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***REVIEW PAPER***
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# A Review on Clinical Properties of Different Leaves

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## ABSTRACT

Leaves, being the principal organs responsible for photosynthesis in plants, encompass a rich assortment of phytochemicals with potential pharmacological efficacy. This review aims to provide an extensive overview of the pharmacological properties associated with leaves, incorporating both traditional applications and contemporary scientific investigations. It discusses the pharmacological effects of leaf extracts and isolated compounds. Furthermore, this review emphasizes the importance of elucidating the phytochemical composition of leaves and understanding their mechanisms of action to effectively utilize their therapeutic potential. Additionally, considerations pertaining to safety, toxicity and the standardization of leaf-derived preparations are addressed. Overall, this review underscores the significance of leaves in pharmacology and highlights the necessity for further exploration and validation of their medicinal properties to facilitate the development of novel therapeutic interventions.

**Keywords:** Leaves, Antioxidants, Clinical, Phenols

## INTRODUCTION

Leaves, the quintessential organs of photosynthesis in plants, have long been recognized for their multifaceted roles in traditional medicine and modern pharmacology (Ghorbani and Esmaeilizadeh, 2017). Their intricate anatomy and biochemical composition make them reservoirs of diverse phytochemicals with potential therapeutic benefits (Wink,1999). Throughout history, various cultures worldwide have utilized leaves for their medicinal properties, often as infusions, poultices, or extracts (Heinrich *et al.,* 2017). With the advancement of scientific research, the pharmacological properties of leaves have garnered significant attention, leading to the identification and exploration of their bioactive compounds and mechanisms of action (Sarker and Nahar, 2012).

The pharmacological potential of leaves extends across a spectrum of health conditions, including but not limited to oxidative stress-related disorders, inflammatory diseases, microbial infections, metabolic disorders like diabetes, cancer and neurological ailments (Patwardhan *et al.,* 2004). Antioxidants present in leaves scavenge free radicals, mitigating cellular damage and promoting overall health (Valko *et al.,* 2007). Anti-inflammatory properties alleviate inflammatory responses, offering relief from conditions such as arthritis and inflammatory bowel disease (Serhan and Petasis, 2011). Furthermore, the antimicrobial activity of leaf extracts has been investigated against a broad range of pathogens, highlighting their potential as natural alternatives to conventional antibiotics (Cowan, 1999).

Moreover, leaves harbor compounds with antidiabetic properties, modulating glucose metabolism and insulin sensitivity (Grover and Yadav, 2004). Their anticancer activity has shown promise in inhibiting tumor growth, inducing apoptosis and preventing angiogenesis (Peng *et al.,* 2011). Additionally, neuroprotective effects of certain leaf constituents have been demonstrated, offering potential therapeutic avenues for neurodegenerative disorders like Alzheimer's and Parkinson's diseases

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(Howes and Perry, 2011).

Despite the burgeoning interest in the pharmacological properties of leaves, challenges remain in standardizing extraction methods, determining optimal dosages and assessing safety profiles (Calixto, 2000). Furthermore, the exploration of synergistic interactions among phytochemicals within leaves presents avenues for future research (Williamson, 2001).

This review aims to provide a comprehensive overview of the pharmacological properties of guava, moringa, papaya, mango and neem leaves, integrating traditional knowledge with contemporary scientific findings. By synthesizing evidence from diverse sources, it seeks to elucidate the therapeutic potential of leaves and their role in the development of novel pharmacotherapeutic agents.

**Review of Literature :**

***Guava Leaves :***

Luo *et al.* (2019) concluded that the isolation of polysaccharides from guava leaves (GLP) and assessment of its antioxidant activity in vitro and anti-diabetic effects on streptozotocin-induced diabetic mice fed a high-fat diet, the findings showed that GLP significantly reduced total cholesterol, triglycerides, glycated serum protein, creatinine and malonaldehyde in addition to demonstrating good DPPH, OH and ABTS free-radical scavenging abilities. of the meantime, it dramatically reduced the damage to the pancreas, liver and kidneys of diabetic mice and raised the activity of the enzyme superoxide dismutase (SOD).

