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Effect of Intragastric Administration of Crude Aqueous Leaf Extract Of *Anacardium occidentale* on Gastric Acid Secretion in Rats

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Summary: The effect of an aqueous leaf extract of *Anacardium occidentale* on gastric acid secretion was tested in rats. Twenty (20) Wistar albino rats were used for the gastric acid assay experiment. The rats were divided into 2 groups of 10 each. Gastric acid output was determined by continuous perfusion of rat stomach in urethane anesthetized rats. Control gastric acid output was obtained using 0.9% sodium chloride as perfusate and extract induced gastric acid output was obtained by perfusion with 0.1% solution of *Anacardium occidentale* Intragastric administration of the extract caused significant increase in mean gastric output ($P<0.05$). Atropine (5µg/100g,) lM and Cimetidine (5mg/100g), IM. significantly inhibited the extract induced gastric acid secretion via muscarinic and histaminic receptors respectively. Our findings showed that the use of the plant extract as a single anti-gastric ulcer therapy may not involve lowering of acid secretions rather it may be due to its anti Helicobacter pylori effect

Keywords; *Anacardium occidentale, aqueous extract, gastric acid secretion, rats, intragastric.*

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INTRODUCTION

The plant, *Anacardium occidentale*. L belongs to the Family; *Anacardiaceae*. It is popularly called cashew. Extracts of the leaf, bark and root of the plant have found wide application in folk medicine.

The plant has been variously used as antidiabetic, antibacterial, anti-inflammatory, purgatives, hypotensive and diuretic. It has been found to be particularly useful in the management of gastrointestinal disorders like colic, dyspepsia, stomachache, dysentery, diarrhea, and stomach ulcer (Leslie, 2005).

The antidiabetic effect of the leaf extract (Leonard *et. al.* 2006) stem bark extract (Ojewole 2003) and the root extract (Evans, 2005), have all been demonstrated scientifically. The mechanism by which *Anacardium occidentale* acts is thought to be through the inhibition of tyrosinase enzyme (Kubo. *et. al.* 1994).Leaf extract of *Anacardium occidentale* has also been reported to have an ameliorating influence on the nephropathy usually associated with diabetes (Leonard,2006).

Also documented by research is the anti inflammatory property of the extract of the plant (Mota, 1983, Ojewole, 2004). The stem bark extract of the plant has been proven to reduce the rat paw edema induced by fresh egg albumen (Ojewole, 2004). The mechanism by which the extract elicits this anti inflammatory effect has been attributed to tannins (Mota. 1985) and flavonoids (Harikrishna, 2004). Another possible mechanism by which the extract exhibits anti inflammatory effect is through the inihibition of Nitric oxide producing inflammatory cells (Olajide, 2004).

Recently, scientists have demonstrated that extracts of *Anacardium occidentale* has inhibitory effect on *Helicobacter pylori*, the infectious agent

incriminated in the pathogenesis of gastric ulcer (Kubo *et. al.,* 1999). *H. pylori* peptic ulcers are treated with drugs that kill the bacteria reduce stomach acid and protect the stomach lining (Anonymous 2004). Treatment usually involves a combination of antibiotics, acid suppressors and stomach protectors (Anonymous 2004). According to Bamberg *et. al.,* (1992) as well as Mohammed and Hunt (1994), anti-secretory drugs have been found to be effective in the treatment of peptic ulcer disease especially where excessive acid secretion is implicated.

Most of the current drugs used against peptic ulcer are not without side effects. Dizziness, headache, vomiting, diarrhea have been associated with multiple therapy (Anonymous, 2005). Considering these challenges, there is a need for the development of safer compounds that could be used as a single therapy for peptic ulcer management.

There is currently a dearth of research publications supporting the folkloric use of this plant in the management of stomach ulcer. Since acid secretory function of the stomach is critical to the pathogenesis of gastric ulcer, there is need to evaluate the acid secretory function of the stomach in response to oral administration of crude extract of the plant.

In the present study, the effect of the aqueous extract or *Anacardium occidentale* was studied in rats. The aim is to determine the effect and also elucidate the probable mechanism of action of the extract.

MATERIALS AND METHODS

Preparation of Crude Extracts

Leaves from *Anacardium occidentale* were collected from the University of Abeokuta's cashew plantation. The plant was identified by trained staff of the University. The plant leaves were dried in the laboratory at room temperature and powdered in a mixer grinder, until a constant weight was obtained. 100grams of ground *Anacardium occidentale* leaves was soaked in 500ml of distilled water for 8 hours and thereafter filtered using Whatman's Nos 1 filter paper. The Filtrate was subsequently evaporated to dryness in an electric oven at 56^{o}C for 72 hours. The resulting dark brown jelly paste was stored in capped bottles in a refrigerator at 4^{o}C until required.

Experimental Animals

Twenty Wistar albino rats of both sexes weighing between 150-220 grams were used for the study. The rats were divided into 2 groups of 10 animals each. The animals were obtained from a commercial rat breeder in Abeokuta. The animals were fasted for 24hours preceding the commencement of the experiment, and were allowed free assess to drinking water.

Gastric Acid Collection and Assay

The method used was essentially the modified continuous perfusion technique of Ghosh and Schild (1958), for continuous recording of gastric acid secretion in rats. Each animal was anaesthetized with 25% (W/V) solution of urethane at a dose of 0.6mls per 100g. intraperitoneally (i.p). The trachea was cannulated with a polythene tubing so as to allow for free breathing during the experiment. A pyloric canula for collection of the stomach effluent was inserted through the incision in the wall of the abdomen and proximal duodenum. The canula was secured around the pyloric ligation. Then an oro-oesophageal tube was passed through the mouth to the stomach and secured with a ligature, this was used for the perfusion of the stomach.

