Research Article

Evaluation of the Potential Anti-diabetic Effect of *Apium graveolens* and *Brassica oleracea* Extracts in Alloxan induced Diabetic Rats

Medhat Mostafa Abozid[*1], Hanaa S. M. Abd El-Rahman[2], Mohamed Salama Mohamed[3]
[1] Biochemistry Department, Faculty of Agriculture, Menoufia University,Shibin El-Kom, Egypt.
[2] Special Food and Nutrition Dept., Food Technology Research Institute, Agricultural Research Center, Giza, Egypt.
[3] Department of Lab, Mashtoul-Elsouk Hospital, Sharqia, Egypt.
Address: Faculty of Agriculture, Mostafa Kamel St. – Shebin El-Kom, Egypt.
***Corresponding author's E-mail:** medhatabozid@gmail.com

Received: 05-03-2018; **Revised:** 01-04-2018; **Accepted:** 15-04-2018.

ABSTRACT

Celery (*Apium graveolens*) leaves and broccoli (*Brassica oleracea*) flowers are used in folk medicine and also they are used in different dishes in Egypt. In the current study, the hypoglycemic and natural antioxidants content of the ethanolic extracts of celery leaves and broccoli flowers were studied. For antioxidant activity, total phenolics (TP), total flavonoids (TF) and vitamin C content were determined; while for hypoglycemic activity diabetes was induced in rats by administration of alloxan (200mg/kg/i.p). Ethanolic extract of celery leaves (CLE) and broccoli flowers (BFE) (150 and 300 mg/kg/b.w for each extract) were administered to diabetic rats for 30 days. Blood glucose (BG), triglycerides (TG), total cholesterol (TC), HDL-cholesterol, LDL-cholesterol, kidney function parameters (urea and creatinine) and liver enzymes (AST and ALT) activities were estimated. Total phenolics (TP) amounts were 30.3 and 38.4 mg/g in CLE and BFE, respectively; total flavonoids (TF) amounts were 18.5 and 22.5 mg/g in CLE and BFE, respectively; while vitamin C was 418.47 and 80.5 mg/kg, respectively. Oral administration of CLE and BFE (150 and 300 mg/kg/b.w) in diabetic rats caused a significant decrease in BG, TG, TC, LDL, urea, creatinine and liver enzymes activities. Our results suggested that CLE and BFE have high content of antioxidants (TP, TF and vitamin C) and also have hypoglycemic effect in diabetic rats.

Keywords: Celery leaves, Broccoli flowers, Hypoglycemic, Antioxidant.

INTRODUCTION

Diabetes is the most common metabolic disorder that has adverse effects on public health, with significant implications for health care systems [1]. With a significant increase in the number of patients in the coming years, diabetes is one of major health challenges on worldwide. Diabetes is closely related with hyperlipidemia [2]. The risk of diabetes is not high blood glucose level, but the source of risk are the major developments that occur to different organs such as liver, kidney, eye and blood vessels resulting from lipid peroxidation due to the formation of free radicals [3-4]. Therefore, stopping the chain reaction of oxidation within the biological systems represents the most important step in protecting cells, especially insulin-producing cells (β- cells in pancreas), and this role can be played by antioxidants [5-6]. The plant kingdom is rich in natural antioxidants such as flavonoids, phenolic compounds and some vitamins (E and C) that can protect pancreatic functions and fight free radicals [7].

Celery (*Apium graveolens*) is one of the plants that are spread in different types of salad and soups throughout the world because of its good taste as well as the high content of secondary metabolites. Celery leaves is rich in flavonoids, carotenoids and it is one of the best vegetables sources for apigenin[8]. The medicinal properties of celery and its use in folk medicine have been known for a long time[9-10]. Broccoli (*Brassica oleracea*) vegetables contain little fat, and so are low in energy. Broccoli flowers have a high antioxidant capacity due to its high concentrations of vitamins A and vitamin C. Broccoli consumption has been shown to be beneficial in protecting against heart disease [11]. Broccoli is widely used in folk medicine because it has therapeutic effects, whether it's essential oil or the extracts of its stems and flowers[12]. In this study, the natural antioxidant content and antidiabetic activity of celery (*Apium graveolens*) leave and broccoli (*Brassica oleracea*) flowers were evaluated.

