Journal of Research in Pharmacy

Research Article

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Evaluation of Anti-Inflammatory and Gastroprotective Activity of Aqueous Peel Extract of *Allium Cepa*

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Received: 6 January 2022 / Revised: 19 April 2022 / Accepted: 19 April 2022

ABSTRACT: *Allium cepa* bulbs (onions) are widely consumed as food, spice and for medicinal purposes. The peels of *Allium cepa* (*A. cepa*) are often discarded as waste but have been reported in literature to contain beneficial phytoconstituents with pharmacologic activity. This study was designed to evaluate the anti-inflammatory and mucosal protective activity of aqueous extract of *Allium cepa* peels. The anti-inflammatory activity was investigated using carrageenan-induced paw edema. Rats were treated orally with extract (200-400 mg/kg) and acetylsalicylic acid (100 mg/kg) as positive control. Thirty minutes after, carrageenan (0.1 ml of 1% w/v) was injected on the sub plantar surface of the right hind paw and edema measured with a digital vernier caliper. The mucosal protective activity was determined with acetylsalicylic acid-induced mucosa damage. The rats were pretreated orally with omeprazole (20 mg/kg) and *A. cepa* peel extract (200 – 400 mg/kg) before the administration of acetyl salicylic acid (300 mg/kg). The stomach of the rats was removed after three hours then examined macroscopically for bands of inflammation, color and hemorrhagic streaks. *A. cepa* peel extract (200 and 400 mg/kg) produced a significant ($p<0.01$) reduction in carrageenan-induced paw edema. The percentage inhibition of inflammation by extract (200 and 400 mg/kg) at 150 minutes post-treatment with carrageenan was 83.39 % and 82.76 % respectively, while acetylsalicylic acid (100 mg/kg) produced an inhibition of 72.41 %. The aqueous peel extract also caused significant ($p<0.001$) inhibition of gastric inflammation induced by acetylsalicylic acid. The percentage inhibition by *A. cepa* extract (200 and 400 mg/kg) was 86.04 % and 92.79 % respectively, while omeprazole (20 mg/kg) produced an inhibition of 77.48 %. The results obtained from this study show the aqueous peel extract of *Allium cepa* has potential anti-inflammatory and gastric mucosa protective activity.

KEYWORDS: *Allium cepa*; Peel; Anti-inflammatory; Gastroprotective; Acetylsalicylic acid

1. INTRODUCTION

Onion (*Allium cepa* L.) of genus *Allium*, Family *Amaryllidaceae*, Subfamily *Allioideae* is used in Nigeria as a spice for food and medicinal purposes. In traditional medicine it is used in the treatment of cardiovascular diseases, diabetes, bronchitis, asthma, stomach ulcer, cancer amongst others [1, 2]. Pharmacological activities of *Allium cepa* bulb includes; hypoglycemic, hypotensive, hepatoprotective, anti-asthmatic, anti-cancer activity [3, 4]. *Allium cepa* bulbs contain phytochemicals such as; flavonoids, phytosterols anthocyanins, phenolic and organo-sulfur compounds [5, 6]. Pharmacological activity of *Allium cepa* bulb has been attributed to the presence of these phytochemicals [7].

The peels of *Allium cepa* which are often discarded as waste products are used as tea in homes and hot aqueous decoction by traditional medicine practitioners in Nigeria for the management of respiratory, cardiovascular and gastrointestinal disorders. The pharmacological activities of onion peel extract have been attributed to the presence of bioactive compounds such as phenolics and flavonoids [8, 9]. The peels of *Allium cepa* have been reported to contain significantly higher concentration of flavonoid when compared with the onion bulb [10]. Quercetin diglucoside, quercetin 4-glucoside, quercetin aglycone are flavonoids present in the onion peel [11]. Quercetin reduces inflammation via modulation of NF-kB pathway with resultant inhibition of cytokines and inducible nitric oxide synthase in vivo [12].

The phytochemical constituent of onion bulb and peels may vary based on time of harvest, geographical region, storage condition and duration of storage after harvest [13]. In addition, varying

How to cite this article: Ayanniyi R, Olumoh-Abdul H, Ojuade F, Akintola J. Evaluatıon of antı-ınflammatory and gastroprotectıve actıvıty of aqueous peel extract of *Allıum cepa*J Res Pharm. 2022; 26(4): 734-741.

http://dx.doi.org/10.29228/jrp.171

ISSN: 2630-6344

concentrations of flavonoids has been reported to be present in the different varieties (red, yellow, white) of onion bulbs and peels [2].

