



Screening of *Carica papaya* Seeds for Pharmacologically Bioactive and Nutritionally Beneficial Substances for Optimization of Its Nutraceutical Potential

**V. H. A. Enemor¹, O. F. Nworji^{1*}, U. C. Ogbodo¹, O. R. Ngwu¹, E. C. Orji¹
and I. O. Ohagim¹**

¹*Department of Applied Biochemistry, Nnamdi Azikiwe University, Awka, Nigeria.*

Authors' contributions

This work was carried out in collaboration among all authors. Author VHAE designed the study. Author IOO performed the experiments. Author OFN performed the statistical analysis, wrote the protocol and the first draft of the manuscript. Authors UCO, ORN and ECO managed the analyses of the study and the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Papaya seeds, though rarely eaten, are used in folk medicine around the world. This study analysed the seeds to evaluate their nutritional and phytochemical content using standard methods. Proximate analysis showed the seeds are a good source of carbohydrate ($48.91\% \pm 0.69$) and protein ($24.33\% \pm 0.74$). Essential minerals such as iron ($70.16 \text{ mg/kg} \pm 0.08$), selenium ($12.50 \text{ mg/kg} \pm 0.08$), and calcium ($26.96 \text{ mg/kg} \pm 0.08$) are present in the seeds at optimal quantities. Amino acid and vitamin analysis indicated that papaya seeds are rich sources of vitamin A ($117.28 \pm 2.09 \text{ mg/kg}$), B₆ ($37.70 \pm 1.84 \text{ mg/kg}$), D ($27.60 \pm 3.96 \text{ mg/kg}$), K ($119.81 \pm 15.88 \text{ mg/kg}$), and all essential amino acids. Phytochemical analysis of the seeds revealed forty-three bioactive compounds including acetic acid and pyrrole, both of which have antimicrobial properties. From the above analytical results, it was revealed that papaya seeds have nutraceutical properties and can be used, in the appropriate quantity as a food or health supplement or an adjunct animal feed.

*Corresponding author: Email: of.nworji@unizik.edu.ng;

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1. INTRODUCTION

Carica papaya L. commonly called pawpaw is an arborescent plant of economic importance that grows perennially in the tropical and subtropical regions of the world [1,2]. It is a dicotyledonous plant that reproduces dioeciously or gynodioeciously [1]. Once harvested, the fruit is eaten raw, juiced, or used to produce candies and jams in Asian and South American countries. Also, the leaves, unripe fruits and flowers are edible when cooked and grounded seeds are used as a spice [1,2]. Nigeria is the biggest producer of pawpaw in Africa and sixth in the world [3]. Here, *C. papaya* is grown mainly for its fruits, which is a good source of iron, calcium, vitamin A and vitamin C [1,4].

C. papaya is revered by herbalists in most African countries because all parts of the plant have diverse medicinal properties. For instance, the leaves and stem have bioactive compounds that inhibit metabolic processes in tumour cells [4]. Extracts from leaves are used, as an antiseptic, blood tonic, for treatment of constipation, obesity, high blood pressure, and heart disorders [5,6]. Mature papaya fruit extracts are used as remedies against malaria and hypertension [5,6]. However, the extracts are harmful to pregnant women because of its abortifacient and teratogenic properties [5]. The unripe fruit extracts are medication for ulcer, diabetes, and sickle cell disorder [4,7]. Commercially, papain, a proteolytic enzyme from unripe pawpaw, is used in industries to clarify beer, tenderize meat, and manufacture drugs for digestive disorders [5,8]. In cosmetic industries, papain is an ingredient in the manufacture of shampoos, soaps, and toothpastes [8]. Respiratory infections and constipation are treated with root extracts [5]. The seeds are used to treat intestinal worms, ulcer, sickle cell disorder and poisoning [5,7,8]. Furthermore, the seed extracts have pharmaceutical potential as a male contraceptive since studies have shown that it inhibits sperm motility in humans and animals [9,10].

C. papaya seeds which forms about 15% of the fruit are mostly agricultural waste [8]. Given its value to folk medicine enthusiasts, papaya seeds are potentially an important source of nutraceuticals. Investigating the nutritional value of *C. papaya* seeds will ensure its value as an additional food source for humans and animals. Likewise, identifying the bioactive compounds

responsible for its efficacy as herbal medicine will add value to its pharmaceutical potential. This study aims to investigate the concentration of medicinally bioactive substances and possible nutritional importance of *C. papaya* seeds obtained from plants grown in South-Eastern Nigeria.

2. MATERIALS AND METHODS

2.1 Sample Collection

C. papaya fruits purchased at Eke-Awka market in Anambra State, Nigeria, were used for the study. The seeds were extracted from the excised fruits, washed, dried then pulverised using a manual grinder. Then the powdered seeds were preserved in an airtight container for further analysis.

