

Research Article

Anti-ulcer and Anti-inflammatory Effects of Hydro-alcohol Extract of *Aloe buettneri* A. Berger (Liliaceae)

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Abstract

Purpose: *Aloe buettneri* A. Berger is commonly used in Togolese folk medicine to treat inflammation and gastric ulcer. In this study we investigated the anti-oedema, analgesic, antipyretic and ulcer healing properties of the hydro-alcohol extract of their leaves.

Methods: Rat oedema paw were induced by the injection of 0.1 ml of formaldehyde 1%, tail flick method is used to study analgesic property, hyperthermia was induced by subcutaneous injection of 15% of a brewers' yeast suspension at dose of 10 ml/kg and ulcers were induced by ethanol or HCl/ethanol mixture.

Results: The extract showed anti-inflammatory properties at doses between 250-500 mg/kg. It inhibited, in a dose- dependent manner, the oedema induced by 0.1 ml of formaldehyde 1%. Scores of 73.70% and 83.63% were obtained when the doses of extract administered were 100 and 500 mg/kg, respectively. The tail flick analgesic index showed an increase of 36.56% when the dose was 500 mg/kg. The extract decreased significantly the hyperthermia induced by the injection of yeast. 1000 mg/kg of the extract inhibited 63.77% of the gastric lesion induced by acid-water-ethanol mixture while daily administration of the same dose accelerated the cicatrization of gastric ulcer induced by 95% ethanol.

Conclusion: The results obtained show that the hydro-alcohol extract of *Aloe buettneri* A. Berger (Liliaceae) has anti-inflammatory, anti-ulcer and wound healing properties

Keywords: *Aloe buettneri*, oedema, analgesic, hyperthermia, ulcer.

INTRODUCTION

Aloe is a plant recognized since antiquity for its therapeutic virtues. It belongs to the family of Liliaceae which garlic and onion belong. *A. barbadensis* or *A. vera* is used in Mexican folk medicine and in other countries as an anti-inflammatory drug and cosmetic product¹ and *A. arborens* was identified as having anti-inflammatory and anti-ulcer properties². Togolese folk medicine uses *Aloe buettneri* to treat gastro-intestinal infections, chronic wounds, cutaneous infections, inflammations and gastrics ulcers³. Species of aloe, particularly *A. schweinfurthii*, *A. saponaria*, *A. arborens* and *A. vera* have been studied for their anti-inflammatory^{2,4} and anti-ulcer⁵ properties. However, to the best of our knowledge, no study has shown the anti-inflammatory and anti-ulcer properties of *A. buettneri*. The aim of these studies is to investigate the anti-inflammatory and anti-ulcer properties of the hydro-alcohol extract of the leaves of *A. buettneri*.

MATERIAL AND METHODS

Plant material

The whole leaves of *A. buettneri* were collected from the botanical garden of the Faculty of Science, Université de Lomé, Togo. The plants were identified by Professor AKPAGANA Koffi de Laboratoire de Botanique et d'Ecologie Végétale. The leaves were then washed, dried under air-conditioning and reduced to powder with electric mill (THOMAS-Wiley). The powder was cold extracted in water/ethanol 95°mixture (1:1) for 72 h. The solvents were evaporated to obtain a dark hydro-alcohol extract whose contained tannins, flavonoids and alkaloids as revealed by phytochemical screening

Animals

Wistar rats, of both sexes, weighing 150-200g were used. They were housed under standard conditions of temperature, humidity and dark-light cycle (12h – 12h). They have free access of water. They were kept in the Animal House of the Faculty.

Anti-inflammatory effect

Oedema was induced according to the method described previously by Sen and Nag⁶ and Agbonon et al⁶. A quantity (0.1 ml) of formaldehyde (1%), was injected into the subplantar right paw of the rats. The treatments were curative or preventive. For the curative group, the rats were administered the extract (100, 250,500 mg/kg) or indomethacin (100 mg/kg) as reference drug, 1 hour after induction of the oedema while for the preventive group, the rats were administered the extract 30 minutes before the induction of the oedema. The volume of the foot paw of each animal was measured by immersion as described by Agbonon and co-workers⁷.

