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A REVIEW ON PHARMACOGNOSY, PHYTOCHEMISTRY AND PHARMACOLOGICAL ACTIVITY OF *CARICA PAPAYA* (LINN.) LEAF

Apurva Priyadarshi * and Bhuwal Ram

Department of Dravyagyuna, Institute of Medical Sciences, Banaras Hindu University Campus, Varanasi - 221005, Uttar Pradesh, India.

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Correspondence to Author:
Apurva Priyadarshi

PhD. Scholar,
Department of Dravyagyuna,
Institute of Medical Sciences,
Banaras Hindu University Campus,
Varanasi - 221005, Uttar Pradesh,
India.

E-mail: apurvayurved@gmail.com

ABSTRACT: Papaya (*Carica papaya* Linn.) is well known for its nutritional as well as medicinal value since long time. The medicinal properties of fruit and other parts of papaya are well known in the different system of traditional medicine including Ayurveda. Its various parts has been reported for various disease conditions *viz*. fever, swellings, jaundice, gonorrhea, bilious fever, itches, eczema, and rheumatism cold, headache, whooping cough, asthma, chicken pox, and bronchitis in various traditional literature. The various remarkable researches on biological activities and medicinal application have been reported during past four decades and established it as an important nutraceuticals agent. *Carica papaya* Linn. leaf has been scientifically studied for various therapeutic activities like antibacterial, antioxidant, antipyretic, insecticidal, antimicrobial, anti-molluscal *etc*. In view of this leaves have been explored through several advanced techniques like phyto-extraction of heavy metals, phytoremediation of particulate pollution and many others. Various studies on phytoconstituents and chemical composition of leaves have been reported in last few decades. The present review aims an exploration of pharmacognostical, phytochemical and pharmacological studies of *Carica papaya* Linn. leaf till now.

INTRODUCTION: *Carica papaya* Linn. is such a marvelous plant, possesses various medicinal properties making it unique among other 22 species of family Caricaceae. It is believed to be originated in the tropics of the Americas, perhaps in southern Mexico and neighbouring Central America. It is polygamous specie and can be specified only at the time of flowering. It exhibits varying degrees of sex reversal [1]. The various parts of this plant are used for curing different ailments.

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Leaves are the most useful part among all used parts for the medicinal purpose. Fomenting breast with hot papaya leaves increases breast milk. Infusion of the fresh leaves is gargled to cure tonsillitis, ulcerative stomatitis, and gingivitis.

Applying the lotion of the leaves stops bleeding and shrinks the haemorrhoids [2]. The tender leaves are used as spinach. Leaves are smoked and inhaled in place of tobacco for the relief in asthma. These are believed to be cardiotonic and also promote sweating hence used in fever also. A fine paste of young leaves (5 - 6 g) is taken internally in severe cases of jaundice. The infusion of tender leaves is used for various urinary complaints and gonorrhoea [3]. The fresh leaves are used for dressing foul wounds as a poultice for sores *etc*. Dried leaves infusion induces purgation and abortion.

In addition to that lots of activities on leaves are reported with scientific data recently. It normalizes the pulse rate in fever and acts as diuretic when administered as decoction [4]. It is attributed to exterminate cough and respiratory, liver and spleen related diseases as well as useful in loss of appetite and oedema [5]. Leaves of *Carica papaya* L. are used in severe jaundice [6] (Reddy, 1986; Raja reddy, 1988), to expel guinea worm [7] (Raj and patel 1978), as a poultice [8] (Banerjee and Banerjee, 1986); in fracture healing [9] (Pal and Srivastava 1976), constipation and indigestion [10] (Megoneitso and Rao, 1983). It has been used to treat oral candidosis, malaria, dengue, yellow fever [11] and as a diuretic in dengue related anaemic [12, 13, 14, 15].

