

## Ingestion of Aqueous Extract of Unripe *Carica Papaya* Has No Adverse Effect on Kidney Function

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**Abstract:** Aqueous extract of unripe *Carica papaya* is being used traditionally as an antisickling agent by some sickle cell patients in Western Nigeria. Investigation into effects of ingestion of the extract on kidney functions in sickle cell patients of different age groups, 2 to < 6 years (x 5.2), 6 to <12 years (x 9.7) and 12 years and above (x 21.4) was conducted using standard techniques. The plasma levels of sodium (Na<sup>+</sup>), potassium (K<sup>+</sup>), chloride (Cl<sup>-</sup>), bicarbonate (HCO<sup>3-</sup>) urea, creatinine, uric acid and calcium before ingestion of the extract and throughout the study period were within the reference range. It was concluded from the results obtained that the extract of unripe *Carica papaya* has no harmful effect on kidney functions.

**Key words:** Antisickling agent • Sickle cell patient • Kidney function • Unripe *Carica papaya*

### INTRODUCTION

The kidney is the chief regulator of all body fluids and is primarily responsible for maintaining homeostasis, or equilibrium of fluid and electrolytes in the body. The kidney main functions are urine formation, regulation of acid-base balance, excretion of waste products of protein metabolism, protein conservation and hormonal function [1, 2].

Nephrons are lost via toxic, anoxic, or immunological injury that may initially injure the glomerulus, the tubule or both together. Glomerular damage can involve endothelial, epithelial, or mesangial cells and/or the basement membrane [2].

Sickle cell disease is a life-long haemolytic anaemia caused by a single point mutation in the beta (β) chain of haemoglobin (Hb). A single nucleotide substitution (GTG for GAG) in the sixth codon of the globin gene results in the substitution of valine for glutamic acid on the surface of the variant-globin chain [3]. This change allows HbS to polymerize when deoxygenated, since valine can dock the complimentary sites on adjacent globin chains. The

polymerization of deoxygenated HbS is the primary indispensable event in the molecular pathogenesis of sickle-cell disease. It is dependent on intraerythrocytic HbS concentration, degree of cell deoxygenation, pH and the intracellular concentration of HbF [4].

The polymer is a rope-like fibre that aligns with others to form a bundle, distorting the red cell into classic crescent or sickled forms. These shapes interfere with a critical erythrocyte feature; its deformability [5]. These rigid sickle cells are responsible for the vaso-occlusive phenomenon that are characteristic of this disorder. The presence of other haemoglobins in the red blood cell, such as haemoglobin F, haemoglobin A, haemoglobin C and haemoglobin D, in that order, has antisickling effect on the polymerization of HbS [6, 7].

The aqueous extract of unripe *Carica papaya* has been reported to possess antisickling properties [8] and it is being used as an antisickling agent by some sickle cell patients in Western Nigeria. The minimum concentration of the extract that achieved maximum antisickling effect was established to be 1g/ml of saline and the antisickling agent was found to reside in the ethyl acetate fraction of

the extract [9]. The extract of unripe *Carica papaya* has been shown to possess no adverse effect on the functions of liver, kidney and bone marrow in Wistar albino rats [10]. Liver function was reported to be normal in seven-year old sickle cell children that ingested the extract for seven days [8], data on safety and therapeutic effect of long term ingestion of the aqueous extract on liver function in different age groups of sickle cell patients has also been documented [11].

Thomas and Ajani [8] reported normal kidney function in seven-year old sickle cell children that ingested the extract for seven days, kidney function on long term ingestion of the extract and in different age groups of sickle cell patients has not been determined, therefore the present work is undertaken to investigate the effect of ingestion of extract of unripe *Carica papaya* on kidney function of sickle cell patients of different age groups over a relatively long period.

## MATERIALS AND METHODS

**Plant Authentication and Extract Preparation:** Matured fresh unripe *Carica papaya* fruit was obtained in a local garden in Ile-Ife and was authenticated at the herbarium of the Botany Department, Obafemi Awolowo University, Ile-Ife, the herbarium number is 14729. The fruit was peeled and the cream coloured seeds inside discarded, 100g of the fruit was immersed in 100ml of water and left at room temperature for 72 hours. The extract was sieved into a clean bottle. The extract was sieved into a clean bottle.

**Category of Patients:** Patients were categorized into three based on their age as follows: there were fifteen patients in each group.

### Category One

**Children:** 2 to <6 years:- (x 5.2) one teaspoonful (5ml) of

aqueous extract of unripe *Carica papaya* was ingested 3 times daily for 6 months.

### Category Two

**Children:** 6 to <12 years(x 9.7) two teaspoonful (10ml) of the aqueous extract of unripe *Carica papaya* was ingested 3 times daily for 6 months.

