**Hypoglycemic Effects Of Ethanol Extract Of Rhizomes Of *Zingiber Officinale* (Ginger)On Some Metabolic Syndrome Indices Of Albino Wistar Rats Fed High-Fat High-Sucrose Diet**

**Christian E. Odo, CHUKWU .O.O**.

Department of Biochemistry, College of Natural Sciences, Micheal Okpara University of Agriculture, PMB 7267, Umudike, Abia State, Nigeria

Email: onyiichuks94@gmail.com

**ABSTRACT**

*Z. officinale* rhizome, known commonly as ginger is extensively used in traditional system of medicine in many countries for the treatment of various disorders. The study was aimed at determining the hypoglycermic effects of the ethanol extract of the rhizomes of *Z. officinale* on some metabolic syndrome indices in albino wistar rats fed high-fat high-sucrose diet. The design consisted of 6 groups. Group 1 received standard feed (vital finisher’s mash) and distilled water, group 2 received high-fat high-sucrose diet only, group 3 received high-fat high-sucrose diet + metformin, groups 4,5 and 6 received high-fat high-sucrose diet + ethanol extract of rhizomes of *Zingiber Officinale* (200, 400 and 800mg/kg body weight respectively). The experiment lasted for 10 weeks. At the end of the experiment, the rats of different groups were sacrificed; body weight and glucose concentration were evaluated using standard methods. Administration with the ethanol extract of *Z. officinale* rhizomes at doses of 200, 400 and 800mg/kg body weight showed significant reduction of body weight and glucose concentration in treated groups observed in the rats of the treated groups. In conclusion, this study reveals that the ethanol extract of the rhizome of *Z. officinale* improved the indices of metabolic syndrome and therefore, justifies its use in the amelioration of metabolic syndrome.

**Keywords:** HFHS diet (high-fat high-sucrose diet), MetS (metabolic syndrome), *Zingiber officinale* (Ginger)

**INTRODUCTION**

Metabolic syndrome including the presence of obesity, insulin resistance and dyslipidaemia that predisposes one to type 2 diabetes mellitus is becoming more prevalent in recent years (Alberti *et al*., 2018; Bergman *et al*., 2018). According to recent estimates, approximately 215 million people worldwide suffer from diabetes and 80–90% of them from type 2 diabetes mellitus (Procopiou and Philippe, 2017). The events of hyperglycaemia and hyperlipidaemia, and their association present major risk factors for the development of diabetic and cardiovascular complications (Salas *et al.,* 2014). To reduce these serious complications and negative outcome of the metabolic syndrome, the control not only of blood glucose but also of lipids is necessary (Moller, 2014). Therefore, new medicinal agents with dual properties on controlling both blood glucose and lipids are in great demand. The currently available therapeutic options such as dietary modification or a combination of synthetic antidiabetic, hypolipidaemic drugs have their own limitations and undesirable side-effects (Salas *et al.,* 2014). Hence, there is an increased demand to search and evaluate traditional approaches for the treatment of metabolic disorders, particularly the use of herbal medicines.

*Z. officinale* commonly known as ginger, a well-known food spice, has been used traditionally in a wide variety of ailments (Afzal *et al.,* 2015; Park *et al.,* 2021). The major chemical constituents of ginger rhizome are essential volatile oils and non-volatile pungent compounds (Govindarajan and Connell, 2021). Low to moderate, but significant blood glucose lowering effect of the juice of *Z. officinale* was observed in both normal and diabetic animals (Sharma and Shukla, 2016). The ethanol extract of *Z. officinale* has also been shown to lower blood glucose in normal rabbits and rats and in alloxan and streptozotocin-induced diabetic rats (Al-Amin *et al*., 2016; Ojewole, 2016). In addition, Singhal *et al* (2021) reported a decrease of blood glucose in normal rats treated with *Z. officinale* rhizomes powder. The anti-obesity actions of ginger extracts were also noticed recently in chemical and in high-fat high-sucrose diet-induced obese mice (Han *et al.,* 2015).

