Effect of *Carica papaya* leaf formulation on Hematology and Serology of normal rat

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**ABSTRACT**

Thrombocytopenia is a disorder in which there is a thrombocyte count of less than 150x10³/µL. Thrombocytopenia is life threatening in many diseases particularly in dengue which is an escalating problem in the world. There was an outbreak of dengue in 2011 in Lahore, Pakistan and it was public opinion that *Carica papaya* leaf extract helps in recovery of platelet count. The aim of present study was to investigate the effect of *Carica papaya* leaf extract on blood chemistry specifically thrombocyte count of rats. Local syrup of papaya leaf extract was used for experimentation. Six animals were used for experiment, 3 as control and 3 experimental. The dose given to experimental animals was 0.5 ml of papaya leaf extract for 7 consecutive days which were at fasting for 4 hours before dose administration. There was a significant increase in mean platelet count, Mean Cell Haemoglobin (MCH) and Mean Corpuscular Volume (MCV) (p<0.05) of the treated animals as compared to control after seven days treatment with *Carica papaya* (CP) leaf formulations. The results described the need for isolation and identification of the C. papaya substances responsible for the release and/or production of thrombocytes. From the experimentation it can be concluded that *C. papaya* leaf extract is associated with rapid increase of platelet count.

**Keywords:** *Carica papaya*, MCH; MCV;

**INTRODUCTION**

Thrombocytopenia is a disorder with platelet count of less than 150x10³/µL. It is the most common cause of defective primary hemostasis that can lead to significant bleeding (Consolini, 2011). As platelet counts are above 20,000/µL, clinical symptoms are often limited to easy bruising; however, below 10,000/µL, the risk of spontaneous mucocutaneous bleeding increases rapidly. Significant quantitative or qualitative platelet dysfunction causes mucocutaneous bleeding (Sekhon & Roy, 2006). Thrombocytopenia stimulates thrombopoiesis, presumably due to thrombopoietin as a result of increased proportion of large young platelets in the peripheral circulation (George & Terrell, 2008). The most common causes of thrombocytopenia are; defective production of platelets by the bone marrow, diminished platelet survival and sequestration of the platelets by the spleen, leptospirosis associated with platelet destruction and bone marrow suppression and sepsis. A combination of above facts also can lead to thrombocytopenia (Li et al., 2001; Rothman & Ennis, 1999; Sheu et al., 2000; Wong & Glader, 2004).

Plants have the main advantage of still being the most effective and cheaper alternate source of drugs. In addition to the nutritional value of its fruit, the leaves of *Carica papaya* (CP) possess medicinal properties and are frequently used in traditional medicines. The antifertility effects of CP seeds in rats and rabbits have been investigated (Lohiya et al., 1994; Lohiya et al., 2000). The leaves of papaya have been shown to contain many active components such as papain, chymopapain, cystatin, tocopherol, ascorbic acid, flavonoids, cyanogenic-glucosides and glucosinolates that can increase the total antioxidant activity in blood and reduce lipid peroxidation level (Otsuki et al., 2010). The alkaloids, flavonoids, saponins, tannin, and glycosides are related with antioxidant activity. CP leaf extract was also found to have antibacterial effect (Romasi & Karina, 2011), antitumor, and immunomodulator activities (Otsuki et al., 2010).

The leaves also contain cardiac glycosides, antherquinones, carpaine, pseudocarpaine, phenolic compounds (Owoyele et al., 2008; Junjar et al., 2011). The contraceptive of CP leaves had been contributed by increased oxidative stress either due to increased free radical release or the decreased antioxidant defense system as well as an associated derangement of protein content of the testes (Kusemiju et al., 2012). An increase in platelet count in mice was reported by Sathasivam et al. (2009). Ahmad et al. (2011) reported that a 45 years old man with dengue fever got increase

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in platelet, leucocyte, and neutrophil count after oral intake of 25 ml water extract of CP twice daily for 5 consecutive days, compared with before treatment. The use of CP for dengue fever patient in Sri lanka had shown increased platelet and leucocyte count of 12 patients in 24 hours after administration of 5 ml CP leaf extract twice daily (Hettige, 2008).

