ACTA SCIENTIFIC NUTRITIONAL HEALTH (ISSN:2582-1423)

Volume 4 Issue 3 March 2020

Research Article

Hypolipidaemic and Antidiabetic Potency of *Allium cepa* (Onions) Bulb in Alloxan-Induced Diabetic Rats

Augustine I Airaodion[1]*, Ime U Akaninyene[2], Kenneth O Ngwogu[3], John A Ekenjoku[4] and Ada C Ngwogu[5]

[1]*Department of Biochemistry, Federal University of Technology, Owerri, Imo State, Nigeria*

[2]*Department of Physiology, Arthur Jarvis University, Akpabuyo, Cross-River State, Nigeria*

[3]*Department of Pathology, Abia State University, Uturu, Nigeria*

[4]*Department of Pharmacology and Therapeutics, Abia State University, Uturu, Nigeria*

[5]*Department of Microbiology, Abia State University, Uturu, Nigeria*

***Corresponding Author:** Augustine I Airaodion, Department of Biochemistry, Federal University of Technology Owerri, Imo State, Nigeria.

DOI: 10.31080/ASNH.2020.04.0648

Received: February 05, 2020

Published: February 20, 2020

Abstract

The aim of this study is to evaluate the hypolipidaemic and antidiabetic potency of *Allium cepa* bulb in alloxan-induced diabetic rats. To achieve this, fresh onion bulbs were purchased from a local market in Owerri, Nigeria and the juice extracted. Thirty-six male albino rats were induced intraperitoneally with alloxan. The rats were grouped into six groups of six animals per group: Group A was not induced with alloxan and untreated, group B animals were induced but not treated, group C animals were treated with glibenclaimide, group D, E and F animals were induced and treated with 1, 2 and 3 mL/100g body weight of *A. cepa* juice respectively. The administration was via oral route for 14 days. The animal's blood sugar levels were determined using glucometer. The lipid profile parameters were determined using standard methods. The animals administered with 1, 2 and 3 mL/100g bodyweight of A. cepa showed significant decrease ($P < 0.05$) in blood sugar level compared to the untreated animals. The decrease in the blood glucose level of the animals following the administration of the juice suggested that the plant possesses antidiabetic effects. The juice of *A. cepa* produces hypolipidaemic effect and this is evident as there were significant decrease in plasma total cholesterol, triglycerides, LDL-cholesterol and an increase in HDL-cholesterol in the treated groups compared to the untreated group. This is an indication that *A. cepa* bulb possessed hypolipidaemic and antidiabetic potency in alloxan-induced diabetic rats.

Keywords: *Allium cepa* Bulb; Alloxan-Induced Diabetes; Fasting Blood Sugar; Lipid Profile

Introduction

Onion (*Allium cepa* L.) is the most widely cultivated species of the genus Allium [1]. The portion of the plant commonly used is the bulb, which is utilized as a food ingredient to give flavour and aroma to a great variety of dishes. Onion is a good source of several phytonutrients as flavonoids, fructooligosaccharides (FOS), and thiosulfinates and other sulfur compounds, recognized as important elements of the Mediterranean diet [2]. In fact, onions contain high levels of phenolic compounds, which have antioxidant properties besides beneficial effects against different degenerative pathologies (cardiovascular and neurological diseases, dysfunctions based on oxidative stress) [3].

Flavonoid is the main phenolic compound in onions, which can be classified to different subclasses (flavones, flavanones, flavonols, isoflavones, flavanonols, flavanols, chalcones, and anthocyanins) on the basis of the degree of unsaturation and the degree of oxidation of the central ring. Flavonoids subclasses can be further differentiated on the basis of the number and nature of substituent groups attached to the rings [4].

Figure 1: *Allium cepa* Bulb.

Flavonols are the most abundant in onions, present as their glycosides, that is, quercetin and kaempferol [5,6], in higher concentration (280 - 400 mg/kg) than other vegetables (i.e., 100 mg/kg in broccoli, 50 mg/kg in apple) [7]. Anthocyanins, belonging to anthocyanidins, are mainly present in red onions (250 mg/kg), besides having a composition rich in flavonols as yellow onions [7]. Fructooligosaccharides (FOS) represent another source of phyto-

chemicals in onions bulbs. They are mainly inulin, kestose, nystose, and fructofuranosylnystose. The health benefits of these carbohydrates have been widely reported in the past years due to their prebiotic effect [8].

In onions, sulfur compounds are responsible for typical odour and flavour and are also active antimicrobial agents [9]; hence, onions may be used as natural preservatives to control microbial growth [10]. They have also protective effects against cardiovascular diseases. The precursors of sulfur-containing compounds are S-alk(en)yl-L-cysteine sulfoxides (ACSOs, i.e., methiin, propiin, and isoalliin) which are hydrolysed by means of alliinase enzyme into pyruvate, ammonia, and a mixture of both volatile and nonvolatile sulfur compounds [11], after the breakage of the tissue caused by cutting, mastication, and cooking.

The concentration of pyruvate produced by alliinase activity allows assessing the pungency of onions [12,13]. The main flavour compounds are generated by spontaneous reactions of the sulfenic acids which latter undergo rearrangement to form a mixture of sulfur-containing compounds (S-compounds) including thiosulfinates, thiosulfonates, and mono-, di-, and trisulfides and specific compounds such as thiopropanal S-oxide, the lachrymatory or tear factor, all responsible for the typical flavour of onions [3].

