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RAISED DOSAGE OF CASHEW LEAVES EXTRACT (ANACARDIUM OCCIDENTALE) MORE POTENT THAN OMEPRAZOLE IN GASTRIC SECRETION ULCER TREATMENT

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ABSTRACT
Effects of ethanolic extract of cashew leaves in thirty six (36) male and female albino rats with induced gastric ulcer were investigated for 14 days. The animals were divided into six (6) groups with six animals in each group. Group I served as control without gastric ulcer. Group II –V with gastric ulcer were administered with various concentrations while group VI group had omeparazole treatment. The mean gastric ulcer count in group II and III was significantly ($P<0.05$) higher than that of control. Group VI had higher ulcer counts than control but lower counts significantly ($P<0.05$) as compared to group II and III. Group V ulcer counts were not different significantly with control but were lower significantly ($P>0.05$) compared with group II, III and IV. The gastric secretion in group II was not different significantly ($P>0.05$) compared to control group, on day 7, increased in group III ($P<0.05$) and on day 14 compared to control. The gastric secretion in group IV was not significantly different ($P>0.05$) as compared to control on day 7, but increased significantly ($P<0.05$) on day 14 compared to control Group V with high dose of extract had low gastric acid secretion on day 7 not significantly different ($P>0.05$) as compared to control and higher significantly on day 14. Group VI with omeprazole treatment had lower gastric secretion significantly different ($P<0.05$) compared to control in day 7 but higher secretion significantly different from that of control on day 14. It was observed that at high dose of the extract low ulcer count and low gastric secretion were recorded compared with the orthodox drug, omeprazole. It is affirmed that cashew leaves extract is a potent antiulcerogenic therapy.

KEYWORDS: Cashew leaves extract, gastric protection, gastric ulcer.

INTRODUCTION
Gastric ulcer is the disease of the gastrointestinal system localized in the stomach as a sore or wound, it occurs due to factors that act against the system and could also be as a result of defective protective system as in gastric barrier, (Fong, 2015). Gastric ulcer may result from Helicobacter pylori, stress, food e.g. beverages, intake of drugs e.g. nonsteroidal anti-inflammatory drugs (Jimmy, 2013), (Gisbert, 2007), (Gamboro, 2005), (Lau, 2001). The prevalence of gastric ulcer is associated with morbidity and relative mortality (Kenneth, 2013). About 4 million or more persons are affected by peptic ulcer disease globally annually, (Zelicson, 2011). Importantly, the perforated peptic ulcer is found to be varied in incidence in some continent in the world and stable in some and the range of incidence is put at 4-11% per population of about 100,000 subjects (Paimela, 1991). The perforated peptic ulcer is often associated with increase morbidity and mortality rates. The incidence rate from the perforated peptic ulcer as per the number of persons affected has shown that the disease is fatal. In Africa epidemiological data on morbidity and particularly hospital-based survey is rare, however, few studies have been reported in autopsy, Olubuyide (1989). This survey showed about 1.5% of the death from this disease accounting for 5% incidence. This implies that the actual population attributable to peptic ulcer is high as the study was done in only a state in Nigeria. The most associated morbidity is found to be bleeding (Tang, 2013) and such is shown to cause as high as 72% of the death from the peptic disease.

The drugs use for the treatment include, H_2 – inhibitors; cimetidine, ranitidine and omeprazole; the proton pump inhibitor (Fong, 2015). Antioxidants and herbal extract are also used. The protection for prostaglandin, source strength for gastric barrier is highly focused with the use of prostaglandin analogue; misoprostol in the treatment, (Zajac 2013) (Wikipedia). The use of herbal remedies in the treatment of gastric ulcer is receiving greater attention as some of such rememdies are with high potency than the Orthodox drugs (Jimmy, 2017). This

study was therefore conducted to evaluate comparative efficacy of ethanolic extract of cashew leaves (anacardium occidentale) and Omeporazole in induced gastric ulcer. Cashew trees are enormous in the tropics with economic benefits particularly the nut eaten when fried with medicinal benefits, (Murthy 1985).

The leaves are reported to have antimicrobial properties, (Ifesan, 2013) (Agedah, 2010) (Omojasola, 2004). The leaves bark and shell oil also have anti-diuretic properties (GreenCottage, 2000). It is also used in the treatment of many kinds of diseases (Arekemase, 2011), including diabetes, inflammation (Akinpeju, 2001). The phytochemcial components include; flavonoids, phenols, terpenoids, xantoprotein, etc.

