Original Article

# Laxative potential of the ethanolic leaf extract of *Aloe vera* (L.) Burm. f. in Wistar rats with loperamide-induced constipation

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## ABSTRACT

**Background:** Constipation is a highly prevalent and often chronic functional gastrointestinal disorder affecting humans irrespective of race and color exposing victims to colorectal cancer. The present study evaluated the efficacy of the ethanolic leaf extract of *Aloe vera* against loperamide-induced constipation in rats. **Materials and Methods:** Rats were constipation induced by the oral administration of loperamide (3 mg/kg body weight) while the control animals received normal saline. Constipated rats were treated with 50, 100, and 200 mg/kg body weight/day of the ethanolic leaf extract for 7 days during which the feeding characteristics, body weight, fecal properties, and gastrointestinal transit ratio were monitored. **Results:** Treatment of constipated rats with the extract at 50, 100, and 200 mg/kg body weight for 7 days improved intestinal motility, increased fecal volume, and normalized body weight in the constipated rats. These are indications of the laxative property of the herb with the 200 mg/kg body weight of the extract showing the best efficacy. **Conclusion:** The effect of the extract compares favorably well with Gaviscon, a standard laxative drug. These findings have therefore lent scientific support to the use of the herb as a laxative agent in Nigerian folkloric medicine.

**Key words:** *Aloe vera*, constipation, ethanolic extract, folk medicine, Gaviscon, intestinal motility

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## INTRODUCTION

Constipation is a highly prevalent and often chronic functional gastrointestinal disorder affecting 3-15% of the general population.[1-4] It is a common clinical problem comprising a constellation of symptoms that include excessive straining, hard stools, feeling of incomplete evacuation, use of digital maneuvers, or infrequent defecation. A number of conditions such as metabolic problems, fiber deficiency, anorectal problems, and drugs can cause constipation. Functional constipation consists of two subtypes, namely, slow-transit constipation and dyssynergic defecation. Some patients with irritable bowel syndrome may exhibit features of both types of constipation.[5]

Laxatives are agents that add bulk to intestinal contents by retaining water within the bowel lumen by virtue of their osmotic effects, or that stimulate intestinal secretion or motility thereby increasing the frequency and ease of defecation.[6,7] The use of chemical drugs such as Senna, Correctol, Exlax, Senokot, and Gaviscon (containing sennosides as active ingredients) for the treatment of constipation is common among affected individuals. However, the use of these orthodox drugs is limited due to their high cost, undesirable side effects (such as stomach pain and cramps), and slow activity (up to 8 h) in relieving constipation.[3,4,8] Therefore, almost half of patients with constipation are not satisfied with the efficacy of orthodox laxatives in improving quality of life.[9,10] Consequently, attention has been shifted to the use of medicinal plants for the treatment of the menace particularly in Nigeria.[11,12] There is the general belief among users that plant extracts are cheap, fast acting, and readily available coupled with the availability of several choices.[13] Therefore, the continuous search for a more natural, effective, affordable and readily available laxative of plant origin necessitated this research.

From time immemorial, aloe plants have been used medicinally for centuries for the treatment of diverse disorders and

ailments such as diabetes and ulcer.[14] There are at least four species of the over 360 known ones that have medicinal properties – *Aloe arborescens* Miller; *Aloe perryi* Baker; *Aloe ferox* Miller, and *Aloe barbadensis* Miller, also known as *Aloe vera*.[14,15] Among them, *A. vera* is the most widely used healing plants in the history of mankind.[16] *Aloe vera* (L.) Burm. f. is perennial, succulent xerophytes which develops water storage tissues in the leaves to survive in dry areas of low or erratic rainfall. The innermost part of the leaf is a clear, soft, moist, and slippery tissue that consists of large, thin-walled parenchyma cells in which water is held in the uniform of viscous mucilage.[17,18] *A. vera* has been part of the traditional medicine practices of many regions of the world for centuries and the medicinal efficacy has been attributed to the aggregation of over 75 bioactive phytochemicals.[19] These comprise basically polysaccharides and anthraquinones which are concentrated in the inner leaf parenchymatous tissues of the plant.[20,21] The medicinal activities of the plant have been reported to be as a result of synergistic action of the compounds (such as cellulose and aloe-emodin) contained therein rather than a single chemical substance.[22] The bioefficacy reports of *A. vera* include antimicrobial,[21,23] antiviral,[24] antioxidant,[25] anti-psoriasis,[26] antidiabetic,[27-30] cardiac stimulatory,[31] antiulcer,[32] immunomodulatory,[33,34] anti-inflammatory,[35,36] anticancer,[37] and hepatoprotective properties.[38]

Although the traditional use of *A. vera* as a laxative is known but little or no scientific credence is available in the literature on the purgative potential of this plant. The present study therefore investigated the laxative/purgative activity of *A. vera* in loperamide-induced constipated experimental animals and the effect was compared with Gaviscon, a standard laxative drug. The result from this study is expected to shed more light on the minimum required dosage of the *A. vera* crude extract that will provide an effective laxative activity.

