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***Review Paper***

# *Psidiumguajava (Guava)* Leaves *as a* Potential Treatment *of* Scurvy

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## Abstract

Psidiumguajava(Guava),*belonging to the Myrtaceae family, is a well-known food crop in subtropical and tropical countries. It is also known for its medicinal value and is widely used as folk medicine around the world. The seed, leaves, fruit and bark of P. guajava tree have been traditionally used for a long time for its medicinal uses that are still in use today.* P. guajava *is known for its antioxidant, analgesic & anti-inflammatory, antispasmodic, hepatoprotective, antidiarrheal, anti-diabetic, anti-cancer activity, antimicrobial and antipyretic properties. Scurvy is a condition (or rather a state)of the human body that occurs due to dietary deficiency of vitamin C, which is primarily the main cause. Chronic malnutrition is an predisposing factor and patients who are suffering from it are the main targets and are at a potential risk . The primates lack the enzymes required to synthesize vitamin C from its precursor. And thus theyhave to supplement Vitamin from exogenous dietary sources to fulfill their needs. Naturally occurring leaves of* Psidiumguajavacan be used as a potential supplement in the treatment of scurvy. The Leaves of this plant provides the all in one treatment of Scurvy. This *Myrtaceae fruit bearing plants are an interesting group offering definite opportunities for future development of excellent natural remedies one can get for treatment of variety of diseases.*

**Keywords:** Scurvy, *Psidiumguajava* Leaves, Vitamin C, Spasmolytic, Analgesic, Anti-inflamatory.

## Introduction

Vitamin C is one of the essential nutrients that isneeded for proper functioning of the body. Primates (including human beings), guinea pigs, bats, and some species of birds lack the enzyme gulonolactone oxidase which is needed for the conversion of gulonolactone to L-ascorbic acid (Vitamin C). And so it can't be synthesized in the body and hence it must be obtained through their diet. Vit. C is a highly active reducing agent and helps in free radical scavenging. It helps in the hydroxylation of proline and lysine in protocollagen to form compounds hydroxylysine and hydroxyproline in mature collagen.

Scurvy, also known as Moeller's Disease, is a clinical condition caused by Vit.C deficiency. Its primary symptoms are-swollen gums with easy bleeding, perifollicular and petechial haemorrhages, ecchymoses. Other clinical features are-haemarthrosis, gastrointestinal bleeding manifestations, and anaemia. Also wound healing is delayed, this is probably due to reduced collagen synthesis as a result of reduced Vit.C level in body.

Vit.C rich fruits (Citrus, Guava, etc) are ideal for the prevention of scurvy. It is usually associated with malnutrition and usually affects the poor people. Treatment of scurvy is usually a Vit.C rich diet or a course of 250mg of Vit. C, 3 times a day should be given. Although prognosis is excellent if treatment is started early, but if not treated may be fatal.

Leaves of guava (Psidiumguajava)can be used as an alternative for the treatment of scurvy. This plant's leaves contain various chemical that can aid in the treatment of scurvy. Guava tree is abundantly found in the subtropical and tropical regions all over the globe. Guava fruit is also rich in Vit.C. Although its fruits are seasonal,but its leaves can be used at any time as these are evergreen trees that can reach up to a height of 33ft, with spreading branches. This plant parts was traditionally used a as natural remedy to a variety of diseases including diarrhea , dysentery, inflamed mucous membranes, digestive problems, edema, gout, hemorrhages, gastroenteritis, gastritis, diabetes.

**Observation:** Morphology: Guava leaves are oval or oblong elliptical shaped, 2 to 6 inches long and 1 to 2 inches wide with an irregular outline. The leaves have short petioles and are oppositely arranged, that are slightly down on the underside. Green in appearance with somewhat leathery texture of veins, this leaves have a pleasant scent.

