RESEARCH ON ANTI-ULCERATIVE PROPERTIES OF THE POLY HERBAL EXTRACT CONTAINING ALLIUM SATIVUM & ZINGIBER OFFICINALE.

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Abstract

Modern medical practise has expanded to include the use of herbal medicines. This research was undertaken to assess the efficacy of the combination therapy of traditional medicinal in the management of induced gastrointestinal damage among albino wistar rats. There were a number of 24 Albino Wistar rats utilised, including both sexes and ranging in weight from 130 to 150 gram. Both the positive and negative control groups were given 1 ml of normal saline, whereas

the indomethacin-treated control group was sacrificed 6 hours after receiving 20 mg/kg. The control group received 20mg/kg of indomethacin whereas the experimental group received 200mg/kg and 400mg/kg of Allium sativum and zingiber officinale extracts, respectively. In contrast to the control group, the gut and duodenum showed no outward signs of ulcers or perforation. All ulcers and perforations were healed on the stomachs of wistar rats when a mixture of plant extracts at doses between 200 and 400mg/kg was administered. Similarly, when these three extracts were combined, all duodenal ulcers caused by indomethacin in Wistar rats healed. Normal mucosa was seen in stomach and duodenum samples from rats that had been administered a 200mg/kg herbs cocktail and indomethacin. Gastroduodenal ulcers were more effectively treated with a combination of the botanicals at a dose of 400 mg/kg. There is promising anti-ulcer action from the combination of plant extracts.

Keywords: Anti-ulcer, Allium sativum, Zingiber officinale, Gastric ulcer, Indomethacin

Introduction

Worldwide, ulcers are becoming more prevalent and frequent. Ulcers affect 14.5 million individuals over the world, and they cause 4.08 million deaths annually. Factors such as stress, bacterial infection, and the use of nonsteroidal anti-inflammatory medicines are thought to contribute to the rising rates at which ulcers are diagnosed and treated in the general population (NSAIDS). Ulcers develop when gastric parietal cells produce too much hydrochloric acid and activate the H+ K-ATPase enzyme, releasing H+ into the stomach lumen and increasing acidity. The released acid then acts on the gastrointestinal mucosa, causing the mucosal protection to be broken down. Consequently, gastric lesions form when the equilibrium between induced gastric and aggressive factors is disturbed, leading to the former. The pathogenicity of gastric ulcers is increased due to a lack of gastric mucus, increased stomach acid output from parietal cells, and increased susceptibility to H pylori infection, all of which cause severe gastric ulcers involving profuse bleeding. Changes in soil structure, etc. Several studies have linked alcohol use to an increased risk of developing stomach ulcers due to portal hypertension. Cancer was also observed to develop in those who had long-term ulcers. Gastric ulcers are caused by a worldwide imbalance between the production of aggressive components like acid and defence components like bicarbonate and mucus. [1, 2]

The prevalence of stomach ulcers is raised by a number of factors, including stress, tobacco, consumption of alcohol, Helicobacter pylori infection, NSAID consumption, inadequate eating habits, and nutritional deficiencies.

Flavonoids found in fruits and vegetables including pears, celery, and onions may help stop H pylori from multiplying and reduce the likelihood of stomach ulcers caused by this bacteria. Fiber-rich meals, including such tubers, bananas, beans, and peas, and vitamin C-rich foods may both reduce the risk of developing duodenal ulcers. [3]

The plant commonly known as garlic, Allium sativum Linn, belongs to the Liliaceae family. In addition to its well-known effects on the vascular system and stomach cancer, garlic is reported to have a wide variety of other pharmacological effects. Garlic has been shown to have effects on the mucosa lining the digestive tract. It's been said that garlic may prevent H pylori from multiplying. Due to its antioxidant qualities, garlic oil is considered to have an antiulcer effect in

ethanol-induced stomach damage. Consuming garlic was believed to help with stomach problems in traditional medical texts. Clinical investigations using different forms of garlic, however, have shown that it may activate the gastrointestinal mucosa, leading to stomach ulcers. Extracts of garlic were also discovered to inhibit the cytoprotective molecule prostaglandin E inside the gut. [5, 6, 7, 8]

The ginger plant, Zingiber officinal, is a perennial herb that grows up to two feet tall and produces blooms that are greenish yellow and resemble orchids. In the dried rhizome, the volatile oils account for about 4% of the total, and these oils are the ones responsible for the distinctive smell and flavour that make ginger so useful medicinally. Studies on the plant's phytochemical composition have shown the abundance of a wide variety of compounds, such as -zingiberene, -bisabolene, gingerols, and shogaols [9]. It has been observed that certain substances have anti-ulcerogenic action. [10]

Material & methods

Preparation of extract

Our ingredients, ginger and garlic, came from a nearby market. Took a week to dry after being sliced and having their skins removed. The dehydrated herbs were then processed using a grinder machine. After that, the plant was ground into a powder and soxhlated with ethanol in a Soxhlet device. Vacuum evaporation was used to concentrate the extract.

