Hypoglycaemic Effects of Dietary Intake of Ripe and Unripe *Lycopersicon esculentum* (Tomatoes) on Streptozotocin-Induced Diabetes Mellitus in Rats

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Abstract: Ripe and unripe tomatoes have been implicated in prevention of chronic diseases such as cancer probably due to their antioxidant, antibiotic, antifungal and anti-inflammatory properties. **Problem statement:** This study was designed to investigate whether ripe and unripe tomatoes will have hypoglycaemic effect in a chronic disease such as diabetes mellitus that has been characterized with hyperglycaemia. **Approach:** Twenty albino Wistar rats were divided into 4 groups (2 control and 2 test groups) of 5 rats each. The normal and diabetic control groups were given citrate buffer (intraperitoneally) and normal rat chow and 65 mg kg^{-1} streptozotocin (intraperitoneally) and normal rat chow respectively. The test groups were given 65 mg kg^{-1} streptozotocin via intraperitoneal route and either a mixture of ripe or unripe tomato and normal rat chow. In all groups, the blood samples were obtained at the tail vein of the animals and the fasting blood glucose level were monitored and determined on the 1st, 3rd and 14th day of consumption of different feed combinations. **Results:** There was significant difference in blood glucose level in animals fed on ripe and unripe *Lycopersicon esculentum* (tomato) compared to the normal and diabetic control groups on the 3rd and 14th day without significant difference on the 1st day. **Conclusion:** Both high-lycopene ripe tomato and high-tomatine unripe tomato have hypoglycaemic effect in diabetic mellitus at short period of dietary intake therefore this suggest that consumers may benefit by not only eating high-lycopene ripe tomatoes, but also high-tomatine unripe tomatoes.

Key words: Hypoglycaemia, *Lycopersicon esculentum*, tomato, diabetes mellitus

INTRODUCTION

Diabetes mellitus is a metabolic disorder that is implicated by oxidative stress which induces insulin resistance in the peripheral tissues and impairs insulin secretion from pancreatic β-cells (Oberley, 1988; Paolisso and Giugliano, 1996; Ceriello and Mortz, 2004; Wang *et al*., 2006). Carotenoids, a group of fat-soluble pigments present in many foods, particularly fruits and vegetables, have abundant conjugated double bonds to interrupt the chain reaction of lipid oxidation and to quench peroxyl radicals (Di Mascio *et al*., 1989; El-Agamey *et al*., 2004). Apart from foods, some major carotenoids are found in the serum or tissues and these are α-carotene, β-carotene, β-cryptoxanthin, lutein/zeaxanthin and lycopene. Among these major carotenoids detected in human tissues or serum, lycopene has shown the most powerful antioxidant properties. Dietary intake of lycopene predominantly comes from the consumption of tomatoes.

In addition, the red color found in ripe tomatoes is due to lycopene; therefore, the redder the tomato, the higher lycopene content. Thus, unripe tomatoes are relatively low in lycopene.

Moreover, the unripe tomatoes have been shown to contain glycoalkaloids, especially tomatine and other phytochemical constituents.

Furthermore, consumption of carotenoid rich food like tomatoes has been associated with several health benefits including their ability to prevent oxidative damage that result to diabetes mellitus (Olmedilla *et al*., 1997).

However, lycopene is not the only constituent of tomatoes that has been reported to prevent occurrence of chronic diseases such as breast, prostate, lung, stomach, colorectal, oral, oesophageal, pancreatic, bladder and cervical cancers, coronary heart disease,

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cataract, age-related muscular degeneration (Giovannucci, 1999; Rao and Agarwal, 1999; Mohanty *et al*., 2002; Khachik *et al*., 2002; Rao, 2002; Sesso *et al*., 2004), tomatine in unripe tomatoes has also been reported to have antifungal, anti-inflammatory, antibacterial and antiviral properties (Fontaine *et al*., 1948; Filderman and Kovacs, 1969; Friedman *et al*., 2009) and inhibit the growth of cancerous cells in the breast, liver, stomach, colon (Friedman *et al*., 2009) with paucity of reports on hypoglycaemic properties.

