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Vijay Yogiraj
Bhupal's Noble Institutes of
Pharmaceutical Sciences,
Udaipur, Rajasthan.

Pradeep Kumar Goyal
Bhupal's Noble Institutes of
Pharmaceutical Sciences,
Udaipur, Rajasthan.

Chetan Singh Chauhan
Bhupal's Noble Institutes of
Pharmaceutical Sciences,
Udaipur, Rajasthan.

Anju Goyal
Bhupal's Noble Institutes of
Pharmaceutical Sciences,
Udaipur, Rajasthan.

Bhupendra Vyas
Bhupal's Noble Institutes of
Pharmaceutical Sciences,
Udaipur, Rajasthan.

Carica papaya Linn: An Overview

Vijay Yogiraj, Pradeep Kumar Goyal, Chetan Singh Chauhan, Anju Goyal, Bhupendra Vyas

Abstract

Papaya (*Carica papaya* Linn) is commonly called as paw-paw and it belongs to the family Caricaceae. Papaya is commonly known for its food and nutritional values throughout the world. The properties of papaya fruit and other parts of the plant are also well known in traditional system of medicine. During the last few decades considerable progress has been achieved regarding the biological activity and medicinal application of papaya and now it is considered as valuable nutraceutical fruit plant. Papaya possess excellent medicinal properties for treatment of different ailments. The different parts of the *Carica papaya* plant including leaves, seeds, latex and fruit exhibited to have medicinal value. The stem, leaf and fruit of papaya contain plenty of latex. The latex from unripe papaya fruit contain enzymes papain and chymopapain. This review focuses on different properties of papaya as a multi-faceted plant.

Keywords: *Carica papaya*, nutraceutical, medicinal plant, multi faceted plant, anti dengue, anti malarial.

1. Introduction

Carica papaya Linn belonging to family Caricaceae is commonly known as papaya in English, Papita in Hindi and Erandakarkati in Sanskrit. The plant is native to tropical America and was introduced to India in 16th century. The plant is recognised by its weak and usually unbranched soft stem yielding copious white latex and crowded by a terminal cluster of large and long stalked leaves, is rapidly growing and can grow up to 20m tall. Traditionally leaves have been used for treatment of a wide range of ailments, like in treatment of malaria, dengue, jaundice, immunomodulatory and antiviral activity. Young leaves are rich in flavonoids (kaempferol and myricetin), alkaloids (carpaine, pseudocarpaine, dehydrocarpaine I and II), phenolic compounds (ferulic acid, caffeic acid, chlorogenic acid), the cynogenetic compounds (benzylglucosinolate) found in leaves. Both leaf and fruit of the *Carica papaya* Linn. possess carotenoids namely β - carotene, lycopene, anthraquinones glycoside, as compared to matured leaves and hence possess medicinal properties like anti-inflammatory hypoglycaemic, anti-fertility, abortifacient, hepatoprotective, wound healing, recently its antihypertensive and antitumor activities have also been established. Leaves being an important part of several traditional formulations are undertaken for standardization for various parameters like moisture content, extractive values, ash values, swelling index, etc [1].

2. Taxonomy, Morphology and Distribution

2.1 Botanical Classification

Domain: Flowering plant
Kingdom: Plantae
Sub Kingdom: Tracheobionta
Class: Magnoliopsida
Subclass: Dilleniidae
Superdivision: Spermatophyta
Phyllum: Steptophyta
Order: Brassicales
Family: Caricaceae
Genus: *Carica*
Botanical Name: *Carica papaya* Linn [2].

2.2 Synonyms of *Carica papaya* Linn.

Indian and International synonyms of *Carica papaya* Linn. and different species of *Carica papaya* Linn. Are described (Table 1, 2 and 3)

Correspondence:

Vijay Yogiraj
Bhupal's Noble Institutes of
Pharmaceutical Sciences, Udaipur,
Rajasthan.

Table 1: Indian Synonyms of *Carica papaya* Linn [3].

Language	Region	Names
1. Hindi	Haryana, Delhi	Papaya, Papita
2. Bengali	West Bengal	Papaya, Pepe, Papita
3. Malyalam	Kerala	Omakai
4. Punjabi	Punjab	Papita
5. Marathi	Maharashtra	Papai
6. Tamil	Tamil Nadu	Pappali
7. Gujarati	Gujarat	Papaya
8. Kannada	Karnataka	Pharangi
9. Rajasthani	Rajasthan	Eerankari

Table 2: International Synonym of *Carica papaya* Linn [3].

