MERIT RESEARCH JOURNALS
www.meritresearchjournals.org
Merit Research Journal of Medicine and Medical Sciences (ISSN: 2354-323X) Vol. 7(10) pp. 374-381, October, 2019
Available online http://www.meritresearchjournals.org/mms/index.htm

Original Research Article

Antifertility Effect of Ethanolic Leaf Extract of *Carica papaya* in Male Wistar Rats

Augustine I. Airaodion[1*], Victor N. Okoroukwu[2], Emmanuel O. Ogbuagu[3], John A. Ekenjoku[3], Uloaku Ogbuagu[1] and Edith O. Airaodion[4]

[1]Department of Biochemistry, Federal University of Technology, Owerri, Imo State, Nigeria*

[2]Department of Pharmacology and Therapeutics, Gregory University, Uturu, Abia State, Nigeria

[3]Department of Pharmacology and Therapeutics, Abia State University, Uturu, Nigeria

[4]Department of Biochemistry, Ladoke Akintola University of Technology, Ogbomoso, Nigeria

***Corresponding Author's E-mail: augustineairaodion@yahoo.com +2347030204212**

Abstract

The use of *Carica papaya* leaves in folklore medicine for its antimalarial and antidiabetic activities without reference to its adverse effect is on the increase globally. This study therefore sought to investigate the antifertility effect of *C. papaya* leaves in male Wistar rats. Fresh and healthy leaves of *C. papaya* disease were harvested from the Institute of Agricultural Research and Training, Moor Plantation, Ibadan. They were dried and extracted using soxhlet apparatus and ethanol as the solvent. Toxicity test was carried out using standard method. Thirty male Wistar rats were grouped into six of five rats each. Animals in groups A, B and C were administered normal saline for 10, 20 and 30 days respectively via oral route. Those in groups D, E and F were similarly treated but with 500 mg/kg body weight of leaf extract of *C. papaya*. At the end of treatment, the animals were sacrificed by cervical dislocation. The internal organs were exposed. Testes and cauda epididymis were removed and kept in sterilized glass. Male fertility parameters were determined using standard methods. Ethanolic leaf extract of *C. papaya* causes decreased sperm count, sperm motility and seminal pH while sperm mortality and abnormality of spermatozoa increased significantly ($p<0.05$) after 10, 20 and 30 days treatment respectively. These effects were dependent on the number of days treated. The normal range of sperm count, sperm motility, seminal pH and abnormality of spermatozoa are essential factors for fertility. Any disturbance of such normal range of seminal quality may affect the fertility of animals. Thus, these changes in seminal quality of *C. papaya* leaf treated-animals showed that *C. papaya* exhibits antifertility activities but this does not automatically translate to such effect on human. Therefore its effect on the fertility of man can be further confirmed.

Keywords: *Carica papaya*, sperm count, sperm motility, sperm mortality, sperm abnormality, seminal pH

INTRODUCTION

The induction of male infertility in experimental animals and humans resulting from treatment with medicinal plants and their products has drawn the attention of researchers. The antisteroidogenic and antifertility activities of extracts from plants with antimalarial properties have also been reported (Lohiya *et al*, 1994; Raji and Bolarinwa, 1997; Raji *et al.,* 2003). With the increased efforts in the development of more potent antimalarial agents as a result of the challenges posed by the resistant strains of the malaria parasite, the evaluation of these antimalarial agents for possible antifertility actions becomes worthwhile. This is in view of

Figure 1. *Carica papaya* Plant (Airaodion *et al*., 2019a)

the fact that both malaria and infertility are worldwide phenomena and the need to avoid the risk of infertility resulting from malarial chemotherapy.

Carica papaya belongs to the family of Caricaceae, and several species of Caricaceae have been used as remedy against a variety of diseases (Munoz *et al*., 2000; Mello *et al*., 2008). Originally derived from the southern part of Mexico, *C. papaya* is a perennial plant, and it is presently distributed over the whole tropical area. In particular, *C. papaya* fruit circulates widely, and it is accepted as food or as a quasi-drug. Many scientific investigations have been conducted to evaluate the biological activities of various parts of *C. papaya*, including fruits, shoots, leaves, rinds, seeds, roots or latex**.** The leaves of *C. papaya* have been shown to contain many active components such as papain, chymopapain, cystatin, à-tocopherol, ascorbic acid, flavonoids, cyanogenicglucosides and glucosinolates that can increase the total antioxidant power in blood and reduce lipid peroxidation level (Seigler *et al*., 2002). Figure 1

Fruit and seed extracts have pronounced bactericidal activities (Emeruwa, 1982). Leaves have been poulticed into nervous pains, elephantoid growths and it has been smoked for asthma relief amongst tropical tribal communities. The antiplasmodial potency of ethanolic leaf extract of *C. papaya* against *Plasmodium berghei* in infected Swiss albino mice has also been reported (Airaodion *et al*., 2019a). Moreover, *C. papaya* leaf extract is consumed for its purported anti-cancer activity by people living on the Gold Coast of Australia, with some anecdotes of successful cases being reported in various publications. *C. papaya* leaf extracts have also been used for a long time as an aboriginal remedy for various disorders, including cancer and infectious diseases.

