

Effects Of Aqueous Extracts Of Seeds And Pulp Of Carica Papaya Linn On The Reproductive Function Of Male Wistar Rats

*Peneme B. M. L¹., Akassa H¹., Ondélé R¹., Moukala E., M¹.,
Bassoueka D¹., Abena A.A².

¹Laboratory of Pharmacognosy and Experimental Pathophysiology (L2PE), Faculty of Sciences and
Technology (FST), Marien University, Ngouabi, B.P. 69, Brazzaville, Republic of Congo

²Laboratory of Biochemistry and Pharmacology, Faculty of Health Sciences (FSSA), Marien Ngouabi
University, B.P. 69, Brazzaville?, Republic of Congo

Abstract:

Carica papaya is a tropical fruit, present in orange red to yellow orange color. The whole plant including fruit, leaves, roots, peel, bark, seed and pulp served as medicine. It is rich in minerals, carotenoids, vitamins, alkaloids, enzymes, lycopene, and flavonoids that provide the papaya with special importance. It is used as a remedy for the treatment of many skin infections, anti fungal, anti viral infections. Its milky juice extracted and dried is used as medicine for digestive disorders and as toothpaste. Carica papaya helps in the treatment of different types of cancer, kidney infections, nervous disorders, etc. Now a days papaya is known as a nutraceutical fruit because of its multifaceted properties. The most enhanced properties of papaya are anti-fungal, anti-fertility, uretonic, anti-hypertensive, hypolipidemic, dengue fever, diuretic, anti-helmintic, wound healing, antibacterial and antitumor activities. This review summarizes the magical pharmacological benefits of Carica papaya.

Keyword: Carica Papaya, Papain, Wound healing, Chymopapain, Nutraceutical.

Date of Submission: 27-09-2023

Date of Acceptance: 07-10-2023

I. INTRODUCTION

For a long time, medicinal plants have been used to treat a huge variety of illness. There were reported a significant diuretic action in plants that are often used for the predictable treatment of renal illnesses. Moreover, medicinal herbs can be an active implement in the hypertension management. Using plants as diuretics agents for treatments of dysuria and hypertension was emphasized in former studies. Presently, the treatment of congestive heart failure (CHF), Hypertention and other cardiovascular diseases includes the use of commercial synthetic Diuretics (Adam, et al; 2018). Carica papaya Linn usually recognized as Pawpaw or papau, Kapaya, Papyas, Papye, Fan mu gua goes to the family Caricaceae. It is supposed that it is a center of nutrients. It raises in all seasons. It is the first inherently adapted fruit (Parle et al., 2011). Usually, its leaves are used for the treatment of diverse illnesses by our descendants, including malaria, dengue, jaundice and viral disorders. Young leaves have additional position in pharmacological researches, as its constituents are further active then, the mature leaf. The leaves behavior also depends on diverse parameters like residue value, dampness, inflammation index etc. (Anuar et al., 2008). The papaya plant has singular compartments named laticifers (Absar et al., 2006). Lactifiers are spread in all tissues of the plant. All Carica papaya parts have pharmacological reputation because of its laticifers and its vigorous components. As studies proved these parts are active for anti-inflammatory, anti-fertility, hepatoprotective wound therapeutic, antihypertensive and antitumor activities. Moreover, it has enzyme-papaintha. This enzyme is used in the allergy's treatment and sports injuries. All its charmed nutrients are very cooperative for the cardiovascular system and defense from heart attacks and colon cancer. Its enchanted fruit has beta-carotene and it rounds against free radicals. It is rich in fiber and keeps the high-density cholesterol level. Its fruit is too cooperative in all abdominal illnesses and the papaya peel is used as wound healing medicine and produces cooling effect. Papaya is benefit for increasing immunity against cough. Besides that, Carica papaya has a combination of alkaline with K₂CO₃ that is active for tumor and for skin treatments such as warts, sinuses and cutaneous tubercles. Today, when referring to drug iatrogenics, there are developing alternative methods to allopathic medicine, namely homeopathy, herbal medicine and acupuncture, due to their relative safety. All other medicines are based on very old and often forgotten knowledge. The current challenge is to update and modernize this knowledge by using new analysis methods (Fabert 2011). In addition, there is even a new trend emerging which consists of looking for new substitute products in food plants to relieve various diseases such as sexual and

digestive disorders, hypertension, diabetes, and even certain cancers. Biological studies on active components of food plants and foods are becoming a very attractive area of research. Thus, food plants such as Cassava, Papaya, Ginger and other vegetables used in human food are subject to various pharmacological tests in order to evaluate their effects on the body major functions. It is well known that sometimes the consumption of certain fruits such as spices and vegetables for nutritional needs causes pharmacological external. Such foods are called nutraceuticals. Research and development of nutraceutical plants could contribute to the treatment of certain pathologies by changing for example the consumption rate of the nutraceutical concerned. Many studies have reported the effects of food plants on reproductive function in humans. This is the case for the phytoestrogenic effects of soy (Feirreira, 2019). According to Debuigne and Couplan (2006), ginger stems have aphrodisiac effects and parsley acts effectively in the case of irregular and painful periods. Papaya seeds are known to have contraceptive effects in men by lowering sperm amount (Absar et al, 2006; Drevert, 2010). The antifertility effects of *C. papaya* seeds on the gonads of male albino rats are reported by Udoh et al. (1999; 2004). Papaya is one of the most consumed fruits in the tropics as a salad, dessert, or drink (Fabert, 2011). This fruit also has various therapeutic properties through its deworming and slightly purgative effects (Debuigne and Couplan, 2006). In India, *Carica papaya* apart from its delicious fruit, its different parts have different pharmacological properties such as dewormer, antibacterial, laxative, anti-inflammatory, male and female contraceptives (Aravind et al., 2013). The present study aims to enhance to compare the effects of papaya pulp with those of the seeds on reproductive function in wistar rats.