In our study, strict comparison of the anti-ulcerogenic potentials of the leaves ethanolic extract with proton pump inhibitor; omeprazole was done to assess the periodic efficacy of this plant. The aim being to find alternative therapy for the treatment of gastric ulcer as the orthodox drugs are with inherent treatment lapses with high degrees of reoccurrence of the disease with attendance high morbidity and mortality.

MATERIALS AND METHODS

Animals: Thirty six (36) male and female albino rats weighing 180-200g and male and female albino mice weighing 20-75g were used for the study. The animals were kept in well ventilated Department of Pharmacology animal house, University of Uyo, and fed with pellets and clean water. They were cared for according to regulation of Institute for Animal Ethical Committee (IAEC) and all the ethical standard laid down in 1964 declaration of Helsinki were observed.

Plant leaves for Extraction: The leaves of cashew tree; anacardium occidentale were obtained from the Faculty of Pharmacy farm, University of Uyo and were identified by a botanist.

Ethanolic Extract Preparation: The fresh leaves of Anacardium occidentale, were washed with clean water, chopped into pieces dried for one week and pulverized into powder form. It was macerated in 70% ethanol and kept for 72hrs. (Trease & Evans). It was filtered and the filtrate concentrated to dryness in water bath at 45oc. The weight of the filtrate was 5g.

Acuit Toxicity Test (LD_{50}): This was done according to methods of Lorke, (1983). It was divided into two phases and a total 36 male and female albino mice weighing 20-25g were used. In the first phase 18 mice were divided into six (6) groups with 3 mice in each group receiving intraperitoneal administration of extract, 1000 mg/kg, 3000 mg/kg and 1000mg/kg. In the second phase another 18 mice were used and divided into 6 groups with 3 mice in each group receiving, 500mg/kg, 750mg/kg and 1000mg/kg of the extract of Anacardium occidentale. The physical signs of toxicity e.g. convulsion, restlessness, decreased respiration and death were observed within 24hrs of the administration of the extract. The acute toxicity (LD50) was calculated from 750mg/kg that produced 0% mortality and 1000mg/kg that produced 1000% mortality.

$$\therefore \text{LD50} = \sqrt{AB} = \sqrt{750 \times 1000}$$

$$= 866.03\text{mg/kg} = 86.60\text{mg/kg}$$

The experimental dosages were based on 10%, 20%, 30% i.e. low dose, medium and high dose of the LD_{50}.

Inducement of Gastric Ulcer

Rats meant for the ulcer study was induced with 2.5m.l/kg of ethanol, given orally and observed for ulceration after 4 hrs. The animals were sacrificed after chloroform anaethesia. The stomach was removed, incised along the greater curvature and the contents washed to observe the ulceration using hand lens. The ulcer count was done by scoring from 0.5 based on the methods of Nwafor 2000.

GROUPING AND TREATMENT OF ULCER

Thirty six (36) albino rats, male and female weighing between 180–200g were divided into six (6) groups with 6 rats in each group. Group I served as control and administered with 10ml/kg of distilled water orally without ulcer inducement. Group 2 was given distilled water but induced with ulcer. Group 3 with induced ulcer was given low dose of 86.60mg/kg of the extract. Group 4 was given medium dose of 173.21mg/kg of the extract while Group 5 was given high dose of 259.81mg/kg of the extract. Group 6 was given 40mg/kg of omerprazole per body weight. The treatment was given orally using canula by passing esophagus and delivered into the stomach (Bertram 2004) and observed for 14 days.

COLLECTION OF GASTRIC SECRETION

On the 7th day after the administration of the extract and drug, the rats were sacrificed after chloroform anaesthesia. The stomach removed washed and filtered 5ml of distilled water added and titrated against, Na0H the same was done for 14 days of the treatment. The titrable acidity was calculated as follows; $\frac{x}{y}$ mmol

Where x is the titre of the acidity

y - original volume of the content

Statistical Analysis

Analysis of variance was used (ANOVA). The results were expressed as mean standard deviation.

RESULTS

The results of the effects of anacardium occidentale on the ulcer scores and gastric acid secretion are presented in tables 1 and 2 as per the period of studies, 7 and 14 days.