The bioaccumulation of organosulfur compounds in onions depends on different factors but especially on the sulfur-based fertilization, the environment, and the genotype of the cultivars [14-16]. Similarly, other compounds such as organic acids and sugars can contribute to the sensory profile of onions. Thus, organic acids influence the acidity and pH of the onion juice at different degrees; the soluble sugars influence the sweetness of onions and hence the acceptability of this vegetable by consumers. In fact, there is increasing interest in the role that some nonstructural carbohydrates play in the taste preference [17].

Diabetes has been reported to be a complex metabolic disorder associated with developing insulin resistance, impaired insulin signaling and β-cell dysfunction, abnormal glucose and lipid metabolism, sub-clinical inflammation and increased oxidative stress. These metabolic disorders has been reported to lead to long-term pathogenic situations including micro- and macro-vascular complications, neuropathy, retinopathy, nephropathy, and a consequent decrease in quality of life and an increase in the rate of mortality [18]. Among the various risk factors underlining the incidence and progression of diabetes, diet has been reported to be the main modifiable factor. Both experimental and epidemiological evidences have proved that the consumption of plant materials rich in variety of phenolic compounds and exhibits high antioxidant potential could have beneficial relationship with the incidence and prevalence of diabetes [19]. Dietary control remains one of the most effective methods in preventing and managing degenerative diseases like diabetes and cardiovascular diseases. Although various plants have been used in traditional medicine to treat diabetes in Nigeria, much still remains to be done scientifically to confirm the potency of these herbal drugs. This study therefore, sought to evaluate the hypolipidaemic and antidiabetic potency of *A. cepa* bulb in alloxan-induced diabetic rats.

Materials and Methods

Collection and extraction of plant material

Fresh onion bulbs were purchased from a local market in Owerri, Imo State, Nigeria and were identified by a botanist. They were cut into small pieces and mashed in a laboratory with a mortar and pestle, and the fluid squeezed out of the resultant slurry on daily basis. The extracted juice was administered to the rats.

Experimental animals

A total of 36 male albino rats with body weight ranging from 120 to 150 g were used for this study. They were acclimatized for 14 days to Laboratory condition. They were kept in plastic cages and fed with commercial rat chow and supplied with water *ad libitum.* The rats were used in accordance with NIH Guide for the care and use of laboratory animals; NIPRD Standard Operation Procedures (SOPs). After the acclimatization period, the rats were injected with alloxan monohydrate dissolved in sterile normal saline in a dose of 150 mg/kg body weight intraperitoneally [20]. After 72 hours of the injection, rats with fasting blood glucose (FBG) at or above 126 mg/dL. (7.0 mmol/L) were considered diabetic.

Grouping of animals

The animals were randomly divided into six groups of six animals each. They were grouped and treated as follows:

- Group A: Normal control (non-diabetic rats)
- Group B: Negative control (diabetic without treatment)
- Group C: Positive control (diabetic + Glibenclamide)
- Group D: Diabetic + 1 mL/100g body weight of *A. cepa* juice
- Group E: Diabetic + 2 mL/100g body weight of *A. cepa* juice
- Group F: Diabetic + 3 mL/100g body weight of *A. cepa* juice.

N.B: Glibenclamide is a standard drug for the management of diabetes.

After fourteen days of treatment, the rats were sacrificed after an overnight fasted under diethyl ether as anesthesia. Blood samples were collected via cardiac puncture.

Determination of fasting blood sugar

The fasting blood sugar of animals was determined three times in the course of this investigation. It was first determined prior to the induction of diabetes by alloxan administration. Secondly, after the induction of diabetes by alloxan administration and lastly, after fourteen (14) days of respective treatment. The blood glucose level were taken by sterilizing the tails of the animals with 10% alcohol, and cutting the tails using scissors then allowing the blood to touch the test strip which was inserted into a calibrated glucose meter (One touch Glucometer, Acon Laboratory INC. San Diego, USA) according to the methods described by Airaodion., *et al.* [21]. This gave direct reading after 5 seconds in mg/dL.

Determination of lipids

Lipids were extracted and determined according to previously described methods [22,23].

Statistical analysis

Data were subjected to analysis of variance using Graph Pad Prism. Results were presented as Mean ± Standard Error of the Mean (SEM). One way analysis of variance (ANOVA) was used for comparison of the means followed by Tukey's post hoc analysis. Differences between means were considered to be significant at $P < 0.05$.

Results

The results of the effect of *A. cepa* bulb on fasting blood sugar and lipid profile are presented in figures 2-10.

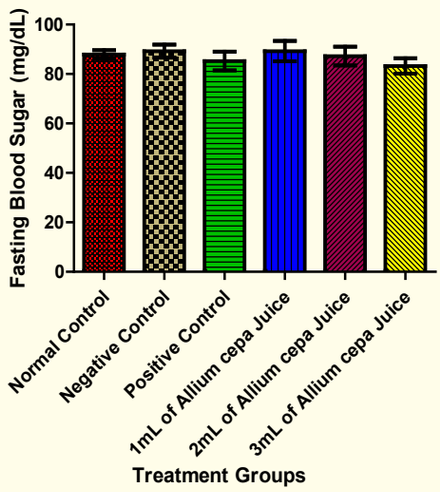

Figure 2: Fasting Blood Sugar of Animals prior to Diabetes Induction. Results are presented as mean ± SEM with n = 6.

