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Full Length Research Article

Antiulcerogenic Effect of Aqueous Seed and Rind Extracts of *Citrullus lanatus* (Water Melon) in Ethanol-Induced Gastric Ulcer Albino Rats

***S. Rabiu and S.A. Muhammad**
Department of Biochemistry, Usmanu Danfodiyo University, Sokoto
[*Corresponding author: Email: abufukaiha@gmail.com; ☎: +234 7032884007]

ABSTRACT: The present study was undertaken to evaluate anti ulcer activity of aqueous seed and rind extracts of *Citrullus lanatus* (watermelon) in ethanol induced gastric ulcer model in albino rats. The experiment was divided in to two models (A: animals pre-treated with aqueous seed extract of watermelon ; B: those per-treated with aqueous rind extract of watermelon) in each, four groups of rats were pre-treated with distilled water (control), Ranitidine (300mg/kg) for each, 150 and 300mg/kg seed and rind extracts were given to pre-treated animals in both models. Rats pre-treated with seed and rind extracts showed significant ($P<0.05$) dose-dependent decrease in gastric lesions formation. Ulcerogenesis was significantly ($P<0.05$) reduced in pre-treated groups compared with control ($P<0.05$). However, the per centage curative effect was effectively high in (seed 75% and rind 70%) and was also dose dependent. The result indicates that *Citrullus lanatus* (watermelon) seed and rind possess potential gastroprotective and antiulcerogenic activities in ethanol induced gastric ulceration. And is probably due to high citrulline and flavonoid contents which might influence both NO synthesis and antioxidant defence mechanism that cumulatively inhibit gastric acid secretion.
Keywords: Ulceration, ulcer index, *Citrullus lanatus*

INTRODUCTION

Peptic ulcer is a worldwide burden. As of 2010, approximately 250,000 people died of peptic ulcer disease (Lozaro, 2012). Its prevalence is quite high in third world countries where an estimated 70% of population is affected (Brown, 2000).Several studies from different parts of Nigeria suggest its occurrence in 4 to 10 per thousand population. Peptic ulcer is one of the most common gastrointestinal diseases. The exact causes of peptic ulcer disease are not known but the pathophysiology may be due to an imbalance between aggressive factors (acid, pepsin, *Helicobacter pylori*, non-steroidal anti-inflammatory drugs etc.) and local mucosal defence factors (mucus, bicarbonate, blood flow, prostaglandins etc.) (Oluwale *et al*., 2013). However, the disease is seen to occur mainly due to persistent intake of NSAIDs, infection by *Helicobacter pylori,* stress or as results of pathological condition such as Zollinger-Ellison syndrome (Dinesh, 2011).

Several synthetic drugs including proton pump inhibitors and H_2 receptor antagonists are available as regimen for peptic ulcer, but are undoubtly associated with number of side effects ranging from diarrhea, headache, drowsiness, fatigue, muscular pain and drug interaction (Anoop and Jagadeesan, 2003). There are many new drugs against ulcer, depending on the type and cause of the ulcer in question. Morbidity rate is more or less reduced, but resulted in many different adverse effects such as relapse of the disease. Therefore, the search for natural product from food and plant as potential therapy with less side effects compared to synthetic compound is strongly encouraged.

Fruits have high vitamins, minerals, fibre, phytochemicals and antioxidants in their pulps, seeds and rinds but they have not been given much attention in the diets of many Nigerians. Most times they are discarded mostly due to ignorance of the nutritive value and curative potentials. (Tindall, 2004).

Watermelon (*Citrullus lanatus*), belongs to family *Cucurbitaceae* originated from southern Africa, and is one of the most common types of melon. The juice is naturally rich in citrulline (El-Razek, 2011). The citrulline in watermelon stimulates Nitric oxide synthase. In the same vein, the citrulline in watermelon can be metabolized to L-Arginine (Collins *et al*., 2007), a known precursor of endogenous NO that inhibits gastric acid secretion (Berg *et al*., 2004) .It also increases plasma concentrations of pancreatic glucagon a potential inhibitor of gastric acid (Loud *et al*., 1981; Oluwale *et al*., 2013). Several studies have indicated that water melon seed, pulp and rind possess significant amount of phytochemical components like flavonoid, saponin, tannins and alkaloid (Johnson *et al*., 2012).

