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ANTI HEMORRHOID EFFECT OF ETHANOL LEAF EXTRACT OF *OCIMUM GRATISSIMUM* ON CROTON OIL INDUCED HEMORRHOID IN RATS

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ABSTRACI

This study was carried out to determine the anti-hemorrhoid effect of ethanol leaf extract of *Ocimum gratissimum* on croton oil induced hemorrhoid in rats. Thirty-five male Wistar albino rats were randomized into five groups A to E, of seven rats each. Group A was not induced and it served as the normal control while groups B to E were induced. Group A was given distilled water only while Group B was left untreated. Group C was treated with standard drug and groups D and E were treated with doses of 100mg/kg and 400mg/kg of extract respectively. The effect of the extract on the animals was monitored by evaluation of their Body Weight dynamics, Percentage rectal water content (Wet weight) and Anorectal coefficient (ARC). While weight loss was averted in animals that were treated with extract, the anorectal evaluation showed that the untreated group B had the highest % rectal water content (76.00 ± 1.00) and Anorectal coefficient, ARC ($5.60\times10^{-3} \pm 3.0\times10^{-4)}$ while the control group A, had the lowest % rectal water content (61.75 ± 2.06) and Anorectal coefficient, ARC ($3.82\times10^{-3} \pm 9.46\times10^{-5}$). Group E had lower % rectal water content (67.00 ± 2.34) and Anorectal coefficient, ARC ($4.15\times10^{-3} \pm 6.45\times10^{-5}$) than group C with % rectal water content (67.75 ± 1.03) and Anorectal coefficient, ARC ($4.85\times10^{-3} \pm 1.76\times10^{-4}$). Significantly, the % rectal water content for group D (67.00 ± 2.08) and Anorectal coefficient, ARC ($4.17\times10^{-3} \pm 6.67\times10^{-5}$) was also lower than that of group C. The difference in % rectal water content was significant ($P<0.05$) when treated group was compared with the rest of the groups. The result indicated highest degree of possible anorectal tissue repair and hemorrhoid healing for animals that were treated with the dose of 400mg/kg extracts (Group E). The anti-inflammatory response which was vital in averting weight loss by the animals that were treated with extract also possibly enhanced its anti-hemorrhoid capacity. The study revealed that the extract was able to reverse the inflammatory and necrotic condition of the anorectal tissue of the induced rats which could eliminate the need for cocktail of drugs or surgery in the treatment of hemorrhoid. Further research is however suggested to elucidate the possible mode of action.

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KEYWORDS:
Ocimum gratissimum, Scent leaf, Anti-hemorrhoid, Anti-inflammatory, Wound healing, Tissue regenerative.

INTRODUCTION

According to Schubert *et al*. (2009), hemorrhoids are clumps or masses of tissues that form in the anal canal and contain blood vessels as well as the surrounding supportive tissues consisting of muscle and elastic fibres that aid in controlling stools. When inflamed or bloated, they develop pathological characteristics called piles (Lorenzo-Rivero, 2009). It frequently results in bleeding, discomfort, anal itchiness, and pain. Infection, faecal incontinence, strangulated hemorrhoids, heavy bleeding, anaemia, blood clots, and perianal thrombosis are complications that can occur (Lohsiriwat, 2012 and Margetis, 2019). Numerous physiological and pathological diseases, including hemorrhoids, are primarily brought on by free radical production (Faujdar *et al*., 2019). Hemorrhoids can be treated surgically, with bulk-forming laxatives, antibiotic-analgesic-steroid-rectal ointments, suppositories, or creams (Kaider-Person *et al*., 2007, Lorenzo-Rivero, 2009, Schubert *et al*., 2009, and Beck, 2011). However, antioxidants work to neutralise free radicals and are crucial in their elimination, which is why they are used to treat hemorrhoids (Johanson *et al*., 1990). Because herbal medicines have reportedly been shown to be safe, affordable, and free from side effects, especially when compared with synthetic pharmaceuticals, there has been a progressive resurgence of interest in the use of medicinal plants in developing nations in recent years (Iniaghe *et al*., 2009). In the tropics of Africa and Asia, *Ocimum gratissimum*, often known as scent leaf, is extensively dispersed. In Nigeria, it is mostly used as a spice and is edible. The plant has a long history of being used for healing, and some of its pharmacological uses have been documented. According to studies, *Ocimmum gratissimum* may be an effective free radical scavenger, minimising the consequences of oxidative stress on the body (Njoku *et al*., 2011). Both antibacterial and antilipidemic effects of *Ocimum gratissimum* essential oil have been demonstrated (Ayinla *et al*., 2011; Omodamiro and Jimoh, 2015). In experimental Rabbits, it enhances the vascular permeability to plasma proteins (Prabhu *et al*., 2009). This is a typical aspect of how a wound heals normally (Orafidiya *et al*., 2005). Due to its capacity to improve wound contraction, studies point to *Ocimum gratissimum*'s methanolic extracts as a possible wound healing agent (Osuagwu *et al*., 2004) and according to Sahouo *et al*. (2003); it has an anti-inflammatory effect as well. Following analgesic tests conducted on mice, there may be analgesic and spasmolytic effects (Aziba *et al*., 1999). The herb can affect and restore the liver's structural integrity as well as cellular activity (Ujowundu *et al*., 2011). Therefore, this study aims to assess the impact of *Ocimum gratissimum* ethanol leaf extract on hemorrhoid indicators.