II. Materials and methods

Plant material

The ripe fruits of the papaya tree (*papaya* or *carica papaya* Linn) as shown in Figure 1, was collected in Congo Brazzaville in October 2022. The seeds were dried for 4 weeks at room temperature ($26 \pm 1^\circ\text{C}$) and ground using a mortar. The powder obtained served as plant material for the study (Figure 2). The pulp was directly transformed into fruit juice and used as an aqueous extract (Figure 3).



Figure 1: a) Photograph of *Carica papaya* Linn b) Photograph Papaya seeds c) Photograph Papaya pulp

Animal material

This study used male and female albino rats of the Wistar strain, and also Swiss mice with an average weight of 130 g and 22 g respectively (Figure 3). These animals were maintained in standard conditions of 12 hours of light and 12 hours of darkness at a temperature of $24 \pm 1^\circ\text{C}$.

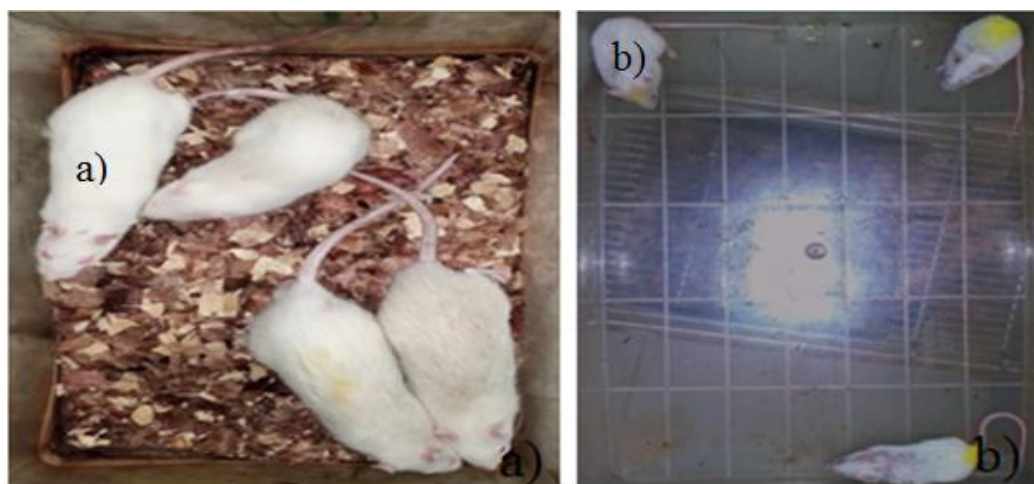


Figure 3: a) Photograph of Wistar rats. b) Photograph and Swiss mice

Preparation of aqueous extracts of carica papaya and solutions used

Preparation of the aqueous extract of carica papaya seeds

The seeds aqueous extract was obtained by maceration at 10% of the dried seed powder. Indeed, 50 g of seed powder were mixed with 500 ml of distilled water in a beaker for 24 hours under a magnetic stirrer. It was followed by filtration (3 times) on hydrophilic cotton and the filtrate was placed at the oven for 48 hours for the complete solvent evaporation. Then, the extract obtained was used for pharmacological activities.

Preparation of the aqueous extract of carica papaya pulp

Papaya pulp was directly transformed into Papaya Juice. In fact, 200 g of papaya pulp was pressed and kneaded then mixed with 1000 ml of distilled water in a beaker. Earlier, the mixture was placed in a blender for good homogenization before being filtered through filter paper to obtain the pulp juice. The juice obtained was used as an aqueous extract for pharmacological tests. The volume of the solution administered was obtained according to the formula below:

$$V = \frac{P \times D}{C}$$

V= Volume of the solution to be administered (ml);

P = Mass of the animal (kg);

D = Administered Dose (mg/kg);

C = Solution concentration (mg/ml).

Evaluation of the acute toxicity of the aqueous extract of papaya seeds and juice

The acute toxicity of the aqueous extract of *C. papaya* seeds and juice was assessed according to OECD Guideline No. 423 (2008). Nine (9) mice were divided into 3 groups of 3 and treated as follows:

- Group 1 or control group received distilled water at a dose of 1 ml/100g of body weight orally;
- Group 2 received 5000 mg/kg of the aqueous extract of *carica papaya* seeds orally;
- Group 3 received 5000 mg/kg of the aqueous extract of *carica papaya* juice orally.

Macroscopic observations were made on ptosis, piloerection, urinary excretion, reaction to external stimuli and the general condition of the animals. This refers to aggression, mobility, vocalization, state of stools, convulsions, etc.). Those observations were made at ½, 1, 2, 3 and 4 hours after administration of each product and mortality was assessed after 48 hours. The mice were left under observation for 14 days in order to monitor food and water consumption and the late appearance of toxicity signs. Thus, body weight was recorded each additional day.

