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ANTIDIARRHOEAL EFFECTS OF AQUEOUS LEAVE EXTRACT OF *CARICA PAPAYA* IN WISTAR STRAIN ALBINO RATS

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Abstract: In the antidiarrheal activity evaluation, the aqueous leave extract of *Carica papaya* was found to be effective against castor oil – induced diarrhea in Wistar strain albino rats at the doses of 200, 400 and 800 mg/kg body weight, the fecal droppings decreased and percentage inhibition was 38.28%, 65.16 % and 23.94 % respectively which was dose – dependent and statiscally significant at ($p < 0.05$). The control group showed typical diarrheal signs with 0.00 % inhibition while the group given the standard antidiarrheal drug loperamide 5 mg/kg body weight was protected 100 %. In the intestinal transit of charcoal meal method, the percentage inhibition of the extract treated rats were 22.80 %, 35.74 % and 31.86%, the atropine sulphate (3 ml/kg) body weight treated group was inhibited by 55.60 % and the inhibition was not dose dependant. In the castor oil induced enteropooling method, the extract inhibited the intestinal fluid accumulation in rats by 28.57 %, 24.49 % and 2.04 % relative to the control group with 0.00% inhibition. The group given atropine sulphate had 89.80 % inhibition. The results of this study suggest that the aqueous leaves of *Carica papaya* has antidiarrheal effect, this might have justified its traditional use in the treatment of diarrhea.

Keywords_Carica papaya Albino Rats, Castor oil, Diarrhea, and Loperamide

INTRODUCTION

Used of traditional medicine practitioners are very common in Nigeria. Besides, herbal medicine practice is also increasing day by day due to fewer side effects [1]. The use and identification of medicinal plants have been in existence throughout human history. Plants have the ability to synthesis a wide variety of chemical compounds that are used to perform important biological functions and to defend against attack from predators such as insects, fungi and herbivorous mammals. At least 12,000 such compounds have been isolated so far. A number estimated to be less than 10% of the total chemical compounds present in plants [2] carry out their functions on humans through processes identical to those already well understood (i.e. chemical compounds in conventional drugs). Herbal medicine does not differ greatly from conventional drugs in terms of how they work [3].

A medicinal plant is any plant used in order to relieve, prevent or cure a disease or to alter physiological or pathological process or any plant employed as a source of drugs or there precursor (4). Medicinal plants are those plants that are used (parts extract etc.) in treating and preventing specific ailment and diseases affect human beings. Knowledge of medicinal plant has resulted from trial and error method and often based on speculation and superstition. In 2001, researchers identified 122 compounds used in modern medicine which were derived from "ethnomedical" plant sources [5]. Herbal medicinal products are assuming greater roles in the lives of the people across the world in the face of global upsurge of drug resistance, toxicity, adverse effects and increasing costs of synthetic products [6]. The use of herbs in the treatment of diseases is very common among non-industrialized societies and often more affordable than purchasing expensive modern pharmaceuticals.

The World Health Organization (WHO) estimates that 80% of the populations of some Asian and African countries presently use herbal medicine for some aspects of primary health care. Studies in the United States and Europe have shown that their use is less common in clinical settings, but has become increasingly more in recent years as scientific evidence about the effectiveness of herbal medicine has become more widely available [7]. *Carica papaya* commonly called *pawpaw* in English, *papita* in Hindi and *Gwanda* in Hausa belongs to the family of Caricaceae with four genera. The plant was originally derived from the southern part of Mexico [8]. *Carica 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 truck is conspicuously scarred where leaves and fruit were borne. The leaves are large, 50-70 [20-28 inches] in diameter, deeply and palmately lobed with seven Alobes [10]. Practically, every part of *Carica papaya* is of economic value and its use ranged from nutritional to medicinal [9]. The fruits are popularly used and processed into juice and wine, while the fruits are cooked as vegetable [11]. The seeds are medically important in the treatment of sickle cell diseases, poisoning related disorder.

