The useful parts of *Annona muricata* include: Fruit (pulp, juice, and seeds), Leaves, Bark, Roots, Seeds. These parts are used for various purposes, including food, medicine, and traditional remedies.

ETHNOMEDICINAL USES

All parts of the *A. muricata* tree, as well as other *Annona* species like *A. squamosa* and *A. reticulata*, are widely utilized in traditional medicine to combat various human ailments and diseases, particularly cancer and parasitic infections.

The fruit of *A. muricata* is used as a natural remedy for arthritic pain, neuralgia, arthritis, diarrhea, dysentery, fever, malaria, parasites, rheumatism, skin rashes, and worms. Additionally, it is consumed to increase a mother's milk production after childbirth.

BIOACTIVE METABOLITES IN *A. MURICATE*

- *Annona muricata* contains a variety of bioactive compounds with potential health benefits. These include annonaceous acetogenins, alkaloids, flavonoids, phenolic acids, and vitamins like Vitamin C and potassium. Additionally, it contains terpenoids, saponins, coumarins, and tannins. *Annona muricata* leaves contain various alkaloids, including aporphines, isoquinolines, imino sugars, and protoberberines. Key flavonoids found in soursop include quercetin and kaempferol. **Phenolic acids** like gallic acid, chlorogenic acid, and ellagic acid, are also potent antioxidants.

Some identified phenolic compounds are phenolic acids, flavonoids and gallotannins. On the other hand, the *A. muricata* leaves and peels have the highest content of alkaloids than stem bark or fresh pulp. The reported alkaloids from *A. muricata* leaves are aporphines, isoquinolines, imino sugars, and protoberberines. About acetogenins, over forty compounds have been isolated from *A. muricata* leaves, and annonacin has been reported as the most abundant.^[6]

A. MURICATA'S REVOLUTIONARY ROLE IN EMT REGULATION

Epithelial-mesenchymal transition (EMT) is a process where epithelial cells change to

become more like mesenchymal cells. This means they lose their tight connections with other cells and gain the ability to move more easily. In cancer, EMT helps cancer cells break away from the main tumor, move to other parts of the body (called metastasis), and become more resistant to cell death. EMT can also make cancer cells more like stem cells, increase drug resistance, and affect how the immune system works. Understanding EMT is important for learning about how cancer spreads.^[7]

Cancer recurrence at the metastatic site is believed to need the reverse process, termed mesenchymal to epithelial transition (MET), following invasion and propagation^[8] For the reversion of migratory mesenchymal neoplastic cells and the subsequent formation of macrometastases, microenvironmental cues are regarded as a crucial deterministic component.

Research suggests that a natural product from the *A. muricata* plant could help prevent cancer cells from spreading. This is because cancer cells use a process called epithelial-mesenchymal transition (EMT) to metastasize, or spread through the body. A key substance that triggers EMT is transforming growth factor-beta 1 (TGF- β 1), which encourages lung cancer cells to move and invade other areas. Interestingly, an extract from *A. muricata* leaves might block TGF- β 1's activity, potentially controlling a subtype of EMT. In animal studies, *A. muricata* extract reduced TGF- β 1 levels in liver tissue of rats with liver damage and was shown to be safe with no harmful effects.^[9]

MUC4, a member of the glycoprotein family, plays a significant role in various cancers like pancreatic, ovarian, and head and neck cancers. It suppresses cell death (apoptosis) and makes cancer cells resistant to some chemotherapy treatments by affecting signaling pathways. Interestingly, *Annona muricata* reduces MUC4 expression, causing metabolic stress and toxicity in pancreatic cancer cells. This reduces the migration and invasion of these cancer cells.^[10]

THE ANTIOXIDANT AND ANTI-CANCEROUS BENEFITS OF ANNONA MURICATA

- More than 120 acetogenins have been identified in ethanolic, methanolic or other organic extracts of different organs and tissues of *A. muricata* such as leaves, stems, bark, seeds, pulp and fruit peel. Annonacin was the most abundant acetogenin reported in both leaves^[11] and fruit of *A. muricata*^[12], but has also been reported in seeds, peel and roots. Some acetogenins

have shown the ability to scavenge free radicals, particularly in studies using the DPPH assay. This suggests a potential role in protecting cells from oxidative stress.

Action of Acetogenins on Tissue Growth: Acetogenins inhibit NADH- ubiquinone oxidoreductase (Complex I) in the mitochondrial electron transport chain. This blocks ATP production. Due to lack of ATP, rapidly dividing cells (like tumor cells, parasites, or insect tissues) undergo cell growth arrest and apoptosis.

Alkaloids are naturally occurring compounds containing basic nitrogen atoms. The most abundant in *A. muricata* are reticuline and coreximine^[13], and leaves contain the higher alkaloid concentration, although they have also been found in roots, stems and fruit.

