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Research Paper

Review of Phytopharmacological Aspects of *Carica Papaya*

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ABSTRACT:
The evolution of humans has been significantly influenced by medicinal plants. The papaya plant has been around since prehistoric times. Carica papaya is extensively grown over the world and used as food and traditional medicine, especially as an antiseptic and contraceptive. Many physiologically active chemicals can be found in papaya. Recent studies in several regions of the world have revealed that C. papaya has a great potential for treating a variety of health issues. In recent years, significant progress has been made in understanding the biological activity and medicinal applications of papaya, and it is now regarded as a valuable nutraceutical fruit plant. The herbs have long been used to cure a variety of ailments, including stomach problems, diarrhea, skin infections, male contraception, and cold home remedies. Lycopene, carotenoids, alkaloids, monoterpenoids, flavonoids, minerals, vitamins, and the enzyme papain are all found in the complete plant. The proteolytic enzyme papain has a wide range of industrial applications. It's utilized in chewing gums and meat tenderizers. Plant juice is used to treat warts, cancer, and tumors in traditional medicine. Papaya has significant therapeutic characteristics that can be used to cure a variety of diseases. The leaves, seeds, latex, and fruit of the Carica papaya plant have all been shown to have a medical use. The body and immune system are nourished by these healthy fruits. Antibacterial, anticancer, insecticidal, wound healing and other therapeutic characteristics have been linked to the plant and its components. The current analysis focuses on some of the most prominent pharmaceutical uses of papaya plants in ancient and modern times.

Keywords: *Carica papaya, Phytoconstituents, Pharmacological activities, Medicinal herbs*

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I. INTRODUCTION:

Ayurveda has about too many plants listed in its medicinal systems. The use of such herbals is mentioned in the ancient Ayurvedic literature like Vedas, Chakara Samhita, and Sushruta Samhita[1, 2]. In this system, the universe is believed to have five elements Prithvi (Earth), Jala (water), Agni (Fire), Vayu (Air), and Akasha (Space). They are known as Panchamahabhoothas (five major elements). These five elements also constitute the human body and the three senses of humor (tridoshas). The tridoshas are Vata (related to air), Pitta (related to fire), and Kapha (related to water). According to Ayurveda, a healthy human body must have to balance this triose. Any imbalance leads to a state of disease. This system of medicine explains the various means to keep tridoshas balanced in various disease conditions, which constitute the therapeutic part[3]. It is an age-old traditional system of medicine that originated in India. Based on the material of origin, Ayurvedic medicines are divided into three classes as shown below; among these, the herbal formulation has gained great importance and rising global attention recently[4].

At least 35,000 plant species are employed for medical purposes around the world, and almost all plant portions are consumed as food as an efficient source of energy. Herb mixes obtained in the wild are commonly used in traditional remedies. However, the therapeutic qualities of plants and plant remedies have received attention in terms of safety, efficiency, economics, and suitability as food for power generation[5]. Medicinal plants have been used to cure health problems and prevent death in virtually all civilizations as a source of medication, culinary6 flavorings, and Medicinal plants have been used to cure health problems and prevent death in virtually all civilizations as a source of medication, culinary flavorings, and preservatives. The biological activities of plants are mainly attributed to active components produced during secondary

metabolism. The antimicrobial activity of a variety of plants has been studied recently to corroborate their historic usage in the treatment of a variety of ailments[6].

Carica papaya is a member of the Caricaceae family, which includes various plants that have been used to treat a range of ailments[5]. Papaya is a nutrient-dense fruit that is available all year round. It's high invitamins C, vitamin A, and vitamin E, all effective antioxidants. Magnesium and potassium, vitamin B pantothenic acid, folate, and fiber are all minerals[7]. Many biologically active chemicals can be found in *Carica papaya*. Chymopapain and papain are two key chemicals that are claimed to help with digestion. Papain is also utilized in the treatment of arthritis. The chemical concentrations differ in the fruit, latex, leaves, and roots. Because each portion of the papaya tree has monetary worth, it is commercially farmed[8].

