

Receptor-Specific Effects Of Aqueous Extract Of *Jatropha tanjorensis* On Gastric Acid Secretion In Male Wistar Rats

Aliyu Ozioma Fati^{1,2}, Abubakar Musa Garba², Umar Zayyanu Usman², Khadija Muhammad Kanoma⁵, Saidu Kasimu³, Onwuchekwa Chinedu², Onyinoyi Bethel Onimisi⁴, Basiru Shuaibu²

¹Department of Physiology, Faculty of Basic Medical Sciences, College of Health Sciences, Prince Abubakar Audu University PMB, 1008, Kogi, Nigeria.

²Department of Physiology, Faculty of Basic Medical Sciences, College of Health Sciences, Usmanu Danfodiyo University PMB, 2254, Sokoto, Nigeria.

³Department of Chemical Pathology and Immunology, Faculty of Clinical Sciences, College of Health Sciences, Usmanu Danfodiyo University PMB, 2254, Sokoto, Nigeria.

⁴Department of Anatomy, Faculty of Basic Medical Sciences, College of Health Sciences, Usmanu Danfodiyo University PMB, 2254, Sokoto, Nigeria.

⁵Department of Obstetrics and gynecology, Federal Medical Center Gusau

Corresponding author's email & Phone no.: fatimatu1515@gmail.com, 08038702504

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ABSTRACT

Background: Gastric acid secretion is regulated by histaminergic, cholinergic, and gastrin-mediated pathways, which are critical in digestion but, when dysregulated, contribute to acid-related gastrointestinal disorders such as peptic ulcer disease. While standard therapies target acid secretion, concerns about their long-term safety have encouraged exploring plant-based antisecretory agents. *Jatropha tanjorensis*, rich in flavonoids, tannins, and saponins, has documented gastroprotective and antioxidant properties but its specific effects on receptor-mediated gastric acid secretion pathways remain unclear. Method: Adult male Wistar rats were pretreated orally with aqueous extract of *Jatropha tanjorensis* (AEJT) at doses of 125, 250, and 500 mg/kg or vehicle. Under anesthesia, gastric acid secretion was measured via continuous perfusion before and after intravenous stimulation with histamine, carbachol, or pentagastrin. Acid output, pH, titratable acidity, and pepsin activity were assessed. Data were analyzed using one-way ANOVA and Tukey's post hoc test with significance at $p < 0.05$. Results: AEJT significantly inhibited basal and histamine-stimulated gastric acid secretion in a dose-dependent manner, with maximal suppression observed at 500 mg/kg ($p < 0.05$). Similarly, carbachol-stimulated acid secretion was significantly decreased by the highest dose of AEJT. In contrast, AEJT treatment significantly increased gastric acid secretion. Conclusion: AEJT exhibits significant, dose-dependent modulation of gastric acid secretion by inhibiting histamine- and cholinergic-induced pathways while enhancing gastrin-mediated secretion. These findings support the therapeutic potential of *Jatropha tanjorensis* as a selective antisecretory and gastroprotective agent, advocating further research into its mechanisms and clinical applications.

Keywords: Carbachol, Gastric acid secretion, Histamine, *Jatropha tanjorensis*, Pentagastrin, proton pump, Wistar rat

1.0 INTRODUCTION

Gastric acid secretion is a highly coordinated physiological process essential for digestion, protein breakdown, and pathogen defence. However, excessive or dysregulated acid secretion contributes to several acid-related gastrointestinal disorders, including gastritis, peptic ulcer disease (PUD), gastroesophageal reflux disease (GERD), and mucosal erosions (Xiang *et al.*, 2021). Acid secretion is regulated by the interaction of three major stimulatory pathways: histaminergic, cholinergic, and gastrin-mediated mechanisms. Histamine stimulates parietal cells through H_2 receptors, enhancing cyclic adenosine monophosphate (cAMP) signaling; acetylcholine, mimicked experimentally by carbachol, activates muscarinic M_3 receptors through calcium-dependent pathways; while gastrin or its synthetic analogue pentagastrin stimulates CCK_2 receptors and also promotes histamine release from enterochromaffin-like

cells (Chen, 2023; Sethi *et al.*, 2022). Because these pathways converge on the H^+/K^+ -ATPase proton pump, agonist-induced secretion models (histamine, carbachol, and pentagastrin stimulation) remain essential tools for evaluating drug candidates and plant extracts with potential antisecretory activity (Kumar *et al.*, 2021; Vela & Xue, 2022).