Table 1: Effect of Amacardium Occidentale on Ulcer Counts of Ethanol Induced Ulceration in Rats

Groups	Day 7 Ulcer Index	P. value	Day 14 Ulcer Index	P. value
Group 1 (control) (10ml/kg of distilled water)	0.00 ± 0.00	P<0.05	0.00 ± 0.00	P<0.05
Group II (Ethanol induce ulcer group) (10ml/kg of distilled water)	4.67±0.33[a]	P<0.05	3.67±0.33[a]	P<0.05
Group III (Low dose extract treatment group) 86.60mg/kg) per oral	4.33± 0.33[a]	P<0.05	3.33± 0.33[a]	P<0.05
Group IV(Middle dose extract treatment group) 173.2mg/kg) per oral	3.00 ±0.58[a.b.c]	P<0.05	1.67 ±0.58[bcd]	P<0.05
Group V (High does extract treatment group) 259.81mg/kg) per oral	1.00 ±0.58[b.c.d]	P<0.05	0.33 ± 0.33[bcd]	P<0.05
Group VI (Omeprazole treatment group) (0.30mg/kg) per oral	0.33 ±0.33[b;cal]	P<0.05	0.00 ± 0.00	P<0.05

Value are presented as mean ± Standard Deviation
a = significantly different from group II (P<0.05)
b = significantly different from group III (P<0.05)
c = significantly different from group IV (P<0.05)
d = significantly different from group V (P<0.05)

Table 2: Gastric Acid Secretion Results

Groups	Day 7 (mmol) Index	P. value	Day 14 Ulcer Index	P. value
Group 1 (control) (10ml/kg of distilled water)	8.67 ± 0.33	P<0.05	8.00 ± 1.53	P<0.05
Group II (Ethanol induce ulcer group) (10ml/kg of distilled water)	5.67±0.33	P<0.05	3.67±0.33[a]	P<0.05
Group III (Low dose extract treatment group) 86.60mg/kg) per oral	28.00± 3.46[a,b]	P<0.05	3.33± 4.00[c]	P<0.05
Group IV(Middle dose extract treatment group) 173.21mg/kg) per oral	8.33 ± 0.33[c]	P<0.05	17.33 ± 0.33[c]	P<0.05
Group V (High dose extract treatment group) 259.81mg/kg) per oral	7.00 ± 0.58[c]	P<0.05	10.67 ± 0.45[c]	P<0.05
Group VI (Omeprazole treatment group) (0.30mg/kg) per oral	0.67 ± 0.33[c]	P<0.05	15.33 ± 0.33[c]	P<0.05

Value are presented as mean ± Standard Deviation
a = significantly different from group II (P<0.05)
b = significantly different from group III (P<0.05)
c = significantly different from group IV (P<0.05)

DISCUSSION

The use of cashew leaves extract (Anacardium occidentale) has shown the variation in its effects at the dosage concentration in gastric acid secretion and the ulcer counts. At low dose the acid output was higher and so the ulcer count, this shows a dose dependent effect. This might have also been due to decreased duodenogastric reflux and gastric total bile acid concentration (Sedef, 2008). However, gastric ulcer does not really mean high acidity to induce the anomaly. And so, many gastric ulcer drugs may not necessarily act by the inhibition of the acid but may act on the causative agent e.g., Helicobacter pylori through combination with antibiotic. But the Helicobacter pylori also increase the tendency of ulceration by it damage to the gastric barrier (Microwiki, 2010), (Olbe, 1996), (Dun, 1993. The study have also compared the anti-ulcerogenic potentials of the cashew leaves extract with the effects of orthodox drug, omeprazole. And has observed a dose dependent decreased in gastric ulcer counts and gastric and gastric acid output in the extract treatment as high dose. This result was similar to the normal dose of omeprazole treatment in the study. The mechanism of this efficacy from the extract might be due to the presence of certain phytochemical components e.g. antioxidants (Morais, 2010). The hydrochloric acid in the leaves of anacardium occidentale can also be the reason for low gastric output as such will inhibit hydrochloric acid as negative feedback mechanism (Gayton, 2011, Barron, 1999). Cashew leaves also contain quercetin glycoside and this constituent is reported to protect gastric macosa by the presence of glycoprotein (Konan, 2007) and hence prevent gastric ulcer. Other phytochemicals include;alkaloids with gastroprotective effects (Gadekar, 2010) also with tannins Saponin (Vasconcelos, 2010, Nwidu, 2009). Also flavonoids content of the leaves and

it cyto protective properties have been reported (Hussani, 2012). Their mechanism of action is reportedly based on the inducement of mucosal prostaglandin production and decrease in histamine secretion and as free radical scavangers, (Sakat, 2009), Whittle, 2003). There are many multifactorial effects in the pathogenesis of peptic ulcer but gastric secretion is pivotal in the causative mechanism of the disease, and so the target of most antiulcerogenic therapies on the gastric acid, either by neutralization as in antacids and histamine blocking as in H_2 blockers or by inhibition of the secretion as in Omeprazole (Sumbul, 2011). Other pathways include the inhibition of acetylcholine and histamine reported in Anacardium occidentale (Sumbul, 2011). This may have been the pathway in our study which reduced the gastric acid secretion though histamine and acetylcholine levels were not determined. But hypergastrinaemia is another mechanism of gastric ulcer inducement (Jimmy 2013). Anacardium, occidentale is thus a very potent and protective antiulcerogenic therapy particularly the anacarcordic acid content which can stimulate mucus and prostaglandin production to protect the gastric intestinal lumen and gastric barrier.