Various plant parts are used to treat a variety of diseases. The leaves are the most useful of all the parts that are used for therapeutic purposes. Its various parts have been described in traditional literature for a variety of disease situations such as fever, swellings, jaundice, gonorrhea, bilious fever, itches, dermatitis, rheumatism cold, and headache, whooping cough, asthma,chickenpox, and bronchitis[9]. Bioactive chemicals have been found in several sections of the papaya plant, including the leaves, fruit, seed, latex, and root. The two most important bioactive components found in *C. papaya* are chymopapain and papain. Tea produced from papaya leaves is used to treat malaria. Some plant preparations have been found to have antimalarial and anti-plasmodial properties. Antimicrobial, antioxidant, and anti-inflammatory properties of *C. papaya*, as well as antitumor and immunomodulatory, anti-diabetic, anthelmintic, wound healing, and analgesic properties[10].

Many active components contained in *Carica papaya* leaves have been shown to increase overall antioxidant capability in the blood and reduce lipid peroxidation. Indigenous peoples have used them to treat several illnesses, including cancer and infectious infections. Crushed *Carica papaya* leaves have been used as an anthelmintic and a fever reducer. In Igboland and Ghana, the bright red parts of dried leaves have been used to cure gastrointestinal ailments. Despite their widespread use, standardized goods or preparations with known content are not commercially available[11].

Food waste or by-products, such as the seed and peel of some fruits, can be used to provide nutrients and antioxidants. Pomegranate peel and grape seed, for example, have been shown to have more antioxidant activity than pulp. Converting these papaya waste seeds into a marketable product will not only help to lower disposal costs but will also give the papaya industry a new source of long-term profit. Processing the seeds into high-protein flours with good nutritional and antioxidant properties, such as protein concentrate and isolate, could be the first step toward employing pawpaw seeds as food ingredients and giving them nutraceutical value in the pharmaceutical and food industries[12]. The seeds are used to cure sickle cell disease and toxicity[13]. The ripe fruit of the pawpaw shrub is commonly eaten as food in numerous parts of the world. The unripe fruit, on the other hand, is employed as a moderate laxative, diuretic, galactagogue, and abortifacient agent[14].

SCIENTIFIC CLASSIFICATION:

The papaya belongs to a taxonomical classification that includes kingdom (Plantae), order (Brassicales), family (Caricaceae), genus (*Carica*), and species (*C. papaya*)[15]. Common names of these plants include papaya, papaw, papita, papaya, papaya-baum, papaia, pawpaw, arand-kharpuja.

VARIOUS CHEMICAL PROPERTIES OF CARICA PAPAYA

Various chemical elements can be found in the fruit, fruit juice, seed, root, leaves, bark, and latex of papaya[7]. Chitinase, glutaminyl cyclase, and cysteine endopeptidases were found in Carica latex (Papain chymopapain and caricain). Carpaine, pseduocarpaine, and dehydrocarpaine I and II are alkaloids found in fruit pulp. Phenols, flavonoids, carotenoids, vital vitamins, and minerals were found in papaya leaves and fruits[14]. Other components such as omega endopeptidase and a combination of cysteine endopeptidases such as papaya endopeptidase II and IV have also been identified[16]. The chemical properties of *Carica papaya* were also examined, and the results revealed the presence of proteins with unknown activities, linamarase, protease inhibitors, and chitinases[17].

TABLE 1:CHEMICAL CONSTITUENTS OF *CARICA PAPAYA* [18, 19, 20]

Part	Constituents
Latex	proteolytic enzymes, papain and chymopapain, glutamine cyclotransferase, chymopapain A, B, and C, peptidase A and B, and lysozyme, glutamine cyclotransferase, chymopapain A, B, and C, peptidase A and B, and lysozyme
Leaves	Alkaloids include carpain, pseudocarpain, and dehydrocarpaine I and II, as well as choline, carposide, vitamin C, andvitamin E.