The global burden of acid-related disease remains significant, especially in developing countries where *Helicobacter pylori* infection, NSAID use, alcohol consumption and stress are prevalent (Edem *et al.*, 2020). Although proton pump inhibitors (PPIs) and H_2 -receptor antagonists remain the standard therapy, concerns about long-term adverse effects — such as micronutrient malabsorption, renal impairment, dysbiosis and rebound hyperacidity — have renewed interest in safer, plant-based antisecretory alternatives (Malaeb & Rachid, 2021; Song *et al.*, 2023). Medicinal



plants contain diverse bioactive compounds including flavonoids, tannins, alkaloids, and saponins, many of which demonstrate anti-ulcer, antioxidant, cytoprotective and antisecretory properties (Manjunatha, 2022; Srivastava *et al.*, 2021). Therefore, assessing herbal extracts using receptor-specific stimulation models provides mechanistic insights and enhances therapeutic development.

Jatropha tanjorensis, a leafy vegetable belonging to the Euphorbiaceae family, is widely consumed in West Africa and traditionally used for ailments such as anemia, diabetes, inflammation, and gastrointestinal disturbances (Oladele *et al.*, 2020; Awote *et al.*, 2023). Phytochemical analyses of *J. tanjorensis* demonstrate abundant flavonoids, phenolics, tannins, saponins, carotenoids and vitamins, which are known for their antioxidant and gastroprotective roles (Awote *et al.*, 2023; Umoren *et al.*, 2023). Flavonoids, for instance, modulate gastric secretion by inhibiting histamine release, suppressing proton-pump activity, enhancing prostaglandin synthesis, and improving mucosal defenses (Francis *et al.*, 2021). Tannins stabilize mucus and form protective complexes with epithelial proteins, while saponins contribute anti-inflammatory and cytoprotective effects (Barde *et al.*, 2020; Yakubu *et al.*, 2022).

Recent pharmacological studies indicate that extracts of *J. tanjorensis* possess anti-ulcer and antioxidant properties. Umoren *et al.* (2023) demonstrated that the extract significantly reduced aspirin-induced gastric lesions, increased gastric mucus production, and ameliorated oxidative stress biomarkers in Wistar rats. Similarly, Antia *et al.* (2021) showed that *J. tanjorensis*-based formulations improved mucosal healing in chemically-induced gastric injuries.

Despite growing interest, the antisecretory potential of aqueous extract of *J. tanjorensis* (AEJT) has not been fully characterized using receptor-specific stimulation models. Most existing studies emphasize antioxidant or anti-ulcer effects using ethanol-, NSAID-, or indomethacin-induced ulcer models (Oladele *et al.*, 2020; Umoren *et al.*, 2023). However, these models do not distinguish whether the plant acts by reducing acid secretion, enhancing mucosal defenses, blocking receptor-mediated signaling, or inhibiting the proton pump directly (Kumar *et al.*, 2021).

If AEJT inhibits histamine-stimulated acid secretion, it would suggest an effect on H₂-receptor pathways or inhibition of histamine synthesis or release (Sethi *et al.*, 2022). Reduction of carbachol-stimulated secretion would indicate muscarinic antagonism or interference with intracellular calcium signaling (Vela & Xue, 2022). Inhibition of pentagastrin-induced secretion could reflect modulation of CCK₂ receptor activity or downstream parietal cell mechanisms (Chen, 2023).

Moreover, demonstrating inhibition across all three pathways would support a possible proton-pump-targeted or multi-pathway inhibitory mechanism.

