

## Effect of *Zingiber Officinale* Ethanol Extract on Serum Electrolytes of Male Wistar Albino Rats Exposed to Inflammation

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**Abstract:** This study investigated the effect of *Zingiber officinale* ethanol extract on serum electrolyte concentrations in male Wistar albino rats exposed to inflammation. Rats were randomly divided into five groups: Group A (blank control), Group B (negative control with induced inflammation and no treatment), Group C (standard control treated with a conventional anti-inflammatory drug), Group D (low-dose *Zingiber officinale* extract), and Group E (high-dose *Zingiber officinale* extract). Serum levels of sodium (Na<sup>+</sup>), potassium (K<sup>+</sup>), chloride (Cl<sup>-</sup>), and calcium (Ca<sup>2+</sup>) were analyzed to assess the impact of treatments. The results revealed that inflammation significantly reduced serum electrolyte levels in the negative control group (B), with marked low sodium ion concentration (87 ± 0.008 mmol/L), low potassium ion concentration (2.2 ± 0.001 mmol/L), depleted level of chloride ion (57.40 ± 0.000 mmol/L), and low calcium ion concentration (2.2 ± 0.000 mg/dL) compared to the blank control group (A), all at p < 0.05. Administration of low-dose *Zingiber officinale* extract (Group D) showed no significant improvement in these electrolyte levels when compared to the negative control (p > 0.05). However, treatment with high-dose *Zingiber officinale* extract (Group E) significantly improved serum concentrations of Na<sup>+</sup> (117 ± 0.003 mmol/L), K<sup>+</sup> (5.6 ± 0.001 mmol/L), Cl<sup>-</sup> (98.0 ± 0.004 mmol/L), and Ca<sup>2+</sup> (4.4 ± 0.003 mg/dL), indicating a dose-dependent restorative effect. These findings inferred that high-dose *Zingiber officinale* ethanol extract may have restored electrolyte balance in inflammatory conditions, potentially serving as a natural therapeutic agent.

**Keywords:** *Zingiber officinale*, inflammation, sodium, potassium, chloride, and calcium.

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## Introduction

### Background of the Study

The intricate biological reaction of bodily tissues to damaging stimuli like infections, irritants, or injuries is called inflammation. According to Chen *et al.* (2019), it includes immune cell activation, the production of inflammatory mediators, and changes to the regular operation of several physiological systems. The equilibrium of serum electrolytes, such as sodium, potassium, chloride, bicarbonate, and calcium ions, which are essential for regular cellular function and general health, can be disrupted by both acute and chronic inflammation. Inflammation-induced serum electrolyte abnormalities can result in further complications like organ failure, neurological dysfunction, and cardiovascular problems (Zhou *et al.*, 2020).

*Zingiber officinale*, has long been valued for its therapeutic qualities in traditional medicine across many countries. Bioactive substances found in ginger, including paradol, shogaol, and gingerol, have been shown to have analgesic, anti-inflammatory, and antioxidant properties (Ríos and Recio, 2018). Particularly well-known for its strong anti-inflammatory qualities, *Zingiber officinale* ethanol extract may help regulate inflammatory reactions and restore electrolyte balance in the blood (Zhao *et al.*, 2019). Considering how common ginger is in traditional medicine, more research is needed to see whether it can help with inflammation-related electrolyte imbalances.

Osmotic pressure, pH balance, cellular functioning, and the general integrity of physiological processes are all dependent on serum electrolytes, which include sodium (Na<sup>+</sup>), potassium (K<sup>+</sup>), calcium (Ca<sup>2+</sup>), bicarbonate (HCO<sub>3</sub><sup>-</sup>), and chloride (Cl<sup>-</sup>) ions (Sharma *et al.*, 2021). The body's need for certain electrolytes may rise or fall during an inflammatory reaction, resulting in imbalances. Serious health effects such dehydration, edema, muscular weakness, heart arrhythmias, and in severe cases, death, can result from these imbalances (Zhao *et al.*, 2019). Therefore, it is essential to look into how natural substances like *Zingiber officinale* may modify electrolyte balance in inflammatory situations in order to create safer, alternative treatment methods.