Bark	β-sitosterol, glucose, fructose, sucrose, galactose, and xylitol
Seed	Carpaine, benzylisothiocynate, benzyl glucosinolate, glucotropaeolin, benzoylthiourea, hentriacontane, Fatty acids, crude proteins, crude fiber, caricin, papaya oil,and the enzyme nyrosin
Fruit	Protein, fat, fiber, carbohydrates, minerals, calcium, phosphorus, iron, vitamin C, thiamine, riboflavin, niacin, and caroxene, amino acids, citric acids, and molic acid (green fruits), volatile compounds: linalol, benzyl isothiocyanate, cis and trans 2, 6-dimethyl-3,6 expoxy-7 octen-2-ol.
Juice	lipids: n-butyric, n-hexanoic, and n-octanoic acids; myristic, palmitic, stearic, linoleic, linolenic acids-vaccenic acidand oleic acids.
Root	Arposide and an enzyme myrosin

TABLE 2: MEDICINAL PROPERTIES OF VARIOUS PARTS OF *CARICA PAPAYA* [19, 20, 21, 22, 23]

Various plant parts	**Medicinal Use**
Ripe fruits	carminative, diuretic, expectorant, sedative, preventive action against dysentery, skin diseases, psoriasis, and ringworm.
Unripe fruits	Laxative, ulcers, and impotence, reduce enlarged spleen and liver and it is used in snakebite to remove poison.
Seeds	NephroProtective Activity, antibacterial properties, anthelmintic and anti-amoebic
Roots	Antifungal activity, diuretic, piles, diuretic
Leaves	Dengue fever, Cancer Cell Growth Inhibition, Antimalarial, and Antiplasmodial Activity, Facilitate Digestion, Antibacterial activity, relieve nausea, Meat tenderizer
Flowers	Febrifuge, jaundice, pectoral properties, emmenagogue
Stem bark	Antifungal activity, jaundice, sore teeth, anti-hemolytic activity

II. PHARMACOLOGICAL ACTIVITIES OF *CARICA PAPAYA*

Antimicrobial activity:

Papaya leaves protect against pathogenic bacteria. Treatment with *Carica papaya* leaf ethyl acetate extract suppressed *B. stearothermophilus*, *L. monocytogenes*, *Pseudomonas sp*, And *E. coli*, according to new research. The activity of the extract was impacted by the pH of the heating process, which was more effective at low pH. Against *B.stearothermophilus* and *E. coli*, the extract activity was modified by NaCl[24]. The bacteriostatic activity was discovered in the seeds of *Carica papaya* against *bacillus subtilis, enterobacter cloacae, Escherichia coli, salmonella typhi, staphylococcus, Proteus Vulgaris, pseudomonas aeruginosa,* and *klebsiella pneumonia*, among other enteropathogens. Gram-negative bacteria were found to be more sensitive to the extract than gram-positive bacteria[19].

Root ethanol extracts demonstrate the greatest activity against the test microorganisms. The root extracts had stronger activity against all of the gram-positive bacteria tested than the gram-negative bacteria, and the aqueous leaf extract had considerable inhibition, with higher activity against the test bacteria than the organic solvents. This also had higher antibacterial activity against all gram-positive bacteria tested than the gram-negative bacteria. Temperature promotes extract activity, but alkaline pH lowers it[25].

The antibacterial potentials of several extracts of *C. papaya* components (dry and crushed leaves, fruit peel, seed) are compared to conventional medications in this study (prefacing and cefuroxime). The extracts of *C. papaya* in petroleum ether demonstrated high antimicrobial activity with a Minimum Inhibitory Concentration (MIC) of 2mg/ml, compared to 4mg/ml and 6mg/ml for prefacing and cefuroxime, respectively. Extracts in 1% HCl and ethanol, on the other hand, demonstrated antibacterial action against all of the gram-positive and negative bacteria tested, whereas extracts in water were exclusively active against *E. coli* and *S. aureus*[26]. In an in-vitro agar well diffusion approach, unripe endocarp acetone extracts were found to be more efficient than leaf extracts against pathogenic Gram-positive bacteria (*B. subtilis*, *B. cereus*, *Micrococcus luteus*, and *S. aureus*) and Gram-negative bacteria (*E. coli* 101 and 119)[27].

