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# Antiulcer Activity of Leaves and Whole Plant Decoctions of *Centella asiatica* (L.) Urb. (*Apiaceae*) in Rat

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**ABSTRACT**

*Centella asiatica* is a perennial herbaceous creeper of local and global health importance. Comparative studies of the leaves and whole plant decoctions have been carried out to investigate their anti-gastric ulcer property, based on their anti-secretory as well as their gastric-mucous-protecting capabilities. The results obtained with absolute ethanol aggression showed that the two decoctions protect the gastric mucosa. The area of hyperemia in the animals treated with both decoctions was inferior compared to the control animals. It was 139.20 ± 1.20 mm2 for the control group, versus 11.02 ± 0.057 and 10.86 ± 0.030 mm2 for the animals which received 200 mg/kg of leaves and whole plant decoctions respectively. After pylorus ligation, the pH of the gastric content of the control group animals is inferior to the treated groups. It was 3.20 ± 0.21 versus 6.30 ± 0.10 and 6.32 ± 0.10 for the animals treated with 200 mg/kg of the leaves and whole plant decoctions respectively. The results show that decoctions of the leaves and that of the whole plant of *C. asiatica* protect the gastric mucosa of the rats against the ulcerogenic effect of absolute ethanol and decreases gastric acidity after pylorus ligation.

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## INTRODUCTION

*Centella asiatica* (L.) Urb. is a perennial herbaceous creeper of the APIACEAE family (Figure 1). The plant has various common names including *Gotu kola***,** *Antanan, Pegaga,* and *Asiatic Pennywort* from its place of origin in Asia and '*Talapetraka*' from Madagascar.

**Figure 1: *Centella asiatica* (L.) Urb. '*Talapetraka*'**

*C. asiatica* is used in traditional medicine for wound healing as in scars and leprosy, and this has been confirmed by scientific reports [1, 2, 3, 4]. The plant is also reported to improve mental activity [5 ] and treats many diseases, including stomach ulcer [3,4] rheumatism [6,7], fever, syphilis [8], arterial hypertension (high blood pressure) [9] depression and general anxiety disorder [10,11].

*C. asiatica* is effective in improving treatment of small wounds, hypertrophic wounds as well as burns, psoriasis, and scleroderma. The mechanism of action involves promoting fibroblast proliferation and increasing the synthesis of collagen and intracellular fibronectin content. It also improves the tensile strength of newly formed skin as well as inhibiting the inflammatory phase of hypertrophic scars and keloids due to the presence of heterosides Madecassoside and Terminoloside [12, 13, 14]. Asiaticoside is responsible for the healing property of the plant and the presence of alkaloids, saponins, tannins [15, 16] have been also reported. Finally, another infection, the stomach ulcer that has common ties to wounds and inflammations is treated with *C. asiatica* [3, 4].

Gastric ulcer is a disease that affects almost 10% of the population, with an overall incidence of 3 new cases per 100 000 inhabitants [17]. This disease is due to an imbalance between aggressor factors (hydrochloric acid, pepsin) and protective factors (bicarbonate, mucus) [18].

The treatment of gastric ulcer, generally, is based on the use of antacids which neutralize the hydrochloric acid secreted by the parietal cells; mucosal protectors that prevent aggressive factors from attacking the gastric mucosa; modulators of acid secretion, or anti-infection that will eradicate *Helicobacter pylori* [19].

In Madagascar, many plants are used empirically in traditional medicine as antiulcer but very few have been the subject of pharmacological studies with the exception of *Stenochlaena tenuifolia* (BLECHNACEAE) (*felipomby*), *Clidemia hirta* (MELASTOMATACEAE) (*mazambody*), *Urophyllum lyallii (*RUBIACEAE*)* (*tamirova*), Avicennia *marina* (AVICENNIACEAE) (*afiafy*) [20] and *Harungana madagascariensis* (GUTTIFEREAE) (*harongana*) [21].

Laboratory studies were carried out to investigate the capabilities of the leaves and whole plant decoctions of *C. asiatica* to protect the gastric mucosa or to reduce gastric acid secretion.

