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Carica Papaya's Activity Related To Platelet Physiology And Thrombocytopenia

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Abstract

Background: *Carica Papaya*, often known as *Papaya*, has long been used in several medical traditions for its bioactive components. Thrombocytopenia is a medical illness marked by a deficiency of platelets, resulting in the potential development of bleeding problems and various associated issues.

Objective : *Papaya* includes several bioactive chemicals that have been extensively researched for its possible impact on platelet function and synthesis. Papain, chymopapain, carpaine, and many flavonoids are among the noteworthy components. These chemicals have anti-inflammatory and antioxidant characteristics, and some studies propose that they could contribute to the improvement of platelet counts. Further investigation should prioritise comprehending the precise mechanisms via which these chemicals engage with the pathways implicated in platelet formation and control.

Method: To conduct a thorough evaluation of the literature, databases from Springer, Elsevier, PubMed, and Science Direct were used.

Conclusion: *C Papaya* has tropical leaves and potential. *Papaya* leaves have phytochemicals. These phytochemicals include carpaine, saponins, terpenes, alkaloids, flavonoids, and antioxidants. Vitamin- and mineral-rich *Papaya*s are low-calorie. Fruit's healthy. Multiple scientific studies provided this data. Thrombocytopenia can result from therapy, dengue, chemotherapy, and pathologies. New and commercial *C Papaya* leaf doses increase platelets and prevent disintegration. No harm occurs. Carpaine, flavonoids, and antioxidants are *Papaya* leaf bioactives.

Keywords: Carpaine, Saponins, Thrombocytopenia, Papain, Papaya

Introduction

Platelet counts are often low in people who have a lot of long-term illnesses. If your platelet count is less than 150 × 109/L, you may have thrombocytopenia. In the medical world, platelet counts less than 100 × 109/L are important[1]. Mild thrombocytopenia is diagnosed when the platelet count falls within the range of 50 to 100 × 109/L. If the platelet count is below 50 × 109/L, it indicates severe thrombocytopenia [2]. Thrombocytopenia can have minor to fatal clinical problems as its aetiology. Still, thrombocytopenia misdiagnosis does happen and may be the outcome of artefacts in the lab [3,4]. Initially, a patient's peripheral blood smear and complete blood count must be checked for thrombocytopenia [1,5]. The

analysis of peripheral blood remains regarded to be a crucial diagnostic tool even if hematology analyzer automation has advanced[1]. The existence of morphological abnormalities that cannot be identified by an automated analyzer is the reason for the provision of an educated interpretation of the data of the total blood count [3,6]. It is essential to make a distinction between thrombocytopenia that is the result of laboratory errors and thrombocytopenia that is caused by actual factors [3]. Thrombocytopenia can be brought on by a number of diseases, including opportunistic infections, myelodysplastic syndrome, aplastic anemia, and cancer [1,7]. Decreased bone marrow thrombopoiesis and increased spleen platelet sequestration may also result in thrombocytopenia. One of the things that can lead to thrombocytopenia is more platelets breaking down around the edges of the blood vessels. A lot of different illnesses, like disseminated intravascular coagulation, thrombotic microangiopathy, and hypersplenism, can kill platelets. Platelets grow up and become more likely to break when these things happen [4,8].

Platelet sequestration in the spleen, insufficient platelet synthesis by the bone marrow, and accelerated platelet breakdown are the three basic reasons of thrombocytopenia. Thrombocytopenia may also be caused by a combination of these problems. People with bone marrow failure syndromes, like aplastic anemia and myelodysplastic syndrome, may not make enough thrombocytes. This can also happen to people with bone marrow-related disorders, like lymphoma, leukemia, multiple myeloma, metastases, and bone marrow granulomas. Some diseases, like immune thrombocytopenia (ITP), DIC, and thrombotic microangiopathies, on the other hand, destroy a lot of thrombocytes. Platelets getting stuck together is a sign of congestive splenomegaly caused by portal hypertension. Some of the conditions that can cause portal hypertension are heart failure, hepatic vein thrombosis, vena cava thrombosis (also known as Budd-Chiari syndrome), cirrhosis (which includes alcoholic liver disease or chronic viral hepatitis), and very rarely arteriovenous malformation of the splenic veins. Platelets are moved from the circulation pool to the splenic pool and stored there. This process is called platelet sequester [9].

