

## ULCEROGENIC AND GASTRIC ACID STIMULATING ACTIONS OF ETHANOLIC ROOT EXTRACT OF *GONGLONEMA LATIFOLIUM* IN RATS.

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### ABSTRACT

This study on the effect of ethanolic root extract of *Gonglonema latifolium* on gastric acid output and ulceration was undertaken due to paucity in scientific reports on the medicinal properties of the root extract especially on gastrointestinal functions. Eighteen (18) albino Wistar rats were randomly assigned into 3 groups of 6 rats each. The control group was fed on normal rat chow + drinking water while the test groups in addition received extract treatment (p.o) at a dose of 100mg/kg and 200mg/kg respectively. The feeding regimens lasted for 14 days. Gastric acid secretion and ulcer studies were done using standard procedures. Results obtained from this study shows that the mean basal gastric acid output (MBGAO) was significantly ( $P < 0.001$ ) higher in the high dose ( $4.00 \pm 0.12$ mmol/L/hr) and lower in low dose ( $2.50 \pm 0.06$ mmol/L/hr) extract treated groups compared with control ( $3.65 \pm 0.05$ mmol/L/hr). The high dose group also showed significant ( $P < 0.05$ ) potentiating effect on histamine induced gastric secretion compared to other groups. The effect of carbachol and atropine on MBGAO was not significantly different among the groups. Mean ulcer scores were also significantly higher in the low dose ( $P < 0.01$ ) and high dose ( $P < 0.001$ ) groups compared with controls. We therefore conclude that ethanolic root extract of *Gonglonema latifolium* contains phytochemical agents that increase gastric secretion at high doses probably via  $H_2$ -histaminergic receptors, suppressing gastric acid production at low doses. The extract also has an ulcerogenic effect on gastric mucosa. Hence the use of crude root extract of *Gonglonema latifolium* should be taken with caution.

**KEY WORDS:** *Gonglonema latifolium*, root extract, gastric acid, ulceration.

### INTRODUCTION

The use of herbs in the treatment and management of ailments is as old as the origin of man, and remains the oldest means of medication known to man. In spite of geographical accessibility to modern health institutions, herbal medicine still remains the first line of medication to many people, (Gedif and Hahn, 2002; Boon, 2002). A vast population resort to this because perceived toxicity of drugs used in orthodox medicine, high cost of western medicine, prolonged treatment protocol and perceived inefficacy (Gedif and Hahn, 2002). Among these plants is *Gonglonema latifolium*, a climbing perennial plant that belongs to the family of asclepidaceae (Okafor and Ejiofor, 1996; Eleyinmi *et al*, 2006).

*Gonglonema latifolium* leaves extract provide a good maintenance mechanism of the normal blood glucose level (Okafor, 2005). Apart from its nutritional

value, this plant shows some anti-hyperglycaemic, anti-hypertensive, hepato-protective and even hypolipodemic effects (Ugochukwu *et al*, 2003; Nwaijo *et al*, 2005). It is also used in the western African sub-region for a number of medicinal and nutritional purposes such as spice and vegetable (Dalziel, 1937). It is commonly called 'Utazi' and 'Arokeke' in the south-eastern part of Nigeria. The plant is traditionally used in the control of weight gain in lactating women and promotes fertility in women (Schneider *et al*, 2003). It is also used to treat malaria, stomach ache, worm infestations, cough, ulcers, and cancers. The hypoglycaemic and anti-hyperglycaemic properties of the ethanolic stem extract of *Gonglonema latifolium* have been reported by Farombi (2003).

*Gonglonema latifolium* leaves extract is rich in proteins (27.2%DM) which compared well with values reported for chickpea (24.0%DM) and other protein rich

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plants. Phytochemical analysis of leaves extract of *Gonglonema latifolium* reveals the presence of essential oil, saponins (asterglycosides), alkaloids, minerals like calcium, phosphorus, magnesium, copper and potassium (Schneider *et al*, 2003; Eleyinmi and Bressler, 2007).