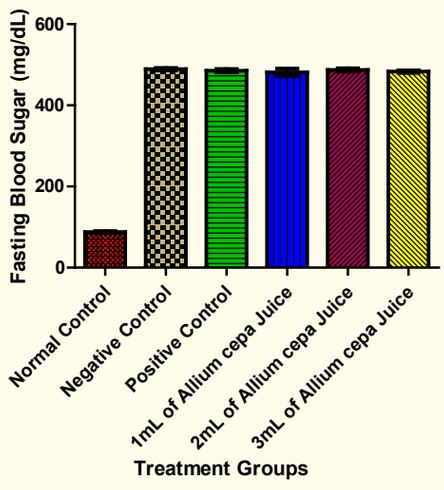

Figure 3: Fasting Blood Sugar of Animals after Diabetes Induction by Alloxan Administration.

Results are presented as mean ± SEM with n = 6.

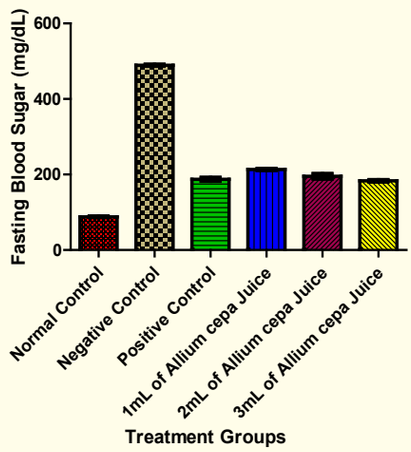

Figure 4: Effect of different Doses of *A. cepa* Juice on Fasting Blood Sugar of Animals after 14 Days of Treatment.

Results are presented as mean ± SEM with n = 6.

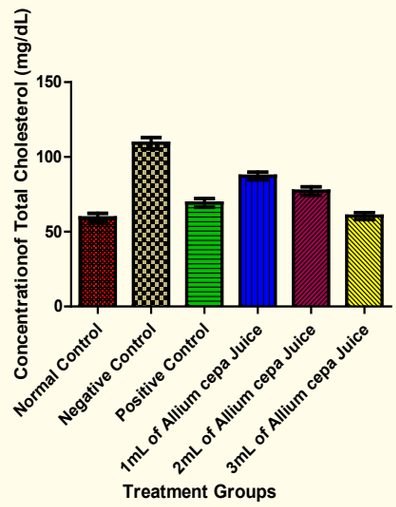

Figure 5: Effect of different Doses of *A. cepa* Juice on Total Cholesterol Concentration of Animals after 14 Days of Treatment.

Results are presented as mean ± SEM with n = 6.

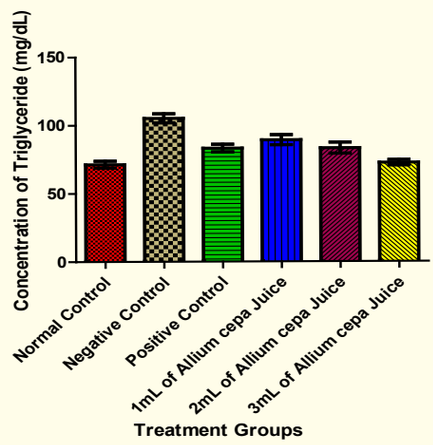

Figure 6: Effect of different Doses of *A. cepa* Juice on Triglyceride Concentration of Animals after 14 Days of Treatment.

Results are presented as mean ± SEM with n = 6.

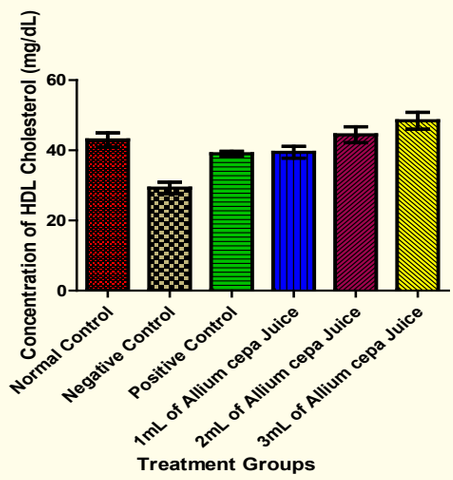

Figure 7: Effect of different Doses of *A. cepa* Juice on HDL-Cholesterol of Animals after 14 Days of Treatment.

Results are presented as mean ± SEM with n = 6.

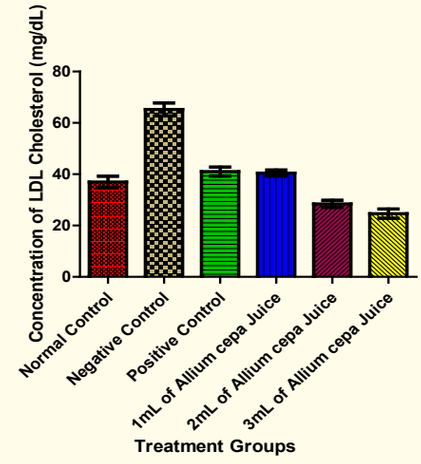

Figure 8: Effect of different Doses of *A. cepa* Juice on HDL-Cholesterol of Animals after 14 Days of Treatment.