Olaniyan (2017) that twenty per cent egg yolk powder of the entire typical rabbit meal can successfully produce hypercholesterolemia. In hypercholesterolemic rabbits, guava leaf extracts—both aqueous and ethanolic—have also been shown to dramatically lower lipid levels; crucially, the extracts did not lower HDL levels, the good kind of cholesterol.

Melo *et al.,* (2020) reviewed the biological activity and the chemical makeup of guava leaf extracts were connected. Phenols, flavonoids, antioxidant qualities, antiviral activity, cytotoxicity and antibacterial activity were tested, respectively, using total phenolics, total flavonoids, ABTS/DPPH, TZMbl, plaque reduction, XTT, spectrophotometric and Kirby-Bauer tests. To ascertain the antiviral selectivity against the human immunodeficiency virus type 1 and the herpes simplex virus type 1, the median cytotoxicity concentration and half-maximum effective concentration values were obtained. A spectrophotometric assay and the Kirby-Bauer test were used to assess the antibacterial activity against *Escherichia coli* and *Bacillus subtilis*. High levels of phenol (0.8 to 2.1 GAE mg/mL) and flavonoids (62.7 to 182.1 Rutin Eq mg/g DW) were found in the guava leaf extracts and these levels were connected with both selective antiviral activity and high antioxidant capacity (therapeutic index values over 10). Antibacterial test results showed that the extracts were active against both gram-positive and gram-negative bacteria.

Ojewole (2006) studied the analgesic impact of the plant extract assessed using the "hot-plate" and "acetic acid" test models of pain in mice, while the anti-inflammatory function of the aqueous leaf extract was studied in rats using fresh egg albumin-induced pedal (paw) edema. Standard reference analgesic and anti-inflammatory drugs were employed for comparison: morphine (10 mg/kg, i.p.) and diclofenac (100 mg/kg, i.p.). Rats treated with P. guajava leaf aqueous extract (PGE, 50–800 mg/kg, i.p.) showed a dose-dependent and significant ($p < 0.05–0.001$) reduction in acute inflammation (edema) caused by fresh egg albumin. Mice exposed to chemical and thermally induced nociceptive pain similarly showed dose-dependent and significant ($p < 0.05$-$0.001$) analgesic effects from the plant extract (PGE, 50-800 mg/kg, i.p.). The plant's abundant tannins, polyphenolic compounds, flavonoids, ellagic acid, triterpenoids, guiajaverin, quercetin and other chemical compounds are thought to be responsible for the plant's leaf extract's documented analgesic and anti-inflammatory properties. Thus, it shows that *P. guajava* leaf aqueous extract has analgesic and anti-inflammatory qualities, supporting ethnomedical and folklore claims that the plant can be used to treat and/or prevent painful, arthritic and other inflammatory illnesses.

Deguchi and Miyazaki (2010). *In vitro* alpha-glucosidase enzyme inhibition, the safety of the extract and Guava Leaf Tea, the reduction of postprandial blood glucose elevation and the amelioration of hyperglycemia, hyperinsulinemia, hypoadiponectinemia, hypertriglycemia and hypercholesterolemia in murine models and multiple clinical trials are all covered in this review. The active component of the aqueous guava leaf extract is also discussed. Type 2 diabetes mellitus is thought to be prevented in part by the long-term reduction of postprandial blood glucose increase and guava leaf tea is thought to be helpful as an alimentotherapy for long-term

treatment.

Jaiarj *et al.* (1999) used rats and guinea pigs to test *Psidium guajava Linn.* (guava) leaf extract's anticough properties. The findings demonstrated that, after 10 minutes of the extract's injection, aqueous extract of the plant at doses of 2 and 5 g/kg, p.o., reduced the frequency of coughs brought on by capsaicin aerosol by (35 and 54%), respectively, in comparison to the control group ($P<0.01$). The anticough action, however, is not as effective as 3 mg/kg dextromethorphan, which reduced cough frequency by (78%) ($P<0.01$). In a test conducted on rat tracheal muscle that was isolated, the extract both directly and synergistically increased muscular contraction and pilocarpine's stimulatory impact. An atropine was utilized to counteract this impact. Furthermore, the disc diffusion method revealed that water, methanol and chloroform extract of dry guava leaves suppressed the development of *Staphylococcus aureus* and β-streptococcus group A ($P<0.001$). Guava leaf extract has an LD50 of greater than 5 g/kg, p.o. These findings imply that guava leaf extract is advised as a cough treatment. With pilocarpine's stimulatory action.