Therefore, the aim of this study is to scientifically evaluate the receptor mediated and gastroprotective effects of the aqueous leaf extract of *Jatropha tanjorensis* (AEJT) against major gastric secretagogues (histamine, carbachol, and pentagastrin) in a perfused rat stomach model.

The specific objectives are:

- To determine the acute and sub-chronic toxicity profile of AEJT (125, 250, 500 mg/kg) in Wistar rats.
- To assess the inhibitory effects of AEJT on basal and secretagogue-stimulated gastric acid secretion, pH, titratable acidity, and pepsin activity.
- To investigate the dose-dependent receptor mediated mechanisms of AEJT compared to omeprazole (20 mg/kg).
- To elucidate potential underlying mechanisms including effects on gastric mucosal defense and antioxidant status.

2.0 MATERIALS AND METHODS

2.1 Experimental animals

Adult male Wistar rats (180–220 g) were housed under standard laboratory conditions (22–25 °C, 12-h light/dark cycle) with free access to food and water. Animals fasted for 24 h before experiment but had free access to water. All procedures were approved by the Institutional Animal Care and Use Committee and complied with standard ethical guidelines.

2.2 Extract Preparation

Leaves of *Jatropha tanjorensis* were collected from, shade-dried at room temperature, pulverized, and extracted with distilled water by maceration (1:10 w/v) for 24 h at room temperature. The extract was filtered, concentrated under reduced pressure at 45°C using a rotary evaporator, lyophilized, yielding 18.5% (w/w), and stored at 4°C. Phytochemical screening confirmed presence of flavonoids, saponins, and tannins (Harborne, 1998). For administration, the aqueous extract of *J. tanjorensis* (AEJT) was reconstituted in distilled water at doses of 125, 250, and 500 mg/kg body weight.

2.3 Experimental design and treatments

Rats were randomly assigned (n = 6/group) to receive orally: (1) vehicle control (distilled water, 10 mL/kg), (2-4) AEJT (125, 250, 500 mg/kg). Treatments were administered 14 days prior to gastric perfusion.

2.4 Gastric perfusion and secretagogue challenge

Under light ketamine anesthesia (50 mg/kg, i.p.), the trachea was cannulated to maintain airway patency. The stomach was perfused continuously with warm isotonic saline (37°C, 1 mL/min) via pyloric ligation

and esophageal cannulation. Basal acid secretion was recorded for 40 min. Subsequently, one secretagogue was administered intravenously via tail vein: histamine (100 µg/kg), carbachol (100 µg/kg), or pentagastrin (100 µg/kg) (Parmer et al., 1984). Gastric perfusate was collected every 10 min for 40 min post-stimulation (total collection: 80 min).

2.5 Measurement of acid output, pH, titratable acidity and pepsin activity

Acid output was determined by titrating perfusate aliquots to pH 7.0 with 0.01 N NaOH; expressed as µEq H⁺/h. Titratable acidity and pH were recorded. Pepsin activity was measured by the hemoglobin-digestion assay (or equivalent standard method).

2.6 Data Analysis

Results are expressed as mean ± SEM. Statistical comparisons among groups were made using one-way ANOVA followed by Tukey's post hoc test. $p < 0.05$ was considered statistically significant.

3.0 RESULTS

3.1 The effects of AEJT on histamine-stimulated gastric acid secretion in rats.

AEJT effects on gastric acid secretion at basal and stimulated phase with histamine. Basal gastric acid secretion was collected every 10 min for 40 min, followed by histamine stimulation (100 µg/kg, IV) with collection every 10 min for 40 min (continuous perfusion: 10 mL/10 min; total 80 min). AEJT (125, 250, 500 mg/kg) produced a dose-dependent decrease in gastric acid secretion ($p < 0.05$ vs control) at 20 min of basal phase and 30 min post-histamine stimulation (Figure 1). The result indicated the inhibitory effects of the AEJT on gastric secretion compared to the normal control.