Results are presented as mean ± SEM with n = 6.

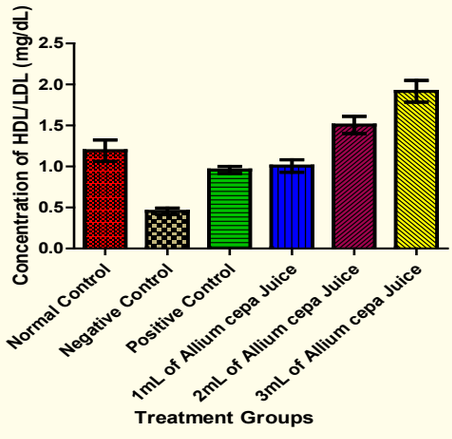

Figure 9: Effect of different Doses of *A. cepa* Juice on HDL/LDL of Animals after 14 Days of Treatment.

Results are presented as mean ± SEM with n = 6.

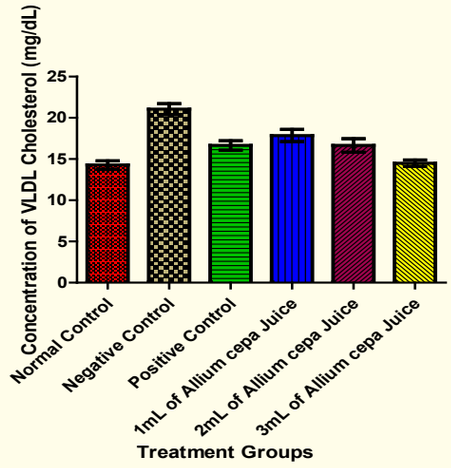

Figure 10: Effect of different Doses of *A. cepa* Juice on VLDL-Cholesterol of Animals after 14 Days of Treatment.

Results are presented as mean ± SEM with n = 6.

Discussion

In this study, diabetes mellitus was induced by exposure of animals to alloxan at a dosage of 140 mg/kg of body weight via intraperitoneal route. This dosage induced diabetes mellitus in the treated rats 72 hours after exposure. Alloxan has been reported to induce diabetes mellitus by selectively destroying beta cells of the pancreas which have been reported to be involved in the synthesis, storage, and release of insulin which is a peptide hormone that regulate carbohydrate, protein, and lipid metabolism [24].

In this study, no significant difference was observed in the fasting blood sugar of all the animals before induction of diabetes (Figure 2). After the induction of diabetes following the administration of alloxan, a significant elevation was observed in the fasting blood sugar of all the treatment groups when compared with the normal control group at $P < 0.05$ (Figure 3). In the normal control group, the pancreatic beta cells which produce insulin are intact and unaffected. Contrarily, alloxan might have destroyed these pancreatic beta cells in treated animals (groups B to F). Therefore, animals exposed to alloxan no longer have functional pancreatic beta cells and might have lost the ability to produce insulin, a hormone required for glucose absorption [25].

At the completion of fourteen days treatment, animals treated with different dosages of *A. cepa* juice had significantly lowered fasting blood sugar when compared with diabetic untreated group (negative control group) as presented in figure 4. This might be an indication that *A. cepa* juice may have an extrapancreatic antihyperglycemic mechanism of action. This is in agreement with the findings of Airaodion., *et al.* [21] on the effect of oral intake of African locust bean on fasting blood sugar and lipid profile of albino rats. It also corresponds with another investigation of Airaodion., *et al.* [26] where they reported the effect of methanolic extract of Corchorus olitorius bulb on hypoglycemic and hypolipidaemic activities in albino rats. Several extracts of different plants have also been reported to have an antihyperglycemic as well as insulin-stim-

ulatory effect [27-30]. Most of the plants extracts with hypoglycemic activities have been found to contain secondary metabolites such as glycosides, alkaloid and flavonoids [31-33]. It is worthy of note that animals treated with 3 mL/100g body weight of *A. cepa* juice reduced blood glucose as much as glibenclamide, a standard diabetic drug. This is suggestive that 3 mL/100g body weight of *A. cepa* bulb juice will yield similar result as glibenclamide in the treatment of diabetes. Glibenclamide has been reported to be a product of chemicals with adverse health effect, thus it is advisable to use *A. cepa* bulb to yield the similar effect with little or no side effect instead of glibenclamide. In the same vein, the juice was able to neutralize the effect of alloxan-induced diabetes in animals as no significant difference ($P < 0.05$) was observed when the fasting blood sugar of animals treated with 3 mL/100g body weight of *A. cepa* bulb juice when compared with the undiabetic animals (normal control) after fourteen days of treatment.