## MATERIALS AND METHODS

### Drugs and chemicals

Loperamide hydrochloride, carmine, and carboxymethylcellulose were procured from Sigma Chemical Co. (St. Louis, MO, USA) while Gaviscon was a product of Reckitt Benckiser Pharmaceutical (Pty) Ltd. (Elandsfontein, South Africa). All other chemicals and reagents used were of analytical grade.

### Plant materials

Fresh, mature leaves of *A. vera* were collected from the Ojo area of Lagos State, Nigeria, from homes where the plant is grown in pots. The plant was authenticated by Mr. OK Oluwa, a biosystemanist in the Department of Botany, Lagos State University, and a voucher specimen (AshMed. 2010/LHB01) was prepared and deposited in the university herbarium.

### Preparation of the ethanolic extract

The leaves of *A. vera* were thoroughly washed with distilled water, cut into thin slices, and air-dried at room temperature to a constant weight. The dried leaves were grinded into a powder and 40 g of the material was extracted by shaking it for 24 h in 500 ml of ethanol. The extract obtained was filtered through Whatman no. 1 (70 mm) filter paper and concentrated on a water bath at 45°C to give a yield of 5.2 g. This was reconstituted in distilled water to give the required doses of 50, 100, and 200 mg/kg body weight for the experiment.

### Animal used

Male albino rats (*Rattus norvegicus*) of the Wistar strain with a mean weight of 150 ± 4.22 g were bred in the animal house of the Department of Biochemistry, Lagos State University. The animals were housed individually in clean metabolic cages placed in a well-ventilated house under optimum conditions (temperature 23 ± 1°C; photoperiod: 12 h natural light and 12 h dark; humidity: 45–50%). They were acclimatized for 7 days after being selected for the experiment, during which they were allowed free access to commercial pelleted rat chow (Lagos State Agro-Products, Agric Farm, Ojo, Lagos) and water *ad libitum*. The cleaning of the cages was done on a daily basis. All animal treatments were in accordance with international ethical guidelines and the National Institute of Health Guide concerning the care and use of laboratory animals. The study was carried out following the approval from the Ethical Committee of the Lagos State University on the use and care of animals.

### Induction of constipation in the rats

Constipation was induced in the animals by the oral administration of 1 ml loperamide (3 mg/kg body weight in 0.9% sodium chloride for 3 days),[39] while the control rats were administered with the normal saline only. The passage of reduced, hard, and dry fecal pellets indicated constipation in the rats.

### Experimental design

A total of 36 Wistar rats were used for the experiment and they were grouped into 6 with each group comprising 6 animals each. Those in Groups 1 (control) and 2 (constipated control) were administered with distilled water. Groups 3, 4, and 5 comprised constipated rats given 50, 100, and 200 mg/kg body weight/day of the *A. vera* ethanolic extract, respectively, while Group 6 consisted of constipated rats administered with Gaviscon. The administration was done using a metal oropharyngeal cannula. The water intake, feed intake, and body weight gain of all the rats were recorded during the experimental period and treatment lasted for 7 days.

### Total number, dry weight, and water content of the fecal pellet

The excreted fecal pellets of individual rats were collected daily at 09:00 am throughout the duration of the experiment. The total number, weight, and water content of the pellets were determined. The water content was calculated as the difference between the wet and dry weights of the pellet.

### Gastrointestinal transit ratio

The gastrointestinal (GIT) ratio was measured according to the method of Nagakura *et al.*[40] On the day 7, 1 ml of carmine (3 g suspended in 50 ml of 0.5% carboxymethylcellulose) was orally administered to the rats. One hour after the marker was administered, the animals were humanely sacrificed and the small intestines were quickly removed. The distance over which the carmine had traveled and the total length of the small intestine were measured. The GIT ratio was expressed as the percentage of the distance travelled by the carmine relative to the total length of the small intestine.

### Statistical analysis

Data were expressed as means ± SD of six replicates and were subjected to one-way analysis of variance (ANOVA) followed by the Duncan multiple range test to determine significant differences in all the parameters. Values were considered statistically significant at $P < 0.05$.