The Carica Papaya is a plant belonging to the Caricaceae family [10]. It is a herbaceous plant that does not have any woody parts. *For example, in Sanskrit it is called Erandakarkati, in Hindi it is called Papita, and in English it is called Papaya. This fruit is the same thing that goes by different names. This plant comes from tropical America and was brought to India in the 1600s. The plant has wide leaves that are arranged in a straight line and are 50 to 70 cm long. Besides that, it bears berries all year long* [11]. Officially known as Carica Papaya, the papaya plant is a perennial native to southern Mexico that is currently seen growing in tropical regions all over the world. Many people believe that the fruit of the C papaya species has medicinal properties. The plant's rinds, fruits, branches, roots, leaves, slime, and seeds are only a few of the sections that have been demonstrated to possess biological impacts [12]. Researchers have found that the leaves of the Carica papaya plant are good for your health in many ways. The leaves of this plant have a lot of fat-soluble vitamins, like A, D, E, and K. They also have a lot of vitamins B and C, iron, salt, and calcium [13]. Furthermore, while the plant undergoes growth, it has the capacity to absorb higher quantities of potassium, nitrogen, and calcium, while exhibiting a significantly reduced uptake of phosphorus [14]. In many Asian nations, the tender leaves of the C Papaya plant are prepared and consumed, similar to spinach, to obtain various health advantages. Papaya leaf juice increases the count of platelets and white blood cells (WBC) in the bloodstream, promoting liver healing and maintaining normal blood coagulation. Several studies have demonstrated that C Papaya leaves, because to their phytochemical makeup, had the capacity to alleviate the complications linked with thrombocytopenia in patients [15].

Many of the currently available anticoagulants (such coumarins and heparin) and antiplatelet medications (like aspirin) have their origins in organic substances [16]. As a result, we suggested doing research on the potentially antithrombotic properties of *Tinospora cordifolia*. *Tinospora cordifolia* is a huge, Menispermaceae family member that is smooth, long-lasting, and climbs. It sheds leaves. It is extensively dispersed over India and South Asia. In addition, there are several more names for it, including gurcha in Hindi, amruthu in Malayalam, amrutha balli in Kannada, guduchi in Marathi, and Sanskrit. Numerous health benefits are associated with it, including hepatoprotective, anti-inflammatory, anti-arthritic, antioxidant, anti-allergic, anti-stress, antileprotic, antimalarial, and immunomodulatory effects [17,18].

Botanical Description

As a consequence of an injury, the *Carica* plant sprouted branches, and the whole plant is composed of a white latex material which can be found throughout its entirety. The stem is hollow and has a cylindrical shape with a diameter ranging from 10 to 30 centimetres. On average, the *Papaya* plant may grow to heights of between two and ten metres. It is an arborescent herb that is perennial. Typically, it has a single trunk; nevertheless, there are instances in which there are leaf scars and spongy-fibrous tissue that are quite visible, has a complex and extensive network of roots that extends far and wide. The arrangement of the leaves is arranged in a spiral pattern, and they are grouped together in the centre of the stem. It is possible for the petiole to reach a length of one metre, and it is hollow and has a hue that is either greenish or purplish-green. The leaf blade is palmate in form and has seven deep lobes. It is spherical in shape and has a diameter that ranges from 25 to 75 centimetres. In addition to being veined heavily, the leaf surface is smooth. Each of the lobes has a wide and deep toothing pattern. The blooms are yellow in colour, not very large, and have the appearance of funnels. They are able to be discovered in the gaps between the leaves either alone or in bunches. Female flowers, male flowers, and hermaphrodite flowers are the three categories of flowers. Female flowers are between three and five centimetres in length and feature a huge pistil that is functional, but they do not have stamens. They possess an ovary that is oval in form. Flowers that are male are located on tall panicles that dangle from the ceiling and contain ten stamens that are grouped in two rows. A pistillode is the only remnant of the gynecium that is present. Female hermaphrodite flowers are bigger than male flowers and feature an ovary that is composed of five carpellate structures. However, the appearance of these blossoms is contingent upon the time of year or the age of the tree. The Carica Papaya plant exhibits a remarkable ability to thrive in diverse geographical regions, spanning from tropical climates to temperate latitudes. Despite this, it is... In order to ensure the plants' success, it is necessary to grow them in areas that are not only warm and bright but also shielded from the wind. In a perfect world, the elevation would be lower than 1500 metres. The effects of strong winds may be detrimental, particularly for soils that are unable to compensate for the loss of substantial amounts of transpiration.