Country	Names
1. India	Papita
2. Holland	Tree melon
3. France	Papaya
4. Australia	Paw paw
5. Brazil	Mamao
6. UK	Papaya, Paw paw

Table 3: Different species of *Carica papaya* Linn [3].

1. <i>Carica candamarcensis</i>	<i>Carica monoica</i>
2. <i>Carica Mexicana</i>	<i>Carica weberbaueri</i>
3. <i>Carica caudate</i>	<i>Carica omnilingua</i>
4. <i>Carica cauliflora</i>	<i>Carica palandensis</i>
5. <i>Carica chilensis</i>	<i>Carica parviflora</i>
6. <i>Carica horovitziana</i>	<i>Carica spruce</i>
7. <i>Carica cundinamarcensis</i>	<i>Carica pubescens</i>
8. <i>Carica dodecaphylla</i>	<i>Carica pulchra</i>
9. <i>Carica glandulosa</i>	<i>Carica quercifolia</i>
10. <i>Carica goudotiana</i>	<i>Carica sphaerocarpa</i>
11. <i>Carica heterophylla</i>	<i>Carica spinosa</i>
12. <i>Carica candicans</i>	<i>Carica nana</i>
13. <i>Carica longiflora</i>	<i>Carica stipulate</i>
14. <i>Carica crassipetala</i>	<i>Carica pentagona</i>

2.3 Botanical Description

Plant

Papaya plant is a large, single-stemmed herbaceous perennial tree having 20–30 feet height (Fig. 1). The leaves are very large (upto 2½ feet wide), palmately lobed or deeply incised with entire margins and petioles of 1-3 feet in length. Stems are hollow, light green to tan brown in color with diameter of 8 inches and bear prominent of scars [4].

**Fig 1:** *Carica papaya* plant

Fruit

The fruits are big oval in shape and sometimes called pepo-like berries, since they resemble melon by having a central seed cavity (Fig. 2). Fruits are borne axillary on the main stem, usually singly but sometimes in small clusters. Fruits weigh from 0.5 up to 20 lbs, and are green unlike ripe, turning yellow or red orange. Flesh is yellow-orange to salmon (pinkish-orange) at maturity. The edible portion surrounds the large central seed cavity. Individual fruits mature in 5-9 months, depending on cultivator and temperature. Plants begin bearing fruits in 6-12 months [4].

**Fig 2:** *Carica papaya* fruit

Flowers

Papaya plants are dioecious or hermaphroditic, producing only male, female or bisexual (hermaphroditic) flowers. Papaya are sometimes said to be “trioecious” meaning that separate plants bear either male, female, or bisexual flowers (Fig. 3). Female and bisexual flowers are waxy, ivory white, and borne on short peduncles in leaf axils, along the main stem. Flowers are solitary or small cymes of 3 individuals. Ovary position is superior. Prior to opening, bisexual flowers are tubular, while female flowers are pear shaped. Since, bisexual plants produce the most desirable fruit and are self-pollinating, they are preferred over female or male plants. A male papaya is distinguished by the smaller flowers borne on long stalks. Female flowers of papaya was pear shaped, when unopened whereas, bisexual flowers are cylindrical [4].

**Fig 3:** *Carica papaya* flowers

2.4 Pollination of *Carica papaya* Linn

Three methods of pollen transfer: - (1) Self-pollination (2) Pollen from same plant but different flower (3) Pollen from different plant (Fig. 4).

Bisexual flowered plants are self-pollinating, but female plants must be cross pollinated by either bisexual or molar plants [4].

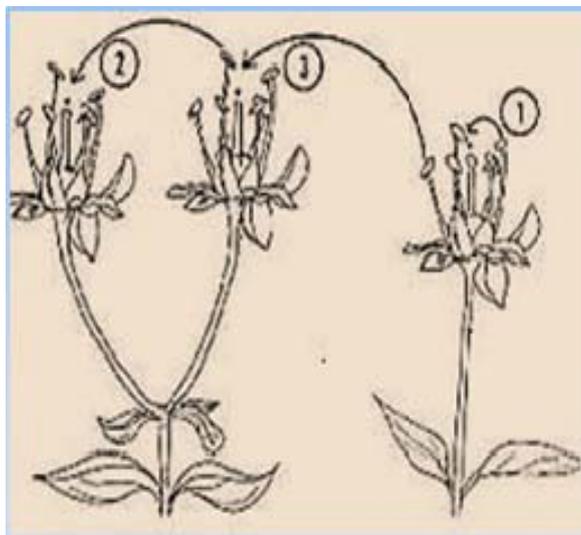


Fig 4: *Carica papaya* pollination

2.5 Geographical Distribution

Though the exact area of origin is unknown, the papaya is believed native to Tropical America, perhaps in Southern Mexico and neighbouring Central America. Successful commercial production today is primarily in Hawaii, Tropical Africa, the Philippines, India, Ceylon, Malaysia and Australia,