Pharmacological tests carried out

Effect of the aqueous extract of the Seeds and Pulp of *C. papaya* on sexual parameters in male rats.

Groups for tests:

6 groups of 4 male rats each were formed receiving *C. papaya* aqueous extracts of pulp and seeds, reference product (Viagra) and distilled water orally for 14 days later as follows:

- Group1 received distilled water at a dose of 1ml/100g of body weight;
- Group 2 received the reference product, Viagra at a dose of 10 mg/kg;
- Group 3 and 4 received the aqueous extract of the seeds at doses of 300 and 600 mg/kg respectively;
- Groups 5 and 6 received the aqueous extract of the pulp at doses of 300 and 600 mg/kg respectively.

Female rats were made receptive by administering orally the estradiol, Oromone at a dose of 1 mg/kg for 3 days, before being mated 6 hours after the last administration.

b. Studies of sexual parameters in male rats

Sexual parameters were evaluated according to the method reported by Ondelé et al. (2015) and Akassa et al. (2019). In fact, the test consisted of mating on the 7th day of the products administration. A male and a female rats made receptive in a cage for 45 minutes. Then, the numbers of sexual mounts, erections, ejaculation and the time of latency were determined by direct observation.

Effect of the aqueous extract of carica papaya seeds and pulp on the plasma testosterone level of rats

Blood sample

At the end of fourteen days of treatment, the animals were anesthetized with diethyl ether. Blood of each rat was taken from the ophthalmic vein using hematocrit tubes (Vitex heparin) and collected in green tubes for centrifugation. After centrifugation of the blood at 3000 rpm for 30 min, the collected plasma was stored in the freezer at -20°C in 1 ml Eppendoff tubes for plasma testosterone determination.

Dosage principle

The testosterone dosage was done by ELISA using the HUMAN technique.

Phytochemical Screening of *Carica Papaya* Seeds and Pulp

The chemical screening of seeds and pulp of *C. papaya* was carried out according to the method described by Sowofora (1996).

III. RESULTS

Acute toxicity of the aqueous extract of *Carica papaya* seeds and pulp

About general condition of the mice

The results on acute toxicity showed that a single dose of 5000 mg/kg, the aqueous extracts of the seeds and pulp of *C. papaya* did not cause notable changes in the general condition and mice behavior compared to the control group. No mortality of the mice was observed after 48 hours, nor after 14 days of observation.

Weight evolution of mice

Figure 4 shows the weight change of the mice during the toxicity test. These results express that the mice treated with the aqueous extract of the seeds or pulp of *C. papaya* at a dose of 5000 mg/kg did not show significant differences ($p > 0.05$) compared to the control group.

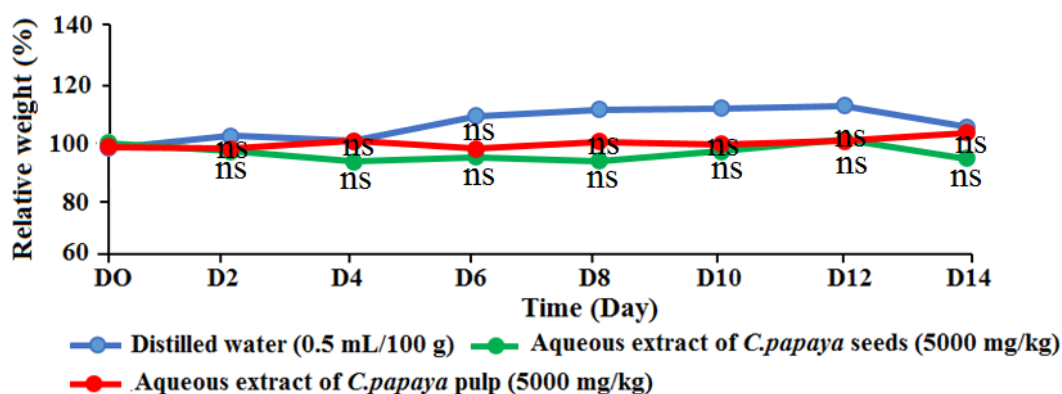


Figure 4: Weight evolution of mice treated with aqueous extracts at a single dose of 5000 mg/kg

Food and water consumption of mice

Figures 5 and 6 respectively show the variations in food and water consumption as a function of time for mice treated with a single dose of 5000 mg/kg. It looks that the aqueous extract of the seeds did not cause any variation in food consumption compared to the control group. However, the aqueous extract of *C. papaya* pulp increased the food consumption of mice in the second week of observation. As for water consumption, it was greater in the mice having received each extract compared to the control mice in the second week of observation. But, these differences are not significant.