Leaves extract of *Gonglonema latifolium* has been reported to contain phytochemical constituents like flavonoids which are capable of promoting gastric mucosal formation, reduce gastric acid secretion and inhibit pepsinogen production, thereby reducing gastric lesions and ulcers (Morebise *et al*, 2001). Due to paucity in scientific reports on the effect of *Gonglonema latifolium* root extract on some gastrointestinal functions, it is therefore the aim of this study to investigate the effect of this extract on gastric acid secretion and ulcerations in rats.

## MATERIALS AND METHODS

### Experimental animals

Albino Wistar rats (weighing between 180-210g) were used for this study. They were obtained from the animal house of the Department of Physiology, University of Calabar-Nigeria and housed at room temperature of  $28 \pm 2^\circ\text{C}$ .

### Experimental plant

Fresh mature roots of *Gonglonema latifolium* were obtained from the botanical garden of Univeristy, Calabar-Nigeria and were identified by the Chief Herbarium Officer of Botany Department, University of Calabar-Nigeria.

### Preparation of plant extract

The roots were washed to free debris, sun dried. They were later oven (Astell Hearson, England) dried at  $35^\circ\text{C}$ - $40^\circ\text{C}$ . The dried roots were ground to fine powder and 500g powder was percolated in 300mls of ethanol (80%v/v, BDH) for 24 hours. It was thereafter filtered with Whatman No. 1 filter paper. The filtrate was then dried to paste at  $45^\circ\text{C}$ . This resulted in 56g (yielding 11.20%) of the crude ethanolic extract. A stock solution of 1g/ml was prepared for the experiments.

### Experimental protocol

Eighteen (18) albino Wistar rats were randomly assigned into 3 groups of 6 rats each. Group 1 was the control group while groups 2 and 3 were the test groups. They were all fed on normal rat chow and drinking water, groups 2 and 3 in addition received 100mg/kg (low dose) and 200mg/kg (high dose) of ethanolic extract of *Gonglonema latifolium* extract (orally, once daily). The feeding regimens lasted for 14 days.

### Preparation of animals for collection of gastric acid

Prior to the collection of gastric acid, animals were fasted for 12 to 18 hours to get rid of any fecal matter in the stomach. This was followed by intraperitoneal injection of 25% urethane at a dose of 6ml per Kg body weight of the animal. The animals were

then laid on the dissecting board, an incision was made on the neck to expose the tracheal for trachea cannulation, and this was to allow for clear airways. Another incision was made on the abdomen about an inch along the linea alba. The stomach was exposed and the thread passed at the pyloric end under the pyloric sphincters. In this case, the small intestine and part of the liver were exposed. A transection of the duodenum was made near the pyloric sphincter and another cannulae placed and firmly held with a thread, care was taken not to rupture blood vessels of the duodenum, and after this the stomach and other exposed structures were put back and covered with normal saline swab. An orogastric infusion tube was carefully passed from the mouth through the oesophagus to the stomach and ligated just behind the tracheal cannula to prevent reflux; care was taken not to damage the vagus nerve. The exposed end of the orogastric tube was passed through a water bath to maintain the perfusate at a physiological temperature ( $37^\circ\text{C}$ ) and to pre-warm the experimental solution. The other end of the orogastric tube was attached to a 50ml syringe mounted on a perfusor pump. The animal was warmed with a table lamp to maintain the body temperature at  $37^\circ\text{C}$ . The temperature was monitored by the help of a rectal thermometer.

### Measurement of gastric acid output

The continuous perfusion method by Gosh and Schild (1958), modified by Amure (1967) was used. The rats were first perfused with 0.9% normal saline at the rate of 1.0ml/min. The aliquots were collected after 10minutes of infusion and were titrated with 0.01N of NaOH using phenolphthalein as an indicator. A pink colour discharge indicated the end point of the titration and the volume of the base used was read off and recorded. The first 10-20 minutes effluent collected was discarded to avoid erroneous acid secretion induced by trauma. When a stable acid secretion was obtained, histamine, ranitidine, carbachol or atropine was administered and acid output determined every 10minutes using the method described above.