MATERIALS AND METHODS

MATERIALS

Plant materials

Fresh leaves of celery plants and broccoli flowers were obtained from the Agriculture Research Center in Giza, Egypt, in winter, (February 2015). The plants were identified in Horticulture Department, Faculty of Agriculture, Minoufia University.

Chemical reagents

Kits of triglyceride (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and glucose, were obtained from Spinreact Company, girona, Spain. Kits for creatinine and urea were obtained from Diamond Company, Cairo, Egypt.

Animals

Sixty Male Wister-albino rats (180 ±10g) were obtained from Research Institute of Ophthalmology (Giza, Egypt) for used in the experiment. The experimental animals were allowed to acclimatize under the laboratory conditions for a minimum period of 2 weeks prior to the experiment. Animals were kept on a standard diet throughout the experimental period [13]. Feed and water were available at all the times during the treatment. Ten animals were used for each group of study.

METHODS

Preparation of extracts

Celery leaves and broccoli flowers were washed and air-dried for 24 hours, then dried at 50°C in oven. The dried samples were grinded into fine powder. Celery leave (400g) and broccoli flowers (400g) were extracted separately with 95% ethanol (3L X 2 times) in a 50°C water bath for 6 h. Two extracts were filtered and concentrated in rotary vacuum evaporator, after that the product was freeze-dried.

Determination of antioxidants in plant extracts

Determination of total phenolics (TP)

The amount of total phenolics (TP) in the studied extracts was determined with the Folin- Ciocalteu reagent. Gallic acid was used as a standard and the total phenolics were expressed as mg gallic acid equivalents (GAE)/g dry weigh. 0.5 ml of samples and standard were putted in test tubes and blended with 2.5 ml of Folin- Ciocalteu reagent (10 fold dilute) and 2 ml of 7.5% Na_2CO_3, then test tubes were covered tightly and allowed to stand for half an hour at room temperature finally, the absorbance was read at 760 nm spectrometrically [14].

Determination of total flavonoids (TF)

The amount of total flavonoids (TF) in two plants was determined according to Aiyegoro and Okoh (2010) [15]. One ml of sample was mixed with 3 ml of methanol + 0.2 ml of 10% $AlCl_3$ + 0.2 ml of 1 M CH_3COOK and 5.6 ml of distilled water and remains at room temperature for half hour. The absorbance was measured at 420 nm with spectrophotometer against blank. The content was determined by using quercetin solution (calibration curve). The results were expressed as mg of quercetin equivalents (QE)/ g dry weight.

Determination of vitamin C by high performance liquid chromatography (HPLC)

Vitamin C was determined by HPLC according to Romeu-Nadal et al., (2006) [16]. The HPLC system consisted of Waters 717 plus Autosampler (USA) with a UV-visible detector. The column used was a Spherisorb C18 (250 x 4.6 mm 5 µm particle size). Mobile phase was double distilled water and acetic acid (0.1% v/v) mixed with methanol in a relative proportion 95:5 (v/v) and the flow rate was 0.7 ml/min. The column temperature was 25°C. Vitamin C was identified by comparison with the retention time for a standard sample of vitamin C at 254 nm.

Evaluation of antidiabetic effect of plant extracts

Induction of diabetes in experimental animals

After 2 weeks of acclimation 50 of rats were injected with a single injection dose of alloxan prepared freshly (dissolved in normal saline) at a dose of 100 mg / kg b.w [17]. Diabetes was confirmed by the determination of blood glucose levels on the third day after administration of alloxan. Rats having blood glucose levels greater than 250 mg/dl were considered diabetic and were used for the study.

Experimental design

Normal and diabetic rats were divided into six groups of 10 rats in each and were treated as follows: group I normal rats were kept without any treatments as negative control (NC); group II diabetic rats were kept without any treatments as positive control (PC); group III and IV diabetic rats administrated with celery leaves extract (CLE) at doses 150 and 300 mg/kg b.w respectively; group V and VI diabetic rats administrated with broccoli flowers extract (BFE) at doses 150 and 300 mg/kg b.w respectively.