Kawakami *et al.* (2012) in this work, demonstrated that guava leaf extracts reduced both the LDL oxidation process, which is driven by the enzyme-overexpressing macrophage-like J774A.1 cells and the leucocyte-type 12-lipoxygenase activity. During 16 weeks, apoE-knockout mice were given 100 mg of dry extracts/kg of body weight orally once a day for 16 weeks. This resulted in a considerable reduction in the area of atherogenic lesions that occurred in the aorta and aortic sinus. The two main substances found in guava leaf extracts that inhibit leucocyte-type 12-lipoxygenase are quercetin and ethyl gallate. The antiatherogenic effect of guava leaf extracts may be due to their inhibitory effects on cell-mediated LDL oxidation and leucocyte-type 12-lipoxygenase activity.

Cheng *et al.* (2009) identified the active component while examining the enhanced effect of aqueous guava leaf extract on glucose absorption in rat clone 9 hepatocytes. To separate the extract into fractions with varying polarity, MeOH-$H_2O$ solutions were eluted via Diaion, Sephadex and MCI-gel columns. To assess the hypoglycemic impact of these fractions, rat clone 9 hepatocytes were subjected to an uptake test of 2-[1-14C] deoxy-D-glucose. High-performance liquid chromatography (HPLC) and nuclear magnetic resonance studies were used to identify the active component. According to the findings, quercetin is the main active ingredient in guava leaf extract, phenolics make up the majority of the extract and high polarity fractions of the extract improve glucose absorption in rat clone 9 hepatocytes. They propose that quercetin, found in the guava leaf aqueous extract, enhances the uptake of glucose by liver cells and, as a result, helps to relieve hypoglycemia in diabetics.

Jang *et al.* (2014) studied at the anti-inflammatory properties of an ethanolic *P. guajava* (guava) leaf extract both *in vitro* and *in vivo*. Our findings showed that, in a dose-dependent way, guava leaf extract (GLE) effectively reduced the synthesis of prostaglandin E2 and nitric oxide that was produced by lipopolysaccharide (LPS). In part, GLE inhibited cyclooxygenase-2 and inducible nitric oxide synthase production and activity via downregulating ERK1/2 activation in RAW264.7 macrophages. Additionally, in two distinct animal models—the rat's Freund's full adjuvant-induced hyperalgesia and the mouse's LPS-induced endotoxic shock—GLE demonstrated strong anti-inflammatory action.

Kawakami *et al.* (2009) examined that prostaglandins, which are implicated in inflammation and cancer, requires the enzyme prostaglandin endoperoxide H synthase (PGHS). The effects of guava leaf extract, which is well-known for its health advantages, on PGHS were examined. It was discovered to suppress the enzyme's ability to produce specific chemicals. One important ingredient, quercetin, also exhibited inhibitory actions. In colon cancer cells, overexpression of PGHS led to an increase in DNA synthesis; however, normal levels were restored by guava extract. This shows that PGHS inhibition plays a role in the extract's antiproliferative effects.

***Moringa Leaves :***

Moyo *et al.* (2011) reported moringa leaf nutritional value using the Van Soest and Proximate techniques. The dried leaves contained 19 amino acids and (30.3%) crude protein. The mineral concentrations of the dried leaves were as follows: (3.65%) of calcium, (0.3%) of phosphorus, (0.5%) of magnesium, (1.5%) of potassium, (0.164%) of sodium, (0.63%) of sulfur, 13.03 mg/kg of zinc, 8.25 per cent of copper, 86.8 mg/kg of manganese, 490 mg/kg of iron and 363 mg/kg of selenium. Out of the 17 fatty acids, α-linolenic acid (44.57%) had the highest value, followed by g-linolenic (0.20%), palmiteic (0.17%), heneicosanoic (14.41%) and capric acid (0.07%). In the

dried leaves, vitamin E was found in the maximum concentration at 77 mg/100 g, compared to 18.5 mg/100 g of beta-carotene. The composition of the fiber was as follows: (11.4%) for neutral detergent fiber, (8.49%) for acid detergent fiber, (1.8%) for acid detergent lignin and (4.01%) for acid detergent cellulose.

