International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 2 Mar-Apr 2022, pp: 1003-1007 www.ijprajournal.com ISSN: 2456-4494

Review on Benefits of Carica Papaya Leaf Extract in Dengue Associated Thrombocytopenia

Adithya Purohit S R[1*], Jhnanitha[2], Shilpashree Vk[3], Ravikumar[4]
1. PG Scholar, Department of Pharmacy Practice, Karavali College of Pharmacy, Mangalore.
2. UG Scholar, Department of Pharmacognosy, Karavali College of Pharmacy, Mangalore.
3. Assistant Professor, Department of Pharmacognosy, Karavali College of Pharmacy, Mangalore
4. Principal, Karavali College of Pharmacy, Mangalore

Submitted: 01-04-2022 Accepted: 11-04-2022

ABSTRACT
Carica papaya leaf has been found to have a potential role in dengue associated thrombocytopenia. In traditional practice Papaya leaf has numerous medicinal benefits. Belonging to the family of Caricaceae, it is being grown in all the tropical and subtropical regions of the world. The main objective of this review is to focus on the benefits of Carica papaya leaf extract for dengue associated thrombocytopenia. Thrombocytopenia is a prominent feature in dengue fever and if left untreated will lead to more severe life threatening complications like internal or external blood loss or haemorrhage. It was found that papaya leaf contains unique plant compounds that have demonstrated wide pharmacological benefits. Presence of bioactive compounds like flavonoids, saponins and other compounds attributes to its antimicrobial/antiviral potential. Article search was conducted using the keywords mentioned below. Relevant clinical studies were identified and analysed on the benefits of Carica papaya leaf extract consumption. Papaya leaf extract was well tolerated by individuals including children. Overall, studies showed an increase in platelet count in patients receiving papaya leaf extract who were diagnosed with dengue. The leaf extract possess a dengue specific neutralising effect that exert a protective role on platelets. Papaya leaf extract along with the standard treatment would help in increasing the platelet levels.

Keywords: Carica papaya, dengue, thrombocytopenia, thrombocyte count, papaya leaf extract, platelet count.

I. INTRODUCTION

Carica papaya is an herbaceous succulent plant which belongs to the family Caricaceae. Central America being the origin, it is now grown in all tropical and subtropical regions of the world. The leaves are palmately-lobed, long and have hollow petioles. The fruit is melon like spherical or long, and will contain over a thousand seeds. Unripe papaya fruit contains papain, chymopapain, endopeptidase papain III and IV, glutamine cyclotransferase, lysozymes, peptidase A and B. Seeds contain benzyl isothiocyanate, benzyl thiourea, beta-sitosterol, papaya oil, caricin and an enzyme myrosin. Leaf of Carica papaya plant contains carpine, carpinine, pseudocarpine, vitamin C, vitamin E, choline and carposide[1].

Carica papaya leaf in traditional practice is used to treat high blood sugar levels. Though there are no trials conducted on humans, papaya leaf has shown its hypoglycaemic activity on diabetic rats as per the study conducted in the Journal of BMC Complimentary and Alternative Medicine[2, 3]. The presence of fibre and other nutrients in papaya leaf may help to reduce digestive disturbances like gas, bloating or heart burn. Papain present in the leaf is a protein dissolving enzyme which acts as an associate exfoliant to get rid of dead skin cells and forestall skin condition. Test-tube studies have shown that papaya leaf extract inhibits the growth of prostate and breast cancer cells, but neither humans nor rats replicate these results[3]. Recent studies has shown multiple roles and benefits of papaya leaf as an anti-inflammatory agent, as an excellent wound healer, anti-tumour as well as immune-modulator and as an antioxidant. A toxicity study (acute, sub acute, and chronic toxicity) conducted on Sprague Dawley rats administered with Carica papaya leaf extract revealed that it was safe for oral consumption[4].

Phytochemical screening of Carica papaya leaf extract identifies the bioactive compounds like saponin, flavonoids, reducing sugar, steroids, tannins and glycosides5,8. The presence of these bioactive compounds infers antimicrobial and antiviral potential in papaya leaf extract5.

