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Evaluation of *hydrated* extract of *phaseolus Vulgaris* L. (bean plant) *on* hypoglycemia and hypolipidemic in streptozotocin-induced diabetic albino *Wistar* rats

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Article History:	ABSTRACT
Received on: 12.07.2019 Revised on: 15.10.2019 Accepted on: 21.10.2019 <i>Keywords:</i> Aldohexose, Bean plant, LDL, glibenclamide, Polygenic disorder, STZ, SGPT	The current research was intended to comprehend hypoglycemic and anti- lipidaemic exercises of hydrated common bean (<i>phaseolus Vulgaris</i> L.) seed extracts on streptozotocin-induced diabetic albino rats. At a set portion fluc- tuate of 100, 200,300 mg/kg body weight of common bean extracts was orally directed as one portion for every day to polygenic disorder rats for a mea- sure of thirty days. The impact of <i>Pvulgaris</i> L. on hypoglycemic, glycosy- lated hemoprotein (HbA1c) and blood serum lipid profile (Total cholesterin), Triglyceride (TG), very low-density lipoprotein (VLDL), low-density lipopro- tein (LDL), High-density lipoprotein (HDL)) in plasma were estimated in the regular and diabetic induced rat. The outcomes demonstrated that quick glu- cose, serum TC, TG, LDL, VLDL, levels were significantly (p<0.05) attenuate, while blood serum HDL, the level was extensively (p<0.05) upgraded inside the diabetic rats. The inconclusive amount of pace of 300 mg/kg is more rea- sonable than that of a hundred mg/kg. Our examination so shows that <i>Phaseo- lus vulgaris</i> L has a powerful adversary to diabetic and anti-lipidaemic impacts on streptozotocin-induced diabetic rats, and results were comparable to ref- erence drug glibenclamide.

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INTRODUCTION

Diabetes mellitus is a persistent disorder featured by a long-lasting indication, resulting from a shortage of hypoglycemic agent production by beta cells or insulin cellular resistance (Shaw *et al.*, 2010). From the outcome attained by the International Diabetes Federation, individuals aged 18-99 years who lived with diabetes internationally in 2017 were 425 million. By 2045 these values were expected to extend to 693 million (IDF, 2017). Diabetes could be a challenging disorder that ends with multiple factors intercommunication like genetic predisposition, environmental risk factors, and behavioral.

Until the improvement of the germ theory of infection within the 19^{th} century, there was the close tie of herbalism and ancient medication. Advanced medication to nowadays has been based on prove gathered by the use of logical strategy from the 19^{th} century. Utilization of pharmaceutical drugs, frequently determined from restorative plants, has generally supplanted home remedies I advanced well being. However, various forms of traditional or alternative medicine are continuously employed by people. A major flavoring part of systems usually is employed. The history of herbalism additionally overlaps with food history, as several of the herbs and spices traditionally employed by humans to season food yield helpful medicative compounds (Tapsell *et al.*, 2006; Lai and Roy, 2004).

Kidney bean, as well as referred to *as Phaseolus vulgaris* L. (Leguminosae), in Asian and Eastern countries, is consumed as food. Ayurvedic and Unani in the Indian subcontinent have practiced this plant for diabetes treatment due to its mechanism (Chopra, 1958). According to a reported by (Roman-Ramos *et al.*, 1995) the activity of antihyperglycemic was observed in aqueous extract of bean pods. (Roman-Ramos *et al.*, 1995) In 100g of *P. Vulgaris* contained 50 mg of flavonoid was reported (Nair *et al.*, 1998). In (Pari and Venkateswaran, 2003) tried the insulinstimulatory result of bean pods from existing β -cells in diabetic rats (Pari and Venkateswaran, 2003).

Phaseolus vulgaris L. is that the desired bean within us and northwestern Mexico (Maize, 2003) and is most frequently eaten whole or sometimes in broth or mashed so refried. Readings have indicated pinto beans will lower the degree of each high-density lipoprotein and cholesterol. Pinto beans have conjointly been shown to contain the Phytoestrogen coumestrol, which incorporates a form of potential health effects (Bhagwat *et al.*, 2008).