Table:1 Botanical Classification of plant

Domain	Flowering plant
Kingdom	Plantae
Sub Kingdom	Tracheobionta
Class	Magnoliopsida
Subclass	Dilleniidae
Super division	Spermatophyta
Phyllum	Steptophyta
Order	Brassicales
Family	*Carica*ceae
Genus	*Carica*
Botanical name	*Carica Papaya* Linn.

PROFILE OF NUTRITION AND PHYTOCHEMICAL APPLICATIONS

According to an analysis, papaya has a high potassium content (223 mg/100 g of fresh fruit), along with high levels of salt, calcium, phosphorus, zinc, iron, copper, manganese, and magnesium. Because papayas are abundant in vitamin A, C, B1, B2, thiamine, folate, riboflavin, niacin, calcium, potassium, iron, and fiber, they are considered extremely significant fruits. Though low in calories, it is high in many different kinds of vitamins and minerals. About 60% of the fruit in every 100 grams is ripe fruit. The papaya has 200 kilojoules of energy per 100 grams. The three main sugars found in the substance are sucrose (48.3 g/100 g), fructose (21.9 g/100 g), and glucose (29.8 g/100 g). Approximately 108 milligrams of ascorbic acid are present in 100 grams of fresh fruit, which is a higher concentration than the 67 milligrams in 100 grams of oranges [19]. Volatile compounds, in particular hydrocarbons, alcohols, terpenes, aldehydes, ketones, esters, benzyl isothiocyanate, and organic acids, are responsible for a substance's flavor and scent [20,21]. The sensory characteristics are the result of these substances. On the other hand, ethyl acetate, ethyl 2-methylbutanoate, and ethyl hexanoate are linked to fruity aromas [22,23]. Among the key chemical groups that are present in significant quantities, aliphatic and volatile hydrocarbons are the ones that play a significant role in contributing to the fragrance [24]. These hydrocarbons are also found in significant quantities. The volatile chemical known as linalool may be discovered in very high concentrations in *Papaya*s, notably in Solo *Papaya* varieties, which contain 94% of the substance. Linalool is the second most abundant component, and Taiwan types contain a high abundance of the oxide cis-linalool. In contrast, Taiwan cultivars have a significant abundance of methanol [25]. Studies show that when the fruit is ripe, the number of aromatic substances like 3-methylbutanol, butanol, terpineol, and benzyl alcohol goes up by a lot. There are 103 different esters that have been found in papaya, and methyl butyrate is the most common one [26]. In addition to linalool, fruit has many other chemicals in it, such as benzyl isothiocyanate [27] and terpene hydrocarbons, amongst others. During the third stage of maturity, the concentration of butanol, 3-methylbutanol, benzyl alcohol, and α-terpineol reaches its maximum level. This concentration is directly proportional to the degree to which the fruit has reached its ripeness [28]. When it comes to the nutritional content of the *Papaya* fruit, the colour of the flesh is considered to be a significant quality [29]. When the fruit softens and changes from amber to orange in color, it is considered mature. This feature distinguishes the fruit from other varieties. This fruit has a flavor that is similar to cantaloupe."There is a slight hint of muskiness present, and it possesses both a sweet and juicy quality simultaneously."[30]. The total soluble solids (TSS) rate in this fruit's flesh can be as low as 10% or as high as 11.5%. The skin, on the other hand, is thought to have fewer phenolic chemicals as the fruit ripens. In fresh fruit, the amounts of caffeineic acid, p-coumaric acid, and ferulic acid run from 175.51 mg/100 g to 112.89 mg/100 g, 229.59 mg/100 g, and 277.49 mg/100 g, respectively. But as the fruit ages, it gives off more vitamin C and the pigments β-cryptoxanthin and lycopene. The amount of lycopene in 100 grams varies from 0.36 mg to 3.40 mg. Vitamin C has between 0.28 mg and 1.06 mg of α-tocopherol and between 0.23 mg and 0.50 mg of β-carotene per 100 grams. Vitamin C can be found in amounts ranging from 25.07 mg to 58.59 mg per 100 grams. Many scientific studies have been done to look at the biological properties of different parts of the papaya plant, such as the fruits, shoots, leaves, seeds, slime, and roots. There are a lot of different chemicals in the plant that can affect different types of cells in different ways. For example, linal can be found in the body of the fruit [31], Together with the alkaloids carpaine and pseudocarpaine, the leaves also contain dehydrocarpaine I and II [32], While class II and III chitinase, cysteine endopeptidases, and glutaminyl cyclase are found in the shoots, glutaminyl cyclase is found in the latex [33], quercetin and kaempferol are present in the shoots [34], cyanogenic compounds can be found in the roots [35], All tissues contain both benzyl glucosinolate and the breakdown product benzyl isothiocyanate. The extracted metabolite undergoes a chemical examination to determine the identities of each of these components