Determination of biochemical parameters in blood

Blood samples were collected from orbital sinus veins technique using heparinized capillary tubes into clean, dry, and labeled eppendorf tubes (1.5 ml). The tubes contained heparin as anticoagulant. Samples were centrifuged at 3600 rpm for 15 min in a centrifuge under cooling (4°C) to separate plasma. Blood glucose (BG) was determined according to enzymatic method of Tinder, (1969) [18], while urea and creatinine in plasma were measured according to Wotton and Freeman, (1982) [19]. For lipid profiles; triglycerides (TG), total cholesterol (TC) and HDL- cholesterol (HDL-C) in plasma were determined according to Bucolo and David, (1973), Richmond, (1973) and Lopez *et al*., (1977) [20 – 22], respectively. LDL – cholesterol (LDL-C) was calculated by using Friedewald formula [23]. Aspartate aminotransferase (AST/GOT) and alanine aminotransferase (ALT/GPT) activities were determined according to Young, (1990) [24].

Statistical analysis

To determine statistical difference between means ($p < 0.01$), ANOVA and Duncan's test were calculated using SPSS statistical software package v.11. Results were expressed as mean values ± SD.

RESULTS AND DISCUSSION

Natural antioxidants in plant extracts

The plants generally contain natural antioxidants represented in phenolic compounds and flavonoids as well as some vitamins that act as antioxidants such as vitamin C. Data in Table (1) showed that TP, TF and

vitamin C in celery leaves were 30.3 mg/g DM, 18.5 mg/g DM and 418.47 mg/kg DM, respectively. These results are similar to previous studies on the same plant [25- 27]. On the other hand, TP, TF and vitamin C in broccoli flowers were 38.4, 22.5 mg/g DM and 85.5 mg/kg DM, respectively; which is similar in turn with confirmed in many previous studies that have been interested in estimating antioxidant activity of broccoli plants [28 – 30]. Studies have showed the positive effect of eating foods rich in their natural antioxidants (phenolics and flavonoids), in the face of many diseases, especially the significant effect of these natural compounds as antidiabetic [31 – 32].

Table 1: Total phenolics (TP), total flavonoids (TF) and vitamin C in two plants

Natural antioxidants	Celery leaves	Broccoli flowers
TP (mg/g DM)	30.3	38.4
TF (mg/g DM)	18.5	22.5
Vitamin C (mg/kg DM)	418.47	85.5

Impact of CLE and BFE on glucose and kidney functions in diabetic rats

Blood sugar level is tightly regulated in the human body. Normally, the blood glucose level is maintained between about 70 to 120 mg/dl. Diabetes is one of the most common metabolic disorders in the world. High blood glucose level is a major stress on the kidneys, leading to deterioration of their functions and kidney disease. Both creatinine and urea are biochemically determined for the efficiency of kidney functions [33]. Diabetic rats (group II) showed a significant increase in BG (295.8 mg/dl), urea (45.42 g/dl) and creatinine (0.94 mg/dl) compared with normal rats (group I) (86.13, 20.31 and 0.51 mg/dl, respectively). Two plant extracts used in both concentrations (150 and 300 mg/kg b.w) showed significant reduction in glucose, urea and creatinine levels compared with diabetic rats (Table 2). The broccoli flower extracts in two concentrations (150 and 300 mg/kg b.w) recorded the lowest values ever of glucose (185.17 and171.38 mg/dl, respectively), urea (32.12 and 30.22 mg/dl, respectively) and creatinine (0.61 and 0.59 mg/dl, respectively).

The use of plants for medical purposes is also widespread in many countries to treat diabetes-related disorders [34]. In the case of diabetes increases the content of glucose in the blood, and resulting in increased activity of the enzyme aldose reductase, which converts the glucose to sorbitol; excessive intracellular accumulation of sorbitol result in chronic complications such as neuropathy, retinopathy, and cataract. Because celery contains high content of flavonoids such as Apigenin, it inhibits this enzyme, which reduces the complications of diabetes [35 – 36].

The hypoglycaemic effect of CLE in our study can be explained by the presence of high content of natural antioxidants (phenolic compounds, falvonoids and vitamin C) [37 – 38]. Previous studies pointed to the effect of broccoli in reducing the level of glucose in rats treated with alloxan and protect cells from damage [39]. There are several proposed mechanisms to explain the action of these plant extracts as they either improved glucose uptake by different cells or increased the rate of liver use of glucose and finally may have improved the secretion of insulin [40]. The high vitamin C contents of celery and broccoli cannot be ignored; especially studies suggest the positive effect of eating foods rich in vitamin C on improving the health status of diabetics [41 – 42]. The resulting improvement in treatment with CLE and BFE can generally be attributed to the high antioxidants content (Table 1), which in turn helps to fight the free radicals that cause most of complications of diabetes.