Thus, the current research was intended to comprehend hypoglycemic and anti-lipidaemic exercises of hydrated common bean (*phaseolus Vulgaris* L.) seed extracts on streptozotocin-induced diabetic albino rats.

MATERIALS AND METHODS

Plant materials

Collection and preparation of material

The healthy seeds of the *Phaseolus vulgaris* L seed were collected from the Erode market, Tamil Nadu, India. The plant specimen was known by a biologist in the Department of Agricultural and Biological science, Biology survey, Coimbatore, India, and assigned voucher number (BSI/SRC/5/23/2018/Tech,3321). The specimens were kept in the Department of Agricultural and Biological science, Biology survey.

Preparation of hydrated crude extract

The seeds were cleaned by removing unhealthy seeds, shaded dried, and then powdered. 50g of the powder was crammed within the thimble and extracted in turn using water 500ml as a solvent for

sixteen hours, and by the help of rotary evaporator at reduced targeted pressure, $60\pm10^{\circ}$ C desired amount of extract was attained. The extract was kept at -20°C and used for further studies.

Experimental animal

Female albino *Wister* rats were chosen for experimental purpose weighing around 180-200g. In the faculty of biotechnology, college of technology (Kalvi Nagar, Tiruchingode) India, rats were provided with standard laboratory whereby they were fed with standard commercial pelleted rat chaw and access to water. House of the animal was maintained with a range of temperature twenty-four -26^oC and relative humidity of the ratio of 30-70%. According to the international regulations for the use of laboratory animals, the experiment was conducted to the institutional Animal Ethics Committee(IAEC), approval number provided, (Reg. No:1826/PO/EReBi/S/15/CPCSEA).

Evaluation of the ant-diabetic activity of *Phaseo-lus vulgaris* L Seed extract

Induction of polygenic disorder in rats

After overnight fast rats were made diabetic by single intraperitoneal (i.p) injection dose of streptozotocin(STZ) at 55 mg/kg body weight, which is dissolved in freshly prepared citrate buffer(0.1 mol/L, pH 4.5). In 72 hours from the day of administration of STZ, blood glucose was determined by withdrawing blood vein from the tail by the help of Dr.Morepen BG 03-GLUCO One glucometer (India). Hyperglycemia (glucose over 250 mg/dl) the level of diabetic rats with this level of blood glucose was taken for experimental.

Grouping of Experimental Animals

6 groups were allocated whereby each group had six rats each as follows

Table 1 shows how the animal has grouped accordingly to their respective groups. Treatment is carried out in four groups- groups 3,4, 5, and 6, while groups 1 and 2 serve as controls.

By the help of intragastric tube, all rats were fed; accordingly, group 1 and 2 rats were fed with water alone, by dissolving the extract and standard drug in water group 3,4,5 and 6 were treated respectively in required quantity for a period of 30 days. In the event of the experiment, Fast Aldo hexose was monitored every week.

Sacrifice study

Overnight fast animals were denied food, and they were sacrificed by decapitation method, wit help of with and without anticoagulant medication tubes blood was collected.

Groups						
Group 1	Distilled water	Negative control				
Group 2	Distilled water	Diabetic induced -streptozotocin management rats				
Group 3	100mg/kg body weight	Diabetic induced rats treated with hydrated Phase- olus vulgaris L. seed extract -30 days				
Group 4	200mg/kg body weight	Diabetic induced rats treated with hydrated Phase- olus vulgaris L. seed extract - 30 days				
Group 5	300mg/kg body weight	Diabetic induced rats treated with hydrated Phase- olus vulgaris L. seed extract - 30 days				
Group 6	600 μ g/kg body weight	Diabetic rats treated with customary drug glibenclamide– 30 days (Pari and Venkateswaran, 2003)				

Table 1: Grouping of experimental animals and dosage allocation

Assurance of the glucose levels

Blood tests were gathered from the tip of the tail for glycemia estimating. During this examination, glucose fixations (mg/dl) decided at the sketched out week after week, by Dr. Morepen BG 03-GLUCO One a hundred glucometer and glucose receptive check strips upheld the glucose enzyme technique.