C. papaya contains two important biologically active compounds viz., chymopapain and papain which are widely used for digestive disorders (Huet *et al*., 2006). It showed that papaya derived papain, caricain, chymopain, and glycerin endopeptidase can improve acidic pH conditions and pepsin degradation. Other active compounds of *C. papaya* are lipase, a hydrolase, which is tightly bonded to the water-insoluble fraction of crude papain and is thus considered as a “naturally immobilized” biocatalyst (Dominguez *et al*., 2006). According to the folk medicine, papaya latex can cure dyspepsia and also applicable for external burns and scalds. Seeds and fruits are excellent antihelminthic and antiamoebic (Okeniyi *et al*., 2007). Airaodion *et al*. (2019b) has also reported that ethanolic extract of *C. papaya* leaves induced miscarriage in pregnant rats.

Furthermore, the leaves and roots of *C. papaya* have been reported to contain cyanogenic glucosides which form cyanide (Bennett *et al*., 1997; Ayoola and Adeyeye, 2010). *C. papaya* latex has been shown to have activities against Candidaalbicans (Giordani *et al*., 1996) Heligmosomoidespolygyrus (Satrija *et al*., 1995), Ascarissuum and Ascaridiagalli (Satrija *et al*., 1994). Aqueous extract of *C. papaya* leaves have shown potential activity in management of dengue fever (Ahmad *et al*., 2011), antitumor and immunomodilatory activities (Otsuki *et al*., 2010). In reproduction, various extracts of *C. papaya* seed have been shown to have antifertility activity in male (Chinoy and Padman, 1996) and female rats (Chinoy *et al*., 1997). It has also been reported to be an arbotifacient and exhibits lactogenic properties (Burkill, 1985). Aqueous extract of *C. papaya* leaf caused reduction in mean values of andrological parameters as a result of lesion of the seminiferous tubule epithelium

(Akinloye and Morayo, 2010). This study therefore sought to investigate the effect of ethanolic leaf extract of *C. papaya* on some male reproductive system.

METHODOLOGY

Collection and Extraction of Plant Material

Fresh and healthy leaves of *C. papaya* free from disease were harvested from the Institute of Agricultural Research and Training, Moor Plantation, Ibadan, Nigeria and were identified by a botanist. They were washed in running water to remove contaminants. They were air dried at room temperature in an open laboratory space for 14days and milled into powder using an electronic blender (Moulinex). The extraction was done using soxhlet apparatus and ethanol as the solvent according to the method described by Airaodion *et al*. (2019c,d). About 25 g of the powder was packed into the thimble of the soxhlet extractor. 250 mL of ethanol was added to a round bottom flask, which was attached to the soxhlet extractor and condenser on a heating mantle solvent was heated using the heating mantle and began to evaporate moving through the apparatus to the condenser. The condensate dripped into the reservoir housing the thimble containing the sample. Once the level of the solvent reached the siphon, it poured back into the round bottom flask and the cycle began again. The process was allowed to run for a total of 18 hours. Once the process was completed, the ethanol was evaporated in a rotary evaporator at 35 ^{o}C with a yield of 2.98 g which represents a percentage yield of 11.92%. The extract was preserved in the refrigerator until when needed.

Oral Acute Toxicity Studies

Oral acute toxicity study was carried out according to the method described by Miller and Tainter (1944) cited in Airaodion *et al*. (2019b). Twenty-five rats were divided into five groups (1–5) consisting of 5 rats per group. Group A was given distilled water (10 ml/kg) while groups B,C, D and E were separately given 500, 1000, 1500, and 2000 mg/kg of the extract respectively. Treatments were administered orally by gastric intubation. The animals were observed for 24 hours post treatment for signs of toxicity and then48 hours for possible death.

Experimental Design and Animal Treatment

Thirty male Wistar rats weighing between 185 and 200 g were purchased from the Central Animal House, College of Medicine, University of Ibadan, Nigeria. They were acclimatized for seven (7) days during which they were fed *ad libitum* with standard feed and drinking water and were housed in clean cages placed in well-ventilated housing conditions (under humid tropical conditions) throughout the experiment. All the animals received humane care according to the criteria outlined in the 'Guide for the Care and Use of Laboratory Animals' prepared by the National Academy of Science and published by the National Institute of Health. They were randomly divided into six groups of five rats each. Animals in groups A, B and C were administered normal saline for 10, 20 and 30 days respectively via oral route. Those in groups D, E and F were similarly treated but with 500 mg/kg body weight of leaf extract of *C. papaya*. At the end of treatment, the animals were sacrificed by the cervical dislocation. The internal organs were exposed. Testes and cauda epididymis were removed and kept in sterilized watched glass.

Determination of Male Fertility Parameters

The cauda epididymides were separated from both of the testes and tinged with 2 mL of normal saline then teased the cauda epididymis of each rat. The suspension was mixed through a metallic net to avoid any other tissue contamination. Sperms counts were done with the aid of hemocytometer according to the method of Eliasson (1975). Motility of spermatozoa was determined according to the methods of Tijee and Oentoeng (1968). For the study of abnormality of spermatozoa, a film of semen was prepared on slide. These films on slide were fixed in methanol. The slides were stained in eosine for 40 minutes. The films were washed in tap water and after drying, the slides were examined under the microscope to see abnormality of spermatozoa. Seminal pH was measured using a pH meter.

Statistical Analysis

Data were subjected to analysis of variance using Graph Pad Prism. Results were presented as Mean ± standard deviation. One way analysis of variance (ANOVA) was used for comparison of the means followed by Tukey's (HSD) multiple comparison tests. Differences between means were considered to be significant at $p<0.05$.

RESULTS

Acute Toxicity Studies

Ethanolic leaf extract of *C. papaya* was safe in rats at the testedoral doses (500–2000 mg/kg). There was no mortality within the study period. However, there were behavioral changes such as depression, reduced motor activity and ataxia. There was also a slight increase in urine output.

