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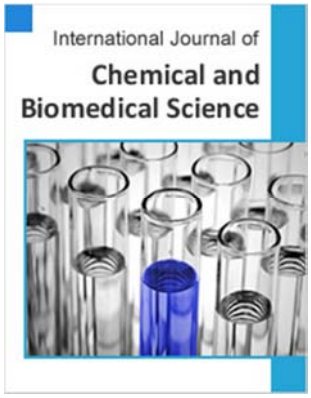

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Effect of Ethanolic Extracts of Selected Dietary Spices on Gastric Acid Secretion in Wistar Rats

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Abstract
The effect of orally ingested substances on gastric function has been a subject of human investigation almost since the discovery of hydrochloric acid in gastric juice. The response of parietal cells of the stomach to the consumption of *Capsicum* peppers, ginger, garlic and *Piper* pepper and their effects on the state of the gastric mucosal integrity was the focal point of investigation in this study. Results obtained showed, ethanolic extract of garlic stimulated the most volume of gastric acid secretion (3.5 ml), followed by paprika pepper (3.25 ml), while habanero pepper extract and the control (normal saline) secreted same gastric acid volume of 3.17 ml. 'Uziza' seed and ginger extract stimulated the least volume of gastric acid secretion, 2.5 ml and 2.17 ml, respectively. The volume of gastric acid secreted by this active components were however not statistically significant ($p < 0.05$), as compared to the control. No measurable gastric lesion(s) were observed in all the groups, there were variations in pH and gastric acid concentration of the secreted gastric juices. The pH ranged between 4.27 and 5.00 and the molar concentrations between 0.015 and 0.036 mol / dm^3. No statistically significant differences ($p < 0.05$) were observed when these mean values were compared with the control. Only the group of rats fed with ethanolic extract of ginger showed any demonstrable increase in growth rate (0.36), albeit statistically insignificant ($p < 0.05$), as compared to the control. The protective potential of ginger and 'uziza' especially on the gastric mucosa- as seen by the relatively smaller volumes of gastric juices they elicited support their espoused anti-ulcerogenic claims.

1. Introduction

Spices are products from plants seeds, fruits, flowers, roots, leaves or bark that are added to food to improve flavour, taste, colour or act to minimize rancidity, and also used as preservatives that suppress microbial activities [1]. Each spice has a unique aroma, flavour and antimicrobial activities which are derived from phytochemicals they contain [2]. Spices are widely used all over the world but more commonly in warmer climates,

maybe due to their anti-microbial properties [3]. The flavour of a spice is derived from volatile oils that evaporate or are oxidized when exposed to air [4]. Studies have revealed that certain spices or their active principles stimulate bile flow and increase biliary bile acids which have an important role in the digestion and absorption of food lipids [5, 6]. The stimulatory action of spices in digestion is thought to be through a stimulation of activities of digestive enzymes. Several of the commonly used spices have recently been observed to have stimulatory influence on pancreatic enzymes and intestinal mucosa in experimental rats [7-9].

Healing and prevention of the recurrence of ulcers represent the central goals of ulcer treatments. The main action of anti-secretory drugs is stomach acid suppression. These agents mostly, have no effects on other factors involved in ulcer pathogenesis and therefore, do not meet all treatment goals. In addition, acid suppressors are expensive and associated with adverse effects and recurrence. Hence, efforts are on to search for suitable alternative treatments from medicinal plant resources [10].

A large percentage of the world population relies on medicinal plants to treat a variety of disorders including peptic ulcer diseases (PUD). In addition to their ability to act on various pathogenic factors, they are cheap and easily accessible. Furthermore, a large number of spices and plant extracts evaluated for their anti-ulcer effects have shown promising outcomes [11-15]. The anti-ulcer effect of spices/herbs is based on their chemical constituents, which attenuate gastric secretion, enhance mucosal integrity, interfere with oxidative burst- NO, SH compounds and inhibit *Helicobacter pylori* growth. Due to their variable phytochemical constituents they may exhibit anti-secretory, cytoprotective or anti-oxidant activities [10].