Guava leaf extract has potent anti-inflammatory, analgesic, hemostatic, hepatoprotective, antimicrobial, antifungal and antioxidant activities. The leaf extract contains Vitamin C in significant amount. They also contain organic compound such as-monoterpene compounds (α-pinene and β-pinene), flavonoids, triterpenoids, caryophyllene oxide, caryophyllene. Menthol, an important analgesic is also present. Along with itavicularin, quercetin-3-α-L-arabinofuranoside and 3-L-4-pyranoside, guaijaverin, guavenoic acid, guajavolide, humulene

(α-humulene), limonene,cardinene is also present. Others compounds such as selinene, tannin, resin, isopropyl alcohol, terpenyl acetate, farnesene, cryptonine, dihydrobenzophenanthridine, prenol, guayavolic acids, oleanolic acid, eugenol, longicyclene, nerolidioltriterpene, β-bisabolene, curcumene, mallic acids, β-sitosterol, ursolic, crategolic and cineol[1], is also found in trace amounts.

α-Pinene acts as an anti-inflammatory agent. Experiments by Nissen and colleagues also proved it to be a broad-spectrum antibiotic[2]. It probably is mediated via PGE1.

Vitamin C (Ascorbic acid) is a nutrient and antioxidant substance. Antioxidant protect cells from the deleterious effect of free radical and helps to scavenge it. A research was done to extract the Ascorbic acid in the leaves of Guava by two methods, in the first method using Ethanol in room temperature and the yield percentage 15.1%, in the other method soxhlet extraction was done and the yield percentage 20.7%[3]. This indicates that Vit.C is present in considerable amount in this leaves. And leaf extract can be used as a rich source of Vit.C in patients with scurvy. Crushed leaves can be taken orally for better use.

Earlier studies indicated that flavonoids may affect anti-inflammatoryeffects. Theycan inhibit reactive oxygen species along with nitrogen compounds[4]. Various enzymes such as - nitric oxide synthase lipoxygenase or cyclooxygenase , exhibitsanti-inflammatoryactivity. It has been proved by various researches that flavonoids can inhibit these anti-inflammatory activities and prevent free radical production[5] .Hence they act as anti-oxidants. But it has been earlier proposed that antioxidant activity of flavonoidsis of negligible amount. Although it has been observed that after intake of foods rich in flavonoids there was a considerable hike in the antioxidant potential ofblood. This discrepancy was later solved by proposing that uric acid, a metabolic product formed as a result of flavonoid depolymerization, was the main cause[6]. Flavonoids alsohave significant antiproliferative activity. Its effect can be best cited in a granuloma where they tend to reduce the volume as well as weight of the granuloma. As it is known that cytokines acts as an important factor in the formation and sustenanceof granuloma, so it is quite evident that flavonoids are mainly responsible for this anti-inflammatory effect and antiproliferative effect[7].

Menthol is a natural analgesic compound found in a wide range of plants.It is also present in significant amount in *Psidiumguajava*. It is finds significant use in minor throat irritation. Opioid analgesics are group of drugs that reduces pain by acting on opioid receptors (mu, kappa and delta). Menthol is a kappa opioid receptor agonist(weak) and acts by inhibiting $Ca^{2+}$ channels at neuronal membranes .As a result the pain pathway is blocked. On tropical administration of menthol, the cold receptors are stimulated and it gives a pleasant cooling sensation due to this effect[8]. *Result of experiments on central action of menthol* indicates that menthol has central analgesic effects acting through the spinal cord. Pain hypersensitivity (contralateral as well as ipsilateralpain) is decreased by menthol. Inflammatory pain is probably inhibited by blockage of voltage gated $Na^+$ and $Ca^{2+}$channels[9]. Hence it can counteract the pain sensation that is caused by swelled up gums in scurvy and give relief to the patient.

β-caryophyllene is chemically a natural bicyclic sesquiterpene compound. It is an important component of oil of *Syzygiumaromaticum* (cloves) and many other essential oils. Clove oil is extracted from its stem and flowers. It has also been extracted from the leaves of*Psidiumguajava* .β-caryophyllene acts as a local anesthetic , thereby reducing the pain in gums due to scurvy[10].

Caryophyllene oxide is a derivative of (−)-β-caryophyllene,also extracted from leaf extracts. Experiments by Chavan, Wakte, and Shindedemonstrated that caryophyllene oxide has potent anti-inflammatory and analgesic activity[11].