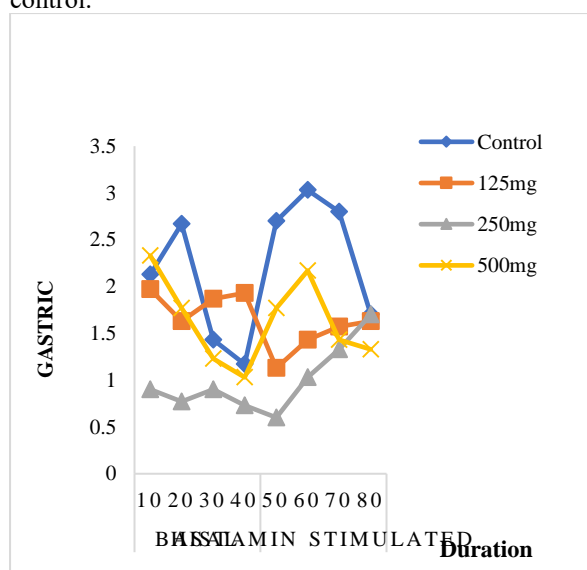


Figure 1: AEJT on Histamine-Stimulated Gastric Acid Secretion in Rats.

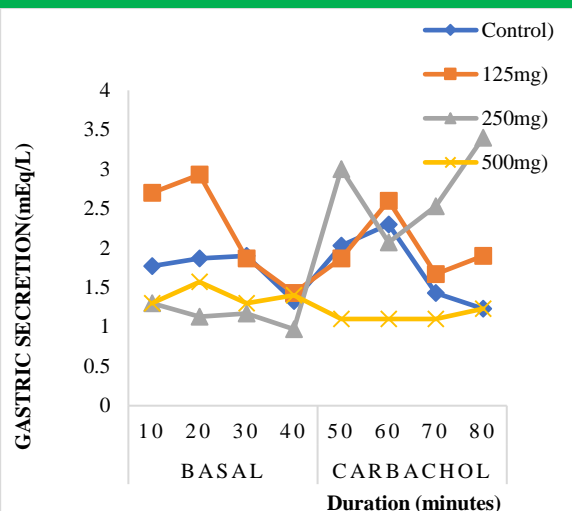


Figure 2: AEJT on carbachol-stimulated gastric acid secretion in rats

3.2 The effects of AEJT on carbachol-stimulated gastric acid secretion in rats

AEJT on gastric acid secretion at basal and stimulated phase with cabachol. Basal gastric acid secretion was collected every 10 minutes, for 40 minutes followed by a stimulated phase with intravenous injection of carbachol in the tail and gastric secretion was also collected for 40 minutes. A continuous gastric perfusion with normal saline adjusted to 10ml/10mins for 80 minutes of gastric juice secretion was carried out in all groups (control, 125, 250 and 500mg/kg). There was significant decrease in gastric secretion ($p < 0.05$) in the 500mg/kg AEJT treated groups at basal phase and upon stimulation with cabachol compared to normal control. The result showed the inhibitory effects of the extract on gastric secretion at a higher dose compared to control (Figure 2).