## MATERIALS AND METHODS

Leaves and whole plant decoctions of *C. asiatica* and experimentally induced ulcer rats were used in the study.

### 1. Preparation of the decoction

The decoctions used were decoctions prepared with 250 g of fresh leaves or 250 g of fresh whole plants in 1 l of water. The mixture was boiled at 100°C temperature to reduce the volume to half.

### 2. Animal used

Seven weeks-old male Wistar rats weighing 200 – 225 g were used. They were bred in the animal house of the *Laboratoire de Pharmacologie Générale, de Pharmacocinétique et de Cosmétologie* (LPGPC), *Faculté des Sciences, Université d'Antananarivo*, Madagascar. They

were kept in cages under standard laboratory conditions of 22 ± 2°C temperature and kept under 12/12 h light/dark cycle.

Animals were fasted 24 h prior to manipulation with free access to water. They were divided into 4 groups of 5 rats per group. The first group served as the control while the other 3 were then treated with the different decoctions.

All the experiments were accepted by the Committee of Animal Ethics at the Sciences Faculty of the University of Antananarivo, Madagascar.

**3. Biological tests**

**a- Activity of the decoctions on gastric hyperhemia**

An anti-ulcer decoction may be able to protect the gastric mucosa against aggressive agents [22].

To investigate the protective effect of the decoctions, the first group of animals served as control and received 10 ml/kg of distilled water, 3 groups received respectively 50, 100 and 200 mg/kg of the leaves decoction, and 3 other groups received respectively 50, 100 and 200 mg/kg of the whole plant decoction by oral route in a volume of 10 ml/kg [23].

Thirty minutes later, 0.5 ml/100 g of absolute ethanol was administered by oral route to the 7 groups of animals, to induce ulcer [23, 24, 25]. After 1h following the ethanol administration, the stomach of the animals was isolated, opened and rinsed with distilled water. The stomach was spread on a flat surface to measure the area of hyperhemia caused by the alcohol ingestion. Hyperhemia was measured by direct planimetry using transparent millimetric paper [26, 27].

**b- Activity of the decoctions on gastric acid secretion**

One of the causes of gastric ulcer is the high secretion of hydrochloric acid [28]. The activity on the gastric acid secretion of the two decoctions was studied in rats fasted 24 h prior to the test. The control group received distilled water while the 3 treated groups received leaves decoction at doses 50, 100, 200 mg/kg respectively, and the other 3 groups received whole plant decoction at doses 50, 100, 200 mg/kg respectively by oral route in a volume of 10 ml/kg [24].

Thirty minutes later, the rats were anesthetized by inhalation of diethyl ether. A 0.5 cm incision was made at the upper part of their abdomen, the pylori were identified and ligatured and afterward, the incision was sutured [28]. The animals were deprived of food and water during the post-operatory period. Four hours later, the animals were sacrificed and their stomachs isolated. The contents of the stomachs were collected, centrifuged at 3000 rpm for 10 min, and the pH of the supernatant was measured [27].

**4. Statistical analysis**

The results were expressed as mean ± s.e.m. Student's 't' test was used to assess the data, a value of $p<0.05$ was considered as significant.

**RESULTS**

After boiling the leaves or the whole plant, 1 ml of the decoction corresponds to 500 mg of leaves or 500 mg of the whole plant, which gives a concentration of 0.5 g/ ml. Our results show that both the leaves and whole plant decoctions prevent ethanol-induced hyperhemia and increase the pH of the gastric content.

**a- Activity of the decoctions on gastric hyperhemia**

One hour after administering alcohol, the gastric mucosa of the animals presents hyperhemia. Its area in the control group is greater than those of the treated groups. In the control, the hyperhemia area is 139.20 ± 1.20 mm2 versus 11.02 ± 0.6 and 10.86 ± 0.30 mm2 in the groups treated with 200 mg/kg of leaves and whole plant decoctions respectively ($p<0.05$). The difference is significant between the control and the treated groups, but not significant between the two groups treated with leaves and whole plant decoction ($p>0.05$) (Table 1).