Thrombocytopenia is life threatening in many diseases particularly in dengue which is an escalating problem in the world. Of the available methods for treating thrombocytopenia, the treatment method mainly depends on the disease severity. Nevertheless, due to certain side effects and the costs involved, the availability of treatment for thrombocytopenia is limited. Present work was done to investigate the effect of leaf extract of *Carica papaya* on hematology and serology of Wistar rats specifically on Thrombocyte count.

**MATERIALS AND METHODS**

**Materials**
Commercially available syrup of CP leaves was used for current study. The study was carried out during November 2011 to June 2012.

**Experimental Animals**
Colony of the Wistar Rats was reared in the animal house of Department of Zoology, University of the Punjab, Lahore-Pakistan. The animals were kept in fully aerated room at room temperature (RT) 23-24°C and maintained with *ad libitum* access to water and food. All experiments were approved by the institutional animal care and use committee.

**Effect of Carica papaya Leaf extract on Blood chemistry**
Six Wistar rats were divided in two groups. Three animals were used as control and three as experimental. The dose given to the experimental animals was 0.5 ml of papaya leaf extract when their weight was 150±25 for 7 consecutive days which were at fasting for 4 hours before dose administration. The animals were kept under constant observation to study their behavior. After 7 days blood was collected. Hematological (CBC) and serological (LFT, LP) analysis were performed in the Clinical Health Center Laboratory of the University of the Punjab.

**Statistical analysis**
The data was presented in terms of mean and SEM, analyzed by descriptive and analytical (student t test) statistics, and P value of less than 0.05 was considered statistically significant. All analyses were made using Graph Pad Prism (version 5.00).

**RESULTS**

**Complete Blood Count (CBC)**
The observations made during the study were quite interesting. The mean total platelet count, MCH and MCV of rats treated with CP leaf formulation were significantly higher (780.00±14.05), (15.2±0.12), and (47.27±0.18) as compared to control receiving distilled water (637.00±40.93), (41.80±1.15), (14.2±0.31) respectively. There was a non-significant (p>0.05) increase in the WBC, hemoglobin (HGB) and hematocrit (HCT) recorded for rats in the test groups relative to that observed in the control group (Table 1).

Table 1. Effect of oral administration of *Carica papaya* leaf extract on hematology and serology of rat.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>Mean ± SEM</th>
<th>Treatment</th>
<th>Mean ± SEM</th>
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<th>Control</th>
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<th>Treatment</th>
<th>Mean ± SEM</th>
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<tbody>
<tr>
<td>PLT (×10^9/l)</td>
<td>637.00±40.93</td>
<td>780.00±14.05*</td>
<td>47.27±0.18*</td>
<td>41.80±1.15</td>
<td>MCV (fl)</td>
<td>7.26±0.51</td>
<td>7.15±0.31</td>
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<td>MCH (pg)</td>
<td>14.2±0.31</td>
<td>15.2±0.12*</td>
<td>37.67±1.20</td>
<td>58.67±4.41 ***</td>
<td>RBC (×10^12/l)</td>
<td>7.26±0.51</td>
<td>7.15±0.31</td>
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<tr>
<td>WBC (×10^9/l)</td>
<td>5.13±0.84</td>
<td>7.10±1.01</td>
<td>30.37±2.07</td>
<td>33.80±1.53</td>
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<td>HCT%</td>
<td>30.37±2.07</td>
<td>33.80±1.53</td>
<td>12.83±0.92</td>
<td>13.43±0.62</td>
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<td>HGB (g/dl)</td>
<td>12.83±0.92</td>
<td>13.43±0.62</td>
<td>8.33±4.33</td>
<td>119.67±2.67**</td>
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<tr>
<td>Blood</td>
<td>Cholesterol</td>
<td>63.00±4.98</td>
<td>65.33±2.85</td>
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<tr>
<td>Lipid Profile</td>
<td>Triglycerides</td>
<td>63.00±4.98</td>
<td>65.33±2.85</td>
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<tr>
<td>V.L.D.L (mg/dl)</td>
<td>18.33±1.76</td>
<td>10.33±3.3*</td>
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Values are expressed as mean ± standard error of mean. PLT; platelet count, MCV; Mean Corpuscular Volume, MCH; Mean Cell Haemoglobin, RBC; Red Blood Cell, WBC; White Blood Cell, HCT; Hematocrit, HGB; Haemoglobin, ALP; Alkaline Phosphatase, ALT; Alanine Amino-transferase , *p & **p value less than 0.05, (p < 0.05) significant value, ***p value significant (p<0.0001).
Effect of C. papaya leaf extract on Liver function test