Chemicals

Analytical-grade omeprazole with indomethacin.

Animals

Male and female albino rats weighing between 150 and 250 grammes were employed for the experiment. As part of the acclimation process following selection, the animals were kept in a climate-controlled facility with natural light levels cycles for a week. We fed them the standard rat pellet diet and let them free access to water.

All of the rats were broken up into four different groups at random. Before receiving the medicine, they fasted for 1 days but had free access to water. The following dosages of the test substances were given by oral gavage using an aqueous phase and suspension:

S. No.	Group	Specification
1	Group I	Distilled water 2ml/kg bodyweight.
2	Group II	Omeprazole 10mg/kg body weight.
3	Group III	Test rats receive aqueous extract 200 mg/kg body weight.
4	Group IV	Test rats receive aqueous extract 400 mg/kg body weight.

Each animal in each group received 20mg of indomethacin per kilogramme of body weight and 1 cc of ethanol per 200 grammes of food half an hour longer to cause stomach injury. The anti-ulcerogenic action of ginger and garlic was tested using the following model.

Acute oral toxicity

The research was conceived in accordance with suggestion No. 423 from the Organization for Economic Co-operation and Development (OECD). The study followed standard procedures. Each dosage was tested on a group of three rats. A loading dosage of 300 mg/kg was given initially. The dosage was also altered to determine the LD50 value, depending on the presence or absence of a chemical linked to mortality and morbidity in the test sample. Between 30 and 60 minutes in, the rats were closely monitored. More volunteers spent four hours in the lab under scrutiny. In addition, for the last two weeks, we've been under constant surveillance.

Indomethacin induced gastric damage in rats.

After 6 hours under ether anaesthesia, the animals were slaughtered. The stomachs were taken out and placed on some filter paper that had been soaked in salt water until they could be examined. The higher curvature was cut longitudinally with sharp shears. With the use of a magnifier, stomach distress was detected by placing it upside down over the index finger. Lesions, either singular or in clusters, were documented. Gastric damage was thought to manifest as erosions, ulcers, perforations, and hyperaemia. It was recorded how often hyperaemia occurred, how prominent the stomach rugae were, and the quantity and severity of the ulcers. [11, 12]

Grades of ulcer severity:

S. No.	Scale	Type of ulcer
1	0	No ulcer
2	1	Superficial ulcer
3	2	Deep ulcer
4	3	Perforation

$$\%\ protection = \frac{control\ mean\ ulcer\ index - test\ mean\ ulcer\ index}{control\ mean\ ulcer\ index} \times 100$$

Ethanol induced gastric ulcer

Before receiving ethanol therapy, which resulted in ulcers, all animals fasted for 24 hours. Each subject was given either a placebo or a conventional drug (10 mg/kg p.o. omeprazole) 1 hour before being subjected to ethanol.

After 1 hour, all of the animals were terminated after receiving 1 ml/200 g of alcohol (90%) intravenously. Ulcer index was determined after stomachs were dissected. [13]

Results

Acute oral toxicity result

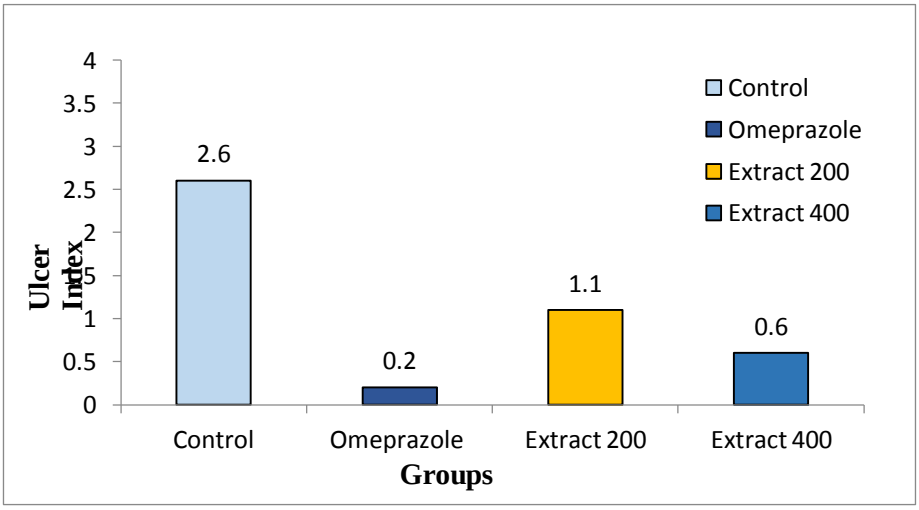
It was due to the victim's behaviour that the acute oral poisoning was detected. At the maximum dosage of 1000 mg/kg weight, the animals were monitored for 14 days. Death rates showed no signs of increasing.