apart from the widespread but smaller scale production in South Africa, and Latin America. In India, papaya is cultivated in Maharashtra, Bengal, Bihar, Haryana, Punjab, Delhi, Andhra Pradesh and Uttar Pradesh [4]. Cultivators of *Carica papaya* are described (Table 4).

Table 4: Cultivators of *Carica papaya* Linn [5].

Variety	Characteristics
1. Mexican Red	Reddish to Red – Orange in color, more elongated in shape and have red flesh
2. Solo	Most common variety, this variety doesn't produce any male tree, Reddish - Orange flesh, pear shaped
3. Sunrise Solo	Pear shaped fruit, smooth skin, Reddish Orange color, sweet, sugar Content high
4. Sunset Solo	Small to medium sized, pear shaped, Orange Red skin
5. Waimanalo Solo(X-77)	Round fruit with neck, cavity star shaped
6. Kamiha	Genetically engineered fruit, well known for its round shape, carry more flesh, most resistant to viruses

3. Chemical Constituents of *Carica papaya* Linn.

Carica papaya Linn. is one of the valuable plant used for various purposes in medicinal field. Leaves, fruit and seeds of the *Carica papaya* are used as ethno medicine.

This work describes biochemical constituents of leaves of *Carica papaya*. Chemical composition of various part of *Carica papaya* plant are described (Table 5).

Table 5: Chemical composition of various parts of *Carica papaya* Linn. Plant [6, 7, 8].

Part	Constituents
1. Fruit	protein, fat, fibre, carbohydrates, minerals, calcium, phosphorus, iron, vitamin C, thiamine, riboflavin, niacin, and caroxene, amino acid, citric acids and molic acid (green fruits), volatile compounds : linalol, benzylisothiocynate, cis and trans 2, 6-dimethyl-3,6 epoxy-7 octen-2-ol. Alkaloid, α , carpaine, benzyl- β -d glucoside, 2-phenylethyl- β -D-glucoside, 4-hydroxyl -phenyl-2 ethyl-B-D glucoside and four isomeric malonated benzyl- β -D glucosides
2. Juice	N-butyric, n-hexanoic and n-octanoic acids, lipids; myristic, palmitic, stearic, linoleic, linolenic acids-vaccenic acid and oleic acids
3. Seed	Fatty acids, crude proteins, crude fibre, papaya oil, carpaine, benzylisothiocynate, benzylglucosinolate, glucotropacolin, benzylthiourea, hentriacontane, β -sistosterol, caricin and an enzyme nyrosin
4. Root	Arposide and an enzyme myrosin
5. Leaves	Alkaloids carpain, pseudocarpain and dehydrocarpaine I and II, choline, carposide, vitamin C and E
6. Bark	β -sitosterol, glucose, fructose, sucrose, galactose and xylitol
7. Latex	proteolytic enzymes, papain and chemopapain, glutamine cyclotransferase, chymopapain A, B and C, peptidase A and B and lysozymes

4. Nutritional Value of *Carica papaya* Linn.

Papaya is common's man fruit, which is reasonably priced and has a high nutritive value. It is low in calories and rich in natural vitamins, and minerals. The comparative low calories content (32 Kcal / 100 g of ripe fruit) make this a favourite fruit of obese people who are into weight reducing regime. Papaya has low carotene compared to other fruit such as apples, guava, sitaphal and plantains, which helps to prevent damage by free radicals. Unripe green papaya is used as vegetable, it does not contain carotene but also all other nutrients are present. The fruit is a rich source for different types of enzymes. Papain, vegetable pepsin present in good amount in unripe fruit is an excellent aid to digestion, which helps to digest the protein in food at acid, alkaline and neutral medium. The celiac disease patients, who cannot digest the wheat protein gliadin, can tolerate it, if it is treated with crude papain, papaya has the property of tenderizing meat. This knowledge is being put to use by cooking meat with raw papaya to make it tender and digestible [9, 10]. The fermented papaya fruit is a promising nutraceutical as an antioxidant. It improves the antioxidant defence in elderly patients even without any overt antioxidant deficiency state at the dose of 9 g/day orally. The papaya lipase, a hydrolase enzyme tightly bonded to the water insoluble fraction of crude papain, is considered as a "naturally immobilized" biocatalyst [11]. Papaya markedly increases iron (Fe) absorption from rice meal, which was measured in parous Indian women, using the erythrocyte utilization of radioactive Fe method. The black seeds edible and have a sharp, spicy taste. They are sometimes ground up and used as a substitute for black pepper. In some parts of Asia the young leaves of papaya are steamed and eaten like spinach [12]. Nutritive value of 100 gm of *Carica papaya* fruit are described (Table 6).