## RESULTS

The administration of loperamide significantly reduced the water intake, the number, water content, and the weight of the fecal pellets [Table 1]. This indicated that constipation had been induced in the rats. However, no significant difference was observed in the feed intake between the control and the constipated animals.

While water consumption decreased in the untreated constipated rats, the administration of the ethanolic extract of *A. vera* significantly increased the water intake in constipated rats [Table 2]. Again, there was no significant difference in the feed intake of all the animals. Similarly, the extract significantly increased the number, water content, and weight of fecal pellets in the constipated rats in a dosage-dependent manner. The body weights of the constipated animals were also normalized following the treatment with the extract.

Loperamide significantly reduced the gastrointestinal motility in the untreated constipated rats [Figure 1]. Treatment with the *A. vera* extract, however, increased the gastrointestinal movement in a dose-dependent manner which compared favorably well with Gaviscon, a standard laxative drug.

## DISCUSSION

Plants have long been a very important source of drugs against several diseases including constipation. In Nigeria, a reasonable percentage of the population depends on herbal medicines because the international commercial medicines are becoming increasingly expensive and out

**Table 1: Effect of the loperamide administration on feed intake, water intake, and fecal properties of constipated rats**

| Parameters | Normal control | Constipated rats |
|---|---|---|
| Feed intake | 16.85 ± 1.21 | 18.76 ± 0.98* |
| Water intake | 20.90 ±1.34 | 9.81 ± 0.85** |
| Number of fecal pellets | 71.14 ± 3.82 | 26.44 ± 1.03** |
| Water content of fecal pellets | 1.67 ± 0.18 | 0.63 ± 0.12** |
| Weight of fecal pellets | 7.02 ± 0.53 | 3.25 ± 0.10** |

Data are mean ± SD values ($n = 6$). *Not significantly different from normal controls ($P < 0.05$). **Significantly different from normal controls ($P < 0.05$).

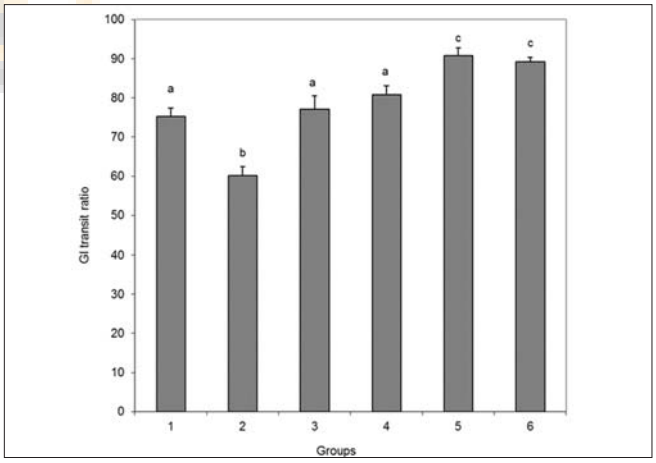


**Figure 1:** Effect of the ethanolic extract of *A. vera* on the GIT ratio in rats with loperamide-induced constipation

**Table 2: Effect of the ethanolic leaf extract of *A. vera* on feed and water intake, body weight gain, and fecal properties of constipated rats**

| Parameters | Constipated + *A. vera* (mg/kg body weight) | | | | | |
|---|---|---|---|---|---|---|
| | Normal control | Constipated control | 50 | 100 | 200 | Gaviscon |
| Feed intake | 25.29 ± 1.62$^a$ | 24.66 ± 1.40$^a$ | 23.21 ± 1.19$^a$ | 22.94 ± 1.18$^a$ | 23.30 ± 1.23$^a$ | 23.12 ± 1.25$^a$ |
| Water intake | 53.80 ± 2.59$^a$ | 42.80 ± 2.86$^b$ | 51.00 ± 2.85$^a$ | 53.78 ± 2.82$^a$ | 54.08 ± 2.56$^a$ | 53.40 ± 2.93$^a$ |
| Number of fecal pellets | 77.80 ± 2.59$^a$ | 36.80 ± 4.94$^b$ | 50.40 ± 3.25$^c$ | 62.20 ± 3.68$^d$ | 74.20 ± 3.75$^a$ | 78.00 ± 3.54$^a$ |
| Water content of fecal pellets (ml) | 1.87 ± 0.08$^a$ | 1.33 ± 0.04$^b$ | 1.43 ± 0.07$^c$ | 1.55 ± 0.06$^c$ | 2.14 ± 0.06$^d$ | 2.08 ± 0.07$^d$ |
| Weight of fecal pellets (g) | 8.77 ± 0.61$^a$ | 3.93 ± 0.27$^b$ | 6.26 ± 0.26$^c$ | 8.52 ± 0.36$^a$ | 8.84 ± 0.32$^a$ | 9.01 ± 0.25$^a$ |
| Body weight gain (g) | 13.20 ± 0.96$^a$ | 31.78 ± 1.00$^b$ | 12.17 ± 0.91$^a$ | 11.12 ± 1.69$^a$ | 10.48 ± 1.55$^a$ | 13.22 ± 1.11$^a$ |