### Category Three

**Adults:** 12 years and above (x 21.4) Three teaspoonful (15 ml) of the aqueous extract of unripe *Carica papaya* was ingested 3 times daily for 6 months.

**Collection of Specimen:** Five milliliters of blood was collected from each of the patients before extract ingestion through clean venepuncture and dispensed into lithium heparin bottle. Blood collection was repeated 24 hours, 1 week, 2 weeks, 3 weeks, 1 month, 2 months, 3 months, 4 months, 5 months and 6 months after daily ingestion of the extract throughout the period of the study. Blood samples were analyzed on the day of blood collection.

**Analytical Procedure:** Sodium (Na) and potassium (K<sup>+</sup>) were determined by flame photometry, chloride (Cl<sup>-</sup>), bicarbonate (HCO<sub>3</sub><sup>-</sup>), urea, creatinine uric acid and calcium were determined using standard techniques [12].

**Statistics:** The mean and standard deviation and the level of significance for the differences between means were computed by students test SPSS 6.

## RESULTS

The effects of intake of extract of unripe *Carica papaya* were presented in Tables 1, 2 and 3. In all age groups, the plasma levels of all the parameters were within

Table 1: Effect of intake of extract of unripe *Carica papaya* on kidney function test in sickle cell patients (2- <6years,x5.2)

Reference Range	Na <sup>+</sup> mmol/L	K <sup>+</sup> mmol/L	CL mmol/L	HCO <sub>3</sub> <sup>-</sup> mmol/L	Urea mmol/L	Cr mmol/L	Uric acid mmol/L	Calcium mmol/L
	120-140	3-5	95-110	20-30	2.5-5.8	50-110	0.12-0.36	2.25-2.75
Intervals	130.13±2.61	3.09±0.10	92.40±2.97	23.87±2.07	2.81±0.28	74.33±6.87	0.14±0.02	2.04±0.18
Before intake								
24 hours after	130.60±2.95	3.09±0.10	91.07±2.78	24.20±1.61	2.79±0.27	75.67±6.68	0.14±0.02	2.07±0.18
1 week after	132.53±2.90	3.23±0.14	93.80±2.30	24.00±1.25	2.82±0.28	77.87±7.91	0.13±0.02	2.17±0.16
2 weeks after	132.13±2.42	3.23±0.25	95.60±1.50	25.33±1.00	2.86±0.33	75.23±6.14	0.16±0.02	2.20±0.11
3 weeks after	132.93±3.47	3.30±0.10	95.00±3.15	24.80±1.15	2.80±0.28	77.50±7.07	0.16±0.02	2.23±0.20
1 month after	131.73±3.90	3.30±0.21	95.80±2.40	25.23±1.00	2.91±0.35	80.60±9.60	0.15±0.01	2.23±0.16
2 months after	132.27±3.47	3.33±0.14	94.00±3.18	25.60±1.68	2.87±0.27	80.14±9.55	0.17±0.02	2.25±0.13
3 months after	134.80±2.62	3.36±0.18	96.33±3.68	25.13±0.83	3.00±0.30	79.64±8.93	0.15±0.02	2.27±0.13
4 months after	133.93±2.73	3.31±0.20	95.67±2.85	25.20±1.37	2.81±0.34	81.46±10.43	0.16±0.03	2.31±0.11
5 months after	134.80±1.42	3.37±0.14	94.87±3.94	25.00±1.36	2.80±0.32	76.30±10.16	0.16±0.03	2.27±0.14
6 months after	133.07±3.10	3.30±0.22	95.89±4.51	25.20±1.15	2.70±0.26	75.26±14.82	0.16±0.03	2.34±0.14

Table 2: Effect of intake of extract of unripe *Carica papaya* on kidney function test in sickle cell disease patients (6- < 12years, x9.7)