### Ulcer study

Animals were starved for about 18hours prior to the start of the experiments. Then they were anesthetized with 25% urethane at a dose of 6ml/kg body weight i.p., the stomach was exposed via a midline incision along the linea alba. 2mls of equal volumes of acid (0.1N HCl) and alcohol (70% ethanol) was introduced into the stomach via a proximal end of the duodenum near the pyloric sphincter and kept in place with an eight shaped ligature a little above the incision. The incision was covered with a cotton wool dapped in normal saline. The animals were then kept for 1 hour. Thereafter, the stomach was isolated and excised through the greater curvature. It was then rinsed with normal saline. Pins were used to fasten the tissues in place for proper visualization. A magnification lens and a Vanier caliper were used to measure the ulcers.

Ulcer scores were determined according to the method of Ohara *et al*, (1995)

**Statistical analysis**

All data are presented as mean ± SEM. The one way ANOVA was used to analyze the data, followed by a post-hoc test (LSD). The results were considered significant at p values of less than 0.05.

**RESULTS**

**Effects of *Gonglonema latifolium* ethanolic root extract on gastric acid secretion in rats**

The mean basal gastric acid output in the control, low and high dose groups were 3.65 ± 0.05mmol/L/hr, 2.50 ± 0.06mmol/L/hr and 4.00 ± 0.13mmol/L/hr respectively. This shows a biphasic effect of the extract on gastric acid secretion, with low doses producing significant (P<0.001) lowering of gastric acid

output and a significant increase (P<0.001) in acid output at high doses, fig. 1.

**Effect of *Gonglonema latifolium* ethanolic root extract on histamine and ranitidine induced gastric acid output in rats**

Administration of histamine was observed to increase the basal gastric acid output in all the groups. The increase was highest in the high dose extract recipients (25.20 ± 6.62mmol/L/hr) compared with low dose (14.25 ± 3.55mmol/L/hr) and control (19.10 ± 5.11mmol/L/hr).

The mean acid output was observed to reduce at almost the same rate in all the groups following ranitidine administration. The values were 8.00 ± 2.21mmol/L/hr, 7.35 ± 1.51mmol/L/hr and 8.30 ± 2.40mmol/L/hr respectively for control, low dose and high dose groups, showing no significant differences among groups, fig. 1.