Platelet physiology

In the first stage of stopping bleeding, called platelet stimulation, there are three steps. There are three steps: adhesion, stimulation, and aggregation. Platelets can stick to the subendothelial surface, which is the bottom layer of damaged blood artery walls. A protein called von Willebrand factor (vWF) helps these cells stick together. After this change in

structure, the platelets make factor V, serotonin, fibrinogen, white blood cells with blood vessels, adenosine diphosphate and triphosphate, and fibrinogen. By binding permanently to the P2Y12 adenosine diphosphate receptor, clopidogrel stops both platelet activity and aggregation at the same time. When the form of the platelet changes, the glycoprotein IIb/IIIa receptors can bind to them. When these receptors connect to fibrinogen, they start the process of platelets sticking together, which can be undone. Antiplatelet drugs injected into the vein, like tirofiban, eptifibatide, and abciximab, can stop fibrinogen from attaching at this time. The third step is the release of arachidonic acid, which is then changed into thromboxane A2. Because of this process, a platelet plug is formed, which is a permanent grouping of platelets. An important part of how aspirin works is that it permanently changes thromboxane A2. In the end, platelets are very important because they provide the phospholipid membrane that finishes the coagulation process [36].

Pathophysiological mechanisms involved in thrombocytopenia

There are many things that can cause your platelet count to be low. These include low platelet counts, bleeding, decreased platelet production, higher platelet loss, higher platelet sequestration, and higher platelet breakdown. Some of the things that can cause low platelet levels in intensive care units (ICUs) are heparin, GP2b3a inhibitors, alcohol, antibiotics, sepsis, major bleeding, and microangiopathic hemolytic anemias like thrombocytopenic thrombotic purpura (TTP), hemolytic uremic syndrome (HUS), and disseminated intravascular coagulation (DIC) [37].When it comes to the effective management of thrombocytopenia in critical care units, having a solid understanding of the various processes and the aetiology is very necessary. For instance, platelet transfusion is used to treat low platelets that are the result of significant bleeding. On the other hand, plasmapheresis is the therapy of choice for illnesses such as transfusion-resistant thrombocytopenia pancreatic syndrome (TTP) and haemoglobin deficiency syndrome (HUS). Many ways can be used to treat heparin-induced thrombocytopenia and thrombosis (HITT), such as quickly figuring out what is wrong, stopping the use of drugs that are linked to heparin, and starting treatment with other blood thinners, such as direct thrombin inhibitors. Platelet production can be slowed down by aplastic anemia, infections, cancer, poor nutrition, and drugs or alcohol that damage the bone marrow [38]. The spleen stores 33% of the platelets in the body. Platelets can move in the body for seven to ten days, depending on physiological factors. If you have cirrhosis or portal hypertension, your spleen may become blocked, which can make it harder for platelets to multiply after a transfer. A lot of people who are getting treatment in critical care units die from a process called fast destruction and consumption. This is similar to sepsis and DIC. Thrombocytopenia can be caused by many things in sepsis, including hemophagocytosis, activation of the complement system, loss of ADAMTS13 protein, and release of histones [39].

Mechanism of action of *Carica Papaya* in Thrombocytopenia

The leaf of the C Papaya plant can effectively treat thrombocytopenia by reducing platelet disintegration. Some chemicals in the leaves of the C. papaya plant, called flavonoids, can bind to proteases, which are needed for viruses to form. Proteases are the components of viruses that are responsible for their replication and functionality. Because of this, the reproduction of the virus is inhibited. This method helps to maintain normal hematocrit levels while also reducing the amount of platelet breakdown. Additionally, the leaf extract exhibits the capacity to scavenge free radicals and perform the function of an antioxidant, so preventing damage and lowering the amounts of hemolysis and bleeding that occur. Furthermore, these extracts enhance platelet formation by significantly amplifying the enzyme activity of ALOX-12 and PTFAR by a ratio of 15 and 13-14, respectively. The presence of carpaine and quercetin in *Papaya* leaves has been shown to increase platelet formation, shield platelets from damage, and preserve the integrity of the platelet membrane. These effects are accomplished via controlling the activity of genes and blocking the action of viral proteases [40].

