



Ant ulcer Activity of *Aloe vera* in Aspirin-Induced Mice

Widyastiwi^{1*}, Nisya Oktaviani¹

¹Department of Pharmacy, Poltekkes Kemenkes Bandung. Jalan Prof. Eyckman No. 24 Bandung, Indonesia.
ZIP code 40161
Corresponding author : widyastiwi@gmail.com

Abstract. Background : Gastric ulcers often characterized by the destruction of the mucosal to muscularis layer of the stomach. One of its major etiology is prolonged NSAIDs use. Its incidence is increasing every year, and often disrupt patients' quality of life. Aloe vera is empirically used as antiulcer in Indonesia, therefore this study was aimed to determine its activity in aspirin induced male-swiss-mice, with ranitidine as comparator.

Methods : Thirty mice were randomized and divided into 6 groups : Negative control, positive control, comparison group (given ranitidine with dose 1,4 mg/20 g), Aloe vera juice group 0,1 ml/20g, 0,3 ml/20g and 0,6 ml/20g. All treatment were administered orally followed by 16.8 mg/20g bw aspirin administration, once a day for three days. Observed parameters including the number and diameter of the ulcer. The results of protection percentage were analyzed statistically using Kruskal Wallis test ($\alpha = 0,05$), then continued with Post Hoc test.

Results : Aloe vera 0.3 ml/20g and 0.6 ml/20g bw possessed a gastric anti-ulcer activity by decreasing number of ulcers in aspirin induced male-swiss-mice significant to control group ($p < 0.05$).

Conclusion : This study propose a potential antiulcer activity of aloe vera. Further research is needed to propose its mechanism of action.

Introduction

Gastric ulcers is a lesion in mucosa, sub mucosa, and muscularis line in gastric. Gastric ulcers occur due to an imbalance disorder between aggressive factors (gastric acid secretion, pepsin, and *Helicobacter pylori* bacterial infection) with defensive factors or mucosal protective factors (prostaglandin production, gastric mucus, bicarbonate, and mucosal blood flow) [1].

NSAIDs are widely used in the community due to its potent activity as pain relievers, antiinflammation, and antipyretic. NSAIDs inhibit COX-1 enzyme and decrease the number of prostaglandin, which played a major role in inflammation and pain [2]. On the other side, gastric mucus, as gastric mucosal protective factors, is also stimulated by prostaglandin E2 and I2, which also directly inhibit gastric acid secretion by parietal cells. Thus, drugs that inhibit prostaglandin formation, such as NSAIDs, decrease mucus secretion and predispose to the development of

peptic ulcer disease. Gastric ulcers develop in up to 15% to 30% of chronic NSAID users with continued use. Between 2% and 4% of patients with an NSAID ulcer will bleed or perforate. Ulcer-related complications and death among regular NSAID users are 3 to 10 times higher compared with nonusers.[3]

Aloe vera L. is a plant belong to Liliaceae family, grows in dry to wet areas (16-33 °C) characterized by its thick and fleshy structure. Aloe vera has a clear gel inside its leaves, and most widely used as medicine [4]. Study showed that aloe vera is rich in enzymes, amino acids, minerals, vitamins, polysaccharides, and other components beneficial for health, including barbaloin, isobarbaloin, aloe-emodin, and aloesin [5]. Aloe vera L. also contains anti-inflammatory agents, including phenolic compounds (flavonoids), anthraquinone glycosides, saponins, tannins, auxin, gibberellins, amino acids, β -sitosterol, lignin, and lectins. This phytochemical properties could be beneficial in gastric ulcer treatment [6].

Many studies has shown aloe vera activity as antinflammation, but there is still limited study of aloe vera as antiulcers. Therefore, we were interested to conduct a study to evaluate effects of aloe vera as antiulcers compared to standard drug ranitidine.

Experimental Section

Materials

Aloe vera juice, acetylsalicylic acid tablet, ranitidine tablet as standard drug, CMC Sodium, Alcohol 70%, NaCl 0,9%, and aquadest.

Animals

Thirty male Swiss-Webster albinomice (20–30 g) obtained from Institut Teknologi Bandung were used for the experiments. The animals were maintained in standard environmental conditions and housed in a light-controlled room at a room temperature, fed on a standard diet with water ad libitum.

Methods

Thirty six Swiss-Webster albino mice were divided into 6 groups. The first and second group served as normal and positive control and was given normal saline. Groups III received standard drug (ranitidine 1,4 mg/20 g), meanwhile group IV, V, and VI received aloe vera juice in three various concentration : 0,1 ml/20g, 0,3 ml/20g and 0,6 ml/20g respectively. Thirty minutes later, each mice in all group, except for normal group, was administered aspirin orally to induced gastric ulcers. This treatment was administered daily for three days.