The leaf tea or extract has a reputation as a tumor destroyer agent and antidiarrhea. The fresh green tea is an antiseptic whilst, the brown dried pawpaw leaves are best served as a tonic and blood purifies [12]. It is traditionally used to treat yellow fever, diarrhoea, eczema, rashes, and stomach ache [13]. In Nigeria, pawpaw is one of the most popular, cheapest, economically important fruit tree grown and consumed for its nutritional content and medicinal purposed [14]. *Carica papaya* contains the enzyme papain, which is present in the fruits, stem and leaves [15]. It contains biologically active compounds such as chymopain and papain which aids in digestion [16]. Diarrhea is described as loose of watery stools that occur more frequently than usual. It could also be defined as the

deviation from normal bowel movement *i.e.* greater looseness of stool. The word "diarrhea" originated from the greek word *diarrhoia. Dia* means "through" and *rheo* means "flow". The term "flowing through" was coined by Hippocrates [17]. Diarrhea is the opposite of constipation and can have many causes which may be infectious or non-infectious. In many cases, diarrhea usually last for few days which is usually termed as acute diarrhea. However, in some cases diarrhea may last for weeks. In this situation, the diarrhea is said to be chronic. Generally there are five types of diarrhea which are the motility diarrhea, secretary diarrhea, osmotic diarrhea, inflammatory diarrhea and dysentery. Diarrhea could be caused by bacteria *Vibrio cholera.* It could also be caused by undigested lactose, too much magnesium, vitamin C. It may also be caused as a result of celiac disease or laxatives [18]. Symptoms of diarrhea may include frequent passage of watery stool, stomach ache, abdominal pain, Nausea (fever), head ache, loss of appetite etc. it could be managed/ treated with medications such as loperamide which slows down the bowels movement and increases the guts absorption. Diarrhea could also be treated by drinking a lot of fluid which helps in replacing the fluid loss and reduce the risk of dehydration. Medicinal plants have now generated renewed interest amongst scientists of various cadres covering agriculture, Veterinary medicine, Human medicine Pharmacognosy etc. the current study was done to evaluate the anti-diarrhea property of *Carica papaya* leaves in albino rats.

Materials and Methods

Collection of the Plant Sample and Identification

Leaves of *Carica papaya* were collected from University of Maiduguri guest house in the month of January 2017. The plant was identified and authenticated by a Botanist from the Department of Biological science, University of Maiduguri.

Preparation of Plant Material

After collection of leaves, it was washed and shade dried at room temperature for 7 days in the Biochemistry Research Laboratory University of Maiduguri. The dried leaves were made coarse by the use of a mortar and pestle. 300 grams of the dried leaves were soaked in 30% methanol and 70% distilled water for three days. The soaked leaves were refrigerated and stirred occasionally. The soaked leaves was filtered using muslin cloth. The residue was discarded and the filtrate was evaporated using a hot plate at a temperature range of 40-45 °C. The weight of the extract obtained was 45.48 grams and the percentage yield was 15.16% [19].

Experimental Animals

Sixty (60) Male Wistar Albino Rats Weighing (120–230) g were obtained from the animal house unit of the Department of Biochemistry, Faculty of Sciences,

University of Maiduguri, Borno State, Nigeria at room temperature for two weeks for acclimatization they had free access to clean water and food. The experiments reported here complied with ethical procedures of animal ethics [20].

Effect of Aqueous Leaf Extract of *Carica papaya* on Castor oil Induced Diarrhea in Wistar Strain Albino Rats

A total of 20 Albino Rats weighing between 135-230 grams were used. The rats were fasted for 18 hours and separated into five groups of four animals each. Group I was treated with (2 ml/kg) body weight of normal saline orally (negative control). Groups II, III, and IV were respectively treated with 200, 400, and 800 mg/kg body weight of aqueous leaf extract of *Carica papaya* orally. Group V (positive control) received 5 mg/kg (intraperitoneal) body weight of loperamide (diphenoxylate). After one hour, the rats were placed singly in cage laid with plain white sheet of paper and each rat was treated with 1ml of castor oil orally. The rats were observed for six (6) hours for watery (wet) or unformed faeces. The watery faeces of each rat were counted at the end of six hours [21-22].

Effect of Aqueous Leaf Extract of *Carica papaya* on Intestinal Transit Time of Charcoal Meal in Wistar Strain Albino Rats

Twenty Albino Rats weighing between 125 to 250 grams were used. The rats were fasted for 18 hours and placed into five groups of four animals each. Group I was treated with 1ml normal saline orally (negative control). Groups II, III and IV were respectively treated with 200, 400 and 800 mg/kg body weight of Aqueous Leaf Extract of *Carica papaya* orally. Group V received 3 ml/kg (intraperitoneal) body weight of atropine sulfate. Thirty minutes after drug and extract administration, 1 ml of 5 % activated charcoal suspension in 10 % aqueous solution of acarcia gum powder was given orally to each rat. The charcoal meal was prepared by dissolving 2.5 g of acarcia gum powder and 2.5 g of activated charcoal in 25 ml of normal saline. After thirty (30) minutes, the rats were sacrificed and then the abdomen opened. The distance travelled by charcoal meal from pylorus were measured and expressed as percentage of the total length of the intestine from the pylorus to the caecum [23-24].