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 2 Mar-Apr 2022, pp: 1003-1007 www.ijprajournal.com ISSN: 2456-4494

CONTENT	PERCENTAGE COMPOSITION
Flavonoid	65.63
Phenol	23.24
Alkaloid	4.88
Saponin	3.30
Glycosides	2.11
Tannins	0.55
Phlobatannin	0.27

Table 1: Phytochemical constituents of ethyl acetate-ethanolic fraction of Carica papaya leaves

Dengue is a mosquito borne viral infection which spread through the bite of an infected Aedes species mosquito[6, 12]. Symptoms of dengue infection are pretty confusing with other illnesses that cause fever, aches, rashes or pain. Generally symptoms like nausea, vomiting, rash, aches and pains suggest a dengue infection[6]. Common laboratory finding in dengue infection is thrombocytopenia. When blood has less blood cell fragments called platelets compared to the normal levels then it is referred to a condition called thrombocytopenia[7]. Both mild and severe dengue infection shows thrombocytopenia and it is beneficial as it helps to correlate with disease severity[8, 9]. It is very important to monitor the platelet and haematocrit count in patients with dengue.

Papaya leaf extract can be consumed at any stage of the infection, preferably from the first day of fever. Leaf of Carica papaya is grounded to obtain an extract that is consumed 25-30 ml 3 times a day by an adult and 5-10ml 3 times a day by children until completely recovered from the illness[6]. There are different methods of preparation of papaya leaf extract for the treatment of dengue[9, 22].

In one of the method, a bunch of fresh papaya leaf is taken and are washed thoroughly with running tap water. The leaves are chopped, weighed (50g) and are crushed with the help of mortar and pestle. 50 ml of boiled cool water is mixed with 25g of sugar and the crushed papaya leaf is added to it. Mixture is kept aside for half an hour and is squeezed to obtain the extract which is consumed and also can be stored for 24 hours.
In another method bunch of papaya leaf is crushed and squeezed to obtain the extract which is directly consumed twice a day[9].

AIM

Aim of this article is to review benefits of Carica papaya leaf extract in dengue associated thrombocytopenia.

METHODOLOGY

All literature was retrieved from databases (Pub Med, Google scholar) using search terms, including "Carica papaya", "dengue", "thrombocytopenia", "thrombocyte count", "papaya leaf extract". Literatures published from 2000 to 2021, investigating the benefits of the Carica papaya plant towards various conditions, were included. Literatures that were not related to dengue associated thrombocytopenia were excluded.

II. RESULT AND DISCUSSION

Thrombocytopenia in dengue patient can occur due to two possible reasons; one reason is more number of platelets being destroyed and cleared from peripheral blood[10, 4]. The other reason is because of the ability of the virus to suppress the bone marrow causing virus to move towards monocytes, macrophages and endothelial cells utilizing all the nutrients from them which could lead to focal apoptosis and sometimes necrosis. Thus leading to infection, platelet aggregation and destruction [4, 20, 21].

Thrombocyte count of less than 100000 cells/mm^3 is an indication of dengue infection. It is very important to normalise these levels in order to prevent further complications. Fresh juice of papaya leaf extract carry essential compounds and play a major role in this process. Compounds like papain and caricain that enhances the platelet count and reduce the infection. Several studies were conducted where rise in platelet count was observed[11].

Studies show that papaya leaf extract is capable of increasing ALOX12 (arachidonate 12-lipoxygenase or platelet type lipoxygenase) by 15 times which plays a beneficial role in promoting platelet production. Platelet specific gene called platelet activating factor receptor (PTFAR) is increased by 13.5 fold following the administration. Quercetin; one of the flavonoid in papaya leaf inhibits the serine protease NS2B and NS3 which plays a key role during virus replication[4, 11].

Asian Pacific Journal of Tropical Biomedicine reported the effectiveness of treatment of dengue, a truck driver who worked in a cement factory was admitted with body temperature 104°F, and the symptoms included breathing problem,

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 2 Mar-Apr 2022, pp: 1003-1007 www.ijprajournal.com ISSN: 2456-4494

severe vomiting, red skin, shivering, severe body pain and high blood pressure. After being diagnosed with dengue patient received 25ml of papaya leaf extract twice every day for five days. A gradual rise in the platelet count and WBC count was noticed after 2 days of treatment[13].

