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Effects of piperine on gastric acid secretion in albino rats

IM Ononiwu, CE Ibeneme and OO Ebong
Department of Pharmacology, University of Port Harcourt, Rivers State, Nigeria

Summary
Piperine, the pungent principle in *Piper nigrum* and *Piper guinensis* was studied for its effect on gastric acid secretion in white albino rats. Increasing the dose from 20 mgkg^{-1} weight to 142 mgkg^{-1} body weight produced dose dependent increases in gastric acid secretion. When compared with control basal acid secretion, these increases were significant (P<0.05). 20 mgkg^{-1} produced a 22.2% (n=7) increase, while the highest dose employed in this study (142 mgkg^{-1}) produced 334.6% (n=7) increase in the gastric acid secretion.Piperine was however about 40 times less effective than histamine in increasing gastric acid secretion. The effect of piperine was significantly antagonized by cimetidine (1 mgkg^{-1}, n=6) but not by atropine (1 mgkg^{-1}, n=6). Any involvement of cholinergic receptors in the observed piperine-induced increase in gastric acid secretion is thus excluded. There is however an indication that stimulation of histamine H2 receptors by piperine is likely to be involved in the increased acidity induced by piperine.

Keywords: *Piperine, gastric acid*

Résumé
Piperine, l'element dans le piper nigrum et piper guiresis etait etudies pourson effect sur-to sevetism de l'acide gstrique chez les rats albinos. L'angumentation de la dose le 20 mg/kg pids a 142 mg/kg poids corporel produsait unes dose dependent, augmentant la secretion de l'acide gstrique. Conyare avec la secretion basale d'acide augmentation significante (P < 0.05) 20mg/kg producait une augment de 22.2% (n=7), Lorgue la , liss grande dose (142 mg/kg) producait une augmentation de 334.6% (n=7). Piperine etait 40 fois plue effaitive que l'histamine l'effect de la piperine etait significament antagoniseu par la cimentidine (1mg/kg, n=6_ mais pas l'atropine 1mg/kg, n=6) L'exclusion de l'enploi des recepteurs cholinergisque sur les recepteurs induits de piperine augmentait la secretion de l'acide gestrique. Il ya cette indication que la stimulation (excitation) des cH2-receptors de l'hitamine par la piperine peut etre utilize par augmentater l'acidite induite par la piperine.

Introduction

Piperine is an alkaloidal constituent of various spices commonly used as food additives in many parts of the world [1]. It is a major chemical constituent of the black peppers including *Piper guinensis*, *Piper nigrum* and *Piper baccatum*. Apart from the Piper species other plant species like *Anethum sowa* are also natural sources of piperine [2]. Some of the peppers are common ingredients in herbal remedies employed in traditional medicine. In Chinese traditional medicine for example a mixture of radish and pepper is employed in the treatment of epilepsy [3]. In Nigeria, especially the South western and South eastern parts of the country, the *Piper species* are commonly used in herbal preparations. Among the Igbos of south eastern Nigeria *Piper guinensis* (called *uziza* in the local language) is a major constituent of any sauce or soup given to post-partum women for its medicinal effects. It is believed among the local populace that keeping the stomach "warm" is the first step to good health and *uziza* keeps the stomach "warm". It is also believed that *uziza* has a stimulant effect on the uterus which helps in stopping post partum haemorrhage.

In recent times attention has been focussed on the effects of common food items and their chemical constituents on gastric acid secretion. Thus studies on *Garcinia cola* [4,5] and *Cola acuminata* [5] have been reported. The present study is a preliminary attempt to investigate the effects of piperine, the pungent principle in the *Piper species* on gastric acid secretion. An attempt was also made to briefly explore the mechanism of its action on gastric acid secretion. This is part of a wider study that aims at investigating the role of different types of spices in gastric acid secretion.

