Journal of Interdisciplinary Histopathology
www.scopmed.org
DOI: 10.5455/jihp.20160321010001

Original Research

Unaltered stroma and parenchyma in vital organs of rat models following administration of low dose of *Carica papaya* leaf

Felix M. Onyije[1], Vivian C. Zenebo[2], Julius K. Bankole[3], Kester A. Digban[4], Godwin O. Avwioro[5]

[1]Department of Medical Laboratory Sciences, Faculty of Basic Medical Sciences, Niger Delta University, Wilberforce Island P.M.B 071, Yenagoa Bayelsa, Nigeria, [2]Histopathology Section, Medical Laboratory Services, Braithwaite Memorial Specialist Hospital, Rivers, Nigeria, [3]Department of Medical Laboratory Science, Ambrose Alli University, Ekpoma, Edo State, Nigeria, [4]Department of Medical Laboratory Science, Faculty of Basic Sciences, Igbinedion University, Okada, Nigeria, [5]Faculty of Science, Delta State University, Abraka, Nigeria

Address for correspondence:
Felix M. Onyije, Department of Medical Laboratory Sciences, Faculty of Basic Medical Sciences, Niger Delta University, Wilberforce Island P.M.B 071, Yenagoa Bayelsa, Nigeria. E-mail: onyijefelix@yahoo.com

Received: January 30, 2016
Accepted: March 21, 2016
Published: April 02, 2016

ABSTRACT

Background: The use of *Carica papaya* leaves for medicines and food in our rural areas is rampant, this is due to its availability and testimonies of its efficacy. **Objective:** This study was aimed at investigating the activities of *C. papaya* on the histo-architecture of some organs. **Materials and Methods:** About 20 Wistar rats were randomly divided into 4 groups of 5 each and received tap water, 2.5, 5, and 7.5 g/kg of ethanolic extract of *C. papaya* PO once a day for 14 days after which biochemical analyses was performed on the blood samples. The tissues were examined histologically. **Results:** Albumin was significantly increased (37.6 ± 2.70) in Group B (5 mg/kg) when compared with the control (32.4 ± 2.30). AST decreased significantly in all the treatment groups (68 ± 1.58, 87.4 ± 403, and 89 ± 1.58) when compared with the control (93.6 ± 1.14). ALT decreased in all groups but was significant in Group C (7.5 mg/kg) 22.8 ± 2.16 when compared with the control (30 ± 2.12). Urea decreased significantly in all the groups (3.34 ± 0.11, 3.78 ± 0.50, and 3.36 ± 0.28), creatinine decreased significantly in Group B (35.4 ± 2.79) when compared to their controls (4.52 ± 0.37 and 50.8 ± 6.37), respectively. Na^+ and K^+ significantly decreased in Groups C and B, respectively; there was no significant difference in other groups and electrolytes. There was increased level of both packed cell volume and hemoglobin significantly. Histologically, there were no tissue alterations in all the treatment groups. **Conclusion:** Complementary and alternative medicine is fast gaining popularity; this necessitates swift research on various dose ranges.

KEY WORDS: Complementary and alternative medicine, hepatocyte, podocyte

INTRODUCTION

The Center for Complementary and Alternative Medicine (CAM) in the US classified CAM into five categories among which include biologically based therapies (herbs, foods, vitamins, and other dietary supplements, including natural products such as shark cartilage). CAM is defined by the National Institute of Health as a group of diverse medical

and health care systems, practices, and products that are not presently considered to be part of conventional medicine [1-4].

The use of plants for medicine in the world predates written history. It was recorded that the ancient Egyptian medicine of 100 BC was basically herbs [5]. The use of CAM and traditional medicine (TM) varies widely between and within countries, in developing nations; TM is the major source of health care [6].

Carica papaya leaf is one of the herbs that has been in use, and there have been different reports on its origin [7] involving most countries of Africa, Asia, and America. It belongs to the family of Caricaceae and is primarily cultivated for the importance of its fruit and leaves [8,9]. Its leaves contain crude protein, carbohydrate, crude fiber, Ca, Mg, and Fe [10], it is a source of carotenoids, vitamin C, thiamine, riboflavin, niacin, vitamin B6, and vitamin K [11]. Phytochemical analysis of *C. papaya* leaf revealed the presence of phenols, alkaloids, steroids, glycosides, saponins, flavonoids, and tannins [12]. It has been reported to be of great medicinal value in the treatment of several diseases which includes tumor [13], colic, beriberi, asthma [14], malaria, fever, antidiabetic, antidiabetic wound healing, and anticancer activities [15-22].