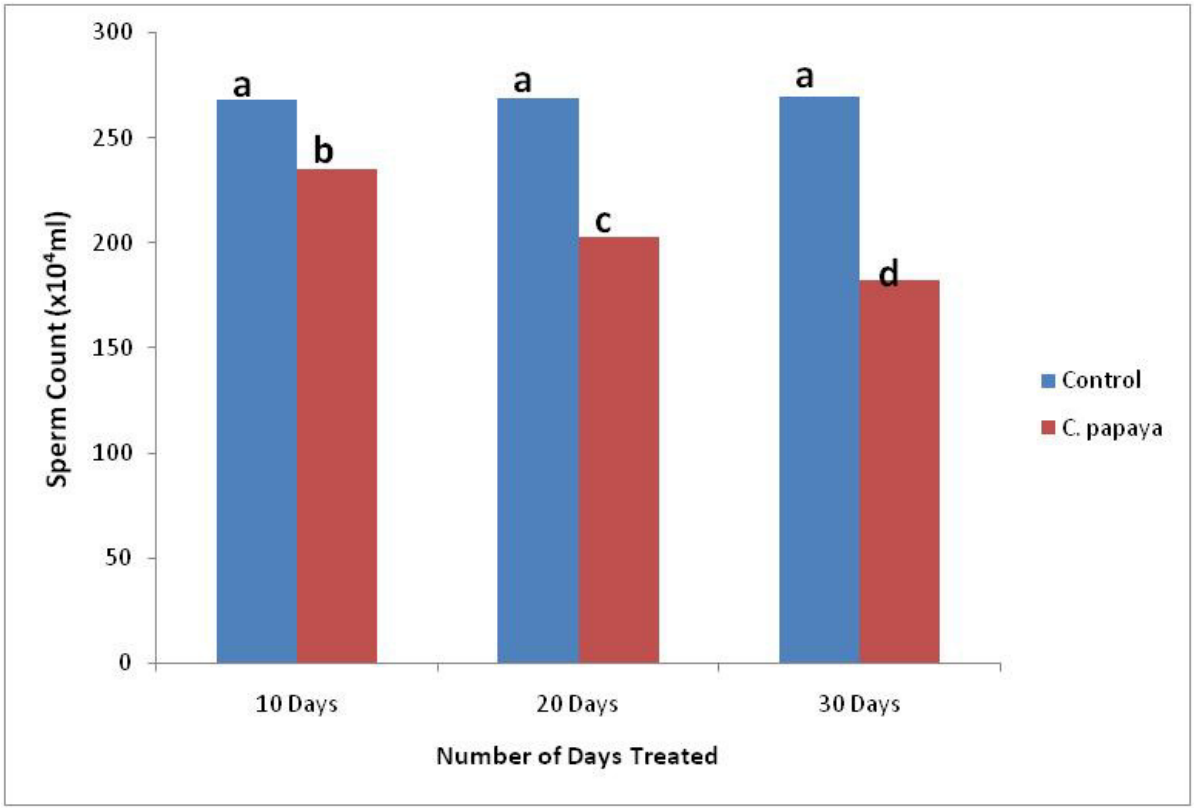

Figure 2. Effect of *C. papaya* on Sperm Count of Animals after 10, 20, and 30 days Treatment respectively. Results are presented as mean values of five rats. Bars with different letters are significantly different at $p<0.05$.