**Table 1. Hyperhemia area induced by absolute ethanol in control and treated groups treated with the decoction of leaves and whole plant of *Centella asiatica*, orally administered ($\bar{m}$ ± s.e.m; n = 6; p<0.05).**

| | Gastric hyperhemia (mm2) | | | p |
|---|---|---|---|---|
| Animals | Control group | Treated with decoction | | |
| Dosage (mg/kg) | | Leaves | Whole plant | |
| 0 (Distilled water) | 139.20 ± 1.20 | - | - | |
| 50 | - | 96.33 ± 3.83 | 95.00 ± 1.20 | N.S |
| 100 | - | 25.66 ± 1.20 | 25.00 ± 0.32 | N.S |
| 200 | - | 11.02 ± 0.60 | 10.86 ± 0.30 | N.S |

**b- Activity of the decoctions on gastric acid secretion**

Four hours after pylori ligation, the pH of the gastric fluid increases in the treated groups. In the control animals, the pH is equal to 3.20 ± 0.21 versus 6.30 ± 0.10 and 6.32 ± 0.10 for the animals treated with 200 mg/kg of leaves and whole plant decoctions respectively (p<0.05).

There is a significant difference between the control and the treated groups but no significant differences between the two groups treated with leaves and whole plant decoction (p>0.05) (Table 2).

**Table 2. pH of gastric fluid after pylorus ligation in control and groups treated with the decoction of leaves and whole plant of *Centella asiatica* administered orally ($\bar{m}$ ± s.e.m; n = 6 ; p<0.05).**

| | pH | | | p |
|---|---|---|---|---|
| Animals | Control group | Treated with decoction | | |
| Dosage (mg/kg) | | Leaves | Whole plant | |
| 0 (Distilled water) | 3.20 ± 0.21 | - | - | |
| 50 | - | 3.90 ± 0.07 | 4.00 ± 0.12 | N.S |
| 100 | - | 4.60 ± 0.23 | 4.70 ± 0.15 | N.S |
| 200 | - | 6.30 ± 0.10 | 6.32 ± 0.10 | N.S |

## DISCUSSION

The activity of leaves decoction as well as a decoction of the whole plant of *C. asiatica* was studied on the experimental ulcer, in rats. Our results show that the two decoctions protect the gastric mucosa after alcohol ingestion and reduce acid secretion after pylorus ligation.

Gastric ulcer was experimentally induced in the rat by the administration of absolute ethanol orally. Ethanol is resorbed in the stomach wall [29] and provokes an acute inflammation characterized by vessel congestion or hyperhemia in the gastric wall due to histamine effect [30-35].

Absolute ethanol precipitates mucosa proteins and thus exposes the gastric mucosa to the proteolytic action of pepsin and hydrochloric acid which cause the destruction of underlying structure [24].

Oral administration of the decoction of leaves and that of the whole plant of *C. asiatica* decreases ethanol-induced hyperhemia. This plant contains heterosides (madecassoside, asiaticoside and terminoloside), which have anti-inflammatory and wound healing properties [13, 34]. The reduction of the hyperemia induced by ethanol in the animals treated with the two decoctions shows that they have increased the protection of the gastric mucosa against the ethanol aggression, by mucous secretion [22, 24].

Pylorus ligation increases acid secretion by stimulating the parasympathetic system and releasing acetylcholine which induces the secretion and accumulation of hydrochloric acid in the stomach [28]. The acid produced in excess erodes the stomach wall, causing the destruction of gastric mucosa. The disappearance of this protective layer allows hydrochloric acid and pepsin to attack the muscular layer of the gastric epithelium resulting in ulcer formation.

Our results also show that the two decoctions increase the pH of gastric fluid. This may be due to the reduction of acid secretion by inhibiting the pump ($H^+/K^+$) ATPase [36] or the neutralization of gastric acidity by increasing the secretion of bicarbonate by the epithelial cells. Prostaglandin E2 and I2 are predominantly synthesized by gastric mucosa and are known to stimulate the secretion of mucous and bicarbonate [19]. The observed increase of gastric mucosal protection against the erosive action of ethanol and the diminution of acidity provoked by the pylorus ligation may be due to the action of the decoctions on the

biosynthesis of prostaglandins. These results suggest an effect of the decoction via prostaglandin synthesis which increases bicarbonate and mucous secretion.

