

## Effect of Sodium Carboxymethylcellulose and Sorbitol on Anti-Peptic Ulcer Activity of *Anredera cordifolia* Leaves Extract

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### Abstract

*Anredera cordifolia* or binahong is one of the Indonesian medicinal plants that is used to treat peptic ulcer. The purpose of this study was to evaluate the effect of the addition of sodium carboxymethylcellulose (CMC) and sorbitol on anti-peptic ulcer activity of *A. cordifolia* leaves extracts in male Wistar rats. The plants were extracted using decoction method and freeze dried. Three liquid formulas were used *i.e.*, i) a combination of sodium CMC and sorbitol; ii) only sorbitol; iii) extract only. The rats were divided into 6 groups, *i.e.*, positive control (sucralfate 35 mg/kg body weight); negative control (80% ethanol); normal control; and 3 formulas. After the administration of the liquid formula, all groups, except normal control, were given 80% ethanol (15 ml/kg body weight) to induce peptic ulcer. Anti-peptic ulcer activity was evaluated using direct observation on rats gastric mucosa, and histopathology assessment. The result showed that the strongest anti-peptic ulcer was shown by sorbitol only (96.95% inhibition), followed by the combination of sodium CMC and sorbitol (92.68% inhibition). The formula which only contained extract showed only 31.70% inhibition. Statistical analysis showed significant differences between formula 1 and 2 with negative controls. In conclusion, *A. cordifolia* leaves extract with the addition of sorbitol showed the strongest anti-peptic ulcer activity.

**Keyword:** *Anredera cordifolia*, peptic ulcer, suspense, Wistar rat.

### Introduction

Peptic ulcer is a medical condition characterized by discontinuation of the lining or mucosa of gastrointestinal tract due to excessive gastric acid secretion. Approximately 8.41 per 100,000 Indonesians died due to peptic ulcer. The risk factors for peptic ulcers were *H pylori* infection; chronic use non-steroid anti-inflammatory drugs; excessive alcohol consumption; and tobacco smoking.<sup>1-4</sup>

*A. cordifolia* or binahong is one of the Indonesian medicinal plants that are empirically used to treat ulcer. It contains flavonoids, alkaloids, terpenoids, oleanolic acid, saponins, proteins, and ascorbic acid. There is limited research on pharmacological activity of *A. cordifolia* as an anti-peptic ulcer.<sup>5-8</sup>

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**Table 1. Anti-Peptic Ulcer Liquid Formula**

Additional Materials	<i>A. cordifolia</i> extract 200 mg/kg body weight		
	Formula 1 (%)	Formula 2 (%)	Formula 3 (%)
USP Syrup	50	50	50
Sodium CMC	0.5	-	-
Sorbitol	20	20	-
Sodium benzoate	0.2	0.2	0.2
Apple essence	qs	qs	qs
Distilled water ad	100	100	100

Sodium CMC is one of the most common suspending agent used in liquid formulation. It is hygroscopic, relatively stable in a liquid solution with a pH of 2.0-10. Sorbitol is a preferable wetting agent due to its pleasant sweet taste and can act as stabilizer.<sup>9,10</sup> We conducted this study to evaluate the effect of different formulas on anti-peptic ulcer activity of *A. cordifolia* leaves extract in male Wistar rats.

## Methods

### Materials

The materials used in this study included *A. cordifolia* leaves which is obtained from Manoko, Lembang, Indonesia; distilled water, 95% and 80% ethanol, toluen, chloroform P, ammonia, Dragendorff reagent, Mayer reagent, hydrochloric acid, sodium hydroxide, magnesium powder, amyl alcohol, iron (III) chloride, gelatin, sodium stearate, Liebermann-Burchard, 10% formalin, USP standard syrup, carrageenan,

sodium benzoate, and apple essence.

### Tools

Tools used in this study included light microscope (Olympus BX51 ®), freeze dryer (Tecstar ®), oral syringes, paper pH indicator, mixer, and silica plate GF 254.

### Animal model

Animals used in this study were white male Wistar rats aged 2-3 months (150-250 g) Acclimatization was performed for one week before the experiment.

### Extraction and formulation of the suspension

*A. cordifolia* leaves were extracted using decoction method. The ratio between the leaves and water was 1:8. The leaves were boiled for 30 minutes. The extract was then filtered and dried using freeze dryer. The yield was calculated. Phytochemical screening was then conducted to determine secondary metabolites in the extract.

**Table 2. Ulcer Assessment**

Ulcer	Score
Normal gastric	1
Bleeding spots	2
The number of ulcers 1 – 3	3
The number of ulcers 4 – 6	4
The number of ulcers 7 – 9	5
The number of ulcers > 9 perforation	6

**Table 3. Damage in Mucosal Integrity**

Damage	Score
No pathological change	0
Eithelial desquamation	1
Erosion of epithelium surface	2
Ulcer in epithelium	3

Table 4. Evaluation of Formula

Evaluation	Formula	Organoleptic			pH	Viscosity	Specific gravity
		Color	Flavour	Aromatic			
Week 1	1	+++	+++	+++	7.6	52	1.093
	2	+++	+++	+++	7.82	14	1.079
	3	+++	+++	+++	7.53	8	1.046
Week 2	1	+++	+++	+++	7.59	52	1.093
	2	+++	+++	+++	7.79	14	1.079
	3	+++	+++	+++	6.64	8	1.045
Week 3	1	+++	+++	+++	7.59	52	1.093
	2	+++	+++	+++	7.79	14	1.079
	3	+++	++	++	6.44	8	1.044
Week 4	1	+++	+++	+++	7.59	52	1.093
	2	+++	+++	+++	7.79	14	1.078
	3	+++	++	+	6.44	7	1.022

Three formulas were used *i.e.*, i) a combination of sodium carboxymethylcellulose (CMC) and sorbitol; ii) only sorbitol; iii) extract only. The complete formula of the liquid preparation can be seen in the table 1. Formulas were then evaluated to examine organoleptic properties, pH, viscosity, and specific gravity.