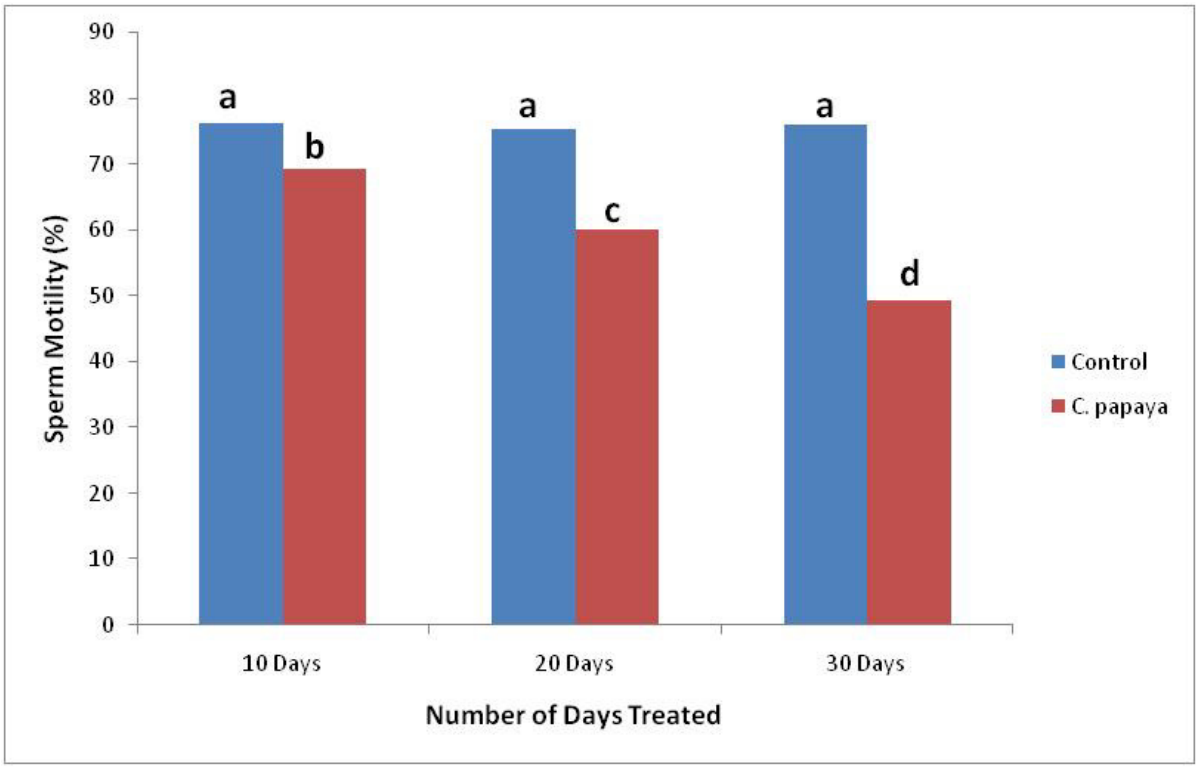

Figure 3. Effect of *C. papaya* on Sperm Motility of Animals after 10, 20, and 30 days Treatment respectively. Results are presented as mean values of five rats. Bars with different letters are significantly different at $p<0.05$.

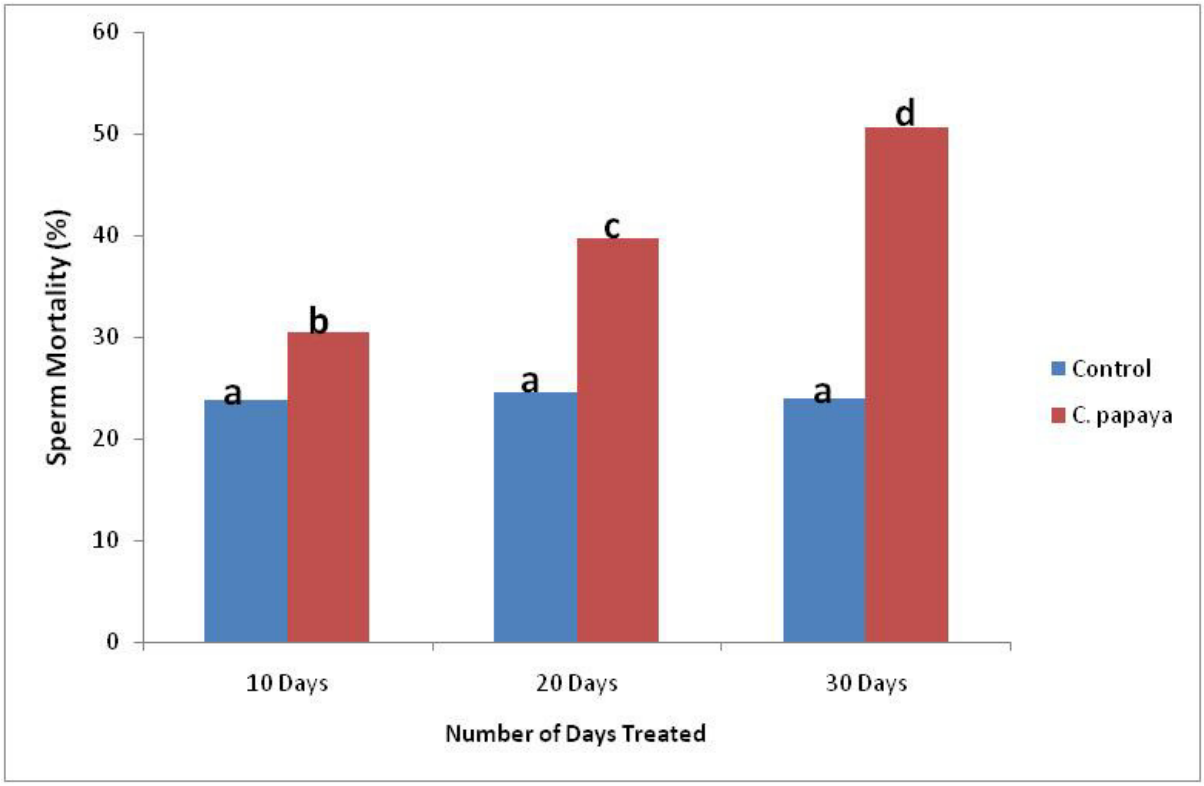

Figure 4. Effect of *C. papaya* on Sperm Mortality of Animals after 10, 20, and 30 days Treatment respectively. Results are presented as mean values of five rats. Bars with different letters are significantly different at $p<0.05$.