Antifungal activity:

Bioactive chemicals were extracted from *Carica papaya* leaves and seeds from discarded ripe and unripe fruit using an ethanol extraction method. The antifungal efficacy of the extracts (LE, SRE, SUE) from the best extraction treatment was determined by testing them against three phytopathogenic fungi: Rhizopus stolonifer, Fusarium spp., and Colletotrichum gloeosporioides. The leaf extract has the broadest range of activity. The MIC50 for Fusarium spp. was 0.625 mg ml-1, and for C. gloeosporioides, it Was 10 mg ml-1, inhibiting mycelial development by around 20% in both cases. *Carica papaya* leaf ethanolic extracts could be a source of secondary metabolites with antifungal activity. Latex is another component of papaya leaves, and it contains chitinases, some of which have been demonstrated to have considerable antifungal action in biochemical studies[9].*C. papaya* latex sap has antifungal action against Candida albicans. When introduced to culture during the exponential development phase, *Carica papaya* latex sap suppresses Candida albicans growth. A combination of *C. papaya* latex (0.41 mg protein/ml) and fluconazole (2 g/ml) inhibited C. Albicans growth in a synergistic manner[28].

Anti-inflammatory activity:

Carrageenan-induced paw edema, cotton pellet granuloma, and formaldehyde-induced arthritis models were used to investigate the ethanolic extract of *C. papaya* leaves in rats. The extract's ulcerogenic properties were also investigated. In the carrageenan test, the extract at a dose of 25-250 mg/kg p.o showed a considerable reduction in paw edema. At higher doses, the extract caused minor mucosal irritation[14]. In a recent in vivo investigation, papaya seeds (methanol and aqueous extract) were discovered to exhibit anti-inflammatory effects. The anti-inflammatory or immunomodulatory properties of nonpolar extracts of any component of the papaya plant have been studied in vivo so far[29].

Alkaloids, flavonoids, saponins, tannins, and glycosides have all been linked to anti-inflammatory properties at variable levels, according to a phytochemical study[30]. The anti-inflammatory benefits seen in this investigation could be attributed to the activity of one or more of the substances identified[31]. Papain is abundant in the latex of the plant's fresh aerial component, the fruit, rather than the dried leaves (used in this study)[32]. Finally, the anti-inflammatory effect of the ethanolic extract of *C.papaya* has been demonstrated in this investigation[33].

Antidiabetic Activity:

An experimental rat model was used to investigate the anti-diabetic efficacy of *Carica papayaL*. leaf extract. In streptozotocin-induced diabetic and non-diabetic rats, a chloroform extract containing steroids and quinine was administered at various dose levels. The sacrifice was carried out after 20 days of treatment, and a biochemical investigation was carried out. Diabetic rats receiving *Carica papayaL*. leaf chloroform extract had significant reductions in serum glucose, transaminases, and triglycerides. According to this study, *C.papaya* leaf can help diabetic symptoms[9].In mice, the anti-diabetic effect of *C. papaya* leaf extracts was examined. The results of this study show that diabetic mice's hyperglycemic levels were normalized after receiving various doses (50,150, and 300 mg/kg BW) of ethanolic leaf extracts. Similarly, *C. Papaya* leaf extracts have been demonstrated to have significant impacts on plasma insulin, triglyceride, cholesterol, and HDL cholesterol levels. Liver enzymes (ALT, AST, and ALP), bilirubin, and blood cells (red cells, white cells, and platelets) all improved in a dose-dependent way. The physiologically active components of papaya leaf extracts are thought to aid in the reduction of diabetes' secondary complications and enhanced insulin sensitivity to glucose uptake by cells[34].

Antioxidant activity:

DPPH test for antioxidant activity of *C. papaya* by comparing the sample extract's DPPH radical scavenging activity IC50 (Inhibitory Concentration) to the standard value of ascorbic acid, the sample extract's DPPH radical scavenging activity was measured. According to the results of the antioxidant activity of *C. papaya* with methanolic extract by the DPPH test, the presence of free radicals is larger and directly proportional to the concentration of the sample. It means that the higher the concentration, the higher the proportion of free radicals in the methanolic extract of *C. papaya* leaves[35].

