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Research

Aloe Vera Heals Gastric Ulcer in 7 Days than Omeprazole and Cimetidine: Prostaglandin?

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ABSTRACT

Peptic ulcer disease is becoming a very common disease as it is associated with lifestyle e.g eating habits more than infection, by bacteria, *H. pylori* [1]. There are many treatments for the disease which are not very potent for the eradication of the disease.

A comparative study was therefore carried out with Aloe Vera, cimetidine and omeprazole to arrive at the most potent treatment drug. A total of thirty (30) male and female rats were used for the study. The Aloe Vera extract with LD_{50} of 1870.83 mg/kg was administered in three dosages; low, medial and high, 187.08 mg/kg, 374.42 mg/kg and 561.25 mg/kg respectively in groups (3-4) while cimetidine and omeprazole in groups V and VI respectively for 28 days. Gastric HCl increased significantly $p<0.1$ in group 3 as compared to the control but was not significant $p>0.01$ in groups 2, 4 and 6. Aloe Vera showed more potent healing than omeprazole and Cimetidine as there were no traces of ulceration observed in the stomach of the rats as early as 7 days of the observation treatment. However, the acid output in the Aloe Vera treated groups were not significantly reduced $p>0.01$ as compared to Cimetidine and omeprazole groups. But the ulceration was significantly eliminated than in the cimetidine and omeprazole treated groups. It is concluded that Aloe Vera probably acts through prostaglandin increase in its ingredient for the healing of the ulcer.

Keywords: Aloe Vera; Cimetidine; Omeprazole; HCl; Gastric ulcer

INTRODUCTION

Gastric ulcer is the disease that affects directly the stomach as a wound in it. It could be caused by infection; e.g *Helicobacter pylori*, [2] or by action of food items e.g. tea and coffee increase intake [1] and by Nonsteroidal Anti-Inflammatory Drugs (NSAID) and by stress-related mucosal damage [3]. It may be due to hypersecretion of hydrochloric acid and pepsin or as a result of an imbalance between the gastric luminal factors and degradation in the protective function of gastric mucosal barrier [4,5]. Peptic ulcer also due to nonsteroidal anti-inflammatory drugs often occurs due to irritation of the gastric epithelial cells and reduced protective prostaglandins [6]. But inhibiting cyclooxygenase (cox 1 × 2 by nonsteroidal anti-inflammatory drugs is another pathway for the peptic ulcer formation. The mechanism involves the inhibition of rate-limiting enzyme in the process of which arachidonic acid is converted to prostaglandin [7].

Cyclooxygenase-2 (COX2) produces prostaglandin associated with inflammation and pains and isoforms of COX1and Cox2 are also inhibited by NSAIDS [8]. The most common symptoms of peptic ulcer disease areepigastric pain, stomach pain immediately after a meal which is very suggestive of gastric ulcer. For duodenal ulcer stomach pains will occur 2 to hours after a meal or when there is no food intake and such are relieved tentatively by intake of food. Unfortunate chronic peptic ulcers may be asymptomatic which may be induced by Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) and may be associated with bleeding and perforation [9]. The diagnosis of peptic ulcers may be by non-invasive test particularly for *Helicobacter pylori* with endoscopy [10]. The non-invasive test includes, (a) the Urea

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Breath Test (UBT), (b) the Fecal Antigen Test (FAT) and (c) the antibody test the urea breath test and the fecal antigen test are preferred [9]. The antibody test is often considered and useful when the test is negative and confirmation of a positive result is required by doing urea breath test or fecal antigen test since such result may be positive for a long time after exposure to *Helicobacter pylori* and so may not be considered as standard diagnostic test [9]. However, methods like Polymerase Chain Reaction (PCR) and culture for the *H. pylori* are employed as such are sensitive. Effective treatment of peptic ulcer, for now, is based on the use of Proton Pump Inhibitor (PPI) and H_2 inhibitor e.g. Omeprazole and cimetidine but are associated with side effects. However, an herbal remedy that is more potent has been invented by the major author of this article. The drug is patented and has won the second position in Nigeria in the 2019 expo exhibition by the Federal Ministry of Science and Technology. The drug novel activity is the occurrence of the nonbonding of three carbon atoms as examined via nuclear magnetic resonance as structurally evident of the active ingredient of this tropical plant. Continuous research for other potent antiulcerogenic drugs is very necessary as per the cost and availability and the readiness for its mass production for the eradication of the peptic ulcer. This prompted the investigation into Aloe Vera as yet another available tropical plant that could alleviate the burden of ulcer in the afflicted population. Aloe Vera is a stemless short plant of (60-100) cm in height. The leaves are thick and fleshy and green with varieties [11] with white spines. The flowers are produced mainly in summer measuring 90 cm in height pendulums with yellow tubular corolla. The phytochemical composition includes anthraquinone c-glycosides, anthrones, lectins [12]. Anthraquinone-rich a Aloe Vera absorbs with violet radiation.