- Coreximine shows anticancer activity by stopping cancer cell growth, inducing programmed cell death (apoptosis), and blocking blood vessel formation that tumors need for survival. It also reduces oxidative stress and inflammation, which further slows cancer progression. Thus, it works as a natural compound with potential use in cancer prevention and treatment.
- Reticuline modulates neurotransmitter systems and this is useful in reducing cancer-related neuropathic pain or neurotoxicity caused by chemotherapy.
- The alkaloids reported in *A. muricata* are mainly of the isoquinoline, aporphine and protoberberine type.^[14] Reticuline has been shown to reduce airway resistance and inflammatory infiltration in lung tissues.^[15] Thirty seven phenolic compounds have been reported to be present in *A. muricata*. The important phenolic compounds found in *A. muricata* leaves include quercetin and gallic acid.^[16]
- Quercetin helps to blocks tumor cell proliferation by halting cycle at G1/S or G2/M checkpoints and also induces apoptosis. Apoptosis induction – Activates p53, caspase-3, and mitochondrial pathways → programmed cell death.
- Gallic acid have Pro-oxidant action in tumor cells .It generates ROS selectively in cancer cells and induces apoptosis. It also activates mitochondrial apoptosis by cytochrome-c release and caspase activation.
- The presence of flavonoids and lipophilic antioxidant compounds such as tocopherols and tocotrienols has been reported to be present in the pulp. Phenolic compounds are considered as the major phytochemicals responsible for the antioxidant activity.^[17]
- Tocopherols enhances immune surveillance by stimulating NK (natural killer) cells and T-lymphocyte activity against tumor cells and it reduces chronic inflammation (a cancer risk

factor) by suppressing COX-2 and inflammatory cytokines.

- Tocotrienols inhibit VEGF (Vascular Endothelial Growth Factor) and other pro-angiogenic factors. Suppress formation of new blood vessels in tumors.
- Anti-tumoral activity has been reported for extracts and some isolated acetogenins of *A. muricata*. It was reported by that the ethanolic extract of *A. muricata* leaves showed greater anti-tumor activity in murine models than curcumin, a known natural chemopreventive.^[18,19]
- The antioxidant activity has been evaluated in fresh and frozen pulp, juice, and fresh or dried leaves also.

Nutritional Facts on Lakshmanaphala(*A. muricata*)

One cup (225 g) of soursop pulp contains 148 calories, 2.3 g of protein, 37.8 g of carbohydrates, and 0.7 g of fat. *Annona muricata* is high in vitamin C, fiber, and potassium.

Calories: 148;

Fat: 0.7 g;

Carbohydrates: 37.8 g;

Fiber: 7.4 g;

Sugars: 30.5 g;

Protein: 2.3 g; Vitamin C: 46.4 mg;

Potassium: 626 mg.

Carbohydrate

Annona muricata has nearly 38 g of carbohydrates per cup. Soursop's carbs come from naturally occurring sugars, and it has more than 7 g of fiber per serving (about a quarter of your recommended daily intake). Sorrel has a low glycemic index.

Fats

This fruit contains very little fat, with less than one gram per serving.

Protein

- *Annona muricata*, like most fruits, contains little protein. A single serving contains only 2.3 g of protein. To meet one's daily protein requirements, one would need to include other protein sources in one's diet, such as salmon, lean meats, and legumes.^[20]

Lakshmanaphala (*Annona muricata*) provides nourishment that supports cancer care by combining vitamins, minerals, and bioactive compounds. Its vitamin C acts as a strong

antioxidant and immunity booster, while dietary fiber improves gut health and helps remove carcinogens. Potassium maintains cellular balance and reduces treatment-related fatigue, and its low fat with natural sugars supplies safe energy without fueling abnormal growth. In addition, its unique acetogenins directly inhibit tumor cell growth and induce apoptosis. Together, this nourishment strengthens the body, reduces cancer risk, and supports recovery during treatment.

AYURVEDIC VIEW ON LAKSHMANAPHALA

Lakṣmaṇaphala, commonly identified with *Annona muricata* (soursop), is not mentioned in classical Ayurvedic texts or *nighaṇṭus* because it is not native to the Indian subcontinent and was introduced much later, likely during the colonial or post-colonial period. Classical Ayurvedic literature such as the *Caraka Saṃhitā*, *Suśruta Saṃhitā*, and later *nighaṇṭus* like *Rāja Nighaṇṭu*, *Bhāvaprakāśa*, and *Dhanvantari Nighaṇṭu* primarily document indigenous plants that were known, used, and studied within the Indian cultural and ecological context at the time. Since *Annona muricata* originates from tropical regions of the Americas and was not part of the ancient Indian flora, it was not observed or evaluated by classical Ayurvedic scholars. Hence, it lacks mention in the foundational texts of Ayurveda, although it may now be studied in the context of integrative or modern herbal medicine.^[21]

CONCLUSION

Lakshmana Phala (*Annona muricata*) emerges as a miracle plant in the fight against cancer. With the alarming increase in cancer outbreaks, it's imperative to explore natural alternatives to allopathic treatments, which often come with debilitating side effects. *Annona muricata* plays a multifaceted role in cancer treatment. It reduces the chances of cancer occurrence, and for those already afflicted, it acts as a *Rasayana*, providing nourishment and rejuvenation to the body's tissues. It controls further cancer growth, prevents metastasis, and exhibits antioxidant properties, which help to combat oxidative stress and promote overall health. Additionally, *Annona muricata* has a significant role in MET (Metastasis), preventing the spread of cancer cells. From its fruit to its leaves, every part of this miracle plant has its own unique action, making it a treasure trove of medicinal properties. Truly, Lakshmana Phala (*Annona muricata*) is a miracle plant that deserves a spot in every cancer-fighting toolkit. Imagine a future where cancer is defeated with the power of this amazing plant.

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