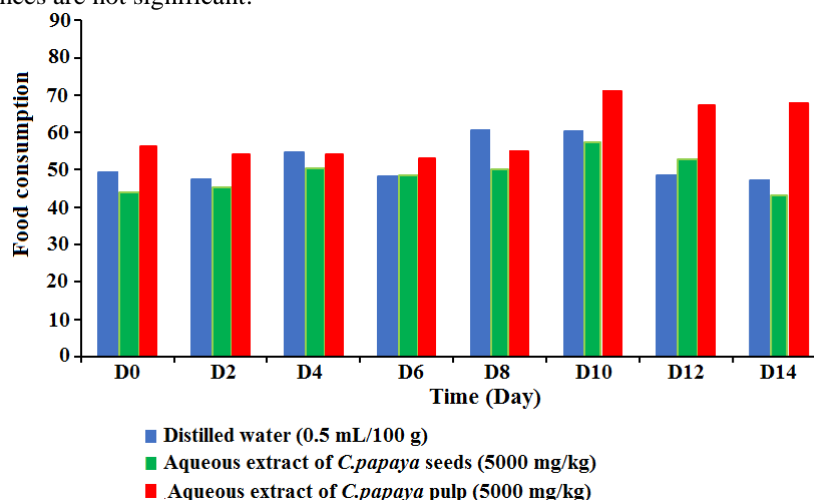


Figure 5: Variation in food consumption of mice treated with the aqueous extract at a single dose of 5000 mg/Kg; (n=3)

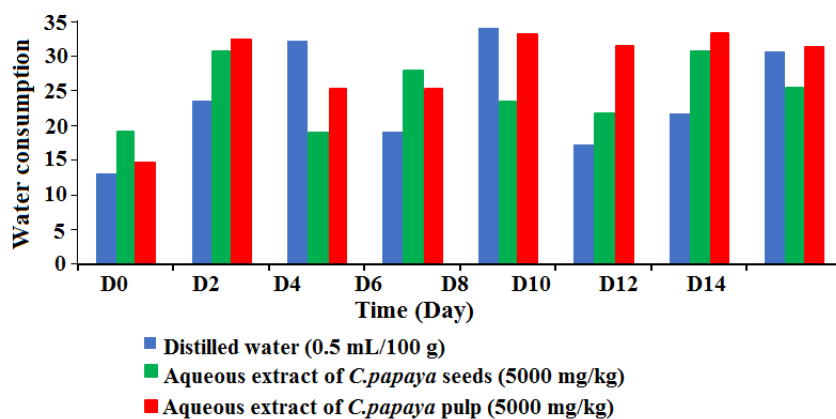


Figure 6: Variation in water consumption of mice treated with the aqueous extract at a single dose of 5000 mg/Kg; (n=3)

Pharmacological tests

Effect of aqueous extract of seeds and pulp of *Carica papaya* on sexual parameters of rats

Number of sexual encounters and erections

Figures 7 and 8 show the effect of the aqueous extract of the seeds and pulp of *C. papaya* on the number of sexual mounts and erections of the rats at seventh day (D7). It gives the idea that the administration of the aqueous extract of the seeds at doses of 300 and 600 mg/kg respectively, resulted a non-significant reduction in the number of sexual mounts and erections compared to the control group (ED). Besides, the administration of the aqueous extract of the pulp at doses of 300 and 600 mg/kg significantly reduced the number of mounts and erections. This reduction was also observed with animals having received the reference molecule.

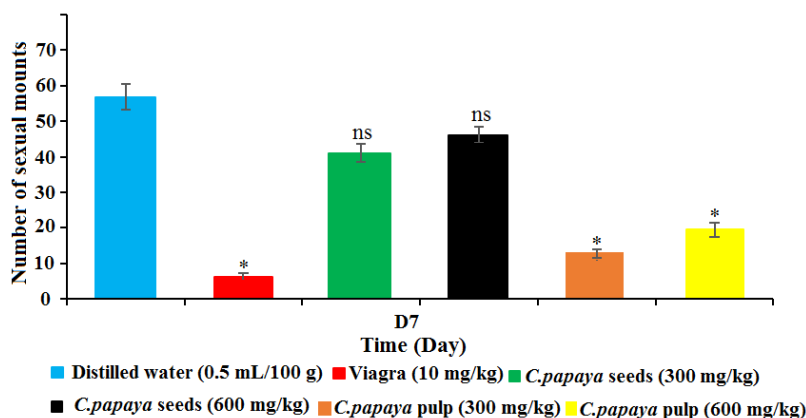


Figure 7: Effects of aqueous extracts of seeds and pulp of carica papaya on the number of sexual mounts in rats

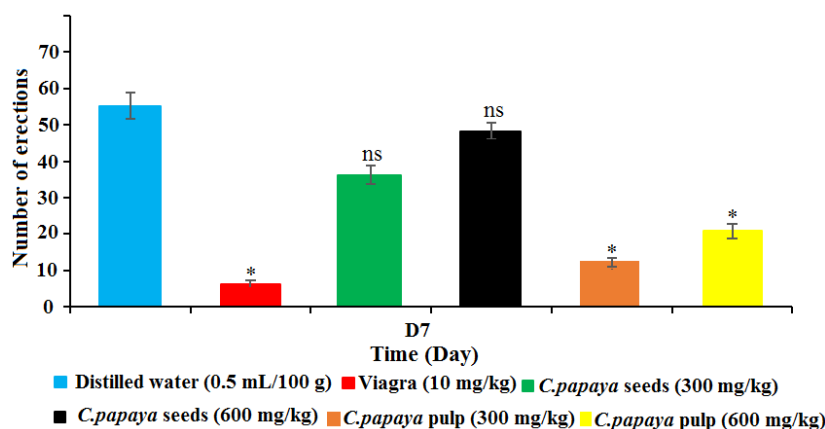


Figure 8: Effects of aqueous extracts of seeds and pulp of carica papaya on the number of erections in rats

Number of ejaculations

Figure 9 shows the effect of the aqueous extract of seeds and pulp of *C. papaya* on the number of ejaculations in rats on the 7th day of treatment. It seems that the administration of aqueous extracts of the seeds and pulp of *C. papaya* at doses of 300 and 600 mg/kg led to a non-significant reduction in the number of ejaculations compared to the control group (ED). The reference molecule also caused a reduction in the number of ejaculations.