MATERIALS AND METHODS

MATERIALS

CHEMICALS, REAGENTS AND EQUIPMENTS

Croton oil, Pyridine and Diethyl ether were procured from Sigma Aldrich, U.S.A.; Daflon (500mg) was procured from Cuzark Pharmacy, Awka, while distilled deionized water was prepared in the Biochemistry lab of Nnamdi Azikiwe University, Awka. All other materials, reagents and equipment used for this study were of analytical grade and were obtained from Docchy analytical laboratories, Awka and IFEs Specialist Diagnostic and Clinic Ltd, Awka.

STUDY SITE

The animal study was done at Chris Experimental animal farm, Awka.

PLANT

Fresh leaves of *Ocimum gratissimum* were purchased from the daily market, Mgbakwu in Awka North Local Government Area of Anambra State, Nigeria and were authenticated by a Taxonomist, Mr Iroka Finan of the Department of Botany, Nnamdi Azikiwe University, Awka, where a voucher has been deposited. The Herbarium no is NAUH 35B.

ANIMAL

Thirty-five (35) male Wistar albino rats weighing between 130g and 150g were procured from Chris Experimental Farm, Awka and maintained in the farm house under standard protocols of animal study. The rats had free access to water and fed *ad libitum*. They were kept for two weeks before the test, to acclimatize.

METHODS

EXPERIMENTAL DESIGN

This research was carried out in two phases;

Phase 1 – Induction of hemorrhoid, monitoring and evaluation

Phase 2 – Treatment and Anorectal evaluation

ANIMAL STUDY DESIGN

The thirty-five (35) male Wistar albino rats weighing between 130g and 150g were randomized into five groups of seven rats each.

Group A: Normal Control (Distilled water only).

Group B: Hemorrhoid – Untreated.

Group C: Hemorrhoid + Standard drug- Daflon

Group D: Hemorrhoid + 100mg/kg ethanol extract of Scent leaf.

Group E: Hemorrhoid + 400mg/kg ethanol extract of Scent leaf.

SAMPLE PREPARATION

PLANT

The leaves were hand-picked, washed and shade dried under room temperature for a period of two weeks. The dried leaves were pulverized to powder and stored in air tight containers for the process of extraction.

EXTRACTION OF PLANT MATERIALS (Nwinyi *et al.*, 2019).

Three hundred (300) grams of the powdered leaves of *Ocimum gratissimum* were soaked in two (2) litres of 70% ethanol and allowed to stand for 24hrs to ensure maximum extraction. The mixture was stirred at 2hrs interval within the 24hrs extraction period. After 24hrs, the mixture was sieved using muslin cloth and filtered with Whatmann-no 1 filter paper. The filtrate was concentrated using water bath at 50℃. The weight of the extract after concentration was 30.2g. **ANIMAL**

PREPARATION OF INFLAMMATION INDUCING AGENT

This followed the method of Nishiki *et al*. (1998). The inducing Croton oil preparation was constituted using deionized water, pyridine, diethyl ether and 6% croton oil in diethyl ether in the ratio of 1:4:5:10. This was done just before the test.

ACUTE TOXICITY STUDIES

Scent leaf is an edible plant, widely consumed and used as spices in the tropics. The acute toxicity of the ethanol plant extract on mice was found to be 2450mg/kg body weight (Njoku *et al*., 2011). The in vivo toxicity of the extract against albino rats showed that the plant extract was safe at various concentrations (Umar *et al.*, 2019). A further toxicity study for this research was therefore not considered expedient.

INDUCTION OF HEMORRHOID

By administering a croton oil formulation, hemorrhoids were caused in all subjects except group A (Normal Control). A cotton swab (4 mm in diameter) was placed into the anus and left there for 10 seconds after being soaked in Croton oil preparation (0.16ml).