Hence, in the present study, the *in vivo* effects of the hypoglycemic effects of ethanol extract of rhizomes of *Z. officinale* on some metabolic syndrome indices in rats fed high-fat high-sucrose diet was investigated.

**Plant Material and extraction:**

Fresh rhizomes of *Z. officinale* were obtained from a local vegetable market (Ubani) in Umuahia North Local Government Area, Abia State and were authenticated by a taxonomist Mr. Ibe K. Ndukwe of the Herbarium Unit of Forestry and Environmental Management Department of Michael Okpara University of Agriculture, Umudike, Abia State.

Extracts from these rhizomes were prepared according to the Soxhlet method described by Jensen (2017).

**Animals**

A total of 30 adult male albino rats aged 8-10 weeks and weighing 80 to 120g and 21 mice were used for the study. Twenty one mice were used for acute toxicity or lethal dose (LD50) evaluation of the extract while 30 rats were used for the high-fat high-sucrose diet study. The animals were obtained from the Animal House of the Department of Zoology and Environmental Biology, Michael Okpara University of Agriculture, Umudike, housed in Aluminum cages (5 rats per cage) and allowed to acclimatize for two weeks to allow for proper adaptation to their new environment and living conditions before commencement of the study. The experimental rats were fed at liberty with vital finisher’s mash (Vital feed, Nigeria) and clean water but starved for 12 hours prior to the commencement of experiment. All animal experiments were conducted in compliance with international guidelines for care and use of laboratory animals (Orieke *et al*., 2019). The study was conducted in the Department of Biochemistry, Michael Okpara University of Agriculture, Umudike.

**Determination of the Acute Toxicity Study and Lethality of the Ethanol Extract of the Rhizomes of *Z. Officinale***

For the acute toxicity evaluation, the Lorke’s method (2019) was adopted with little modification.

**Experimental Design**

Thirty (30) adult albino rats assigned to 6 groups of 5 rats each were treated according to the order below:

**Group 1:** Normal control

**Group 2:** Negative control (high-fat high-sucrose diet only)

**Group 3:** High-fat high-sucrose diet + metformin **(**100 mg/kg body weight)

**Group 4:** High-fat high-sucrose diet + ethanol extract of the rhizomes of *Z. officinale* **(**200 mg/kg body weight)

**Group 5:** High-fat high-sucrose diet + ethanol extract of the rhizomes of *Z. officinale* **(**400 mg/kg body weight)

**Group 6:** High-fat high-sucrose diet + ethanol extract of the rhizomes of *Z. officinale* **(**800 mg/kg body weight).

Treatment lasted for 10 weeks during which body weights were taken at two weeks intervals from beginning to end of treatments using an electronic balance (DJ-A1000, China).

**Determination of Blood Glucose Concentration**

The experimental animals were tested for fasting blood glucose levels using ACCU-CHEK Active glucometer and test strips supplied by Roche Diagnostics Mannheim, Germany.

**Statistical Analysis**

Data obtained were presented as mean ± standard error of mean and analyzed using oneway Analysis of Variance of SPSS software. The variant mean was separated by least significant difference of the different groups. Significance was accepted at the level of P < 0.05.

**RESULTS AND DISCUSSION**

**Figure 1: Effect of Ethanol Extract of Rhizomes of *Z. officinale* on Bodyweight Changes of Albino Wistar Rats Fed High-Fat High-Sucrose Diet**

The results are presented as mean ± standard deviation (n = 5); bars with different letter superscripts are significantly different (P<0.05).

**Figure 2:** **Effect of Ethanol Extract of Rhizomes of *Z. officinale* on blood glucose concentration levels of Albino Wistar Rats fed High-fat High-sucrose Diet**.

The results are presented as mean ± standard deviation (n = 5); bars with different letter superscripts are significantly different (P<0.05).