MATERIALS AND METHODS

Collection and Ethanolic Extraction of *C. papaya* Leaves

The leaves of *C. papaya* were obtained from the premises of the School of Health Science and Technology, Port Harcourt, located between Latitude 4°45'N and Latitude 4°55'N, and Longitude 6°55'E and Longitude 7°05'E in Rivers State, Nigeria. The leaves were dried and pulverized. The powered material was extracted in 95% ethanol for 48 h, filtered and concentrated using a regulated water bath. The extract obtained was reconstituted with water to give the required dosage of 2.5.5, and 7.5 mg/kg body weight.

Experimental Animals

Twenty Wistar rats were obtained from the animal house of Nnamdi Azikiwe University, Nnewi Campus, Anambra State and kept in the School of Health Science and Technology, Port Harcourt. The animals were acclimatized for 7 days in cages under standard laboratory conditions of 27 ± 2°C, relative humidity 50 ± 15%, and normal photo period (12 h dark/12 h light).

Experimental Design

The animals were divided into four groups of five rats each, and the extract was administered once per day PO for 14 days as follows. They also had normal feeds and water regularly.

Control group: Received water.
Group A: Received 2.5 mg/kg of *C. papaya* extract.
Group B: Received 5 mg/kg of *C. papaya* extract.
Group C: Received 7.5 mg/kg of *C. papaya* extract.

Serum Analysis

Blood samples obtained from the rats were kept in a plain vial and centrifuged at 5000 rpm for 10 min at room temperature to obtain serum. Serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), albumin, total bilirubin, urea, creatinine, and electrolytes were determined using standard methods.

Packed Cell Volume (PCV) and Hemoglobin (Hb)

Blood was collected into ethylenediaminetetraacetic acid vial for the analysis of PCV and Hb using standard method.

Tissue Preparation for Microscopy

The respective organs were dissected and fixed in 10% formal saline. They were processed by dehydrating in ascending grades of alcohol followed by impregnation and embedding in paraffin wax. Paraffin sections were cut at 5 μm thickness and stained with hematoxylin and eosin (H and E) for general tissue architecture.

Statistical Analysis

Data were analyzed using one-way Analysis of Variance (ANOVA), and group means were compared using the Dunnett's Multiple Comparison Test using GraphPad Prism® software Version 5.01. $P < 0.05$ were considered statistically significant.

The research was conducted in line with the animal research: Reporting *in vivo* experiments (ARRIVE) guidelines [23].

RESULT

Biochemical Analysis

In evaluating the liver function biochemically, there was no significant difference in total bilirubin when compared the treatment groups (5 ± 2.12; 5 ± 0.17; and 5 ± 1.41, respectively), when compared with the control (5 ± 2.82). There was increased albumin and was found to be statistically significant ($P < 0.05$) (37.6 ± 2.70) in Group B (5 mg/kg) when compared with the control (32.4 ± 2.30). AST decreased significantly in all the treatment groups (68 ± 1.58, 87.4 ± 403, and 89 ± 1.58) when compared with the control (93.6 ± 1.14). ALT decreased in all the groups but was significant in Group C (7.5 mg/kg) 22.8 ± 2.16 when compared with the control (30 ± 2.12) as seen in Table 1. Two kidney function markers (urea and creatinine) were analyzed and urea decreased significantly in all the groups (3.34 ± 0.11, 3.78 ± 0.50, and 3.36 ± 0.28), whereas creatinine decreased in Group C (50.4 ± 5.68) but was statistically significant ($P < 0.05$) in Group B (35.4 ± 2.79) when compared to their controls (4.52 ± 0.37 and 50.8 ± 6.37), respectively, as illustrated in Table 2. In Table 3, electrolyte analysis (Na^+, K^+, HCO_3^-, Cl^-, and AG) Na^+ and K^+ significantly decreased in Groups C and B, respectively; there was no significant difference in other groups and electrolytes.