Gastrointestinal disorder such as inflammation of gastric mucosa and ulcer affects about 5-10 % of the population [14]. This may result from over production of gastric acid, *Helicobacter pylori* infection, and use of non-steroidal anti-inflammatory drugs (NSAIDs). Acetylsalicylic acid is known to produce irritation, inflammation of the gastric epithelium [15].

Traditional medicine practitioners use the decoction from the red peels of *Allium cepa* in treatment of gastrointestinal disorders. There are limited scientific reports on the anti-inflammatory and gastro-protective activity of the red peel extract of *Allium cepa*. In previous studies, only the anti-inflammatory activity of peel extract of *Allium cepa* was evaluated with no study on the gastro-protective activity.

This study aims to evaluate the anti-inflammatory as well as protective activity of the aqueous peel extract of *Allium cepa* on acetylsalicylic acid-induced gastric inflammation.

2. RESULTS

2.1 Anti-inflammatory activity of aqueous peel extract of *Allium cepa*

Pre-treatment of rats with aqueous peel extract of *Allium cepa* produced significant reduction in carrageenan-induced paw edema which was time-dependent. Reduction in paw edema was observed between 30-210 minutes after administration of carrageenan (Table 1).

Table 1. Effect of aqueous extract of *Allium cepa* peels on paw edema induced by carrageenan

Time (Minutes)	Paw edema (mm)			
	Control	Acetylsalicylic acid (100 mg/kg)	*A. cepa* extract (200 mg/kg)	*A. cepa* extract (400 mg/kg)
30	0.526 ± 0.109	0.448 ± 0.099	0.380 ± 0.083	0.356 ± 0.079
60	0.782 ± 0.125	0.600 ± 0.123	0.416 ± 0.089	0.466 ± 0.106
90	1.056 ± 0.096	0.716 ± 0.126*	0.474 ± 0.09***	0.506 ± 0.084**
120	1.430 ± 0.249	0.632 ± 0.130**	0.350 ±0.079**	0.350 ± 0.079**
150	1.276 ± 0.320	0.352 ± 0.076**	0.212 ± 0.049**	0.220 ± 0.069**
180	1.340 ± 0.412	0.510 ± 0.116	0.450 ± 0.154	0.436 ± 0.158
210	1.084 ± 0.228	0.576 ± 0.073	0.418 ± 0.089*	0.492 ± 0.142*

Mean ± SEM, * p<0.05, **p<0.01, ***p< 0.001 vs control, n=5

Maximal reduction in paw edema occurred after 150 minutes. The percentage inhibition of inflammation produced by 200 and 400 mg/kg at 30, 60, 90, 120, and 150 minutes post-treatment with carrageenan was (27.75 % and 32.32 %); (46.80 % and 40.41 %); (55.11 % and 52.08 %); (75.52 % and 75.52 %); (83.39 % and 82.76 %) respectively (Figure 1).

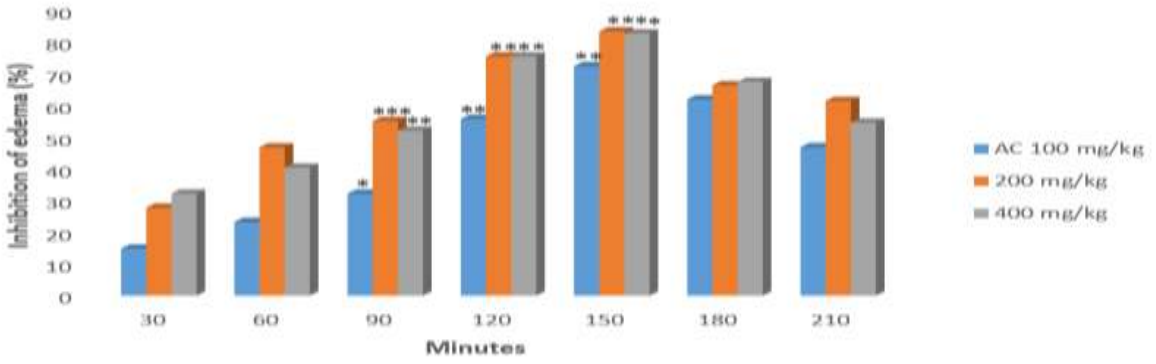

Figure 1. Inhibitory activity of Acetylsalicylic acid 100 mg/kg (AC), *Allium cepa* extract 200 mg/kg, 400 mg/kg on carrageenan-induced paw edema. Mean ± SEM, * p<0.05, **p<0.01, ***p< 0.001 vs control, n=5