Interestingly, over the years, dietary consumption of vegetables and fruits (tomatoes) rich in carotenoids has been recommended for diabetic patients to be a protective factor against hyperglycemia (Suzuki *et al*., 2002; Bantle *et al*., 2006; Rao and Rao, 2007; Ali and Agha, 2009) but dietary consumption of high-tomatine unripe tomatoes (*Lycopersicon esculentum*) has not been recommended for diabetes mellitus. Therefore, the aim of this study was to investigate the hypoglycaemic effects of both high-lycopene ripe tomato and high-tomatine unripe tomatoes on streptozotocin-induced diabetes mellitus using rat as a case study.

MATERIALS AND METHODS

Plants: Some quantities of ripe and unripe *Lycopersicon esculentum* (tomato) were obtained from Songhai Farm, a government subsidiary, Old Nekede, Owerri, Imo State, Nigeria. Both ripe and unripe *Lycopersicon esculentum* were properly washed and grinded into aqueous form using the manual grinding machine. They were put in different air tight containers and refrigerated. As 80 g of rat chow was weighed and 10% of the 80 g of rat chow was mixed properly with 10% of prepared *Lycopersicon esculentum* (ripe and unripe) to feed the test groups.

Animals: Albino wistar strain rats with body weight of 100-150 g were used in this study. The animals were obtained from the animal house of the Faculty of Basic Medical Science, University of Nigeria, Nsukka, Nigeria. The animals were kept in cages with suitable temperature, humidity, water and normal rat chow for 2 weeks to acclimatize.

Induction of diabetes mellitus: The animals were weighed and injected via intraperitoneal route, 65 mg kg^{-1} of streptozotocin (Sigma) dissolved in citrate buffer (0.01 M, pH 4.5).

Assessment of blood glucose level: Diabetes Mellitus was confirmed after 72 h of streptozotocin injection by testing the fasting blood glucose levels using glucometer and glucose test strip. The accuracy of the test result was confirmed by the use of glucose test kit.

Experimental procedure: This work was carried out on 4 groups of rats which comprises of 2 control groups (normal and diabetic controls) and 2 test groups; each group contained 5 rats and was placed in different cages for proper identification.

Group I-normal control: The animals in this group were given citrate buffer via intraperitoneal route and they were fed on normal rat chow and water *ad libitum*.

Group II-diabetic control: The animals were injected intraperitoneally with 65 mg kg^{-1} of streptozotocin to induce diabetes mellitus. Also, the animals were fed on normal rat chow and water *ad libitum*.

Group III-diabetic rats fed on ripe *Lycopersicon esculentum* and normal rat chow: Each animal in this group was injected (intraperitoneally) with 65 mg kg^{-1} of streptozotocin. The animals were fed on mixture of 10% of prepared ripe *Lycopersicon esculentum* and 10% of 80 g of normal rat chow and water *ad libitum*.

Group IV-diabetic rats fed on unripe *Lycopersicon esculentum* and normal rat chow: Also, each animal was treated (intraperitoneally) with 65 mg kg^{-1} of streptozotocin and the animals were fed on mixture of 10% of prepared unripe *Lycopersicon esculentum* and 10% of 80 g of normal rat chow and water *ad libitum*.

In all groups, the blood samples were obtained at the tail vein of the animals and the fasting blood glucose level were monitored and determined via glucometer on the 1st, 3rd and 14th day of consumption of different feed combinations

RESULTS

The results obtained were presented as mean ± SEM and analyzed using Analysis Of Variance (ANOVA) with post-hoc test (LSD). The results were considered significant at $p < 0.05$.

Effects of normal saline and normal rat chow: The results in the Table 1 showed that citrate buffer and normal rat chow have no effect on fasting blood glucose in non-diabetic and diabetic rats in normal (Group I) and diabetic (Group II) controls respectively.

Effects of ripe and unripe *Lycopersicon esculentum* on 1st day of treatment: As summarized in the Table 1, there was no significant difference in fasting blood glucose levels in the test groups when compared with the diabetic control group (200.00±11.80 mg dL^{-1}) on the 1st day of the experiment.