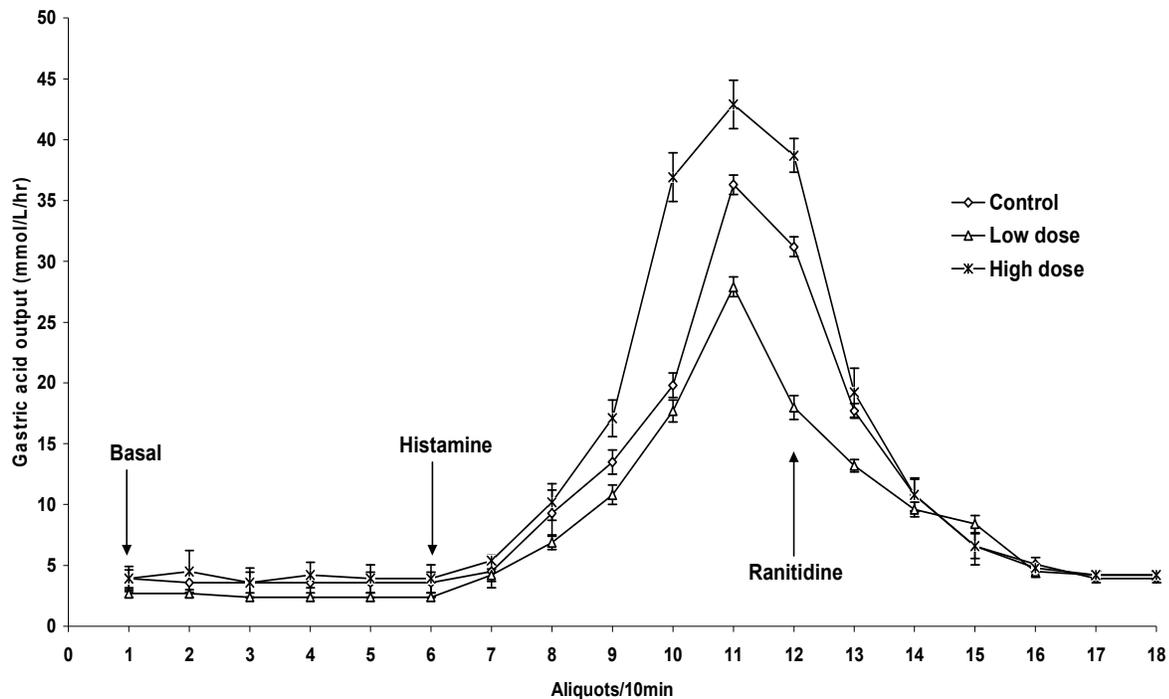


Fig. 1 Comparison of gastric acid secretion following administration of histamine and ranitidine in the different experimental groups. Values are mean ± SEM, n = 6.

**Effect of root ethanolic extract of *Gonglonema latifolium* on carbachol and atropine induced gastric acid secretion**

Carbachol was observed to increase mean basal gastric acid output to 7.65 ± 1.20mmol/L/hr in the control group. In the low and high dose group, the increases were 8.27 ± 1.06 and 9.25 ± 1.42mmol/L/hr

respectively, showing no significant differences among groups.

Administration of atropine thereafter reduced the mean gastric acid output to 3.55 ± 0.26, 3.35 ± 0.25 and 3.75 ± 0.29mmol/L/hr for control, low dose and high dose groups respectively. Fig. 2.