Estimation of organic chemistry parameters

Blood samples from six groups were collected with the help of the EDTA tube after the animal was sacrificed by the end of 30 days. With the technique of auto-analyzer "Architect C8000" by manufactured (Abbott), separated plasma was carried out on test of total cholesterol, lipid profile levels, renal marker enzymes, alkaline phosphate, SGPT, and SGOT.

Statistical analysis

One-way ANOVA analysis was the method used for parameter values to be analyzed. For 6 rats in each group, results were expressed as mean \pm SEM, and the result was significant when the value is P<0.05.

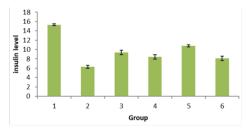
RESULTS AND DISCUSSION

Changes in weight, insulin, blood sugar and c-peptide

As shown in Table 2. It's obvious that the induction of polygenic disorder led to increased blood glucose, decreased bodyweight, insulin, and the C peptide level as a result of muscle wasting. The destruction of β -cells of the pancreas caused insulin inhibition release. (Ahmed *et al.*, 2016). The accelerator of the breakdown of proinsulin is done by c-peptide and hypoglycemic agent and distribution into circulation in equimolar concentration. Rather insulin working alone activity of C-peptide and hypoglycemic agent levels is known to be of great importance in insulin secretion. Administration of hydrated *Phaseolus vulgaris* L. seed extract orally significantly magnified the amount of plasma hypoglycemic agent and amino acid, blood sugar was equally reduced. The prospective way by which *Phaseolus vulgaris* L. reduced blood sugar could be either enhanced by the hypoglycemic agent by increasing the release of insulin from present beta cells.

Figure 1 shows the level of insulin level in experimental animals. The diabetic control group without treat showed a decreased level of insulin when compared with the normal control group. At the concentration of 300 mg/kg body weight of *Phaseolus vulgaris*, L. blood insulin level increased when comparing to the untreated diabetic group.

Figure 2 shows the bodyweight of experimental groups. The diabetic control group showed a reduction in body weight when compared with normal control after a period of 30 days. Administration of *Phaseolus vulgaris* L. improved body weight level most improvement is observed in group 5(diabetic treated 300mg/kg) and 6(standard drug).



Group 1- Normal control; Group 2 -Diabetic control; Group 3 -dose 100 mg/kg *Phaseolus vulgaris*; Group 4 -200 mg/kg *Phaseolus vulgaris*; Group 5-300 mg/kg *Phaseolus vulgaris*; Group 6- glibenclamide

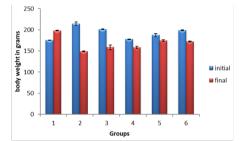
Figure 1: Impact of *Phaseolus vulgaris* L on hypoglycemic agent level

Figure 3 shows the level of lipid values in experimental groups. The diabetic control group showed ele-

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Groups	Blood glucose (mg/dl)	Hypoglycemic agent(µU/ml)	Amino acid (mg/ml)
Control	112.4 ± 1.18^a	15.14 ± 0.19^a	7.59 ± 0.02^a
Diabetic	370 ± 4.67^{ba}	6.09 ± 0.35^{ba}	3.135 ± 0.10^{ab}
100 mg/kg P.vulgaris	196 ± 0.87^{ba}	9.56 ± 0.45^{ab}	4.63 ± 0.11^{ba}
200 mg/kg P.vulgaris	178 ± 2.09^{ba}	8.55 ± 0.48^{ab}	4.54 ± 0.43^{ba}
300 mg/kg P.vulgaris	140 ± 1.61^{ba}	10.75 ± 0.22^{ab}	$6.81{\pm}~0.17^{ab}$
glibenclamide	158 ± 0.98^{ba}	7.70 ± 0.48^{ab}	4.43 ± 0.30^{ba}