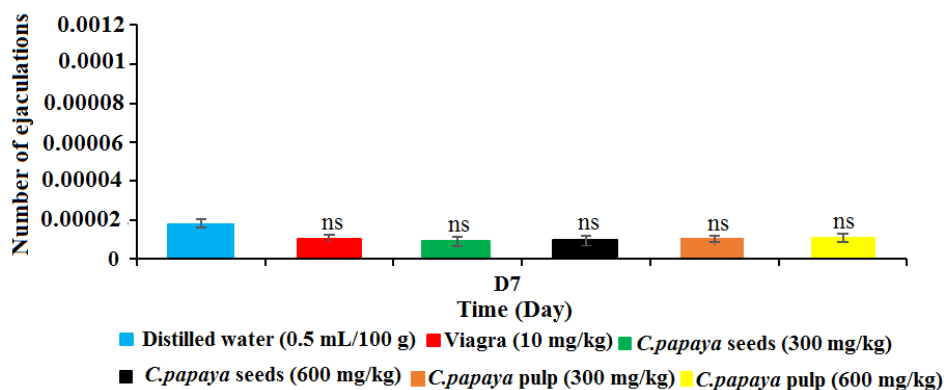


Figure 9. Effects of the aqueous extract of seeds and pulp of carica papaya on the number of ejaculations in rats

Latency time

Figure 10 shows the effect of the aqueous extract of the seeds and pulp of *C. papaya* on the latency time in rats on the seventh day (D7) of treatment. It looks that the administration of the aqueous extract of carica papaya seeds at doses of 300 and 600 mg/kg respectively led to a significant increase in latency time compared to the control group (ED). But with the aqueous extract of the pulp the difference is not significant. While, the increase in latency time was very significant with the reference molecule at a dose of 10 mg/Kg.

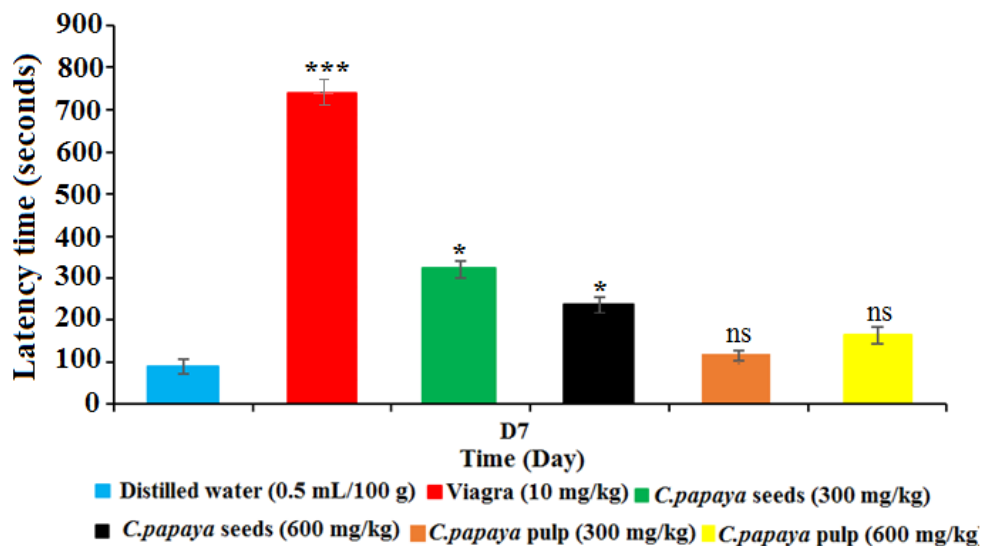


Figure 10: Effects of aqueous extracts of carica papaya seeds and pulp on latency time in rats

Effects of the aqueous extract of seeds and pulp of *C. papaya* on plasma testosterone levels

Figure 11 shows the results of testosterone dosage in animals treated with aqueous extracts of *C.papaya* seeds and pulp. It is shown a non-significant decrease in the testosterone level in the groups treated with the aqueous extract of the seeds at 300 and the extract at 600 mg/kg and the pulp at 300 mg/kg in rats with Viagra as well compared to the control group (ED). On the other hand, this figure shows a non-significant increase in the aqueous extract of the pulp at 600 mg/kg.