Investigation into the chemical composition and antioxidant properties of *A. cepa* bulb has shown that they contain secondary metabolites such as flavonoids, alkaloids, glycoside, and phenolic compounds as well as possesses remarkable antioxidant activity [34]. These metabolites might be responsible for the hypoglycemic effect of *A. cepa* bulb observed in this present study. The fasting blood sugar reducing effect of *A. cepa* bulb could also an indication that it possesses antidiabetic properties which could control hyperglycemia. It has been reported that one of the approaches in the treatment of early stage of diabetes is to decrease postprandial hyperglycemia [21,26]. This is done by slowing down the absorption of glucose through the inhibition of the carbohydrate-hydrolyzing enzymes, α-amylase and α-glucosidase, in the digestive tract [26]. Consequently, inhibitors of these enzymes cause a decline in the rate of glucose absorption and thus blunting the post-prandial plasma glucose increase [35]. Based on these investigations, it could be suggested that *A. cepa* bulb may inhibit platelet aggregation and enhance vasodilatation, exerting a vital protective role in the prevention of the development and progression of vascular complications caused by the hyperglycemic state. In fact, researches have shown that polyphenolic compounds present in some plant extracts has the ability to inhibit the process of thrombus formation [36,37].

Apart from the regulation of sugar in the body, insulin has been reported to have a crucial function in the metabolism of lipid. Insulin deficiency, as observed in diabetes mellitus, is related to hypercholesterolemia and hypertriglyceridemia, which occur in experimental diabetic rats [38-40]. Hypercholesterolemia has been reported to result in a relative molecular ordering of the residual phospholipids, resulting in a decrease in membrane fluidity [41]. Accumulation of triglycerides is one of the leading risk factors in coronary heart disease (CHD). Lipid and lipoprotein abnormalities play an important role in the pathogenesis and progression of several disease conditions [42].

From the result of this present study, total cholesterol and triglycerides levels were observed to have reduced significantly when diabetic animals treated with glibenclamide and varying dosages of *A. cepa* juice were compared with those of the negative control group (diabetic but untreated animals) at $P < 0.05$ (Figures 5 and 6 respectively). The similar result obtained for glibenclamide and *A. cepa* bulb could be an indication that *A. cepa* bulb possesses the potential in preventing the progression of CHD. This potential might have resulted from its high phytochemical content and antioxidant potential reported by Liguori., *et al.* [34]. Despite the availability of known anti-diabetic medications, remedies from medicinal plants are used with increasing success to treat this disease and manage its complications better [26,43]. Furthermore, it has been suggested that plant drugs and herbal formulations are less toxic and are free from side-effects when compared with synthetic drugs, leading to an increasing preference for herbal remedies over synthetic drugs [44-48]. Increased results of therapeutic effectiveness of herbal medicines could have influenced the interest of world health organization (WHO) in hypoglycemic agents of plant origin used in the traditional treatment of diabetes [49].

Hypertriglyceridaemia has been reported in diabetic animals [26,50]. This was observed to be due to elevated absorption and formation of triglycerides in the form of chylomicrons sequel to exogenous consumption of diet rich in fat or through elevated endogenous production of triglyceride-enriched hepatic VLDL-cholesterol and decreased triglyceride uptake in peripheral tissues [26,27]. The effect of *A. cepa* bulb observed in this study might be suggestive that *A. cepa* bulb have the propensity to reduce the absorption and formation of triglycerides in the form of chylomicrons. Hypercholesterolaemia has also been reported in diabetic animals [21,50]. This was associated to the elevated dietary cholesterol absorption from the small intestine sequel to the intake of high fat diet in a diabetic state [27].

However, the concentrations of serum triglyceride, VLDL-cholesterol and total cholesterol were significantly lowered in animals treated with varying doses of *A. cepa* juice when compared with those of the negative control group (diabetic but untreated animals) in the present study. Moreover, it can be conjectured that the lipid lowering effects of *A. cepa* bulb could be due to the inhibition of hepatic cholesterol, triglyceride and possibly fatty acid synthesis by the phenolic constituents of *A. cepa* bulb [27].

Hypertriglyceridaemia is a predictor of high blood pressure [51]. In the peripheral vascular system, endothelial cells rely on lipoproteins for the transfer of neutral sterols at this site. Although free cholesterol is transferred to HDL-cholesterol particles through the functioning of a designated HDL-cholesterol receptor, lecithin cholesterol acyl transferase (LCAT) serves to maintain the concentration toward the HDL core and preserve the hydrophobic nature that facilitates the transfer. Esterification of cholesterol produces cholesterol ester (CE), which is concentrated in HDL core, and may be transferred by cholesterol ester transfer protein (CETP) in the plasma compartment to apo-B containing lipoproteins in exchange for triglyceride. Increased CETP activity would suggest an enrichment of apo-B lipoproteins in plasma, while simultaneously de-

creasing HDL-cholesterol, and has generally been considered pro-atherogenic [21,52]. This probably explains why *A. cepa* bulb may lead to a reduction in the risk of developing heart diseases since a high HDL-cholesterol/LDL-cholesterol ratio has been shown to be beneficial and is indicative of a lower risk of cardiovascular diseases [27,53].

HDL and LDL are two of the four main groups of plasma lipoproteins that are involved in lipid metabolism and the exchange of cholesterol, cholesterol ester and triglycerides between tissues [54,55]. Several researches have reported an inverse relationship between plasma HDL-cholesterol levels and risk of cardiovascular disease, implying that factors attributed with HDL-cholesterol protects against atherosclerosis [27,33]. Some of these factors appear to have antioxidant and anti-inflammatory effects which may obviate processes that initiate atherogenesis [56,57].