Table 1: Liver function analysis

Parameter	Control	Group A (2.5 mg/kg)	Group B (5 mg/kg)	Group C (7.5 mg/kg)
Total Bilirubin	5±2.82	5±2.12	5±0.17	5±1.41
Albumin	32.4±2.30	31.6±1.14	37.6±2.70**	31.4±1.14
AST	93.6±1.14	68±1.58***	87.4±4.03**	89±1.58*
ALT	30±2.12	27.4±4.82	28±2.91	22.8±2.16*

Each value represents the mean±standard deviation, values are statistically different from control (* p < 0.05, **p <0.01 and *** p<0.001)
One-way Analysis of Variance (ANOVA)+Tukey-Kramer multicomparison test, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase

Table 2: Serum urea and creatinine analysis

Parameter	Control	Group A (2.5 mg/kg)	Group B (5 mg/kg)	Group C (7.5 mg/kg)
Urea	4.52±0.37	3.34±0.11***	3.78±0.50*	3.36±0.28***
Creatinine	50.8±6.37	51.8±0.83	35.4±2.79***	50.4±5.68

Each value represents the mean±standard deviation, values are statistically different from control (* p < 0.05, **p <0.01 and *** p<0.001)
One-way Analysis of Variance (ANOVA)+Tukey-kramer multicomparison test

Table 3: Electrolyte analysis

Parameter	Control	Group A (2.5 mg/kg)	Group B (5 mg/kg)	Group C (7.5 mg/kg)
Na^+	137.6±2.88	135.8±0.83	138±2.91	132.8±2.16*
K^+	7.8±0.46	6.14±0.11***	8.18±0.24	7.64±0.23
Cl^-	103±1.93	-	103.4±2.50	98.2±2.28
HCO_3^-	14.2±2.86	14.1±0.54	12.8±2.16	15.2±2.16
Ag^+	23.8±9.28	20.4±1.14	21.8±3.76	20.4±4.33

Each value represents the mean±standard deviation, values are statistically different from control (* p < 0.05, **p <0.01 and *** p<0.001)
One-way Analysis of Variance (ANOVA)+Tukey-Kramer multicomparison test

PCV and Hb

The PCV of the animals increased in all the groups (36 ± 2.54, 38 ± 3, and 44.4 ± 2.30) and was statistically significant in Group C (44.4 ± 2.30) when compared to the control (34 ± 3.16) [Figure 1]. Similarly, the Hb also increased in all the groups (12.00 ± 0.863, 12.68 ± 0.8438, and 14.80 ± 0.7714) and was significant in Group C (14.80 ± 0.7714) too when compared to the control (11.34 ± 1.060). This is illustrated in Figure 2.

Histological Analysis

Photomicrographs of liver Slides 1 and 2 (control) show normal portal triad with well-radiating hepatocytes and sinusoid [Figure 3]. Groups A-D also display normal central vein, hepatocyte, and sinusoid. Figure 4 photomicrograph of kidney, Slides 1 and 2 (control) with normal renal corpuscle and proximal convoluted tubules. Figure 5 photomicrograph of heart, Slides 1 and 2 (control) with normal myocardium and well-branching fibers with nuclei. There were no histological differences between the experimental groups [Slides 3-8 of Figures 3-5] when compared with the control slides.

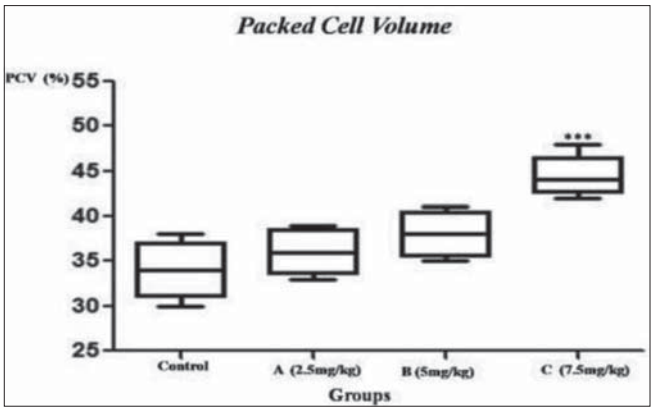

Figure 1: Packed cell volume. Each value represents the mean ± standard deviation, values are statistically different from control at P < 0.05*** 0.0001 One-way Analysis of Variance + Tukey-Kramer multicomparison test