Table 6: Nutritive value of 100 gm of *Carica papaya* Linn. Fruit [13].

Constituents	Ripe Papaya	Green Papaya
1. Protein	0.6 g	0.7 g
2. Minerals	0.5 g	0.5 g
3. Fibre	0.8 g	0.9 g
4. Fat	0.1 g	0.2 g
5. Carbohydrates	7.2 g	5.7 g
6. Energy	32 Kcal	27 Kcal
7. Total	2,740 µm	0
8. Carotene	888	0

5. Medicinal and Pharmacological properties of various parts of *Carica papaya* plant

5.1 Leaves

Papaya leaf has a numberless of benefits. In some parts of Asia, the young leaves of the papaya are steamed and eaten like spinach.

- Dengue fever- Commencing on studies of Dr. Sanath Hettige, who conducted the research on 70 dengue fever patients, said papaya leaf juice helps increase white blood cells and platelets, normalizes clotting, and repairs the liver.
- Cancer cell growth inhibition- Recent research on papaya leaf tea extract has demonstrated cancer cell growth inhibition. It appears to boost the production of key signaling molecules called Th1-type cytokines, which help regulate the immune system.
- Antimalarial and antiplasmodial activity- Papaya leaves are made into tea as a treatment for malaria. Antimalarial and antiplasmodial activity has been noted in some

preparations of the plant, but the mechanism is not understood and not scientifically proven

- Facilitate digestion- The leaves of the papaya plants contain chemical compounds of carpain, Substance which kills microorganisms that often interfere with the digestive function.

Additional Benefits of Papaya Leaves: As an acne medicine, Increase appetite, Ease menstrual pain, Meat tenderizer, Relieve nausea [14].

5.2 Fruit

Papaya fruit is a rich source of nutrients such as provitamin A, carotenoids, vitamin C, vitamin B, lycopene, dietary minerals and dietary fibre. Danielone is a phytoalexin found in the papaya fruit. This compound showed high antifungal activity against *Colletotrichum gloeosporioides*, a pathogenic fungus of papaya.

- Laxative- Ripe papaya fruit is laxative which assures of regular bowel movement.
- Indigestion- The milky juice which is tapped from the green, mature fruit while still in the tree contains an enzyme known as "papain". People use this in the preparation of different remedies for indigestion.
- Void the heart attack or stroke- The folic acid found in papayas is needed for the conversion of homocysteine into amino acids such as cysteine or methionine. If unconverted, homocysteine can directly damage blood vessel walls, is considered a significant risk factor for a heart attack or stroke [14].

5.3 Seeds

The black seeds of the papaya are edible and have a sharp, spicy taste. They are sometimes ground and used as a substitute for black pepper.

- Nephro - protective activity- In wistar rats nephro-protective activity was observed in dose. Concentration of urine and creatinine were evaluated.
- More potent- The papaya seeds are very pungent and peppery, making them almost unpalatable. However the seeds seem to have more potent medicinal values than the flesh.

Papaya seeds have antibacterial properties and are effective against *E. coli*, *Salmonella* and *Staphylococcus* infections, Papaya seeds may protect the kidneys from toxin - induced kidney failure. Seeds can eliminate intestinal parasites, and help detoxify the liver. Used as a skin irritant to lower fever. Cure for piles and typhoid and anti-helminthic and anti-amoebic properties. Dried papaya seeds actually look quite similar to peppercorns and can be used in just the same way. Grinding a couple over a meal, especially protein rich meals, is a simple way to add extra enzymes to your diet and improve your digestive health [14].

5.4 Peel

Papaya peel is often used in cosmetics. The papaya peel can also be used in many home remedies.