2.2 Mucosal protective activity of aqueous peel extract of *Allium cepa*

Acetylsalicylic acid (300 mg/kg) produced inflammation and redness of gastric mucosa. Pretreatment of rats with aqueous extract of *Allium cepa* peels (200 and 400 mg/kg) caused an inhibition of 86.04 %, and 92.7 % respectively in inflammation and redness of gastric mucosa (Table 2).

Table 2. Inhibitory effect of aqueous extract of *A. cepa* peels on acetylsalicylic acid-induced mucosal injury

Treatment	Mean Inflammation Index	% Inhibition
Normal saline	44.40 ± 3.58	00.00
Omeprazole (20 mg/kg)	10.00 ± 2.35***	77.48
A. Cepa extract (200 mg/kg)	6.20 ± 2.27***	86.04
A. Cepa extract (400 mg/kg)	3.20 ± 2.06***	92.79

Mean ± SEM, ***p< 0.001, n=5

The mucosa of rats in control group showed no bands of inflammation, hemorrhagic streaks and redness on macroscopic examination (Figure 2a). Mucosa of rats treated with acetylsalicylic acid showed bands of inflammation, hemorrhagic streaks and redness (Figure 2b). Examination of the mucosa of rats pre-treated with extract of *Allium cepa* (200 and 400 mg/kg) and then administered acetylsalicylic acid (300 mg/kg) revealed a reduction in inflammation, hemorrhagic streak and redness (Figures 2c and d). Omeprazole (20 mg/kg) also produced a decrease in inflammation, hemorrhagic streak and redness (Figure 2e).

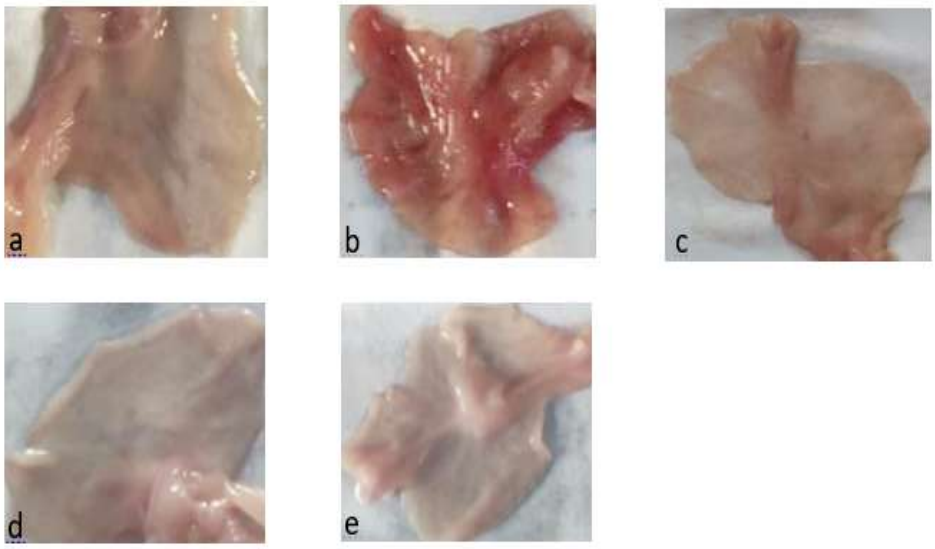

Figure 2. Stomach of rats pre-treated with extract against acetylsalicylic acid-induced mucosal inflammation. 40x magnification. a) Control; b) Acetylsalicylic acid 300 mg/kg; c) Omeprazole 20 mg/kg; d) *Allium cepa* 200 mg/kg; e) *Allium cepa* 400 mg/kg

3. DISCUSSION

In this study, anti-inflammatory and mucosal protective activities of aqueous peel extract of red *Allium cepa* were investigated. The extract produced a significant reduction in carrageenan-induced inflammation of rat's right hind paw. The percentage inhibition of inflammation produced by 200 and 400 mg/kg at 150 minutes post-treatment with carrageenan was 82.47 % and 82.76 % respectively. The inflammatory response produced after injection of carrageenan occurs in two phases. In the first phase, there is the release of vasoactive substances such as; prostaglandins, bradykinins, serotonin and histamine. In the second phase there is production of metabolites of arachidonic acid and infiltration of neutrophils [16].