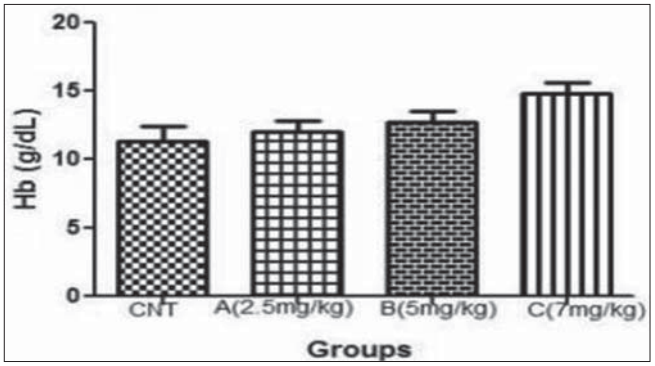

Figure 2: Determination of hemoglobin. Each value represents the mean ± standard deviation, values are statistically different from control at P < 0.05*** 0.0001 One-way Analysis of Variance + Tukey-Kramer multicomparison test

DISCUSSION

Histologically, the liver is made up of lobules, which are hexagonal in shape; the main functional cell of the liver is the hepatocyte. These cells are in a thin plate separated by fine vascular sinusoids through which blood flows. The portal vein, hepatic artery, and bile duct (portal triads) travel together through the liver parenchyma. Each of the liver lobules has a central vein, which drains the lobule. The liver which detoxifies drugs and chemicals in the body is also responsible for fat metabolism, carbohydrate metabolism, protein metabolism, storage, intermediary metabolism, and secretion [24]. Our results revealed no visible alteration in the liver using the light microscope [Figure 3], which is similar to the researches of Zakiah *et al*. [25] and Umana *et al*. [26] where they reported normal histology of the liver following administration of *C. papaya* leaf and seed extract, respectively. The histology result of the liver in this research corroborates with the liver function biochemical (bilirubin, AST, and ALT) analysis [Table 1], where there was no significant difference in total bilirubin of treatment groups (5 ± 2.12, 5 ± 0.17, and 5 ± 1.41, respectively), when compared with the control (5 ± 2.82). The nonsignificant decrease of serum