Epidemiological studies have also shown that increased levels of total cholesterol and/or LDL-cholesterol in the blood are serious risk factors for coronary heart disease [33,58]. Most extra-hepatic tissues, although having a requirement for cholesterol, have low activity of the cholesterol biosynthetic pathway. Their cholesterol requirements are supplied by LDL, which is internalized by receptor-mediated endocytosis [27]. A major function of HDL-cholesterol is to enhance reverse cholesterol transport by scavenging excess cholesterol from peripheral tissues followed by esterification through lecithin: cholesterol acyltransferase and delivering it to the liver and steroidogenic organs for subsequent synthesis of bile acids and lipoproteins and eventual elimination from the body [59,60]. This role of HDL-cholesterol has been reported to be responsible for its atheroprotective properties [21,33]. HDL-cholesterol also regulates the exchange of proteins and lipids between various lipoproteins [26,27].

In addition, HDL-cholesterol provides the protein components required to activate lipoprotein lipase which releases fatty acids that can be oxidized by the ß-oxidation pathway to release energy [54,55]. Most importantly, HDL-cholesterol can reduce the oxidation of LDL-cholesterol and the atherogenic effects of oxidized LDL-cholesterol by virtue of its antioxidant property [21,60]. LDL is a lipoprotein that transports cholesterol and triglyceride from the liver to peripheral tissues. It enables fat and cholesterol to move within the water-blood solution of the blood stream [33]. LDL is often called bad cholesterol; hence low levels are beneficial [21,26].

Interestingly, the administration of *A. cepa* bulb in varying dosage in this study caused a significant increase in the serum level of HDL-cholesterol when compared with the negative control animals (diabetic but untreated animals) (Figure 7) at $P < 0.05$. HDL-cholesterol is usually referred to as the 'good cholesterol' [22]. Again, *A. cepa* bulb administration significantly decreased the concentration of LDL-cholesterol (bad cholesterol) when compared with that of the negative control group (diabetic but untreated animals) at $P < 0.05$ (Figure 8). This result is in agreement with the findings of Airaodion., *et al.* [33] who studied the hypoglycemic and hypolipidaemic activities of methanolic extract of *Talinum triangulare* bulb in Wistar rats but contradicts another finding of Airaodion., *et al.* [21] who reported a non-significant difference in the LDL-cholesterol concentration when animals were treated with African locust bean for 14 days. The combined effect of increased HDL-cholesterol (good cholesterol) and decreased LDL-cholesterol (bad cholesterol) in the present study resulted in an increased HDL-cholesterol/LDL-cholesterol ratio in animals treated with varying dose of *A. cepa* juice when compared with the negative control group (Figure 9). This strongly supports the believe that dietary supplementation with *A. cepa* bulb may lead to a reduction in the risk of developing heart diseases, because a high HDL-cholesterol/LDL-cholesterol ratio has been shown to be beneficial and is indicative of a lower risk of CHD [27]. Although, the activities of enzymes were not investigated in this study, but it is possible that *A. cepa* bulb decreased the activity of 3-hydroxy-3-methylglutaryl coenzyme A (HMG CoA) reductase (the rate-limiting enzyme in cholesterol biosynthesis) [23]. This implies that *A. cepa* bulb is of significant health importance as far as hyperlipidaemic and hyperglycemic are concerned.

Conclusion

The result of this study indicates that *A. cepa* bulb possesses hypolipidaemic and antidiabetic potency in alloxan-induced diabetic rats.

Conflict of Interest

Authors declare that no conflict of interest exist in this publication.

Bibliography

1. Bindu B ad Podikunju B. "Performance evaluation of onion (*Allium cepa* L. Var. Cepa) varieties for their suitability in kollam district". *International Journal of Research in Agricultural Sciences* 1.1 (2015): 18-20.

2. Slimestad R., *et al*. "Reviews. Onions: a ˚ source of unique dietary flavonoids". *Journal of Agricultural and Food Chemistry* 55.25 (2007): 10067-10080.

3. Grifths G., *et al*. "Onions—a global benefit to health". *Phytotherapy Research* 16.7 (2002): 603-615.

4. Perez-Gregorio RM., *et al*. "Identifcation and quantifcation of flavonoids in traditional cultivars of red and white onions at harvest". *Journal of Food Composition and Analysis*. 23.6 (2010): 592-598.

5. Santas J., *et al*. "Antimicrobial and antioxidant activity of crude onion (*Allium cepa* L.) extracts". *International Journal of Food Science and Technology*. 45.2 (2010): 403-409.

6. Prakash D., *et al*. "Antioxidant and free radical scavenging activities of phenols from onion (*Allium cepa*)". *Food Chemistry*. 102.4 (2007): 1389-1393.

7. De-Ancos B., *et al*. "Bioactive compounds from vegetable and fruit 8 Journal of Food Quality by-products". in Biotechnology of Bioactive Compounds. Sources and Applications. Section I, V. K. Gupta and M. G. Tuohy, Eds., 3-36, Wiley Blackwell (2015).

8. Ben´ıtez V., *et al*. "Study of bioactive compound content in different onion sections". *Plant Foods for Human Nutrition* 66.1 (2011): 48-57.

9. Rose P., *et al*. "Bioactive S-alk(en)yl cysteine sulfoxide metabolites in the genus *Allium*: the chemistry of potential therapeutic agents". *Natural Product Reports*. 22.3 (2005): 351-368.

10. Pszczola DE. "Antimicrobials: setting up additional hurdles to ensure food safety". *Food Technology* 56.6 (2002): 99-107.