Various Ayurvedic texts quote *Carica papaya* L. with different synonyms *viz*. Eraṇḍachirbhit [16, 17]. Vṛkṣacirbhiṭa, Nalikādal [17], Gopālakarkaṭi [4], Viṣapatra [5], Nālaparṇi, Kāśakarkaṭi, Kṣīrasravā, Śuklapuṣpi, and Eraṇḍapatrikā [5] and Eraṇḍakarkaṭi. The fruits are specifically termed as kumbhaphalā and madhukarkaṭi [17]. It is aphrodisiac, tonic and pacifies the tridosh (three basic components of body *i.e.* Vāta, Pitta and Kapha) [18]. These synonyms have been prearranged in order to denote different aspects of this plant. Apart from various differences somewhat external morphological appearances of plant and its parts resemble with *Ricinus communis* Linn. (Eraṇḍa), *Cucumis momordica* Roxb. (Cirbhiṭa) and *Luffa species* (karkaṭi) which seems to be the foremost base of the synonyms ascribed for *Carica papaya* L. *i.e.* Eraṇḍachirbhit [17] Vṛkṣacirbhiṭa [17], Gopālakarkaṭi [4], Kāśakarkaṭi, and Eraṇḍapatrikā [5] and Eraṇḍa-karkaṭi. The synonym Viṣapatra [5], has been given to it due to some poisonous material containing leaves (seems to explaining pharmacological quality) whereas the synonym Nalikādal and Nālaparṇi attributed to it due to long and hollow petioled (Nāla) leaves (Parṇi or Dal). On the basis of its milky exudation it is said Kṣīrasravā and has been termed as Śuklapuṣpi because of its white colored flowers.

Pharmacognostical Studies: The papaya is a small, usually a single stemmed tree with sparsely branching. It grows from 15 - 30 ft tall having leaves spirally arranged and confined to the top. The lower trunk contains conspicuous scars of leaves and fruits.

The leaves are deeply palmately lobed with seven lobes, large, 50 - 70 cm (20 - 28 in) in diameter. The trees are dioecious containing latex in all parts. The flowers are highly dimorphic having 5 parts and, the stamens fuse to the petals of male flowers. A superior ovary and five contorted petals remain present in female flowers. Male and female flowers remain in the leaf axils. The sweet-scented flowers remain open at night. It bears a large berry-like fruit with 10 - 30 cm diameter and 15 - 40 cm long.

The analysis and documentation of *Carica papaya* Linn. leaves have been done for the development of quality standards. The microscopic study reveals the presence of epidermis, collenchymas and parenchyma, sclerenchyma, xylem, phloem, and pith was found to be absent. Successive extractive value has been found highest in petroleum ether extract 20.44%. Moisture content found to be 7.77% whereas mean ash values were 16.72% (total), 3.25% (acid insoluble ash) and 6.05% (water-soluble ash) [19]. Abundance of spheraphides and rhomboidal calcium oxalate crystals and starch grains are reported in leaf powder. No trichomes found whereas the stomatal index was found to be 31.56 ± 3.41, vein termination number 3-4 and palisade ratio as 12.65 ± 1.57.14 [20].

Phytochemical Studies: The popularity of herbs in traditional medicine has been linked to their higher likelihood of containing pharmacologically active compounds compared to woody plant forms [21, 22]. Studies report that leaves are the most widely used parts of plant [23]. The leaves of *Carica papaya* L. contain the alkaloid carpaine [24], pseudocarpaine[25] and dehydrocarpaine I & II [26]. The alkaloid Carpaine (first isolated by Greshoff in 1890), has been found to possess antitumor activity *in-vitro* against mouse lymphoid leukemia L1210, lymphocytic leukemia P388 and Ehrlich ascites tumor cells. It also shows anti tubercular activity against *Mycobacterium tuberculosis* H37 Rv. It is a heart poison and lowers the pulse frequency and depresses the CNS. It is reported to be a potent amoebicide [3].

Pseudocarpaine is isomeric with carpaine only difference is in the configuration at the alcoholic carbon atom. It differs from carpaine in melting point and rotation [25].

Presence of choline and carposide, anthraquinone, vitamin C and vitamin E are also reported. These molecules have a wide range of biological activities. Leaves of plants have been reported to accumulate insulin, tannins and other alkaloids which may be responsible for their medicinal properties [25].

Seven flavonoids including quercetin 3-(2G-rhamnosyl-rutinoside), kaempferol 3-(2G-rhamnosyl-rutinoside), quercetin 3-rutinoside, myricetin 3-rhamnoside, kaempferol 3-rutinoside, quercetin, and kaempferol have also been reported and has been assessed for their antioxidant activities [27]. The flavonols and alkaloidal fractions are reported by HPLC-based activity profiling. Among flavonol type four were found as – manghaslin, clitorin, rutin, and nicotiflorin and the alkaloid fraction constituted five compounds which were isolated as piperidine alkaloids [28].