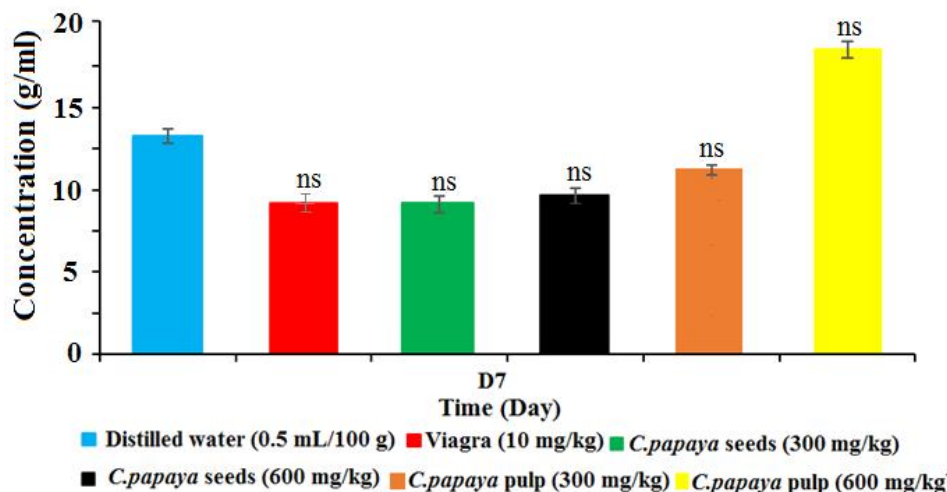


Figure 11: Effects of *Carica papaya* seed and pulp extracts on testosterone levels in rats

Phytochemical profile of the aqueous extract of *C. papaya* Seeds and Pulp

Table I illustrates the results of the chemical screening carried out on the Seeds and Pulp of *C. papaya*. It is noted the presence of a few highlighted chemical families.

Table I: Results of Chemical Screening

Chemical families	Results (<i>C. papaya</i> seeds)	Results (Pulp of <i>C. papaya</i>)
Tannins	+	+
Alkaloids	+	+
Flavonoids	+	+
Dares	+	+
Mucilage	-	+
Free anthraquinones	+	-
Steroids and terpenoids	+	+

(+) presence; (-) absence

IV. DISCUSSION

This study expected to compare the effects of aqueous extracts of the seeds and pulp of *C. papaya* on the reproductive function in male wistar rats. The acute toxicity study showed that at a dose of 5000 mg/kg, the two extracts did not show any sign of perceptible toxicity after 48 hours in mice. These results are comparable to those obtained by Etame et al, (2017). This author reported the absence of toxicity of the wine extract of *Carica papaya* seeds up to a dose of 5000 mg/kg. Monitoring the weight change of mice treated with a single dose of 5000 mg/kg of each *Carica papaya* extract did not show significant differences with the control group. Even, the variations in food and water consumption for two weeks of monitoring acute toxicity did not show significant variations between the treated groups and the control group. It shows the good tolerance of the aqueous extracts of the seeds and pulp of *Carica papaya* at a high dose. These results corroborate the different uses in traditional and modern medicine of *Carica papaya* reported by Febert (2011) and Nguyen et al, (2013).

Pharmacological effects of the two extracts

The decrease in the number of sexual mounts of rats treated with the two extracts compared to control rats, indicates that the aqueous extracts of *C. papaya* could contain substances that lower libido and sexual desire. Indeed, previous studies have revealed that the increase in the number of sexual mounts of males on females is related to the increase in libido which accentuates the physical attachment among animals (Ondel e et al., 2015; Erhabor and Idu , 2017; Eudes, 2019; Akassa et al., 2019). However, according to Febert (2011) the main alkaloid of *Carica papaya* which is carpain has amoebicidal properties being potentially bradycardic and hypotensive in rats. This could explain the decrease in the libido of rats observed in this study. On the other hand, the drop in the number of mounts with Viagra as is an aphrodisiac substance (Sabrina, 2018), could be explained by the usage of the dose of 10 mg/kg which would be too strong for the rat in the present work. Indeed, Lechat (2006) reported that in hormonology, a high dose can cause an effect contrary to that which is sought. This study also showed that

the administration of aqueous extracts of the seeds and pulp of *C. papaya* at doses of 300 and 600 mg/kg caused respectively a non-significant and significant reduction in the number of erections and ejaculations in some rats. These results suggest that the aqueous extracts inhibit the phenomenon of erection by reducing the virility of rats. Indeed, the reduction in the number of erections and ejaculations implies a reduction in blood flow in the corpora cavernosa (Ernest, 1998; Droupy, 2005; Ammari et al, 2012). These observations also showed that the administration of each *C.papaya* extract increased the latency time which confirms the decline in libido and virility in animals. This study also showed that aqueous extracts of *Carica papaya* seeds and pulp have similar effects on lowering sexual parameters. A drop in sexual parameters is comparable with the results obtained by Drevet et al. (2010). This author reported the contraceptive effects of *Carica papaya* seeds through the reduction of spermatozoa. Administration of the aqueous extract of *C.papaya* seeds at doses of 300 and 600 mg/kg and pulp at 300 mg/kg led to a non-significant reduction in plasma testosterone levels in rats. This reduction suggests that papaya seeds and pulp contain substances that inhibit testosterone production. These results are comparable to those obtained by (Udoh et al, 2008) who showed that the alkaloid activity of the extract of *C. papaya* seeds on the reproductive function in male wistar rats reduces the production of testosterone. Besides, this result corroborates the studies reported by Absar (2006), Drevet et al. (2010) who showed that daily consumption of papaya seeds led to a considerable reduction in the number of spermatozoa in rats. This effect is non-toxic because it stops at the end of the treatment. The similar effects of papaya pulp and seeds on lowering sexual parameters and decreasing testosterone levels suggest that papaya consumption could be well encouraged among men who no longer have the desire to have children and those suffering from advanced prostate cancer. Indeed, it is known that prostate cancer is a hormone-dependent pathology in more than 80% whose treatment in the advanced stage requires lowering testosterone levels (Decapeptyl Monograph, Vidal, 2020). Moreover, the drop in sexual parameters with these two aqueous extracts of *Carica papaya* is contrary to the results obtained by Onde (2016) and Akassa (2020) which demonstrated the increase in sexual parameters with respectively the aqueous extracts of *Buchholzia Coriacea* and *Pausinystalia yohimbe* by increasing testosterone levels. However, the non-significant increase in testosterone levels with papaya pulp extract at a dose of 600 mg/kg indicates that at high doses, the pulp could cause the opposite effects to those of the seeds by increasing the androgenic effect. This effect of high dose pulp could be exploited to correct pathologies related to androgen deficiencies. This result is close to that of Aravind et al. (2013) who reported that the *Carica papaya* fruit stimulates the reproductive organs in humans. This increase in plasma testosterone levels in rats with the high dose of the pulp extract is comparable to the aphrodisiac effect of papaya reported by certain traditional practitioners and Clara (2018). On the other hand, the drop in testosterone levels with Viagra although it is an aphrodisiac molecule and could be explained by a negative feedback mechanism. This work which made it possible to make a comparison between the effect of the pulp of *Carica papaya* regularly consumed in human food and the seeds, showed the similar and sometimes opposite effects of the two organs of this plant depending on doses used. This study helped to highlight the hidden therapeutic virtues of this delicious fruit. It would therefore be sufficient to adapt the doses of papaya consumed according to needs to obtain the desired physiological and pharmacological effects. This implies limiting the consumption of papaya if the desire for paternity is still necessary. While, it could be increased when there is no longer the desire and above all to probably prevent the development of prostate cancer.