Within 7-8 hours of the introduction of croton oil, a linear progression of oedema was seen. Prof. Okani, a Consultant Histopathologist at the Chukwuemeka Odumegwu Ojukwu University Teaching Hospital in Awka, reaffirmed this.

The animal study started on August 29, 2022 and ended on September 15, 2022. Body weight was checked weekly while treatment was given daily for 14 days.

MONITORING AND WEIGHT EVALUATIONS

The rats were physically monitored and body weights were measured weekly. Data was collected throughout the duration of the experiment and recorded.

TREATMENT AND ANORECTAL EVALUATION

After 24 hrs of induction, one rat was taken from group A and used for pilot study; while one rat each was taken from groups B to D and used for Wet weight determination as baseline studies. Treatment was then given to all the groups daily for 14 days. The standard drug used for group C was Daflon at the dose of 1g (3x per day) for 4 days, then 1g (2x per day) subsequently while 100mg/kg of extract was used to treat group D and 400mg/kg of extract was used for group E. The control group A was given distilled water only. On day 14, all

animals were euthanized under anesthesia and the anorectal portions were subsequently cut and evaluated.

DETERMINATION OF WET WEIGHT AND ANORECTAL COEFFICIENT

Twenty millimeter of the anorectal portion was cut and the wet weight recorded before drying. After drying, the dry weight was also recorded. The values were used to calculate the % rectal water content by the method of Liu *et al*. (2012).

The % rectal water content was calculated using the formula,

$$\% \text{ rectal water content} = \frac{Wet\ weight - Dry\ weight}{Wet\ weight} \times \frac{100}{1}$$

The Anorectal Co-efficient (ARC) was calculated using the formular,

$$\frac{Water\ Content\ (ml)}{Body\ weight\ (g)}$$

STATISTICAL ANALYSIS

The values obtained and the significance between the treated and control group was analyzed by one-way ANOVA using the SPSS version 17 and $P < 0.05$ was considered to be statistically significant.

RESULTS

RESULT OF MONITORING AND WEIGHT EVALUATION OF THE ANIMAL IS SHOWN BELOW.

The induced animals (Groups B to E) found it difficult to defecate. Some did not pass faeces until after 15hrs of induction. From the bar chart, the induction of group B animals which were not treated was followed by about 1.9% weight loss after 14 days against 18% weight gain by the control group A. The group C, treated with standard drug had an initial 8.6% weight gain in the first 7 days before dropping to a 4.9% weight increase thereafter while group D, treated with extract (100 mg/kg) had 12.3% weight increase and group E, treated with extract (400 mg/kg) displayed 13.2% weight increase within the given period of 14 days.

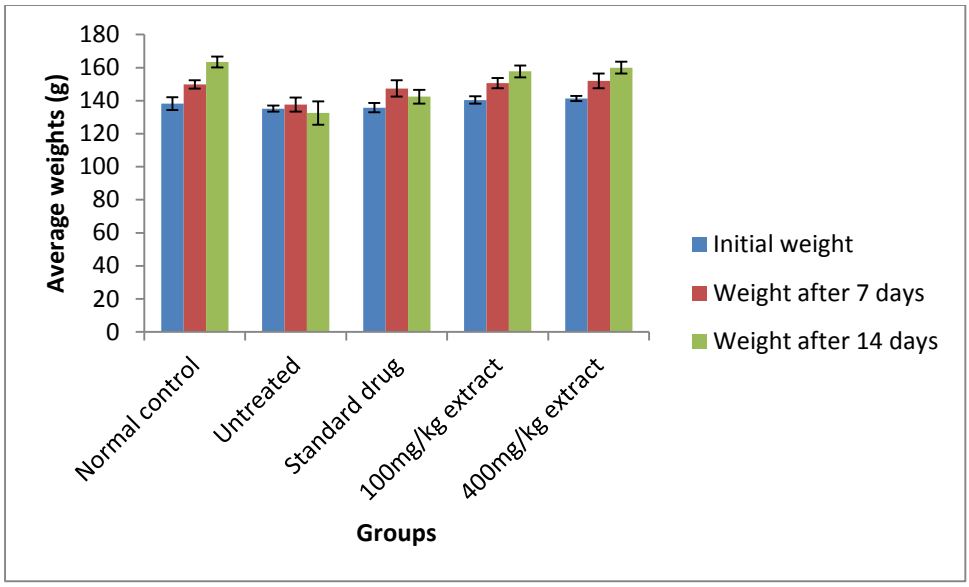

FIGURE 1: **Bar chart showing average weight of the various groups during the experimental period**

RESULT OF THE ANORECTAL EVALUATION AFTER TREATMENT IS SHOWN BELOW.