### Justification of the Study

Finding efficient therapies that can control inflammation and its related consequences, such as electrolyte imbalances, is crucial given the rising incidence of inflammatory disorders throughout the world. The kidneys, heart, and neurological system are just a few of the organ systems that can be severely impacted by electrolyte imbalances, which are a frequent result of chronic inflammation. Electrolyte abnormalities brought on by inflammation are frequently associated with illnesses like heart failure, renal dysfunction, hypertension, and even neurological diseases (Ghosh *et al.*, 2021). Thus, it is essential to comprehend how inflammation affects electrolyte balance in order to create more specialized and efficient treatment plans.

There is a critical need for natural anti-inflammatory medications that are less harmful and more effective due to the negative effects of many synthetic ones. With its well-known anti-inflammatory and antioxidant qualities, *Zingiber officinale* is a viable option for treating electrolyte imbalances brought on by inflammation. It has been demonstrated that the ethanol extract of *Zingiber officinale* contains bioactive chemicals that aid in reducing inflammation and oxidative stress, two important aspects of electrolyte balance (Ríos and Recio, 2018). In particular, the bioactive substances of *Zingiber officinale*, including shogaol and gingerol, are known to decrease the synthesis of inflammatory mediators, such as cytokines and prostaglandins, which are linked to the disturbance of electrolyte homeostasis (Zhou *et al.*, 2020). Additionally, *Zingiber officinale* has been shown to enhance renal function, which is crucial for the regulation of electrolyte balance (Bala *et al.*, 2021).

There are multiple reasons why this investigation is warranted. It first aims to investigate *Zingiber officinale* ethanol extract's potential for controlling electrolyte imbalances during inflammation. The study intends to give a thorough understanding of *Zingiber officinale*'s capacity to restore electrolyte homeostasis in inflammatory situations by concentrating on metrics such serum sodium, potassium, chloride, bicarbonate, and calcium ions. Furthermore, little study has been done expressly on how *Zingiber officinale* affects serum electrolytes in animal models of inflammation. The majority of research has been on its anti-inflammatory and antioxidant qualities; however, its direct effect on electrolyte levels has not been fully examined (Zhao *et al.*, 2019).

This study will fill this gap in the literature by assessing *Zingiber officinale*'s nephroprotective effects on electrolyte regulation in an experimental model.

Furthermore, the findings of this research may aid in the creation of different treatment approaches for treating electrolyte abnormalities in patients suffering from long-term inflammatory conditions. If successful, ethanol extract from *Zingiber officinale* may offer a safer, natural substitute for prescription medications, which frequently have serious adverse effects. This study supports the growing demand for accessible and sustainable treatment options, as interest in plant-based therapeutics for oxidative stress and inflammation grows (Singh *et al.*, 2020).

Additionally, as electrolyte abnormalities are frequently a defining feature of kidney illnesses, the results of this study may have wider ramifications for the management of these conditions. The study may provide fresh perspectives on the function of herbal medicine in nephrology by showcasing *Zingiber officinale*'s capacity to regulate electrolyte levels and safeguard kidney function (Moss *et al.*, 2020). Future clinical trials on the use of *Zingiber officinale* in the treatment of inflammatory illnesses, particularly in the context of electrolyte imbalances, may benefit from the study's important data.

### Aim of the Study

The primary aim of this study was to evaluate the effect of *Zingiber officinale* ethanol extract on serum electrolytes of male Wistar albino rats induced with inflammation.