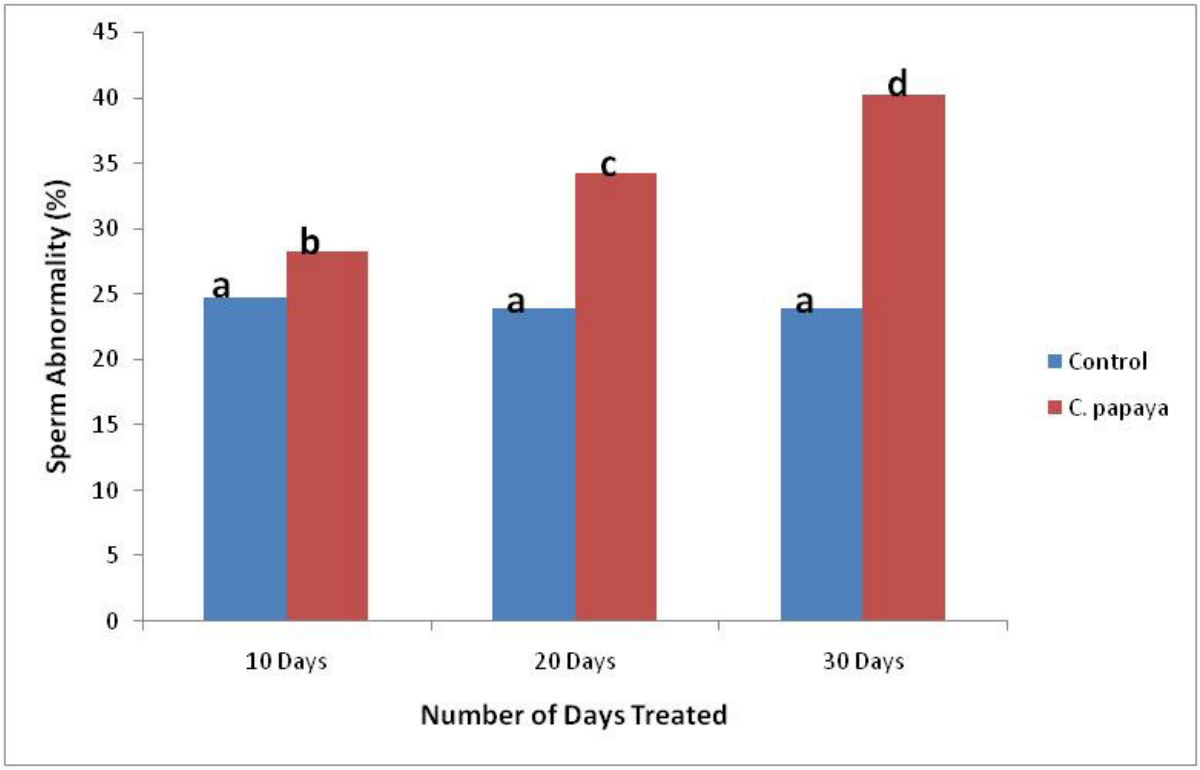

Figure 5. Effect of *C. papaya* on Sperm Abnormality of Animals after 10, 20, and 30 days Treatment respectively. Results are presented as mean values of five rats. Bars with different letters are significantly different at $p<0.05$.

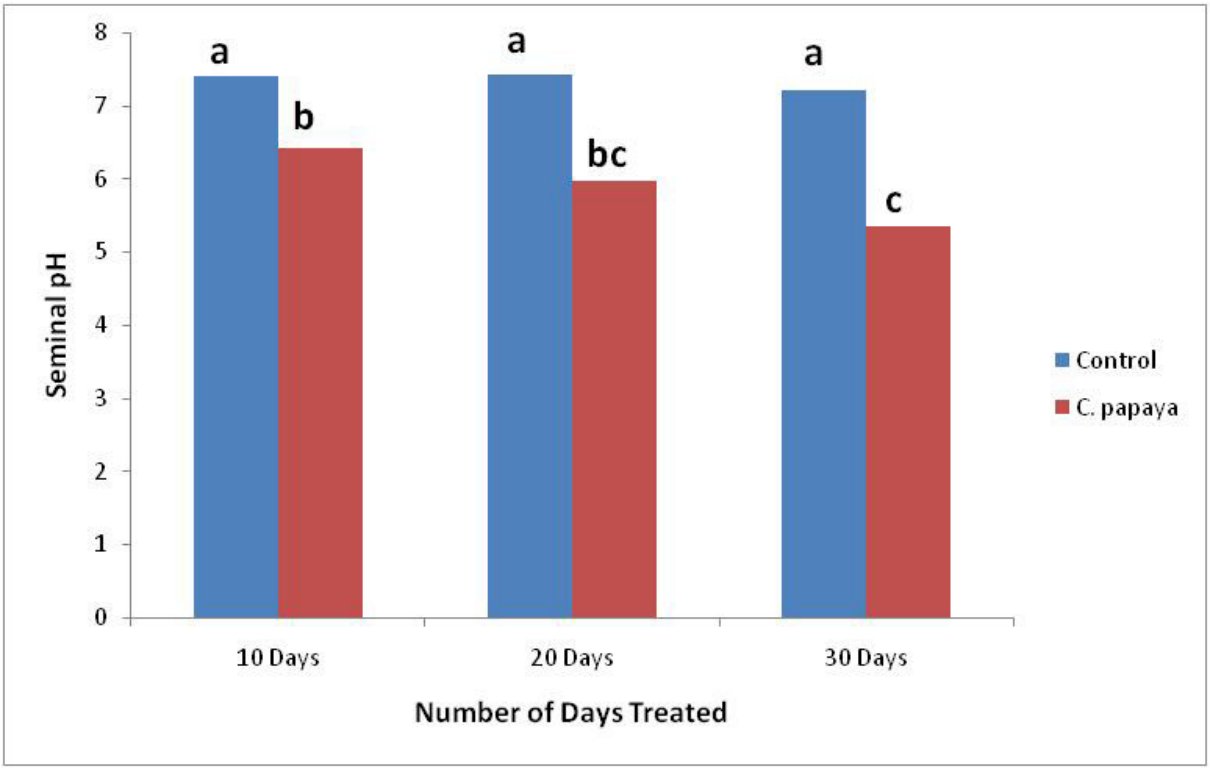

Figure 6. Effect of *C. papaya* on Seminal pH of Animals after 10, 20, and 30 days Treatment respectively. Results are presented as mean values of five rats. Bars with different letters are significantly different at p<0.05.