The extractive yields of leaf tissue remains less than that of other plant parts *i.e.* ripe and unripe fruits [29]. The chemical analysis of leaves of *Carica papaya* L. growing in the semi-arid zone has also been done through the most reliable and accurate as well as non-destructive and consistent method for analysis for major and traces elements *i.e.* EDXRF. The leaves were subjected to Energy Dispersive X-ray Fluorescence (EDXRF) and then analyzed for different mineral composition. The higher amount of that oxygen 87%, calcium (4.47%), magnesium (3.37%) potassium (1.49%) was found, compared to that of other elements. Some other elements like silicon, (0.805%) aluminum, phosphorus, chloride, sulphur, stannous, strontium, also found but in less amount. The element like chromium (0.0129%) has also been quantified in it, whereas heavy metals like zinc (0.0039%), manganese (0.0031%), copper (0.0017%) and rubidium (0.0015%) were also noted to be present in the leaves of *C. papaya*. Vanadium, Titanium, Cobalt, and Tantalum remain absent in it [30].

Pharmacological Studies:

1. Antithrombocytopaenic Activities: Carpaine is reported to exhibit potent activity in sustaining platelet counts up to $555.50 \pm 85.17 \times 10^9$/L on busulfan induced thrombocytopenic Wistar rats exhibiting no acute toxicity [31]. In order to determine the platelet count increasing potency *Carica papaya* L. leaf extract a study was carried (Singhal Abida *et al*., 2013) in a murine model. Results were very significant as increased platelet and RBC count in the test group compared to that of controls was observed. Starting from day 3 ($3.4 \pm 0.18 \times 10^5$/mil) the platelet count increased to almost fourfold higher at day 21 (11.3×10^5/mil) in test group which was almost more than double in comparison to control. The RBC also increased significantly. Hence, through this study, the conclusion was made to appreciate the recommendation of *Carica papaya* L. leaf extract to boost thrombopoiesis and erythropoiesis in humans and animals where these cell lineages have been compromised [32].

Regarding the role of *Carica papaya* L. leaves in a patient suffering from dengue fever, a case study has also been discussed (Nisaar *et al*., 2011). The 45-year-old patient suffering from dengue fever was administered with 25 ml aqueous extract of *Carica papaya* L. leaf twice a day for 5 consecutive days. Pre and post-treatment blood samples were analyzed for platelet count, WBC, and neutrophils. PLT count increased from 55×10^3 µl to 168×10^3 µl. Hence threefold increase in PLT, twofold in WBC and 70% increase in neutrophils were observed. So it was concluded from patients feeling and blood reports that *Carica papaya* L. leaves aqueous extract exhibit potential activity against dengue fever [33].

2. Analgetic Activity: The three extracts of leaves of *Carica papaya* L. have been evaluated for their analgesic activity in mice model having acetic acid-induced pain (Siegmund method).These three extracts (*n*-hexane, ethyl acetate, and ethanol extracts) exhibited significant analgesic activity at all the three dose levels (0.175, 0.35 and 0.70 mg/kg bw orally) when compared to aspirin (taken as the standard drug) [34].

3. Antiplasmodial Activity: Leaf extracts of *Carica papaya* L. exhibit high antiplasmodial activity with low cytotoxicity. This activity is shown by three alkaloids [7, 8, 9]. Compounds were tested for bioactivity *in-vitro* against four parasites (*Trypanosoma brucei rhodesiense*, *Trypanosoma cruzi*, *Leishmania donovani*, and *Plasmodium falciparum*), and in the Plasmodium berghei mouse model.

This study concludes that the antiplasmodial activity of papaya leaves was confirmed and might be linked to alkaloids. Among these alkaloids, carpaine was highly active and selective *in-vitro* [28].

4. Antitumor and Immunomodulatory Activity: A study has been completed to assess the antitumor and immunomodulatory activity of *Carica papaya* L. leaf aqueous extract. In this study, the effects of *Carica papaya* L. extract on the proliferative response of tumor cell lines were observed. Through [3H] thymidine incorporation the cytotoxic activities of human peripheral blood mononuclear cells (PBMC) was also assessed. Results were indicative of significant growth inhibitory activity of this extract on tumor cell lines. As far as PBMC concerned the leaf extract reduced the production of IL-2 and IL-4.

The expression of 23 immunomodulatory genes was enhanced by this extract. Index markers of immunomodulatory effects were also found. Conclusively this study revealed that the *Carica papaya* L. leaf extract may mediate a Th-1 type shift in the human immune system. The extract may potentially provide a link for treatment of carcinoma, allergic disorders and serve as immuno-modulator in human [35]. The antiproliferative response of *Carica papaya* L. leaf juice has been assessed on a range of cell lines representing benign hyperplasia, tumorigenic and normal cells of prostate origin. A time course analysis of before and after *in-vitro* digestion and of the molecular weight based fraction of leaf juice showed significant antiproliferative response.