11. Block E. "The organosulfur chemistry of the genus *Allium*—implications for the organic chemistry of sulfur". Angewandte Chemie—International Edition. 31.9 (1992): 1135-1178.

12. Schwimmer S and Weston WJ. "Onion flavor and odor: enzymatic development of pyruvic acid in onion as a measure of pungency". *Journal of Agricultural and Food Chemistry* 9.4 (1961): 301-304.

13. Bacon JR., *et al*. "Quantitative analysis of flavour precursors and pyruvate levels in different tissues and cultivars of onion (*Allium cepa*)". *Food Chemistry*. 64.2 (1999): 257-261.

14. Yoo KS., *et al*. "Differences in onion pungency due to cultivars, growth environment, and bulb sizes". *Scientia Horticulturae* 110.2 (2006): 144- 149.

15. Chope GA., *et al*. "Preharvest application of exogenous abscisic acid (ABA) or an ABA analogue does not affect endogenous ABA concentration of onion bulbs". *Plant Growth Regulation* 52.2 (2007): 117-129.

16. Soumya KR., *et al*. "Evaluation of cytotoxic effects of synthetic pesticide 'Attack' on Root Meristems of *Allium cepa* L". *South Indian Journal of Biological Sciences* 2.1 (2016): 35.

17. Terry LA., *et al*. "Nonstructural carbohydrate profles in onion bulbs influence taste preference". in Proceedings of the Information and Technology for Sustainable Fruit and Vegetable Production (Frutic '05), Montpellier, France (2005).

18. Santaguida PL., *et al*. "Diagnosis, prognosis, and treatment of impaired glucose tolerance and impaired fasting glucose". *Evidence Report Technology Assess* 12 (2008): 1-11.

19. Bahadoran Z., *et al*. "The association of dietary phytochemical index and cardio-metabolic risk factors in adults: Tehran lipid and glucose study". *Journal of Human Nutrition and Diet* (2013).

20. Prince PSM and Menon VP. "Antioxidant action of Tinosporacordifolia root extract in alloxan diabetic rats". *Phytotherapy Research*. 15.3 (2001): 213-238.

21. Airaodion AI., *et al*. "Effect of Oral Intake of African Locust Bean on Fasting Blood Sugar and Lipid Profile of Albino Rats". *Asian Journal of Research in Biochemistry* 4.4 (2019): 1-9.

22. Owoade AO., *et al*. "Toxicological assessment of the methanolic leaf extract of Bridelia ferrugelia". *The Journal of Phytopharmacology* 7.5 (2018): 419-424.

23. Owoade AO., *et al*. "Levofloxacin-induced dyslipidemia in male albino rats". *Asian Journal of Pharmacy and Pharmacology*. 4.5 (2018): 620-629.

24. Luka, C.D., *et al*. "Hypoglycaemic Properties of Aqueous Extracts of Anacardium occidentale, Moringa oleifera, Vernonia amygdalina and Helianthus annuus: A Comparative Study on Some Biochemical Parameters in Diabetic Rats". *International Journal of Pharmaceutical Science Invention* (2013): 2319 - 6718.

25. Meigs JB., *et al*. "The natural history of progression from normal glucose tolerance to type 2 diabetes in the Baltimore longitudinal study of Aging". *Diabetes* 52 (2003): 1475-84.

26. Airaodion AI., *et al*. "Effect of methanolic extract of Corchorus olitorius leaves on hypoglycemic and hypolipidaemic activities in albino rats". *Asian Plant Research Journal*. 2.7 (2019): 1-13.

27. Airaodion AI., *et al*. "Antidiabetic effect of ethanolic extract of Carica papaya leaves in alloxan-induced diabetic rats". *American Journal of Biomedical Science and Research* 5.3 (2019): 227-234.

28. Venkateswaran S., *et al*. "Effect of Phaseolus *vulgaris* on circulatory antioxidants and lipids in streptozotocin-induced diabetic rats". *Journal of Medicinal Food* 5 (2002): 97-104.

29. Loew S and Kaszkin M. "Approaching the problem of bioequivalence of herbal medicinal products". *Phytotherapy Research* 16 (2002): 705-711.

30. Ogbuagu EO., *et al*. "Effect of methanolic extract of Vernonia amygdalina leaves on glycemic and lipidaemic indexes of Wistar rats". *Asian Journal of Research in Medical and Pharmaceutical Sciences* 7.3 (2019): 1-14.

31. Airaodion AI., *et al*. "Comparative assessment of phytochemical content and antioxidant potential of Azadirachta indica and Parquetina nigrescens leaves". *Asian Plant Research Journal* 2.3 (2019): 1-14.

32. Airaodion AI., *et al*. "Evaluation of Phytochemical Content and Antioxidant Potential of Ocimum gratissimum and T. occidentalis leaves". *Asian Journal of Research in Medical and Pharmaceutical Sciences* 7.1 (2019): 1-11.

33. Airaodion AI., *et al*. "Hypoglycemic and hypolipidaemic activities of methanolic extract of Talinum triangulare leaves in Wistar rats". Intern*ational Journal of Bio-Science and Bio-Technology* 11.5 (2019): 1-13

34. Liguori L., *et al*. "Chemical Composition and Antioxidant Properties of Five White Onion (*Allium cepa* L.) Landraces". *Journal*

of Food Quality (2017): 1-9.