The plant is native to South West Arabian Peninsula but it is widely cultivated throughout the world [13]. The exudate of the plant; aloin is found to be a dietary supplement for weight loss and as constipation therapy [14]. However, it has some level of toxicity at some dosage levels on ingestion and topical application [15]. However, the toxic components aloin may be removed via processing but the excess amount of aloin may have side effects [16]. The juice is said to be marketed for digestive problems but the full explanation for the digestive problem not explained. Aloe Vera is also used as moisturizer and anti-irritant and as straps shaving cream, shampoos, etc. [6]. It has anti-aging effects onVit A, treating burns, stomach ulcers treatment, and AIDS [17]. But the leaf extract is said to contain a substance that can cause cancer [18]. It is also associated with abdominal cramps and diarrhea [18]. But the topical application is not associated with any side effects [18].

MATERIALS AND METHODS

Animals

A total of 57 animals were used for the study consisting of 27 albino mice for the toxicity study (LD_{50}) and 30 albino rats for the main study. The animals were weighed (14-25.5) kg and (110-170) kg respectively. The animals were kept in a ventilated animal house of the Department of Pharmacology, Faculty of Pharmacy, University of Uyo. They were fed with clean water and pellets using the guidelines of the Helsinki ethical committee 1964.

Acute toxicity test LD_{50}

The acute toxicity test was done according to Lorke method 1983. Twenty-seven mice were used in the study and were divided into three groups of nine mice each. The mice were administered intraperitoneally at a starting dose of 500 mg/kg to 2000 mg/kg. A toxic dosage was established between 5000mg/kg and 20000mg/kg with physical signs of restlessness, writhing, and death finally. The acute toxicity was obtained from the square root of the maximum dosage that produced 0% mortality and the minimum dosage that produced 100% mortality=$\sqrt{a \times b}$

$Ld_{50} = \sqrt{a \times b} = \sqrt{1750 \text{ mg} \times 20000} = 1870.83$ mg/kg

This was further subdivided into the low dose, medial and high dosages by 10%, 20% and 30% multiplication as follows: 10%=(10% of LD_{50})=187.08 mg/kg

20% of LD_{50}=374.42 mg/kg

30% of LD_{50}=561.25 mg/kg

RESULTS

The results of the study are shown in the Tables 1 and 2 and Figures 1 and 2 are summarized as follows.

Table 1: Effects of treatment groups on gastric acid output from (7-28) days.

Group/Treatment	Gastric output/mmol/l
Group 1 (control)	0.0009750 ± 0.00068496
Group 2 (Aloe Vera dose)	0.001765 ± 0.0012882
Group 3 (Aloe Vera medium dose)	0.0023750 ± 0.00198389
Group 4 (Aloe Vera high dose)	0.0013250 ± 0.0071356
Group 5 (Cimetidine)	0.0009500 ± 0.00061914
Group 6 (omeprazole)	0.0013500 ± 0.00096782

The results showed that the volume of gastric acid secretion increased significantly ($p<0.1$) in group 3, 0.0023750 ± 0.00198389 as compared to group 1, normal control; 0.0009750 ± 0.00068496. But was not significant ($p>0.1$) in group 2 treated with low dose Aloe Vera high doses, 0.0017675 ± 0.00112882, 0.0013250 ± 0.00071356 and omeprazole group 6 0.000950 ± 0.00061914 when compared with control, 0.0009750 ± 0.0008496. The results revealed that Aloe vera is more potent at

medium dosage than omeprazole in the treatment of gastric ulcers.

Table 2: Effects of treatment groups on gastric acid output (7-28) days (mmol/L).

Group	Day 7	Day 14	Day 21	Day
1	0.0019 ± 0.0079	0.002 ± 0.00816	0.0028 ± 0.0079	0.007 ± 0.0152
2	0.0028 ± 0.0096	0.0001 ± 0.00181	0.0019 ± 0.0079	0.0006 ± 0.0044
3	0.0052 ± 0.0131	0.0006 ± 0.0044	0.0016 ± 0.0073	0.0021 ± 0.0083
4	0.0006 ± 0.0044	0.23 ± 0.0875	0.0013 ± 0.0065	0.0011 ± 0.0060
5	0.0006 ± 0.0044	0.0018 ± 0.0078	0.0010 ± 0.0003	0.0004 ± 0.0001
6	0.0009 ± 0.0047	0.0009 ± 0.0054	0.0028 ± 0.0079	0.00008 ± 0.005