Effect of Aqueous Leaf Extract of Carica papaya on Castor Oil Induced Enteropooling in Wistar Strain Albino Rats

Twenty (20) Albino Rats weighing between 135 to 230 g were used. The rats were fasted for 18 hours and separated into five groups of four rats each. Group I rats were treated with 2 ml/kg body weight of normal saline orally (negative control). Groups II, III, and IV were respectively treated with 200, 400 and 800 mg/kg body weight of aqueous leaf extract *Carica papaya* orally. Group V received ml/kg (intraperitoneal) body weight of atropine sulfate. After thirty minutes (30) each rat was treated with 1ml of castor oil. One hour after castor oil treatment, the rats

were sacrificed and the small intestine removed, tied on both ends with thread and weighed. The intestinal content was collected by milking and the volume measured. The intestine thereafter weighed and the differences between full and empty intestine were calculated [24, 25].

Statistical Analysis

The result were expressed as mean ± standard error of mean (SEM). Statistic analysis were performed using one way analysis of variance (ANOVA) (Turkey: Compared all pairs of column or Dunnett tests). Values of $p<0.05$ were considered significant. *Computer software GraphPad InStat® @* USA. 2003 [26].

Results

The results shows that there was highly significant ($p<0.05$) decrease in faecal dropping in group treated with 200, 400 and 800ml/kg. The control drugs has the highest % inhibition while in the calculated % inhibition of faecal dropping, there was significant ($p<0.05$) decrease in % inhibition. And the percentage inhibition was 38.28, 65.18 and 23.94%. The control drug loperamide (diphydroxylate) inhibit the castor oil induced diarrhea by 100%.

Table 1: Effect of Aqueous Leaf Extract of *Carica papaya* on Castor Oil- Induced Diarrhea in Wistar Strain Albino Rats

Treatment Dose	Fecal Dropping	%Inhibition
Normal Saline (control) 2ml/kg	13.75±0.48	-
Extract 200ml/kg	8.50±0.65***	38.28
Extract 400ml/kg	4.75±0.63***	65.16
Extract 800ml/kg	10.50±1.04***	23.94
Control drug (loperamide) 5ml/kg	0.00±0.00***	100.00

Mean ± SEM, n=*** ($p<0.05$). There was highly significant decrease in % inhibition compare with the control. The effect of aqueous leaf extract of *Carica papaya* on castor oil induced diarrhea was presented on table **1.**

The result of the transit of charcoal meal was presented on table 2. The result shows that, there was significant ($p<0.05$) decrease in the transit of charcoal meal in groups treated with 200, 400 and 800mg/kg of the extract, while the control drugs has the highest inhibition of charcoal transit. The rats were reduced by 22.80%, 35.74% and 31.86% while the atropine sulfate 3ml/kg by 55.60%.

Table 2: Effect of Aqueous Leaf Extract of Carica papaya on Intestinal Transit Time of Charcoal Meal in Wistar Strain Albino Rats

Treatment Dose	Distance Travelled by Charcoal Meal (cm)	Total Length of Intestine (cm)	% Inhibition
Normal Saline 2ml/kg	87.00± 1.08	92.43± 4.42	-
Extract 200mg/kg	67.00±4.26*	103.70±6.94	22.80
Extract 400mg/kg	55.90± 1.49***	94.28.± 3.07	35.74
Extract 800mg/kg	59.23± 0.88***	84.25± 2.20	31.86
Control Drug Atropine 3ml/kg	38.48± 3.13***	82.45 ±6.04	55.60

Mean ± SEM, n= 4 ***P<0.05 highly significant compared with the control. *P<0.001 slightly significant compared with the control.

There was a statistically significant difference (P<0.05) in the weight of full intestinal contents of rats in the groups treated with various Doses and that of the control group. However, there was a significant difference (P<0.05) in the weight of full intestinal contents of rats treated with 400 and 800mg/kg of extract compared to that of the control group (Table 3). There was also a significant (P< 0.05) marked inhibition of the intestinal fluid volume in the rats treated with 400 and 800mg/kg. There percentage inhibition at 200, 400 and 800mg/kg was 28.57, 24.49 and 2.04% respectively. While in the atropine sulfate treated (positive control drug), there was marked inhibition of 89.80 % intestinal fluid volume at 3 ml/kg