Humulene **(α-humulene)** is a naturally occurring monocyclic sesquiterpene. It is constituent of Guava leaves extract. It produces similar effects to dexamethasone[12]. Recent studies have found outthat the *Cordiaverbenacea*'s essential oil, α-humulenehas anti-inflammatory properties. Experimental animal models of rats and mice having inflammation, responded well to oral treatment.α-humulene can also reduce platelet activating factors. Edema(caused by histamine injection) was also reduced by alpha humulene. Significant results were found out when in it was used for systemic treatment in experimental rats (injected with carrageenan). Interleukin-1β (IL-1β) and tumornecrosis factor- α were markedly reduced. This compound was also found to reduce various other factors including prostaglandins $E_2$ ($PGE_2$). Along with it, it alsoreduced the expression of various enzymes including cyclooxygenase and nitric oxide synthase (iNOS).So it is quite evident that this compound is a potential anti-inflammatory agent. Surprisingly animals treated with dexamethasoneshowed similar pattern of activity[13].

Avicularin (quercetin-3-α-L-arabinofuranoside) is another important compound found in the leaf extract. Avicularinhas anti infectious and anti-inflammatory properties. Studies revealed that synthesis of inducible nitric oxide synthase as well as cyclooxygenase is reduced by avicularin .So as a result nitric oxide and prostaglandins, which are proinflammatory mediators are reduced. Hence inflammatory responses can't be generated. Another factor NF-κB is responsible for production of proinflammatorycytokines, it acts by activating genes in the nuclues. But LPS-induced degradation of IκB, which is responsible for cytoplasmic retention of NF-κB, is suppressed by avicularin. As a result the inflammatory cytokines are reduced producing a marked anti-inflammatory action[14].

The spasmolytic activity of the *Psidiumguajava*leaf has been shown experimentally. Quercetin, aaglyconepresent in the leaf

and in the extract, gets activated on hydrolysation by gastrointestinal fluid[15]. Oral administration of the leaf extract is effective in producing mark spasmolytic action.

Jaiarj, Wongkrajang, Thongpraditchote, Peungvicha, Bunyaprap hatsara and Opartkiattikul experimented on the bleeding time and hemostasis property of guava leaf extract. Hemostasis involves three vital components vasodilatation, platelet aggregation and coagulation of blood. In vivo models showed that dosage of guava leaf extract is directly proportional to the amount of platelet aggregation occurred. Increase in amount of leaf extract increases its effect.Also vascular tissue of animal models (rabbit) earlier treated with phenylephrine, showed marked vasoconstriction on application of this extract. All this factors proved to be beneficial but further experiments revealed counter mechanism. Blood coagulation time was considerablyincreased. Rise in APTT (activated partial thromboplastin time )($p<<0.05$)was directly proportional to the amount of extract given. Bleeding time was unaffected [16]. Although guava leaf extract may not be a complete hemostatic agent (as it prolongs coagulation time) but still others beneficial effects give it a minor hemostaticproperty. Platelet aggregation and vasoconstriction may be able to control minor bleeding manifestations in scurvy which will be a beneficial effect to ascorbic acid which has the major role.

Guaijaverin (quercetin-3-*O*-*α*-L-arabinopyranoside) is an active flavonoid compoundfound in guava leaves. It has antiplaque property. The growth of bacteria *Streptococcus mutans* was inhibited by guaijaveri[17]. *Plaque is an important factor that is to be considered in scurvy. It can further complicate the disease by invading the swollen gums, which act as potential breeding grounds for microorganisms and causing secondary dental problems*. This leaf extract acts by inhibiting growth of other microorganism on the inflamed gums and teeth and prevents it from getting further complicated. Hence plaque cannot get deposited on the teeth and they are saved from further damage.
Guava Leaves Extract has antimicrobial activity. Birdi et al. and Birdi et al.stated that P. guajava leaves can be effective in treating diarrhea as it has a broad spectrum of antimicrobial action[18]. Flavonoids which is an active component of this leaf is primarily responsible for this antimicrobial activity. Experiments by H.ARIMA & DANNO on guava leaf extract have revealed four flavonoids quercetin ,guaijavarin, morin-3-*O*-α-L-lyxopyranoside , morin-3-*O*-α-L-arabopyranoside that has potent antimicrobial action[19].Guava leaf extract also suppressed growth of a gram positive bacteria(including *Staphylococcus aureus andBacillus cereus*).Antimicrobial effects of guava leaves was further pronounced by experiments that showed that extract prepared from dry leaves was effective in inhibiting the growth of β-streptococcus group A bacteria[20]. So it is quite evident that the leaf extract contain antimicrobial agents that can be made use of in treating microbial diseases. These leaf extracts when used in scurvy treatment has double beneficial effects, apart from providing Vit.C (which treats the main cause),it is also providing protection against various microorganisms that may invade the already injured gums and teeth.