Other Therapeutic Potentials of *C Papaya* Leaf

For thousands of years, the medicinal benefits of C papaya leaf have been recognized. The leaf possesses therapeutic properties that can effectively treat a wide range of illnesses. These curative roles include:

Immunomodulatory Activity

It is possible to deliberately weaken the immune system through a certain method. This is what immunomodulation means. The goal of this study was to find out if freeze-dried C papaya leaf juice (FCPLJ) could be used to keep the immune system from overreacting in AG129 mice that were infected with a clinical type of DENV-2 (DMOF015). People who were infected took part in a three-day study to see what would happen if they took 500 or 1000 mg/kg/day of FCPLJ by mouth. The plasma of sick mice had higher amounts of GM-CSF, GRO-alpha, IL-1 beta, IL-6, MCP-1, and MIP-1 beta. These chemicals were found in smaller amounts in the plasma of mice that were not hurt. It was also seen that the amounts of viral RNA and IL-6 in the hepatocytes went down. It was made clear in this study that the FCPLJ may be able to affect the immune system in a model of dengue fever that doesn't kill [41]. In order to test how well C papaya leaf works in regular immune therapy, six Wistar rats were put into each group. The rats were given pure mature leaf doses by mouth every day for three days in a row. The doses were 0.18, 0.36, and 0.72 mL/100g BD. The study used different amounts of mature leaf concentrate of C. papaya (MLCC) to look at how peritoneal macrophages ate bacteria and the cytokine reactions that went along with it. They also looked at how bone marrow cells and splenocytes grew outside of living organisms. More leukocytes, platelets, lymphocytes, bone marrow cells, and monocyte subpopulations were found after oral MLCC was given by gavage. When rats were given the highest dose of MLCC, levels of pro-inflammatory cytokines, especially TNF and IL-6, dropped by a large amount. When the MLCC was taken by mouth at all three dose levels, it greatly increased the number of peritoneal macrophages in rat tissue. The MLCC successfully increased the rat PMS's ability to take in foreign particles in the lab and triggered an immune response that led to the activation of Th1 cells. The researchers found that MLCC, when taken in small amounts (31.25 g/mL), helped bone marrow cells (BMC) grow outside of the body. It helped stem cells (SC) grow at 31.25 and 62.5 g/mL as well. The lab was the place where these two processes took place. Higher amounts (500 and 1000 g/mL, on the other hand) changed cytokine levels and were harmful to both BMC and SC. The immunomodulatory benefits of MLCC were found by giving it to people by mouth [42].

Antimalarial Activity

People in South Asian countries often use papaya leaf (C Papaya plant) to get rid of malaria. In vitro testing was used to see how well C papaya leaf extracts worked against Plasmodium falciparum strains 3D7 and Dd2. A dichloromethane extract from papaya leaves showed a high level of effectiveness in treating malaria. Researchers used bioassay-guided separation to find a form of carpaine that works better. The half-life of this type of carpaine was found to be 2.19 ±0.60 g/mL (4.57 m) and 2.01 ±0.18 g/mL (4.21 m) for both forms. One thing that was very different about the leaf extract was that it didn't hurt healthy, virus-free human red blood cells. The results of this experiment [43] provided evidence that antimalarial activity was present. In order to investigate the possible antimalarial effects of methanolic leaf extract of *C Papaya*, Swiss mice were first infected with Plasmodium berghei NK65 and then given the extract after the infection. Six groups of six different mice were made from the 36 mice that were there. People in Group B were the control group for the sick people, and people in Group A were the control group for the healthy people. Groups C and D were given artesunate (10 mg/kg body weight) and chloroquine (10 mg/kg body weight). Both of these doses were put into the bodies of the subjects. There were two groups, E and F. They were given 400 mg and 600 mg of methanolic leaf extract from C. papaya, respectively. Leaf extract mixed with methanol was given to groups E and F. It was tested on people and found that giving 400 mg/kg BD and 600 mg/kg BD of C papaya plant extract reduced blood bugs by 56.76% and 75.56%, respectively. The number of parasites dropped by 92.86% for artesunate and 90.67% for chloroquine when given at doses of 10 mg/kg BD. The extract greatly increased the amounts of hematocrit and hemoglobin in the mice that were given it, while it greatly decreased the number of white blood cells. It was also talked about mice that were infected but did not react to treatment. Scientists did an experiment and found that C. papaya leaf extract in methanol could kill malaria eggs [44].