No abnormalities in the fur, pigment, or smoothness of the skin were seen, and normal behavioural characteristics were recorded. There was no evidence of itching, spasms, or anxiety, and the eyes were a healthy pink with normal movement.

Indomethacin induced ulcer

The herbal extract dramatically reduced ulcer lesions compared to the control group after stomach resection. Even while the 200mg/kg dosage had some effect, the 400mg/kg dose had far more powerful antiulcer effects. Results are presented as means standard error of means (SEM). One-way analysis of variance (ANOVA) as well as Barlett's Test were used to examine the data. The cut-off for significance was set at P 0.05.

Dose	Ulcer Index	% Protection
Control	2.6	----
Omeprazole	0.2	92.3%
Extract 200	1.1	57.6%
Extract 400	0.6	76.92%

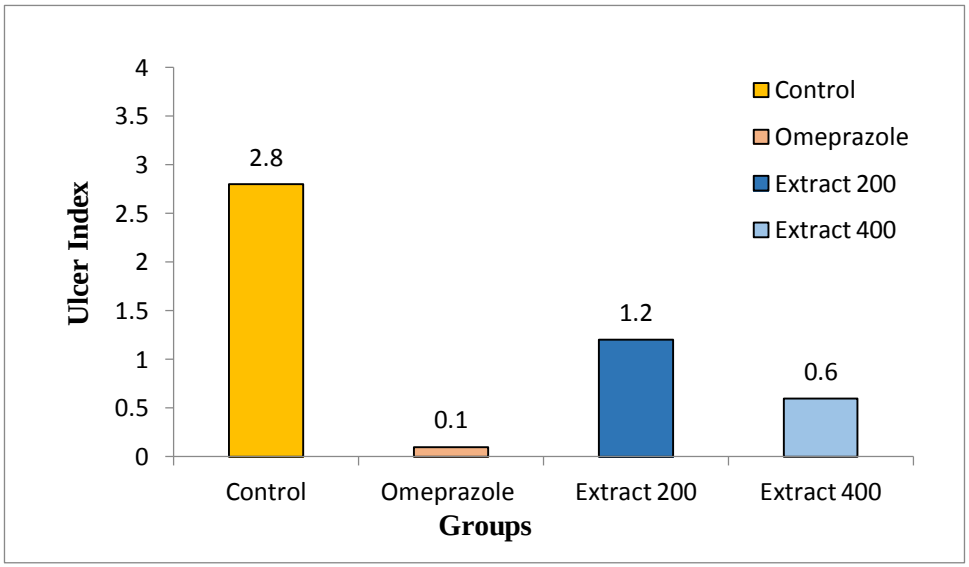


Ethanol induced ulcer

The herbal extract dramatically reduced ulcer lesions compared to the control group after stomach resection. It was shown that although both dosages had some effect, the 400mg/kg dose had far more potent antiulcer effects than the 200mg/kg dose.

Dose	Ulcer Index	% Protection
Control	2.8	----
Omeprazole	0.1	96.4%

Extract 200	1.2	57.1%
Extract 400	0.6	78.57%



The results of the current investigation reveal that, compared to the control group, both the extract and omeprazole utilised in the study had considerable gastro protective benefit. Results from the overall intensity score and lesion index in gastric tissue showed that indomethacin administration led to stomach damage; however, the combination of indomethacin plus either extract or omeprazole reduced the severity of the damage. When indomethacin was combined with extract or omeprazole, the average number of ulcers in the indomethacin group has increased. When compared to omeprazole, the proportion of ulcer growth suppression by extract for stomach distress was similar. The data show that ginger and garlic extract may protect the stomach from the side effects of indomethacin (a non-steroidal anti-inflammatory drug). Overproduction of leukotrienes and other products of the 5-lipoxygenase pathway is thought to be the main cause of gastric ulceration when taking NSAIDs like indomethacin, with the primary cause being the inhibition of "cytoprotective prostaglandins," e.g., PGEs and PGI2, by inhibition of the cyclooxygenase pathway of arachidonic acid metabolism.

For both the stomach and duodenum, the ulcerative index was reduced in indomethacin-treated Wistar rats. The gastrointestinal ulcer index dropped to practically nil after taking ginger and garlic. Treatment with ginger, garlic, or both resulted in a markedly reduced ulcerative index compared to pre-treatment values.