2.2 Proximate Analysis

The proximate composition of *C. papaya* seeds was determined by following standard procedures recommended by the Association of Analytical chemists (AOAC) [11]. Ash content was evaluated by incineration in a muffle furnace at 500°C for 3 hours. Moisture content was analysed by gravimetric process at 100°C. Protein, fat, and fibre content were measured by Kjeldahl, Soxhlet, and enzymatic-gravimetric methods, respectively. Carbohydrate content was calculated by difference.

2.3 Mineral Analysis

Mineral content was determined as described by AOAC [11]. The sample (2 g) was ashed in a furnace at 550°C for 2 hours, then the residue digested with 10 ml of 20% H₂SO₄, filtered and diluted by a factor of 10 with deionised water. The mineral content of the resulting solution was measured using an atomic absorption spectrophotometer (240AA FS, Agilent).

2.4 Vitamin Analysis

Vitamin content was determined, as described by Kirk and Sawyer [12]. β-carotene, thiamine, riboflavin, cobalamin, cholecalciferol, α-tocopherol, and phyloquinone, concentration in the seeds, was estimated by colourimetric assay using a spectrophotometer (Jenway 60610), with absorbance measured at 325 nm, 261 nm, 242

nm, 361 nm, 264 nm, 410 nm and 635 nm respectively. Evaluation of niacin, pyridoxine and ascorbate concentration was by titration method.

2.5 Amino Acid Analysis

Amino acid profile was determined as described by Cohen and Strydom [13]. The sample was hydrolysed with 6 N HCl at 110°C for 24 hours and then filtered through a 0.50 µm membrane filter (Millipore). Afterwards, the solution was derivatised using phenyl isocyanate and analysed with HPLC (Aligent) following the manufacturer's instruction. Identification of amino acid was done by comparing their retention times with those of the standards.

2.6 Phytochemical Analysis

The phytochemical constituents of *C. papaya* seeds were determined with GCMS (GCMS-QP-2010, Shimadzu, Japan) as described by Yang et al. [14]. A HP-5ms GC column was used, with the sample injected in splitless mode. Helium was the carrier gas at a flow rate of 1 ml min⁻¹. The injector and ion source temperature were 250°C. The column temperature was at 50°C for 1 minute, then ramped to 250°C at 5°C min⁻¹. The temperature was held at 250°C for 20 mins then ramped to 280°C. Identification of the chromatogram peaks was with the NIST/ETA/NIH database.

2.7 Data Analysis

Data were analysed using GraphPad Prism software 8. The experiments were in triplicates and, data presented as mean ± standard deviation where appropriate.

3. RESULTS AND DISCUSSION

3.1 Proximate Composition

The proximate composition of *C. papaya* seeds is summarised in Table 1. The seeds had a moisture content of 2.30% which suggests that they were less susceptible to putrefaction. An ash content of 10.88% and fibre content of 12.94% indicates that the seeds are a potential supplementary source of essential minerals and dietary fibre. Protein, lipid, and carbohydrate content were 24.33%, 0.65% and 48.91% respectively which suggests that the seeds are nutritionally valuable, especially for individuals requiring a lower cholesterol diet. Earlier studies reported protein and ash content of *C. papaya* seeds that are comparable with the results from this study [15,16].

Table 1. Proximate composition of *C. papaya* seeds

Parameters	Composition (%)
Moisture	2.30 ± 0.15
Ash	10.88 ± 3.66
Lipid	0.65 ± 0.21
Protein	24.33 ± 0.74
Fibre	12.94 ± 0.27
Carbohydrate	48.91 ± 0.69

*Values are expressed as Mean ± SD (n = 3)

3.2 Mineral Analysis

Table 2 outlines the mineral content of *C. papaya* seeds. Iron, the predominant mineral in the seeds is important for haemoglobin synthesis and its deficiency associated with anaemia, high infant mortality rate and impaired immune function in adults [17]. From the results, 100 g serving of papaya seeds will provide 25% of the recommended daily iron intake for pregnant women [18]. Other essential minerals present in ample quantities in the seeds include calcium and magnesium. These minerals are important for building bones, regulating blood pressure, blood clotting and muscle contraction. The seeds also contain adequate amounts of selenium, a powerful antioxidant that attenuates mercury, cadmium, and arsenic toxicity [19]. Furthermore, epidemiological evidence has shown that selenium deficiency is associated with increased cancer risk [19]. An earlier study reported similar amounts of Iron for *C. papaya* seeds, however, the concentration of other identical minerals was significantly higher than reported in this study [20]. The seeds also contained toxic metals such as arsenic, cadmium, lead, and mercury. The provisional tolerable weekly intake (PTWI) for arsenic, cadmium, lead, and mercury are 15 µg/kg, 7 µg/kg, 25 µg/kg, and 4 µg/kg body weight, respectively [21]. At 30 mg/kg, arsenic is present in the seeds at toxic levels, to adults of healthy weight, possibly, because of soil pollution or the use of arsenic based pesticides.