Antiviral Efficacy

Over the course of many decades, viruses have been the cause of terrible diseases that have been passed on to people. Significant advancements have been made by the pharmaceutical sector in terms of the mechanisms and targeting of antiviral drugs. However, these ground-breaking breakthroughs have also resulted in an increase in the resistance of viruses to the immune system. As a result of the challenges that have been encountered in the pursuit of a cure, the emphasis of therapy has switched from synthetic pharmaceuticals to natural remediesThe text is absent. The C papaya plant's papaya leaf is essential to the generation of viruses, according to scientific research. In a dengue-sick mouse model, researchers discovered that freeze-dried CPLJ significantly improved the reduction of viremia and NS1 levels [45]. This was found out during the probe. In this work, new strains of the dengue virus from New Guinea C (DEN-2) were given to AG129 mice. These new strains were not adapted to mice. The people were then given freeze-dried CPLJ by mouth for three days straight, right after the first dose, at 500 mg/kg/day and 1000 mg/kg/day amounts. Some twenty-four different chemicals were found in freeze-dried CPLJ. In addition, giving CPLJ by mouth to AG129 mice that had the disease reduced the number of deaths. To prove that C papaya leaf can fight viruses, another in vitro experiment was done on C6/36 cells that had been infected with DENV-1. Plates were used in the test. Quantitative real-time polymerase chain reaction, or qRT-PCR, was used to test the normal control sample as well as four samples that were infected and then treated with C papaya leaf extracts. To find out how much DENV-1 RNA was there, the dengue general real-time RT-PCR method was used. The chemical sensitivity of this method is 1 × 103 copies/M1. Four standard dilutions of the positive control's replication, a positive control, a negative control, and a positive control obtained from an analytical system were used to do this. The test on cell shape showed that dilutions of C papaya leaf extract from 1/16 to 1/512 did not have any negative effects. It was found that dilutions between 1/32 and 1/256 were the best ones to use to treat an experimental DENV-1 illness. DENV RNA was found in the positive control, the normal controls, and the untreated control that had the DENV-1 infection in the qRT-PCR study. The four samples that were treated with DENV-1 and had different amounts of papaya leaf extracts, along with the negative control, did not have any DENV RNA. These are the reasons why experiments have shown that C papaya leaf extract can stop DENV-1 infections [46]. An investigation on the antiviral capabilities of silver nanoparticles made from C papaya leaf extract was conducted recently. Cell lines from Kidney Vero E2 were used in the study. The method included synthesizing and characterizing silver nanoparticles after performing both aqueous and non-aqueous extractions. To investigate possible interactions between the viral NS5 protein and the medicinal compounds found in C papaya leaf extract, molecular docking simulations were performed. The highest degree of strong action potential was observed when silver nanoparticles were produced using the methanol extract of C papaya leaves. The IC50 value of the nanoparticles was 9.20 µg/mL. Molecular docking experiments showed that 5,7-dimethoxycoumarin has its greatest affinity toward the NS5 protein, making it the most advantageous ligand. The results of the study indicate that MCPLE silver nanoparticles significantly reduce the development of dengue virus type.

Anticancer Properties

Scientific research has shown that the leaf of the C papaya plant can stop progression of several types of cancer. We used different types of cells, including those from prostate cancer, normal prostate cells, and benign hyperplasia, to test how well C juice made from papaya leaves and its many products kill cells. Lab tests on leaf juice that were eaten for 24, 48, and 72 hours showed that it stopped cell growth, stopped the S phase of the cell cycle, and caused apoptosis. The values fluctuated between 0.1 mg/mL to one milligram per milliliter. The procedure of sorting chemicals based on their molecular weight supported the investigation's conclusions. The results of the investigation showed that the medium-polar component of the leaf juice successfully stopped invasive PC-3 cells from adhering to and migrating onto it [47]. Rats were given ethanol solutions containing papaya and moringa leaves in place of surgery. Delaying the growth of cancerous cells was the treatment's main goal. There is strong evidence that the effective inhibition of cancer cell growth occurs when a dosage of 150 mg per kg of body weight is administered [48].