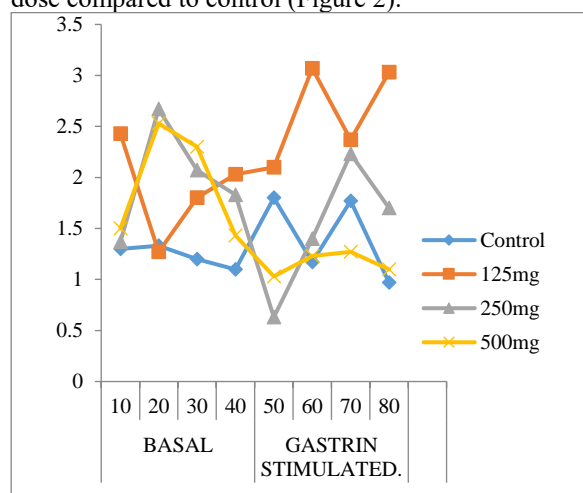


Figure 3: AEJT on Penta-Gastrin-Stimulated Gastric Acid Secretion in Rats

3.3 The effects of AEJT on penta-gastrin-stimulated gastric acid secretion in rats

Figure 4.18 shows the effect of the aqueous extract of *Jatropha tanjorensis* leaf on gastric acid secretion at basal and stimulated phase with penta gastrin. Basal gastric acid secretion was collected in the first 40 minutes followed by a stimulated phase with intravenous injection of penta gastrin for the next 40 minutes. A continuous gastric perfusion with normal saline adjusted to 10ml/10mins for 80 minutes in all groups. There is significant increase ($p < 0.05$) in gastric acid secretion in treatment groups at 10min and 40min of basal phase and throughout the stimulated phase with penta gastrin.

4.0 DISCUSSION

The findings indicate that AEJT significantly decreased gastric acid secretion during both basal and histamine-stimulated phases in a dose-dependent manner. This inhibitory effect supports the hypothesis that AEJT acts by modulating histaminergic pathways involved in gastric acid regulation. Similar results have been reported by Kampal *et al.* (2024), who found that aqueous extracts of medicinal plants exhibit potent antihistaminergic properties that reduce gastric acid output. Additionally, Awote *et al.* (2023) demonstrated that *Jatropha tanjorensis* alleviates acid hypersecretion and protects gastric mucosa, reinforcing the antisecretory capacity of AEJT through histamine receptor antagonism or proton pump modulation. These findings confirm and extend the known antisecretory effects of *Jatropha tanjorensis* in ulcer management.

At higher doses, AEJT significantly inhibited carbachol-stimulated gastric acid secretion, indicating an anticholinergic effect. Carbachol stimulates acid secretion via muscarinic receptor activation, and the inhibition seen suggests AEJT may interfere with these receptors or downstream intracellular signaling. This is in agreement with Onyekwelu *et al.* (2021), who reported that several plant polyphenols exert antisecretory effects by antagonizing cholinergic receptors in gastric parietal cells. Such mechanisms contribute to the protective properties of plant extracts, including AEJT, against acid-related gastric disorders, broadening its pharmacological profile.

Contrary to its inhibitory actions on histamine and carbachol pathways, AEJT significantly increased gastric acid secretion stimulated by penta-gastrin. Gastrin acts on cholecystokinin-2 receptors to promote acid secretion, and the potentiation suggests AEJT may sensitize parietal cells or enhance gastrin receptor signaling. This stimulatory effect is distinct from reports on other plant extracts like garlic, which inhibit gastrin-induced secretion (Tariq *et al.*, 2020). The unique dual modulatory effect observed with AEJT highlights the complexity of its bioactive compounds and their selective influence on gastric acid secretory

mechanisms.

Collectively, these findings demonstrate that AEJT exhibits complex, stimulus-dependent modulation of gastric acid secretion: inhibiting histamine- and cholinergic-mediated acid release while enhancing gastrin-induced secretion. The dose-dependent antisecretory effects reinforce the potential clinical application of *Jatropha tanjorensis* in managing acid-related diseases, including peptic ulcers, as supported by similar protective effects described by Awote *et al.* (2023) and Usunobun (2024). Further studies are warranted to elucidate the molecular mechanisms underlying AEJT's dual modulatory actions and to explore its therapeutic utility.

5.0 CONCLUSION

The aqueous extract of *Jatropha tanjorensis* (AEJT) exhibits significant and dose-dependent modulation of gastric acid secretion in rats. AEJT effectively inhibits acid secretion stimulated by histamine and carbachol, indicating its potential antagonism of histaminergic and cholinergic pathways involved in gastric acid regulation. Conversely, AEJT enhances penta-gastrin-stimulated gastric acid secretion, suggesting a unique stimulatory effect on gastrin-mediated pathways. These differential effects highlight the complex pharmacological profile of AEJT, which may involve multiple receptor targets or intracellular signaling mechanisms.

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