At the fourth day, mice were sacrificed using neck dislocation method. Abdomen were performed, and gastric were collected to be analyzed. Scoring for number of ulcers were categorized as shown in table 1, meanwhile for ulcer severity were categorized by diameter of ulcers as shown in table 2.

Table 1. Scoring of Ulcer Number

Score	Kategori
1	Normal Gastric
2	Bleeding spots
3	1-3 number of ulcers
4	4-6 number of ulcers
5	7-9 number of ulcers
6	>9 number of ulcers

Table 2. Scoring of Ulcer Severity

Score	Kategori
1	Normal Gastric
2	Ulcers with diameter <0,5 mm
3	Ulcers with diameter 0,5 – 1,5 mm
4	Ulcers with diameter 1,6 – 4,0 mm

5	Ulcers with diameter >4 mm
6	Ulcers with perforation

The results of the experiments were expressed as Mean \pm S.D. The mean values of control groups were compared with the mean value of treated groups using Kruskal Wallis. Results were considered significant at $P < 0.05$.

Results and Discussion

The purpose of this study was to evaluate effects of aloe vera as antiulcers compared to ranitidine as standard drug. Antiulcers activity was shown by a decrease in the number and severity of ulcers after chronic induction using aspirin solution per orally.

Ranitidine inhibit acid production by reversibly competing with histamine for binding to H₂ receptor on basolateral membrane of parietal cells. The long safety and efficacy with the H₂ receptor antagonist eventually let to their availability without prescription. [1] In Indonesia, ranitidine can be accessed by patients without prescription, as long as supervised by pharmacist. It is the most common used drug for gastric ulcers besides antacids. In this study, mefenamic acid is preferred as standard drug to represent activity of antiulcers in community.



Fig 1. Gastric appearance of control and treatment groups

Figure 1 showed appearance of gastric lumen of all groups in this study. As seen above, gastric lumen of negative control group seems normal without any lesion, meanwhile ulcers is clearly visible in positive control group. In standard group and aloe vera group treatment, ulcers is visible in various degree although it is not as severe as in positive control group.

Score of ulcer number were evaluated after three days of treatment. The average score of ulcer number is shown in Figure 2, and average score of ulcer severity is shown in Figure 3.

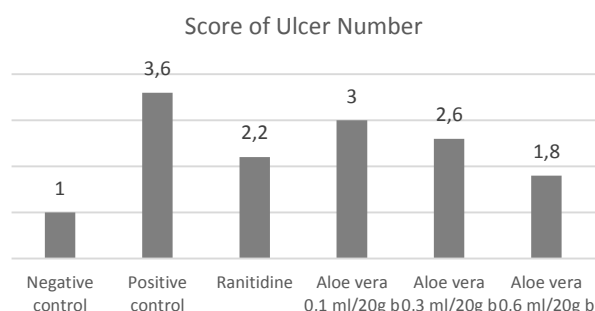


Fig 2. Average average score of ulcer number

Figure 2 showed that positive control group (induced, not treated) exhibit the highest average score of ulcer number, meanwhile aloe vera 0,6 ml/20g bwere lowest, even lower than standard drug ranitidine.

Figure 3 showed similar result as positive control group exhibit the most severe ulcer, meanwhile aloe vera 0,6 ml/20gbwere slightly better than ranitidine in reducing ulcer severity by reducing its diameter.

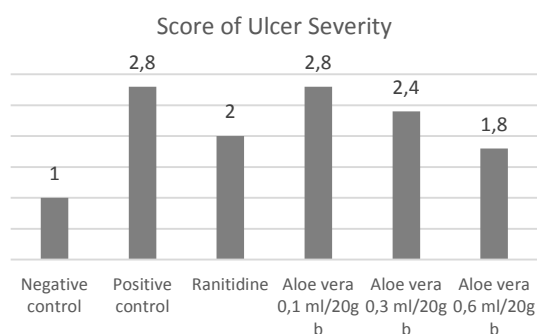


Fig 3. Average average score of ulcer severity

Statistical analysis were performed to compare aloe vera and standard drug activity in reducing number and severity of ulcer. Statistical Analysis is shown in Table 3 below.

Table 3. Statistical Analysis for Antiulcer Activity of Aloe vera

Groups	Score of Ulcer Number	Score of Ulcer Severity
Negative control	1,00±0,00	1,00±0,00
Positive control	3,6±0,55	2,80±0,45 ^b
Ranitidine	2,2±1,10 ^a	2,00±1,00
Aloe vera 0,1 ml/20g b	3,00±0,00 ^b	2,80±0,45 ^b
Aloe vera 0,3 ml/20g b	2,60±0,89 ^{a,b}	2,40±0,89 ^b
Aloe vera 0,6 ml/20g b	1,8±1,10 ^a	1,80±1,10

^asignificantly different to positive control group
^bsignificantly different to negative control group

As shown in table 3, ulcer number in ranitidine group were significantly different with positive control group. Aloe vera 0,3 ml/20 gb and 0,6 ml/20 gb also indicate similar results.