Anti-diabetic Activity

The prevalence of diabetes along with the unfavorable effects of synthetic drugs has led to a more thorough search for low-risk and affordable alternatives. Using alloxan as a research tool, an investigation was carried out on the antidiabetic effects of the ethanolic extract from C. papaya leaves in rats that had been given a diabetes inducer. In order to provide benchmarks, Groups A and B were used as positive and negative controls, respectively. Glibenclamide was given to Group C, whereas an ethanolic leaf extract from C papaya leaves was given to Groups D, E, and F at doses of 200, 400, and 600 mg/kg BD, in that order. The oral administration of extracts led to a significant ($p < 0.05$) reduction in blood sugar levels during a two-week period. While HDL levels increased, plasma levels of triglycerides, total cholesterol, and LDL all showed declines[49]. Following that, HDL levels went up. It was looked into whether the C papaya leaf juice could be used to treat diabetes. The experiment was done on mice that were given alloxan and then got diabetes. Five groups of six people each were formed. People in Group I and Group II were given 0.1 mL of a vehicle solution to use as positive and negative samples, respectively. A 600-gram amount of glibenclamide was given to Group III based on their body weight. Groups IV and V, on the other hand, were given 250 milligrams and 500 milligrams per kilogram of body weight, respectively. After taking the medicine for 28 days, lipid profiles, blood glucose levels, and biochemical markers linked to heart disease risk and the start of artery disease were significantly lower ($p < 0.05$). Furthermore, it is important to note that the serum HDL values rose significantly ($p < 0.05$) [9].

Anti-angiogenic Activity

Angiogenesis is the process by which new blood vessels grow out of existing ones. A series of binary switches that either promote or inhibit blood vessel growth regulate this process. One of the potential effects of the process modification is developing cancer. Using molecular docking, it was possible to determine the potential binding sites for the angiogenic receptors VEGFR1 and VEGFR2 and how bioactive compounds in leaves interact with them. The aim of the investigation was to identify potential binding sites for these receptors. Using an aqueous leaf extract, the chorioallantoic membrane egg-yolk angiogenesis model could be successfully inserted. This completes the task. There is evidence that the blood capillaries' width, length, and interconnectedness are all reduced by the C papaya plant's leaf. Furthermore, research indicates that some compounds such as quercetin, ascorbic acid, lycopene, and riboflavin are reduced when the leaf is removed. The study's conclusions were supported by these findings. It also had the effect of reducing the quantity of angiogenesis cases that occurred in unhealthful settings [8].

Anti-oxidant Activity

Oxidative stress is a big risk factor that leads to many serious illnesses. There is evidence that a product from C papaya leaves may be able to lessen the effects of oxidative stress. A test was done on Swiss mice to look into the reactive stress that cyclophosphamide results in. Every day for fifteen days, 250 mg of C papaya leaf extract was given to each animal based on its weight in kg. Studies have shown that the leaf extract of the C papaya plant helps fight oxidative stress and may even help protect DNA from damage [50]. The antioxidant and antimutagenic qualities of extracts from Anastatica hierochuntica, Lepidium sativum, and Carica papaya were investigated in this work using Swiss albino mice. EAC-cell injections into the mice's peritoneal cavity caused Ehrlich ascites cancer. On the other hand, when all extracts were taken orally for seven days at a 500 mg/kg bodyweight dose, oxidative stress, chromosomal aberration, DNA breakage, and inflammation decreased. As stated in the reference, the biomarkers linked to kidney and liver function showed improvement [51].

Antibacterial Activity

The causation of diseases by germs has been established as a significant obstacle, exacerbated by the increasing resistance of bacteria to therapeutic treatments. The agar well-diffusion method was used to show that C papaya leaf extracts can kill S. aureus, B. subtilis, E. coli, and S. typhi bacteria. Based on the data, E. Coli had the most action, being much more effective against the microorganisms that were being studied. CPLE separation of methanol led to the creation of seven

different parts. The five parts that have shown the most effectiveness against Escherichia coli are listed below. The green part of the C papaya plant has chemicals that might be able to treat a number of illnesses, such as typhoid fever, wound infections, gastroenteritis, and urethritis. The above factors are what made this happen.