Table 2: Effect of celery leaves extract (CLE) and broccoli flowers extract (BFE) on glucose and kidney functions in diabetic rats

Groups	BG (mg/dl)	Urea (mg/dl)	Ceratinine (mg/dl)
Group I	86.13 ± 3.8 a	20.31 ± 1.4 a	0.51 ± 0.048 a
Group II	295.8 ± 4.2 f	45.42 ± 2.5 e	0.94 ± 0.054 f
Group III	210.77 ± 1.5 e	36.1 ± 1.6 d	0.66 ± 0.037 e
Group IV	196.33 ± 3.6 d	32.9 ± 1.8 c	0.64 ± 0.041 d
Group V	185.17 ± 3.1 c	32.12 ± 1.7 c	0.61 ± 0.053 c
Group VI	171.38 ± 2.8 b	30.22 ± 2.3 b	0.59 ± 0.062 b

Values represent means ± S.D obtained from 10 rats, numbers in the same column followed by the same letters do not differ significantly, and when the numbers followed by different letters differ significantly at ($p \geq 0.01$).

Impact of CLE and BFE on lipid profiles in diabetic rats

One of the most important complications of diabetes is the high level of serum lipids, especially triglycerides, total cholesterol and LDL-cholesterol [43]. Table (3) showed that diabetic rats (group II) caused a significant increase in TG (127.33mg/dl), TC (195.23 mg/dl) and LDL-C (139.64 mg/dl) compared with normal rats (group I) values (84.75, 125.34 and 52.67 mg/dl, respectively); while caused a significant decrease in HDL-C (30.12 mg/dl) in comparison to group I (55.67 mg/dl). These results are similar to those confirmed in earlier studies on the coloration between diabetes and elevated lipid profile in blood [44 – 46]. The high values of triglycerides (TG) are attributed to higher rates

of production of very low density lipoprotein (VLDL); which rich in TG to decreased removal of TG by adipose tissue and muscle [47]. A high cholesterol levels can be explained in the case of diabetes by increasing the activity of the 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase enzyme (HMG-CoA reductase), which plays a key role in the synthesis of cholesterol as well as increase the absorption of cholesterol from diet [48]. Lower HDL-C in diabetes may be due to reduced lipoprotein lipase activity; because of lipoprotein lipase is primarily responsible for the analysis of TG from chylomicrons and VLDL, which leading to production of HDL particles [49].

The results in Table (3) showed that the CLE with both concentrations (150 and 300 mg/kg b.w) resulted in a significant reduction in the levels of TG (100.3 and 96.12 mg/dl, respectively), TC (160.23 and 155.67 mg/dl, respectively) and LDL-C (93.9 and 93.3 mg/dl, respectively) compared with diabetic rats (group II); while a significant increase in HDL-C was observed. These results are largely consistent with the results of many researchers [50 – 51] who studied the effect of celery on blood lipid levels. The main problem that causes all complications of diabetes is the lack of insulin, and previous studies indicate the role played by celery in improving the production of insulin from the pancreas, which works to reduce blood glucose levels and thus a significant improvement in blood lipids [36, 52]. The supplementation with BFE resulted in a significant increment in the level of HDL-C, and on the other hand, a significant reduction in the levels of TG, TC and LDL-C, compared with all studied groups; the best effect at all was treated with BFE in dose 300mg/kg b.w. Previous studies have supported our findings [53 – 55], which strongly suggests our expectations for the positive role of broccoli in reducing the harmful effects of diabetes. Table (1) showed high content of broccoli content of total phenolics and flavonoids. Phenolics and flavonoids may influence expression of genes relevant for the development of type2 diabetes, i.e. genes regulating glucose transport, insulin secretion or action, antioxidant effect, lipid metabolism [56 – 58].