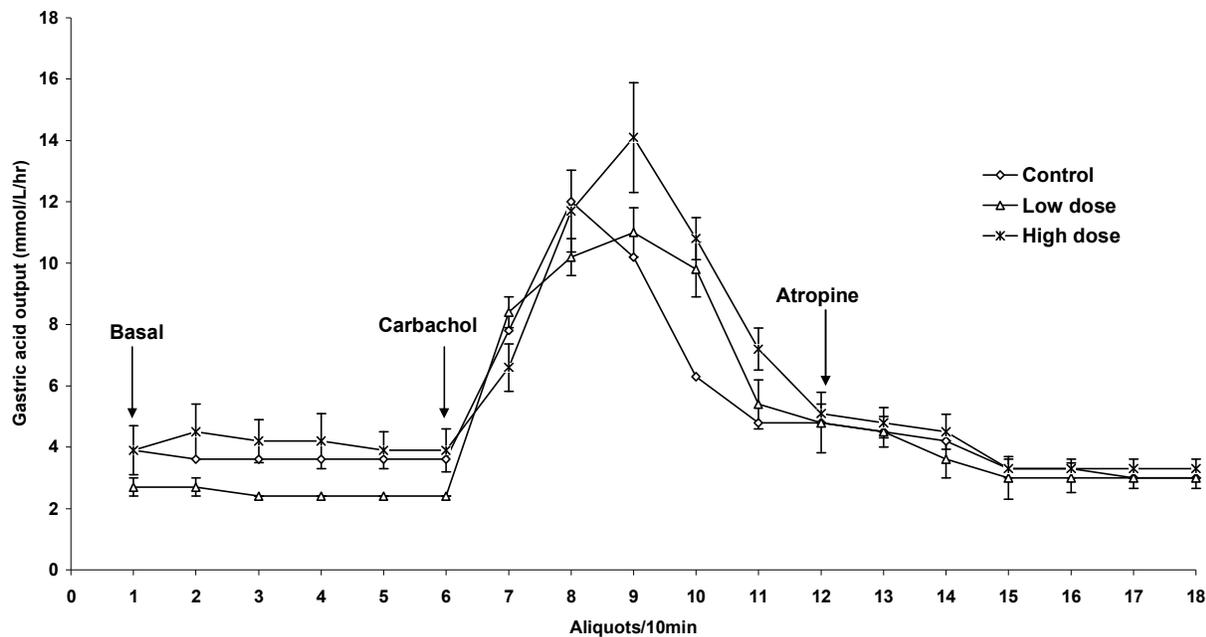
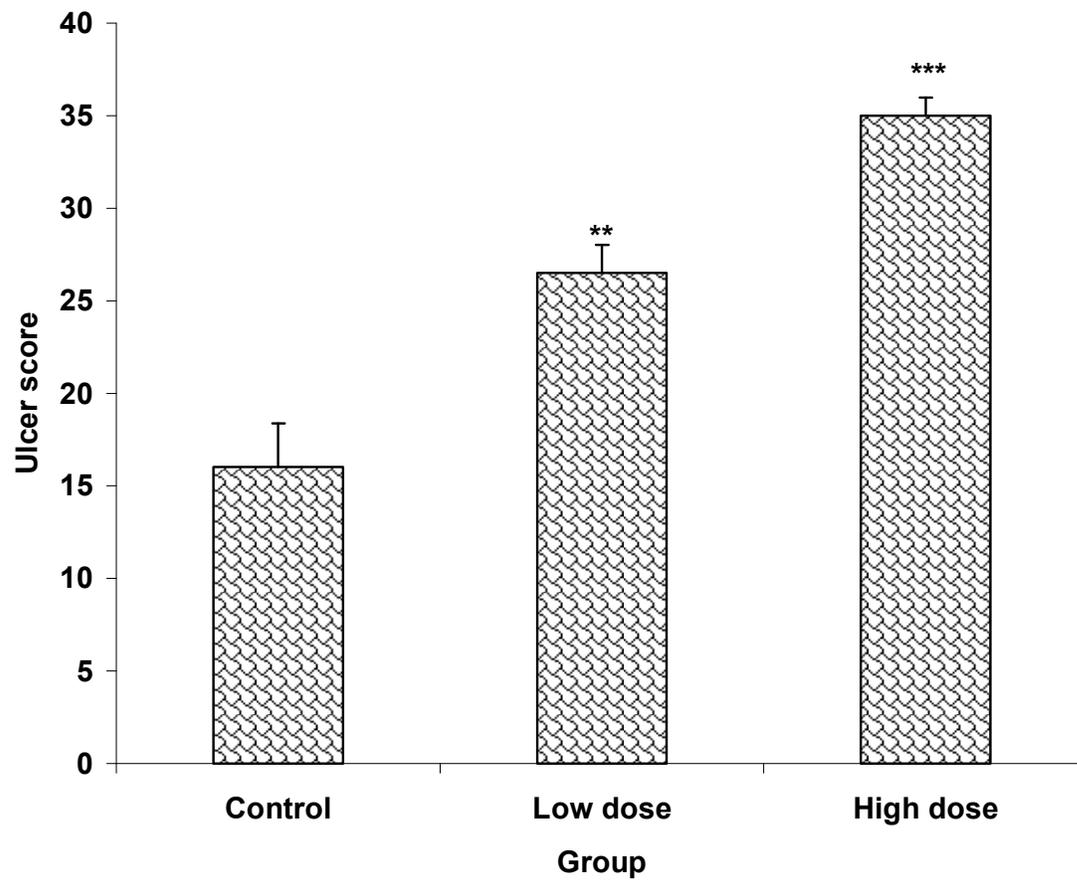


Fig. 2 Comparison of gastric acid secretion following administration of carbachol and atropine in the different experimental groups. Values are mean  $\pm$  SEM, n = 6.