Table 1: The fasting blood glucose levels on the 1st, 3rd and 14th day in non-diabetic rats fed on normal rat chow and diabetic rats fed on normal rat chow, ripe and unripe *Lycopersicon esculentum* (Tomato) (n = 5)

Day	Group I-normal control (mg dL^{-1})	Group II-diabetic control (mg dL^{-1})	Group III-diabetic rats fed on ripe tomato (mg dL^{-1})	Group IV-diabetic rats fed on unripe tomato (mg dL^{-1})
1st	103.50±5.10	200.00±11.80*	201.00±16.32*	210.00±23.52*
3rd	104.00±3.75	194.27±19.97*	151.20±10.10***	153.10±11.03***
14th	106.00±6.10	198.00±8.40*	108.80±5.20**	108.40±3.94**

*: Significantly different from normal control group (p<0.05); **: Significantly different from diabetic control group; ***: Significantly different from normal and diabetic control groups. Values are mean ± SEM

Effects of ripe and unripe *Lycopersicon esculentum* on 3rd day of treatment: Also, from the Table 1, there was significant difference in fasting blood glucose level in animals fed on ripe *Lycopersicon esculentum* (151.20±10.10 mg dL^{-1}) and animals fed on unripe *Lycopersicon esculentum* (153.10±11.03 mg dL^{-1}) compared to the values in normal (104.00±3.75 mg dL^{-1}) and diabetic (194.27±19.97 mg dL^{-1}) control groups.

Effects of ripe and unripe *Lycopersicon esculentum* on 14th day of treatment: On the 14th day as presented in the Table 1, there was significant decrease in fasting blood glucose level in animals fed on ripe *Lycopersicon esculentum* (108.80±5.20 mg dL^{-1}) compared to the diabetic control group (198.00±8.40 mg dL^{-1})

Also, there was significant decrease in fasting blood glucose level in animals fed on unripe *Lycopersicon esculentum* (108.40±3.94 mg dL^{-1}) compared to the diabetic control group (198.00±8.40 mg dL^{-1}).

DISCUSSION

The hypoglycaemic effect of ripe and unripe tomatoes on streptozotocin-induced diabetes mellitus was examined in this study. The normal control group has normal fasting blood glucose level while the diabetic control group has sustained hyperglycaemia throughout the experiment, thus this showed that normal rat chow and citrate buffer have no effects on the fasting blood glucose levels. In other words, it has been revealed in this study that the animals that were confirmed diabetic without dietary intake of either ripe or unripe tomato has sustained hyperglycaemia throughout the experimental duration while on the other hand, diabetic animals with dietary intake of either ripe or unripe tomato has hypoglycaemia at the 3rd and 14th day (the last day of the experimental duration). The ripe tomatoes significantly reduced the fasting blood glucose level in diabetic rats at 3rd and 14th days compared to diabetic control group (Group II), probably due to their phytochemical constituents, especially carotenoids and chromium which have been reported to have effects on glucose metabolism and possibly

insulin secretion (Anderson, 2000; Head and Chowka, 2003; Ylonen *et al*., 2003; Jain *et al*., 2007). In addition, it has been concluded in some studies that intake of carotenoid rich tomato protect against hyperglycaemia in diabetes mellitus (Suzuki *et al*., 2002; Ali and Agha, 2009; Ylonen *et al*., 2003).

Also, it has been reported that unripe tomatoes inhibit cancerous growth in the breast, liver, stomach, colon probably due to the presence of glycoalkaloids, especially tomatine which has antifungal, anti-inflammatory, antibacterial and antiviral properties (Friedman *et al*., 2009). In this study, unripe tomatoes have significantly reduced blood glucose level as in ripe tomatoes probably due to the presence of large amount of glycoalkaloids such as tomatine, dehydrotomatine, tomatidine. The process by which unripe tomatoes caused hypoglycaemia at 3rd and 14th days in diabetic rats as ripe tomatoes is unknown yet but it may be due to its phytochemical constituents especially tomatine.

Furthermore, the ripe tomatoes slightly decreased the blood glucose levels than the unripe tomatoes but the level of the decrease was not so much therefore it is not unreasonable to suggest that unripe tomatoes are effective like ripe tomatoes in reducing blood glucose level (hypoglycaemia) in diabetes mellitus and contribute to the maintenance of good health.

CONCLUSION

Conclusively, it is advisable that consumers may benefit by not only eating high-lycopene ripe tomatoes, but also high-tomatine unripe tomatoes.

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