RECOMMENDATION

The extract of Anacardium occidentale is therefore recommended as antiulcerogenic therapy but usage shall await further test.

REFERENCES

1. Agedah, C. E, Bano, D. D., Nyananyo, B. L. Identification of antimicrobial properties of cashew, Anacardium occidentale (Family, Anacardiacea). *Journal of Applied Science and Environment Management*, 2010; 14(31): 25-27.
2. Akinpelu, D. A. Antimicrobial activity of Anacardium occidentale bark. Filoterapia, 2001; 72(3): 286-287.
3. Arekamase. M. O. Oyeyiola, G. P., Aliya, M. B. Antibacterial activity of Anacardium occidentale on some enterotoxin producing bacteria. *International Journal of Biology*, 2011; 3(4): 968-973.
4. Barran, J. (1999). Digestive problems/natural health remedies (Baseline of Health foundation, http//jonbarron.ng/article/your stomach-part-3.
5. Bertam, G. In Basic and Clinical Pharmacology, 9th ed. New York, Chicago Sanfrancisco, London, 2004.
6. Dun, B. F. Pathogenic Mechanism of Helicobacter pylori. *Gastroenterol. Clin Northam*, 1993; 22(1): 43-57.
7. Fong, S. Y., Wong, Y. C. Xic, C., Zko, Z. Herb-drug interactions between scutellarieze and mefenamic acid. Simultaneous investigation of pharmacokinetics, anti-inflammatory effects and gastric damage in rats. *Journal of Ethnopharmacology*, 2015; 170: 101-16.
8. Gadekar, R. P. L., Chaurasiya, P. K, Pawa, R. S., Patil U. K. A potential of some medicinal plants as an antiulcer agents. *Pharmacognosy Review*, 2010; 4: 136-46.
9. Gambero, A., Becker, T. L., Zago, A. S., De Olivesra, A. F., Pedrazzoli, J. J. Comparative study of anti-inflammatory and Ulcerogenic activities of different cyclo-otygenase inhibitors Inflamaopharmacology 2005; 13: 441-54.
10. Gisbert, J. P., Legido, J. Gracia, S., Pajares, J. M. H. Pylori and perforated peptic ulcer prevalence of the inflection and role of nonsterodal anti-inflammatory drugs, Dig. Liver dis., 2004; 36: 116-120.
11. Greencottage, D. (2000). Vegetable oils, cashew nut (Anacardium occidentale Linn) http://www.greencottage.corn/oil./cashew.html.
12. Guyton, A. C., John, H. E, In text both of Medical Physiology, 2011; 20th ed.
13. Hussaini, J., Othman, N. A., Abdulla, N. A., Majid, H. M. F. Gastro protective effects of Dicranopieris linearis leaf extract against ethanol-induced gastric mucosal injury in rats Science Research. Essay, 2012; 7.
14. Ifesan, B. O. T., Fashakin, J. F., Ebosele, F., Oyenride, A. S. Antioxidant and antimicrobial properties of selected plant leaves. *European Journal of Medicinal Plant*, 2013; 3(3): 465-473.
15. Jimmy, E. O. Novel compounds with antiulcerogenic potentials unveiled in plantain leaves isolates isolater. Accepted for Publication Journal of drug discovery and therapy, 2017.
16. Jimmy, E. O., Odeh, S., Adelaiye, A. B. Hypergastrinaemia and raised HCL in tea drinking anoceated gastric ulcer. *Journal of Physiobiochemical and metabolism*, 2013; 2(2): 2-4.
17. Kenneth, T., Jon, A. S., Jan, t. K., Tom, G. and Kjetil, S. Epidemiology of perforated peptic ulcer: Age and gender-adjusted analysis of incidence and mortality. *World Journal of Gastroenterol*, 2013; 19(3): 347-354.
18. Konan, N. A., Bacchi, E. M., Lincopan, N., Varela, S. D. and Varanda, E. A. /Acute-subacute toxicity and genetoxic effect of hydroethanolic extract of the cashew (Anacardium occidentale L). *Journal of Ethnopharmacology*, 2007; 110: 30-38.
19. Leau, J. Y., sung, J., Hiu, C., Henderson, C. W., Metz, D. C. Systematic Review of epidemiology of complicated peptic ulcer disease incidence, recurrence risk factors and mortality. *Digestion*, 2011; 84: 103-113.
20. Lorke, D. A new approach to practical Acute toxicity testing. *Archieves of Toxicology*, 1983; 54: 275-287.
21. Microwiki. Gastritio and peptic ulcer disease, caused by helicobacter pylori, 2010.
22. Morais, T. C., Pinta, N. B., Carvalho, K. M. M. B. Rios, J. B. and Santos, F. A. Protective effect of Anacardic acid from cashew (Anacardium occidentale) on Ethanolic Induced Gastric Damage in Mice. Chemical Biological Interaction, 2010; 183: 264-29.