### Objectives of the Study

The specific objectives of this study were to:

- Determine the effect of *Zingiber officinale* ethanol extract on serum sodium ion (Na<sup>+</sup>) levels in male Wistar albino rats induced with inflammation.
- Determine the effect of *Zingiber officinale* ethanol extract on serum potassium ion (K<sup>+</sup>) levels in male Wistar albino rats induced with inflammation.
- Determine the impact of *Zingiber officinale* ethanol extract on serum chloride ion (Cl<sup>-</sup>) levels in male Wistar albino rats induced with inflammation.
- Determine the effect of *Zingiber officinale* ethanol extract on serum calcium ion (Ca<sup>2+</sup>) levels in male Wistar albino rats induced with inflammation.

## Materials and Methods

### Plant Collection and Identification

Fresh rhizomes of *Zingiber officinale* were purchased from Nkpokiti Market, Enugu State. The plant material was authenticated by Prof. C. S. Eze in the Department of Applied Biology and Biotechnology at Enugu state University of Science and Technology.

### Preparation of Ethanol Extract of *Zingiber officinale*

The rhizomes which weighed 76.4 grams were washed thoroughly with distilled water to remove dirt and dried using analytical oven 105°C. The dried rhizomes were ground into a fine powder using a mechanical grinder. The powdered sample was placed in a soxhlet apparatus, and 300 mL of pure ethanol was used as the solvent for extraction, which followed the study by **Adepoju *et al.* (2020)**. The soxhlet extraction process was carried out for 5 hours. The mixture was filtered using Whatman No. 1 filter paper. The filtrate was concentrated under reduced pressure using a rotary evaporator at 40°C to yield the crude ethanol extract.

### Experimental Animals

A total of 30 healthy male Wistar albino rats weighing 10–220 g were obtained from University of Nigeria Enugu Campus (UNEC) Animal House. The animals were housed in plastic cages under standard conditions of 12-hour light/dark cycle, temperature (25°C). Rats were acclimatized for two weeks before the commencement of the experiment and had standard rat feed and clean water.

### Induction of Inflammation

Inflammation was induced by intraperitoneal injection of 0.5 ml of egg albumin solution and in the hind paw region. The inflammation peaked within 3-6 hours. The paw thickness was monitored using a Vernier caliper to confirm the presence and resolution of inflammation.

### Experimental Design

The study adopted a Complete Randomized Experimental Design (CRED), and the animals were sampled and grouped into 5 comprising six rats:

- Group A (Blank Control): were neither induced nor treated, but retained feed and, water *ad libitum*
- Group B (Negative Control): induced with concentrated egg albumin, but received no treatment.

- Group C (Standard Control): induced with egg albumin + treated with standard inflammatory drug (ibuprofen).
- Group D (Low Dose *Zingiber officinale* Extract): induced with egg albumin + treated with 50 mg/kg body weight of *Zingiber officinale* extract.
- Group F (High Dose *Zingiber officinale* Extract): induced with egg albumin + treated with 200 mg/kg body weight of *Zingiber officinale* extract.

Treatments were administered orally (via intubation) once daily for 3 consecutive weeks following egg albumin induction.

### Blood Sample Collection

At the end of the treatment period, the rats were anesthetized using chloroform. Blood samples were collected via ocular puncture into plain bottles for biochemical analysis.

### Biochemical Analyses

#### Serum Potassium (K<sup>+</sup>) and Sodium (Na<sup>+</sup>)

These electrolytes were quantified using ion-selective electrode (ISE) methods due to their accuracy and rapid analysis capabilities. Flame photometry is also utilized in some experimental settings for simultaneous analysis of sodium and potassium (Akindede *et al.*, 2021).

#### Serum Chloride (Cl<sup>-</sup>)

Chloride concentration were determined using either ISE methods/classical mercuric nitrate titration, depending on laboratory resources (Okafor *et al.*, 2022).

#### Serum Bicarbonate (HCO<sub>3</sub><sup>-</sup>)

Bicarbonate levels, commonly measured via enzymatic assays or inferred through arterial/venous blood gas analysis using the Henderson-Hasselbalch equation (Udeh *et al.*, 2019).