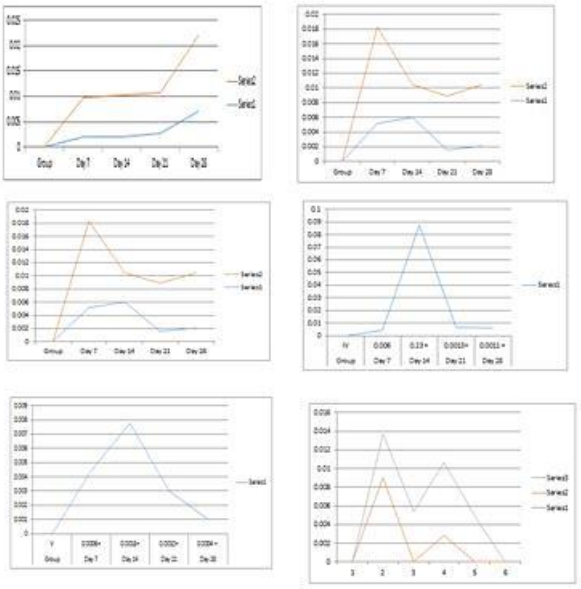

Figure 1: Effects of treatment groups on gastric acid output from (7-28) days.

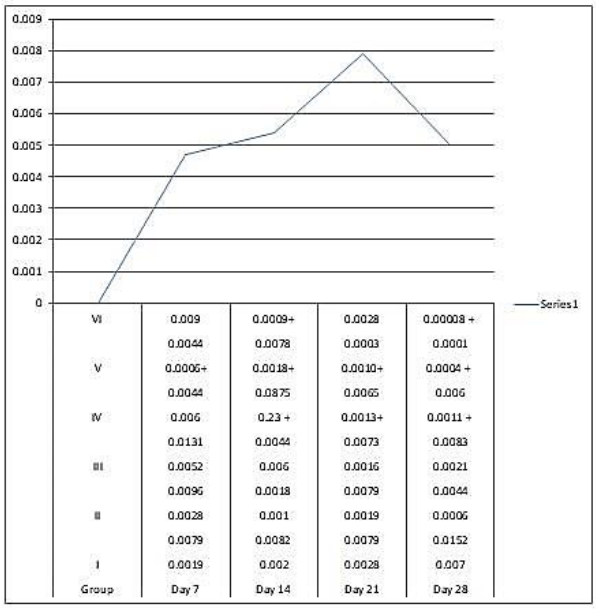

Figure 2: Combine treatment groups with acid output mmol/l

DISCUSSION

The study has shown the potency of Aloe vera extract as compared with cimetidine and omeprazole. The hydrochloric acid output in the two drug groups compared with Aloe vera has shown that there is a reduction in the gastric acid output particularly in the high dose group as compared with the omeprazole group, in line with the previous study in acid output reduction [19]. The mechanism of action of acid reduction is considered to be due to amino acid and fatty acids, prostaglandins [20]. The amino acid in the form of protein tends to increase hydrochloric acid levels to convert inactive pepsinogen to pepsin which may account for a slight increase in the gastric acid output in the Aloe vera treatment group. Aloe vera has also been found to contain fatty acids, auxins, and gibberellin [21]. Fatty acids increase prostaglandin levels which modulates inflammation while auxin and gibberellin enhance wound healing. Prostaglandinhas been

found to increase in omeprazole and cimetidine administration in gastric ulcer which led to higher ulcer healing in the study with tropical plants [22]. In this study, it has been found that the administration of Aloe vera within 7 days led to the healing of gastric ulcer whereas the groups administered with cimetidine and omeprazole had no such healing. Aloe vera decrease acid output with increasing usage as observed for 28th day as against its high dosage. It means periodic increase enhances the production of prostaglandin for mucus protective synthesis as observed in the previous study with a tropical plant [22]. Prostaglandin was not analyzed in this study but in the previous study [22] it was shown that prostaglandin levels were increased from day 7 to 28 days of the study and hence the healing of the gastric ulcer. The healing was more in the extract used in the study than the orthodox drugs; cimetidine and ranitidine. This implies that potent herbal remedies potentiate the prostaglandin increase pathway via the fatty acid synthesis in the healing process.

Prostaglandins are autocoids and potent vasodilator [7] and derived from unsaturated fatty acid and arachidonic acid. Prostaglandins are primarily released into the gut human upon vagal and hormonal stimulation [23]. The endogenous prostaglandins are involved in the maintenance of mucosal integrity, control of mucosal, control of mucosal blood flow, protection against harmful agents, inhibition of acid synthesis increase secretion of protective mucus and protection against ulcer gastric injury, ulcer healing and cytoprotective agent [7].

CONCLUSION

In the study Aloe Vera showed a clear potency lead on the cimetidine and even the omeprazole in the reduction of acid output even at its low dose. This means this crude extract has a lot more if purified the more as this will be the next approach based on its inherent toxicity.

RECOMMENDATION

The study recommends Aloe Vera for the treatment of gastric ulcer but under the supervision of researchers and clinicians in gastroenterology.

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