Data are mean ± SD values ($n = 6$). Row values with superscripts different from the control are significantly different ($P < 0.05$).

of reach coupled with the undesirable side effects.[11,12] The present study has clearly demonstrated that the aqueous extract of *A. vera* has a laxative activity, which is comparable to Gaviscon.

The use of loperamide as a constipation inducer is well documented. The drug is an opioid agonist antidiarrheal that inhibits intestinal water secretion and colonic peristalsis.[41,42] This inhibition extends fecal evacuation time and delays intestinal luminal transit.[43] Loperamide-induced constipation is therefore considered to be a model of spastic constipation.[44]

The observed reduction in the number, weight, and water content of fecal pellets following the treatment with the drug indicated induction of constipation in the rats. A similar observation was reported by Shimotoyodome *et al*.[45] and Wintola *et al*.[3] The reduction in the water consumed by the constipated animals may also be due to the effect of the drug which probably accounted for the reduction in the water content of the fecal pellets. However, the drug did not prevent the animals from feeding adequately.

The administration of the ethanolic leaf extract of *A. vera* to the constipated rats was effective in influencing the increased defecation frequency, fecal volume, and motility of the colon. These are indications of the laxative property of the plant extract. This may be due to the presence of anthranoid glycosides derivatives of which aloin is the main compound.[46] According to Izzo *et al*.,[47] aloin is metabolized by the colonic flora to reactive aloe-emodin which is responsible for the purgative activity of this plant. This compound possibly exerts its action by disturbing the equilibrium between the absorption of water from the intestinal lumen via an active sodium transport[48] and the secretion of water into the lumen by a prostaglandin-dependent mechanism.[49]

Although the feed intake did not differ among the groups, the gain in body weight was higher in the untreated constipated rats compared to the extract-treated groups. This may be due to the accumulation of fecal pellets in their bodies, thus accounting for the extra weight. This clearly indicates that the plant extract increased intestinal secretion and motility in the constipated rats. A similar observation was reported by Niwa *et al*.[50] where dietary fiber was used for the treatment of morphine-induced constipation in rats. Wintola *et al*.[3] also recorded a similar observation during the treatment of constipated rats with *A. ferox*. Of particular interest is the fact that the effect of the *A. vera* extract was dose dependent in this study. The effect of the highest dosage actually compared favorably well with Gaviscon.

The transit process of the entire gastrointestinal tract reflected the overall gastrointestinal motor activity. Measuring the colonic transit time is useful in constipation, abdominal bloating, and refractory irritable bowel syndrome.[3] It also provides quantitative information about the colonic transit, enables the identification and characterization of transit abnormalities, and allows the assessment of the severity of the problem as well as the response to therapy.[51] In this study, carmine was used as the marker to measure the colonic movement. The *A. vera* ethanolic extract increased the intestinal motility which, in turn, enhanced colonic peristalsis in the rats. The possible mechanism of the extract in this process may be enhancing the release of fluid thereby increasing intestinal secretion. The laxative effect of the extract could also be attributed to changes in the intestinal motility, which produced an increase in the intestinal transit and colonic movement.[52] Generally, the effect of the treatment with the extract compared favorably well with Gaviscon. The present study compares favorably well with that of Wintola *et al*.[3] where an *A. ferox* extract was used. This is an indication that the herb was effective in ameliorating bowel obstruction, thereby enhancing easy movement in the intestine.

## CONCLUSION

The present study revealed that oral administration of the ethanolic extract of *A. vera* exhibited a laxative activity in rats with loperamide-induced constipation rats. This suggests the beneficial effects of the herb in improving intestinal motility. Noteworthy is the fact that the extract at the highest dose of 200 mg/kg body weight showed the best laxative action, which compared favorably with Gaviscon. These findings have lent scientific support to the use of *A. vera* as a laxative agent in Nigerian folkloric medicine.

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