Abalaka *et al.* (2012) using Agar Diffusion Methods, the antibacterial activity of leaf extracts from the *Moringa oleifera* Lam family of plants was ascertained. The plant's active ingredients were extracted using two solvents: chloroform and water. *Escherichia coli*, *Salmonella Typhi* and *Pseudomonas aeruginosa* all showed remarkable growth inhibition activity against the crude chloroform extract, with respective diameter zones of inhibition (DZI) of 30±0.01, 26±0.03 and 20±0.04. *P. aeruginosa* was resistant at all test concentrations, however the aqueous extract of this plant's leaf shown activity against *E. Coli* and *S. Typhi*, displaying diameter zones of inhibition of 20±0.03 and 18±0.01, respectively. range of the minimum bactericidal concentration is 20–40 mg/ml and the range of the minimum inhibitory concentration (MIC) is 10–20 mg/ml. Alkaloids, flavonoids, saponins and tannins were among the secondary metabolites found in the samples after phytochemical screening. *M. oleifera* may be a useful medicine for the treatment of infections brought on by the test organisms if properly investigated into and improved with the determination of its toxicity.

Fokwen *et al.* (2018) proposed study was to determine how the color variation of *Moringa oleifera* leaves affected their nutritional content, phytochemical makeup and antioxidant capacity. Fresh moringa leaves, both green and yellow, were dried for 48 hours at 45 °C in an oven before being mixed. Each plant material's powder was separated into two sections: one was used to measure the material's proximate composition and mineral content and the other to measure the amount of phenolic content and antioxidant activity. The findings demonstrated that the proximate composition, phenolic content, metal chelation activity and ferric reducing antioxidant capacity of *Moringa oleifera* leaves remain unaffected by their color change. The iron content and radical scavenging activity of the leaves increase (from 61.41 to 96.68%) when they turn from green to yellow. It does, however, considerably lower the leaves' contents of potassium (3144 to 131.20%), sodium (141.70 to 15.90%), calcium (2346.80 to 1576%) and magnesium (657.50 to 471.40%). When compared to yellow leaves, green *Moringa oleifera* leaves have a higher nutritional value (mineral element).

Peixoto *et al.* (2011) assessed how well gram-positive and gram-negative bacteria are inhibited by aqueous and ethanolic moringa leaf extracts (*Moringa oleifera*). 100, 200, 300 and 400L of extract were soaked into paper disks at 20 g/180 mL and 10 g/190 mL.*Escherichia coli* (ATCC25922), *Staphylococcus aureus* (ATCC25923), *Vibrio parahaemolyticus*, *Enterococcus faecalis* (ATCC29212), *Pseudomonas aeruginosa* (ATCC27853), *Salmonella enteritidis* (IH) and *Aeromonas caviae* were the microorganisms against which all extracts were tested. To conduct the susceptibility experiments, the modified disk diffusion method was employed. All of the therapies failed to affect the strains of *S. enteritidis* (IH), *P. aeruginosa* and *E. coli*. Disks containing 400 L of extract were often the most effective against *A. caviae*, *V. parahaemolyticus*, *S. aureus* and *E. faecalis*.According to the study, aqueous and ethanolic moringa leaf extracts show promise as a complementary treatment for infections brought on by the strains that were studied.

Leone *et al.* (2015) reported that numerous studies conducted in vitro assessed the anticancer effects of water and alcohol extracts of *Moringa oleifera* leaves on various tumor cell lines. A study also discovered that the KB human tumor (KB) cell line's ability to proliferate was inhibited in a dose-dependent manner by the aqueous extract of *Moringa oleifera* leaves. DNA fragmentation, morphological alterations and the activation of apoptosis were also linked to this antiproliferative effect.