In human skin, Detroit 550 fibroblasts, *C. papaya* seeds water extract, acts as an antioxidant against hydrogen peroxide (H_2O_2) oxidative damage. The aqueous extract of *C. papaya* seeds is nontoxic and acts as a potent free radical scavenger, preventing H_2O_2 oxidative stress in Detroit 550 fibroblasts. As a result, it has the potential to defend against oxidative stress[36].

Analgesic Activity:

There are analgesic properties in the three extracts made from Carica papaya L. leaves [37]. These three extracts (n-hexane, ethyl acetate, and ethanol extracts) displayed considerable analgesic effectiveness at all three dose levels (0.175, 0.35, and 0.70 mg/kg BW orally) when compared to aspirin in a mouse model of acetic acid-induced pain (Siegmund technique) (taken as the standard drug)[9, 38].The best analgesic activity was found in an ethanol extract of *Caricapapaya* leaves, which was comparable to aspirin[39].

Wound healing activity:

Excision and dead space wound models were used in streptozotocin-induced diabetic rats to examine the aqueous extract of *C. papaya* fruit [100 mg/ kg^{-1}, 1 day 1 for 10 days] for wound healing activities[40]. The aqueous extract shows a 77 % reduction in wound area when compared to the control 59% wound contraction. As a result, researchers discovered that the aqueous extract of *C. papaya* has potent wound-healing effects[16, 41]. In 2009, researchers looked into the papaya latex synthesized in the Carbopol gel, which was proven to be effective in the treatment of burns and so encouraged wound healing activity. They also discovered that plant-derived papain enzymes can cure gangrenous wounds and hard skin[42].

Antimalarial activity:

The rind of raw papaya fruit extract contains a substantial amount of petroleum ether, which has antimalarial properties. Extracting the active ingredient from this plant, which grows abundantly across the tropics and whose rind is discarded as waste, could have great commercial potential for antimalarial action[57]. Antimalarial properties of a decoction of S. macrophylla seeds have been reported[43]. The antimalarial efficacy of S. macrophylla seed methanol extract against Plasmodium falciparum was examined[46]. On chloroquine-resistant P. falciparum strains, the bark extract of S. macrophylla demonstrated high antimalarial efficacy (78 percent inhibition at 100 g/mL) (Indo). The bark extract inhibited the rat malaria P. vinckeipetteri 279BY by 73 percent in an in vivo investigation at 250 mg/kg body weight[45]. In addition to antimalarial action against P. falciparum, the aqueous extract of S. macrophylla seeds showed antibabesial activity[44].

Anthelmintic activity:

Traditional medicine has employed a variety of plants and plant extracts to treat helminth infections, including papaya, which is high in proteolytic enzymes that disintegrate worm cuticles, has low toxicity, and has been used in traditional medicine to treat gastrointestinal nematodes for decades. The worm digesting activity of a papain preparation made from *C.papaya* latex as described in 1940, as they quickly digested the Ascaris[19].*Carica papaya* seeds have anthelmintic effects against the eggs, infective larvae, and adult worms of the parasitic nematode Trichostrongylus colubriformis in vitro[47].In papaya seed ex- tracts, benzyl isothiocyanate is the primary or single anthelmintic[48]. Papaya latex has antihelmintic action against Heligmosomoides polygyrus infections in mice[49]. The mouse gastrointestinal nematode Heligmosomoides polygyrus was used to test the anthelmintic efficiency of cysteine proteinases from papaya and other plants in vitro. Cysteine proteinases induced significant damage to the cuticle of adult male and female Heligmosomoides polygyrus worms after only 2 hours of incubation, as evidenced by the loss of surface cuticular layers.The plant enzymes' mechanism of action (attacking the worm's protective cuticle) suggests that resistance would take a long time to emerge in the wild. Because of their potency and method of action, plant cysteine proteinases are promising candidates for a new class of anthelmintics that are desperately needed for the treatment of humans and domestic livestock[50].