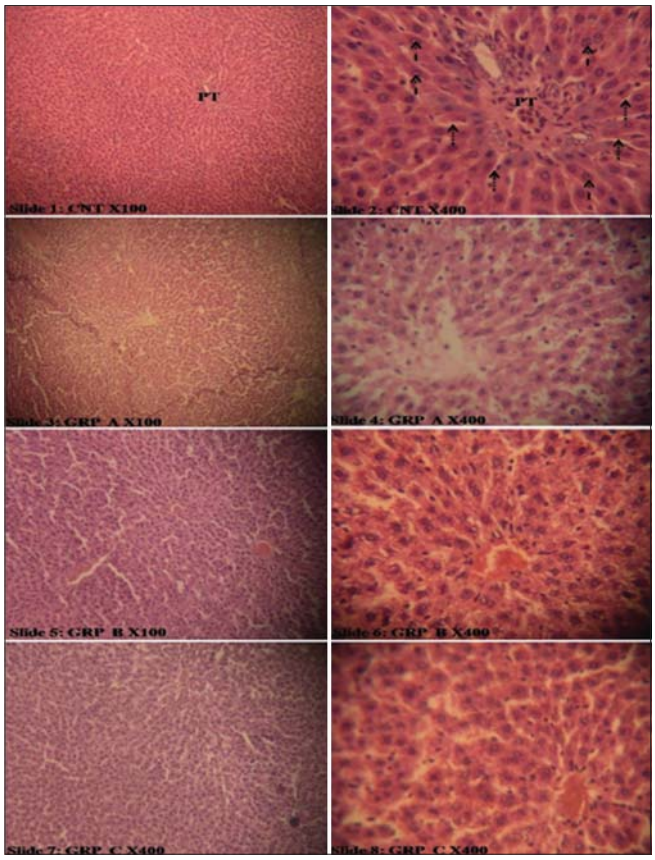

Figure 3: Photomicrograph of liver: Slide 1 and 2 controls (CNT) with normal portal triad (PT) with well-radiating hepatocyte (dash arrow) and sinusoid (dot arrow). Group A to D also displays normal central vein, hepatocyte, and sinusoid. There are no histological differences between in the experimental groups (Slides 3-8) when compared with the control group (Slides 1 and 2). H and E, ×100 and ×400

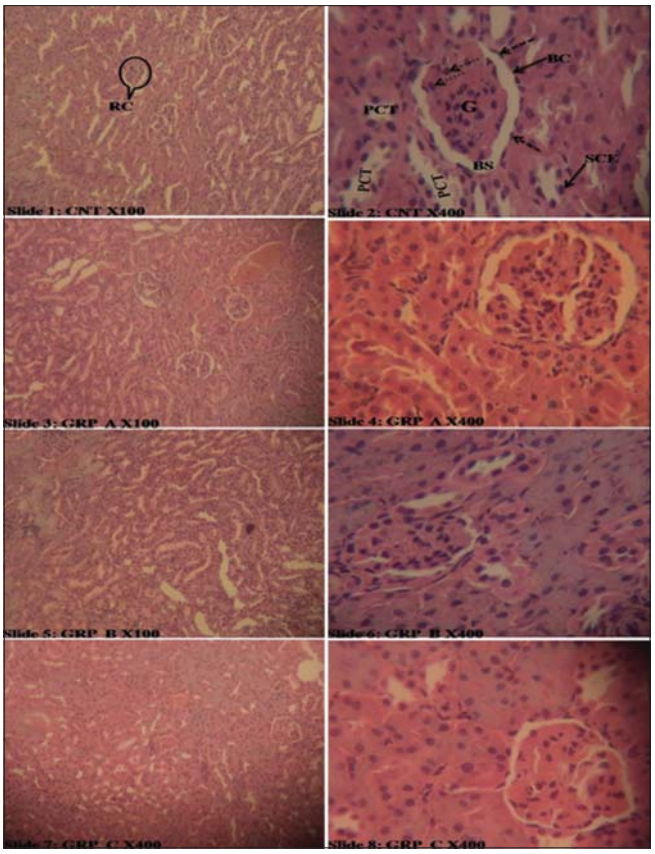

Figure 4: Photomicrograph of kidney Slides 1 and 2 controls (CNT) with normal renal corpuscle (RC) formed by the glomerulus (G) with well circumscribed Bowman's capsule (BC). A space that demarcates glomerulus (G) from the Bowman's capsule (BC), the Bowman's space (BS) is visible. The proximal convoluted tubules (PCT), it is simple cuboida epithelium (SCE). Simple squamous epithelium (dash arrow) and Podocytes (dot arrow) are all normal. There are no histological differences between in the experimental groups (Slides 3-8) when compared with the control group (Slides 1 and 2). H and E ×100 and ×400