***Mango Leaves :***

Reddeman *et al.* (2019) examined mango leaf extract (*Mangifera indica*), which contains (60%) mangiferin (MLE), was the subject of a series of toxicological investigations that complied with OECD and GLP regulations. A bacterial reverse mutation assay revealed no genotoxic evidence (Ames). An in vitro test for chromosomal aberration revealed signs of clumpogenic activity, while an in vivo test using a mammalian micronucleus revealed no results up to the maximum dosage (2000 mg/kg bw). Rats were used in a 90-day repeated dose oral toxicity trial at dosages of 0, 500, 1000 and 2000 mg/kg bw/day (vehicle control). The maximum dose examined, 2000 mg/kg bw/day, was shown to be the NOAEL for MLE in Han:Wist male and

female rats, based on the absence of toxic effects or death over the 90-day trial.

Infante-Garcia *et al.* (2017) found that natural polyphenols, specifically *Mangifera indica* Linn extract (MGF), had antidiabetic, antioxidant and anti-inflammatory properties. After long-term MGF treatment of db/db mice, the role of MGF in central problems associated with T2D was examined. In db/db mice treated with MGF for 22 weeks, metabolic parameters (body weight, glucose and insulin levels) as well as central consequences such as brain shrinkage, inflammatory processes, spontaneous bleeding, tau phosphorylation and cognitive performance were measured. MGF prevents obese db/db mice from gaining too much weight. MGF-treated rats exhibited longer-term maintenance of insulin and C-peptide levels, which are indicative of pancreatic function. By reducing the number of microglia in the cortex and the hippocampus, MGF was able to diminish central inflammation. Similarly, in db/db mice, there was a considerable decrease in central spontaneous bleeding. Following MGF treatment, db/db animals showed a reduction in cortical and hippocampal shrinkage as well as a decrease in tau hyperphosphorylation, leading to a partial recovery of learning and memory deficits.

Severi *et al.* (2009) The purpose of this study was to ascertain whether a *Mangiferai ndica* leaf decoction (AD) had any gastroprotective effects on several mouse experimental models. When administered to treated animals up to a dose of 5 g/kg (p.o.), AD considerably reduced the severity of stomach injury generated by different gastroprotective models without causing any toxic signs or symptoms. When mice and rats with gastric lesions caused by HCl/ethanol, absolute ethanol, non-steroidal anti-inflammatory drugs (NSAIDs), or stress-induced gastric lesions were given oral pre-treatment with AD (250, 500, or 1000 mg/kg), the lesions significantly decreased. Bioactive phenolic components were found in AD composition phytochemical studies, accounting for (57.3%) of the extract's total phenolic content. Two primary phenolic compounds were identified, namely C-glucosyl-benzophenone (3-C-β-D-glucopyranosyl-4',2,4,6-tetrahydroxybenzophenone) and mangiferin (C-glucopyranoside of 1,3,6,7-tetrahydroxyxanthone). These results suggest that the aqueous infusion made from the leaves of *M. indica* may have gastroprotective qualities.

Kanwal *et al.* (2009) isolated Five flavonoids, *viz.,* (–)-epicatechin-3-O-β-glucopyranoside (1), 5-hydroxy-3-(4-hydroxylphenyl)pyrano[3,2-g]chromene-4(8H)-one (2), 6-(p-hydroxybenzyl)taxifolin-7-O-β-D-glucoside (tricuspid) (3), quercetin-3-O-α-glucopyranosyl-(1'!2)-β-glucopyranoside (4) and (–)-epicatechin(2-(3,4-dihydroxyphenyl)-3,4-dihydro-2H-chromene-3,5,7-triol) (5), from the leaves of mango (*Mangifera indica* L.). Different quantities of these flavonoids (100, 300, 500, 700, 900 and 1000 ppm) were tested for their antibacterial activity against four different bacterial species: *Bacillus sp.*, *Escherichia coli*, *Lactobacillus sp.* and *Azospirillium lipoferum*. The growth of all five tested bacterial species was considerably inhibited by all tested doses of flavonoids. There were, nevertheless, clear variations in the flavonoids' antimicrobial activity. Compound 1 showed the least amount of antibacterial activity, which led to a (7–75%) decrease in the various bacterial species' development. Compound 5 had the strongest antibacterial efficacy, with bacterial growth being reduced by (45–99.9%) at varied doses. *Bacillus species* and *A. lipoferum* had the greatest vulnerability to this chemical. Additionally, compounds 2-4 showed strong antibacterial activity. The amount of these substances that inhibited bacterial growth varied from (52%) to (96%). Based on the current investigation, compound 5 has been found to be the most efficacious flavonoid against *A. lipoferum* and *Bacillus sp.*