This study evaluated the effects of ethanol extract of the rhizomes of *Z. officinale* on some metabolic syndrome indices on albino wistar rats fed high-fat high-sucrose diet. Metabolic syndrome (MetS) is a range of cardiovascular risk factors increasing the development of type 2 diabetes mellitus and cardiovascular diseases. *Z. officinale* commonly known as ‘ginger’ has its origin traced to Asia. It has a lot of medicinal uses as far as herbal medicine is concerned. It has been proven to have anticovulsant, antidiuretic, antiinflammatory, diuretic, antifungal, antihypertensive, antispasmodic, antitumor, and anticancer effects (Agrawal *et al.,* 2021).

The results of the effect of ethanol extract of rhizome of *Z. officinale* on body weight (Figure 1) shows that the groups co-treated with metformin and the extract had significantly lowered body weight gain when compared with the negative control. Metformin is known to act on the hypothalamus, leading to decreased neuropeptide Y and increased pro-opiomelanocortin (Sarda *et al.,* 2017). Metformin can also reduce food intake by ameliorating the leptin and insulin sensitivity (Coll *et al.,* 2020). The low body weight of animals on the groups consuming HFHS diet and metformin maybe due the effect of metformin on the body. The combined effects of various phytochemicals such as flavonoids and phenolics in the extract could be responsible for lowering the body weight in the groups treated with graded doses of the extract. HFHS diet used is a model for induction of MetS in animal model that mimics human feature of the disease (Sharma and Shukla, 2016). This diet leads to increase body weight, dyslipidemia and other features of MetS as demonstrated in this study. The increase in body weight is associated with increment of calorie intake which causes excessive energy to be stored as triglyceride (TG) (Falz-Hassan *et al.,* 2021). It is then stored in the adipose tissue and acts as an energy reservoir leading to accumulation of abdominal adipose fats (Al-min *et al.*, 2016). In HFHS diet, sucrose increases via its ability to stimulate hunger, blocking satiety responses and reducting resting energy expenditure as in overweight and obese subjects (Cusi and Defronzo, 2018). Weight gain observed in the group fed HFHS diet only was driven primarily by increased energy intake from fat and reduced metabolism rate as a consequence of high fructose from sucrose intake induced leptin resistance in rats (Kuate *et al.,* 2015), as well as induction hyperinsulinemia, state which increases the accumulation of fat by activation of lipoprotein lipase of adipocytes (Goossens, 2017). *Z. officinale* is a food fiber and many studies revealed that consumption of dietary fibers is associated to a reduction of body weight (Delzenne and Cani, 2015); by affecting satiety which results in the reduction of dietary intake. These results corroborate those obtained on *Irvingiagabonensis* (Ngondi *et al.,* 2016).

The result of blood glucose concentration showed that the group given the highest doses of the extract had significantly reduced blood glucose concentration compared with other treatments and the group given high-fat high-sucrose diet only (Figure 2). Faizi-Hassan *et al.* (2021) reported that the hypoglycemic property of ethanol extract of rhizomes of *Z. officinale* is due to the presence of phytochemicals. The cause of the potent action of the ethanol extract of rhizomes of *Z. officinale* is not known but maybe ascribed to the synergistic effects of bioconstituents that serve as antioxidant which may have scavenged free radical species generated by the HFHS diet, thus preventing the destruction of pancreatic beta cells and maintain physiological functions of body organs (Muhammad *et al.,* 2013).

**CONCLUSION**

*Z. officinale* used as whole plant supplement in HFHS diet is able to reduce body weight and blood glucose concentration. The ethanol extract of the rhizomes of *Z. officinale* at doses of 200, 400 and 800 mg/kg body weight ameliorated the studied bio-indicators of metabolic syndrome brought about by the high-fat high-sucrose diets and supports the local application of the ethanol extract of the rhizomes of *Z. officinale* in the management of metabolic syndrome and possibly the incorporation of ginger an integral part of our diets.

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