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An Experimental Study on the Abortificient Potentials of Unripe Seed Extract of *Carica papaya* in Adult Female Wistar Rats

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Abstract

This study is aimed at investigating the abortifacient potentials of *Caricapapaya (C. papaya)* using adult female rats as a model. Female rats (CP1 – CP5) served as the experimental group while female rats (CP6 and CP7) served as the control group. Each rat in both groups was given 20g of normal rat chow and water *adlibitum* during the experiment. In addition to this diet, each rat in the experimental group was force fed orally with 1ml/kg body weight of aqueous seed extract of unripe *C. papaya* form by dissolving 1gram of blended fresh *C. papaya* seed in 10ml for 2hrs. Administration of aqueous seed extract of *C. papaya* begins from the 5th day to 15th day. The results showed that mean body weights were significantly lower ($p<0.05$) in the group treated with extract of *C. papaya* at the second (233.00±20.00g versus 194.00±22.21g) and third week (272.40±45.50g versus 185.00±21.25g) of pregnancy compared to the control. Our findings indicate that *C. papaya* seed is abortifacient. It also showed that the time window of pregnancy at which the seed extract of *C. papaya* exhibited abortifacient effect was from the second trimester of pregnancy and resulted into zero fetus at the end of the third trimester.

Keywords

Carica papaya, Abortion, Pregnancy, Female

1. Introduction

The papaya (from Carib via Spanish), papaw, or paw paw is the fruit of the plant *Caricapapaya*, the sole species in the genus *Carica* of the plant family *Caricaceae*. It is native to the tropics of the Americas, perhaps from southern Mexico and neighbouring Central America (Boning and Charles, 2006). The papaya is a large, tree-like plant, with a single stem growing from 5 to 10 m (16 to 33 ft) tall, with spirally arranged leaves confined to the top of the trunk. The lower trunk is conspicuously scarred where leaves and fruit were borne. The leaves are large, 50–70 cm (20–28 in) in diameter, deeply palmately lobed, with seven lobes. Unusually for such large plants, the trees are deciduous. The tree is usually un-branched, unless lopped (Echeverri*et al.,* 1997). The flowers are similar in shape to the flowers of the Plumeria, but are much smaller and wax-like. They appear on the axils of the leaves, maturing into large fruit - 15–45 cm (5.9–17.7 in) long and 10–30 cm (3.9–11.8 in) in diameter.

In some parts of the world, papaya leaves are made into tea as a treatment for malaria (Rahmat, 2009). Antimalarial and antiplasmodial activity has been noted in some preparations of the plant (Morton, 1987), but the mechanism is not understood and no treatment method based on these results has been scientifically proven (Lohiya*et al.*, 2002). In belief that it can raise platelet levels in blood, papaya may be used as a medicine for dengue fever. Papaya is marketed in tablet form to remedy digestive problems. Papain is also applied topically for the treatment of cuts, rashes, stings and burns. Papain ointment is commonly made from fermented papaya flesh, and is applied as a gel-like paste. Harrison Ford was treated for aruptured disc incurred during filming of Indiana Jones and the Temple of Doom by papain injections (Boning and Charles 2006). Women in India, Bangladesh, Pakistan, Sri Lanka, and other countries have long used green papaya as an herbal medicine for contraception and abortion. Enslaved women in the West Indies were noted for consuming papaya to prevent pregnancies and thus preventing their children from being born into slavery (Titanji*et al.*, 2000).

Birth control, also known as contraception and fertility control, is a method or device used to prevent pregnancy

(Taliaferro *et al.*, 2011). Planning, provision and use of birth control is called family planning (Rang *et al.*, 2012). Safe sex, such as the use of female condoms, can also help prevent sexually transmitted infections (Chin *et al.*, 2012). Birth control methods have been used since ancient times, but effective and safe methods only became available in the 20th century (Hanson *et al.*, 2012). Some cultures deliberately limit access to birth control because they consider it to be morally or politically undesirable (Sitruk-Ware *et al.*, 2007). The most effective methods of birth control are sterilization by means of vasectomy in males and tubal ligation in females, intrauterine devices (IUDs) and implantable contraceptives. This is followed by a number of hormonal contraceptives including oral pills, patches, vaginal rings, and injections. Less effective methods include barriers such as condoms, diaphragms and contraceptive sponge and fertility awareness methods. The least effective methods are spermicides and withdrawal by the male before ejaculation. Sterilization, while highly effective, is not usually reversible; all other methods are reversible, most immediately upon stopping them (Taliaferro *et al.*, 2011). Emergency contraceptives can prevent pregnancy in the few days after unprotected sex. Some regard sexual abstinence as birth control, but abstinence-only sex education may increase teen pregnancies when offered without contraceptive education (DiCenso*et al.*, 2002).