Effect of *C. papaya* on Male Fertility Parameters of Animals

The results of the effect of *C. papaya* leaf extract on male fertility parameters of animals are presented in figures 2-6.

DISCUSSION

Herbs have been used for centuries in the treatment of different ailments (Subaprinya and Nagini, 2005; Siraji *et al*., 2008). Some of them have unexploited effects which can result in serious unplanned consequences. These consequences could be teratogenic, and as such babies born of such pregnant mothers can be malformed with ignorance of its cause (Togun *et al*., 2008). This study therefore sought to investigate the effect of ethanolic leaf extract of *C. papaya* on some male reproductive parameters.

In this study, it could be clearly demonstrated that sperm count declined significantly (p<0.05) when animals treated with leaf extract of *C. papaya* were compared with the control groups throughout the period of administration as presented in figure 2. This result is similar to the findings of Ekenjoku*et al*. (2019) who treated animals with *Vernonia amygdalina* leaf extract. It also corresponds with the report of Kumari *et al*. (2017) who treated animals with *C. papaya* seed extract. This might be suggestive that leaf extract of *C. papaya* interfered with steroid hormone biosynthesis, which results in impaired spermatogenesis (Lakhman *et al*., 2013). Disturbance in steroid hormone biosynthesis as well as spermatogenesis may affect the seminal quality of animals. The decrease in sperm count observed in this study is dependent on the number of days treated. This is indicative that continuous use of *C. papaya* leaves will sustain reduction in sperm count.

In this study, a significant (p<0.05) decrease was observed in sperm motility of animals treated with leaf extract of *C. papaya* when compared with the control group throughout the period of administration. This corresponds to the findings of Ekenjoku*et al*. (2019) who treated animals with *Vernonia amygdalina* leaf extract. It also agrees with the report of Kumari *et al*.(2017) who treated animals with *C. papaya* seed extract. It might be an indicator that *C. papaya* leaf extract has the ability to reduce the ATPase activity level in all tissue of the animals used in this study (Hasim *et al*., 2013). This causes suppression of energy metabolism. If ATPase activity is decreased, it could suppress the motility rate of sperm, as ATP is the main energy source of sperm and it is directly related to sperm motility. Lohiya *et al*. (2000) observed total inhibition of motility in human sperm after

treatment with *C. papaya* seed extract. *C. papaya* seed extract has also shown inhibitory action on sperm motility in rats (Lohiya *et al*., 2002; Pathak *et al*., 2013). The inhibitory motility observed in the sperm of rats treated with leaf extract of *C. papaya* in this study might follow the same mechanism as that reported for the seed extract of *C. papaya*. The decrease in sperm motility observed in this study is dependent on the number of days treated. This is indicative that continuous use of *C. papaya* leaves will sustain reduction in sperm motility.

In this study, leaf extract of *C. papaya* was observed to increase the number of abnormal spermatozoa when compared with the control animals after 10, 20 and 30 days treatment respectively. Increased abnormality of spermatozoa in *C. papaya* treated animals might be as a result of damage of sertoli cell (Maninvanan *et al*., 2009). For normal testicular function sertoli cell plays vital role in maintaining conducive environment for spermatogenesis. Damage in sertoli cell may affect the maturation process of spermatozoa, which might result in increased abnormality of sperms observed in this study.

Seminal pH was observed to decline when animals treated with leaf extract of *C. papaya* were compared with the control animals after 10, 20 and 30 days treatment respectively. This is contrary to the findings of Ekenjoku *et al*. (2019) who reported a significant decrease in seminal pH only after 30 days treatment with *Vernonia amygdalina*. This might be that *C. papaya* leaf extract affects the normal pH range even after 10 days treatment. If the pH is decreased, the medium of seminal plasma becomes acidic which in turn makes sperms highly fragile, thus leading to higher rate of mortality.

A significant increase was observed in sperm mortality of animals treated with leaf extract of *C. papaya* when compared with the control groups after 10, 20 and 30 days treatment respectively. This also contradicts the findings of Ekenjoku *et al*. (2019) who reported a significant increase in sperm mortality only after 30 days treatment with *Vernonia amygdalina*. This result might be attributed to the significant ($p<0.05$) decrease in seminal pH throughout the period of treatment. Low pH of epididymal fluid of bovine has been reported to result in increased rate of mortality of spermatozoa (Acott and Carr, 1984).

Generally, antimalarial remedies have been reported to have antifertility effects. Some of these remedies reported include chloroquine (Adeeko and Dada, 1998), *Azadirachta indica,* (Raji *et al., 2004), Alstonia boonei* (Oze *et al.,* 2007) and dihydroartemisinin (Nwanjo *et al.,* 2007). Airaodion *et al*. (2019a) has reported that *C. papaya* has antimalarial properties. Thus, there is a possible relationship between its antimalarial properties and antifertility activities. Aqueous extract of *C. papaya* leaves have been reported to produce similar antifertility effects on male rats (Akinloye and Morayo, 2010). The exact mechanism by which *C. papaya* leaves reduced sperm count is unknown, but it has been suggested that it contain a compound called papain which possibly cross the blood testes barrier to exert harmful effects on the seminiferous tubules of the testes (Akinloye and Morayo, 2010). Studies have reported the presence of proteins in the sperm as well as the semen. Edwards *et al.* (1981) reported the presence of serum proteins (albumin, lactoferrin), glycoproteins, akinase and prostatic. These proteins nourish the sperm cell. The reduction in sperm count observed in animals treated with leaf extract of *C. papaya*, might be attributed to the proteolytic action of the proteases in *C. papaya:* papain and chymopapain. These enzymes may have hydrolysed the semen proteins, making them unavailable for use by the sperm cells, thereby leading to malnutrition and defects seen in the cells.