Table 3: Effect of celery leaves extract (CLE) and broccoli flowers extract (BFE) on lipid profiles in diabetic rats

Groups	TG (mg/dl)	TC (mg/dl)	HDL-C (mg/dl)	LDL-C (mg/dl)
Group I	84.75 ± 2.9 a	125.34 ± 5.2 a	55.67 ± 3.5 f	52.72 ± 2.3 a
Group II	127.33 ± 2.1 e	195.23 ± 3 f	30.12 ± 2.77 a	139.64 ± 3.22 e
Group III	100.3 ± 3.2 d	160.23 ± 2.6 e	46.23 ± 2.55 e	93.9 ± 2.33 d
Group IV	96.12 ± 2.8 c	155.67 ± 2.5 d	43.16 ± 1.67 d	93.3 ± 1.44 d
Group V	99.34 ± 1.8 d	148.24 ± 3.6 c	41.13 ± 2.86 c	87.2 ± 2.66 c
Group VI	93.26 ± 2.5 b	139.22 ± 2.9 b	38.34 ± 3.67 b	82.2 ± 2.9 b

Values represent means ± S.D obtained from 10 rats, numbers in the same column followed by the same letters do not differ significantly, and when the numbers followed by different letters differ significantly at ($p \geq 0.01$).

Impact of CLE and BFE on AST and ALT enzymes activity in diabetic rats

AST and ALT activities were significantly elevated in group II compared with group I. The rise in these enzymes activities were significantly improved in both plant extracts (CLE and BFE) dose dependently (Figure 1). The BFE at dose 300mg/kg b.w decreased the levels of liver enzymes activity significantly ($p \geq 0.01$) compared with all treated groups.

An Increasing in liver enzymes activity (AST, ALT and ALP) as well as total protein and albumin levels are indicators of liver injury. The elevation on AST and ALT activities are the most frequently measured indicator of liver damage and occurs in diabetics more frequently than in the general population [59].

The elevated in AST and ALT activities in diabetic rats confirmed, which has been observed in previous studies [60 – 61].

On the other hand, our results are in line with previous studies pointed to the improvement effects of celery [62] and broccoli [63] on liver function in diabetic animals. The improvement in liver functions when treated with CLE and BFE can be explained by the high content of the two plants by natural antioxidants, which protect the liver cells from damage.

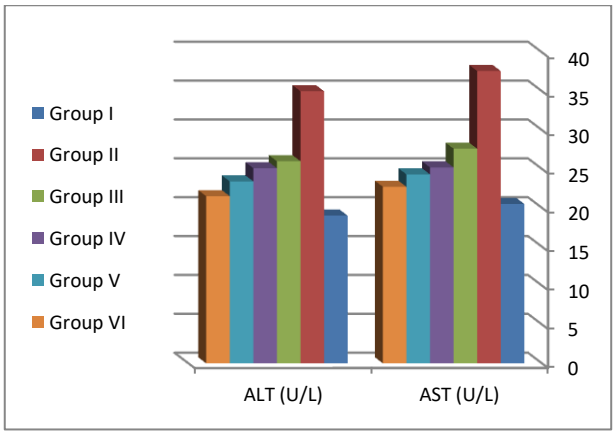

Figure 1: Effect of CLE and BFE on AST and ALT enzymes activity in diabetic rats

CONCLUSION

Our results speculated that the observed hypoglycemic and hypolipidemic effects of celery leaves and broccoli flowers might be related to the total phenolics and

flavonoids contents. Celery leaves and broccoli flowers can be used by diabetic patients to reduce the bad effects of the disease. Further studies are needful to fractionate and identify the active compounds in CLE and BFE and mode of action for these compounds in diabetic animal models.

Acknowledgment: We gratefully acknowledge Prof. Dr. Youssef Amin Ashoush and Prof. Dr. Ahmed Mohamed Farid Ali (Faculty of Agriculture, Menoufia University) for their recommendations and advice during the research period.