Analgesia

Analgesia was studied according to the method of Sewell and Spencer⁸ or Tail Flick method. Twenty-five male and female rats, divided into five groups of five rats each, were used. The tail of the animal was immersed in hot water at 50°C in a thermostated bain-marie. The time of withdrawal of the tail was measured and recorded as the reaction time. One hour after beginning of the experiment, the rats received by the oral route, water or the *A. buettneri* extract (100, 250, 500 mg/kg) or DL-Lysine Acetylsalicylate (Sanofi-synthelabo) as reference drug (50 mg/kg).

Antipyretic effect

Hyperthermia was induced by subcutaneous injection of 15% of a Brewer's yeast suspension at a dose of 10 ml/kg. Twenty four hours before the induction of hyperthermia, 16 male rats were fasted. At the end of the fasting period, the rectal temperature of the rats was recorded as the basal temperature and then Brewer's yeast suspension was injected. Eighteen hours after, hyperthermia was checked and then the animals received by the oral route water or the Aloe extract (100, 250, 500mg/kg). The rectal temperature was then recorded every hour up to 6th hour.

Anti-ulcer effect

For the preventive studies, ulcer was induced according to the method of Yamahara et al⁹. Thirty rats of either sex weighing 150-200g were fasted for 24 hours and divided into six

groups of five each. One hour before ulcer induction, the rats received water or Aloe extract (250, 500, 1000, 2000 mg/kg) or sucralfate 0.5 mg/kg. Gastric lesion was induced by the administration of HCl/ethanol mixture (ethanol 95°: 60 ml, HCl 1N: 1.7 ml, Water: 38.3 ml) at a dose of 0.4ml/kg. One hour after ulcer induction the animals were ether-anesthetised, sacrificed by cervical dislocation, and then the stomach was removed. The stomach was incised along the axis of greater curvature after immersion in 2% formaldehyde. The dimension of ulcer was measured with a planimeter

For curative studies, rats were fasted overnight prior to ulcer induction. Ulcer was induced by the oral administration of 95% ethanol at a dose of 0.5 ml/100g¹⁰. The rats were divided into ten groups of five rats each (group I to X). Group I to V are the control groups while group VI to X are the treated groups. Two groups (control and treated) of rats were sacrificed, respectively, on day 0, day 2, day 4, day 6, day 8 following ulcer induction. Day 0 is ulcer induction day. The treated groups received 1000 mg/kg of the Aloe extract while the control groups received distilled water. Ulcers were evaluated with a planimeter.

Statistical analysis

The results were treated using SYSTAT 5.0 software and expressed as mean \pm S.E.M. Statistical analyses of data were carried out using Student's t- test. Results were considered significant if $P < 0.05$.

RESULTS

Antinflammatory effect of the Aloe extract

Injection of 0.1ml of formaldehyde 1% induced rat paw oedema. The hydro-alcohol extract of *A. buettneri* administered orally at 100, 250, 500 mg/kg 30 minutes before the formaldehyde injection inhibited oedema 3.14%; 28.26% and 46.22% ($p < 0.05$), respectively, one hour after oedema induction. Three hours later, inhibition was 82.52; 86.87; 89.81% ($p < 0.01$), respectively (see Figure 1).

For the curative studies, the increase in oedema paw volume was 46.72 \pm 1.34% in the

control rats, but was only 26.92 \pm 0.66; 15.22 \pm 2.48; 12.77 \pm 1.29% three hours after induction in the rats which received 100, 250, 500 mg/kg of Aloe extract (see Figure 2).

Analgesic effect of the extract of *A. buettneri*

Analgesia was evaluated by immersing the tail of the rats in maintained hot water at 50°C. The time of immersion of the tail increased with the dose. It was 4.15 \pm 0.17 seconds for control rats, and 5.16 \pm 0.21; 7.04 \pm 0.25; 7.07 \pm 0.28 seconds, respectively, for the rats which received 100, 250 and 500 mg/kg of the extract. Thus the doses of 250 and 500mg/kg had practically the same effect (Figure 3).