Discussion

Treatments for peptic ulcers in past research tended to entail the use of a particular plant preparation [14, 15, 16]. Some herbal remedies have been demonstrated to be more effective when combined with other treatments often used in orthodox medicine [17]. In this investigation, the ulcerative index was almost at zero after treatment with ginger and garlic. Both the stomach and duodenum of Wistar rats treated with the herbal mixture differed significantly from controls. The potential for additive or synergistic effects during treatment of an illness motivates the use of many plant species in a single preparation. Extract of herbal combination treatment has aided ulcer healing and decreased recurrence rates as well [18, 19]. In this research, the indomethacin-induced damage to the upper gastrointestinal tract was healed by a mixture of ginger and garlic. The study's findings suggest that ginger and garlic help prevent stomach acid production and ulcers caused by acidified ethanol. Therefore, both garlic and ginger aid in preventing ulcer development and decreasing acid secretion.

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Declarations

The authors declare that they have no competing interests.

Reference

1. Langmead L, Rampton DS. Herbal treatment in gastrointestinal and liver disease – benefits and dangers. Aliment Pharmacol Ther 2001; 15:1239.
2. Thamlikitkul V, Banyapraphatsara N, Dechatiwongse T, Theerapong S, Chantrakul C, Thanaveersuwan T. Randomized double blind study of Curcoma domestica Val. For dyspepsia. J Med Assoc Thai 1989; 72:613-20.
3. Crawford JM. The gastrointestinal tract in Robbin's Pathologic basis of disease. Citron, Kumar and Collin (Eds), Saunders; New Delhi, 2003:787-802.
4. Kokate CK, Purohit AP, Gokhale SB. Pharmacognosy. Pune, India: Nirali Prakashan; 2004: pp347- 48
5. Rahman K, Lowe GM. Garlic and cardiovascular disease: a critical review. J Nutr 2006 Mar; 136(3suppl):736S-40S.
6. Milner JA. Preclinical perspectives on garlic and cancer. J Nutr 2006 Mar; 136(3Suppl):827S-31S.
7. Mahady GB, Matsuura H, Pendland SL. Allixan, a phytoalexin from garlic, inhibits the growth of Helicobacter pylori in vitro. Am J Gastroenterol 2001 Dec; (12):3454-5.
8. Gaffen JD, Tavares IA, Bennett A. The effect of garlic extract on contractions of rat gastric fundus and human platelet aggregation. J Pharm Pharmacol 1984 Apr; 36(4):272-4

9. Khushtar ,M.,V Kumar, K Javed,and Uma Bhandari. Protective Effect of Ginger oil on Aspirin and Pylorus Ligation-Induced Gastric Ulcer model in Rats. Indian JPharm Sci.2009 Sep-Oct; 71(5): 554-558.
10. Chioma A Anosike, Onyechi Obidoa, Lawrence US, Ezeanyika and Meshach M Nwuba. Anti-inflammatory and anti-ulcerogenic activity of the ethanol extract of ginger(Zingiberoficinale). African Journal of Biochemistry Research Vol.3(12),pp379-384, December, 2009.
11. Gerhard Vogel H etal. DrugDiscovery and Evaluation. 2nd edition Germany: Springer - Verlag Berlin Heidelberg. 2002. 825-946.
12. Kulkarni SK. Hand book of experimental pharmacology. 3rded. New Delhi: Vallabh prakashan; 1999:pp148-50.
13. Khan HA. Computer assisted visualization and quantitation of experimental gastric lesions in rats. J Pharmacol Toxicol Methods 2004; 9: 89–95
14. Oguwike FN, Offor CC, Nwadighoha AN, Ebede SO. Evaluation of Efficacy of Cabbage Juice (Brassica Oleracea Linne) As Potential Antiulcer Aggent and Its Effect on the Haemostatic Mechanism of Male Albino Wistar Rats. J Dental Med Sci 2014; 13:92-97.
15. Azamthulla M, Asad1 M, Prasad VS. Antiulcer activity of allium sativum bulb juice in rats. Saudi Pharmaceut J 2009; 17: 70-7.
16. Borra SK, Lagisetty RK, Mallela GR. Anti-ulcer effect of Aloe vera in non-steroidal antiinflammatory drug induced peptic ulcers in rats. African J Pharmacol 2011; 5(16):1867-71.
17. Adnan M, Ullah I, Tariq A, Murad W, Azizullah A, Khan AL, Ali N. Ethnomedicine use in the war affected region of northwest Pakistan. J Ethnobiol Ethnomed 2014; 10:1-16
18. Dai XP, Li JB, Liu ZQ, Ding X, Huang CH, Zhou B. Effect of Jianweiyuyang granule on gastric ulcer recurrence and expression of VEGF mRNA in the healing process of gastric ulcer in rats. World J Gastroenterol 2005; 11:5480–84.
19. Ling JH, Li JB, Shen DZ, Zhou B. Nuclear factor-kappaB mRNA and protein expression in stomach tissue of rats with gastric ulcer recurrence and effect of jianwei yuyang granule on its expression. Zhongguo Zhongxiyi Jiehe Zazhi 2006; 26:228.