Islam *et al.* (2010) carried this study to examine the analgesic, anti-inflammatory, antibacterial and antifungal effects of *Mangifera indica* ethanol leaf extract. Swiss albino mice and Wistar albino rats were employed as models for the acetic acid-induced writhing response and the carrageenan-induced paw edema, respectively, to assess the analgesic and anti-inflammatory qualities. The effects of the leaf extract were compared with those of Diclofenac Sodium, a widely available analgesic and anti-inflammatory medication, in both cases. Oral administration of the ethanol leaves extract considerably ($P<0.01$) decreased the writhing reaction in the analgesic bioassay. Comparing the degree of inhibition of the leaf extract to that of the common analgesic medicine was (55.8%), while for Diclofenac sodium, was 75.28 per cent.However, despite the fact that leaf extract reduces paw edema, no discernible difference was seen. The antibacterial and antifungal properties of the leaf extract were also evaluated using the poisoned food and disc diffusion techniques. The leaf extract demonstrated a zone diameter ranging from 7.0 mm to 11.5 mm in the antibacterial assay, inhibition against two Gram negative bacteria (*Shigella flexneri* and *Shigella sonei*) and six

Gram positive bacteria (*Staphylococcus aureus*, *Streptococcus agalactiae*, *Bacillus cereus*, *Bacillus megaterium*, *Bacillus subtilis* and *Lactobacillus vulgaricus*). However, *Proteus sp*. and *Salmonella typhi* exhibited adverse effects on leaf extract. Three different fungus species (*Aspergillus ustus*, *Aspergillus niger* and *Aspergillus ochraceus*) were targets of the antifungal activity of *Mangifera indica* leaf extract.

***Papaya Leaves :***

Ugo *et al.* (2019) study's results showed that the following were present: protein (6.50%), fat (2.01%), ash (2.18%), moisture (57.01%), crude fiber (3.10%) and carbohydrates (29.20%). Vitamins B1 (199.31 mg/100g), B2 (295.63 mg/100g), C (68.59 mg/100g), beta carotene (303.55 mg/100g) and E (39.78 mg/100g). Minerals: calcium (1086.53 mg/100g), potassium (80.13 mg/100g), sodium (30.42 mg/100g) and phosphorus (1971.17 mg/100g) (1086.53 mg/100g). Flavonoids: 899.53 mg/100g, alkaloids: 1569.13 mg/100g, saponins: 898.07 mg/100g and tannins: 310.50 mg/100g are the phytochemicals. According to this study, *Carica papaya* extracts are an excellent supply of proximate composition and a rich source of vitamins, minerals and phytochemicals.

Owoyele *et al.* (2008) examined rats to test the anti-inflammatory properties of an ethanolic extract of *Carica papaya* leaves utilizing models of formaldehyde-induced arthritis, cotton pellet granuloma and paw oedema caused by carrageenan. The reference group was given indomethacin at a dose of 5 mg/kg, whereas the experimental animals were given extracts or saline (control group) at a dose of 25–200 mg/kg orally. Investigations were also conducted into the extract's ulcerogenic potential. The carrageenan test findings indicate that the extracts considerably ($p < 0.05$) decreased paw oedema. Similarly, the extract led to a noteworthy decrease in the quantity of granuloma formation, which decreased from 0.58 ±0.07 to 0.22 ±0.03 g. From the fourth to the tenth day of the study, the extracts dramatically decreased the persistent oedema in the formaldehyde arthritis model. At high doses, the extracts also caused a minor irritability of the mucosa. The research validates the anti-inflammatory properties of papaya leaves from Carica.