Anti-sickling activity:

When a glutamic acid at position 6 of hemoglobin in red blood cells is changed to valine, it causes sickle cell disease (SCD). The unripe papaya fruit extract has been shown in recent tests to have anti-sickling properties[51].In a dose-dependent way, another study demonstrated the effective antisickling property of *Carica*

papaya leaf extract[52].When administered orally to rats at a concentration of 10 mg/kg, papaya aqueous root extract significantly increases urine production and displays urinary electrolyte excretion profiles that are comparable to those of hydrochlorothiazide[53]. Under osmotic stress, a methanolic extract of *C. papaya* at a concentration of 10 mg/mL decreased hemolysis and protected erythrocyte membrane integrity in vitro[7]. The extract of unripe papaya fruit contains anti-sickling properties[19].The most effective doses of the *C. papaya* leaf extract were determined to be 5 and 10 mg/ml, which significantly influenced the time course for sickling and had a notable antisickling action[54].

Antiplasmodial Activity:

Carica papaya L. leaf extracts have significant antiplasmodial efficacy and low cytotoxicity. Three alkaloids, 7, 8, and 9, demonstrate this action[55]. The bioactivity of compounds was investigated in vitro against four parasites (Trypanosoma brucei rhodesiense, Trypanosoma cruzi, Leishmania donovanii, and Plasmodium falciparum), as well as in a Plasmodium berghei animal model. The antiplasmodial action of papaya leaves was validated in this investigation, and it may be linked to alkaloids. Carpaine was the most active and selective of these alkaloids in vitro[9].evaluating the effectiveness of an ethanolic papaya leaf extract against Plasmodium berghei infected Swiss albino mice[56].The active components found in the extracts, including flavonoids, alkaloids, anthraquinones, tannins, saponins, terpenoids/steroids, diterpenoids, and cardiac glycosides, may be responsible for their antiplasmodial effect. Therefore, against malarial infections, we advised 400 mg/kg of *C. papaya* extract[57].

Anticancer activity:

The anticancer activities of *C. papaya* have been discovered in vitro. The plant includes papain, an enzyme that is found in papaya and is useful in the treatment of cancer[58]. Fibrin is broken down by papain, which covers tumor cells and converts them to amino acids[59]. Inside papain contains the pigment lycopene, which is extremely reactive to free radicals and oxygen. Isothiocyanate, found in papaya, prevents breast, prostate, pancreatic, lung, leukemia, and colon cancer[60].

In a study, it was discovered that *C. papaya* leaf extract can slow the progression of malignant cells[61]. Various markers such as CA15-3 and LDH are key biochemical parameters for detecting malignant cells, and it was discovered that a dose of 200 mg/kg body weight of the leaf extract had a substantial effect on lowering these markers in the treatment of cancer[62].

The anticancer effects of petroleum ether, ethyl acetate, chloroform, and methanol (80 percent) extracts of aerial portions of *C. papaya* were investigated in UACC62 (melanoma), TK10 (renal), and MCF7 (breast) cancer cells. The petroleum extract of papaya aerial parts was found to have a substantial effect on MCF7 (breast) cancer cells[63]. According to one study, black seed from yellow ripe papaya has a direct influence on reducing prostate cancer cell proliferation[64].The prostate cancer cell line was examined with a methanolic extract of black seed (ripe papaya) and white seed (unripe papaya)[65]. The black seed extract is effective against prostate cancer cells, whilst the white seed has been shown to stimulate preexisting prostate cancer cells[66]. In another investigation, papaya leaf juice was found to have an antiproliferative effect on prostate cancer cells[67].

Hepatoprotective activity:

The fruit's ethanol and aqueous extracts have impressive hepatoprotective properties against CCl4-induced hepatotoxicity. However, the hepatoprotective mechanism, as well as the active ingredients responsible for this plant's hepatoprotective action, are unknown[57].Rats were used to test the hepatoprotective effects of aqueous and ethanol extracts of *Carica papaya*[68]. Both the aqueous and the ethanol extracts of *C. papaya* significantly reduced the liver damage caused by carbon tetrachloride[69]. Biochemical markers like serum bilirubin, alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase were used to assess the protective efficacy. The liver's histological alterations were evaluated in comparison to the control[70].