1.1. Aim of the Study

This work is intended to study the effect and abortifacient potential of *C. papaya* on pregnancy, using the Sprague-Dawley rats.

1.2. Statement of the Problem

Nigerian adolescents and single women with unwanted pregnancy have resort to the use of concoction made from venom herbs, including *C. papaya* for inducing abortion. Also, death has been reported by Nigerian Newspapers to occur in some of the women ingesting concoction for pregnancy termination. This study is therefore necessary to determine the effect of *C. papaya* on pregnancy.

1.3. Scope of the Study

This study is restricted to the observation of the abortifacient effect of *C. papaya* seeds on pregnancy as indicated by weight changes, presence or absence of delivery at the end of the gestational period, and also the effect on the fetal size.

2. Materials and Method

2.1. Pilot Study

The aim of the pilot study was to select viable fertile male and female rats to be used for the experiment. Twenty Sprague Dawley rats (10 females and 10 males) of the same strain were obtained from the animal house at college of medicine, Ambrose Alli University Ekpoma.

The rats weighed within 150g to 180g. The Sprague Dawley rats were moved to the experiment site with proper ventilation at Antonio Research Center, No 40 Ujoelen Extention Road, Ekpoma, Edo State. They were all weighed before acclimatization and kept in a twenty cells cage, wide enough to accommodate three rats. During acclimatization they were also fed with normal rat chow (grower mesh) and clean drinking water. Their bedding was made of saw dust and was changed daily in order to improve animal wellbeing and obtain an accurate result.

The ten female Sprague Dawley rats were separated into ten cells in the cage labeled CP1 to CP10. The male Sprague Dawley rats were also placed in ten separate cells labeled M1 to M10. All the rats (male and female) were observed during two weeks of acclimatization, the purpose of acclimatization is to subject the Sprague Dawley rats to the new environment in which the experiment is to be carried out to enhance their performance under a new environmental condition.

After two weeks of acclimatization, a pilot study was carried out. In this case, ten male rats were randomly allocated to ten female rats and left to cohabit for three days, so that mating could take place. Thereafter, the males were withdrawn and were put in separate cells labeled (MM1 to MM10) below the female rat each male rat mated with. The female rats were left in their maternity cages for 18-25 days to observe birth.

2.2. Selection of Fertile Rats for the Study

The experimental study involves the selection of fertile adult male and female Sprague Dawley rat from the pilot study. Seven adult female rats; F2, F3, F4, F5, F6, F7, and F9 littered during the pilot study, were all selected. Their selection also involved the selection of the male Sprague Dawley rat that was involved in the pregnancy. The male rats were all selected because they proved to be fertile during the pilot study. The entire selection was carried out for the purpose of achieving a good experimental result at the end of the experiment. During the experimental study, both male and female Sprague Dawley rats were under constant inspection. Each of these rats was fed with normal rat chow, clean drinking water and their beddings were changed as in the previous study.

2.3. Substance of Study

Aqueous extract of unripe *C. papaya* seed

2.4. Experimental Animal

Fourteen Sprague Dawley rats (seven female and seven male) of proven fertility during the pilot study were used for the experimental study. These rats were 15 weeks old and were all kept in the same ventilated environment.

From the seven groups of female Sprague Dawley rats, CP1, CP2, CP3, CP4, and CP5 served as the experimental group, while CP6 and CP7 served as the control group.

The aim of this procedure is to compare the performance of the substance to be given to the experimental group with the control group that were given normal feeds. Also the male

Sprague Dawley rats were used again as in the previous study, with each assigned to its previous female counterpart.

2.5. Collection of Sample and Preparation

Unripe *C. papaya* fruits were collected from Edeogbon Street, at G1 road Ihumudumu, Ekpoma Edo State in Nigeria. The Unripe *C. papaya* was sliced open and seeds obtained and sun dried. The seeds were ground into paste using a mortar. To obtain the aqueous extract, one gram (1g) of the *C. papaya* seed paste was weighed using a digital measuring scale and then dissolved in ten ml (10ml) water and allowed to stand for two hours. Then extract was collected with the use of a filter paper. In other to avoid fermentation of *C. papaya* aqueous seed extract, this preparation was done daily.