The cytotoxic effect of medium polarity fraction of leaf juice (0.03-0.003 mg/mL) was seen on all prostate cells excepting of the normal cells. The medium polar fraction has also been found to inhibit migration and adhesion of metastatic PC-3 cells. The S phase cell cycle arrest and apoptosis were thought to be a possible mechanism for these activities on the basis of flow cytometric study.

Hence this study reports about the antiproliferative and antimetastatic properties of *Carica papaya* L. leaf extract against prostatic diseases including PCa [36]. Proliferative Activity of Saponin-Reducing *Carica papaya* L. leaves extracts on human lung fibroblast cell (IMR90) has also been studied [37].

5. Antidiabetic Activity: A study regarding the assessment of antidiabetic activity of *Carica papaya* L. leaf extract was carried out in an experimental rat model. The chloroform extract which consist steroid and quinines was administered at various dose levels in streptozotocin-induced diabetic and non-diabetic rats. After 20 days of treatment, the sacrifice was done and the biochemical study was carried out. There was a significant reduction in serum glucose, trans-aminases and triglyceride observed in diabetic rats after the administration of *Carica papaya* L. leaf chloroform extract. This study concludes the potential activity of *C. papaya* leaf to treat the symptoms of diabetic patients [38].

6. Antimicrobial activity: In order to investigate the antimicrobial activity of different extracts of leaves of *Carica papaya* L. (Baskaran *et al*., 2012), it was observed that the ethanol, methanol, ethyl acetate, acetone, chloroform, petroleum ether, hexane and aqueous extract showed activity against bacteria and fungus. Among these extracts, the chloroform extract was found more active against *Micrococcus luteus* bacteria whereas acetone extract was more active against *Candida albicans* fungus.

Hence it was concluded that extracts of *Carica papaya* L. leaves possess antibacterial and antifungal activity against several human pathogenic bacterias and fungi [39]. The 20% aqueous and alcoholic extracts of leaf was screened for antibacterial activity against *Staphylococcus aureas* and *Escherischia coli* (George *et al*., 1947) [40]. Carpine isolated from plant exhibited slight inhibitory activity against *M. tuberculosis* H37Rv (Ramaswamy and Sirsi, 1960, 1967) [41, 42]. The leaf extract inhibited the growth of ring worm causing fungi, *Epidermophyton floccosum* (52.37%), *Trichophyton mentagrophytes* (24.3%) and *Microsporum gypseum* (20.32%) (Mishra *et al*., 1991) [43].

The aqueous extract of leaves showed 30 and 40 percent mycelia inhibition of *Aspergillus flavns* and A versicolor respectively (Dubey *et al*., 1982) [44] and mycelia inhibition of skin disease causing fungi *Trichophyton rubrum* and *Epidermophyton floccosum* (Kishore and Dubey, 1988) [45].

The aqueous leaf extract in another study showed growth and spore production of three fungal pathogens of rice, *Pyricularia oryzae*, *Drechslera oruzae* and *Corticium sasakii* (Tewari and Dath, 1984) [46]. The three phytopathogenic fungi: *Colletotrichum gloeosporioides*, *R. stolonifer* and *Fusarium spp.* were subjected for assessment of the antifungal activity of *Carica papaya* L. leaf and seed extracts (Seed ripe extract, Seed unripe extract). Among them, the broadest action spectrum was exhibited by the leaf extract. The MIC 50 (minimum inhibitory concentration 50) for the leaf extract was found to be >10 mg ml^{-1} for *C. gloeosporioides* and 0.625 mg ml^{-1} for *Fusarium spp.*

Approximately 20% mycelial growth inhibition was observed in both. Hence the ethanolic extracts from leaves of *Carica papaya* L. may be taken as a potential antifungal agent having the source of secondary metabolites [29]. The antifungal activity of aqueous extracts of leaves has also been found against *Colletotrichum gloeosporioides* [47]. The antimalarial activity of *Carica papaya* L. leaves extract has also been established through a study (kovendan *et al*., 2012). During this study, the activity of ethanol extract on blood stages of CQ sensitive and CQ resistant strains against *Plasmodium falciparum* (target species) was assessed.

The highest larval mortality was observed in first to fourth instars larvae and pupae were evaluated. The plant extract exhibited moderate to good antiparasitic effects. In four concentrations the extract showed promising inhibitory activity against the CQ sensitive strain and in CQ resistant to *P. falciparum*. The result concluded that the *Carica papaya* L. leaf ethanol extract has the potential to be used as an ideal eco-friendly approach for the control of vector mosquitoes [48].