CONCLUSION

The results obtained from this study revealed that ethanolic leaf extract of *C. papaya* causes decreased sperm count, sperm motility and seminal pH while sperm mortality and abnormality of spermatozoa increased significantly. The normal range of sperm count, sperm motility, seminal pH and abnormality of spermatozoa are essential factor for fertility. Any disturbance of such normal range of seminal quality may affect the fertility of animals. Thus, these changes in seminal quality of *C. papaya* leaf treated-animals showed antifertility effects, but this does not automatically translate to such effect on human. Therefore, its effect on human fertility can be further confirmed.

CONFLICT OF INTEREST

Authors wish to declare that no conflict of interest exist in this study and publication.

REFERENCES

Acott TS, Carr DW, (1984). Inhibition of bovine spermatozoa by caudal epididymal fluid: 2 Interaction of pH and acquiescence factor, Biol. Reprod. 30, 926-935.

AdeekoAO, Dada OA (1998). Chloroquine reduces fertilizing capacity ofepididyma sperm inrats. Mr. J.Med. Sci., 27:63-64.

Ahmad N, Fazal H, Ayaz M, Abbasi BH, Mohammad I, Fazal L (2011). Dengue fever treatment with *Carica papaya* leaves extracts. Asian Pac. J. Trop. Biomed.,1:330-333.

Airaodion AI, Airaodion EO,Ekenjoku JA,Ogbuagu EO, Ogbuagu U (2019a). Antiplasmodial Potency of Ethanolic Leaf Extract of *Carica papaya* against *Plasmodium berghei* in Infected Swiss Albino Mice. Asian J. Med. Principles and Clinical Practice. 2(2):1-8

Airaodion AI, Ogbuagu EO, Airaodion EO, Ekenjoku JA, Ogbuagu U. (2019c). Pharmacotherapeutic effect of methanolic extract of *Telfairiaoccidentalis* leaves on glycemic and lipidemic indexes of alloxan-induced diabetic rats. Int. J. Bio-Sci. and Bio-Technol. 11(8):1-17.

Airaodion AI, Ogbuagu EO, Ekenjoku JA, Ogbuagu U, Airaodion EO.

(2019d). Therapeutic effect of methanolic extract of *Telfairia occidentalis* leaves against acute ethanol-induced oxidative stress in Wistar rats. International Journal of Bio-Science and Bio-Technology. *11(7):179-189.*

Airaodion AI, Ogbuagu EO, Okoroukwu VN, Ogbuagu U (2019b). *Carica papaya* Leaves might Cause Miscarriage. Asian Research Journal of Gynaecology and Obsterics. 2019;2(4):1-8.

Akinloye OO,Morayo OM (2010). Evaluation ofandrological indices and testicular histology followingchronic administration ofaqueous extract of*Carica papaya* leaf inWistar rat. Mr. J.Pharm. Pharmacol., 4:252-255.

Ayoola PB, Adeyeye A (2010). Phtyochemical and nutrient evaluation of *Carica papaya*(pawpaw)leaves.Int. J.Res. Rev. AppliedSci., 5:325-328.

Bennett RN, Kiddie G, Wallsgrov RM(1997). Biosynthesis of benzylglucosinolate, cyanogenic glucosides and phenylpropanoids in *Carica papaya*. Phytochem, 45: 59-66.

BurkillHM (1985).The Useful Plants ofTropicalWest Africa. Vol.l,Royal BotanicGardens Kew, Sydney,pp: 604.

Chinoy NI, Padman P (1996). Antifertility investigations on the benzene extract of*Carica papaya* seeds in male albino rats. J. Med.Aromatic Plant Sci., 18:489-494.

ChinoyNI, Harsha J, Shilpa G (1997). Antifertility investigations ofalcoholicpapaya seed extract infemale rats. J. Med.Aromatic Plant Sci., 19:422-427.

Dominguez de Maria P, Sinisteraa JB, Tsai SW, Alcantara AR (2006). Biotech Adv. 24: 493-499.

Edwards JJ, Tollaksen SL, Andersom NG (1981). Proteins of human semen. Two-dimensional mapping ofhuman seminal fluid. Clin. Chern., 27: 1335-1340.

Ekenjoku JA, Airaodion AI, Okoroukwu VN, Ogbuagu EO, Ogbuagu U. Oral administration of ethanolic extract of *Vernonia amygdalina* leaves might impact negatively on fertility in male wistar rats. Asian Journal of Medical Principles and Clinical Practice.

Eliasson R (1975). Analysis of Semen. In progress in infertility. Eds. S.J. Behrman and R.W. Kistner, Little Brown and company Boston, Vol-II in edition Chapter-33, 693.

Emeruwa AC (1982). Antibacterial substance from Carica papaya fruit extract. J Nat Prod. 45: 123-127.

GiordaniR, Cardenas ML, Moulin-Traffort J, Regli P, (1996). Fungicidal activity oflatex sap from *Carica papaya* and antifungal effect ofD(+)-glucosamine on *Candida albicans* growth. Mycoses,39: 103-110.

Hasim BS, Goverdhan NA, Vengaiah V, Changamma C (2013) Impact of *Carica papaya* Linn. Seed extraction on some Marker Enzymes in Male Albino Rats, Int. J. Pharm. Sci. 22 (2), 214-217.