- Sunscreen and soothing slave- The presence of vitamin A helps to restore and rebuild damaged skin. Applied papaya peel used as skin lightening agent. When peel mixed with honey and applied it can act as soothe and moisturizers the skin.
- Fight dandruff- The papaya vinegar with lemon juice can be applied to the scalp for 20 minutes prior to shampooing to fight dandruff.

- c) Muscle Relaxant- Adding papaya oil and vinegar to bath water, along with essential oils like lavender, orange and rosemary can be nourishing, refreshing and relaxing, and can work as a pain reliever and muscle relaxant [14].

5.5 Roots

Juice from papaya roots is used in some countries of Asia to ease urinary troubles. Papaya leaf when dried and cured like a cigar, is smoked by asthmatic persons. An infusion of fresh papaya leaves is used by person to expel or destroy intestinal worms. Fresh young papaya are also used to remedy colic, a certain stomach disorder or cramp. A decoction formed by boiling the outer part of the roots of the papaya tree in the cure of dyspepsia [14].

5.6 Latex

The milky sap of an unripe papaya contains Papain and chymopapain. chymopapain was approved for intradiscal injection in patients with documented herniated lumbar intervertebra discs and who had not responded to "conservative therapy". Papain is also used to treat commercial beer, to degum natural silk, as a meat tenderizer and in the production of chewing gums. Cosmetically it is used in Shampoos and in a number of face-lifting operations. In humans papain slows down the heart and thus reduces blood pressure.

It is also used in Antihelmintic, relieves dyspepsia, cures diarrhea, pain of burns and topical use, bleeding haemorrhoids, stomachic, whooping cough [14].

5.7 Other Uses

- a) Colon cancer- The fiber of papaya is able to bind cancer-causing toxins in the colon and keep them away from the healthy colon cells. These nutrients provide synergistic protection for colon cells from free radical damage to their DNA.
- b) Anti-Inflammatory effects- Protein enzymes including papain and chymopapain and antioxidant nutrients found in papaya; including vitamin C, vitamins E, and beta-carotene, reduce the severity of the conditions such as asthma, osteoarthritis, and rheumatoid arthritis.
- c) Rheumatoid arthritis- Vitamin C - rich foods, such as papaya, provide humans with protection against inflammatory polyarthritis, a form of rheumatoid arthritis involving two or more joints.
- d) Promote lung health- If you are smoker, or if you are frequently exposed to second hand smoke. Eating vitamin A rich foods, such as papaya, help your lung healthy and save your life.
- e) Anti-sickling activity- Current research proves that papaya is having an anti-sickling activity.
- f) Prevent prostate cancer- Men consuming lycopene - rich fruits and vegetables such as papaya, tomatoes, apricots, pink grape fruit, watermelon, and guava were 82 % less likely to have prostate cancer compared to those consuming the least lycopene - rich foods.
- g) Anticoagulant effect- Injection of papain extract in a dog increases prothrombin and coagulation threefold. It is also claimed that the enzyme eliminates necrotic tissues in chronic wounds, burns and ulcers. Papain is also of commercial importance in the brewery industry, in the food industry and in the textile industry [14].

6. Preliminary research on *Carica papaya* Linn.

Natarjan Sudharkar explained that *Carica papaya* Linn is commonly called as paw-paw and it belongs to the family Caricaceae. Papaya possess excellent medicinal properties for treatment of different ailments. The different parts of the *Carica papaya* plant including leaves, seeds, latex and fruit exhibited to have medicinal value. The stem, leaf and fruit of papaya contain plenty of latex. The latex from unripe papaya fruit contain enzymes papain and chymopapain; other components include a mixture of cysteine endopeptidases, chitinases and an inhibitor of serine protease. Phytochemical analysis of *Carica papaya* leaf extract revealed the presence of alkaloids, glycosides, flavanoids, saponins, tannins, phenols and steroids. This study focuses on different properties of papaya such as antioxidant and free radical scavenging activity, anticancer activity, anti-inflammatory activity, treatment for dengue fever, anti-diabetic activity, wound healing activity and antifertility effects. Thus *Carica papaya* acts as a multi faceted plant. It is also imperative to identify the mechanism of the plant compounds and studying the active principle of the extract. Thus, we should include the papaya in our diet as fruit salads, fruit juice, leaf extract, decoction prepared through papaya leaves, etc. However, including papaya seeds in any of the form should be avoided for young men and pregnant women, since it possess antifertility effects that was demonstrated well in animal models [15].