Chemical screening

The phytochemical study of the aqueous extracts of the seeds and pulp of *Carica papaya* highlighted the presence of alkaloids, steroids, terpenes, flavonoids and tannins. Also, the presence of mucilages in the pulp and anthraquinones in seeds. This result is comparable to the results of Nwofial et al. (2012), Pallavi et al., (2018), Bomo et al, (2022) who worked respectively on the physicochemical, nutritional and toxicity parameters of *Carica papaya* seeds. These phytochemicals could be responsible of the pharmacological effects observed. Indeed, according to Febert (2011), the main alkaloid of *Carica papaya* has bradycardic and hypotensive properties in rats. These properties of papaya could be attributed to the reduction in sexual performance of rats receiving aqueous extracts of papaya in the present work. Besides, Latex is present in all parts of *Carica papaya*, its main enzyme which is papain would also be involved in the reduction in sperm production without being toxic (Etame, 2017; Drevet, 2010).

V. CONCLUSION

In assumption, this study designates that also nonedible parts of *C. papaya*, in particular seeds and pulp extract, may be a hopeful source of reproductive disorders treatments with therapeutic implications. In effect, we showed that *C. papaya* seeds and pulp could be very important to play an important role to treat many diseases. The present study showed that in mice, the aqueous extracts of *Carica papaya* seeds and pulp are not toxic up to a dose of 5000 mg/kg; with an LD50 greater than 5000 mg/kg. In male rats, the aqueous extracts of the seeds and pulp of *Carica papaya* at doses of 300 and 600 mg/kg have similar effects on the reduction of sexual parameters and lead to a non-significant reduction in testosterone levels, except the pulp extract at a dose of 600 mg/kg which

increases it. It would be desirable to evaluate the biological effects of the extract of *Carica papaya pulp* on the quality and number of spermatozoa in the epididymis and to establish a phytomedicine based on *Carica papaya pulp* for the treatment of reproductive disorders.