The food particles remaining inside the stomach were washed out by passing normal saline and gently pressing the stomach to expel the gastric contents. This was continued until a clear solution completely free of food particles was obtained. Finally the stomach and intestine were returned to their proper places and the abdominal wounds closed by putting moist cotton wool soaked in 0.9% normal saline over the wound.

The animals were allowed 60 minutes after surgery for stabilization. The rat stomach was perfused through the oro-esophageal tube with 0.9% saline at 37^{o}c and at 1.0ml/min.Since the normal body temperature was 37^{o}C, the temperature of liquid going into the stomach was maintained at this temperature. This was done by using an organ bath whose thermostat was set at 37^{o}C. The infusion tube was coiled several times into the organ bath before finally going into the esophagus.

The effluent was collected at 10 minutes intervals for 60 minutes and assayed for its acid content by titrating against 0.01M NaOH. When a steady basal acid secretion had been obtained with saline, the stomach was then perfused with the extract at a concentration of 1gm/L also in saline (0.9%) at the rate of 100ml/min. (Ita *et. al.,* 2005). The initial pH of the extract was 5.6 but was adjusted to 7.0 with 0.01M NAOH before it was used for perfusion. Samples were collected at 10 minutes interval for another 60 minutes (Osim, *et.al*. 1991). In the group A rats, after the peak acid output had been obtained, a blocking agent Cimetidine (5mg/100grams) was administered intramuscularly and gastric effluent samples were collected for a further 60 minutes. Group B rats were treated with atropine administered intramuscularly and samples of gastric effluent were collected for 60 minutes as in group A.

Data was expressed as Mean ± SEM. Differences in means between and across groups were compared using student t-test. P< 0.05 was considered significant.

RESULTS

Anacardium Occidentale extract increased gastric acid secretion. The basal output for GroupA rat was 0.81 ± 0.036 Meq/10 minutes and the mean output through out the period of extract administration was 18.8 ± 0.7 Meq/10 minutes. 30 minutes after Administration.

For the group B rats, the effect of Atropine on extract was tested. The mean basal output was 0.76 ± 0.031 Meq/10 minutes and the mean output during administration of extract was 13.7 ± 0.62Meq/10 minutes. This represents a significant increase over the control acid output.

Atropine significantly (P<0.05) reduced the extract stimulated acid output to 1.07 ± 0.05 Meq/10 minutes, thirty minutes after administration of extracts.

Table 1:
Effect of Extract and Drugs on gastric output in Group A and B

	Basal Acid output (Meq/10min)	**Extract induced acid output (Meq/10min)**	**Acid output after administration of blockers (Meq/10min)**
Group A (CIMET)	0.81 ±0.36[a]	12.8 ±0.71[b]	0.75 ±0.038[a]
Group B (ATRP)	0.76 ±0.031[a]	13.7 ±0.62[b]	1.07 ±0.05[a]

CIMET = Cimetidine; ATRP = Atropine
Values in the column with different super scripts are significantly different at P<0.05. Values are expressed as mean ± SEM.

DISCUSSION

The experiment has clearly demonstrated that intra-gastric administration of 0.1% aqueous leaf extract of *Anacardium occidentale* markedly increased the gastric output in both group A and B rats as shown in Table 2. Since intramuscular administration of Atropine and Cimetidine to both groups A and B rats respectively completely reversed the increased acid output due to the extract. Its mechanism of action may probably involve both muscarinic and histaminic H_2 receptors.

The significant increase in gastric acid output evoked by the extract may be due to parasympathetic stimulation and the release of acetylcholine, which is known to stimulate the release of gastric juice rich in acid (Schubert and Shamburek; 1990). It is therefore likely that the secretory action of the crude extract was caused by the release of acetylcholine like agent from the nerve endings of the stomach.

The binding of secretagogue to the oxyntic cell receptors is coupled to at least 2 possible intracellular messengers Ca^{2+} and cyclic AMP. Cholinergic action controls the influx of extracellular Ca^{2+} into the oxyntic cells with subsequent activation of undefined intracellular events resulting in acid secretion.

In the group A rats, that received cimetidine (30 minutes) after administration of the extract, acid output was also reduced. This could be as a result of competition between the agonist and antagonist leading to the displacement of chemical compounds in the extract that has affinity for the H_2 receptors.

From observations made in these experiments, one could therefore infer that the action of the extract is probably exerted through a dual pathway mechanism; one is via the muscarinic cholinoceptors in which acetylcholine-like agent is the transmitter and is blocked by atropine. The other pathway is probably via the H2-receptor sub type in which histamine like agent is the transmitter; and is blocked by the anti histamine, Cimetidine. Histamine does not require extra cellular calcium (Ca^2+) for stimulation of acid secretion. Cyclic AMP is the intracellular messenger coupling the effect of Histamine to hydrogen ion production and secretion.

Since gastric ulcer does not necessarily involve high gastric acidity, many gastric ulcer drugs do not act via inhibition of acid secretion, rather their ameliorative effects is through the inhibition of *H. pylori*, the causative agent of the disease. Although our extract, based on the findings of this study did not inhibit acid secretion, it could still be useful as an anti-gastric ulcer agent because of its proven effect on *H. pylori* (Kubo *et al* 1999).

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