Arvind G studied that *Carica papaya*, is a lozenge tropical fruit, often seen in orange-red, yellow-green and yellow-orange hues, with a rich orange pulp. The fruit is not just delicious and healthy, but whole plant parts, fruit, roots, bark, peel, seeds and pulp are also known to have medicinal properties. The many benefits of papaya owed due to high content of Vitamins A, B and C, proteolytic enzymes like papain and chymopapain which have antiviral, antifungal and antibacterial properties. *Carica papaya* can be used for treatment of a numerous diseases like warts, corns, sinuses, eczema, cutaneous tubercles, glandular tumors, blood pressure, dyspepsia, constipation, amenorrhoea, general debility, expel worms and stimulate reproductive organs and many, as a result *Carica papaya* can be regarded as a Neutraceutical. The present study reviews the pharmacological uses of *Carica papaya* and side/toxic effects. *Carica papaya* contains an enzyme known as papain which is present in the bark, leaves and fruit. The milky juice is extracted, dried and used as a chewing gum for digestive problems, toothpaste and meat tenderizers. It also contains many biological active compounds including chymopapain and papain which is the ingredient that aids digestive system, and again used in treatment of arthritis [16].

Zunjar V investigated the microscopic evaluation of leaves of *Carica papaya* Linn to establish the salient diagnostic features for the leaf. The leaf shows abundant sphaeraphides and rhomboidal calcium oxalate crystals. The leaves shows no trichomes. Microphological studies conducted on the leaf gave value of stomatal index to be 31.56 ± 3.41 , vein termination number 3-4, and palisade ratio to be 12.65 ± 1.57 . The leaf shows a continuous network of veins. Histo chemical tests perform indicate the presence of alkaloids and starch. Powder study shows the presence of sphaeraphides, starch grains and rhomboidal calcium oxalate crystals, apart from regular characters such as stomata and spiral xylem. Physiochemical parameters such as extractive values, ash values and moisture content have also been studied for the leaf. The result of this study could be useful in setting some diagnostic indices for

identification, authentication and preparation of the monograph of the plant [17].

Varisha Anjum study was performed for the development of physico-chemical parameters of *Carica papaya* Linn. Leaves belonging to family Caricaceae. The study comprises physico-chemical and phytochemical evaluation to confirm purity and authenticity of *Carica papaya* leaf based on WHO guidelines. Microscopy of the leaf showed presence of epidermis, collenchyma, and parenchyma, sclerenchyma, xylem, phloem and pith was found to be absent. Successive extractive value is found highest in petroleum ether extract 20.44 % (on dry weight basis). Mean ash values (%) are 16.72 (total), 3.25 (acid insoluble ash), and 6.05 (water soluble ash) and moisture content is found to be 7.77 % and the phytochemical analysis indicate the presence of carbohydrates, terpenoids, flavonoids, phenolic compounds in different extracts of *Carica papaya* Linn. leaf. TLC fingerprinting profile of different extract was also developed which exhibited presence of several medium polar compounds [18].

Harrison Abia investigated the efficacy of treatments with *Carica papaya* is dependent on the quantity of the different chemical substances present in the preparation. The quantity of chemical substances varies in the fruit, latex, leaves, and roots and varies with the extraction method, age of the plant part, and the cultivar and sex of the tree. The antibacterial and antifungal ability of both fresh and dried leaves of *Carica papaya* against bacteria and fungi of medical importance was carried out. The aqueous, ethanol and acetone extract of both the dried and fresh leaves were tested at 25, 50 and 100 mg/ml concentrations on both the bacteria and fungi isolates using the disc diffusion method. Results showed very significant broad spectrum antimicrobial activity against Gram-negative and Gram-positive bacteria and fungi. The organic extracts were more effective than aqueous extracts. The result further showed that the dry sample was effective against both Gram-positive and Gram-negative bacteria while the fresh sample was more effective against Gram-negative bacteria. The dried leaf extract was potent against some of the bacteria which standard antibiotics were not able to inhibit. *Carica papaya* leaves showed a better antibacterial activity than antifungal activity. Demonstration of antimicrobial activity against the test isolates is an indication that there is possibility of sourcing alternative antibiotic substances in this plant for the development of newer antibacterial agents [19].

Ravi kumar Pigli explained in his study that dengue fever or dengue hemorrhagic fever is the most prevalent viral disease caused by dengue virus a family of flavivirus transmitted through aedes aegypti mosquito. Approximately 2.5 billion people world wide affected by this virus. Dengue is single stranded RNA virus, has four serotypes i.e. type 1, 2, 3 and 4. There are no approved antiviral agents or vaccine is available for the treatment of this virus which causes increasing the mortality rate all over the world. As there are no synthetic drugs available, now it is need to focus on medicinal plants which are considered to be effective, safer and non-toxic. There are several medicinal plant extracts were found to have anti dengue activity, but they are not approved for dengue viral treatment. The present article reviews on the medicinal plants available for their anti-dengue activity and also provided the phytochemical constituents present in those medicinal plants [20].