Anti-fertility activity:

According to reports, the white rat spermatozoa are resistant to the antifertility effects of the ethyl acetate extract of *C. papaya* seeds (Rattus norvegicus)[71]. The 1,2,3,4-tetrahydropyridine-3-yl-octanoate chemical was visible in an extract of ethyl acetate[27].In conclusion, the detected drug significantly differed in activity from the control and had an impact on the motility, viability, and abnormalities of the spermatozoa, as well as their activity[72].the male albino rats' gonads were affected negatively in terms of fertility by pawpaw seeds. The germinal epithelium and germ cells degenerated, there were fewer Leydig cells, and there were vacuoles in the tubules, according to histological studies at a high dose of 100 mg.kg-1 body weight[73].

On the seminiferous tubules of rats, a crude extract of *C. papaya* bark [5-10 mL/ (kg. d), p.o for 4 weeks] exhibited complete loss of fertility, which was attributed to a decrease in sperm motility and morphology. As a result, the bark indicated that the environment was secure and that it may be used[74].

Anti-ulcer activity:

Alcohol-induced acute stomach injury and blood oxidative stress in rats were treated with aqueous seed extract of *C. papaya* at doses of 50 mg/kg and 100 mg/kg p.o. The stomach acidity of rats given 100 mg/kg of the extract was dramatically reduced[16].papaya plant leaves' ethanolic extract, which was discovered to be useful against ulcers[75].Using ethanol and indomethacin-induced stomach ulcer models in rats, the antiulcer potentials of aqueous and methanol extracts of whole unripe papaya fruit were examined[76].It was discovered that an aqueous extract was more successful at treating ethanol-induced stomach ulcers[77]. It was determined that the papaya fruit seed oil contains benzyl isothiocyanate and that the proteolytic enzyme papain from the unripe fruit latex had potent antiulcer properties[78].

Anti-dengue activity:

In a dose-dependent way, *C. papaya* latex extracts in chloroform, methanol, and aqueous form were effective against *C. quinquefasciatus* and *Aedes aegypti larvae* [79]. Chloroform extract > methanol extract > aqueous extract is the order of cytotoxic impact[80]. According to one report on a clinical trial with *C. papaya*, patients with dengue fever had a higher platelet count and recover faster[81]. Two teaspoons of C. papaya leaf juice were administered to 5 dengue patients three times per day for 6 hours, using the customary approach[82]. It was discovered that leaf juice causes a significant increase in platelet counts within 24 hours of treatment (An increase in platelet count was observed when a patient was given a *C.papaya* leaf extract tablet three times daily for five days) and that this effect could be due to the expression of the platelet-activating factor receptor gene, which is responsible for platelet formation[29]. Another study discovered that the leaves of *C.papaya* have a promising effect in increasing a dengue patient's platelet count[83].

Antiprotozoan activity:

In vivo and in vitro studies were conducted on the activity of the petroleum ether extract of *C. papaya* seeds against the ciliate protozoan Ichthyophthirius multifiliis[84].Infected goldfish (Carassius auratus auratus) were immersed in pools containing *C. papaya* extract for 96 hours[85]. When compared to untreated control, I. multifiliis populations on fish were reduced by 90% after treatment with bath plant extract at 200 mg/l. As a result, parasite-induced fish mortality was dramatically reduced[86]. In vitro experiments revealed that I. multifiliis died completely after 6 hours in 200 mg/l of *C. papaya* extract[87]. Plant extracts may have antiprotozoal activity, which could help control I. multifiliis effectively[88].

Molluscicidal activity:

Snails, despite being harmless in their eating habits, serve as intermediate hosts for helminth parasites, allowing serious parasitic illnesses to spread[89].Fasciola hepatica and Schistosoma produce fasciolosis and schistosomiasis, respectively, which are transmitted by snails[90].Freshwater snails Lymnaea acuminate (Lymnaeidae) and Indoplanorbis exustus (Planorbidae) serve as intermediary hosts in the parasite's life cycle.In the gonadal/nervous tissue of Lymnaea acuminata, feeding snail attractant pellets containing papain (40 percent of 24 h LC50) resulted in significant reductions in protein, amino acids, DNA, RNA, and AChE activity[91].Except for the root, papain may be found in all parts of the tree[86]. The toxicity of lyophilized latex from the skin of unripe fruits and pure papain against L. acuminate is similar across all exposure periods, whereas the toxicity of a column purified fraction of *C. papaya* seed is lower than that of lyophilized latex[92]. It's because the latex of *C. papaya* contains a higher concentration of papain than the seed[93].