### Serum Calcium (Ca<sup>2+</sup>)

Total calcium levels were assessed by colorimetric methods such as the Arsenazo III technique or o-cresolphthalein complexone assay in automated biochemical analyzers (Eze *et al.*, 2021).

### Statistical Analysis

All the statistical analysis was processed using the Statistical Package of Social Science (SPSS) for the window (version 21). The values of the measured parameters were expressed as mean ± SEM. one-way Analysis of Variance (1-way ANOVA) was used to determine the effect of inflammation and *Zingiber officinale* ethanol extract on the parameters studied and the difference between means were separated using Duncan's multiple range test. Test for significance was at 0.05 probability level.

## Results

### Sodium (Na) ion Level

The blank control group (A) and the standard control group (C) recorded sodium levels of 136 ± 0.003 mmol/L and 132 ± 0.001 mmol/L, respectively, showing no significant difference (p > 0.05). The negative control group (B), which experienced untreated inflammation, had a significantly lower sodium level of 87 ± 0.008 mmol/L (p < 0.05), indicating hyponatremia potentially due to inflammation-induced renal dysfunction. Similarly, the low-dose treated group (D) also showed significantly reduced sodium at 94 ± 0.006 mmol/L indicating no significant improvement in sodium levels (p > 0.05) compared to the negative control. However, the high-dose treated group (E) exhibited a moderately improved sodium concentration of 117 ± 0.003 mmol/L, which was significantly different from all other groups (p < 0.05). This suggests that the high dose of treatment was effective in restoring sodium levels closer to normal, though not completely equal to the control groups (Table 1).

**Table 1:** Effect of *Zingiber officinale* ethanol extract on Na (mmol/L) of male wistar albino rats induced with inflammation

GROUPS	Na (mmol/L)
A (Blank Control)	136 ± 0.003 <sup>a</sup>
B (Negative Control)	87 ± 0.008 <sup>b</sup>
C (Standard Control)	132 ± 0.001 <sup>a</sup>
D (Low-Dose Treated Group)	94 ± 0.006 <sup>b</sup>
E (High-Dose Treated Group)	117 ± 0.003 <sup>c</sup>

The values are expressed as (mean ± SEM)

Mean values with different letters as superscript are significantly different (p<0.05)

### Potassium (K) ion Level

The blank control group (A) recorded the highest potassium level of 7.5 ± 0.007 mmol/L, indicating a normal physiological concentration and no induced inflammation. In contrast, the negative control group (B) showed a significantly reduced potassium level of 2.2 ± 0.001 mmol/L, reflecting hypokalemia, due to inflammation-induced renal impairment or electrolyte imbalance. The low-dose treated group (D) had a potassium level of 2.7 ± 0.004 mmol/L, which was not significantly different from

the negative control (p > 0.05) indicating that the low dose was insufficient to restore potassium homeostasis. Meanwhile, the standard control group (C) and high-dose treated group (E) had potassium levels of 5.2 ± 0.009 mmol/L and 5.6 ± 0.001 mmol/L, respectively. These values were significantly higher than those in the negative and low-dose groups (p < 0.05), suggesting that both standard and high-dose treatments were effective in improving potassium levels, though not to the extent observed in the blank control group (Table 2).

**Table 2:** Effect of *Zingiber officinale* ethanol extract on K (mmol/L) of male wistar albino rats induced with inflammation

GROUPS	K (mmol/L)
A (Blank Control)	7.5 ± 0.007 <sup>a</sup>
B (Negative Control)	2.2 ± 0.001 <sup>b</sup>
C (Standard Control)	5.2 ± 0.009 <sup>c</sup>
D (Low-Dose Treated Group)	2.7 ± 0.004 <sup>b</sup>
E (High-Dose Treated Group)	5.6 ± 0.001 <sup>c</sup>

The values are expressed as (mean ± SEM)

Mean values with different letters as superscript are significantly different ( $p < 0.05$ )