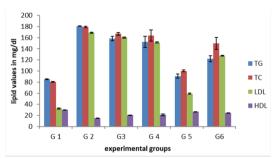
Table 2: Impact of oral administration of Phaseolus vulgaris L. extract on blood sugar, Hypoglyceamic agent and amino acid levels

Data proceed expressed as mean \pm SEM (N = 6). Down the column values with completely different superscripts are significantly different at P < 0.05. a NC(Normal control) group different. b DC(diabetes control) group



Group 1- Normal control; Group 2 -Diabetic control; Group 3 -dose 100 mg/kg Phaseolus vulgaris; Group 4 -200 mg/kg Phaseolus vulgaris; Group 5-300 mg/kg Phaseolus vulgaris; Group 6- glibenclamide

Figure 2: Impact of Phaseolus vulgaris L hydrated seed extract on weight in grams



Group 1- Normal control; Group 2 -Diabetic control; Group 3 -dose 100 mg/kg *Phaseolus vulgaris*; Group 4 -200 mg/kg *Phaseolus vulgaris*; Group 5-300 mg/kg *Phaseolus vulgaris*; Group 6- glibenclamide

Figure 3: Impact of *Phaseolus vulgaris* L hydrated seed extract on lipoid profile

vated lipid values for total cholesterol, low-density lipoprotein, and triglyceride, while high-density lipoprotein level was low when comparing the normal control group. After treatment with *Phaseolus vulgaris L* with varying concentration and glibenclamide, an improvement was observed, group 5 and group 6 responded well to treatment. Treatment with *Phaseolus vulgaris* L. extract in 200-DC and 300-DC groups showed a significant decrease in the levels of serum TG, TC, and LDL-C and a simultaneous significant increase in the level of HDL-C when compared with DC group. Only the serum HDL-C return to the basal level of the NC group, the serum TG, LDL-C, and TC did not return to the basal level of the NC group.

Changes in urea, creatinine, ALP and SGOT levels

Table 3 shows the level of the liver marker and kidney marker enzymes plasma level of experimental rats. There was a drastic rise in SGOT and ALP levels in the untreated diabetic group when compared with the normal control group. After treatment, diabetic rats with *Phaseolus vulgaris* extract and standard drug reduction of SGOT and ALP levels were observed. Renal markers in the untreated group increased more than for the normal control group. Treatment *Phaseolus vulgaris* extract and standard drug help in the reduction of the renal values.

The current statistics showed that at the dose of 300 mg/kg of *Phaseolus vulgaris* L. extract, aldohexose, glycerides, total steroid alcohol, high-density lipoprotein, low-density lipoprotein, SGOT, urea, and creatinine attenuate significantly. Moreover, the extract enhanced monosaccharide tolerance in treated diabetic rats as compared with the management of diabetic rats. The hydrated extract of legume showed a comparable anti-diabetic impact to glibenclamide, a customary hypoglycaemic drug that's used as a usual anti-diabetic agent to measure the anti-diabetic activities in investigational polygenic disease studies (Jain *et al.*, 2010; Ramkumar *et al.*, 2011).