total bilirubin is probably not of clinical significance, unlike its increase, which is an indication of hepatocellular damage. In the same vein, the significant decrease of AST in all the treatment groups (68 ± 1.58, 87.4 ± 403, and 89 ± 1.58) when compared with the control (93.6 ± 1.14) and ALT which decreased in all the groups though significant in only Group C (22.8 ± 2.16) when compared with the control (30 ± 2.12) is an indication of hepatoprotective activity of *C. papaya* leaf extract. This agrees with the report by Aashish *et al.* [27] where the activity of C. papaya leaf was evident by the significant reduction in the levels of all serum markers. Increased levels of the two parameters are indicative of necrosis of hepatocytes, myocardial cells, erythrocytes, or skeletal muscle cells [28-30]. The glomeruli and tubules (nephron) are the basic functional unit of the kidney playing a role in excretion of waste products, elimination of foreign substances, regulation of water, and control of most compounds among others. Urea and creatinine were analyzed to ascertain the integrity of kidney function; urea decreased significantly in all the groups (3.34 ± 0.11, 3.78 ± 0.50, and 3.36 ± 0.28), while creatinine decreased in Group C (50.4 ± 5.68) but was statistically significant in Group B (35.4 ± 2.79) when compared to their controls (4.52 ± 0.37 and 50.8 ± 6.37), respectively [Table 2] [31]. Increase in serum urea and creatinine has been reported as an indication of renal impairment [28]. The reduction of the two parameters [Table 2] in this research is a pointer of normal renal function, this in evident in the photomicrograph of the kidney [Figure 4] where there was no histological distortion seen. This is in agreement with the research of Zakiah *et al*. [25] who report no effect on the kidney treated with *C. papaya* leaves and also the work of Tarkang *et al*. [32] where aqueous extract of the leaves of *C. papaya* treated for 28 and 90 days did not show any abnormality in renal parameters and liver enzymes. The leaves of *C. papaya* have been reported to be blood booster for the body [33], and also Claude and Paule [34] reported that the presence of iron in *C. papaya* leaves is an indication of its antianemic activity. These reports concur with this present study which is evidence in the PCV (36 ± 2.54, 38 ± 3, and 44.4 ± 2.30) and Hb (12.00 ± 0.863, 12.68 ± 0.8438, and 14.80 ± 0.7714) of the animals treated with *C. papaya* leaves increased in all the groups and was statistically significant in Group C of both PCV and Hb (44.4 ± 2.30 and 14.80 ± 0.7714), respectively, when compared to their controls (34 ± 3.16 and 11.34 ± 1.060) [Figures 1 and 2]. In the same vein, Claude and Paule [34] and Ayoola and

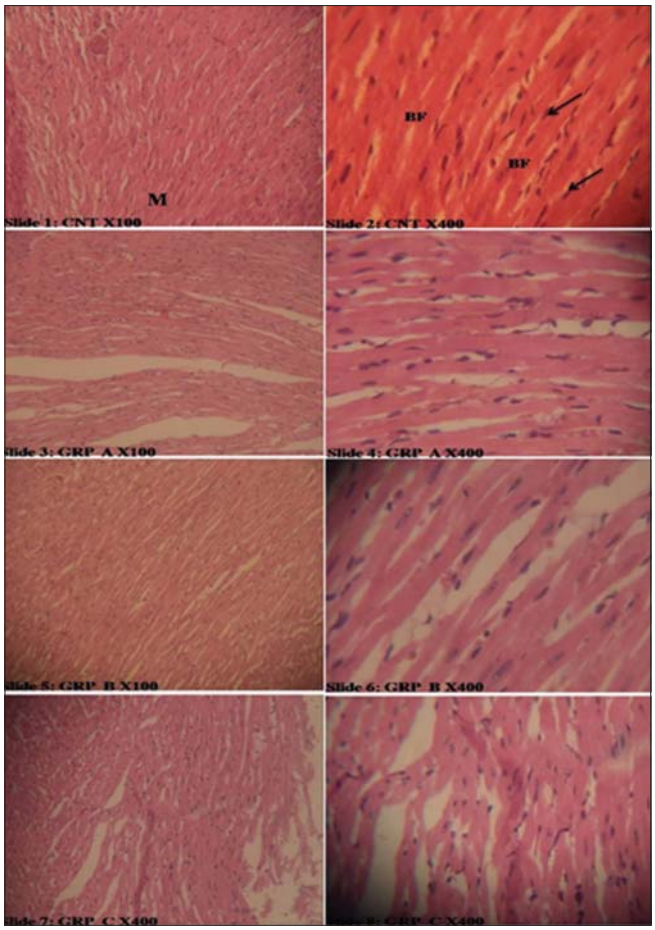

Figure 5: Photomicrograph of heart: Slide 1 and 2 (CNT) with normal myocardium (M), well-branching fibers (BF) with nuclei (arrows). There are no histological differences between in the experimental groups (Slides 3-8) when compared with the control group (Slides 1 and 2), H and E, ×100 and ×400

Adeyeye [13] also stated that presence of minerals such as Mg, K, Ca, Mn, Na, and Fe in *C. papaya* leaves indicate its usefulness in the functioning of the heart. The histological assessment of the heart in this research show normal histological features when examined with the light microscope [Figure 5]. This is similar to the result of Oduola *et al*. [35] where they reported that all tissues examined (normal and experimental) were essentially normal.