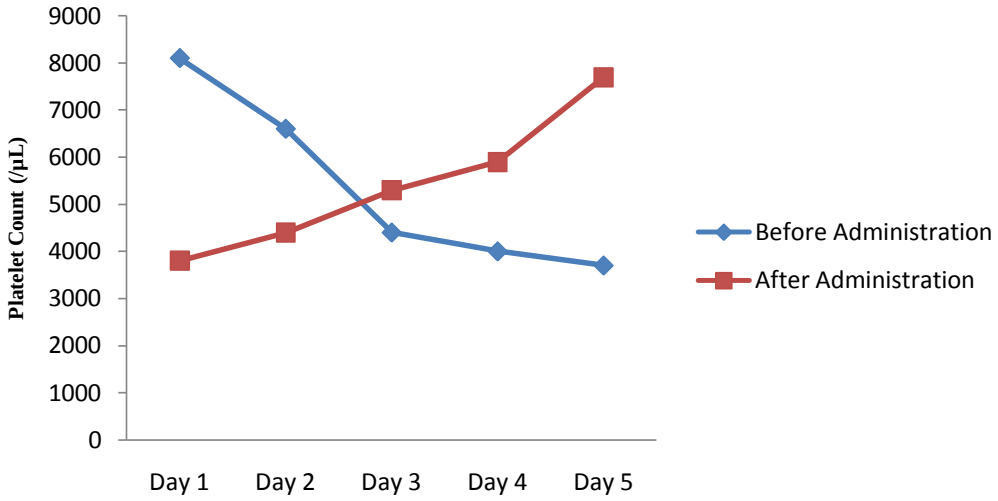

Fig 1: Comparison of platelet count before and after the administration of papaya leaf extract

According to the reports of British Medical Journal, two children suffering from dengue infection had a speedy recovery after the consumption of a spoonful of papaya leaf extract every four hours. Gradual increase was seen in the platelet counts of both the children after 12 hours. After a couple of days the platelet count were found to stably increase and normalise[14].

Multi-centric double blinded placebo controlled randomised observational study conducted by Kasture PN et al on 300 patients across 5 centres in India indicates significant increase in the platelet count over the 5 day therapy duration in patients with dengue. Authors observed gradual increase in platelet count on the 3rd day in the test group when compared to control group (82.96±16.72, 66.45±17.36 thousands). On the 4th and 5th day platelet counts were found to be higher in test group when compared to the control groups[15, 23].

A similar randomized controlled study was conducted in involving 227 patients with dengue fever and dengue hemorrhagic fever. Patients received papaya leaf extract for 3 consecutive days and were compared with patients (control) receiving standard treatment. Significant increase in platelet count was observed in patients receiving papaya leaf extract when compared to the control group[4].

A double blinded randomised prospective study was conducted in a tertiary healthcare hospital in India where patients with dengue fever and thrombocyte count below 30000/µL were included in the study. The study showed that Carica papaya leaf extract was safe and was well tolerated. Patients in test group administered with Carica papaya leaf extract showed gradual increase in platelet count compared to the patient in control group[16].

A study was conducted in Indonesia where Carica papaya leaf extract capsules (CPC) were used. High fever for more than 2 days, thrombocyte count <150000/µL and hematocrit of 20% or more were the inclusion criteria where 80 patients met this criteria. They were divided into two randomised groups where one group received CPC along with standard treatment and the other received only the standard treatment. It was found that platelet count increased in patients receiving CPC along with standard treatment[17].

A study in International Journal of Applied and Basic Medical Research reported an increase in platelet count in dengue patients who consumed the papaya leaf extract. Four randomised control study was conducted to prove the safety and efficacy of papaya leaf extract. 439 subjects who met the inclusion criteria were included and it was found that were Carica papaya leaf extract was beneficial in increasing the platelet count and decreasing the number of days of hospitalisation[18].

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 2 Mar-Apr 2022, pp: 1003-1007 www.ijprajournal.com ISSN: 2456-4494

The Journal of Medicinal and Aromatic Plants included a study which incorporated 5 patients with dengue who consumed papaya leaf extract. Reports suggest a gradual increase in the platelet levels within 24 hours[19].

