

Effects of papaya leaves on thrombocyte counts in dengue — a case report

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Abstract

Dengue fever is on the rise in developing nations like India, Pakistan, Sri Lanka and Bangladesh. There is no anti-viral chemotherapy or vaccine for dengue virus and management of the disease is done on supportive measures. The decline in the thrombocyte count leads to dengue haemorrhagic fever accounting for complications and mortality. Oral administration of *Carica papaya* leaves extract is said to have a positive impact on thrombocyte count. A 23-year-old man was administered a calculated dose for five days. Blood samples were tested for complete blood count before and after the administration of the juice. Thrombocyte count had increased from 28000/micro liter to 138000/micro liter at the end of five days. We present our experience here.

Keywords: Dengue fever, Thrombocyte count, *Carica papaya* leaves.

Introduction

Carica papaya L. is the only species within the Caricaceae genus, and the palm-like tree has segmented leaves, yellow flowers and large black seeded yellow to orange fruits.¹ *C. papaya* L. fruit juice and leaves extracts have demonstrated anti-cancer,² anti-oxidative,³ anti-inflammatory,⁴ anti-bacterial,⁵ nephro-protective,⁶ hepato-protective⁷ activity against toxins, hypoglycaemic, hypolipidaemic effects⁸ and anti-sickling properties in sickle cell disease.⁹

Dengue fever (flaviviridae family of viruses) is an arthropod-borne disease carried by *Aedes ayegypti* with four different serotypes 1, 2, 3 and 4.¹⁰ Dengue fever cases have been on the rise in Pakistan and other developing countries. It is estimated that there are between 50 and 100 million cases of dengue fever (DF) and about 500,000 cases of dengue haemorrhagic fever (DHF) each year which require hospitalisation.¹⁰ There is no known anti-viral chemotherapy for DF yet. Many vaccine trials have been done, but none has produced a satisfactory

outcome.¹⁰ Management includes supportive measures like anti-pyretic, hydration, blood and blood products and pain killers. Infection induces a life-long immunity to that particular serotype, but secondary infection with another serotype is dangerous and life-threatening due to higher risks of DHF.¹¹ The only way to prevent dengue virus acquisition is to avoid being bitten by a vector mosquito.¹⁰

With such high rates of incidence and mortality it would be useful to have a regimen improving the outcome of the disease. Investigating the effect of papaya leaves on the platelets can help our physicians in helping patients with diseases like DF where the platelets are the major cause of complications and mortality. Here we present a DF case who responded positively to the administration of papaya leaves extract.

Case Report

A 23-year-old male, medical student by profession, a swimmer by hobby and a resident of Karachi was brought to Sunset Poly Clinic with a fever of 102°F for the preceding 2 days. Symptoms included nausea, red skin, severe body ache and weakness. He reported that he used to visit friends and poorly managed tea stores after sunset every evening after his swimming sessions. He was bitten by a mosquito somewhere. After 2 days he had high-grade fever with severe body ache, weakness and nausea. The symptoms would increase at some times of the day and decrease at other times.

He was admitted and tested for typhoid, malaria and dengue. Dengue Rapid N51 antigen was found to be positive. The haematological reports also revealed an abrupt decline in the patient's thrombocyte counts. He was given azithromycin 250mg once daily, acetaminophen 8-hourly and tremendous amounts of hydration orally, but there were no signs of improvement and the condition got worse with time. After obtaining consent from the patient, *C. papaya* leaves extract was administered orally to the patient to test the popular belief of the leaves increasing thrombocyte counts under the supervision of the senior physician at the clinic. The leaves were collected and thoroughly washed with

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Table-1: Results before administration of *C. papaya* leaves extract.

Days	1	2	3	4	5
Platelets / μ L	177000	143000	72000	54000	28000
WBCs / μ L	7200	6700	5400	4300	3000
Hemoglobin g/dl	14.5	14.5	14.5	14.2	13.1

Table-2: Results after administration of *C. papaya* leaves extract.