RESULTS OF WET WEIGHT AND ANORECTAL COEFFICIENT ARE SHOWN IN THE BAR CHARTS BELOW.

From the results, the untreated group B had highest percentage rectal water content (76.00 ± 1.00) and ARC ($5.60\times10^{-3} \pm 3.0\times10^{-4}$) while the control group A had the lowest % rectal water content (61.75 ± 2.06) and ARC ($3.82\times10^{-3} \pm 9.46\times10^{-5}$). The group E, treated with dose of 400mg/kg extract had lower percentage rectal water content (67.00 ± 2.34) and ARC ($4.15\times10^{-3} \pm 6.45\times10^{-5}$) than group C, treated with standard drug which exhibited % rectal water content (67.75 ± 1.03) and ARC ($4.85\times10^{-3} \pm 1.76\times10^{-4}$). Significantly, group D treated with dose of 100mg/kg extract showed % rectal water content (67.00 ± 2.08) and ARC ($4.17\times10^{-3} \pm 6.67\times10^{-5}$), which was also lower than that of group C.

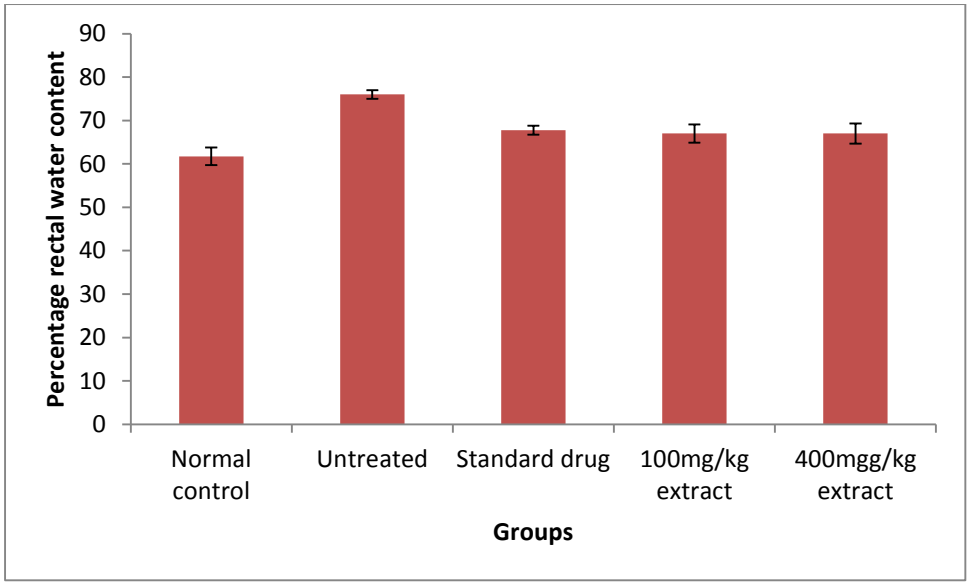

FIGURE 2.1: Bar chart showing % rectal H_20 content

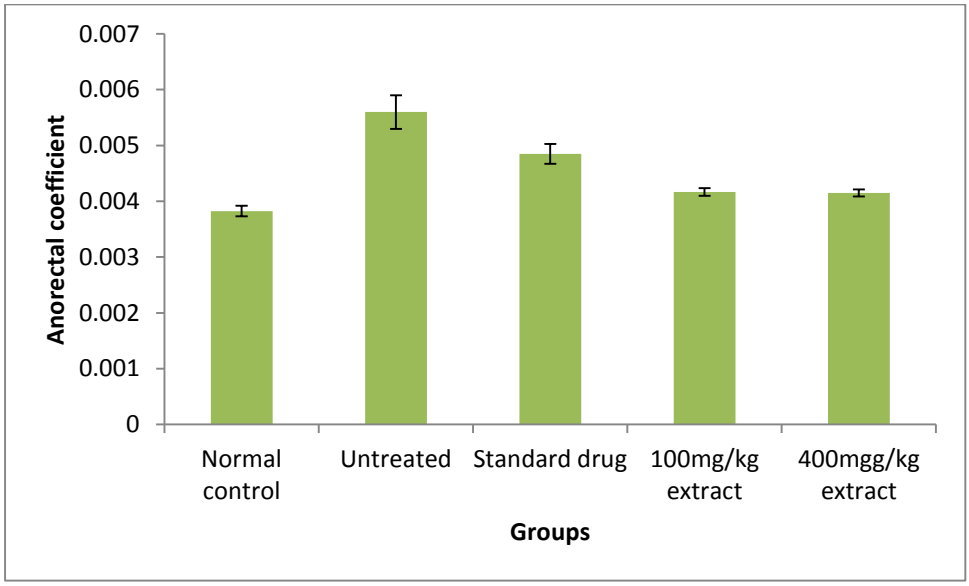

FIGURE 2.2: **Bar chart showing average ARC in the various groups**

DISCUSSION

Hemorrhoids have been attributed to inflammation caused primarily by generation of excess free radicals in the body (Faujdar *et al*., 2019). Complications lead to abnormal distortion of the vascular channel together with necrosis of the supporting anorectal tissue, excessive bleeding, anaemia, infection and pain (Lohsiriwat, 2012 and Margetis, 2019). This study of the anti-hemorrhoid effect of ethanol leaf extract of scent leaf on croton oil induced hemorrhoid in rats investigated the possible anti-inflammatory, wound healing and tissue regenerative

capacity of the extract which could reverse the inflammatory and necrotic conditions of the induced anorectal portion and possibly ameliorate the pathological effects of hemorrhoid.

The report by Yun-Zi *et al*. (2017) on the common pathway of stress-related diseases showed that elevated inflammatory mediators such as TNFα, IL1β, cytokine inducers like LPS or vaccination lead to chronic stress. The discomfort and weight loss by the experimental animals may be as a result of inflammatory stress that was associated with the induced hemorrhoid. This is corroborated by earlier study which showed that repeated acute stress induced change in weight and may represent a change in homeostasis which has potential to inhibit food intake and reduce body weight (Harris *et. al*., 2002). It is also in agreement with previous finding which indicated that inflammation demands the convergence of more cells at the site of activity by way of secreting inflammatory cytokines and chemokines which can cause the animals to lose weight due to high energy expended in the process (Huang and Lee, 2018). Phytochemicals have been reported to reduce cytokine gene expression of IL-1β, IL-6 and TNF-α which are pro-inflammatory cytokines and increase IL-10 which is