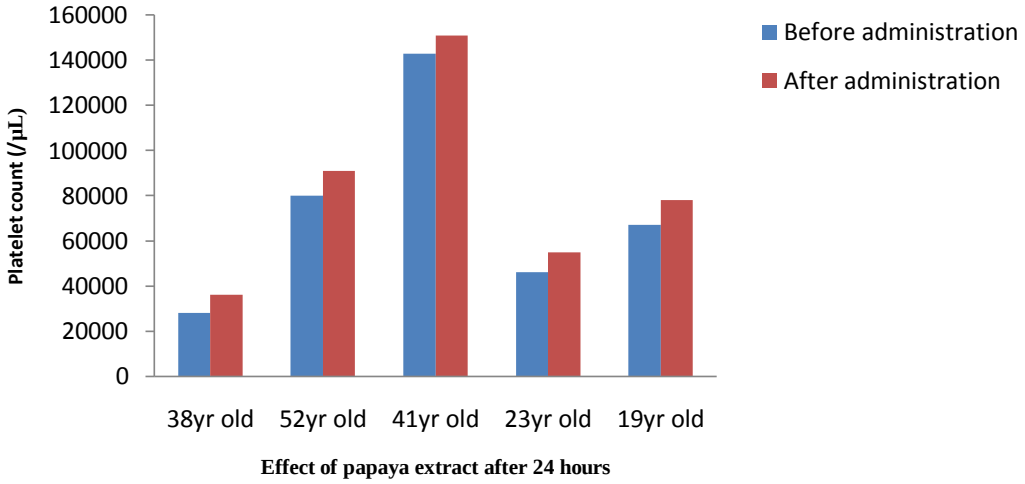

Fig2: Graph showing increase in platelet count after 24 hour of administration

III. CONCLUSION

From this review it is observed that Carica papaya leaf extract does show its importance in dengue. Good improvements in platelet counts were observed. This might be feasibly attributed to its membrane-stabilizing property. The flavonoids and other phenols present within the juice of Carica Papaya leaf are suggested to supply the beneficial effects. The leaf extract possess a dengue specific neutralising effect that exert a protective role on platelets. Papaya leaf extract along with the standard treatment would help in increasing the platelet levels.

CONFLICT OF INTEREST

The authors have no conflicts of interest regarding this review.

REFERENCES

[1]. Sharma DK, Tiwari B, Singh RK, Sahu S, Mathur SC, Singh RM, et al. Estimation of minerals in Carica papaya Leaf found in Northern India by using ICP-OES technique.IntJ SciEngRes.2013;4:2012–9.

[2]. Juárez-Rojop IE, Díaz-Zagoya JC, Ble-Castillo JL, Miranda-Osorio PH, Castell-Rodríguez AE, Tovilla-Zárate CA, et al. Hypoglycemic effect of Carica papaya leaves in streptozotocin-induced diabetic rats. BMC Complementary and Alternative Medicine [Internet]. 2012 Nov 28 [cited 2022 Mar 9];(1).

[3]. Ansley. 7 Emerging Benefits and Uses of Papaya Leaf [Internet]. Healthline. Healthline Media; 2020 [cited 2022 Jan 9].

[4]. Subenthiran S, Choon TC, Cheong KC, Thayan R, Teck MB, Muniandy PK, et al. Carica papayaLeaves Juice Significantly Accelerates the Rate of Increase in Platelet Count among Patients with Dengue Fever and Dengue Haemorrhagic Fever. Evidence-Based Complementary and Alternative Medicine [Internet]. 2013 [cited 2022 Feb 2];1–7.

[5]. Research, Shubham S, Mishra R, Dutta K. (PDF) Phytochemical Analysis of Papaya Leaf Extract: Screening Test [Internet]. ResearchGate. unknown; 2019 [cited 2022 Mar 8].

[6]. Rasana Patil, Tina Makhija, H. P. Suryawanshi, S.P. Pawar. A Review on – Dengue. Research J. Pharm. and Tech. 6(9): September 2013; Page 930-936.