Days	1	2	3	4	5
Platelets / μ L	28000	50000	64000	84000	138000
WBCs / μ L	3000	3700	5400	5900	7800
Hemoglobin g/dl	13.1	13.3	13.3	13.6	13.6

boiled and cooled water. One-and-a-half leaf was ground in a grinder with water to make a juice of 150ml. As the taste of the *C. papaya* leaves is extremely bitter, the patient would have alternate sips between the *C. papaya* extract and commercially-made fruit juices. Around 150ml of extract was given to the patient once daily for five consecutive days. The extract was given to the patient as a single dose. Platelet count before the administration of extract had been done every day and the routine was followed during the 5 days of extract administration as well.

Haematological assessment revealed that platelets and white blood cells showed continuous decrease with a slight decrease in haemoglobin initially (Table-1). The results of the 5 days after the leaves extract was given improved manifold (Table-2). The family was warned about platelet transfusions if required and the patient was kept on fluid diet with intravenous hydration. The patient remained in the hospital throughout the 10 days of treatment.

With every successive administration of the extract, the reports revealed a continuous rise in platelets; a rise from 28000/micro liter to 138000/micro liter by the end of the fifth day of taking the *C. papaya* leaves extract.

Amongst the clinical signs and symptoms, fever, body ache and nausea also resolved with the therapy.

Discussion

The main objective was to investigate the role of *Carica papaya* leaves in DF. A toxicity study (acute, sub-acute, and chronic toxicity) conducted on Sprague Dawley rats administered with *Carica papaya* leaves juice (CPLJ) of the sekaki variant revealed that it was safe for oral consumption.¹² There are no anti-viral chemotherapeutic agents yet discovered for DF. The journey to drug

discovery through the study of immune-modulatory effects against dengue infection is based on the research of generic compounds and natural products.¹³

C. papaya L. has been used for centuries in ethno-medicine to treat many diseases and symptoms, and mature ripe fruits have been used as an effective remedy against ringworms.¹⁴ Green fruits, on the other hand, have been used to lower blood pressure, and as an aphrodisiac. *C. papaya* Leaves were eaten and used as a heart tonic and analgesic. In traditional medicine, they were used to reduce inflammation and pain due to their analgesic properties.¹⁴ We further investigated their role in DF and effects on thrombocyte counts.

Our investigation revealed positive findings in the role of *C. papaya* leaves for the treatment of dengue, and for improving platelet counts. This was also observed in another study on a 45-year-old man where counts increased from 55000/micro liter to 168000/micro liter.¹⁵ Our study showed a dramatic increase in thrombocyte count from 28000/micro liter to 138000/micro liter within 5 consecutive days of administration. This is further supported by another study in which the PTAFR gene, which is known to be responsible for increased platelet production and aggregation, was expressed 13.42-folds among the patients who consumed the papaya juice as compared to the control group, indicating that the juice had played an important role in addressing the arresting of bleeding tendencies among these patients.¹⁶

Our study further depicted the improvement in the symptoms of dengue during and following the administration of the extract. Along with the increasing thrombocyte counts, the anti-hemolytic action of *C. papaya* leaves could have a potential therapeutic efficacy in the disease processes, causing destabilisation of biological membranes.¹⁷

The patient's recovery and progressive increase in thrombocyte counts could have been spontaneous since DF is a self-limiting disease with sufficient supportive therapy. This factor can be investigated in a further study using controls.

Plants are a useful source of medicine and *C. papaya* is one of them. Our study supports the popular claim of the use of *C. papaya* leaves in treating DF by increasing platelet counts and alleviating symptoms.

Conclusion

Dengue is on the rise again in our part of the world and better understanding of the management of dengue is important to avoid dengue haemorrhagic fever. *C. papaya*

leaves seems to be a promising solution to our problem. Dengue fever continues to be a nuisance, causing several deaths every year, and a further detailed study on investigating this topic might help in reducing the associated mortality.