Leaves are reported to support the growth and development of the larvae of the pest Diacrisia oblique (Deshmukh *et al*., 1979) [49]. An alcoholic extract of the leaves was found to inhibit the growth of *Neurospora crassa* whereas the extracts of leaves and fruits show antibacterial activity against several bacteria. The alcoholic extract of the leaves also possesses molluscicidal activity against *Bulinus globosus* [50].

7. Anthelmintic Activity: After performing epidemiological survey for relevance of guinea worm infection it was found to be 2.85% and more common in males. A paste of leaves of the plant with opium and common salt applied for 3 days was helpful in relief of symptoms and easy extraction of worms from the body (Sanghvi, 1989) [51, 52]. The leaf extract of papaya showed light mortality against meloidogyne incognito and *Rotylenchulus reniformis* nematodes (Mahemood *et al*., 1979) [53].

8. Central and Cardiovascular Effects: The alcoholic extract of leaves (10 mg/kg ip) showed dose dependent sedative effect in male rats. The extract (5 mg/kg ip) induced central muscle relaxation. The extract at dose of 50 mg/kg ip completely protected the rats against pentylene-tetrazol induced seizures, while 50 percent protection was observed with dose of 5 mg/kg ip. The extract at dose of 100 and 200 mg/kg ip showed 100% protection against maximum electroshock induced convulsions. The behavioral effects of extract were associated with an initial desynchronization of EEG and increased activity of EMG (Gupta *et al*., 1990) [54]. The leaf extract showed cholinestrage activity (Gupta and Gupta 1997) [55].

The major alkaloid found in leaves carpaine has been reported for cardiovascular effects using Wistar rats [56]. Increased dosage of carpaine showed progressive decrease in systolic, diastolic, and mean arterial blood pressure. Atropine sulfate (1 mg/kg) or propranolol hydrochloride (8 mg/kg) also did not change the circulatory response to carpaine. Carpaine in 2 mg/kg dosage is reported to reduce cardiac output, stroke volume, stroke work, and cardiac power, but has no effect on total peripheral resistance.So it can be said that carpaine affects the myocardium [57].

9. The Anti-inflammatory Activity: The ethanolic extract of *Carica papaya* L. leaves have been also investigated for its anti-inflammatory activity in rats using paw oedema (carrageenan test), formaldehyde induced arthritis models and cotton pellet granuloma. Experimental animals were treated with 25 - 200 mg/Kg (orally) of the extracts or saline (control group) and the reference group was given indomethacin 5 mg/Kg bw.

The ulcerogenic activity of the extract was also investigated. It was observed that there was a significant ($p<0.05$) reduction in paw oedema in the carrageenan test. A significant reduction in the amount of formation of granuloma (from 0.58 ± 0.07 to 0.22 ± 0.03 g.) was also observed. The extract exhibited a significant reduction in persistent oedema from the 4th day to the 10th day of the investigation was observed in formaldehyde arthritis model. Slight mucosal irritation has also been seen at high doses of extract. Conclusively the anti-inflammatory activity of *Carica papaya* L. leaves has been established [58].

10. Nephroprotective Activity: A study dealing with nephrotoxicity of Pb (II) and its amelioration through *Carica papaya* L. leaves powder has been done in experimental rats. In Pb(II) ions 1.000 mg/L i.p administered rats experimental rats the increased levels of serum biochemical parameters and oxidative stress including SGPT, SGOT, urea, creatinine, and malondialdehyde were seen. Whereas pre-treatment with papaya leaves powder reduced the levels of SGPT, SGOT, urea, creatinine, and malondialdehyde significantly, compared to Pb(II) treated group only. Pb(II) exposure induced severe necrosis of kidney cells and swelling of tubular cells whereas pre-treatment with *C. papaya* leaves powder reduced the damage effects. It has been concluded from this study that pre-treatment with *C. papaya* leaves powder antidote to serve preventive effects against Pb(II) induced nephrotoxicity in experimental rats [59].

11. Wound Healing Activity: The wound healing competence of *Carica papaya* L. leaves powder has been evaluated in an experimental study. Here the propylene glycol was taken as control check and the rate of wound closure; wound contraction, fibroblast cell count, and histology of granulation tissue were the assessment criteria. The insignificant wound contraction was noticed. But significant wound closure and fibroblast cell count were observed in *Carica papaya* L. leaves powder treated group. As a conclusive remark, this study provides a scientific background for leaves of *Carica papaya* L. having remarkable wound healing potential [60].

Due to platelet increasing property of the leaves of *Carica papaya* L., various supplements having it as a content are nowadays being marketed rapidly. On average reviews indicate that various manufacturing techniques used in several marketed *C. papaya* leaves formulations may degrade the phytochemical which will suppress the beneficial effects of this component. Hence the traditional method of its presentation should be made in practice but it also needs some more updations [61].