Materials and methods

White albino rats of both sexes weighing between 100 and 200g were employed in this study. They were kept in rat cages under the same environmental conditions of temperature and humidity and fed on growers marsh *ad libitum* for a period of one week. After this period of acclimatization, the rats were divided into experimental groups depending on the type of experiments that were to be carried out. Before any set of experiments was carried out, both the test and control groups of the rats were subjected to a 24-hour fast. They were then weighed and anaesthetised with urethane (6 mlkg^{-1} body weight) administered intraperitoneally and observed for a period of 30-45min. until anaesthesia was fully established. A tracheostomy was then performed on the rat and the trachea cannulated. An incision was also made along the linea-alba of the upper abdominal wall of the rat to expose the stomach. The junction between the duodenum and the pyloric end of the stomach was identified and a little incision through which a cannula was inserted was made. The cannula was then firmly ligatured in position. The stomach was perfused with normal saline through an oesophageal cannula until the effluent became clear. A continuous perfusion of the stomach with normal saline at a constant perfusion rate of 0.5mlmin^{-1} was then carried out.

Drugs used

The drugs used are histamine phosphate (Sigma), Cimetidine (Smithkline Beecham), Atropine sulphate (Sigma) and Piperine. Stock solutions of the drugs were prepared with normal saline. 2g of piperine was first dissolved in a 0.5ml quantity of ethanol and then made up to 10ml with normal saline.

Experimental procedure

The Gosh and Schild technique as modified by Ibu [6] and Ibu *et al* [4] was used throughout this study. After adjusting the perfusion rate to a constant value of 0.5ml min^{-1}, effluents from the stomach were collected every 10 minutes for 60 minutes. Each aliquot was then titrated to phenolphtalein end point with 0.0025N sodium hydroxide (NaOH) solution. The calculated concentration of the acid was taken to be the basal gastric acid

Correspondence: Dr I M. Ononiwu, Department Pharmacology, College of Health Sciences, University of Port Harcourt, Nigeria. E-mail: ugoeze_inno@yahoo.com

secretion. Thereafter graded doses of the test drugs: piperine 0.5-142mgkg^{-1} or histamine 0.5-6mgkg^{-1} were administered intraperitoneally (i.p) while equivolumetric doses of normal saline were administered to animals in the control group. Gastric effluents were also collected and analysed by titration to phenolphtalein end point with 0.0025N NaOH. In experiments in which the H_2 receptor antagonist cimetidine 1mgkg^{-1} (i.p) or the muscarinic receptor antagonist atropine 1mgkg^{-1} (i.p) were administered, these antagonists were administered 1 hour before piperine 40mgkg^{-1} was administered.

Analysis of data

The results obtained from n number of rats in each group were pooled together and the values presented here are the group means ± the standard error of mean (s.e.m). Student's t-tests were employed in calculating the significance of differences. Significant differences were assumed when $P<0.05$.

Results

The mean basal gastric acid secretion was 2.25 ± 0.03mMol L^{-1}. Piperine administered intraperitoneally produced dose-dependent increases in the gastric acid secretion as shown in table 1. The lowest dose of piperine (20 mgkg^{-1} body weight.) employed in the present investigation produced a significant increase (about 22.2% ; n=7) over the basal gastric acid secretion while the highest dose employed in this experiment (142 mgkg^{-1} body weight) produced 334.6% (n = 7) increase over the basal gastric acid secretion. The effect of piperine compared with histamine on the gastric acid secretion is shown in fig 1. Piperine was found to be less effective as a secretagogue than histamine. Atropine 1mgkg^{-1} administered 1 hour before piperine (40 mgkg^{-1} n = 6) did not produce any significant changes on the piperine-induced increase in gastric acid secretion as shown in fig. 2(a). However cimetidine 1mgkg^{-1} produced a significant decrease in the piperine-induced gastric acid secretion (fig.2b)

Table 1: Effect of piperine on gastric acid secretion in rats.