REFERENCES

- [1]. Adam, Y., Nasaruddin, A.A., Zuraini, A., Arifah, A. K., Fauzee, M.S.O., Zakaria, Z. A. And Somchit, M. N. (2018). Diuretic Activity Of Roots From *Carica Papaya L.* And *Ananascomosus L.* International Journal Of Pharmaceutical Sciences Review And Research, 23(1): 163-167.
- [2]. Parle M, Guditta. Intern Res J Pharm 2011; 2(7): 6-12.[2] Anjum V, Ansari SH, Naquvi KJ, Arora P, Ahmad A. Sch Res Lib 2013; 5(2): 370-76.
- [3]. Anuar NS, Zohari SS, Taib IA, Rahman MT. Food Chem Toxicol 2008; 46: 2384-89.
- [4]. <https://doi.org/10.1016/j.fct.2008.03.025>
- [5]. Absar A.Q., Dhirendra B., Sanghai, Et Padgilwar S.S., (2006). Herbal Options For Contraception. A Review. Pharmacognosie Magazine (Phcog Mag), 2 (8) : 0973-1296.
- [6]. Akassa H., Ondélé R., Pénéme BML., Etou Ossibi AW., Morabandza CJ., Tamboura HH., Abena AA. (2019), Aphrodisiac Activity And Study Of The Mechanism Of Action Of The Aqueous Extract Of *Pausinystalia Yohimbe Kschum (Rubiaceae)* In Wistar Rats. Journal Of Animal Et Plant Sciences Vol. 39, Issue 1 : 6372-6383.
- [7]. Ammari JE., Riyah O, Aballal Y., Mellas S., Tazi ME., Khallou KA., El Fassi MJ., Farib My H., (2012), Physiology And Pathophysiology Of Erection. Urology, 6p.
- [8]. Aravind.G ; Debjit. B ; Duraivel. S ; Gudivada H, (2013). Traditional And Medicinal Uses Of *Carica Papaya*. Journal Of Medicinal Plants Studies 1(1):7-15.
- [9]. Bomo J. A, Michel A.N, Pascal L.E, Véronique C, Séraphin K (2022), Physicochemical Parameters And Nutritional Composition Of The Pulp Of 4 Varieties Of *Papaya (Carica Papaya)* Sold On The Abidjan Market (Ivory Coast).
- [10]. Debuigne G. Et Couplan F., (2006). Small Larousse Of Plants That Heal: 500 Plants. Paris, France, 893 P.
- [11]. Droupy S. (2005). Epidemiology And Pathophysiology Of Erectile Dysfunction. Medico-Surgical Encyclopedia, Urology, 18-720-A-10.
- [12]. Ernst E., (1998). Yohimbine For Erectile Dysfunction: A Systematic Review And Meta-Analysis Of Randomized Clinical Trials, J. Urol., 159(2): 433-436.
- [13]. Erhabor J., Et Idu MD., (2017), Aphrodisiac Potentials Of The Ethanol Extract Of *Aloe Barbadensis Mill.* Root In Male Wistar Rats. Research Article, 10p.
- [14]. Etame Loe Gisèle1, Yinyang Jacques1, Okalla Ebongue Cécile, Makondo Brice Vivien1, Ngaba Guy Pascal, Mpondo Mpondo. Emmanue Et Dibong Siegfried Didier, (2017). Study Of The Acute And Subacute Toxicity Of The Wine Extract Of *Carica Papaya Linn* Seeds. Journal Of Applied Biosciences: Vol. 120:12077-12085. ISSN 1997-5902.
- [15]. Eudes F., (2019), Premature Ejaculation And Its Treatments In 2019. Doctoral Thesis. Caen University Of Normandy. 178p.
- [16]. Fabert C.M., (2011). The *Papaya Tree, Carica Papaya L.*, From Traditional Medicine To Current Medicine. Botanical And Pharmacognosic Studies. Thesis For The State Diploma Of Doctor Of Pharmacy. Faculty Of Pharmacy Limoge, 128p
- [17]. Lechat P., (2006). Pharmacology DCEM1 Level. Pharmacology Department. Pierre And Marie Curie University, 349p.
- [18]. Nwofia, G. E., Ojmelukwe, P. Et Eji, C. (2012). Chemical Composition Of Leaves, Fruit Pulp And Seeds In Some Morphotypes Of *Carica Papaya (L)*, International Journal Of Medicinal And Aromatic Plants, 2 (1), 200-206.
- [19]. Nguyen.T. T, Shaw.P. N,Parat, M. O.Et Hewavitharana, A. K, (2013). Anticancer Activity Of *C. Papaya*: A Review.Molecular Nutrition & Food Research,57 (1),153-164.
- [20]. Organisation De Coopération Et De Développement Economiques (OCDE), (2008). OECD Guidelines For Testing Of Chemicals - Acute Oral Toxicity - Upstream And Downstream UDP Procedure. France.OECD, 425p
- [21]. Ondélé R., Etou Ossibi A.W., Bassoueka D.J., Peneme M., Elion R., Binimbi A., Et Abena A.A., (2015). Acute Toxicity And Aphrodisiac Effect Of The Aqueous Extract Of *Rauvolfia Obscura K.Schum (Apocynaceae)*, Afrique SCIENCE 11(3), 172-180.
- [22]. Ondélé R. (2016), Aphrodisiac And Cardiovascular Effects Of The Aqueous Extract Of The Trunk Bark Of *Buchholzia Coriacea Engl. (Caparaceae)* In The Wistar Rat, Doctoral Thesis, Marien NGOUABI University. 126p.
- [23]. Peneme B.M.L., 2017. Ethnopharmacological Study Of Presumed Contraceptive Plants In Brazzaville. Thesis In Biological Sciences, Faculty Of Science And Technology, Marien NGOUABI University. 138 P.
- [24]. Pallavi S., Nainika T., Trisha S., Aishwarya G And Sargam V. (2018). Phytochemical Screening And Analysis Of *Carica Papaya, Agave Americana* And *Piper Nigrum*. International Journal Of Current Microbiology And Applied Sciences. ISSN : 2319-7706. 9p
- [25]. Sabrina I. (2018). Study Of The Consumption Practice Of *Viagra* Among Undiagnosed Young Men. Master's Thesis, University Of Friborg (CH). 194p.
- [26]. Udoh. F.V, Udoh. P.B Et Umoh. E.E, (2008). Evaluation Of The Alkaloid Extract Of *C. Papaya* Seeds On Reproductive Functions In Male Wistar Rats. Pharmaceutical Biology 563-567.
- [27]. Udoh P, Nju R, Udoh F (2004b). The Effect Of *Carica Papaya* On The Pituitary-Thyroid And Parathyroid Glands Of Male Albino Rats. Global J Pure App Sci 10:515-517.
- [28]. Udoh P, Kehinde K (1999). Studies On The Anti-Fertility Effect Of *Pawpaw* Seeds (*Carica Papaya*) On The Gonads Of Male Albino Rats. Phytopte Res 13: 226-228.