[7]. Lale A, Lale S, Bick R, Fareed J. Dengue Fever and Thrombocytopenia: A Deadly Duo. Blood [Internet]. 2006 Nov 16 [cited 2022 Mar 15];(11):3978–3978.

[8]. Jonas LT MDReviewed by Dr Damien. Papaya Leaf Extract and Platelet Count [Internet]. News-Medical.net. News-Medical; 2018 [cited 2022 Jan 9].

[9]. Method 3 | The Times of India [Internet]. The Times of India. Times of India; 2017 [cited 2022 Feb 2].
[10]. Rajapakse S, de Silva NL, Weeratunga P, Rodrigo C, Sigera C, Fernando SD. Carica papaya extract in dengue: a systematic review and meta-analysis. BMC Complementary and Alternative Medicine [Internet]. 2019 Oct 11 [cited 2022 Jan 9];(1).
[11]. Chao C-H, Wu W-C, Lai Y-C, Tsai P-J, Perng G-C, Lin Y-S, et al. Dengue virus nonstructural protein 1 activates platelets via Toll-like receptor 4, leading to thrombocytopenia and hemorrhage. Kuhn RJ, editor. PLOS Pathogens [Internet]. 2019 Apr 22 [cited 2022 Jan 9];(4):e1007625.
[12]. Gibbons RV. Dengue: an escalating problem. BMJ [Internet]. 2002 Jun 29 [cited 2022 Jan 9];(7353):1563–6.
[13]. Ahmad N, Fazal H, Ayaz M, Abbasi BH, Mohammad I, Fazal L. Dengue fever treatment with Carica papaya leaves extracts. Asian Pacific Journal of Tropical Biomedicine [Internet]. 2011 Aug [cited 2022 Jan 9];(4):330–3.
[14]. Kularatne SAM. Dengue fever. BMJ [Internet]. 2015 Sep 15 [cited 2022 Jan 9];h4661.
[15]. Pangtey Ghan Shyam, Prakash A, Munjal Y. Journal of the Association of Physicians of India - JAPI [Internet]. Journal of the Association of Physicians of India - JAPI. [cited 2022 Jan 19].
[16]. Sathyapalan DT, Padmanabhan A, Moni M, P-Prabhu B, Prasanna P, Balachandran S, et al. Efficacy & safety of Carica papaya leaf extract (CPLE) in severe thrombocytopenia (≤30,000/µl) in adult dengue – Results of a pilot study. Price MA, editor. PLOS ONE [Internet]. 2020 Feb 19 [cited 2022 Jan 19];(2):e0228699
[17]. Yunita F, Hanani E. The effect of Carica papaya L leaves extract capsule on platelet count and hematocrit level in dengue fever patient. Int J Med Aromat Plants. 2012;2:573–8.
[18]. Charan J, Saxena D, Goyal J, Yasobant S. Efficacy and safety of Carica papaya leaf extract in the dengue: A systematic review and meta-analysis. International Journal of Applied and Basic Medical Research [Internet]. 2016 [cited 2022 Jan 19];(4):249.
[19]. Prakash Kala C. Leaf Juice of Carica papaya L.: A Remedy of Dengue Fever. Medicinal & Aromatic Plants [Internet]. 2012 [cited 2022 Mar 15];(06).
[20]. Thomas L, Jonas D. Papaya Leaf Extract and Platelet Count [Internet]. News-Medical.net. News-Medical; 2018 [cited 2022 Mar 12]
[21]. Ansari R. Extract of Carica papaya L. leaves: Standardising its use in dengue fever. Indian Journal of Pharmacology [Internet]. 2016 [cited 2022 Mar 12];(3):338.
[22]. Baheerati M.M. Natural Therapy for Dengue Fever. Research J. Pharm. and Tech. 7(2): Feb. 2014; Page 269-271.
[23]. Kasture PN, Nagabhushan KH, Kumar A. A Multi-centric, Double blind, Placebo controlled, Randomized, Prospective study to evaluate the Efficacy and Safety of Carica Papaya Leaf Extract, as empirical therapy for thrombocytopenia associated with dengue fever. J Assoc Physicians India 2016; 64:15-20