Table 3: Effect of Aqueous Leaf Extract of *Carica papaya* on Castor Oil Induced Enteropooling in Wistar Strain Albino Rats

Treatment Dose	Weight of full Intestine (g)	Weight of Empty Intestine (g)	% Inhibition
Normal Saline 2ml/kg	5.100± 1.32	3.86± 0.14	-
Extract 200mg/kg	5.23±0.40*	4.58±0.30	28.58
Extract 400mg/kg	5.33± 0.47***	4.40.± 0.58**	24.49
Extract 800mg/kg	5.83± 0.48***	4.63± 0.23	2.04
Control Drug Atropine 3ml/kg	4.05± 030**	3.93 ±0.30	89.80

Mean ± SEM, n= 4
*** P < 0.05, highly significant compared with the control
**P<0.01 moderate significant compared with the control
*P<0.001 slightly significant compared with the control.

DISCUSSION

In this study, the evaluation of the aqueous leaf extract of antidiarrheal effect of *Carica papaya* comprised evaluation of its effects on castor oil-induced diarrhea, its effects on gastrointestinal transit of charcoal meal and castor oil-induced enteropooling was also investigated with reference to actions of drugs like atropine sulfate in reducing gastrointestinal transit and fluid accumulation and also drugs like loperamide which reduces secretory diarrhea. Castor oil, a very

effective laxative is hydrolyzed in the upper small intestine to ricinoleic acid, which can stimulate fluid secretion, inhibit water and electrolyte absorption, reduce active sodium and potassium absorption and decrease Na, K-ATPase in the small intestine and colon. The use of castor oil induced –diarrhea as a model is logical in our study because the autacoids and prostaglandin are involved in the causation of diarrhea [27, 28]. The liberation of ricinoleic acid from castor oil results in irritation and inflammation of the intestinal mucosa, leading to release of prostaglandin which stimulates motility and secretion [29]. In this study, the results showed that aqueous extract of *Carica papaya* leaf could in a dose – dependent manner, reduce castor oil-induced diarrhea as well as the number of diarrheal feces and total weight of feces, which could be taken as antidiarrheal activities. Loperamide is one of the most efficacious and widely used antidiarrheal drugs. Loperamide effectively antagonized the diarrhea induced by castor oil. The therapeutic effect of loperamide is believed to be due to its antimotility and antisecretory activity; atropine produced a significant reduction in both the intestinal fluid accumulation and transit time because it is a competitive antagonist of acetylcholine. It acts by blocking the muscarinic receptors of the acetylcholine causing muscle relaxation thereby treating diarrhea [30].

Loperamide (a standard antidiarrheal drug) is a synthetic opiate analogue developed specifically for use in diarrhea. All opiate agonists have effects on intestinal smooth muscle. Loperamide regulates the gastrointestinal tract by inhibiting the propulsive motor activities, predominantly in the jejunum and this effect is partially inhibited by opiate antagonists. Other effects on intestinal motility may be mediated through inhibition of prostaglandin stimulation of gut motility and/or through calcium antagonist action [31]. Antidiarrheal properties of medicinal plants were found to be due to tannins, flavonoids, alkaloids, saponins, reducing sugars, sterol, and glycosides. Hence, tannins, reducing sugars, flavonoids and saponins may be responsible for mechanism of antidiarrheal activity of Aqueous Leaf Extract of *Carica papaya.* These provide a scientific basis for the potential use of *Carica papaya* leaf in gastrointestinal disorders such as diarrhea [32].

The Aqueous Leaf Extract of *Carica papaya* exhibited significant antidiarrheal activity on gastrointestinal transit of charcoal meal in rats. Hyper motility characterizes forms of diarrhea where the secretory components are not the causative factor. The aqueous leaf extract of *Carica papaya* suppressed the propulsive movement of gastrointestinal transit of charcoal meal which clearly indicates that extract may be capable of reducing the frequency of stools in diarrheal conditions [33]. Aqueous leaf extract of *Carica papaya* was found to possess an anti enteropooling in castor oil-induced diarrhea in albino rats by reducing both weight and volume of intestinal content. These effects are direct

consequences of reduced water and electrolytes secretion in small intestine, suggesting that extract may enhance water and electrolyte absorption from intestinal lumen.

CONCLUSION

The extract of *Carica papaya* showed antidiarrheal activity in rats' model. Moreover, the extract found to be safe at dose of 200mg/kg in rats model. The findings suggest the validity of the acclaimed effect of *Carica papaya* as antidiarrheal agent in traditional herbal medicine.

Conflict of Interest

The author has declared that there is no conflict of interest related to this paper.

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