Reference Range	Na <sup>+</sup> mmol/L	K <sup>+</sup> mmol/L	CL mmol/L	HCO <sub>3</sub> <sup>-</sup> mmol/L	Urea mmol/L	Cr mmol/L	Uric acid mmol/L	Calcium mmol/L
	120-140	3-5	95-110	20-30	2.5-5.8	50-110	0.12-0.36	2.25-2.75
Intervals Before intake	127.93±6.98	3.57±0.41	96.87±3.07	22.67±2.85	3.15±0.47	87.60±5.49	0.18±0.02	2.15±0.09
24hours after	128.33±6.96	3.51±0.35	97.13±2.33	24.33±3.24	3.15±0.42	87.60±5.70	0.18±0.02	2.14±0.09
1 week after	129.40±6.84	3.48±0.33	97.73±1.87	24.93±1.53	3.15±0.35	87.27±4.76	0.19±0.02	2.18±0.09
2 weeks after	129.27±5.93	3.45±0.29	97.20±2.93	24.93±1.44	3.10±0.39	87.13±7.87	0.18±0.02	2.24±0.07
3 weeks after	129.20±5.82	3.57±0.19	97.53±2.93	23.47±5.57	3.22±0.31	91.07±5.47	0.18±0.02	2.27±0.10
1 month after	127.87±3.89	3.50±0.26	96.47±3.09	24.33±1.45	3.28±0.38	89.60±5.51	0.19±0.02	2.27±0.09
2 months after	128.13±4.48	3.49±0.31	97.47±3.00	25.00±1.31	3.31±0.42	88.93±4.89	0.19±0.02	2.27±0.09
3 months after	128.20±4.78	3.34±0.25	97.47±2.13	25.00±1.31	3.29±0.26	91.60±4.97	0.19±0.02	2.27±0.10
4 months after	130.07±5.08	3.48±0.27	97.27±v4.30	26.07±0.88	3.10±0.26	91.13±6.92	0.18±0.02	2.34±0.12
5 months after	130.60±6.33	3.45±0.16	96.13±1.81	25.13±1.13	3.23±0.27	89.80±5.63	0.18±0.03	2.32±0.11
6 months after	130.40±6.01	3.60±0.22	95.20±2.78	25.73±1.28	3.21±0.31	88.13±5.39	0.19±0.04	2.35±0.10

n=15

Table 3: Effect of intake of extract of unripe *Carica papaya* on kidney function test in sickle cell disease patients (12 years and above, x 21.4)

Reference Range	Na <sup>+</sup> mmol/L	K <sup>+</sup> mmol/L	CL mmol/L	HCO <sub>3</sub> <sup>-</sup> mmol/L	Urea mmol/L	Cr mmol/L	Uric acid mmol/L	Calcium mmol/L
	120-140	3-5	95-110	20-30	2.5-5.8	50-110	0.12-0.36	2.25-2.75
Intervals before intake	130.07±5.66	3.51±0.43	96.47±4.22	21.60±1.12	3.22±0.35	83.20±6.48	0.17±0.02	2.15±0.11
24 hours after	129.47±5.75	3.52±0.30	97.87±4.03	23.20±1.26	3.27±0.35	83.00±6.44	0.17±0.02	2.16±0.09
1 week after	129.93±6.16	3.60±0.24	97.93±4.50	25.00±1.00	3.23±0.24	83.33±6.68	0.17±0.02	2.22±0.09
2 weeks after	131.27±6.09	3.60±0.24	98.60±3.70	25.07±1.22	3.28±0.38	82.67±6.61	0.16±0.03	2.22±0.09
3 weeks after	130.87±4.75	3.54±0.29	97.87±1.88	24.87±0.99	3.28±0.48	84.67±6.77	0.17±0.03	2.21±0.14
1 month after	130.47±3.07	3.59±0.14	97.73±2.89	24.47±1.92	3.27±0.41	84.53±7.93	0.17±0.03	2.21±0.14
2 months after	129.53±4.93	3.60±0.21	98.89±3.38	24.27±1.39	3.27±0.33	82.71±6.00	0.18±0.04	2.25±0.05
3 months after	129.53±5.19	3.55±0.23	97.67±3.83	24.87±1.25	3.29±0.30	83.00±7.24	0.18±0.04	2.25±0.11
4 months after	128.80±4.51	3.44±0.21	98.13±2.90	25.33±1.11	3.25±0.37	84.20±7.40	0.18±0.04	2.23±0.11
5 months after	129.33±4.20	3.43±0.17	99.07±3.33	24.87±0.64	3.21±0.28	85.12±7.20	0.17±0.04	2.30±0.12
6 months after	130.47±3.56	3.50±0.19	99.07±3.01	24.80±0.94	3.24±0.30	84.52±6.01	0.17±0.04	2.30±0.15

the reference range before intake of the extract and throughout the period of the study.

## DISCUSSION

The present study established non-toxic effect of intake of extract of unripe *Carica papaya* on kidney function in sickle cell patients. The results obtained in this study were in agreement with the report of Thomas and Ajani [8] where normal kidney function was established before intake and after daily intake of aqueous extract of unripe *Carica papaya* for seven days. In the present work, the plasma levels of all the parameters measured especially urea and creatinine were within the reference range before intake of the extract and throughout the six months of study. Normal plasma levels of urea and creatinine is recognized as normal kidney function [8].

In conclusion, it was established from the present study that the intake of aqueous extract of unripe *Carica papaya* has no harmful effect on kidney function. Work is going on to isolate and characterize the active ingredients in unripe *Carica papaya* fruit. Its mechanism of action is also being studied.

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