No significant differences were noted with regards to the effects of the decoctions of the leaves and that of the whole plant in reducing acid secretion and protecting the mucosa against alcohol-aggression.

## IV- CONCLUSION

Both the leaves and the whole plant decoctions of *C. asiatica* are effective against gastric ulcer. There are no significant differences between the effects of the two decoctions. This activity may be due to madecassoside, asiaticoside or terminoloside present in the decoctions, which could increase the prostaglandins secretion. Further investigations will show the molecule(s) responsible for this activity, and elucidate its mechanism of action.

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## REFERENCES

1. Grimes Ch. Le traitement de la lèpre par l'Hydrocotyle asiatica. Bull Soc Path Exo XXXII. 1939; **6**: 692-02.
2. Hausen B.M. *Centella asiatica* (Indian pennywort), an effective therapeutic but a weak sensitizer. Contact Dermatitis. 1993*;* **29**:175–79.
3. Cheng C.L.' Koo M.W. Effects of *Centella asiatica* on ethanol induced gastric mucosal lesions in rats. Life Sci. 2000; **67**: 2647–53.
4. Quansah N., Randrianavony P. Natures' Gift to Humanity: Natural Remedies for selected common health problems. Author House, Bloomington, IN., USA. 2012.
5. Jana U., Sur T.K., Maity L.N., Debnath P.K., Bhattacharyya D. A clinical study on the management of generalized anxiety disorder with *Centella asiatica*. J Nepal Med Coll. 2010; **12** (1):8-11.
6. Newall C.A., Anderson L.A., Phillipson J.D. Hydrocotyle. Herbal Medicines. A Guide for Health Care Professionals. London: The Pharmaceutical Press. 1996; 170-72.
7. Liu M., Dai Y., Yao X., Li Y., Luo Y., Xia Y. Anti-rheumatoid arthritic effect of madecassoside on type II collagen-induced arthritis in mice. Int Immunopharmacol. 2008; **8**:1561–66.
8. Kashmira J.G., Jagruti A.P., Anuradha K.G. Pharmacological Review on *Centella asiatica*: A Potential Herbal Cure-all. Ind J Pharmac Sci. 2010; **72** (5): 546-56.
9. Singh P., Singh J.S. Recruitment and competitive interaction between ramets and seedlings in a perennial medicinal herb, *Centella asiatica*. Basic Appl Ecol.2002; **3**: 65-76.
10. Cauffield J. S., Forbes, H.J. Dietary supplements used in the treatment of depression, anxiety, and sleep disorders. Lippincotts Prim Care Pract. 1999; **3**: 290–04.