Anti-diarrheal responses:

Raw *C. papaya* chloroform extract (25 mg/mL) and ripe *C. papaya* acetone extract (25–0.39 mg/mL) both demonstrated antidiarrheal action against gut pathogens[94].The antidiarrheal activity of ripe *C. papaya* extract against Plesiomonas shigelloides was widely observed, with concentrations ranging from 50 mg/mL to 0.39 mg/mL. DAS77 (an herbal mixture made from dried papaya root and young Mangifera indica bark) is beneficial in the treatment of diarrhea.DAS77 was tested on mice, and the results revealed that it has anti-diarrheal properties. In another study, the antidiarrheal activity of *C. papaya* leaf aqueous extract was examined in a rat model, and the extract was reported to have good antidiarrheal action and to be safe at 200 mg/kg in the rat model[95,96].

III. PHYTOCHEMICAL STUDIES:

Herbs are more likely than woody plant forms to have a pharmacologically active chemical, which explains their appeal in traditional medicine[97]. According to studies, leaves are the most extensively used plant parts. Carpaine, pseudocarpaine, and dehydrocarpaine I & II are alkaloids found in the leaves of *Caricapapaya L.* In vitro tests on mouse lymphoid leukemia L1210, lymphocytic leukemia P388, and Ehrlich ascites tumor cells revealed that the alkaloid Carpaine (originally discovered by Greshoff in 1890) exhibits anticancer action.

It also inhibits Mycobacterium tuberculosis H37Rv, a tuberculosis pathogen. It's a heart toxin that reduces pulse frequency and depresses the central nervous system. It is said to be an effective amoebicide.

The only difference between pseudocarpaine and carpaine is the arrangement of the alcoholic carbon atom. It has a different melting point and rotation than carpaine. Choline and carposide, anthraquinone, vitamin C, and vitamin E are all claimed to be present. These compounds are involved in a wide range of biological processes. Insulin, tannins, and other alkaloids have been found in plant leaves, which may be responsible for their therapeutic benefits.

Seven flavonoids have been identified, including quercetin 3-(2G-rhamnosyl-rutinoside), kaempferol 3-(2G-rhamno- syl-rutinoside), quercetin 3-rutinoside, myricetin 3 - rhamnoside, kaempferol 3-rutinoside, quercetin, and kaempferol 27. HPLC-based activity profiling is used to report the flavonols and alkaloidal fractions. Manghaslin, clitorin, rutin, and nicotiflorin were discovered among the flavonols, while the alkaloid fraction contained five substances that were identified as piperidine alkaloids.

Leaf tissue has lower extractive outputs than other plant sections, such as ripe and unripe fruits. Chemical analysis of *Carica papaya* L. leaves growing in the semi-arid zone was also carried out using the most reliable, accurate, non-destructive, and consistent approach for a major and trace element analysis, EDXRF. The leaves were evaluated for distinct mineral compositions using Energy Dispersive X-ray Fluorescence (EDXRF). When compared to other elements, higher amounts of oxygen (87%), calcium (4.47%), magnesium (3.37%), and potassium (1.49%) were discovered. Other elements such as silicon, aluminum (0.805 percent), phosphorus, chlorine, sulfur, stannous, and strontium were also detected, but in smaller amounts. Chromium (0.0129 percent) has also been discovered[9].

IV. CONCLUSION:

Papaya is well-known around the world for its outstanding and therapeutic characteristics. Traditional medicine uses the entire papaya plant, including its leaves, seeds, ripe and unripe fruits, and juices. Papaya is high in phytochemicals such as vitamins, antioxidants, flavonoids, polyphenols, and several minerals, as well as enzymes such as papain, lycopene, isothiocyanate, and some proteolytic enzymes that help to treat health problems. As a result, regular consumption of papaya will improve our health by quenching free radicals in the body and enhancing our immune system's ability to fight foreign pathogens. *Carica papaya* is a nutraceutical plant with several pharmacological properties.

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