Antipyretic effect of the extract of *A. buettneri*

Injection of 15% of Brewers' yeast at 10 ml/kg increased the rectal temperature of the rats for 1.5°C. This hyperthermia remained the same for control rats with small fluctuations over 24-hour period. Administration of the extract, 18 hours after the induction of hyperthermia, decrease the temperature from 38.78 \pm 0.024°C to 38° \pm 0.05°C three hours after the administration of the extract. The reduction was dose- and time-dependent in that 6 hours after the administration of the extract, the recorded temperature was 38.70 \pm 0.3°C for the control while it was 37.70 \pm 0.07°C; 37.00 \pm 0.03°C and 36.85 \pm 0.15°C, for rats which received the extract at doses of 100; 250 and 500 mg/kg, respectively (see Figure 4).

Anti-ulcer effect

Ulcer was induced by two different methods. While ulcer induced by the administration of water-HCl-ethanol mixture produced ulceration of 19 \pm 1.00 units 1 hour after induction, ethanol only induced ulceration of 9.20 \pm 0.58 units 2 hours after induction. In both cases, we noted a lesion characterized by an abrasion of the gastric epithelium, erosion associated with one necroses ischemic.

As Table 1 indicates, *Aloe buettneri* extract inhibited dose-dependently the gastric lesion with the percentage of inhibition 25.16 \pm 11.21;

63.77 ±11.67 and 74.48 ±15.23%, respectively, for rats which received 500, 1000 and 2000 mg/kg of extract. The doses of 1000

and 2000 mg/kg had a significant effect on the gastric lesions (p <0.01). For ulcerations induced by oral administration of ethanol 95%,

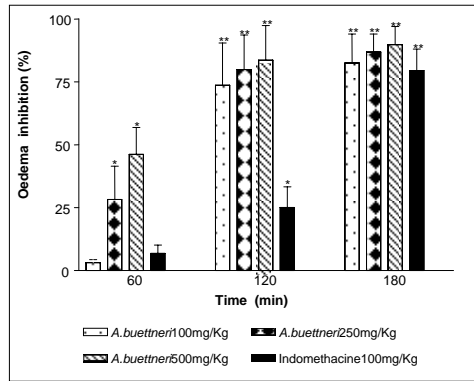


Figure 1: Effect of the extract of *A. buettneri* administered thirty minutes before the induction of the oedema with 0.1 ml of 1% formaldehyde. Values represent the mean ± S.E.M. of five rats. * P < 0.05; ** P < 0.01 (extract vs. control).

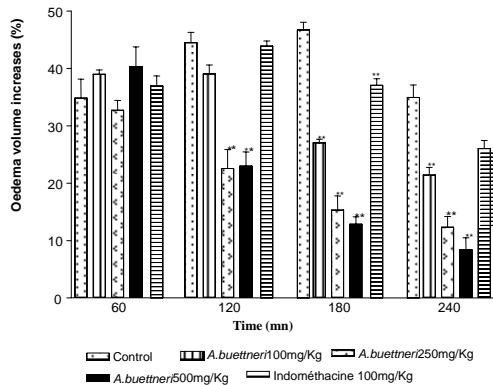
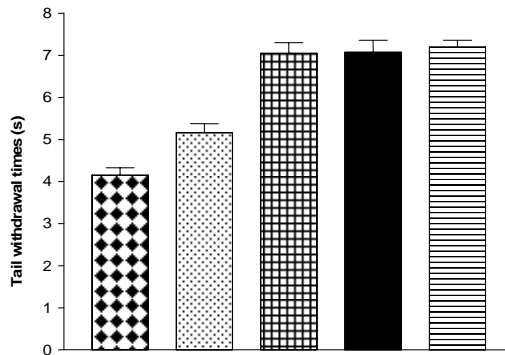