CONCLUSION: Herbal products are preferred as a symbol of safeguard in comparison to synthetic one which shows various untoward effects on health. The present literature review supports the broadness of activity present in the leaves of *Carica papaya*. The advanced phytochemical analysis entails us the presence of a variety of active molecules which may be responsible for its various biological activities. More research can be done to explore the unknown and unexplored potential of leaves of *Carica papaya* L. Further analysis of leaves of *Carica papaya* L. (active compounds) can be carried out by way of making use of different advanced investigative methods.

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REFERENCES:

1. Bedi R: Bedi vanaspati kosh. Kitabghar publication, New Delhi; First edition 2005; 1: 440-453.
2. Pullaiah T: Encyclopaedia of world medicinal plants. Regency publication, New Delhi 2006; 1: 446-449.
3. The wealth of India, raw materials Ca-Ci: CSIR, New Delhi 1992; 3: 290. ISBN-81-85038-97-X
4. Trikamji AY: Dravyagunavigyanam uttaraardha. Sharma ayurved mandir datiya (MP) 2001; 5: 212-213.
5. Bapalal VG: Nighantu Adarsh Chaukhambha bharati Academy, Varanasi, Reprint 2007; 1: 613-616.
6. Reddy RK: Folk medicines from Chittoor district, Andhra Pradesh, India, used in the treatment of Jaundice. International Journal of Crude Drug Research 1988; 26: 137-140.
7. Raj, KPS and Patel MR: Some medicinal plants of Cambay and its immediate vicinity and their uses in Indian indigenous system of medicine. Indian drugs 1978; 15: 145-152, 160.
8. Banerjee AK and Banerjee: A survey of medicinal plants in Shevaroy hills. J Econ Tax Bot. 1986; 8: 271-290.
9. Pal SC and Srivastava SN: Preliminary notes on the ethnobotany of Singhbhum District, Bihar. Bull. Bot. Surv. India 1976; 18: 247-250.
10. Megoneitso and Rao RR: Ethnobotanical studies in Nagaland, sixty two medicinal plants used by the Angami-a Naga, J. Econ. Taxon. Bot. 1983; 4(1): 167-172.
11. Kisangau DP, Hosea KM, Joseph CC and Lyaruu HV: *In-vitro* antimicrobial assay of plants used in traditional