## Methodology

My present study emphasize the various important medicinal property of guava leaves and its usefulness in the treatment of scurvy. Various research have been previously done on this species to demonstrate its various properties. Fruits, seeds and leaves all have been extensively studied. Experiments have been done to reveal the various chemicals this leaves contain. Also the pharmacological and pathophysiological properties of this leaves are being extensively studied. All these studies and research aided me on this research and provided valuable information.

Scurvy as a disease mainly prevails because of the deficiency of Vitamin C in the diet, which is one of the essential micronutrients that is needed for proper functioning of body. This plant which is a good source of vitamin C is also a good source of other chemicals that aid in the treatment of this dreadful disease. All these factors add up to prove the qualitative treatment this plant might have in the treatment of scurvy. Much needed chemical trials and other research is needed to ascertain its utility. But theoretically it is quite efficient. Also individual research work done for the various components of this leaves proved to be quite beneficial.

## Results and Discussion

Various results indicate that Psidiumguajava leaves extract is providing an excellent treatment in Scurvy. Although few pathophysiological action of its is still in a hazy state. This plant has extreme potential to be a source of natural remedies to a number of diseases. Although scurvy is not much common these days due to proper dietary plans implementation. But it still prevails in developing countries. Malnutrition is the major cause of it. Usually it is accompanied by marasmus and other nutritional deficient diseases. Guava plant is quite common is tropical regions. Its fruit is a rich source of Vitamin C and dietary fibers. Also it as a good source of calcium,vitamin A, iron ,manganese , malic acids, oxalic acid, saponin, flavonoids, phosphoric acid, quercetin, guaijavarin. Also its seed contains various essential oils. The leaves are equally valuable and can be used as an immediate remedy as it available the whole year round, not like the fruits which is seasonal.

It is a good source of Ascorbic acid that helps to recover from scurvy. It is also a good antimicrobial agent and antiplaque agent, that protects the gums from getting infected during the recovery phase of the patient. Bleeding manifestation in the form of gum bleeding, petechichial and perifolicularhemorrhages, gastrointestinal bleeding is seen. Platelet aggregation and vasoconstriction effect of Guava leaf extract can be used to preventthese bleeding manifestations. Also if these bleeding manifestaions are controlled then anaemia

due to blood loss will be automatically corrected.*P.guajava leaves also has analgesic, anesthetic and spasmolytic action, which helps to get relief from pain.*

*P.guajava leaves also has a potent* antioxidant activity which helps to protect the cells from reactive free radicals.Also they have anti inflammatory effects that may be helpful in control of haemathrosis. They also have anti diabetic, anti diarrheal property.It is also hypoglycemic agent so it has double benefits in case of controlling obesity related diabetes reducing both weight and also acting against diabetes. They have hepatoprotective action and hence can be used as a liver tonic in jaundice .It is currently being researched for its anti-cancer properties. Traditionally they have been used in the treatment of malaria, as a oral care agent and in the control of vaginal odours.

## Conclusion

Nature is the treasure house of medicines. Cure of every disease lies in nature itself. *This plant Psidiumguajava of* Myrtaceae family are an interesting group offering definite opportunities for future development of excellent natural remedies one can get for treatment of variety of diseases.Every part of this plant has immense medicinal value.Its fruit, flowers, seeds, leaves all have its own medicinal value.This study provides only a glimpse of the potency of this plant to cure scurvy and its pharmacological properties. Evidence suggests P. *guajava* can a be a great natural remedy for the treatment of various diseases and only the seeds of time can provide it be likewise.

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