On the other side, in terms of ulcer severity, there were no significantly different score among all groups. This is probably caused by aspirin induction which only conducted for three days. Further research is needed to evaluate aloe vera effect in reducing severity of ulcer in chronic use of NSAIDs.

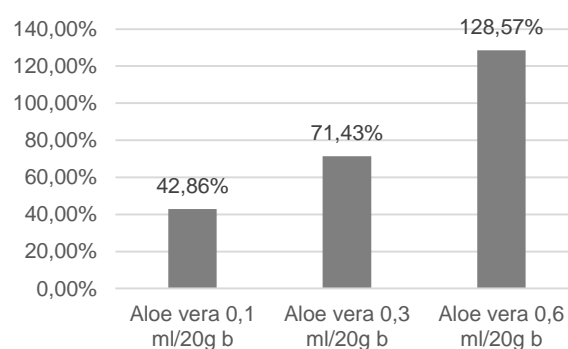


Fig 4. Effectivity Percentage of aloe vera compared to ranitidine

In addition statistical analysis, pharmacological effect of substance also often expressed as percentage of effectivity. This analysis can be done by comparingscore in treatment group to ranitidine as standard drug. Percentage of effectivity of aloe vera in three different doses compared to ranitidine is shown in figure 3. It is showed that aloe vera 0,6 ml/20g bw is 128,57% effective compared with ranitidine, or simply concluded that aloe vera 0,6 ml/20g bw is 1,28x more effective compared to ranitidine in reducing number of ulcer in mice.

In a previous study conducted by Gopinaptan and Rameela (2014), aloe vera juice 20 ml/kgBBcombined with amlajuce effective in alcohol-induced acute gastric ulcer acute. Tissue damage in the stomach can increase levels of protein and carbohydrates in gastric juices. Mechanism proposed by Gopinatan and Rameela is aloe juice can reduce levels of protein and carbohydrates in gastric juices. The flavonoid content in aloe juice also theoretically can inhibit the 5- lipooxygenase pathway or leukotriene antagonist activity. Gastric mucosa protection by flavonoids content in aloe vera could play a significant role in treatment of acute and chronic gastric ulcerations. [7]

Jimmy and Udim (2015) propose another antiulcer activity of aloe vera. Aloe vera is known to have antacids and H₂ receptor antagonis like effect. It its probably due to lectin content in aloe vera that inhibit acid secretion. Lectin is a glycoprotein that is able to bind with carbohydrates and inhibit aminopirin uptake by parietal cells, which is needed to secrete acid to gastic lumen. [8]

Conclusion

This study conclude a potential antiulcer effects of aloe vera. Further research is needed to propose its mechanism of action and its role as complimentary therapy in ulcer management.

Competing Interest

The authors of this paper have no competing interest to report.

Acknowledgement

The authors of this paper have no acknowledgement to report.

References

- [1]. Brunton, Laurence dan Parker, Keith. (2010). Pharmacoterapy of PepticUlcer. Dalam Goodman, L.S., & Alfred G. Goodman & Gilman's Pharmacological Basis of Teurapetics. Edisi 12. New York: Mc Graw Hill Medical.
- [2]. Katzung, Bertram G. & Trevor, Anthony J. (2015). *Basic & Clinical Pharmacology (13th Ed.)*. United States: McGraw-Hill Education.
- [3]. Dipiro.JT., 2009, Pharmacoterapy Handbook 7th edition, Mc Graw Hill, New York.
- [4]. Dalimartha, Setiawan. (2008). *Atlas TumbuhanIndonesia*. Jilid V. Jakarta: PustakaBunda
- [5]. Agoes, Azwar. (2010). *TanamanObatIndonesia*. Buku III. Jakarta: SalembaMedika
- [6]. Mani, Pandey, Neelesh, Mehra, Sourabh, Kosey dan Gaurav, Midha . (2015). Treatment and Replenishment of G.I. Tract with CombinedRegimenTherapy (CRT) of Allopathic (PPIs) and Ayurvedic (Aloe Vera) Medicine in PepticUlcerDisease to Counteract Relapse. *Journal of Gastrointestinal& Digestive System*, 5 (2), 1-8.
- [7]. Gopinathan S. dan Rameela N.(2014). Anti UlcerActivity of Aloe Vera Juice and Aloe Vera and Amla Fruit Combined Juice in Ethanol InducedUlcerated Rats. *International Journal*

of Pharmacy and Pharmaceutical Science, 6 (6), 190-197

- [8]. Jimmy E.O dan Udim N.A. (2015). DurationalEnhancedAntiulcerogenicPotentials of Aloe Vera withOmeprazol in GastricUlcer. *EuropeanJurnal of Pharmaceutical and MedicalResearch*, 2 (4), 59-70, ISSN: 3294-3211.