2.6. Administration of Sample

Each rat in the experimental group was force fed orally with 1ml/kg body weight with 1g/10ml of aqueous seed extract of unripe *C. papaya*. Dose was chosen after determination of lethal dose (LD_{50}) from the result of Bankole et al., (2012)

2.7. Experimental Design

The seven selected female rats of proven fertility from the pilot study where allocated into cells. Female rats (CP1 – CP5) served as the experimental rats while female rats (CP6 and CP7) served as the control rats. The seven selected male rats of proven fertility from the pilot study were randomly allocated to the seven cells containing seven female rats so that each cell contained one female rat and one male rat. They were left in their various cages for three days to allow mating occur. After three days when mating was confirmed by the presence of sperm in vaginal smears examined under a light microscope. The day sperm/vaginal plug found was taken as the first day of gestation (GD 1). The males were withdrawn from the females. The male rats were put in separate cages with reference to the female rat each male rat mated with. The female rats were left in their initial cages so that each female rat occupied a separate maternity cage.

The female rats; both the control and experimental groups, were fed with 20g of normal rat chow and water given *ad libitum* from the 4th day to the end of the experiment. On day five all the rats (experimental and control group) were weighed using a digital measuring scale. The experimental group was force fed orally with 1ml/kg of sample (unripe *C. papaya* aqueous seed extract), after which normal rat chew of 20g was given. Administration of drug lasted for the period of ten days (day 5 to day 15), while the control was given no treatment.

2.8. Body Weight Measurement

All animals were weighed before mating, after mating and daily during the experiment using the digital measuring scale to determine body weight. The values were obtained and recorded. This was then typed into the SPSS (version 20) for statistical analysis.

3. Results

3.1. Result of the Pilot Study

After three weeks of separation of the female rats from the male rats from the first day of exposure with periodic examination and with notification of good health, the female Sprague Dawley rats; F2, F4, F5, F6, littered on the twenty first (21st) day, F3, F7, F8, littered on the twenty second (22nd) day, while F1, F8 and F10 did not litter.

After delivery, the adult female rats were allowed to nurse their young for a 21 day period before their young were relocated to another cage, while the adult female Sprague Dawley rats retained their normal cells.

Table 1. *Weekly mean body weight changes in pregnant rats fed C. papaya compared with control.*

Groups	Weight changes in grams				
	Before mating	After mating	1st week of pregnancy	2nd week of pregnancy	3rd week of pregnancy
Control group	177.40±9.50	177.40±18.50	214.40±21.50	233.00±20.00	272.40±45.50
Test group	172.20±24.77	174.00±24.38	193.60±25.46	194.00±22.21*	185.00±21.25*

Values are mean ± Standard deviation;
*indicates statistical significance compared to control at $p<0.05$.

3.2. The Abortive Potential of Seed Extract of *C. papaya* Indicated Via Mean Body Weight Gain of Pregnant Rats

Table 1 shows that mean weekly body weight changes of pregnant rats treated with seed extract of *C. papaya* for 10 days compared with control. Increasing mean body weight gain was observed throughout the experiment in the control group. In the group fed seed extract of *C. papaya* there was shape increase in mean body weight gain in the first week (193.60±25.46g) and a slight increase in the second week (194.00±22.21g) but with about 10gram weigh lost in the third week (174.00±24.38g) compared to weight in the second week. Compared with the control, mean body weights were significantly lower ($p<0.05$) in the group treated with seed extract of *C. papaya* at the second (233.00±20.00g versus 194.00±22.21g) and third week (272.40±45.50g versus 185.00±21.25g) of pregnancy.

3.3. Comparative Daily Pattern of Weight Changes in Pregnant Rats Fed Seed Extract of *C. papaya* and Control Pregnant Rats

Figure 1 shows the pattern of daily weight changes in the group fed seed extract of *C. papaya*. It was observed that mean

daily body weight gain begins to reduce at the 9th day through the 17th day (see figure 1 for detail). Figure 2 compares the average mean body weight gain pattern between the control and the group fed seed extract of *C. papaya*. While the control presented steady body weight increase to the 21st day, the test group presented a decreased at day 3 and increase from day 6 to 13 and a decrease in day 14 to 19 (see figure 2).