Anti-inflammatory effect of the leaf extract of *Allium cepa* observed in the present study may be attributed to inhibition of arachidonic acid metabolism to prostaglandins and leukotrienes [17]. In addition, anti-inflammatory effect of onion peels and bulbs have been attributed to its membrane stabilizing activity which was found to be higher in the peels compared with the bulbs [8, 18]. The significant anti-inflammatory activity exhibited by the peel extract is beneficial and may be responsible for some of its biological activity in acute and chronic inflammatory conditions.

The gastroprotective activity of the aqueous peel extract of *Allium cepa* was also evaluated as most orthodox anti-inflammatory drugs induce gastric mucosa inflammation and ulceration [19]. Gastric mucosa inflammation was induced acutely with high dose acetylsalicylic acid (300 mg/kg). The gastric mucosa of the untreated control group revealed bands of inflammation, hemorrhagic streaks and redness on macroscopic examination. Conversely, pre-treatment of rats with peel extract of *Allium cepa* caused a significant reduction in inflammation index (inflammation, hemorrhagic streaks and redness) in acetylsalicylic acid-induced mucosal injury. On macroscopic examination the degree of inflammation observed on gastric mucosa of rats treated with extract (200 and 400 mg/kg) was less compared with rats in control group. In addition, the degree of inflammation for 400 mg/kg group was less than the rats in 200 mg/kg group.

The percentage inhibition of gastric inflammation produced by (200 and 400 mg/kg) of extract was 86.04 % and 92.79 % respectively. This was similar to 77.48 % inhibition observed with omeprazole (20 mg/kg). Acetylsalicylic acid produces gastric mucosa inflammation and injury by inhibiting the synthesis of prostaglandins. Prostaglandins protect the gastric mucosa by inhibiting both gastric acid secretion and release of mediators of inflammation [20]. Gastroprotective effect of the peel extract of *Allium cepa* thus may be mediated through the production of prostaglandin and inhibition of mediators of inflammation [21, 22].

Polyphenolic compounds such as flavonoids and phenolic acids present in the peel extract of *Allium cepa* have been reported to suppress inflammation and may be responsible for the anti-inflammatory and

gastroprotective activity of onion peel extract [23, 24]. This study has revealed the dual therapeutic benefits of red onion peel extract by exhibiting both anti-inflammatory as well as gastroprotective activities.

4. CONCLUSION

Allium cepa peel extract produced a significant reduction in carrageenan-induced paw edema. In addition, the peel extract also caused significant inhibition of gastric inflammation induced by acetylsalicylic acid. These findings show that peel extract of *Allium cepa* has potential anti-inflammatory and mucosal protective activities which provides support for the ethno-medicinal use of onion peel extract. Further research needs to be carried out to isolate, characterize and standardize the bioactive constituents.

5. MATERIALS AND METHODS

5.1 Plant material

The red peels of *Allium cepa* were obtained from the Mandate market in Ilorin, Kwara State, Nigeria. Debris and soil were removed by rinsing with water. The peels were dried under a shade and reduced to power before extraction.

5.2 Drugs and Chemicals

Acetylsalicylic acid, omeprazole, ketamine, xylazine, methanol (Loba Chemie Pvt Ltd)

5.3 Experimental animals

Male albino rats (100-120 g±10 g) were used for this study. The animals were acclimatized in animal house of the Department of Pharmacology and Toxicology, University of Ilorin, Ilorin, Kwara State, Nigeria. Animals were cared for according to United States National Institute of Health Guidelines for the Care and Use of Laboratory Animals (NIH publication No 85-23) and allowed free access to animal feed and water (*ad-libitum*).

Ethics clearance was obtained from the University of Ilorin Ethics Review Committee with approval number (UERC/ASN/2019/1861). Experiments were carried out according to the guidelines of University of Ilorin Ethics committee on Research, and also the International Animal Care and Use Committee (IACUC) in Nigeria.