In the present study, as shown in Figure 2, weight loss was observed due to the induction of polygenic disorder by streptozotocin. Administration of *Phaseolus vulgaris* L. extract and standard drug drastically improved a load of weight loss when comparing untreated diabetic control. Due to insulin deficiency degradation of protein and lipids are known to contribute to weight loss (Irudayaraj *et al.*, 2012). By treatment, the diabetic rats with *Phaseolus vulgaris* L. extract as well as standard drug-enhanced

Group	Hepati	c Markers	Renal Markers	
	SGOT (U/L)	ALP (U/L)	Urea (mg/dl)	Creatinine (mg/dl)
Control	40.83 ± 0.22^a	49.69 ± 0.65^a	36.63 ± 0.45^{a}	1.69 ± 0.12^a
Diabetic	117.62 ± 1.64^{b}	127.30 ± 0.94^b	81.84 ± 1.47^b	6.64 ± 0.17^b
100mg/kg P.vulgaris	99.13 ± 2.32^{ab}	$104.25{\pm}2.24^{ab}$	$\textbf{72.57} \pm \textbf{3.21}^{ab}$	$4.55{\pm}0.49^{ab}$
200 mg/kg P.vulgaris	77.16 ± 0.84^{ab}	$83.94{\pm}~0.77^{ab}$	66.70 ± 0.75^{ab}	$3.19 {\pm}~0.15^{ab}$
300 mg/kg P.vulgaris	54.13 ± 0.21^{ab}	46.43 ± 0.96^b	40.09 ± 0.31^{ab}	$1.51 {\pm}~ 0.17^b$
Standard	47.25 ± 1.15^{ab}	$49.83 {\pm}~0.17^{ab}$	$41.29\pm0.52^{\mathit{ab}}$	1.87 ± 0.07^{ba}

Table 3: Impact of oral administration of Phaseolus vulgaris L. extract on SGOT, ALP, urea, and Creatine

Data proceed expressed as mean \pm SEM (N = 6). Values with completely different superscripts down the column are significantly different at P < 0.05. a NC(Normal control) group. b DC(diabetes control) group

glucose metabolism and so improved body weight.

A secondary complication of diabetes is mostly brought out by metabolic disorders of polygenic disorders (Chehade et al., 2013). Hypercholesterolemia and hypertriglyceridemia are reportable to occur in diabetic rats (Wang et al., 2010; Balamurugan and Ignacimuthu, 2011). The hydrolysis of triglycerides and mobilization of free fatty acids takes place when lipolytic hormones action is activated by insulin in normal conditions (Ruge *et al.*, 2012). Inversely, in the diabetic state, there is a deficiency of insulin leading to reduced lipoprotein activity, this makes the liver to overproduce lowdensity lipoprotein, and hypertriglyceridemia condition is observed. Treated diabetic animals suggested that the extract holds tropic insulin results or insulin-mimetic activity as it is evident by a significant reduction of plasma, low-density lipoprotein, cholesterol, and triglyceride.

In line with our results, untreated diabetic rats showed a significant elevation of urea and creatinine levels, which is used to assess the nephritic pathology (Honoré *et al.*, 2012). Hyperglycemia in diabetic condition leads to attenuation of metabolic alteration in protein and nucleic acid metabolism, from our study we observed by treatment of *Phaseolus vulgaris* L. to diabetic rats a meaningful decrease in some in urea and creatinine was observed.

From earlier studies, liver damage is reported to occur due to the increase in ALP and SGOT activities in diabetic conditions (Florence *et al.*, 2014). We came to an agreement in our study that the damage of hepatocellular could be brought up by an increase

of ALP and SGOT in diabetic rats. By administration of glibenclamide and *Phaseolus vulgaris* L. for 30 days to diabetic rats showed great improvement of these enzymes in plasma. Our result was in agreement with earlier report *piper longum* root extract on antidiabetic effect on diabetic rats (Nabi *et al.*, 2013) and indicated the hepatoprotective results of legume against STZ-induced toxicity.

Phaseolus vulgaris L has been reportable earlier to contain bioactive compounds like flavonoids. The medication activity of *Phaseolus vulgaris* L is due to the presence of a flavonoid compound. (Chaves *et al.*, 1997, 1993) Phenolic and flavonoids compounds are major symptoms to the activities of numerous healthful plants (Romano et al., 2013). From studies report that flavonoids have medicinal properties. As a result, to stimulate glucose metabolism in peripheral tissue aerophilous stress throughout diabetic conditions (Eid et al., 2010; Rauter et al., 2010). They additionally exert a stimulatory result on hypoglycaemic agent secretion by energizing Ca2+ concentration (Babujanarthanam et al., 2009). However, the resolute medication activity is additionally attributable to the synergistic result of varied classes of bioactive compounds gift in Phaseolus vulgaris L extract.