The effects of orally ingested substances on gastric function in humans have been a subject of investigation almost since the discovery of hydrochloric acid in gastric juice. Gastric juice (gastric acid) is a digestive fluid formed in the stomach and it is composed of high proportion of hydrochloric acid, and also potassium chloride and sodium chloride, in small proportion [16]. Gastric acid is produced by the parietal cells (also called oxyntic cells) lining the stomach and are coupled in feedback systems to increase acid production when needed [3, 16]. The nervous and endocrine systems collaborate to increase gastric secretion and motility when food is eaten and to suppress them as the stomach empties [17]. A gastric ulcer is a distinct breach in the mucosal lining of the stomach, a result of caustic effects of acid and pepsin in the lumen. Ulcers can also occur in parts of the intestines just beyond the stomach – these are known as duodenal ulcers. Both stomach and duodenal ulcers are sometimes referred to as peptic ulcers. Studies in the varying occurrence of ulcers in third world countries despite high *Helicobacter pylori* colonization rates suggest dietary factors play a role in the pathogenesis of the disease [18].

Spices, despite their nutritive value, when they reach the digestive tract may cause irritation to the stomach's mucosal lining [19]. Most spices thus, tend to stimulate increase in acid secretion in the stomach and reduce the strength of the mucosal barrier. They have been found on analysis to contain high amounts of acid [11-15]. So, over-indulgence on spicy foods may directly cause gastric ulcers and various degrees of stomach ailments with potential for causing gastric ulcers [14]. Salivary and gastric secretions are increased when the nerve centres are stimulated by the sense of smell and by the presence of pungent principles in the foodstuff [20].

The present study investigates the effect of the ethanolic extract of some selected dietary spices viz: garlic (*Allium sativum*), "Uziza" seed (*Piper guineense*), ginger (*Zingiber officinale*), habanero pepper (*Capsicum chinense*), paprika (*Capsicum annuum*), on gastric acid secretion in wistar albino rats.

2. Materials and Methods

2.1. Materials and Reagents

All materials and glass wares used in this study were washed with detergent and rinsed with sterile deionized water. All reagents used were standard reagents of analytical grade and were products of Sigma Chemical Co. St. Louis MO, USA or BDH Chemical Ltd, Poole, England.

2.2. Spices Collection and Preparation of Extracts

Fresh spices of habanero pepper, paprika pepper, 'uziza' seeds/guinea pepper, ginger and garlic were obtained from the open market in Makurdi, Nigeria and were washed properly prior to use for experimentation. The peppers of habanero and paprika were then sliced before drying, to enhance the drying process. 'Uziza' seeds/guinea peppers were also sun- dried along with habanero and paprika peppers for 14 d, and then ground with an electric miller. However, garlic and ginger were not dried, to avoid destruction of their active ingredients. The fresh garlic and ginger were ground using an electric blender. Cold extraction was then carried out on the ground spice samples separately by measuring 50 g each of the ground spice using an electric weighing balance (model AQT 1500) and then soaking each in separate 200 ml of 80% ethanol in an Erlenmeyer flask for 48 h. The flasks were sealed with aluminium foil throughout extraction period and shaken at intervals to ensure proper extraction of the active ingredients.

After the 48 h extraction period, the extracts were filtered using a Whatman No. 1 filter paper. The filtrates were collected in beakers and were concentrated using a stirring water bath set at a temperature of 45°C. The concentrated samples were then diluted with 80 ml of normal saline, which served as the vehicle for the administration of these ethanolic extracts to the rats. The resultant solutions of habanero, paprika, garlic, ginger and 'uziza' seed/guinea pepper were then stored in a refrigerator at 4°C.

2.3. The Experimental Animals

18 wistar albino rats, mixed sexes, weighing between 95 g

to 190 g were used for this study, and were obtained from the Central Animal House of the College of Health Sciences, Benue State University, Makurdi. The animals were housed under standard laboratory conditions and fed with standard livestock feeds (Livestock Feeds Ltd, Makurdi). They were given water *ad libitum*, but the feed given was regulated during the spice extract administration period. Ethical regulations were followed in accordance with national and international guidelines for the protection of animals' welfare during the experimental process.

2.4. Experimental Design

The 18 rats were randomly divided into 6 groups of 3 rats each (Table 1). The animals were allowed to acclimatize for 2 wk prior to the commencement of the study. The rats in each group were fed and given water *ad libitum.* They were fed just enough quantity of feed to allow for complete digestion before dawn. This was to ensure the rats were hungry during administration of extract to achieve maximum efficacy of the dose. The weights of the rats were constantly measured to determine the effect of the spice extracts on the feeding habits of the various rats in each group.

The administration of the spice extract was done for 2 wk, after which the rats were fasted for 12 h prior to the time they were sacrificed. The rats were euthanized by inhalation of overdose of chloroform and their stomachs opened along the greater curvature.

Biochemical parameters investigated included: Gastric acid secretion, gastric acidity, gastric ulcer determination and gastric acid pH determination.