3.3 Vitamin analysis

The most abundant vitamin in *C. papaya* seeds, as shown in Table 3, was vitamin C. As a powerful antioxidant, vitamin C helps prevent age-related cognitive decline and enhances the absorption of iron [22]. Considerable quantities of vitamin A, B₆, D and K were also present in seeds. Vitamin A preserves optimal vision, reduces the risk of cervical cancer and is necessary for immune health [23,24]. Vitamin B₆ is essential for the synthesis of

neurotransmitters, haemoglobin, and glucose metabolism [25]. Vitamin D and K work together to increase bone density in osteoporotic patients [26]. Following the WHO's dietary recommendation [18], 100 g of *C. papaya* seeds will give 14% of dietary reference intake for vitamin C and over 100% for vitamins A, B₆, D and K.

Table 2. Mineral composition of *C. papaya* seeds

Mineral	(mg/kg)
Aluminium	0.05 ± 0.00
Arsenic	30.68 ± 0.79
Cadmium	0.12 ± 0.00
Calcium	26.94 ± 0.08
Copper	0.16 ± 0.01
Iron	70.16 ± 0.08
Lead	0.45 ± 0.06
Magnesium	22.92 ± 0.81
Manganese	0.69 ± 0.00
Mercury	1.03 ± 0.01
Nickel	0.21 ± 0.00
Potassium	8.62 ± 0.09
Selenium	12.50 ± 0.08
Sodium	12.96 ± 0.04

*Values are expressed as Mean ± SD (n = 3)

3.4 Amino Acid Profile

From the results in Table 4, the total amino acid content was 63.01 g per 100 g of protein. Amino acids play a significant role in maintaining metabolic efficiency [27]. Isoleucine, an essential amino acid required for normal muscle function, is the predominant amino acid found in *C. papaya* seeds [27]. Other essential amino acids present in substantial quantities include lysine and threonine. Lysine is vital for calcium absorption while threonine is necessary for protein biosynthesis [27]. Methionine which is critical for normal cell function is the least abundant essential amino acid in the seed [28]. Despite this, all the essential amino acids in the seeds are present in quantities that are above the recommended daily estimates for adults within a healthy weight range. Non-essential amino acids present in sufficient quantities include glutamate and serine. Glutamate is crucial for learning, perception, and memory while serine is important for brain development and protein biosynthesis [28]. Cysteine, a non-essential amino acid vital for glutathione metabolism [29], is the least substantial in the seeds.

Table 3. Vitamin composition of *C. papaya* seeds

Vitamin	Seed concentration (mg/kg)
A	117.28 ± 2.09
B ₁	2.05 ± 00.06
B ₂	2.03 ± 00.09
B ₃	0.04 ± 00.00
B ₆	37.70 ± 1.84
B ₁₂	4.22 ± 00.02
C	128.92 ± 11.82
D	27.60 ± 3.96
E	0.64 ± 00.04
K	119.81 ± 15.88

*Values are expressed as Mean ± SD (n = 3)

Table 4. Amino acid profile of *C. papaya* seeds

Amino acid	(g/100g protein)
Alanine	2.85
Arginine	2.90
Aspartate	3.49
Cysteine	1.07
Glutamate	4.76
Glycine	3.48
Histidine	3.99
Isoleucine	5.49
Leucine	3.84
Lysine	4.85
Methionine	1.56
Phenylalanine	3.59
Proline	2.78
Serine	4.75
Threonine	4.58
Tryptophan	2.46
Tyrosine	3.39
Valine	3.18
Total	63.01

3.5 Phytochemical Analysis

Mass Spectral analysis of *C. papaya* seeds yielded forty-three bioactive compounds as presented in Table 5. Nona-3,5-dien-2-ol is the most abundant phytochemical in the seeds. A search of the spectral databases, Dr. Duke's Phytochemical and Ethnobotanical Databases (Dukes) [30], Chemical Entities of Biological Interest (ChEBI) [31], and Human Metabolome Database (HMDB) [32] gave insight to the medicinal properties of ten phytochemicals. Acetic acid is commonly used as a food acidity regulator and it also has antimicrobial, anti-inflammatory, mucolytic, pesticide, protistocidal, osteolytic, ulcerogenic, and spermicide properties [30,31]. Urea is used as a fertilizer,