Otsuki *et al.* (2010) investigated how aqueously extracted *Carica papaya* leaf fraction affects the development of different tumor cell lines as well as the ability of human lymphocytes to combat cancer. Significant growth inhibition of tumor cell lines was observed by the CP extract. CP extract reduced the production of IL-2 and IL-4 in PBMC, but it did not impede growth in the production of IL-12p40, IL-12p70, IFN-, or TNF-. Activated human peripheral blood mononuclear cells PBMC's cytotoxicity against K562 cells was increased by CP extract. 23 immunomodulatory genes, including CCL2, CCL7, CCL8 and SERPINB2, were found to be upregulated by microarray analysis, indicating their potential use as index markers for the immunomodulatory effects of CP extract. Molecular weights less than 1000 in the active ingredients of the CP extract enhanced anti-tumor actions and prevented the development of tumor cells. CP leaf extract has the potential to be used as an immunoadjuvant for vaccination therapy as well as a treatment and preventive measure for a number of human diseases, including cancer and several allergy disorders.

Juárez-Rojop *et al.* (2012) reported that in diabetic rats, the *Carica papaya* aqueous extract (0.75 g and 1.5 g/100 mL) effectively lowered blood glucose levels ($p<0.05$). Additionally, it lowered blood levels of aminotransferases, triacylglycerol and cholesterol. After therapy, low plasma insulin levels in diabetic rats did not alter, but in non-diabetic rats, they climbed dramatically. In non-diabetic treated animals, pancreatic islet cells were normal; however, in diabetic treated rats, *C. papaya* could aid in islet regeneration, which showed up as the preservation of cell size. In the livers of diabetic rats, *C. papaya* inhibited hepatocyte disruption and glycogen and lipid buildup. Lastly, it was shown that *C. papaya* extract had an antioxidant impact on diabetic rats.

Nirosha and Mangalanayaki (2013) opined that Papaya leaves extract could possess antibacterial effect. Three different types of solvents, including ethanol and ethylacetate, were used in the maceration procedure to extract papaya leaves. By using the diffusion method, papaya leaf and stem extracts were evaluated against a variety of Gram positive and Gramnegative bacteria, including *Salmonella typhi*, *Bacillus cereus*, *Streptococcus pneumonia*, *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeroginosa*. When compared to Gram positive bacteria, the extract showed greater activity against all Gram negative bacteria tested; *Salmonella typhi* showed the highest activity (16 mm zone of inhibition). An increase in temperature increased the extracts' activity, whereas an alkaline pH reduced it. The extracts' Minimum Inhibitory Concentration (MIC)

varied from 50 to 200 mg/ml. Alkaloids, tannins, saponins and phenols were identified in the extracts based on preliminary phytochemical tests. Typhoid fever, otitis media, uretritis, gastroenteritis and wound infections can all be treated with carica papaya.

Hasimun and Ernasari (2014) suggested the analgesic properties of *Carica papaya* leaves (CPL) extracts (n-hexane, ethyl acetate and ethanol), using an acetic acid-induced pain model in mice (Siegmund technique). Eleven groups of experimental animals were assigned and they were given 50 mg/kg bw of aspirin along with n-hexane, ethanol and acetate extracts at concentrations of 0.175, 0.35 and 0.70 mg/kg bw orally; the control group was given (0.5%) CMC-Na. The findings demonstrated that, in comparison to the control group, all extracts at dosages of 0.175, 0.35 and 0.70 mg/kg bw exhibited considerable analgesic effect ($p<0.05$). At a dose of 0.70 mg/kg bw, the ethanol extract of CPL had the highest analgesic action, matching aspirin in effectiveness.

Aruljothi (2014) studied the antibacterial properties using the agar well diffusion method of the extract were investigated against microorganisms that cause wound infections, including *Escherichia coli*, *Staphylococcus aureus*, *Proteus vulgaris*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. The leaf extracts containing acetone had a strong antibacterial impact on gram-negative bacteria, particularly *Pseudomonas sp*. According to the study, papaya leaves may include potent antibacterial substances that prevent the growth of microorganisms that cause wound infections in vitro. The outcomes amply demonstrated the value of using papaya leaf extracts topically to treat wound infections, as has long been the custom.

