Selenium Treatment Ameliorates Experimentally Induced Diarrhoea in Albino Rats

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ABSTRACT

Diarrhoea is one of the leading causes of death in children worldwide, accounting for 1 out of every 9 deaths in children. Therefore, in an attempt to tackle this disease, we investigated the effects of selenium on experimentally induced diarrhoea in animals. Female albino rats weighing 100 - 150 g were used and diarrhoea was induced by oral administration of castor oil, after which the animals were treated with 100 or 200 µg/kg selenium orally to investigate its effect on the number of wet faeces output. Experiments on intestinal enteropooling and intestinal motility of activated charcoal meal were also carried out. The two doses of selenium (100 and 200 µg/kg) significantly (P < 0.01) reduced the number of wet faeces and also significantly (P < 0.001) reduced the volume of intestinal fluid content, with 200 µg/kg producing 43.81% inhibition of fluid content, while the standard drug loperamide caused 54.30% inhibition. Furthermore, 100 µg/kg and 200 µg/kg selenium significantly (P < 0.001) reduced intestinal motility; producing 28.49% and 29.91% motility inhibition respectively with respect to control, while atropine inhibited intestinal movement by 49.2% with reference to control. In conclusion, selenium possesses anti-diarrhoeal effects through anti-secretory and anti-motility mechanisms.

Keywords: Diarrhoea, Selenium, Anti-secretory, Anti-motility.

Introduction

Diarrhoea is one of the leading causes of child mortality and morbidity in the world and is responsible for the death of about 525 000 children every year.1 Causes of diarrhoea include bacteria, viral or parasitic infections. Other causes include malnutrition, transmission from person-to-person, poor personal hygiene and consumption of contaminated food. The disease can last for several days, in which the patient suffers severe body water and electrolyte loss, which might result in death.1,2,3 Selenium (Se) is an essential micronutrient that was first described in 1817.4 Studies show that balanced selenium levels are essential for the normal functioning of the body systems, whereas abnormal status can cause diseases.5 There are pieces of evidence linking low selenium status with the development of several chronic diseases, including cardiovascular disease, cancer, diabetes and obesity.6,10 On the other hand, higher selenium status has been linked to enhanced immune competence, with better outcomes for cancer, viral infections, HIV progression to AIDS, male infertility, pregnancy, cardiovascular disease, mood disorders and bone health.11-14 Dietary selenium intake also has a strong inverse association with obesity.15 There are various forms of selenium used for dietary supplementation, however selenium-enriched yeast (Se-yeast) is a common form used for this purpose. It is capable of increasing the activity of selenoenzymes and its bioavailability has been found to be higher than that of inorganic selenium sources.16,17 Moreover, several intervention studies have been done using selenium yeast to raise selenium status.18-20

The relevance of selenium in health and disease is becoming so obvious. A study in Tanzania revealed that daily supplementation with 200 µg selenium decreased the risk of diarrhoeal morbidity among HIV infected women.21 Another study in Ethiopia discovered the high prevalence of selenium deficiencies in HIV seropositive and seronegative diarrhoeal patients.22 These suggest that the selenium status and treatment might be important in combating diarrhoeal disease. In a recent study by Sinaga et al., it was found that treatment with selenium reduced the frequency and duration of diarrhoea; it also improved the stool consistency and the recovery time.23 All these reports point out that selenium could be used in the treatment of diarrhoea, but the actions of selenium treatment in the gut during diarrhoea has not yet been investigated. Therefore, in this research, diarrhoea was induced in Wistar rats using castor oil, they were then treated with selenium yeast to observe the effect of this treatment on passing out wet faeces. We proceeded to investigate the mechanism by which selenium yeast reduce the number of wet faeces by conducting experiments on intestinal enteropooling and intestinal transit time of charcoal meal.

Materials and Methods

Animals

A total of 40 healthy female albino-Wistar rats weighing 100 - 150 g were used. They obtained from the Animal House, College of Health Sciences, Kogi State University, Anyigba, Nigeria and housed within the same facility under standard controlled environmental conditions, with a 12-hour light/dark cycle. They were kept in wire meshed cages and fed with standard pellet diet (Vital Feeds, Grand Cereals LTD, Jos, Nigeria) with water ad libitum. The rats were allowed to acclimatize for two weeks before the experiments. This study was granted ethical clearance by the Institutional Research and Ethics Committee of Kogi State University, Anyigba, Nigeria (KSU/CHS/REC/004/VOL2) and the animals were handled in line with the guidelines of the Committee, which is in accordance with the Guide for the Care and Use of Laboratory Animals (1996, published by National Academy Press, 2101 Constitution Ave. NW, Washington, DC 20055, USA).