Table 5. Phytochemical compounds in *C. papaya* seeds

Compound	Retention Time (min)	% Peak Area
Propargylamine	5.631	0.48
Silane, (fluoromethyl) dimethyl-	6.716	2.40
Ethanamine, N-methylene-	32.769	1.77
Acetic acid	32.962	1.78
Urea	33.660	0.62
2-Butanamine, (S)-	56.301	0.44
Guanidine, methyl-	56.960	1.33
2-Propynenitrile, 3-fluoro-	57.386	1.00
Pyrrrole	58.045	0.48
Hydrazine, 1,1-dimethyl-	58.356	1.08
Difluoramine	58.666	1.18
Ethyleniminoacetonyl	59.092	0.86
Propanamide	59.325	0.83
Thiirane	59.519	0.28
Cyanamide, dimethyl-	59.751	0.83
1,1'-Bicyclopropyl	59.829	0.26
Cyclopropaneethanol	60.139	2.03
2-Hexyne	60.643	2.07
Pyridazine, 3-amino-6-chloro-, 2-oxide	60.914	0.46
1,14-Tetradecanediol	61.186	1.55
6-Octen-1-ol, 3,7-dimethyl-, (R)-	61.651	1.83
2-Octyne	61.806	1.39
10-Undecen-1-ol	62.000	0.75
Octanenitrile	62.155	1.30
4-Hexenoic acid, 3-methyl-, methyl ester	62.698	4.40
Chloromethyl 6-chloroundecanoate	62.814	1.65
1,15-Pentadecanediol	63.047	1.19
Citronellol	63.240	1.78
(Z)-4-Decen-1-ol, trifluoroacetate	63.667	5.32
Trans-2,3-dimethylbicyclo [2.2.2] octane	64.326	2.28
7-Octenoic acid	64.442	2.09
2,7-Octadiene, 4-methyl-	64.830	3.00
3-Decen-1-ol, (Z)-	64.946	1.67
7-Oxabicyclo [4.1.0] heptane, 3-oxiranyl-	65.567	8.61
E-7-Tetradecenol	65.683	2.45
Nona-3,5-dien-2-ol	66.187	13.55
3-Buten-2-one, 4-(5-hydroxy-2,6,6-trimethyl-1-cyclohexen-1-yl)-	66.303	0.85
Cyclopentaneundecanoic acid	66.419	0.58
13-(2-Cyclopenten-1-yl) tridecanoic acid	66.691	6.29
Salicylic acid, 2TMS derivative	66.846	2.70
Cyclopropanecarboxylic acid, dodec-9-ynyl ester	67.040	1.68
11-Dodecenol	67.195	1.26
Hexanoic acid, 6-cyano-	67.350	2.70

pharmaceutical and cosmetic agent, and for flour treatment [31,32]. 2-Butanamine, (S)- is an antifungal agrochemical [31]. Guanidine, methyl- is a uremic toxin [31].

Pyrrole is a flavouring agent and has antitumor, anti-inflammatory, and antimicrobial activity [32]. Hydrazine, 1,1-dimethyl- is teratogenic, carcinogenic, and used as fuel in rockets [31]. Citronellol is used as a surfactant, emulsifier, allergenic, antibacterial, antiseptic, antifungal, herbicide, nematocide, trichomonacide, pesticide, sedative and in perfume compositions [30,32]. 10-Undecen-1-ol is an emulsifier, surfactant, and a flavouring agent in detergents and soaps [32,33]. 13-(2-Cyclopenten-1-yl) tridecanoic acid is an antibacterial, antileptic and antisarcoidotic agent [30]. Studies have shown that propargylamine has neuroprotective and antiapoptotic activities [34,35]. Thiirane containing compounds are associated with antitumor, antimicrobial, and immunosuppressant activities [36]. Identified phytochemicals such as acetic acid and pyrrole affirm the use of papaya seeds in folklore medicine. The findings indicate that the seeds contain an extensive range of phytochemicals that could be of considerable interest to pharmaceutical companies. Future investigations will focus on using in-silico methods such as molecular docking, genome-wide functional screening, and quantitative or qualitative structure-activity relationship (QSAR) modelling to elucidate the properties of other phytochemicals identified in the seeds.

4. CONCLUSION

This study assessed the nutritional and chemical profile of *C. papaya* seeds. The results indicate that the seeds are a useful source of carbohydrate, protein, and essential amino acids. Also, the presence of essential mineral elements such as magnesium, calcium and iron and vitamins A, B₆, D and K enhances the nutritional quality of the seeds. The rich phytochemical profile of the seeds explains its value as herbal medicine and its potential to the pharmaceutical industry as a source of bioactive drug candidates. However, research to determine the bioavailability and the antinutritional properties of *C. papaya* seeds is necessary before they are used in animal feeds or consumed as part of a nutritious diet.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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