***Neem Leaves :***

Khillare and Shrivastav (2003) determined the optimal concentration of aqueous extract from tender, old *Azadirachta indica* (neem) leaves in order to instantly immobilize and destroy all human spermatozoa. The spermicidal activity of neem leaf extract was investigated using the Sander–Cramer test. For both old and tender leaf extracts, the minimum effective spermicidal concentrations under test circumstances were 2.75 ± 0.754 mg/million sperm and 2.91 ± 0.669 mg/million sperm, respectively. Researchers also looked at how extracts affected the morphology and viability of sperm, finding no changes in the morphology of the head, midpiece, or tail and no evidence of viable sperm. The leaf extracts were discovered to have a carbohydrate and water-soluble character. Additionally, the impact of varying extract concentrations (old and tender) on the sperm motility was investigated. The percentage motility decreases linearly with concentration and reaches zero in 20 s at a dose of 3 mg.

Mahmoud *et al.* (2011) determined how neem leaf extracts, in vitro, affected the growth of several human pathogens, including *Aspergillus flavus*, *Aspergillus fumigatus*, *Aspergillus niger*, *Aspergillus terreus*, *Candida albicans* and *Microsporum gypseum*. The test pathogens' ability to proliferate was decreased at several concentrations (5, 10, 15 and 20%) made from these extracts and the effect grew with concentration. When compared to the activity achieved by the other extracts at the same concentration, the (20%) ethyl acetate extract exhibited the highest inhibition. A primary component (nimonol) was identified by High Performance Liquid Chromatography (HPLC) examination of the ethyl acetate extract. This component was purified and chemical confirmation was obtained using Nuclear Magnetic Resonance (NMR) spectroscopy study. After filtering out the nimonol, the (20%) ethyl acetate extract lost some of its antifungal activity and the amount of this activity loss varied depending on the pathogens under study. When tested against all six fungal infections, the pure nimonol as a stand-alone chemical exhibited negligible antifungal action.

Dholi *et al.* (2011) explained *Azadirachta indica*'s pharmacological hypoglycemic effect in rats with diabetes. Following a 24-hour treatment period, a single dose research using 250 mg/kg of *Azadirachta indica* showed reductions in glucose (18%), cholesterol (15%), triglycerides (32%), urea (13%), creatinine (23%) and lipids (15%). Moreover, a 15-day research with multiple doses decreased glucose, triglycerides, urea, lipids and creatinine. In a test of their glucose tolerance, diabetic rats treated with 250 mg/kg of neem extract showed much lower glucose levels than the control group. At day 15, diabetic rats treated with *Azadirachta indica* also showed significant reductions in glucose levels. *Azadirachta indica* is a viable substitute for traditional methods in the treatment of diabetes mellitus. It lowers elevated blood sugar levels in diabetes patients, which should be investigated further with oral hypoglycemic medication.

Hla *et al*. (2011) assessed using the DPPH free radical scavenging assay, the antioxidant activity of the watery extract and (95%) ethanol extract from the dried Neem leaves. The watery Neem leaf extract has stronger antioxidant activity than the (95%) ethanol extract, as evidenced by the (50%) oxidative inhibitory concentrations (IC50) of the two extracts being 0.26 and 3.99 µg/ml, respectively. Neem leaves have antioxidant properties, which make them a potential antioxidant agent for the treatment of oxidative stress-related illnesses like diabetes, cancer, tumors, aging and inflammation, among others.

Udeinya *et al.* (2008) concluded the efficacy of a crude neem leaf extract (IRAB) in vitro against the sexual (gametocytes) and asexual (trophozoites/schizonts) forms of the malarial parasite *Plasmodium falciparum*. Asexual parasites and mature gametocytes treated with IRAB (0.5 µg/mL) in separate 72-hour cultures showed parasite counts that were less than (50%) of those in control cultures, which had parasitemia levels of (8.0%) and (8.5%), respectively. A sexual parasites and mature and immature gametocytes were decreased to (0.1%), (0.2%) and (0%) parasitemia, respectively, in cultures containing 2.5 µg/mL. The cultures with 5.0 ìg/mL did not contain any parasites.

**Conclusion :**

In conclusion, guava leaves, mango leaves, papaya leaves, neem leaves, and moringa leaves all exhibit remarkable pharmacological properties, contributing to their traditional and modern medicinal uses. However, among these, guava leaves stand out as particularly superior due to their rich reservoir of bioactive compounds and versatile therapeutic benefits.

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