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Selenium yeast
Selenium yeast containing 200 µg/kg selenium per tablet was purchased from Mason Vitamins Inc. Miami Lakes, USA. For treatment, rats were fed with 0.5 mL of the different concentration of the selenium, dissolved in distilled water and the drug was prepared fresh per experiment. The drug calculation for preparation of stock is as shown below:

For rats that took 100 µg/kg selenium and weigh 150 g:

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200 \text{ µg/kg (1 tablet) of selenium yeast was dissolved in 6.67 mL distilled water, thus every 0.5 mL of the solution contains 100 µg/kg selenium.}
\]

For rats that took 200 µg/kg selenium and weigh 150 g:

\[
200 \text{ µg/kg (1 tablet) of selenium yeast was dissolved in 3.33 mL distilled water, thus every 0.5 mL of the solution contains 200 µg/kg selenium.}
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Toxicity of selenium yeast
Acute toxicity studies indicate that the LD₅₀ for selenium yeast was 37.3 mg/kg and chronic administration of selenium yeast up to 800 µg/d provides no evidence of toxicity.¹⁶

Castor oil (CO) induced diarrhoea
Diarrhoea was induced by oral administration of castor oil and the anti-diarrhoeal activity of selenium was then investigated according to the method previously described by Teke et al.²⁴ The Rats were fasted for 18 hours, divided into four groups of five animals each. The animals were kept in separate cages in which the floor was lined with white paper, and wire gauge was placed 2 cm above the floor of each cage to prevent the animals from making direct contact with the excrement. Each rat was given 1 mL castor oil and unless otherwise noted, all treatments in this experiment were administered orally. After 30 minutes, the rats in the different groups were treated as follows: group I received the 0.5 mL of normal saline; group II, 100 µg/kg selenium; group III, 200 µg/kg selenium and group IV, 3 mg/kg loperamide. The fecal pellets from each rat were counted every 1 hour from the time of selenium treatment for the first 5 h. The number of wet feaces was recorded for each animal.

Castor oil-induced enteropooling
After the first experiment, the animals were returned to their diet and they recovered from the effect of treatment with castor oil within one day by passing out the normal solid feaces. They were then allowed to rest for 2 weeks before being used for the enteropooling experiment. They were fasted for 18 h and divided into 4 groups of five animals each. One hour prior to administration of 1 mL castor oil, each group was treated as follows: group I, received 0.5 mL normal saline (control group); group II received 100 µg/kg selenium; group III received 200 µg/kg selenium; group IV received the standard drug loperamide (3 mg/kg). One hour after castor oil administration, the rats were sacrificed; the ends of the small intestine were tied with thread before i

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= \frac{|\text{distance travelled|ctl} - \text{distance travelled |tm}|}{\text{distance travelled|ctl}} \times 100
\]

Intestinal motility
The intestinal motility test was conducted according to the method of Akomolafe et al.²⁶ A further 20 rats were used for this experiment; they were divided into 4 groups of five animals each. Each rat in group I was given 0.5 mL of normal saline. Groups II and III received 0.5 mL of 100 µg/kg and 0.5 mL of 200 µg/kg selenium, respectively and Group IV received 5 mg/kg of standard drug atropine. After 30 minutes, the rats were given 0.5 mL of freshly prepared charcoal meal (CM; 10% deactivated charcoal in 0.1% Tween 80). After another thirty minutes, the rats were sacrificed by cervical dislocation and the anterior abdominal wall was immediately cut open to dissect out the whole small intestine (pylorus to caecum). The length of the small intestine and the distance between the pylorus region and the front of the charcoal meal was measured. This distance was expressed as a percentage of the length of the small intestine and the inhibition of movement was calculated as:

\[
= \frac{|\text{distance travelled|ctl} - \text{distance travelled |tm}|}{\text{distance travelled|ctl}} \times 100
\]

Significance
Results are presented as mean ± standard error of mean (SEM). Statistical significance was calculated using ANOVA with Bonferroni post hoc test. The values were considered significant when P < 0.05. Data was analyzed using SPSS version 20 software.