REFERENCES

1. Bowling AC, Beal MF, Bioenergetic and oxidative stress in neurodegenerative diseases, Life Sciences, 56, 1995, 1151-1171.
2. Taskinen MR, Diabetic dyslipidemia, Atherosclerosis, Suppl 3, 2002, 47-51.
3. Hunt JV, Dean RT, Wolff SP, Hydroxyl radical production and autoxidative glycosylation. Glucose autoxidation as the cause of protein damage in the experimental glycation model of diabetes and aging, Biochemical Journal, 256, 1988, 205-212.
4. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, Nathan DM, Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin, The New England Journal of Medicine, 346(6), 2002, 393-403.
5. Gordon M, Dietary antioxidants in disease prevention, Natural Product Reports, 13, 1996, 265-273.
6. Murthy VK, Shipp JC, Hanson C, Shipp DM, Delayed onset and decreased incidence of diabetes in BB rats fed free radical scavengers, Diabetes Research and Clinical Practice, 18, 1992, 11–16.
7. National Nutrition Council, Finish Nutrition Recommendations. Committee report 1998, Ministry of Agriculture and Forestry, Helsinki, Finland, 1999, 9.
8. Joao SD, Nutritional Quality and Health Benefits of Vegetables. Food and Nutrition Sciences, 3, 2012, 1354-1374.
9. Atta AH, Alkofahi A, Anti-nocicepite and antiinflammatory effects of some Jordanian medicinal plant extract, Journal of Ethnopharmacology, 60, 1998, 117–124.
10. Saleh MM, Zwaving JH, Malingre TM, Bos R, The essential oils of Apium-graveolens var secalinum and its cercaricidal activity, Pharmaceutisch weekblad-Scientific edition, 7, 1985, 277–279.
11. Elizabeth HJ, Marcela A, Physiological effects of broccoli consumption. Phytochemistry Reviews, 8(1), 2009, 1568-7767.
12. Miraj S, Broccoli (*Brassica Oleracea var. Italica*): Potential candidate in the health management, Der Pharmacia Lettrem 8 (14), 2016, 61-65.
13. Reeves RG, Nielsen FH, Fahey GC, Purified diets for laboratory rodents. Journal of Nutrition, 123(1), 1993, 1939-1951.
14. Kim DO, Jeong SW, Lee CY, Antioxidant capacity of phenolic phytochemicals from various cultivars of plums, Food Chemistry, 81, 2003, 321–326.
15. Aiyegoro OA, Okoh AI, Preliminary phytochemical screening and in vitro antioxidant activities of the aqueous extract of *Helichrysum longifolium*, BMC Complementary and Alternative Medicine, 10, 2010, 21-28.
16. Romeu-Nadal M, Morera-Pons S, Castellote AI, Lopez-Sabater MC, Rapid high-performance liquid chromatographic method for Vitamin C determination in human milk versus an enzymatic method, Journal of Chromatography B, 830, 2006, 41-46.
17. Chen HX, Zhang M, Xie BJ, Components and antioxidant activity of polysaccharide conjugate from green tea, Food Chemistry, 90, 2005, 17-21.
18. Tinder P, Determination of blood glucose using oxidase system with a non- carcinogenic chromogen, Annals of Clinical Biochemistry, 6, 1969, 24-31.
19. Wootton ID, Freeman H, Micro Analysis in Medical Biochemistry, 6th ed, Churchill Living Stone Publication, London, 1982, 68.
20. Bucolo G, David H, Quantitative determination of serum triglyceridesby the use of the enzymes, Clinical Chemistry, 19, 1973, 475.
21. Richmond W, Preparation and properties of a cholesterol oxidase from *Nocardia sp.* and its application to the enzymatic assay of total cholesterol in serum, Clinical Chemistry, 19, 1973, 1350-1356.
22. Lopez MF, Stone S, Ellis S, Collwell JA, Cholesterol determination in high density lipoproteins separated by three different methods, Clinical Chemistry, 23, 1977, 882-886.
23. Friedewald WT, Levy RI, Fredrickson DS, Estimation of theconcentration of low- density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge, Clinical Chemistry, 18, 1972, 499–502.
24. Young DS, Thomas DW, Friedman RB, Pestaner LC, Effects of drugs on clinical laboratory tests, Clinical Chemistry, 18(10), 1972, 1041.
25. Elliot JG, Application of antioxidant vitamins in foods and beverages, Food Technology, 53, 1999, 46-48.
26. Jovanka K, Mira P, Momir M, Radoslav M, Ljiljana G, Protective effects of celery juice in treatments with doxorubicin, Molecules, 14, 2009, 1627-1638.
27. Jung WS, Chung IM, Kim SH, Kim MY, Ahmad A, Praveen N, In vitro antioxidant activity, total phenolics and flavonoids from celery (Apiumgraveolens) leaves. Journal of Medicinal Plants Research, 5(32), 2011, 7022-7030.
28. Alsuhaibani AMA, Effect of broccoli on the antioxidant activity of experimental rats ingested thermally oxidized oil, Nature and Science, 11 (12), 2013, 1-7.
29. Grover JK, Yadav S, Vats V, Medicinal plants of India with anti-diabetic potential, Journal of Ethnopharmacology 81, 2002, 81-100.
30. Hu CH, Zuo AY, Wang DG, Pan HY, Zheng WB, Qian ZC, Zou XT, Effects of broccoli stems and leaves meal on production performance and egg quality of laying hens, Animal Feed Science and Technology, 170, 2011, 117–121.
31. Hertog ML, Feskens EJ, Hollman PH, Katan MB, Kromhout D, Dietary antioxidants flavonoids and the risk of coronary heart disease: the zutphen elderly study, Lancet 342, 1993, 1007-1011.
32. Kako M, Miura T, Nishiyama Y, Ichimaru M, Moriyasu M, Kato A, Hypoglycemic activity of some triterpenoid glycosides, Journal of Natural Products; 60, 1997, 604-605.
33. Schutte JE, Longhurst JC, Gaffney FA, Bastian BC, Blomqvist CG, Total plasma creatinine: an accurate measure of total striated muscle mass, Journal of Applied Physiology: Respiratory, Environmental and Exercise Physiology, 51, 1981, 762- 766.
34. Rajasekaran S, Ravi K, Sivagnanam K, Subramanian S, Beneficial effects of *Aloe veraleaf* gel extract on lipid profile status in rats with streptozotocin diabetes, Clinical and Experimental Pharmacology and Physiology 33(3), 2006, 232-237.
35. Kanter M, Meral I, Yener Z, Ozbek H, Demir H, Partial regeneration/ proliferation of the β-cells in the islets of langerhans by *Nigella sativa L.* in sterptozotocin-induced diabetic rats, Tohoku Journal of Experimental Medicine, 201, 2003, 213-219.
36. Niaz K, Gull S, Azia M, Antihyperglycemic/Hypoglycemic effect of celery seeds (Ajwain / Ajmod) in streptozotocin induced diabetic rats, Journal of Rawalpindi Medical College, 17(1), 2013, 134-137.

