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EFFECTS OF *Carica papaya* LEAF EXTRACT SUSPENSION ON CARBOPLATIN INDUCED THROMBOCYTOPENIA IN MICE

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AUTHORS' CONTRIBUTIONS

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Plants and plant-based products have been active to stop numerous human diseases since ancient times. *Carica papaya Linn*. From the Caricaseae family, is perennial usually unbranched, smooth stem and long-stalked leaves. Papaya leaf extract (PLE) has a therapeutic role in the action of numerous human diseases due to the existence of rich source of phytochemicals, minerals and vitamins. From this study it was found that *Carica papaya* leaf significantly increases the thrombocyte count and prevents chemotherapy induced thrombocytopenia. The effect starts immediately from day2. But the effect on neutrophil count is not conclusive as the count increased only on the last four days of observation. In future if developed as an anti-cancer drug, it can be either given alone without any complication of thrombocytopenia or can be combined with other anticancer drugs preventing thrombocytopenia induced by them. However the substances responsible for this action have to be identified and isolated. There is also need for further studies on experimental animals and human beings that may provide definitive and sure data regarding its usefulness, exact mode of action and therapeutic utilization. Once the exact mode of action is known it can be tried in other thrombocytopenic conditions and also will be a new generation of drugs in the treatment of cancer.

Keywords: *Carica papaya* leaf; neutrophil count; carboplatin; thrombocytopenia.

1. INTRODUCTION

Thrombocytopenia is a relative decrease of platelets in blood.A normal human platelet count ranges from 150,000 to 450,000 platelets per microliter of blood. These limits are determined by the 2.5th lower and upper percentile, so values outside this range do not necessarily indicate disease [1]. Low platelet levels

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do not lead to clinical problems; rather, they are picked up on a routine full blood count. Occasionally, there may be bruising, particularly purpura in the forearms, petechiae, nosebleeds and bleeding gums. Inspection typically reveals evidence of bleeding (petechiae or ecchymoses), along with slow, continuous bleeding from any injuries or wounds. Adults may have large, blood-filled bullae in the mouth. If the person's platelet count is between 30,000 and 50,000/mm3, bruising with minor trauma may be expected; if it is between 15,000 and 30,000/mm3, spontaneous bruising will be seen (mostly on the arms and legs). Life-threatening bleeding also can occur [2].

Cancer prevention includes primary and secondary prevention methods. Primary prevention refers to avoiding cancer-causing substances in the environment or dietary elements associated with increased risk; dietary supplementation with putative protective agents. Secondary prevention aims at early detection and removal of benign tumors of oral, cervical and breast cancers [Osborne et al (1997)]. It was estimated that in the year 2000, worldwide over 10 million new cases of cancer occurred (approximately 5.3 million men and 4.7 million women) and over 6 million people died from cancers [3]. The most frequently affected organs are lung, breast, colon, rectum, stomach and liver. The absolute number of new cancer cases is increasing rapidly, due to growth in size of the population, and increase in the proportion of elderly persons as a result of improved life expectancy following control of communicable diseases. In India, the life expectancy at birth has steadily risen from 45 years in 1971 to 62 years in 1991, indicating a shift in demographic profile. *Carica papaya* belongs to family caricaceae is a large plant, like a tree, without branches and it is a herbaceous plant because the stem does not have much wood and remains soft and green until its death [4]. The single stem grows from 5 to 10 m tall with all the leaves on the top. The leaves are large, deeply lobed, palmate, with long petiole; 50-70cm wide. Some plants have perfect (with female and male organs) flowers but other plants have flowers with only one sex (female or male) [5,6].

Generally, the fruit is oval to nearly round single chambered, cylindrical or spherical in size and, in some cases, like a big pear. Fruits are 15-50 cm long and 10-20 cm wide, and weigh up to 9 kg. The skin of the fruit is thin and tough; it is not eaten because it is too bitter. First, the skin is green but it changes to yellow in ripe fruits. In a ripe fruit, the pulp is yellow, orange, pink and even light red. Inside the fruit, there are many small black seeds.

The present study aimed to analyses effect of *Carica papaya* leaf suspension on neutrophil count of carboplatin given mice.

Picture 1. Morphological view

2. MATERIALS AND METHODS

Raw, mature and fully green *Carica papaya* leaf was obtained from the local market in the month of December 2009 and identified in department of Botany, University of Madras. Mice (mus musculus) of either sex weighing 20-30 gm were procured from Kings Institute, Guindy and were maintained at standard housing conditions. The mice were housed in cages (6 per cage) and provided with water and food *ad libidum.* The cage bed consisted of sawdust and was changed every three days to maintain good hygiene. Carboplatin reconstituted with sterile 0.9% NaCl and injected IP at a dose of 125 mg/kg to induce thrombocytopenia Carboplatin injected to mice as a single intraperitoneal injection at a dose of 125 mg/kg causes a significant, but reversible, thrombocytopenia. Peripheral platelet numbers stayed at pre injection levels for the first 5 days after injection of carboplatin and then droped rapidly over days 6 to 8. The thrombocytopenia plateaus between days 8 to 15. Platelet numbers rapidly returned to a control level over the next 2 days [7-9]. The data were statistically analyzed by using student t-test. P- value of less than 0.01 was considered to be highly significant.