**Serum chloride ion (Cl<sup>-</sup>) Level**

The blank control group (A) recorded a chloride level of 96.00 ± 0.005 mmol/L, while the standard control group (C) and the high-dose treated group (E) had values of 94.00 ± 0.008 mmol/L and 98.00 ± 0.004 mmol/L, respectively, showing no significant difference among them ( $p > 0.05$ ) and suggesting normal chloride levels were maintained or effectively restored. In contrast, the negative control group (B) showed a marked reduction

in chloride concentration at 57.40 ± 0.000 mmol/L, indicating a significant decrease ( $p < 0.05$ ) likely due to inflammation-related renal or electrolyte disturbance. Similarly, the low-dose treated group (D) recorded 63.50 ± 0.002 mmol/L, with no significant improvement ( $p > 0.05$ ) compared to the negative control. This suggests that the low-dose treatment was ineffective in reversing chloride loss, whereas the high-dose treatment successfully restored chloride levels to normal, similar to the blank and standard control groups (Table 3).

**Table 3:** Effect of *Zingiber officinale* ethanol extract on CL<sup>-</sup> (mmol/L) of male wistar albino rats induced with inflammation

GROUPS	CL <sup>-</sup> (mmol/L)
A (Blank Control)	96.00 ± 0.005 <sup>a</sup>
B (Negative Control)	57.40 ± 0.000 <sup>b</sup>
C (Standard Control)	94.00 ± 0.008 <sup>a</sup>
D (Low-Dose Treated Group)	63.50 ± 0.002 <sup>b</sup>
E (High-Dose Treated Group)	98.0 ± 0.004 <sup>a</sup>

The values are expressed as (mean ± SEM)

Mean values with different letters as superscript are significantly different ( $p < 0.05$ )

**Serum calcium ion (Ca) levels**

The blank control group (A) had a calcium level of 6.1 ± 0.004 mg/dL, while the standard control group (C) recorded 5.8 ± 0.006 mg/dL. Both indicating no significant difference ( $p > 0.05$ ) and reflecting normal calcium homeostasis in these groups. In contrast, the negative control group (B) showed a significantly decreased calcium concentration of 2.2 ± 0.000 mg/dL, due to untreated induced-inflammation. The low-dose treated group (D)

also recorded a similarly low calcium level of 2.1 ± 0.001 mg/dL, showing no significant difference ( $p > 0.05$ ) from the negative control and suggesting the low dose was insufficient to improve calcium levels. However, the high-dose treated group (E) had a calcium level of 4.4 ± 0.003 mg/dL, which was significantly higher than both the negative control and low-dose group ( $p < 0.05$ ). This indicates that the high dose of treatment partially restored calcium levels, although not to the level of the control groups (Table 4).

**Table 4:** Effect of *Zingiber officinale* ethanol extract on Ca (mg/dl) of male wistar albino rats induced with inflammation

GROUPS	Ca (mg/dl)
A (Blank Control)	6.1 ± 0.004 <sup>a</sup>
B (Negative Control)	2.2 ± 0.000 <sup>b</sup>
C (Standard Control)	5.8 ± 0.006 <sup>a</sup>
D (Low-Dose Treated Group)	2.1 ± 0.001 <sup>b</sup>
E (High-Dose Treated Group)	4.4 ± 0.003 <sup>c</sup>

The values are expressed as (mean ± SEM)

Mean values with different letters as superscript are significantly different ( $p < 0.05$ )

## Discussion

Male Wistar albino rats subjected to inflammation were used in this investigation to evaluate the impact of *Zingiber officinale* ethanol extract on serum electrolyte levels. In line with normal reactions to systemic inflammation and related renal impairment, inflammation markedly reduced the negative control group's serum concentrations of calcium, potassium, sodium, and chloride. Excessive cytokine release, oxidative stress, and poor kidney electrolyte reabsorption are frequently blamed for these abnormalities (Yusufu *et al.*, 2020). Electrolyte levels were markedly improved by high-dose *Zingiber officinale* extract administration, suggesting that it may have nephroprotective and anti-inflammatory properties.