CONCLUSION

In conclusion, hydrated seed extract of *Phaseolus vulgaris* L. was significant to STZ-induced diabetic rats since decreasing aldohexose levels was observed. Hypo lipidemic result was inarguable by a significant reduction in plasma lipid parameters. This result makes sure the employment of this plant to achieve polygenic disorder complications. To extensively understand the mechanism of action results due to the presence of bioactive compounds involved in these medical field activities remain to be confirmed.

Conflict of Interest

We declare that we've no conflict of interest

REFERENCES

- Ahmed, K., Zameer, S., Sidhra, S. Z. A., Ponmurugan, P., Kumar, B. S. 2016. Ameliorative potential of Solanum trilobatum leaf extract and fractions on lipid profile and oxidative stress in experimental diabetes. *Pakistan Journal of Pharmaceutical Sciences*, 29(5):1571–1578.
- Babujanarthanam, R., Kavitha, P., Pandian, M. R. 2009. Quercitrin, a bioflavonoid, improves glucose homeostasis in streptozotocin-induced diabetic tissues by altering glycolytic and gluconeogenic enzymes. *Fundamental & Clinical Pharmacology*, 24(3):357–364.
- Balamurugan, R., Ignacimuthu, S. 2011. Antidiabetic and Hypolipidemic effect of methanol extract of Lippia nodiflora L. in streptozotocin-induced diabetic rats. *Asian Pacific Journal of Tropical Biomedicine*, 1(1):60117–60119.
- Bhagwat, S. H., David, B., Holden, J. M. 2008. USDA-Iowa State University database on the isoflavone content of foods. US Department of Agriculture.
- Chaves, N., Escudero, J. C., Gutierrez-Merino, C. 1993. Seasonal variation of exudate of cistus ladanifer. *Journal of Chemical Ecology*, 19(11):2577–2591.
- Chaves, N., Escudero, J. C., Gutierrez-Merino, C. 1997. Role of Ecological Variables in the Seasonal Variation of Flavonoid Content of Cistus ladanifer Exudate. *Journal of Chemical Ecology*, 23(3):579–603.
- Chehade, J. M., Gladysz, M., Mooradian, A. D. 2013. Dyslipidemia in Type 2 Diabetes: Prevalence, Pathophysiology, and Management. *Drugs*, 73:327–339.
- Chopra, R. N. 1958. Chopra's indigenous drugs of India. Dhur, Calcutta. Ram Nath. 2d ed.
- Eid, H. M., Martineau, L. C., Saleem, A., Muhammad, A., Vallerand, D., Benhaddou-Andaloussi, A., Haddad, P. S. 2010. Stimulation of AMP-activated protein kinase and enhancement of basal glucose uptake in muscle cells by quercetin and quercetin glycosides, active principles of the antidiabetic medicinal plant Vaccinium Vitis-idea. *Molecular Nutrition & Food Research*, 54(7):991–1003.

Florence, N. T., Benoit, M. Z., Jonas, K., Alexan-

dra, T., Désiré, D. D. P., Pierre, K., Théophile, D. 2014. Antidiabetic and antioxidant effects of Annona muricata (Annonaceae), aqueous extract on streptozotocin-induced diabetic rats. *Journal of Ethnopharmacology*, 151(2):784–790.