2.1 Preparation of Extract

Medium sized fresh papaya leaves were washed with water. The leaves were crushed and squeezed through muslin cloth to obtain the juice. To standardize preparation no water was added and moderate pressure was applied during squeezing so that about 10 ml juices was obtained from each leaf. Fresh juice was prepared daily. Then the leaves juice extract was treat with rats as per animal design.

3. RESULTS AND DISCUSSION

This study was carried out with an attempt to evaluate effect of *Carica papaya* leaf suspension on carboplatin induced thrombocytopenia m mice. Data collected from the study are summarized below (Table 1 and Table 2).

In this study the *Carica papaya* leaf suspension shows increase m platelet count from day2 and remains increased till dayl 7. The increase in thrombocyte count in thrombocytopenia induced mice receiving papaya leaf shows significant ($p < 0.01$) rise on comparing with carboplatin alone group. In their study three groups were used. Group one received normal saline, group two received palm oil and group three received papaya leaf suspension. Thrombocyte counts were analyzed before (0 hour) and at 1, 2, 4, 8, 10, 12, 24, 48 and 72 hours after dosing. The thrombocyte counts in the control mice having received palm oil showed a similar rise as that observed in the saline controls. This therapeutic potential should be further investigated by a dose response experiment and by isolating and identifying the substances responsible for the release and/or production of the thrombocytes, followed by studies based on the use of the pure substances in suitable formulations [10-11].

Table 1. Results of Student's t-test for the platelet count comparison between, palm oil controls, carboplatin alone and animals having received carboplatin + *C. papaya* leaf suspension

Sl. no.	Days	Palm oil *vs* carboplatin alone		Carboplatin alone *vs* carboplatin + PLS	
		t	p	t	p
1	Dl	0.468	0.669	-0.722	0.489
2	D2	0.470	0.833	-6.091	0.000*
3	D3	0.11O	0.167	-9.081	0.000*
4	D4	4.413	0.4833	-12.362	0.000*
5	D5	4.155	0.4167	-20.612	0.000*
6	D6	3.508	0.06	-28.127	0.000*
7	D7	7.407	0.000*	-9.358	0.000*
8	D8	7.067	0.000*	-27.759	0.000*
9	D9	10.088	0.000*	-29.278	0.000*
10	D10	6.860	0.000*	-37.300	0.000*
11	D11	6.918	0.000*	-20.741	0.000*
12	D12	11.399	0.000*	-22.418	0.000*
13	D13	5.974	0.000*	-20.142	0.000*
14	D14	2.303	0.044	-19.277	0.000*
15	D15	-0.720	0.488	-10.911	0.000*
16	D16	-0.455	0.659	-17.025	0.000*
17	I D17	-0.930	0.374	-9.463	0.000*

** - $p < 0.01$ (statistically significant)*

Table 2. Results of Student's t-test for the white blood cell count comparison between, palm oil controls, carboplatin alone and animals having received carboplatin + *C. papaya* leaf suspension

Sl. no.	Days	Palm oil vs carboplatin alone		Carboplatin alone vs carboplatin +PLS	
		t	p	t	p
1	DI	-0.869	0.405	0.769	0.460
2	D2	-0.406	0.693	0.145	0.888
3	D3	-0.947	0.366	-0.243	0.813
4	D4	-0.884	0.397	-0.660	0.524
5	D5	-0.689	0.506	1.754	0.110
6	D6	2.498	0.032	-2.429	0.36
7	D7	2.224	0.50	1.255	0.238
8	D8	4.038	0.002	-1.374	0.199
9	D9	4.499	0.001*	-2.191	0.53
10	D10	2.672	0.023	-3.518	0.06
11	D11	4.682	0.001*	-4.229	0.02
12	D12	4.963	0.001*	-4.376	0.01
13	D13	5.488	0.000*	-6.948	0.000*
14	D14	14.303	0.000*	-6.165	0.000*
15	D15	7.048	0.000*	-8.324	0.000*
16	D16	8.558	0.000*	-4.425	0.01
17	D17	7.665	0.000*	-5.662	0.000*

- $p < 0.01$ (statistically significant)

4. CONCLUSION

The above findings suggested that *Carica papaya leaf* suspension significantly prevents the thrombocytopenia induced by chemotherapy m mice. From the present new data, it may decide that papaya leaf (*Carica papaya*) interruption have antimicrobial effect and effect on blood constituents, growth performance. Papaya leaves extract can also be considered as leukocyte enhancer, efficient growth promoter and remarkable role in treating thrombocytopenia.

ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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