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References

- Jayaweera DM. Medicinal plants (indigenous and exotic) used in Ceylon. Colombo: National Science Council of Sri Lanka; 1981.
- Rahmat A, Rosli R, Wan Nor IW, Endrini S, Sani HA. Anti-proliferative activity of pure lycopene compared to both extracted lycopene and juices from watermelon (*Citrullus vulgaris*) and papaya (*Carica papaya*) on human breast and liver cancer cell lines. *J Med Sci* 2002; 2: 55-8.
- Mehdipour S, Yasa N, Dehghan G, Khorasani R, Mohammadirad A, Rahimi R, et al. Antioxidant potentials of Iranian *Carica papaya* juice in vitro and in vivo are comparable to alpha-tocopherol. *Phytother Res* 2006; 20: 591-4.
- Owoyele BV, Adebukola OM, Funmilayo AA, Soladoye AO. Anti-inflammatory activities of ethanolic extract of *Carica papaya* leaves. *Inflammopharmacology* 2008; 16: 168-73.
- Yismaw G, Tessema B, Mulu A, Tiruneh M. The in vitro assessment of antibacterial effect of papaya seed extract against bacterial pathogens isolated from urine, wound and stool. *Ethiop Med J* 2008; 46: 71-7.
- Olagunju JA, Adeneye AA, Fagbohunka-Bisuga NA, Ketiku AO, Benebo AS, Olufowobi OM, et al. Nephroprotective activities of the aqueous seed extract of *Carica papaya* Linn. in carbon tetrachloride induced renal injured Wistar rats: a dose and time dependent study. *Biol Med* 2009; 1: 11-9.
- Rajkapoor B, Jayakar B, Kavimani S, Muruges N. Effect of dried fruits of *Carica papaya* Linn on hepatotoxicity. *Biol Pharm Bull* 2002; 25: 1645-6.
- Adeneye AA, Olagunju JA. Preliminary hypoglycemic and hypolipidemic activities of the aqueous seed extract of *Carica papaya* Linn in Wistar rats. *Biol Med* 2009; 1: 1-10.
- Ogunyemi CM, Elujoba AA, Durosinmi MA. Anti-sickling properties of *Carica papaya* Linn. *J Nat Prod* 2008; 1: 56-66.
- Maheswaran R, Satish S, Ignacimuthu S. Larvicidal activity of *Leucas asper* (Willd) against the larvae of *Culex quinquefasciatus* Say. and *Aedes aegypti* L. *Inter J Integrative Biol* 2008; 2: 214-7.
- Morens, Fauci, Brody JE. Mosquito thrives; so does dengue fever. Geneva: WHO; 2008.
- Halim SZ, Abdullah NR, Afzan Z, Abdul Rashid BA, Jantan I, Ismail Z. Acute toxicity of *Carica papaya* leaf extract in Sprague Dawley rats. *J Med Plants Res* 2011; 5: 1867-72.
- Selisko B, Dutartre H, Guillemot JC, Debarnot C, Benarroch D, Khromykh A, et al. Comparative mechanistic studies of de novo RNA synthesis by flavivirus RNA-dependent RNA polymerases. *Virology* 2006; 351: 145-58.
- Morton JF. Fruits of Warm Climates. Miami, FL: Creative Resource Systems Inc; 1987; pp 336-46.
- Ahmad N, Fazal H, Ayaz M, Abbasi BH, Mohammad I, Fazal L. Dengue fever treatment with *Carica papaya* leaves extracts. *Asian Pac J Trop Biomed* 2011; 1: 330-3.
- Subenthiran S, Choon TC, Cheong KC, Thayan R, Teck MB, Muniandy PK, et al. *Carica papaya* leaves juice significantly accelerates the rate of increase in platelet count among patients with dengue fever and dengue hemorrhagic fever. *Evid Based Complement Alternat Med* 2013; 2013: 616737. doi: 10.1155/2013/616737.
- Ranasinghe P, Ranasinghe P, Abeysekera WPKM, Premakumara GAS, Perera YS, Gurugama P, et al. In vitro erythrocyte membrane stabilization properties of *Carica papaya* L. leaf extracts. *Pharmacognosy Res* 2012; 4: 196-202.