- Honoré, S. M., Cabrera, W. M., Genta, S. B., Sánchez, S. S. 2012. The protective effect of yacon leaves decoction against early nephropathy in experimental diabetic rats. *Food and Chemical Toxicology*, 50(5):1704–1715.
- IDF 2017. The International Diabetes Federation. Atlas Eighth edition 2017. pages 31679–31687.
- Irudayaraj, S. S., Sunil, C., Duraipandiyan, V., Ignacimuthu, S. 2012. Antidiabetic and antioxidant activities of Toddalia Asiatica (L.) Lam. leaves in streptozotocin-induced diabetic rats. *Journal of ethnopharmacology*, 143(2):515–523.
- Jain, S., Bhatia, G., Barik, R., Kumar, P., Jain, A., Dixit, V. K. 2010. Antidiabetic activity of Paspalum scrobiculatum Linn. in alloxan-induced diabetic rats. *Journal of Ethnopharmacology*, 127(2):325–328.
- Lai, P., Roy, J. 2004. Antimicrobial and Chemopreventive Properties of Herbs and Spices. *Current Medicinal Chemistry*, 11(11):1451–1460.
- Maize 2003. CGC meeting.
- Nabi, S. A., Kasetti, R. B., Sirasanagandla, S., Tilak, T. K., Kumar, M. V. J., Rao, C. A. 2013. Antidiabetic and antihyperlipidemic activity of Piper longum root aqueous extract in STZ induced diabetic rats. *BMC Complementary and Alternative Medicine*, 13(1).
- Nair, S., Nagar, R., Gupta, R. 1998. Antioxidant phenolics and flavonoids in common Indian foods. *The Journal of the Association of Physicians of India*, 46:708–718.
- Pari, L., Venkateswaran, S. 2003. Effect of an aqueous extract of Phaseolus vulgaris on plasma insulin and hepatic key enzymes of glucose metabolism in experimental diabetes. 58(12):916–915.
- Ramkumar, K. M., Vanitha, P., Uma, C., Suganya, N., Bhakkiyalakshmi, E., Sujatha, J. 2011. Antidiabetic activity of alcoholic stem extract of Gymnema montanum in streptozotocin-induced diabetic rats. *Food and Chemical Toxicology*, 49(12):3390–3394.
- Rauter, A. P., Martins, A., Borges, C., Mota-Filipe, H., Pinto, R., Sepodes, B., Justino, J. 2010. Antihyperglycaemic and protective effects of flavonoids on streptozotocin-induced diabetic rats. *Phytotherapy Research*, 24(S2):133–138.
- Roman-Ramos, R., Flores-Saenz, J. L., Alarcon-Aguilar, F. J. 1995. Anti-hyperglycemic effect of

some edible plants. *Journal of Ethnopharmacology*, 48(1):25–32.

- Romano, B., Pagano, E., Montanaro, V., Fortunato, A. L., Milic, N., Borrelli, F. 2013. Novel Insights into the Pharmacology of Flavonoids. *Phytotherapy Research*, 27(11):1588–1596.
- Ruge, T., Sukonina, V., Kroupa, O., Makoveichuk, E., Lundgren, M., Svensson, M. K., Eriksson, J. W. 2012. Effects of hyperinsulinemia on lipoprotein lipase, angiopoietin-like protein 4, and glycosylphosphatidylinositol-anchored highdensity lipoprotein binding protein 1 in subjects with and without type 2 diabetes mellitus. *Metabolism*, (5):652–660.
- Shaw, J. E., Sicree, R. A., Zimmet, P. Z. 2010. Global estimates of the prevalence of diabetes for. *Diabetes, Res. Clin. Pr*, 87:4–14.
- Tapsell, L. C., Hemphill, I., Cobiac, L., Sullivan, D. R., Fenech, M., Patch, C. S., Inge, K. E. 2006. Health benefits of herbs and spices: the past, the present, the future. *Medical Journal of Australia*, (S4):185– 185.
- Wang, L., Zhang, X. T., Zhang, H. Y., Yao, H. Y., Zhang, H. 2010. Effect of Vaccinium bracteatum Thunb. Leaves extract on blood glucose and plasma lipid levels in streptozotocin-induced diabetic mice. *Journal of ethnopharmacology*, 130(3):465–469.