anti-inflammatory cytokine, in LPS-activated cells (Ghareeb *et al*., 2013). Phytochemicals also induced molecular changes in NF-KB pathway (Lee *et al*., 2018). The anti-inflammatory response of the extract could therefore be vital in averting the weight loss among the treated animals and possibly enhanced its anti-hemorrhoid capacity. The response of the extract is supported by Sorhue *et al*. (2021) who reported that *Ocimum gratissimum* increased IL-10 expression while simultaneously decreasing IL-1β expression in experimental animals.

The efficacy of the treatment in this study could be determined by the ability of the extract to reverse the inflammatory and necrotic conditions of the induced anorectal portion which is exhibited by percentage rectal water content or suppressed Wet weight effect and Anorectal Co-efficient (ARC). The degree of suppression is proportional to the potency of the extract. This is in agreement with the report of Huiyi (2013), which showed that cerebral water content measurement is used for detecting the severity of the brain swelling and can be used as a means to indirectly reflect the extent of brain tissue damage. Consequently, the results obtained from this work indicated highest degree of possible anorectal tissue repair and hemorrhoid healing for animals that were treated with dose of 400mg/kg extract (Group E) since it presented the lowest percentage rectal water content and anorectal coefficient (ARC) among the induced groups. The healing potential of the extract was not dose dependent as even a lower dose of 100mg/kg (Group D) showed significant healing potential. The group that was treated with standard drug (Group C) showed the least healing potential among the treated groups. This

result is consistent with the anti -inflammatory response of the extract which revealed that weight loss associated with inflammatory stress was averted in animals that were treated with the extract.

CONCLUSION

This study showed that the ethanol leaf extract of scent leaf possesses possible anti-inflammatory response capability and anorectal tissue repair capacity which may be instrumental to its anti-hemorrhoid activity. The extract was able to reverse the inflammatory and necrotic conditions of anorectal portion of induced rats which could eliminate the need for cocktail of drugs or surgery in the treatment of hemorrhoids.

RECOMMENDATION

Based on the above result, *Ocimum gratisimmum* could be recommended as an anti-hemorrhoid agent. Further research is however suggested to elucidate the possible mode of action.

CONTRIBUTION TO KNOWLEDGE

The study revealed that ethanol leaf extract of scent leaf was able to reverse the inflammatory and necrotic conditions of anorectal tissue of induced rats which could eliminate the need for cocktail of drugs or surgery in the treatment of hemorrhoids.

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