Table 1. *Table showing grouping of rats, administration and doses of ethanolic extracts of various spices.*

Groups	Ratsper group	Spice ethanolic extract administered	Dose of the extract administered mg/mL*
1	3	Habanero pepper	143.37
2	3	Paprika pepper	107.50
3	3	'Uziza' seed/guinea pepper	152.50
4	3	Ginger	5.00
5	3	Garlic	81.25
6	3	Normal saline (vehicle of administration)	9×10^{-6}

*doses administered based on the LD_{50} oral toxicity value of the spice extracts.

2.5. Gastric Acid Secretion Assay

The gastric acidity assay was performed using the method described by Gehan *et al.* [19]. The stomachs of the rats were ligated at the pylorus and then cut open. The gastric contents from were then drained into centrifuge tubes. 5 ml of distilled water was added to each tube and the resultant solution centrifuged at 3,000 rpm for 10 min. Gastric acid output was determined in the supernatant by titration with 0.0025N NaOH [21].

2.6. Gastric Ulcer Determination

Gastric ulcer determination was carried out by the method described by Raji *et al.* [22]. The emptied stomachs were washed with normal saline and then pinned flat on a cork board. The gastric mucosa of each rat was then viewed microscopically (x10) for the presence of any score(s) of ulceration and each given a severity rating [23] as follows:

<1mm = 1

>1mm - < 2mm = 2

> 2mm - < 3mm = 3

The gastric ulcer lesions formed were scored and the mean Ulcer Index (U.I) was calculated as shown in equation 1:

$$\text{Ulcer Index (U.I)} = \frac{Mean\ degree\ of\ ulceration \times \%\ of group\ of\ ulceration}{100} \quad (1)$$

2.7. Gastric pH Determination

The pHs of the centrifuged gastric juices were determined from the supernatants using a pH paper (Whatman narrow range pH 4-6).

2.8. Statistical Analysis

A one-way between subjects ANOVA was conducted. The values presented are mean ± standard deviation.

3. Results

3.1. Gastric Acid Secretion

Table 2 shows the effect of the ethanolic aqueous extracts of the different spices on the volume of gastric acids secreted. The results presented are the means ± standard deviation. Analyses of the results using ANOVA (P< 0.05) showed no statistical significance (P= 0.352) compared to the control group.

Table 2. *The effect of the administration of the various spice extract on volume of gastric acid secretion in the rats.*

Groups	Spice Extract	Gastric Acid Volume*ǂ
Group 1	Control	3.17 ± 0.83
Group 2	Habanero	3.13 ± 0.81
Group 3	Paprika	3.25 ± 0.66
Group 4	'Uziza' seed	2.50 ± 0.50
Group 5	Ginger	2.17 ± 0.76
Group 6	Garlic	3.50 ± 0.50

*The values of gastric acid volume in the table are presented as mean ± standard deviation. ǂ P= 0.352

3.2. Gastric Acid Concentration

The gastric acid concentration was determined from the molar concentration and volume of the base (0.0025N NaOH) used in the titration of the acid. Table 3 shows the effect of the aqueous ethanolic extracts of the spices on gastric concentration (mol dm^{-3}) of the secreted juices. The results indicate that the gastric acid secreted by the control group had the highest concentration, followed by that secreted by habanero ethanolic extract, and then, the extracts of ginger and 'uziza' seeds. Aqueous ethanolic extract of garlic and paprika showed the least concentration. Statistical analysis of the results showed no significant differences (p= 0.325) at 95% confidence level.

Table 3. *Table of gastric acidity against the spice extracts administered in each experimental group and the control.*

Groups	Spice Extract	Gastric Acid Concentration (mol/dm^3)* †
Group 1	Control	0.036 ± 0.0280
Group 2	Habanero	0.035 ± 0.0097
Group 3	Paprika	0.015 ± 0.0041
Group 4	'Uziza' seed	0.031 ± 0.0087
Group 5	Ginger	0.033 ± 0.0160
Group 6	Garlic	0.016 ± 0.0022

*The values of gastric acidity in the table are presented as mean ± standard deviation.
† P= 0.325 (P < 0.05)

3.3. Gastric Ulcer Determination

The stomachs of the rats were ligated at the pylorus and then cut open along the greater curvature. The stomach mucosas of the rats were then observed physically and microscopically for any possible score(s) of ulceration. No ulcer scores were observed in the gastric mucosa of the rats' stomach. Colour variations of the gastric mucosa were, however, observed ranging from pink to brown (Table 4).