Watermelon is also known to be a good source of vitamin A, C and the antioxidant lycopene (Gill *et al.*, 2010).It is used diuretic and as antihypertensive (Figueroa *et al.*, 2012). Rats treated with juice extract of *Citrullus lanatus* showed significant dose-dependent decrease in the gastric lesions formation, lowered gastric acid secretion and significant inhibition of ulcer (Oluwale et al., 2013).Several researches have been performed to evaluate the anti-ulcer and gastroprotective activities of *Citrullus lanatus* (Sharma *et al*., 2012; Bhardwaj *et al*., 2012). The present study was conducted to investigate anti-ulcerogenic effect of aqueous seed and rind extracts of watermelon in ethanol- induced peptic ulcer model in albino rats.

MATERIALS AND METHODS

Watermelon Seed and Rind Extraction

Ten (10) fruits of watermelon were bought from Sokoto central market in Sokoto north Local Government Area of Sokoto State, Nigeria. The samples were bought in their fresh state and in sufficient quantity for the analysis. The fruit was washed to remove dirt and cut into smaller pieces. The thick outermost back and the seeds were removed and washed with tap water and dried under shed. The seed and rind were pulverized into powder and soaked in 500ml distilled water overnight. The extracts were filtered using No 1 Whatman filter paper. The filtrates were then dried in a drying cabinet and stored until required.

Experimental Animals

A total of forty eight (48) albino rats of both sexes weighing between 250 and 265g were used for the study and obtained from Animal House, Biological Sciences Department of Usmanu Danfodiyo University, Sokoto, Nigeria. The animals were monitored under standard laboratory conditions and fed with routine commercially formulated rat feed (purchased from Rahusa vital feeds, Sokoto). Clean tap water was supplied ad libutum and allowed to acclimatize for two weeks under same conditions. The animals were divided into two models (A: animals pre-treated with aqueous seed extract of watermelon; B: those per-treated with aqueous rind extract of watermelon) each of twenty four (24) animals.

The first study involved ethanol-induced peptic ulceration in rats treated with aqueous seed extract of watermelon. While the second study involved animals that were placed under same condition but treated with aqueous rind extract of different concentrations. In each of the studies, the animals were later randomly sub grouped into a control (distilled water) and experimental (150 and 300mg/kg aqueous extracts of seed and rind watermelon pre-treatment) groups with six (6) animals each as follows:

Model A
Group – I (Control): Distilled water
Group – II (Standard): Ranitidine (300mg/kg)
Group – III: Seed Extract (150mg/kg)
Group – IV: Seed Extract (300mg/kg)
Model B
Group – I (Control): Distilled water
Group – II (Standard): Ranitidine (300mg/kg)
Group – III: Rind Extract (150mg/kg)
Group – IV: Rind Extract (300mg/kg)

The animals were starved for forty eight (48hr) prior to the inducement to ensure an empty stomach. Excessive dehydration and abnormal metabolic flux during the fasting period were prevented by supplying sucrose 8% (w/v) solution in NaCl 0.2% (w/v) which was removed 1 hr before the experiment. In the first day, normal oral feeding of water was continued and the animals of II, III and IV were given two doses of ranitidine (300mg/kg), Seed extract (150mg/kg), Seed extract (300mg/kg) respectively for two days at six (6) hrs interval. After 90 minutes of pre-treatment (on the second day), 80% ethanol was given to all the animals at a dose of 8ml/kg. Four hours later, the animals were sacrificed, stomach were removed and cut along the greater curvature to measure the ulcer index and same treatment was applied to the rats in the second model.

Estimation of Ulcerogenesis

The lesion (appears as dots) on the wall of the stomach was visible and counted, each five (5) lesions were considered as one(1) millimetre ulceration (Elegbe, 1978;Mallika *et al.,* 2009). The sum total length of the ulcers in each group of the animals divided by its number gives the ulcer index (mm) while % curative effect is given by:

Curative effect(%) = UIC-UIT/UICx100
Where
UIC = Ulcer Index in Control
UIT = Ulcer Index in the test group
The ulcer score criteria used is presented in Table 1.

Data Analysis

Data obtained from this study were analysed using the InStat statistical software (version 3.0 for windows,

Santiago USA). Analysis of variance (ANOVA) was used to compare means, and values were considered significant at $p<0.05$.

Table 1: Ulcer score Criteria

Ulcer Score	Criteria
0	Normal Stomach/No ulcer
0.5	Punctuate or pinpoint ulcers
1.0	Two or more small haemorrhagic ulcers
2.0	Ulcers greater than 3mm in diameter.

RESULTS AND DISCUSSION

Phytochemical analyses of the aqueous seed and rind extracts of watermelon showed the presence of alkaloids, flavonoids, saponins, tannins, citrate and volatile oil (Table 2). Aqueous Seed and Rind extracts of Watermelon were evaluated for its anti-ulcer activity against ethanol- induced gastric ulcer model in albino rats. The degree of ulceration (determined by the Mean Ulcer Score) in all the treatment groups was significantly lower than that in animals given distilled water only (control) and is dose dependent. The results are presented in Tables 3 and 4 respectively.