5.4 Extraction of *Allium cepa* peels

The onion peels were macerated (ratio 100 g of the peels to 1 liter of distilled water) for 24 hours and the aqueous extract was decanted, filtered using Whatman filter paper 125 mm (No 1). The filtrate was evaporated to dryness on a water bath at 45 °C, and then stored at -4 °C for later use. The percentage yield was calculated as follows;

$$\text{Percentage yield} = \frac{weight\ of\ dried\ extract}{weight\ of\ powdered\ onion\ peels} \times 100\%$$

5.5 Determination of anti-inflammatory activity of aqueous extract of *Allium cepa* peels

Anti-inflammatory activity of *Allium cepa* peels extract was carried out using carrageenan-induced paw edema. The method of Winter *et al*., 1962 was used with slight modifications [25]. Twenty male albino rats were divided into four groups of five animals each and the animals were treated as follows:

- Group I: negative control was treated with distilled water.
- Group II: standard drug (acetylsalicylic acid, 150 mg/kg orally).
- Group III-IV: 200 and 400 mg/kg orally of aqueous extract of *Allium cepa* peels.

Thirty minutes after these treatments, the rats in all groups were injected 0.1ml carrageenan (1 % w/v) in 0.9 % saline on the sub plantar surface of the right hind paw. Paw edema was measured using a digital vernier caliper before administration of carrageenan and at thirty-minute intervals for a period of 3 hours. The anti-inflammatory activity was calculated as the difference in the paw edema sizes at various time intervals.

$$\frac{\text{(Vt-Vo) control} - \text{(Vt-Vo) treated}}{\text{(Vt-Vo) control}}$$

Where, Vt control= paw edema of control at a particular reading time

Vo control= paw edema of control at 0 minute
Vt treated= paw edema of treated at a particular reading time
Vo= paw edema of treated at 0 minute

Percent inhibition of paw edema at different time interval was calculated as follows:

$$\%\ inhibition\ of inflammation\ = \frac{control - treated}{control} \text{ x } 100$$

5.6 Determination of mucosal protective activity of aqueous extract of *Allium cepa*

Acetylsalicylic acid-induced mucosal inflammation was carried out using the method of Trabadela et al., 2008 with modifications [26]. Twenty-five male albino rats divided into five groups of five animals each. All animals were fasted for 18 hours but allowed to have free access to water. Acetylsalicylic acid (300 mg/kg) was administered to rats in groups II-V and after 3 hours the animal was treated as follows;

- Group I: negative control (distilled water, 1 ml/kg orally)
- Group II: normal control (distilled water, 1 ml/kg orally)
- Group III: standard drug (omeprazole, 20 mg/kg orally)
- Group IV-V: (200 and 400 mg/kg, PO) of aqueous peels extract.

After three hours, animals were euthanized using intraperitoneal injection of ketamine (60 mg/kg) and xylazine (7.5 mg/kg). The stomach was excised following standard experimental procedure [27].

5.6.1 Inflammation scoring method

The level of damage to the stomach was assessed by dissecting along its greater curvature and placed on a board. Macroscopic examination was carried out with aid of a hand lens checking the bands of inflammation, color and hemorrhagic streaks. The method of Praveen and Paradhasaradhi, 2013 was used to score and determine degree of gastric damage [29].
Normal colored stomach = 0, Red coloration = 1, Hemorrhagic streak = 2, Bands of inflammation = 3. Given by;

$$Inflammation\ index\ (II)\ = \frac{Total\ inflammation\ score}{No.\ of\ animals\ with\ inflammed\ mucosa}$$

$$\%\ inhibition\ of inflammation\ = \frac{II\ control - II\ test}{II\ control} \text{ x } 100$$

5.7 Statistical analysis

Data was expressed as mean ± S.E.M. and analyzed using GraphPad Prism 7.0 (GraphPad Software, Inc., San Diego, CA). Statistical analysis comparing the control and treatment groups was carried out using one-way ANOVA. Statistical significance was taken at $p<0.05$.

Acknowledgements: The authors acknowledge Mr. Abdulrahman Shittu of Department of Pharmacology and Toxicology, Faculty of Pharmaceutical Sciences, University of Ilorin, Ilorin, for his technical support during the course of this work.
Author contributions: Concept – R.A., H.O-A.; Design – R.A., H. O-A.; Supervision – R.A., F.O., H. O-A.; Resources – R.A., J.A.; Materials – J.A., F.O.; Data Collection and/or Processing – J.A., F.O.; Analysis and/or Interpretation – R.A., J.A., F.O.; Literature Search – R.A., J.A.; Writing R.A., J.A.; Critical Reviews – R.A., J.A., H.O-A., F.O.

Conflict of interest statement: "The authors declared no conflict of interest" in the manuscript.

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