medicine in Bukoba Rural district, Tanzania. Afr J Tradit Complement Altern Med 2007; 4: 510-523.
12. Ghoti H, Fibach E, Dana M, Abu Shaban M and Jeadi H: Oxidative stress contributes to hemolysis in patients with hereditary spherocytosis and can be ameliorated by fermented papaya preparation. Ann Hematol 2011; 90: 509-513.
13. Aruoma OI, Hayashi Y, Marotta F, Mantello P and Rachmilewitz E: Applications and bioefficacy of the functional food supplement fermented papaya preparation. Toxicology 2010; 278: 6-16.
14. Iweala EE, Uhegbu FO and Ogu GN: Preliminary *in-vitro* antisickilng properties of crude juice extracts of *Persia Americana*, *Citrus sinensis*, *Carica papaya* L. and Ciklavit (R). Afr J Tradit Complement Altern Med 2010; 7: 113-117.
15. Sripanidkulchai B, Wongpanich V, Laupattarakasem P, Suwansaksri J and Jirakulsomchok D: Diuretic effects of selected Thai indigenous medicinal plants in rats. J Ethnopharmacol 2001; 75: 185-190.
16. Sharma PV: Ayurved ka Vaigyanik itihasa; Chaukhambha Orientalia, Varanasi 1996; 3: 380.
17. Shaligram VL: Shaligram nighantubhushan; khemraj srikrishnadass, Mumbai 2011; 928-929.
18. Sharma PV: Priyanighantu; Chaukhambha surabharati prakashan, Varanasi 2004; 193.
19. Anjum V, Ansari SH, Naquvi KJ, Arora P and Ahmad A: Development of quality standards of *Carica papaya* L Leaves; Scholars Research Library, Der Pharmacia Lettre 2013; 5(2): 370-376.
20. Zunjar V, Mammen D, Trivedi BM and Daniel M: Pharmacognostic, Physicochemical and Phytochemical studies on *Carica papaya* Linn. leaves: Pharmacognosy Journal 2011; 3(20): 5-8.
21. Thomas E, Vandebroek I, Sanca S and Van Damme P: Cultural significance of medicinal plant families and species among Quechua farmers in Apillapampa, Bolivia. J Ethnopharmacol 2009; 122: 60–67
22. Sagnia B, Fedeli D, Casetti R, Montesano C, Falcioni G and Colizzi V: Antioxidant and Anti-Inflammatory Activities of Extracts from *Cassia alata, Eleusine indica, Eremomastax speciosa, Carica papaya* L. and *Polyscias fulva* medicinal plants collected in Cameroon; Plos one 2014; 9(10).
23. Focho DA, Newu MC, Anjah MG, Nwana FA and Ambo FB: Ethnobotanical survey of trees in Fundong, Northwest Region, Cameroon. J Ethnobiol Ethnomed 2009; 5: 17.
24. Ramasawamy AM and Sirsi M: Antituberculosis Activity of Some Chemical Constituents from Higher Plants. Indian J. Pharm 1960; 22: 34-35.
25. Govindachari TR, Pai BR and Narasimhan NS: Pseudocarpine, a new alkaloid from *Carica papaya* L. J. Chem. Soc., 1954; 0: 1847-1849.
26. Chung-Shih T: New macrolcyclic, Δ1-piperideine alkaloids from papaya leaves: dehydrocarpaine I and II; Phytochemistry 1979; 18(4): 651-652.
27. Agung N, Hesty H, Jae SC and, Hee-Juhn P: Identification and quantification of flavonoids in *Carica papaya* L. leaf and peroxynitrite-scavenging activity; Asian Pacific Journal of Tropical Biomedicine 2017; 7(3): 208-213.
28. Tasqiah: HPLC- based activity profiling for antiplasmodial compounds in the traditional Indonesian medicinal plant *Carica papaya* L. Journal of Ethnopharmacology 2014; 155(1): 426-434.
29. Chavez Quintal P, Gonzalea-Flores T, Rodriguez-Buenfil and Gallegos-Tintore S: Antifungal activity in Ethanolic Extracts of *Carica papaya* L cv Maradol leaves and seeds; Indian Journal of Microbiology 2011; 51(1): 54-60.
30. Ram PN, Ram VR, Khatri TT, Vyas SJ and Dave PN: XRF analysis of *Carica papaya* L. leaves of semi arid region of Kachchh; International Letters of Natural Sciences 2014; 19: 15-24.
31. Vishwanath Z, Prasad DR, Mehul J, Trivedi B and Nivsarkar M: Antithrombocytopenic activity of carpaine and alkaloidal extract of *Carica papaya* Linn. leaves in busulfan induced thrombocytopenic Wistar rats; journal of ethanopharmacology 2016; 181(2): 20-25.
32. Dharmarathna SLCA, Wickramasinghe S, Waduge RN, Rajapakse RPVJ and Kularatne SAM: Does *Carica papaya* L. leaf extract increase the platelet count? An experimental study in a murine model; Asian Pacific Journal of Tropical Biomedicine 2013; 3(9):720-724.
33. Ahmad N: Dengue fever treatment with *Carica papaya* L leaves extracts; Asian Pacific Journal of Tropical Biomedicine 2011; 4: 330-333.
34. Suwendar PH and Ernasari GI: Analgetic activity of Papaya (*Carica papaya* L.) leaves extract; Procedia Chemistry 2014; 13: 147-149.
35. Otsuki N, Dang NH and Morimoto EKASC: Aqueous extract of *Carica papaya* L. leaves exhibits anti tumor activity and immunomodulatory effects; Journal of Ethnopharmacology 2010; 127(3): 760-767.
36. Pandey S, Walpole C, Cabot PJ, Shaw PN, Jyotsna B and Hewavitharana AK: Cancer; Biomedicine and Pharmacotherapy 2017; 89: 515-523.
37. Abidina NZ, Omara H, Empungana AJ, Kamalaldinb NA, Yahayab BH and Zubairia SI: Proliferative Activity of Saponin-Reducing *Carica papaya* L. Leaves Extracts on Human Lung Fibroblast Cell (IMR90). Journal Teknologi November 2016.
38. Juarez-Rojop IE: Phytochemical screening and hypoglycaemic activity of *Carica papaya* L. leaf in streptozotocin- induced diabetic rats; Revista Brasileira de Farmacognosia 2014; 24(3): 341-347.
39. Baskaran C, Rathabai V, Velu S and Kubendiran K: The efficacy of *Carica papaya* L. leaf extract on some bacterial and a fungal strain by well diffusion method; Asian Pacific Journal of Tropical Disease 2012; 2(2): s658-s662.
40. George M, Venkataraman PR and Pandalai KM: Investigation on plant antibiotics part II; A search for antibiotics substances in some Indian medicinal plants. Journal of science and industrial research 1947; 6B: 42-46.
41. Ramasawamy AS and Sirsi M: Antituberculosis Activity of Some Chemical Constituents from Higher Plants. Indian J. Pharm. 1960; 22: 34-35.
42. Ramaswamy AS and Sirsi M: Antitubercular activity of some natural products; Indian Journal of Pharmacology 1967; 29: 157-158.
43. Mishra DN, Dixit V and Mishra AK: Mycotoxic evaluation of some higher plants against ring worm causing fungi; Indian Drugs 1991; 28: 300-303.
44. Dubey NK, Dixit SN and Bhargava KS: Evaluation of leaf extracts of higher plants against some storage fungi; Indian Journal of Botany 1982; 5: 20-22.
45. Kishore N and Dubey NK: Fungitoxicity of some higher plants aginst *Trichophyton rubrum* and *Epidermophyton floccossum*. Indian Journal of Pharmaceutical Sciences, 1988; 50: 323-325.
46. Tewari SN and Dath AP: Effect of leaf extract of some plants on the growth of three fungal pathogens of rice. Indian Phytopathol 1984; 37: 458-461.
47. Bautista-Baños S, Barrera-Necha LL, Bravo-Luna I and Bermudes-Torres L: Antifungal activity of leaf and stem