CONCLUSION

This basic research tilts toward the safety of *C. papaya* leaves as evident in various results. Its uses for many generations also attest to this, despite the various reports of its revisable and irreversible danger in some parts of the body. However, molecular analysis to ascertain the level of safety is strongly recommended.

ACKNOWLEDGMENTS

Authors wish to acknowledge Iboomni L, Mbaba O, Eletuo PC, Ugwu C, and Joshua AR for their contribution toward this research.

REFERENCES

1. National Center for Complementary and Alternative Medicine (NCCAM). The Use of Complementary and Alternative Medicine in the United States. Bethesda, MD: National Institutes of Health; 2008. Available from: http://www.nccam.nih.gov/news/camstats/2007/camsurvey_fs1.htm. [Last accessed on 2015 Oct 25].
2. Kwan D, Hirschkorn K, Boon H. U.S. and Canadian pharmacists' attitudes, knowledge, and professional practice behaviors toward dietary supplements: A systematic review. BMC Complement Altern Med 2006;6:31.
3. Waldman SA, Terzic A. Pharmacology and Therapeutics: Principles to Practice. Philadelphia: Elsevier, W.B. Saunders; 2008. p. 1536.
4. Vohra S, Feldman K, Johnston B, Waters K, Boon H. Integrating complementary and alternative medicine into academic medical centers: Experience and perceptions of nine leading centers in North America. BMC Health Serv Res 2005;5:78.
5. Aggarwal BB, Sundaram C, Malani N, Ichikawa H. Curcumin: The Indian solid gold. Adv Exp Med Biol 2007;595:1-75.
6. Richardson MA, Straus SE. Complementary and alternative medicine: Opportunities and challenges for cancer management and research. Semin Oncol 2002;29:531-45.
7. Aradhya MK, Manshardt RM, Zee F, Morden CW. A phylogenetic analysis of the genus *Carica L*. (Caricaceae) based on restriction fragment length variation in a cpDNA intergenic spacer region. Genet Resour Crop Evol 1999;46:579-86.
8. Ong HC, Ruzalila BN, Milow P. Traditional knowledge of medicinal plants among the Malay villagers in Kampung Tanjung Sabtu, Terengganu, Malaysia. Indian J Tradit Knowl 2011;10(3):460-5.
9. Dick G. Papaya. A tantalising taste of the tropics, Maricopa County Master Gardener Volunteer Information, University of Arizona Cooperative Extension, 2003.
10. Godson E, Nwofia PO, Chinyere EJ. Chemical composition of leaves, fruit pulp and seeds in some *Carica papaya* (L) morphotypes. Int J Med Arom Plants 2012;2(1):200-6.
11. Suhas JV, Taslim TK, Vijay RR, Pragnesh ND, Hitendra SJ. Biochemical constituents in leaf of *Carica papaya* - Ethnomedicinal plant of Kachchh region. Int Lett Nat Sci 2014;12:16-20.
12. Natarajan S, Theivanai VR. Potential medicinal properties of *Carica papaya* Linn. - A mini review. Int J Pharm Pharm Sci 2014;6:2.
13. Ayoola PB, Adeyeye A. Phytochemical and nutrient evaluation of *Carica papaya* (Pawpaw) leaves. IJRRAS 2010;5:325-8.
14. Krishna KL, Paridhavi M, Patel JA. Review on nutritional, medicinal and pharmacological properties of papaya (*Carica papaya* Linn.). Nat Prod Rad 2008;7:364-73.
15. Otsuki N, Dang NH, Kumagai E, Kondo A, Iwata S, Morimoto C. Aqueous extract of *Carica papaya* leaves exhibits anti-tumor activity and immunomodulatory effects. J Ethnopharmacol 2010;127:760-7.
16. Adebayo JO, Krettlia AU. Medicinal plants used in Nigeria for the treatment of malaria. J Ethnopharm 2011;88:34-7.
17. Oboh G, Olabiyi AA, Akinyemi AJ, Ademiluyi AO. Inhibition of key enzymes linked to Type 2 diabetes and sodium nitroprusside - Induced lipid peroxidation in rat pancreas by water-extractable phytochemicals from unripe pawpaw fruit (*Carica papaya*). J Basic Clin Physiol Pharmacol 2013;46(30):1-14.
18. Mahmood AA, Sidik K, Salmah I. Wound healing activity of *Carica papaya* L. Aqueous leaf extract in rats. Int J Mol Med Adv Sci 2005;1:398-401.
19. Nayak SB, Pinto Pereira L, Maharaj D. Wound healing activity of *Carica papaya* L. in experimentally induced diabetic rats. Indian J Exp Biol 2007;45:739-43.
20. Nayak BS, Ramdeen R, Adogwa A, Ramsubhag A, Marshall JR. Wound-healing potential of an ethanol extract of *Carica papaya* (Caricaceae) seeds. Int Wound J 2012;9:650-5.
21. Gurung S, Skalko-Basnet N. Wound healing properties of *Carica papaya* latex: *In vivo* evaluation in mice burn model. J Ethnopharmacol 2009;121:338-41.
22. Collard E, Roy S. Improved function of diabetic wound-site macrophages and accelerated wound closure in response to oral supplementation of a fermented papaya preparation. Antioxid Redox Signal 2010;13:599-606.
23. Kilkenny C, Browne WJ, Cuthill IC, Emerson M, Altman DG. Improving bioscience research reporting: The ARRIVE guidelines for reporting animal research. PLoS Biol 2010;8:e1000412.