37. Middleton E, Kandaswami C, Theoharides TC, The effects of plant flavonoids on mammalian cells: implications for inflammation, heart disease and cancer, Pharmacological Reviews 52, 2000, 673–751.

38. Singh A, Handa SS, Hepatoprotective activity of *Apium graveolens* and *Hygrophila auriculata* against paracetamol and thioacetamide intoxication in rats, Journal of Ethanopharmacology, 49(3), 1995, 119-126.

39. Dembinska-Kiec A, Mykka-nen O, Kiec-Wilk B, Mykka-nen H, Antioxidant phytochemicals against type 2 diabetes, British Journal of Nutrition, 99, 2008, 109-117.

40. Latha P, Chandra-Sekhar KB, Sujatha D, Evaluation of antidiabetic potential of ethanolic extract of *Caseria elliptica* in sterptozotocin induced diabetic rats, International Journal of Research in Pharmaceutical Sciences, 8(3), 2017, 291-297.

41. Mayer-Davis EJ, Bell RA, Reboussin BA, Antioxidant nutrient intake and diabetic retinopathy: the San Luis Valley Diabetes Study, Ophthalmology, 105, 1998, 2264–2270.

42. Millen AE, Gruber MS, Klein R, Relationships of serum ascorbic acid and alpha-tocopherol to diabetic retinopathy in the Third National Health and Nutrition Examination Survey, American Journal of Epidemiology, 158, 2003, 225–233.

43. Pushparaj PN, Low HK, Manikandan J, Tan BK, Tan CH, Anti-diabetic effects of *Cichorium intybus* in streptozotocin- induced diabetic rats, Journal of Ethnopharmacology, 111(2), 2007, 430-434.

44. Falko JM, Parr JH, Simpson RN, Wynn V, Lipoprotein analyses in varying degrees of glucose tolerance: Comparison between non-insulin-dependent diabetic, impaired glucose tolerant, and control populations, The American Journal of Medicine, 83(4), 1987, 641-647.

45. Shankarprasad DS, Gundalli S, Mahantesh B, Kashinakunti SV, Sunitha P, Lipid profile in diabetes mellitus, Indian Journal of Pathology and Oncology, 2(4), 2015, 290-294.