extracts from various plant species on the incidence of *Colletotrichum gloesporoides* of papaya and mango fruit after storage. Rev Mex Fitopatol 2002; 20: 8-12.
48. Kovendan K: Antimalarial activity of *Carica papaya* L. (Family: Caricaeae) leaf extract against *Plasmodium falciparum*; Asian Pacific Journal of Tropical Disease 2012; 2(1): 306-311.
49. Deshmukh PD, Rathore YS and Bhattacharya AK: Larval survival of Diacrisia oblique Walker on several plant species; Indian Journal of Entomology 1979; 41(1): 5-12.
50. Adetunji VO and Salawu OT: Efficacy of ethanolic leaf extracts of *Carica papaya* L. and *Terminalia catappa* as molluscicides against the snail intermediate hosts of schistosomiasis; Journal of Medicinal Plants Research 2010; 4(22): 2348-2352,
51. Sanghvi PK: Epidemiological studies on guinea worm in some newly discovered villages of Jhabua district (M.P) and test of *Carica papaya* L. leaves of Guinea worm infection. Indian Journal of Medical Sciences 1989; 43: 123-124.
52. Reviews on Indian Medicinal Plants ICMR, New Delhi 2007; 5: 500-551 ISSN- 0972-7957.
53. Mahamood L, Masood A, Saxena SK and Hussain SI: Effect of some plant extracts on the mortality of *Meloidogyne incognita* and *Rotylenchulus reniformis*; Acta Bot Indica 1979; 7: 129-132
54. Gupta A, Wambebe Co and Parsons DL: Central and Cardiovuscular Effects of the Alcoholic Extract of the Leaves of *Carica papaya* L, International Journal of Crude Drug Research 1990; 28(4): 257-266.
55. Gupta A and Gupta R: A survey of plants for presence of cholinestersse activity. Phytochemistry 1997; 46(5): 827-831.
56. Hornick CA, Sanders LI and Lin YC: Effect of carpaine, a papaya alkaloid, on the circulatory function in the rat. Research Communications in Chemical Pathology and Pharmacology 1978; 22(2): 277-289.
57. Burdick and Everette M: Carpaine. An alkaloid of *Carica papaya* L. Chemistry and pharmacology. Economic Botany 1971; 25(4): 363-365.
58. Owoyele BV, Adebukola OM, Funmilayo AA and Soladoye AO: Anti-inflammatory activities of ethanolic extract of *Carica papaya* L leaves; Inflammo-pharmacology 2008; 16: 168-173.
59. Suyono T, Fachrial E, Zein R, Chaidir Z, Tjong DH and Aziz H: The Effect of Pb(II) in the Kidney of Experimental Rats and the effectiveness of Papaya (*Carica papaya* L.) leaves powder as an antidote; Research Journal of Pharmaceutical, Biological and Chemical sciences, January 2016.
60. Ukoba O, Adfisan IE and Aguawa US: The wound healing effect of powdered *Carica papaya* L. leaves. IMPACT: International Journal of Research in Applied, Natural and Social Sciences (IMPACT: IJRANSS) 2016; 4(3): 1-10.
61. Hossain N, Kumar PV and Wei YS: Dengue and drawbacks of marketed *Carica papaya* L. leaves supplements; International Journal of Green Pharmacy 2016.

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