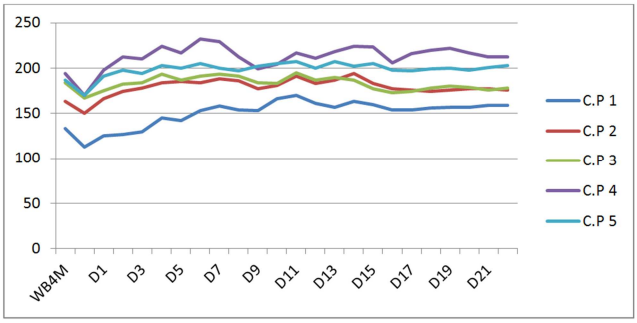

Figure 1. *Shows the pattern of daily weight changes in the group fed C. papaya. (Key: C.P = C. papaya, 1 to 5 represent rat 1 to rat 5; D = day; WB4M = weight before mating).*

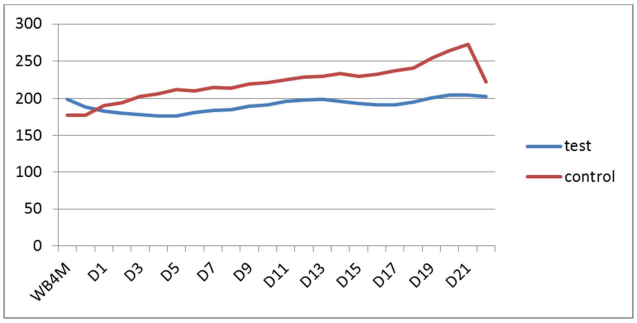

Figure 2. *Compares the average mean body weight gain pattern between the control and the group fed C. papaya. (Key: Control, test = fed C. papaya, D1 to 21 number of days; WB4M = weight before mating).*

4. Discussion

This study investigates the abortifacient potential of seed extract of unripe *C. papaya* in pregnant rats. The results of this study showed that seed extract of unripe *C. papaya* possesses abortifacient potentials. This was indicated by the weight loss observed in the 3rd week and the significant reduction ($p<0.05$) in mean body weight in the 2nd and 3rd week of pregnancy in test group compared with the control. The comparable mean body weight increase in the control and test at the 1st week indicates that the rats in both groups were actually pregnant. However, at the end of 21day, rats in control rats gave birth while those in test did not, hence indicating that the seed extract of unripe *C. papaya* fed to test group has abortifacient capacity. These findings collaborate with the reports by Chinoy *et al*. (2006) and Adebiyi *et al*. (2003) who reported that the seed extract of *C. papaya* is abortifacient. Hence, the present study has further confirmed the findings of Adebiyi *et al*. (2003), Oderinde *et al*. (2002) and Chinoy *et al*. (2006) who showed that extract of *C. papaya* seeds has adverse effects on female reproduction.

In line with the findings of this study, in India, south-east Asia and Indonesia, the fruit is widely classified as harmful in pregnancy, hence pregnant women are strictly forbidden from eating it for fear of its teratogenic and abortifacient effects (Adebiyi *et al*., 2002, 2003). Chinoy *et al*. (2006) has proved the anti-fertility, anti- implantation and abortifacient properties of extracts from papaya seeds. By implication, the findings in this study are in accordance.

As observed in this study, administration of the seed extract of *C. papaya* at the first trimesters of pregnancy did not result in abortions in the treatment groups. This was indicated by the mean body weight gain in the first trimester compared with the control. This finding agrees with the study of Oyelowo *et al*. (2014) which in his study showed that the group administered the extract throughout pregnancy (D21) manifested abortificient properties which led to the zero fetal births as observed in this study. Also, the study by Raji *et al*. (2005) where extract was administered to the animals two weeks before mating and throughout pregnancy reported abortion on the 1st and 2nd week which is in line with this study considering the weight changes at day 9 through day 14. However, the study of Oyelowo *et al*. (2014) reported abortion to occur at the 3rd trimester where extract was administered after when pregnancy was already established. In agreement with the findings of this study, *C. papaya* seed has been identified to have anti-fertility, anti-implantation as well as abortificient properties in female albino rats (Adebiyi *et al*., 2002, Oderinde *et al*., 2002, Raji *et al*., 2005).

5. Conclusion and Recommendation

Our study revealed that *C. papaya* seed is abortifacient. It also showed that the time window of pregnancy at which the seed extract of *C. papaya* exhibited an effect was from the second trimester of pregnancy and resulted into zero foetus at the end of the third trimester. Based on these findings, it is recommended that pregnant women take notice of this fruit during pregnancy. In addition, its use in folklore medicine during pregnancy should be discouraged.

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