V Krishna Prabha formulate a ready to serve beverage incorporate with papaya leaves and guava against Dengue fever. Papaya leaves contain various nutrients and

pytoconstituents like saponins, tannins, cardiac glycosides and alkaloids. These constituents can act on the bone marrow, prevent its destruction and enhance its ability to produce platelets. The guava fruits are rich in vitamin C (ascorbic acid) content. It can be concluded that the papaya leaves induce the rapid increase in platelet count and immunity. It may play a valuable role in the management of dengue fever in the future [21].

Soobitha Subenthiran investigated the platelet increasing property of *Carica papaya* leaves juice (CPLJ) in patients with dengue fever (DF). An open labeled randomized controlled trial was carried out on 228 patients with DF and dengue hemorrhagic fever (DHF). Approximately half the patients received the juice, for 3 consecutive days while the others remained as controls and received the standard management. Their full blood count was monitored 8 hours for 48 hours. Gene expression studies were conducted on the ALOX 12 and PTAFR genes. The mean increase in platelet counts were compared in both groups using repeated measure ANCOVA. There was a significant increase in mean platelet count observed in the intervention group but not in the control group 40 hours since the first dose of CPLJ. Comparison of mean platelet count between intervention and control group showed that mean platelet count in intervention group was significantly higher than control group after 40 and 48 hours of admission. The ALOX 12 (FC=15.00) and PTAFR (FC=13.42) genes were highly expressed among those on the juice. It was concluded that CPLJ does significantly increase the platelet count in patients with DF and DHF [22].

Fenny Yunita found that Indonesia is one of the countries with the highest cases of dengue fever in South East Asia. The number of patient and distribution area increases with increasing mobility and population density. *Carica papaya* Linn. Belongs to Caricaceae family is a widely cultivated plant in Indonesia and has many health benefits. The leaves were believed to increase platelet count and dengue fever patient benefit, but there were very limited published reports on scientific evident. The objective of the study was randomized clinical trial with a sample size of 80 subjects. These subjects were randomized into two groups of 40, including the control and intervention group (received two CPC three times daily). The result showed that CPC had significant increased the platelet count ($P < 0.05$), maintained stability of hematocrit in the normal level, shorten hospitalization ($P < 0.05$) in dengue fever patients and accelerates the increased in platelet count compared with control group [23].

Swati patil determined the effect of *Carica papaya* leaves aqueous extract in increasing the platelet count in thrombocytopenic rat model. Aqueous extract of *Carica papaya* leaves at concentration of 400 mg/kg and 800 mg/kg were given to cyclophosphamide induced thrombocytopenic rats for a period of fifteen days. Blood was withdrawn at various time intervals to determine the platelet count. Also, the clotting time was determined on the 15th day of the study by capillary method. *Carica papaya* leaf extract was found to increase the platelet count and also to decrease the clotting time in rats. The study aims at determining the possible effects of papaya leaves in thrombocytopenia occurring in dengue fever [24].

Susiji Wickramasinghe investigated the potential role of fresh *Carica papaya* leaf extract on haematological and biochemical parameters and toxicological changes in a murine model. In total 36 mice were used for the trial. Fresh *Carica papaya* leaf extract [0.2 mL (2 g)/mouse] was given only to the test group

(18 mice). General behaviour, clinical signs and feeding patterns were recorded. Blood and tissue samples were collected at intervals. Haematological parameters including platelet, red blood cell (RBC), white blood cell (WBC), packed cell volume (PCV), serum biochemistry including serum creatinine, serum glutamic-oxaloacetic transaminase (SGOT) and serum glutamic-pyruvic transaminase (SGPT) were determined. Organs for possible histopathological changes were examined [25].

C Baskaran evaluated the qualitative analysis of phytochemicals and antimicrobial activity of various solvent extracts of *Carica papaya*. The antimicrobial activities of different solvent extracts of *Carica papaya* were tested against the Gram-positive and Gram-negative bacterial strains and fungus by observing the zone of inhibition. The Gram-positive bacteria used in the test were *Staphylococcus aureus*, *Bacillus cereus* and *Micrococcus luteus*, and the Gram-negative bacteria were *Escherichia coli*, and *Klebsiella pneumoniae*, fungus like *Aspergillus niger*, *Aspergillus flavus*, *Candida albicans*, *Candida tropicalis*, *Cryptococcus neoformans*, and *Candida kefyr* [26].