24. Barbara Y, James SL, Alan S, John WH. Wheater's Functional Histology. A Text and Colour Atlas. 5th ed. Edinburgh: Elsevier; 2006. p. 288-94.
25. Ismail Z, Halim SZ, Abdullah NR, Afzan A, Abdul Rashid BA, Jantan I. Safety evaluation of oral toxicity of *Carica papaya* Linn. Leaves: A subchronic toxicity study in Sprague Dawley rats. Evid Based Complement Alternat Med 2014;2014:741470.
26. Umana U, Timbuak JA, Musa SA, Hamman WO, Samuel A. Acute hepatotoxicity and nephrotoxicity study of orally administered aqueous and ethanolic extracts of *Carica papaya* seeds in adult Wistar rats. Asian J Med Sci 2013;5(3):65-70.
27. Aashish P, Tarun S, Pallavi B. Ameliorative effect of leaves of *Carica papaya* in ethanol and anti-tubercular drug induced hepatotoxicity. Br J Pharm Res 2013;3:648-61.
28. Uthman ED. Interpretation of Lab Test Profiles. Available from: http://www.web2.airmail.net/uthman/lab_test.html. [Last accessed on 2015 Oct 19].
29. Tietz NW. Clinical Guide to Laboratory Tests. Philadelphia: Saunders; 1983.
30. Friedman RB, Young DS. Effects of Diseases on Clinical Laboratory Tests. Washington, DC: American Association of Clinical Chemistry; 1980.
31. Lutz S. Blue. 2012. Histology - Female Reproductive System. The University of Western Australia Online Publication. Available from: http://www.bluehistology.com. [Last accessed on 2015 Oct 19].
32. Tarkang PA, Agbor GA, Armelle TD, Yamthe TL, David K, Mengue NY. Acute and chronic toxicity studies of the aqueous and ethanol leaf extracts of *Carica papaya* Linn. in Wistar rats. J Nat Prod Plant Resour 2012;2:617-27.
33. Giove Nakazawa RA. Traditional medicine in the treatment of enteroparasitosis. Rev Gastroenterol Peru 1996;16:197-202.
34. Claude B, Paule S. The Manual of Natural Living. 1st ed. Guildford: Biddles Ltd.; 1979. p. 98-101.
35. Oduola T, Bello I, Idowu T, Avwioro G, Adeosun G, Olatubosun L. Histopathological changes in Wistar albino rats exposed to aqueous extract of unripe *Carica papaya*. N Am J Med Sci 2010;2:234-7.

Source of Support: Nil, Conflict of Interest: None declared.