Dose of piperine	Mean concentration acid output (mMol L^{-1}Hr^{-1}) N=7	% increase over basal secretion (N = 7)
20 mgkg^{-1}	2.75 ± 0,52	22.2
40 mgkg^{-1}	5.23 ± 0.67	132.4
57 mgkg^{-1}	7.00 ± 0.48	211.1
114 mgkg^{-1}	9.62 ± 0.26	327.6
142 mgkg^{-1}	9.78 ± 0.53	334.6

Mean basal acid secretion = 2.25± 0.03 mMol L^{-1} Hr^{-1}

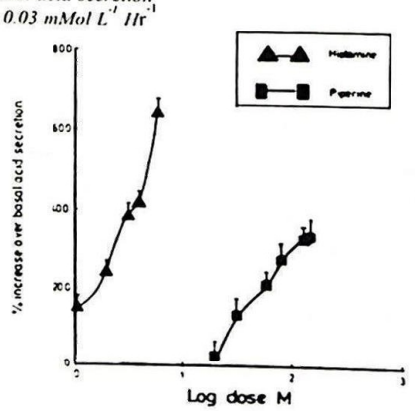

Fig. 1

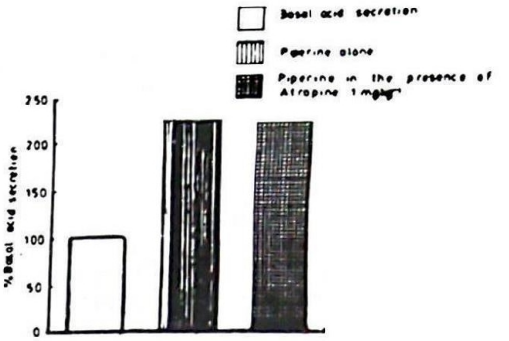

Fig. 2a:

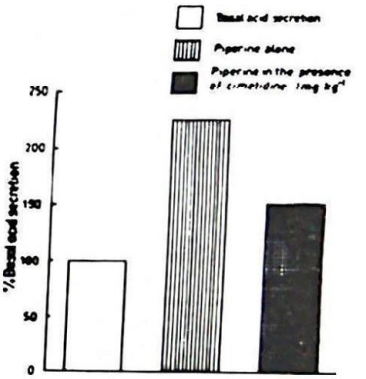

Fig. 2b:

Discussion

From the current study, piperine was found to produce significant increases in the gastric acid secretion in a dose-dependent manner. 20 mgkg^{-1} of piperine which was found in preliminary tests to produce significant increases in gastric acid secretion produced about 22.2% increase while the highest dose of 142 mgkg^{-1} body weight employed in the present study produced 334.6% increase over the basal gastric acid. The increases in the gastric acid secretion could be attributed to piperine and not necessarily to volume effect. Equal volumes of normal saline administered to control animals did not produce any significant changes from the basal gastric acid secretion. A small quantity of 60% ethanol (about 0.5ml) was used in dissolving the piperine (2g) before making up the volume of the stock solution (10ml.) with normal saline. Pre-test experiments with similar combination of ethanol and normal saline (without piperine) did not produce significant effects on the gastric acid secretion Thus the increases in the gastric acid secretion could not have been produced from any other source other than the piperine. Compared with a pure synthetic secretagogue histamine, piperine was found to be less effective in increasing gastric acid secretion.

The significance of these observations however lies in the fact that as the major constituent of peppers which may be consumed daily over a long period, the frequency of introducing piperine into the body system may be high enough to cause frequent increase in gastric acid secretion. Furthermore, heavy pepper users are likely to experience episodic upsurge in gastric acid secretion.

In the present study an attempt was made to explore the mechanism by which piperine produces the increase in gastric acidity. The possibility of a cholinergic receptor involvement was ruled out by the inability of the muscarnic receptor antagonist atropine to block the piperine-induced increase in gastric acid secretion. However there is an indication from the present study that the stimulation of histamine receptors may be involved. The H_2 receptor antagonist cimetidine produced significant inhibition of the piperine-induced increase. This however needs to be investigated a lot more in detail in a more quantitative manner.

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