23. Murthy, B. G. K., Sivasamban, M. A. Recent trends in utilization of cashew Research and development. Proceedings of the International Cashew symposium, Cochin, Keraca, India, 1985; 201-207.
24. Nwafor, P. A., Okwuassamba, F. K. Binda, L. G. Antidiarrhoreal and antiulcenogenic effect of methanolic extract of Asparagus pubescens root in rat. *Journal of Ethnopharmacology*, 2001; 72: 421-427.
25. Nwidu, L. L. and Nwafor, P. A. Gastroprotective effects of leaf extract of carpolobia Lutea (polygalacea) in rats. *African Journal of Biotechnology*, 2008; 8: 012-019.
26. Olbe, L. Hmlet, A., Dalenback, T., Fandrisks, L. Mechanism in which Helicobacter pylori infection of antrum contributes to the development of duodenal ulcer. *Gastroenterology*, 1996; 110(5): 1386-1394.
27. Olubuayide, I. O. An autopsy survey of peptic ulcer disease at Ibadan. *African Journal of Medicine*, 1989; 35(10): 1-6.
28. Omojasola, P. F. and Arue, S. The antibacterial activity of the Anacardium leaf on some selected microorganism. *Biosciences Research Communications*, 2004; 60(1): 25-50.
29. Paimela, H., Tuoumpo, P. K., Rerakyl, T. K., Hoc Kerstedt, K., Kivilaakso, E. Peptic ulcer surgery during the H_2-receptor antagonist: A population based epidemiological study of ulcer surgery in Helsiriki from 1972-1987. *Br. J. Surg*., 1991; 78: 28-31.
30. Saikat, S., Raja, S., Biplab, B., Joydep, M. Plants and Phytochemicals for Peptic Ulcer: An Overview. *Pharmacognosy*, 2009; 3(6): 220-289.
31. Sedef, K., Erkan, P., Gulden, A., Satrite, K., Nurgul, S., Ali, O. and Buhan, S. Bile reflux index after therapeutic biliary procedures, BMC Gastroentemol, 2008; 8: 4
32. Sumbul, S., Ahmad, M. A., Asif, M. and Akhta, M. Role of Phenolic compounds in peptic ulcer: An overview. *Journal of Pharmacology, Bioallied Sciences*, 2011; 3: 361-367.
33. Tang, S. J. Endoscopic treatment of hyper gastrointestinal ulcerbleeing. *Video Journal and Encyclopedia of GI Endoscopy*, 2013; 1(1): 143-147.
34. Trease & Evans: In Trease & Evans text book of Pharmacognosy, 1996.
35. Vasconcelos, P. C., Andreo, M. A., Vilegas, W., Hiruna-Lime, C. A. and Pellizzon, L. H. Effect of mouriri pusa tannins and flavonoid on prevention and treatment against experimental gastric ulcer. *Journal of Ethno Pharmacol*, 2010; 131: 146-161.
36. Whittle, B. J. R. Fruits IV in H. Manrse (ed.) volatile compounds in Foods and Beverages. New York, 1991.
37. Zajac, P., Holbrook, A. Super, M. E., Vogt, M. An overview: Current clinical guidelines for the evaluation diagnosis, treatment and management of dyspepsia. *Osteopathic Family Physician*, 2013; 2: 79-85.
38. Zelicson, M. S. Broncer, C. M. Johnson, B. L., Camanas, J. A., Smith, D. E., Rawlinson, D. Von, S. Stone, H. H., Taylor, S. M. Helicobacter pylori is not the predominant etiology for peptic ulcers requiring operation. *Am. Surg*, 2011; 71: 1054-1060.