Table 4. *Effect of spice extracts on the gastric mucosa appearance.*

Spice extracts	Gastric mucosa colour
Control	Rat 1= Deep pink Rat 2= Light pink Rat 3= Pink
Habanero	Rat 1= Deep pink Rat 2= Light pink Rat 3= Pink
Paprika	Rat 1= Pink Rat 2= Light brown Rat 3= Pink
'Uziza' seed	Rat 1= Pink Rat 2= Light pink Rat 3= Pink
Ginger	Rat 1= Pink Rat 2= Light brown Rat 3= Pink
Garlic	Rat 1= Pink Rat 2= Light brown Rat 3= Pink

3.4. Gastric Juice pH

The pHs of the gastric juices of the various rats were determined using a Whatman narrow range (pH 4-6) pH paper. The pH of the gastric juices were weakly acidic, ranging from 4.27 to 5.0 among the rats as shown in Table 5. Among the experimental groups, the gastric acid stimulated by garlic ethanolic extract had the strongest acidic pH, and that stimulated by 'uziza' seeds extract had the weakest pH compared to the control. The results showed no statistical significance ($p < 0.05$) compared to control, although $p = 0.05$.

Table 5. *The effect of the administration of the spice extracts, in the experimental groups, and normal saline, of the control groups, on the pH of the secreted gastric acid.*

Spice Extracts	Gastric Acid pH* †
Control	4.27 ± 0.25
Habanero	4.93 ± 0.12
Paprika	4.83 ± 0.29
'Uziza' seed	5.00 ± 0.00
Ginger	4.83 ± 0.58
Garlic	4.43 ± 0.12

*The values of gastric acid pH in the table are presented as mean ± standard deviation.
† P= 0.05

3.5. The Weight of the Rats

The weight gain, growth rate and percentage growth rate of the experimental rats are presented in Table 6. The rats administered with ginger extract gained more weight than the other experimental rats, with the control having the next highest weight gain. It appears that the aqueous extracts of habanero, paprika, 'uziza' seed, ginger and garlic affected the feeding pattern of the rats as their weight gain was less than that of the control, although this was statistically not significant ($p < 0.05$).

The growth rate and percentage growth rate of the rats were calculated from the rats' weights from equations 2 and 3 respectively:

$$\text{Growth rate} = \frac{\text{Final weight gain} - \text{Initial weight gain}}{\text{Initial weight gain}} \quad (2)$$

$$\text{Percentage growth rate} = \text{Growth rate} \times 100\% \quad (3)$$

The growth rate did not show any statistical significance ($p = 0.05$), as $p = 0.29$.

Table 6. *Variation in the weight gain and growth rate of the rats ‡.*

Spice Extract	Weight Gain (G)*	Growth Rate*	% Growth Rate
Control	26.23 ± 22.32	0.23 ± 0.21	23
Habanero	20.90 ± 16.30	0.20 ± 0.15	20
Paprika	19.10 ± 8.91	0.14 ± 0.08	14
'Uziza seed'	14.20 ± 6.33	0.12 ± 0.09	5
Ginger	39.77 ± 7.91	0.36 ± 0.06	26
Garlic	21.00 ± 13.16	0.16 ± 0.11	16

* p = 0.364
* p = 0.29
‡The values of weight gain and growth rate are presented as mean ± standard deviation.

4. Discussion

The mechanism by which dietary spices cause dyspepsia and epigastric pain in certain individuals has yet to be defined and poorly understood. This is in part due to the paucity of studies on the subject, and the fact that the few studies that have appeared in the literature have reported conflicting findings on the effect of spicy foods, spices or their active ingredients on both gastric secretion and mucosal integrity. Although, Sanchez [24] reported that black and red pepper cause gastric distress, but do not stimulate gastric acid secretion, Myers *et al.* [25] observed that red and black pepper significantly enhance parietal secretions. The result of this research work showed that there was no statistically significant difference ($p < 0.05$) between group means of gastric acid volume secreted [$F(5,12)= 1.235$, $p= 0.352$] although, red (habanero) and black (uziza) peppers both caused the secretion of gastric acid (but not in significant amounts compared to control). It is perhaps possible that increase in gastric acid volume may be proportional to the quantity of the spice extract administered in a dose-dependent manner.