#### Anti-peptic ulcer activity

The rats were divided into 6 groups, *i.e.*, positive control (sucralfate 35 mg/kg body weight); negative control (80% ethanol); normal control; and 3 formulas. Animal was fasting for 18 hours before the administration of

the treatment. One hours after the administration of the treatment, all groups except normal control were given 80% ethanol 15 ml/kg bw to induce peptic ulcer. After 4 hours, animals were sacrificed.<sup>11</sup> Anti-peptic ulcer activity was evaluated using direct observation on rats gastric mucosa, and histopathology assessment. Gastric pH, the number and severity of ulcers, the ratio of ulcer inhibition were measured. Gastric histopathology assessment was performed using hematoxylin staining with eosin. Mucosal damage was measured. Statistical analysis was conducted using analysis of variance (ANOVA).  $P < 0.05$  defined statistical significance.

Table 5. Number and Severity of Ulcers

Group	Average number of ulcers	Average severity of ulcers
Normal Control	0 ± 000	0 ± 000
Negative Control	5.75 ± 4.112	4.5 ± 2.380
Positive Control	0.25 ± 0.500	0.25 ± 0.500
Formula 1	0.5 ± 0.577b	0.5 ± 0.577b
Formula 2	0.25 ± 0.500b	0.25 ± 0.500b
Formula 3	3.5 ± 2.380a,c	3.5 ± 0.577a,c

Description: a = different with normal group, b = different with the positive control, c = different with the negative control

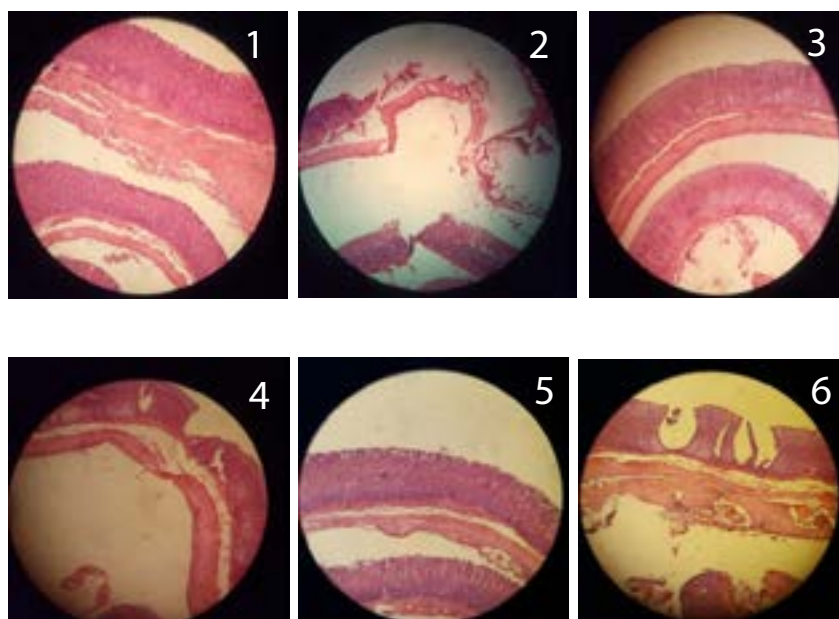
**Table 6. Peptic Ulcer Index and Inhibition Percentage**

Group	Peptic Ulcer Index	Inhibition Percentage (%)
Normal Control	0.00	100.00
Negative Control	2.05	0.00
Positive Control	0.06	96.95
Formula 1	0.15	92.68
Formula 2	0.06	96.95
Formula 3	1.40	31.71

### Results and Discussion

The extraction of 250 g of *A. cordifolia* leaves with 2l of distilled water resulted in 46 g of dried extracts (18.4%). Phytochemical screening showed that the extract and all suspensions contained alkaloid, phenol, tannin, quinones, flavonoids, monoterpene sesquiterpene, steroid, and triterpenoide.

Evaluation of characteristics of formula for 1 month is presented in the table 4. The addition of sodium carboxymethylcellulose and sorbitol affected the organoleptic properties, pH, viscosity, and specific gravity. Formula 1 and 2 showed good characteristics.



**Figure 1. Histopathology of Male Wistar Rats Gastric**

Description: 1 = Normal control  
2 = Negative control  
3 = Positive control  
4 = Formula 1  
5 = Formula 2  
6 = Formula 3

Anti-peptic ulcer activity test was conducted to evaluate which formula that showed strongest activity. The strongest ulcer inhibition was shown by formula 2, with 96.95% inhibition. It was followed by formula 1 with 92.68% inhibition, while formula 3 only inhibited 31.70% of the ulcers.

Gastric histopathology observation also showed that formula 2 exhibited better results. In the formula 2, the average gastric mucosal damage was 0.25, indicating no pathological change of the mucosa. Based on Barthel-Spoiled indicator, epithelial desquamation and surface erosion were observed in the ulcer. Addition of sodium carboxymethylcellulose and sorbitol could influence the anti-ulcer activity since it might affect the absorption rate and bioavailability of the active compounds.<sup>11-13</sup>

## Conclusion

*A. cordifolia* leaves extract with the addition of sorbitol showed the strongest anti-peptic ulcer activity.

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## Conflict of Interest

None declared.

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