Serum activity of ALK-Phosphatase, biomarker of liver toxicity was significantly elevated in treated group (194.00±24.36 U/L) when compared to control (58.67±4.41 U/L) (p< 0.0001) (Table 1), while other two markers of liver toxicity, bilirubin and ALT had non-significant rise 0.43±0.03, 30.50±2.50 as compared to controls 0.41±0.01, 37.67±1.20 respectively (Table 1).

Effect of C. papaya leaf extract on Lipid profile

Serum cholesterol and Very low density lipids (V.L.D.L) in CP leaf extract treated rats showed a significant rise (119.67±2.67), (10.33±1.76) in comparison to control (82.33±4.33), (18.33±1.76), respectively (Table 1). There was a slight increase observed in triglycerides (65.33±2.85) compared with control (63.00±4.98) but this increase was non-significant (p>0.05) (Table 1).

DISCUSSION

Herbal medicines are used because of the fact that plants contain natural ingredients that can promote health and alleviate illness (Komal et al., 2010). They make an enormous contribution to primary health care and have shown great potential in modern phytomedicine against numerous infirmities and the complex diseases and ailments of the modern world. There will always be risks when appropriate regulations do not handle the appropriate formulation of the remedies or when self-medication fosters abuse (Mukesh et al., 2010).

The CP leaf extract was well tolerated by rats showing no overt signs of stress, aversive behavior or behavioral changes. Previous observations have shown no adverse effects or mortality under acute toxic condition due to orally administered CP leaf extract at 2000 mg/kg body weight (Afzan et al., 2012). Present study showed statistically significant rise in the mean Thrombocyte count values of rats after oral administration of Carica papaya leaf extract relative to the rats in the control group receiving distilled water. Mean MCV, and MCH values also increased. These results are in agreement with previous observations of increase in platelet count after treatment with leaf extract of Carica papaya. CP leaf extract has been found to accelerate the increase in platelet count, and shortened the hospitalization period (Yunita et al., 2012). A significant increase in the platelet counts has been observed after oral administration of freshly prepared, mature leaf concentrate of C. papaya. Both mature and immature leaves of C. papaya have the potential to be developed as a plant based therapeutic agent for thrombocytopenia (Gammulle et al., 2012). Juice consumption during the course of dengue infection had the potential to induce the rapid production of platelets (Subenthiran et al., 2013).

Liver function test to explore the hepatotoxicity had shown a significant rise in ALK-Phosphatase activity which indicated some kind of abnormality in bile duct. Level of cholesterol and very low density lipids were also increased significantly, which had an associated risk for cardiovascular disease. One previous study had described safety for oral consumption of CP leaf extract over a period of 3 days without hepatotoxicity, renal toxicity, haematotoxicity and neurotoxicity. Hepatotoxicity in present experiment might be due to administration of dose for longer period of time although dose used in the experiment (0.5ml) was lower than used in other experiment (0.72ml/100g) (Gammulle et al., 2012).

The platelet increasing effect after 7 days oral adminstration of the CP leaf extract was evident from the present study that illustrated an exact mechanism of Thrombocyte formation from megakaryocyte as under normal healthy body conditions, platelets are produced from megakaryocytes within 4 to 6 days (Choi et al., 1995). From this it could be concluded that increased platelet production may be due to megakaryopoietic stimulatory activity. Increased platelet production by C. papaya leaf extract might be due to Vitamin C present in CP leaf (Nwofia & Ojmelukwe, 2012). Vitamin C is a powerful antioxidant and high doses of it might prevent free-radical mediated damage of the platelets (Olas & Wachowicz, 2002).

It can be concluded from the present study that Carica papaya leaf extract might be associated with the increase of thrombocyte count but consumption for longer period could cause hepatotoxicity and risk for cardiovascular disease.

REFERENCES