No gastric lesion formation was observed in the stomachs of the experimental rats, but slight changes in colour of the gastric mucosa observed were in consonance with the findings of Graham *et al.* [26], who had reported that ingestion of spicy foods, as much as 30 g of jalapeno peppers (red pepper), failed to induce the formation of endoscopically observable gastric lesions in human subjects. This contrasts with the observations of Myers *et al.* [25] who had reported a significantly enhanced dose-dependent gastric cell exfoliation and mucosa micro-bleeding on administration of red and black pepper. No such observations were made in the present study- although, the observed colour changes in the gastric mucosa observed may be the onset of gastric cell exfoliation which may have been more visible if the spice extract administration period was extended.

Garlic extract caused the highest secretion of gastric acid ($p < 0.05$) in line with the observations of Fatemeh *et al.* [27] and Anderson [28], that allicin (garlic extract) stimulates gastric glands causing increased production/release of basal acid in a dose-dependent manner based on the stimulation of the stomach's mucous membrane. Allicin also combines with the stomach's natural proteins, reducing the excessive activity which can lead to indigestion [28]. The gastric mucosal integrity of the rats treated with garlic extract was unaltered, as no gastric lesions were observed. De Wet *et al.* [29] had reported that allicin (garlic extract) has antibacterial effect against *Helicobacter pylori*, thus, garlic extract probably protects the integrity of the stomach.

The reduction in the volume of gastric acid secreted in the group administered with ginger (compared to the control group in Table 2) had been previously reported by Okumi *et al.* [30]. They observed that 6-gingerol, the active ingredient in ginger extract inhibits gastric acid secretion through the activation of transient receptor potential vanilloid-1 in the gastric lumen. 6-Gingerol is thus known as a dietary agonist of transient receptor potential vanilloid-1. This was properly why the mucosal integrity of the rats administered ginger extract was unaltered as no score(s) of ulceration were recorded. Zhongzi *et al.* [31] had observed that 6-gingerol have a protective effect on the gastric mucosa against aspirin-induced gastric ulcers in rats, and does not aggravate the ulcers. Furthermore, the observed decrease in gastric acid volume secreted on administration of 'uziza' seed extract (Table 2) conflicts with the findings of Ononiwu *et al.* [32] and Raji *et al.* [22], that reported a dose- dependent increase in gastric acid volume secreted in rats fed on this spice. Although, the decrease in gastric acid volume was not statistically significant ($p < 0.05$), it may be due to the relatively small dose of 'uziza' seed administered- 15.25 mg, compared to 25.56 mg reported by Ononiwu *et al.* [32]. Also, no gastric lesions were observed in the rats fed with this spice. Whether this was due to the antioxidant properties of 'uziza' seed [33](Okwute, 1992) or not requires further investigation.

The pHs of the gastric acid secreted (Table 5) were all weakly acidic, ranging from 4.27-5.00. Although, there were slight variations among the rats, the results were not statistically significant [$F (5, 12) = 3.107$, $p= 0.05$]. In spite of the fact that gastric juice pHs are reported to be between 1.8 – 3 (Guyton and Hall, 2006)[16], the weaker pHs observed in the present study may not be unconnected with the 5 ml of normal saline used in washing the gastric content off the gastric mucosa as described by Gehan *et al.* [19]. Perhaps, washing off the gastric content with smaller volumes of a recommended external liquid might affect the pH much less. Nevertheless, there appeared to be a seemingly weak correlation between pH of the gastric juices and the overall flavour strength of the spices. The pungency of 'uziza' seed/guinea pepper and habanero pepper were the strongest among the spices used, and consequently elicited the stimulation of gastric juices with the highest pH values. Paprika pepper is less pungent compared to habanero pepper, but about the same as ginger extract. The pHs of the gastric juices elicited by paprika and the ginger extract were about the same. Garlic was the least pungent and expectedly, stimulated gastric juices with the least pH, albeit with the highest concentration (0.1244 mol / dm^3).

Although the ginger extract did not have any measurable effect on the mucosal integrity of the rats, the growth rate of the rats it was administered to was the highest (0.36), albeit, statistically insignificant ($p < 0.05$). Generally, the growth rate of the rats in Table 6, showed no statistically significant difference between the group means [$F (5, 12)= 1.407$, $p= 0.29$]. The ability of the ginger extract to increase weight in the rats is still unclear and needs further investigation.

5. Conclusion

Dietary spices are a major component of diets around the world especially in Africa and Asia. The protective potential of ginger and 'uziza' especially on the gastric mucosa- as seen by the relatively smaller volumes of gastric juices they

elicited support their espoused anti-ulcerogenic claims. Although, the effects of the individual spices on the measured parameters were statistically not significant, in most diets, a combination of spices (2 or more) is used. Hence, it is probable that the synergistic effect of the spices may elicit greater effects.

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