In model-A, the seed extract at dose of 150 and 300mg/kg showed significant % curative effect of 65.8% and 75.0% compared with standard drug Ranitidine 66.7%. While in model-B, with rind extract, 66.9 and 70.2 % curative effect were observed against 66.9% of Ranitidine.

In the both models, the seed and rind showed a protective effect on the stomach mucosa against experimentally-induced ulceration. There was a significant reduction ($P < 0.05$) in ulcerogenesis in test animals pre-treated with aqueous extracts of seed and rind in concentrations of 150 and 300mg/kg respectively, when each was compared individually with the control. And the reduction was dose-dependent.

Phytochemical analyses of watermelon seeds show that secondary metabolites such as saponins, flavonoids, tannins, alkaloids and volatile oil are present (Braide *et al*, 2012). These secondary metabolites are responsible for the pharmacological activities such as, analgesic and anti-inflammatory of seeds (Madhavi *et al*, 2012), anti-ulcerative activity (Alok, 2012).

Peptic ulcer has long been known to be one of the most significant gastrointestinal burdens afflicting million around the Globe. With ever growing search in herbal medicine that would effectively cure and reduce complications observed with synthetic drugs.

Watermelon is rich in amino acid citrulline (Perkins, 2008), and it has been reported that the body records a significant amount of citrulline after consumption of several kg (Mandel *et al,* 2005). The citrulline which exists in watermelon especially in the rind is a known stimulator of Nitric Oxide. Similarly, L-Arginine, a known source of endogenous NO, inhibits gastric acid secretion (Berg *et al*., 2004), and increased in plasma concentrations of pancreatic glucagon was noticed in rats fed with watermelon seed (Loud *et al*., 1981) Nitric oxide was shown to inhibit gastric acid secretion in rats (Hasebe *et al.*,1998; Hasebs *et al.*, 2001).

Table 2: Phytochemical Analysis of *C. lanatus* extracts

phytoconstituents	Seed	Rind
Flavonoid	+	+
Saponin	+	+
Alkaloid	+	+
Tannins	+	+
Volatile Oil	+	_
Citrate	+	+
Glycosides	+	+
Anthraquines	–	_

+: Depicts presence of the metabolite
–: Depicts absence of the metabolite

Table 3: Effect of aqueous seed extract of Watermelon (*C. lanatus*) on ethanol – induced ulcer in rats

Group	Dose (mg/kg)	Ulcer Index	Curative Effect (%)
Control	-	1.20±0.25	-
Ranitidine	300	0.40±0.31*	66.7
Extract	150	0.41±0.31*	65.8
Extract	300	0.30±0.30*	75.0

Values are expressed as Mean±S.D, n=6, *P<0.05 as compared with control

Table 4: Effect of aqueous Rind Extract of Watermelon (*C. lanatus*) on Ethanol-Induced Ulcer in Rats

Group	Dose (mg/kg)	Ulcer Index	Curative Effect (%)
Control	-	1.21±0.25	-
Ranitidine	300	0.40±0.31*	66.9
Extract	150	0.40±0.31*	66.9
Extract	300	0.36±0.27*	70.2

Values are expressed as Mean±S.D, n=6, *P<0.05 as compared with control

On this note, it can be speculated that, the mechanism by which either of these extracts cause a decrease in gastric secretion that led to ulceration was probably by increasing citrulline contents that triggers an increase in NO synthesis (Brown *et al*., 1993). Gastro protective effect of watermelon in Indomethacin-induced peptic ulcer has been reported (Kato *et al*., 1998).methanolic extract of seeds showed significant decrease in the gastric volume, free acidity and total acidity and significant percentage inhibition of ulcer (Gill *et al*., 2011).

CONCLUSION

The present study reports that watermelon seed and rind possess significant gastroprotective, antiulcerative effect on the stomach in experimental animal model. The remarkable reduction in mean ulcer score in this work may likely be explained by the anti gastric acid secretion effect of watermelon, which significantly reduces the formation of ulcers when compared with reference drug (Ranitidine).The anti ulcer activity is probably due to high citrulline and flavonoid contents of the extracts that have great influence on NO synthesis which has been reported to have antisecretory and antioxidant effects respectively. Moreover, watermelon seed and rind are frequently used in traditional system of medicines. Further studies are needed to characterize and explore the other therapeutic potential of the compounds present in the extracts.

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