11. Chen Y., Han T., Qin L., Rui Y., Zheng H. Effect of total triterpenes from *Centella asiatica* on the depression behavior and concentration of amino acid in forced swimming mice. Zhong Yao Cai. 2003; **26**:870–73.
12. Wieslawa B., Paulina Z.A., Elzbieta S.S., Malgorzata B. *Centella asiatica* in cosmetology. Adv Dermatol Allergol. 2013; **30** (1): 46–49.
13. Allegra C. Comparative Capillaroscopic study of certain bioflavonoids and total triterpenic fractions of *Centella asiatica* in venous insufficiency. Clin Ther. 1981; **99**: 507–13.
14. Kartnig T. Clinical applications of *Centella asiatica*. J Herbs Spices Med Plants. 1998; **3**: 146-73.
15. Haftek M., Mac-Mary S., Le Bitoux M.A. Clinical, biometric and structural evaluation of the long-term effects of a topical treatment with ascorbic acid and madecassoside in photoaged human skin. Exp Dermatol. 2000; **17**:946–52.
16. Nikitakis J., Breslawec H.P. International Cosmetic Ingredient Dictionary and Handbook. Ed. 14 (Washington). 2014.
17. Thorsen K., Soreide J. A., Kvaloy J. T., Glomsakert, Soreide K. Epidemiology of perforated peptic ulcer: Age and gender-adjusted analysis of incidence and mortality. World J Gastroenterol. 2013; **19:** *347 - 54.*
18. Divakar M.C., Lakshmi D.S. Anti-ulcer activity of *Wrightia tinctoria* ( Roxb.) R.Br. Der Pharmacia Sinica. 2011; **2**(2):355-60.
19. Sherwood L. Physiologie humaine. *2ème Ed. De Boeck*, Paris. 2010.
20. Rabeson N., Randrianarivo E., Ralaiarimanana N., Rakotoarison O., Randriantsoa A. Etude des effets d'extraits de *Clidemia hirta* (Melastomaceae) et *Stenochlaena tenuifolia* (Blechnaceae), sur l'ulcère expérimental chez la souris. Ethnopharmacologia. 2005 ; **36:**61-67
21. Randrianavony P., Ratsimiala Ramonta I., Andriamalala S.G., Andriamampianina T, Quansah N., Randimbivololona F. *Harungana madagascariensis* (Clusiaceae) et ulcère gastrique. Ethnopharmacol**.** 2016; **56** : 62-66.
22. Nabavizadeh F., Alizadeh M.A., Adeli S., Golestan M., Moloudian H., Kamalinejad M. Gastroprotective effects of *Stachys lavandufolia* decoction on experimental gastro ulcer. Afr J Pharm. 2011; **5** (2): 155-59.
23. Diehl K-H., Hull R., Morton D., Pfister R., Rabemampianina Y. et al. A good practice to the administration of substances and removal of blood, including routes and volumes. J Appl Toxicol. 2001; **21**:15-23.
24. Oates P.J., Hakkinen J.P. Studies on the mechanism of ethanol-induced gastric damage in rats. Gastroenterol. 1988; **94** (1):10–21,
25. Kinger K.H., Gupta K.M. Evaluation of anti-ulcer activity of *Polygonum barbatum* line (whole plant). J Biomed Pharm Res. 2012; **1**(2):34-37.
26. Manjusha K., Vipin K., Surender S. Gastroprotective activity of Methanol leaves decoction of *Barleria prionotis* Linn on ethanol and indomethacin-induced ulcer in rats. Br J Pharm Res. 2013; **3** (4): 817-29.
27. Kumar M.S., Aparna P., Poojitha K., Karishma S.K., Astalakshm N. A comparative study of *Michelia champana Linn.* Flower and leaves for anti-ulcer activity. Int J Pharm Res. 2011; **2**(6):1554-58
28. Shay H., Komarov S.A., S.E. Fels, D. Meraze, M. Gruenstein, H. Siplet. A simple method for the uniform production of gastric ulceration in the rat. Gastroenterol. 1945;**5**: 43-61.
29. Lands W.E.M. A review of alcohol clairance in human. ALCOHOL. 1998; **15**: 147-60.
30. Mozafar K., Hossen S. Protective effect of *Falcaria vulgaris* decoction on ethanol induced gastric ulcer in rat. Ir J Pharmacol Ther. 2006; **5**: 43-46.
31. Jyoti G., Dinesh K., Ankit G. Evaluation of gastric anti-ulcer activity of methanolic decoction of *Cayrati trifolia* in experimental animals. Asian Pac J Trop Dis. 2012; **2**: 99-02.
32. Dale H.H., Laidlaw P.P. The physiological action of β-iminazolylethylamine. J Physiol. 1910 ; **41**: 318-44.
33. Fauve R.M., Hevin M. Réaction inflammatoire et réactions immunitaires. Inflammation Russo-Marie, Ed. John Libbey Eurotext (Paris). 1998.
34. Gohil K.J., Patel J.A., Gajja A.K. Pharmacological Review on *Centella asiatica*: A Potential Herbal Cure-all. Indian J Pharm Sci. 2010; **72** (5): 546-56.
36. Ishii Y. Critical studies of the pylorus ligated rats (Shay rat). Jpn J Pharmacol. 1969; **19**: 125-37.