35. Chen X., *et al*. "One of the most important α- glucosidase inhibitors". *Current Medical Chemistry* 13 (2006): 109-116.

36. Dohadwala MM and Vita JA. "Grapes and cardiovascular disease". *Journal of Nutrition* 139(9) (2009): 1788-1793.

37. Gresele P., *et al*. "Effects of resveratrol and other wine polyphenols on vascular function: An update". *Journal of Nutritional Biochemistry* 22.3 (2011): 201-211.

38. Loci AS., *et al*. "Hypoglycemic effect of a valuable extract on some blood parameters in diabetic animals". *Journal of Ethnopharmacology* 43 (1994): 167-171.

39. Ahardh CD., *et al*. "The effect of tolnetamide in lipoproteins and lipoprotein lipase and hormone sensitive lipase". *Diabetes Research and Clinical Practice* 46 (1999): 99-108.

40. Frayn KN. "Insulin resistance and lipid metabolism". *Current Opinion Lipidology* 4 (1993): 197-204.

41. Bopanna KN., *et al*. "Antidiabetic and antihyperlipidemic effect of neem seed, kernel powder on alloxan diabetic rabbits". *Indian Journal of Pharmacology* 29 (1997): 162-167.

42. Rotimi OS., *et al*. "Amoxillinand pefloxacin-induced cholesterogenesis and phospholipidosis in rat tissues". *Lipids in Health and Disease* 14 (2015): 13-30.

43. Bhattaram VA., *et al*. "Pharmacokinetics bioavailability herbal medicinal products". *Phytomedicine* 9 (2002): 1-36.

44. Airaodion AI., *et al*. "Investigation of aqueous extract of Zingiber officinale root potential in the prevention of peptic ulcer in albino rats". *International Journal of Research and Innovation in Applied Science* 4.2 (2019): 64-67.

45. Airaodion AI., *et al*. "Prophylactic efficacy of aqueous extract of Curcuma longa against indomethacin-induced ulcer". *International Journal of Research* 6.1 (2019): 87-91.

46. Airaodion AI., *et al*. "Evaluation of Moringa oleifera leaves potential in the prevention of peptic ulcer in wistar rats". *International Journal of Research* 6.2 (2019): 579-584.

47. Saravanan R and Pari L. "Antihyperlipidemic and antiperoxidative effect of diasulin, a polyherbal formulation in alloxan induced hyperglycemic rats". BMC Complement. *Alternative Medicine* 5 (2005): 14-34.

48. Airaodion AI., *et al*. "Efficacy of Combined crude Extract of Curcuma longa and Moringa oleifera in the Prevention of Peptic Ulcer in Albino Rats". *Asian Journal of Research in Medical and Pharmaceutical Sciences* 7.2 (2019): 1-8.

49. Shoback DG and Gardner D. "Chapter 17". Greenspan's Basic and Clinical Endocrinology (9th Ed.). New York: McGraw-Hill Medical (2011). ISBN: 978-0-07-162243-1.

50. Saliu JA., *et al*. "Antidiabetic Potentials of Jute Bulb (*Talinum triangulare*) On Type-2 Diabetic Rats". *Journal of Emerging Trends in Engineering and Applied Sciences* 6.7 (2015): 223-230.

51. Allen RR., *et al*. "Daily consumption of a dark chocolate containing flavanols and added sterol esters affects cardiovascular risk factors in normotensive population with elevated cholesterol". *Journal of Nutrition* 138 (2008): 725-731.

52. Greene CM., *et al*. "Maintenance of the LDL-cholesterol/ HDL-cholesterol ratio in an elderly population given a dietary cholesterol challenge". *Journal of Nutrition* 135 (2005): 2793-2798.

53. Perona JS., *et al*. "Reduction in systemic and VLDL triacylglycerol concentration after a 3-month Mediterraneanstyle diet in high-cardiovascular-risk subjects". *Journal of Nutrition Biochemistry* 9 (2010): 892-898.

54. Gordon DJ and Rifkind BM. "High-density lipoprotein: The clinical implications of recent studies". *New England Journal of Medicine* 321.19 (1989): 1311-1316.

55. Sviridiv D. "Intracellular cholesterol trafficking". *Histology and Histopathology* 14 (1999): 305-319.

56. Navab M., *et al*. "The Yin and Yang of oxidation in the development of the fatty streak. A review based on the George Lyman Duff Memorial Lecture". *Arteriosclerosis and Thrombosis in Vascular Biology* 16 (1994): 831-842.

57. Oram JF and Lawn RM. "ABCA1: The gatekeeper for eliminating excess tissue cholesterol". *Journal Lipid Research* 42 (2001): 1173-1179.

58. Law MR. "Lowering heart disease risk with cholesterol reduction: Evidence from observational studies and clinical trials". *European Heart Journal* 1 (1999): S3-S8.

59. Stein O and Stein Y. "Atheroprotective mechanisms of HDL-Atherosclerosis". 144 (1999): 285-303.

60. Airaodion AI., *et al*. "Pharmacotherapeutic effect of methanolic extract of Telfairia occidentalis leaves on glycemic and lipidemic indexes of alloxan-induced diabetic rats". *International Journal of Bio-Science and Bio-Technology* 11.8 (2019): 1-17.