Figure 2: Effect of the extract of *A. buettneri* administered 1h after the induction of oedema with 0.1ml of 1% formaldehyde. The values represent the mean ± S.E.M. of groups of five rats. ** P < 0.01 (extract vs control)



the length of ulceration decreased from 9.20 ± 0.58 units (day 0) to 5.40 ± 0.51 units (day 4) and to 0.00 unit (day 8) for control animals. These dimensions decreased to 7.20 ± 1.20 ; 1.00 ± 0.45 and 0.00 ± 0.00 units, respectively, on day 2, day 4 and day 6 in the rats treated with the hydro-alcohol extract of *A. buettneri*. These results show that the extract accelerated the cicatrization of the ulcerous wounds

DISCUSSION

Our results show that the extract of *A. buettneri* has anti-oedema, analgesic, antipyretic and anti-ulcer properties. These properties could be attributed to the following

phytochemical compounds: tannins, flavonoids and alkaloids (revealed by phytochemical screening) which are present in the extracts. As previously described, oedema and pain induced by formaldehyde are mediated by substance P, bradykinin, histamine, serotonin and prostaglandins¹¹. Inhibition of oedema induced by the extract (500 mg/kg) and the increase in the immersion time of the tail in hot water suggest that the extract probably inhibits the production of bradykinin and substance P. In addition, rats which received the extract one hour after injection of formaldehyde showed oedema volume decreases. This could indicate that the extract also inhibits the

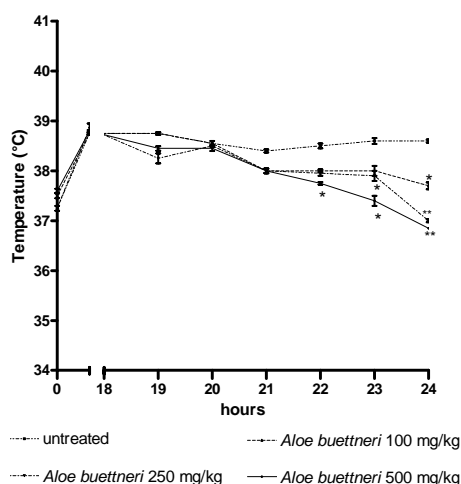


Figure 4: The effect of the extract of *A. buettneri* on induced hyperthermia. The values represent the mean \pm S.E.M. of four rats. * $P < 0.05$; ** $P < 0.01$ (extract vs. control).

Table 1: Dimensions (in arbitrary units) of ulcer induced by oral administration of ethanol-water mixture (1:1)

Treatment	Ulceration (arbitrary units)
Control	19.00 \pm 1.00
<i>Aloe buettneri</i> 250 mg/kg	16.66 \pm 0.66
500 mg/kg	14.33 \pm 0.88*
1000 mg/kg	07.00 \pm 0.58**
2000 mg/kg	05.00 \pm 1.15**
Sucralfate 0.5 mg/kg	11.00 \pm 2.15**

The data were expressed as mean \pm S.E.M.; ** $p \leq 0.01$ (extract vs. control). Each arbitrary unit corresponds to 25 mm².

synthesis of prostaglandins¹¹. Indeed, flavonoids are known to inhibit the metabolism of the arachidonic acids whereas the tannins inhibit the synthesis of prostaglandins¹².

Furthermore, the extract administered 18 hours after the induction of hyperthermia decreased body temperature. The extract may have acted like antagonists of pyrogenic endogenous molecules (interleukines 1). Their mechanisms have already been described for the extract of *A. barbadensis*^{13, 14}. Another important finding is the anti-ulcer effect of the extract. Indeed the extract at a dose of 1000 mg/kg reduced gastric lesion by 63.77 ± 11.67 % and accelerated the ulcers wounds healing. It is known that the gastric ulcers are due to acid hypersecretion which is often stimulated by the production of histamine, or to a reduction in the production of mucus. Thus, it is possible that the extract acted by inhibiting acid secretion via the blocking of the histaminic receptors and/or by the stimulation of mucus production. Sadiq et al¹⁵ have shown that the cytoprotective effect of the extract of *A. vera* is due to the inhibition of acid secretion by interaction with H₂ – histaminic receptors.

CONCLUSION

The results obtained have demonstrated the anti-inflammatory, anti-ulcer and wound healing properties of *A. buettneri* and thus buttresses its use in Togolese folk medicine. Further investigations are required to fully elucidate the mechanisms of action of the extract.

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