46. Sosenko JM, Breslow JL, Miettinen OS, Gabbay KH, Hyperglycemia and plasma lipid levels -A prospective study of young insulin-dependent diabetic patients, The New England Journal of Medicine, 302(12), 1980, 650-654.

47. Nikkila EA, Kekki M, Plasma triglyceride transport kinetics in diabetes mellitus, Metabolism, 22(1), 1973, 1-22.

48. Saudek CD, Young NL, Cholesterol metabolism in diabetes mellitus: The role of diet.Diabetes, 30S (2), 1981, 76-81.

49. Clee, SM, Zhang H, Bissada N, Miao L, Ehrenborg E, Benlian P, Shen GX, Angel A, LeBoeuf RC, Hayden MR, Relationship between lipoprotein lipase and high density lipoprotein cholesterol in mice: modulation by cholesteryl ester transfer protein and dietary status. Journal of Lipid Research, 38, 1997, 2079-2089.

50. Kooti W, Ghasemiboroon M, Asadi-Samani M, Ahangarpoor A, Noori A, Abadi M, Afrisham R, The effects of hydro-alcoholic extract of celery on lipid profile of rats fed a high fat diet, Advanced in Environmental Biology, 8(9), 2014, 325-330.

51. Perumalraja R, Sharief SD, Antihyperlipidemic activity of ethanolic extract of celery stem on rats, International Journal of Pharmaceutical and Biological Archives, 4(4), 2013, 731-734.

52. Veermanic C, Pushpavalli G, Pugalendi KV, Antihyperglycemic of *Cardispermum halicacabum Linn.* Leaf extract on STZ induced diabetic rats, Journal of Applied Biomedicine, 2008; 6, 19-26.

53. Chisolm GM, Steinberg D, The oxidative modification hypothesis of atherogenesis: an overview, Free Radical Biology and Medicine, 28, 2000, 1815–1826.

54. Christiansen B, Bellostas MN, Petersen AM, Ingestion of broccoli sprouts does not improve endothelial function in humans with hypertension, Food Chemistry, 5, 2010, 124- 131.

55. Stranges S, Dorn J, Donahue R, Oxidation, type 2 diabetes and coronary heart disease: A complex interaction, Diabetes Care, 31, 2008, 1864–1866.

56. Das UN, GLUT-4, tumor necrosis factor, essential fatty acids and daf-genes and their role in insulin resistance and non-insulin dependent diabetes mellitus, Prostaglandins Leukotrienes Essential Fatty Acids, 60, 1999, 13–20.

57. Moskaug JO, Carlsen H, Myhrstad M, Blomhoff R, Molecular imaging of the biological effects of quercetin and quercetin-rich foods, Mechanism of Ageing and Development, 125, 2004, 315–324.

58. Thirunavukkarasu M, Penumathsa SV, Koneru S, Juhasz B,Zhan L, Otani H, Bagchi D, Das DK, Maulik N, Resveratrol alleviates cardiac dysfunction in streptozotocin induced diabetes: role of nitric oxide, thioredoxin, and hemeoxygenase, Free Radical Biology and Medicine, 43, 2007, 720–729.

59. Everhart JE, Diabetes in America, 2nd ed, National Institute of Diabetes and Digestive and Kidney Diseases, Washington, DC. GPO 1995, 457-483.

60. Erbey JR, Silberman C, Lydick E, Prevalence of abnormal serum alanine aminotransferase levels in obese patients and patients with type 2diabetes, American Journal of Medicine, 109, 2000, 588–590.

61. Wannamethee SG, Shaper AG, Lennon L, Whincup PH, Hepatic enzymes, the metabolic syndrome, and the risk of type 2 diabetes in older men, Diabetes Care, 28, 2005, 2913-2918.

62. Venkateswaran S, Pari L, Antioxidant effect of *Phaseolus vulgaris* in streptozotocin induced diabetic rats, Asia Pacific Journal of Clinical Nutrition, 11, 2002, 206- 209.

63. Bahadoran Z, Mirmiran P, Hosseinpanah F, Hedayati M, Hosseinpour-Niazi S, Azizi F, Broccoli sprouts reduce oxidative stress in type 2 diabetes: a randomized double-blind clinical trial, European Journal of Clinical Nutrition, 65(8), 2011, 972–977.

Source of Support: Nil, **Conflict of Interest:** None.