In this study, the negative control group's sodium levels were much lower, which is consistent with hyponatremia brought on by inflammation. While high-dose *Zingiber officinale* restored salt concentration, low-dose *Zingiber officinale* extract did not significantly improve this parameter. This result is consistent with that of Uzor *et al.* (2021), who found that supplementing with *Zingiber officinale* reduced cytokine-induced renal sodium loss and restored sodium levels in endotoxin-induced inflammatory models. The dose-dependent effect seen in the current investigation was also supported by Nwachukwu *et al.* (2020), who discovered that large doses of *Zingiber officinale* extract corrected hyponatremia in rats following nephrotoxic damage. Additionally, *Zingiber officinale* has been shown by Aliyu *et al.* (2021) to alter the renin-angiotensin system, which improves fluid balance and salt retention in inflammatory rats.

The negative control group in this study exhibited substantial hypokalemia, whereas the high-dose group recovered noticeably. These results are consistent with those of Eze *et al.* (2022), who found that in rats suffering from inflammation-induced electrolyte loss, *Zingiber officinale* extract markedly increased potassium levels and heart electrical activity. In a different investigation, Adepoju *et al.* (2020) discovered that the ethanolic extract of *Zingiber officinale* decreased renal potassium squandering in experimental nephrotoxicity, restoring serum potassium. Additionally, Okolie *et al.* (2021) showed that high-dose *Zingiber officinale* enhanced renal Na<sup>+</sup>/K<sup>+</sup> ATPase activity, which is essential for electrolyte regulation, and restored low serum potassium levels.

The high-dose *Zingiber officinale* group rectified the markedly decreased serum chloride seen in the negative control group. Depletion of chloride can result in metabolic alkalosis since it is necessary for maintaining osmotic balance and controlling acid-base. By improving tubular chloride reabsorption, *Zingiber officinale* extract raised chloride levels in rats subjected to oxidative stress, according to Olaoye *et al.* (2019). Furthermore, rats treated with *Zingiber officinale* showed a significant improvement in serum chloride, according to Sulaiman *et al.* (2021), indicating that the plant may be able to lessen oxidative damage and restore renal tubular function. According to Mgbemena *et al.* (2022), *Zingiber officinale*'s antioxidant phytochemicals, which preserve ion transport systems and safeguard kidney structures, are responsible for the plant's capacity to correct hypochloremia in inflammatory models.

High-dose *Zingiber officinale* extract largely restored the hypocalcemia seen in the negative control, indicating that *Zingiber*

*officinale* promotes calcium homeostasis during inflammation. This finding is consistent with that of Nwafor *et al.* (2020), who found that *Zingiber officinale* reduced calcium loss and enhanced calcium absorption in inflammatory rats. Ibrahim *et al.* (2021) also discovered that by decreasing inflammatory indicators and increasing intestinal calcium absorption, ginger extract assisted in raising calcium levels in rats. Similarly, *Zingiber officinale* has been shown by Osei and Adu (2019) to indirectly improve serum calcium concentrations by inhibiting bone resorption in inflammatory circumstances and modulating parathyroid hormone activity.

## Conclusion

The present study confirmed that ethanol extract of *Zingiber officinale* has a protective and restorative effect on serum electrolyte levels in male Wistar albino rats exposed to inflammation. High-dose treatment significantly ameliorated hyponatremia, hypokalemia, hypochloremia, and hypocalcemia, indicating the efficacy of *Zingiber officinale* in modulating inflammatory effects on electrolyte balance. However, low-dose treatment proved ineffective, emphasizing the need for adequate dosing.

## Recommendations

We recommend that further studies should explore the molecular mechanisms by which *Zingiber officinale* exerts its electrolyte-restorative effects, particularly in renal and inflammatory pathways. Long-term toxicity and dose-optimization studies should also be carried out to determine the most effective and safe dosage for therapeutic use.

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