Hepatoprotective Activity

The fruit's ethanol and aqueous extracts exhibit notable hepatoprotective effects. However, the hepatoprotective mechanism and the active ingredient responsible for the plant's effects are still unknown.

Table-2: Marketed formulation of *Carica Papaya*

Company name	Brand name	Dosage form
Rochway	*Papaya* leaf extract capsules	All of the dry leaves that make up the capsule are finely powdered and come from natural papaya components.
Rochway	*Papaya* leaf extract – 500 ml	*Papaya* leaf extract that is dry and 100% bio-fermented from *Carica Papaya*
Herbal *Papaya*	*Papaya* Leaf (Paw Paw Twig) Extract (alcoholfree)	sixty vegetable capsules made from dried *Papaya* leaf
Iowa Select Herbs LLC	*Papaya* leaf extract 4 oz (120 ml)	An extract of *Papaya* leaves in liquid form
SidoMuncul Herbal	Sari Daun Pepaya	For every capsule, there is 500 mg of dried extract of *Caricae* folium, also known as *Papaya* leaf.
Celebration Herbals	This product is a herbal tea, which is manufactured only from papaya leaves. There is no caffeine in it. The container measures 1.33 ounces (38 grams) and includes 24 tea bags.	(*Papaya* leaves that have been fermented) Tea bags

Micro lab limited	Caripill	Extract of dried *Carica Papaya* leaves contained in a tablet

Future Perspective

Carica papaya shows promising promise in treating thrombocytopenia, which gives us reason to be optimistic; nevertheless, this could only be achieved via more scientific research, standardization, and regulatory assistance. It is important to use both scientific and traditional information to get the best results from papaya for treating thrombocytopenia. Carpaine, chymopapain, papain, and many flavonoids are some of the important chemicals. A number of studies have shown that these chemicals may be involved in the process of increasing platelet counts. In addition, these compounds have anti-inflammatory and antioxidant characteristics. In the future, research may concentrate on gaining a knowledge of the exact mechanisms that these chemicals use to interact with the pathways that are involved in the generation and control of platelets.

Conclusion

The *Papaya* plant, also known as *C Papaya*, is a tropical plant that offers amazing potential in its numerous components, notably the leaves. There are several different types of phytochemicals that may be found in *Papaya* leaves. These phytochemicals include carpaine, saponins, terpenes, alkaloids, flavonoids, and antioxidants. A *Papaya* is a fruit that is very low in calories, despite the fact that it has a high concentration of vitamins and minerals. It is a fruit that is quite nutritious. The sensory qualities of this fruit are regulated by volatile molecules, and the pulp of this fruit includes dynamic compounds that have a variety of effects on various tissues. When the number of platelets in the blood is less than 150 × 109/L, it is called thrombocytopenia. This illness could have more than one reason. The leaf of the C papaya plant has a special mix of chemicals that make it look like it might be very good for treating a lot of different illnesses. There are special things about papaya leaf that make it a good medicine that can help with many health problems, like diabetes, malaria, viral illnesses, cancer, oxidative stress, and weak immune systems. A lot of research has shown that C papaya leaf can help treat thrombocytopenia. It does this by targeting genes like ALOX-12, PTFAR, and CD110. A lot of science studies have led to this information. Thrombocytopenia can be caused by many things, such as drugs, viral illnesses like dengue, chemotherapy, and other medical and physiological conditions. Both the newly developed dosages and the widely available dosages of C papaya leaf are meant to raise the number of platelets in the blood while also stopping them from breaking down. This is accomplished without causing any damage. *Papaya* leaf contains a number of phytochemicals, including carpaine, flavonoids, and antioxidants, which are considered to be among the most important bioactive components. New studies suggest that the leaf belonging to the C papaya plant might be able to help people who have low platelets. This is accomplished by reducing the disintegration of platelets, containing flavonoids that bind to viral assembly proteases, preventing viral replication, and increasing platelet synthesis. In addition, it has antibacterial, anticancer, antiangiogenic, anticancer, anticancer, and antiangiogenic activities. Urethritis, gastroenteritis, wound infections, and typhoid fever are some of the conditions that might potentially be treated with this substance.

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