Huet J, Looze Y, Bartik K, Raussens V, Wintjens R, Boussard P (2006). Structural haracterization of the papaya cysteine protinases at low pH. Biochem Biophy Res Commun. 341: 620-626.

Kumari S, Kumar R, Singh VN (2017). Contraceptive Effects of Aqueous Extract of *CaricaPapaya* (Linn.) Seed on Seminal Profile of Swiss Albino mice. International Journal of Science and Research. 6(8):1963-1965.

Lakhsman J, Changamma C (2013). Antispermatogenic effect of *Carica papaya* seed extract on steroidogenesis in albino rats. Int. Journal of Pharmacy and pharmaceutical science. 5 (1).

Lohiya NK, Goyal RB, Jayaprakash D, Ansari AS, Sharma S. (1994). Antifertility effects of aqueous extract of *Carica papaya* seeds in Male rats. Planta. Med 60: 400 – 404

Lohiya NK, Kothari LK, Manivannan B, Mishra PK, Pathak N (2000). Human sperm immobilization effect of *Carica papaya* seed extract: In vitro study, Asian journal of andrological 2 (2), 103-110.

Lohiya NK, Manivannan B, Mishra PK, Pathak N, Sriram S, Bhande SS, Panneerdoss S (2002). Chloroform extract of *Carica papaya* seeds induced long-term reversible azospermia in lengur monkey. Asian journal of Andrology 4 (1): 17-26.

Manivannan B, Mittal R, Goyal S, Ansari AS, Lohiya NK (2009). Sperm characteristics and ultrastructure of testes of rats after long-term treatment with the methanol subfraction of *Carica papaya* seeds. Asian J Androl; 11:583–99.

Mello VJ, Gomes MT, Lemos FO, Delfino JL, Andrade SP, Lopes MT (2008). The gastric ulcer protective and healing role of cysteine proteinases from Carica candamarcensis. Phytomedicine. 15: 237-244.

Miller LC, Tainter MC (1944). Estimation ofthe $LD_{50}$and its errors by means of the logarithmic-probit graph paper. Proc. Soc.Exp. Biol. Med. 57:261-264.

Munoz V, Sauvain M, Bourdy G, Callapa J, Rojas I, Vargas L (2000). The search for natural bioactive compounds through a multidisciplinary approach in Bolivia Part II. Antimalarial activity of some plants used by Mosetene indians. J Ethnopharmacol. 69:139-155.

Nwanjo HU, Iroagba LN, Nnatuanya IN, Eze NA (2007). Antifertility activity of dihydroarteminisinin in male albino rats. Internet J. Endocrinol., Vol.4

Okeniyi JA, Ogunlesi TA, Oyelami OA, Adeyemi LA (2007). Effectiveness of dried Carica papaya seeds against human intestinal parasitosis: a pilot study. J Med Food. 10: 493-499.

Otsuki N,Dang HN, Kumagai E, Kondo A, Iwata S, Morimoto C (2010). Aqueousextract of *Carica papaya* leaves exhibits anti-tumor activity and immunomodulatory effects. J. Ethnopharmacol., 127: 760-767.

Oze G, Nwanjo H, Oze R, Akubugwo E, Orisakwe E, Aka P (2007). Reproductive impairment associated with the Ethanolic extract of*Alstonia boonei* (De-wild)stems bark in male rats. Int. J. Lab. Med., Vol.3*1O.5580/1e9c*

Pathak N, Mishra PK, Manivannan B, Lohiya NK (2000). Sterility due to inhibition of sperm motility by oral administration of benzene chromatographic fraction of the chloroform extract of the seed of *Carica papaya* in rats. Phytomedicine; 7: 325-333.

Raji Y, Bolarinwa AF (1997). Antifertility activity of *Quassia amara* in male rats – *in vivo* study. Life sciences, 61(11): 1067-1074.

Raji Y, Udoh US, Mewoyeka OO, Ononye FC, Bolarinwa AF (2003). Implication of reproductive endocrine malfunction in male antifertility efficacy of *Azadirachta indica* extract in rats Afr. J. Med. Med. Sci 32: 159-165.

Raji Y,Ogunwande IA, Osadebe CA, John G (2004). Effects of*Azadirachta indica* extracton gastric ulceration and acid secretionin rats. J. Ethnopharmacol., 90: 167-170.

Satrija F, Nansen P, Bjorn H, Murtini S, S. He S (1994). Effect ofpapaya latex against *Ascaris suum* in naturally infectedpigs. J. Helminthol., 68: 343-346.

Seigler DS, Pauli GF, Nahrstedt A, Leen R (2002). Cyanogenic allosides and glucosides from Passiflora edulis and Carica papaya. Phytochemistry. 60: 873-882.

Siraji D, Islam N, Begum N, Ferdousi S (2008). Effect of Ocimum sanctum Linn (Tulsi) on body weight and some biochemical parameters in restraint stressed albino rats. J Bangl Soc Physiol. (3):29-34.

Subaprinya R, Nagini S (2005). Medicinal properties of neem leaf: a review. Curr Med Anti-Conc Agent. 5(2): 146-9.

Tijee DY, Ontoeng S (1968). The viscosity of Human Semen and the percentage of motile spermatozoa, Fertile Steril, 19, 562-565.

Togun RA, Emma-Okon BO, Aboderin AA (2008). Lectins, mitogenicity and seed germination: a comparative study with the seeds of Telfairia occidentalis (Hook, F.) (Curcurbitaceae), Carica papaya (Linn) (Caricaceae) and Artocarpus communis (J.R. & G. Forst) (Moraceae). Biokemistri. 20(1): 11-15.