R Sumathi collected the plant materials such as leaves, stem and root of disease free *Carica papaya* from Kaveripakkam, Vellore district, Tamilnadu. The dried powdered plant material is subjected to solvent extraction using the solvents cold water, hot water and ethanol. Antimicrobial assay of plant extract against clinical isolates by AWD assay. Only the leaf extracts showed inhibitory effect against *Candida albicans*, whereas stem and root extracts were ineffective. Among the leaf, stem and root extracts, the leaf extract is found to exhibit more antimicrobial activity than the stem and root [27].

Sheikh Fauziya suggested that papaya (*Carica papaya* Linn.) is well known for its exceptional nutritional and medicinal properties throughout the world. The whole plant including its leaves, fruits, seed, bark, latex and their juice are use as medicine. Papaya is considering as Nutraceutical fruits due its multifaceted properties. The whole plant of papaya contain enzyme Papain, Lycopene, Isothiocyanate, important Mineral, Vitamins, Carbohydrates, Carotenoids, Flavonoids. These important nutritious fruits feed the body and immune system. A papaya in vitro study shows that it will treat many cancer cell line and papaya physiochemical having anticancer activities. Papaya is rich in enzyme papain which is effective against cancer. Papain breaks down the fibrin cancer cell wall and protein into amino acid form. Other than papain it also contain lycopene which highly reactive towards oxygen and free radical. Isothiocyanate effective against breast, lung, colon pancreas, prostate as well as leukemia. These enzymes capable of inhibiting both formation and development of cancer cell [28].

Khaled Rashed research work deals with the evaluation of anti-HIV-1 effect of *Carica papaya* aerial parts polar extracts and also the investigation of the chemical content from the polar extracts of the plant. The methanol and aqueous extracts of *Carica papaya* were tested for their anti-HIV-1 activity using the syncytia formation assay. Methanol and aqueous extracts of *Carica papaya* aerial parts showed activity as anti-HIV-1 agents, both of the extracts therapeutic index (TI) of 5.51 and 7.13 compared with the standard drug. Phytochemical analysis of both the extracts proves the presence of phytochemicals as flavonoids, tannins, alkaloids, carbohydrates and triterpenes. The results have shown that *Carica papaya* methanol and aqueous extracts have drug ability as anti- HIV-1 agents [29].

Achini Gammulle investigated that management of thrombocytopenia is by drugs and blood products, both of which are costly. Conversely, Sri Lankan traditional medicine use mature leaf concentrate of *Carica papaya* to treat this condition. This claim was scientifically validated. Adult wistar rats (N=6/group) with Hydroxyurea - induced thrombocytopenia (model established for the first time), were orally administered, once daily on 3 consecutive days with three doses of fresh mature leaf concentrate of *Carica papaya* (0.18, 0.36 and 0.72 ml/100g), while controls received water. Standard protocols were used to establish their platelet, WBC and RBC counts. Effects of mature leaf concentrate of *Carica papaya* on carrageenan induced edema in rats, on rat erythrocyte membrane stabilization, and on acetic acid-induced vascular permeability in mice, as well as acute toxicity studies were conducted using standard methodology. High dose of mature leaf concentrate of *Carica papaya* in thrombocytopenic rats significantly (P<0.05) increased platelets by 76.5%, WBC by 30.51% and RBCs by 9.08%, when compared with controls. High dose of mature leaf concentrate of *Carica papaya* also significantly (P<0.5) inhibited carrageenan induced rat paw edema and impaired in vivo vascular permeability in mice (by 82%), while inducing maximum (10.11%) membrane stabilizing activity of rat RBCs at 8mg/ml of mature leaf concentrate of *Carica papaya*, suggestive of effective anti-inflammatory activity. Administration of high dose of mature leaf concentrate of *Carica papaya* on 3 consecutive days neither provoked overt signs of toxicity nor stress, where hepatotoxicity, renotoxicity, hematotoxicity and neurotoxicity were also ruled out. Thus freshly prepared mature leaf concentrate of *Carica papaya* is orally active, effectively increases rat platelet, WBC and RBC counts with no acute toxicity, and possesses potent anti-inflammatory activity, that overly justify claims of traditional medicine [30].

7. References

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