Results and Discussion
In this research, diarrhoea was induced by administering castor oil to each rat. This model of diarrhoea induction is often used in research, because castor oil contains ricinoleic acid, which stimulates the release of endogenous prostaglandin.²⁷ The prostaglandin then cause arachidonic induced diarrhoea, which is characterized by an increase in intestinal transit time and increased accumulation of fluid in the intestine.²⁸ The standard drug loperamide was also used as a positive control; loperamide increases the colonic phasic segmenting activities by inhibiting the pre-synaptic cholinergic nerves in the sub-mucosal and myenteric plexuses. These then cause an increase in faecal water absorption, thereby reducing the frequency of defecation.²⁹ The result of this study show that all rats treated with castor oil passed out wet feaces. Furthermore, treatment with 100 µg/kg and 200 µg/kg selenium doses dependently and significantly (P < 0.01) reduced the number of wet faecal pellet dropping of rats at the end of 5 hours when compared with control. Loperamide also caused a significant decrease (P < 0.01) in the number of wet fecal pellets, which correlated significantly different from that obtained with 100 µg/kg and 200 µg/kg selenium as shown in Table 1. This finding agrees with the claims that selenium could be used to treat diarrhoea.²²,²³

In the enteropooling experiment, selenium treatment was found to significantly (P < 0.001) reduce intestinal fluid content (data shown in Table 2); 100 µg/kg selenium produced 41.07% inhibition of fluid accumulation with respect to control and 200 µg/kg selenium treatment produced 63.81% inhibition, while loperamide caused 54.30% inhibition of fluid accumulation. There were however, no significant differences between the effects of both doses of selenium and loperamide on fluid accumulation. Reduction in the volume of intestinal fluid content is important in the treatment of diarrhoea; hence many anti-diarrhoeal agents prevent or reduce the severity of diarrhoea by reducing the intestinal fluid content. These include herbal portions of Rubia cordifolia, Maturicia excelsa L. (Chamomile), Matricaria chamomilla Linn, and Pelargonium luridum (Andrées) sweet root.³⁰,³¹ In line with this, the antidiarrhoeal activity of selenium could be mediated via counter activity to the mechanisms that mediate diarrhoea induction by castor oil; that is, selenium could increase water and electrolyte absorption or decrease the secretion of fluid and electrolytes. Further, selenium might exert anti diarrhoeal effects by inhibiting the effect of the ricinoleic acid on prostaglandin E₂ receptors, thereby blocking the release of prostaglandin, which could in turn cause increase fluid secretion and increase intestinal motility.²⁸

Selenium treatment in this study significantly reduced intestinal motility as shown in Table 3. Selenium at doses of 100 µg/kg and 200 µg/kg significantly (P < 0.001) reduced the intestinal transit time of charcoal, with reference to the control animals. While the standard drug atropine caused a more significant (P < 0.01) reduction in the intestinal transit time of charcoal, when compared with 5e treated and control, which refers to a greater percentage inhibition of intestinal motility (Table 3). Diarrhoea is characterized by abnormal intestinal motility and increase in propulsion commonly observed. Therefore most anti-diarrhoeal drugs possess the ability to slow down intestinal movement. This antimotility effect of selenium is similar to those of; Rubia cordifolia, Cordia Africana, Lantana camara Linn and Pelargonium luridum (Andrées).²²,²³,²⁸ All these treatments abolish peristalsis in the colon and hence significantly delay passage of feaces through the bowel. The delayed transit through the bowel also increases the opportunity for increased absorption of fluid from the feaces, producing a drying effect on the stool that further slows its progress through the bowel. Selenium could inhibit intestinal motility by inhibiting cholinergic and serotoninergic receptors of the gut.³³

Selenium is considered a cornerstone of the body's antioxidant defense mechanism.

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²² When incorporated into the various selenoenzymes, selenium increases antioxidant capacity and influences the inflammatory signaling pathways that modulate reactive oxygen species (ROS) by inhibiting the nuclear factor-kappa B (NF-kB) cascade, resulting in a suppressed production of interleukins and tumor necrosis factor alpha (TNF-α).³⁵ 48 Adeniyi et al., 2018

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Majority of selenoproteins are classified as antioxidants, because they regulate various signaling processes by influencing the redox homeostasis and cellular Ca²⁺ influx. On the other hand, literature confirmed that oxidative stress and reduced antioxidant status of the gut are involved in the etiology of many gastrointestinal disorders including diarrhoea. Therefore, the anti-diarrhoecal effects of selenium could be due to its antioxidant activity.

**Conclusion**

In developing countries, diarrhoea represents one of the leading causes of death of children under five years with a huge financial burden, however, it is both preventable and curable. The disease has continued to be a menace despite many research, government and non-governmental organization interventions, hence, other ways to tackle this problem are being sought. The result of this study thus suggests that selenium, an essential micronutrient could be very useful in the prevention and treatment of diarrhoea. Furthermore, it ameliorates diarrhoea via anti-secretory and anti-motility mechanisms.

**Conflict of interest**

The authors declare no conflict of interest.

**Authors’ Declaration**

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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