**Effect of *Gonglonema latifolium* ethanolic root extract on gastric ulcers in rats**

The mean gastric ulcers in the control, low dose and high dose groups were  $16.00 \pm 2.38$ ,  $26.50 \pm 1.51$  and  $35.00 \pm 0.95$  respectively. It was significantly higher in the low dose ( $P < 0.01$ ) and high dose ( $P < 0.001$ ) groups compared with controls. Fig. 3



**Fig. 3** Effect of *Gonglonema latifolium* root extract on gastric ulceration in rats. Values are mean  $\pm$  SEM, n = 6. \*\*P<0.01, \*\*\*P<0.001 vs control. a = P<0.05 vs low dose.

## DISCUSSION

This research work was designed to investigate the effect of ethanolic root extract of *Gonglonema latifolium* on gastric acid secretion and ulceration. Results obtained show that mean basal acid output in the high dose extract recipients was significantly higher compared with control and low dose groups. The low dose recipients in turn were observed to have a significantly lower acid output compared to the other groups. The extract also dose dependently increased gastric ulcerations compared with control.

The stomach continuously secretes gastric acid from the parietal cells. The acid is prevented from damaging the mucosal walls because of the mucus cells that secrete very viscid and adherent mucus and the tight gap junctions between its adjacent epithelial cells. Inflammation of the gastric mucosa, excessive production of gastric acid could break this barrier and disposes the mucosa to gastric injuries and ulcers (Guyton and Hall, 2006).

Leaves extract of *Gonglonema latifolium* has been reported to contain phytochemical constituents like flavonoids which are capable of promoting gastric mucosal formation, reduce gastric acid secretion and inhibit pepsinogen production, thereby reducing gastric lesions and ulcers (Morebise *et al*, 2001). Other components like saponins and tannins are also present in the leaf extract of *Gonglonema latifolium* which tend to exhibit some anti-inflammatory and anti-oxidant properties.

On the contrary, our preliminary study on the root extract of *Gonglonema latifolium* shows that it is deficient of the above mentioned components but rich in substances like polyphenols, alkaloids, glycosides and some reducing sugars with opposite effect to that described above for the leaves extract. It is obvious that the high levels of acid secretion and ulceration produced by the root extract of *Gonglonema latifolium* could be due to the presence of these components or some other mechanisms yet identified.

The extract was also observed to potentiate the effect of administered histamine on gastric acid secretion. It has been suggested that subcutaneous histamine stimulates copious secretion of acid in rat's stomach through the H<sub>2</sub> receptor, and the cellular mechanism involves the activation of cyclic adenosine monophosphate (cAMP) a process that is driven by H<sup>+</sup>/K<sup>+</sup> ATPase (Garrison, 1992). It is therefore possible that the extract could increase gastric acid secretion by acting on and stimulating the histaminergic H<sub>2</sub>-receptors. This evidence is supported by the fact that the high dose recipient group also potentiated the effect of histamine induced secretion of gastric acid. Ranitidine was also observed to reduce acid output induced by histamine in all the groups studied. This is in consonance with reports that ranitidine is a pharmacological agent that blocks the action of histamine on the H<sub>2</sub> receptors (Boucher, 1977; Garrison, 1992).

Carbachol, a muscarinic receptor agonist was also observed to induce secretion of acid secretion in all the groups under investigation. The increase in gastric output induced by carbachol was not significantly different among the groups, ruling out the involvement of the muscarinic receptors in the action of the root extract of *Gonglonema latifolium*. Atropine a muscarinic

receptor blocker was also observed to block carbachol induced acid secretion equally in all the study groups.

We therefore conclude that ethanolic root extract of *Gonglonema latifolium* contains phytochemical agents that increase gastric acid secretion and ulceration probably by stimulating the histaminergic receptors or probably causing gastric irritations.

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