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Research Article

IN VITRO ANTIDIABETIC ACTIVITY OF AQUEOUS FRUIT EXTRACT OF *Solanum torvum* Sw.

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ABSTRACT

Anti-diabetic activity of aqueous fruit extract of *Solanum torvum* was aimed at detecting the phytochemicals and ascertains the anti-diabetic activity using *in vitro* experimental models. In this study, physiochemical parameters were carried out and the content of phyto organic constituents such as total alkaloids, flavonoids, phenols, carbohydrates, fats, proteins and crude fiber were determined. LC-MS/MS have been used for detecting the phytochemicals. Different concentrations of the extract have been screened for their anti-inflammatory and antidiabetic activities. Aqueous fruit extract of *S. torvum revealed* the presence of (iso)pentyl dihexoside, quinic acid derivative, chlorogenic, caffeoylglucaric acid and dicaffeoylquinic acid by LC-MS/ MS analysis. The extract exhibited maximum anti-inflammatory activity of 23.95 % at 1000 µg/ml in inhibition of albumin denaturation, 59.00% at 1000 µg/ml in inhibition of protease denaturation and 64.00% at 1000 µg/ml by HRBC membrane stabilization assay, which are comparable to that of standard aspirin. The extract exhibited maximum anti diabetic activity of 72.00 % at 1000 µg/ml in inhibition of α-amylase activity, 63.00% at 1000 µg/ml in inhibition of α-glucosidase activity and 78.00% at 1000 µg/ml in glucose uptake by yeast cells, which are comparable to that of standard acarbose. From the results, the aqueous fruit extract of *S. torvum* might possess antidiabetic activity due to the presence of bioactive compounds.

Keywords: Anti-inflammatory activity, Anti diabetic activity, *Solanum torvum* SW

INTRODUCTION

Diabetes mellitus (DM) is one of the most common endocrine metabolic disorder resulting from a defect in insulin secretion, insulin action, or both [1-3]. Insulin deficiency in turn leads to chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism. Diabetes is a growing challenge in India with estimated 8.7% diabetic population in the age group of 20 and 70 years. By the year 2010, it is estimated that more than 200 million people worldwide will have DM and 300 million will subsequently have the disease by 2025, which causes the various micro vascular complications includes retinopathy [4-5], neuropathy [6-7], nephropathy [8-9] and macro vascular complications includes heart attack, stroke, peripheral vascular diseases [10-11] and ulceration [12]. Population growth, inadequate supply of drugs, prohibitive cost of treatments, side effects of several allopathic drugs, and development of resistance to currently used drugs have led to an increased emphasis on the use of plant materials as a source of medicine for a wide variety of human ailments. As part of the strategy to reduce the financial burden on the human population in developing countries, increased use of plant drugs will be recommended. India is sitting on a gold mine of well recorded and traditionally well practiced knowledge of herbal medicines such as Siddha and Ayurveda. So, the researchers are investigating and try to find more effective and safer hypoglycemic agent without causing any side effects. Concerning these points on mind, we selected fruits of *Solanum torvum* for this work.

S. torvum (*Solanaceae* family) is a cultivated relative of eggplant *S. melongena* L. [13]. It is a prickly creeping shrub native to India [14]. Phytochemical screening of sun-dried *S. torvum* fruits gave positive tests for alkaloids, flavonoids, saponins, tannins, glycosides, fixed oil, vitamin B group, vitamin C and iron salts[15]. *S. torvum* possesses antifungal [16], immunomodulatory and erythropoietic [17], antioxidant [18], analgesic and anti-inflammatory [19], anti-ulcerogenic[20], cardioprotective[21], nephroprotective [22], antidiabetic [23], angiotensin and serotonin receptor blocking activities [24]. So, this study is to investigate the anti-diabetic activity of aqueous extract of *S. torvum* fruit, a common vegetable used by the Indians, on *in vitro* models.

MATERIALS AND METHODS

Collection of plant material

The friuts of *S. torvum* was collected from Herbal Garden of STET College on the month of April 2017. Taxonomical identification was done by Prof. P.Brindha, Associate Dean and Co-ordinator, CARISM, SASTRA Deemed University, Tirumalaisamudram and authentication was done by Dr.S.John Britto, RAPINAT Herbarium and Centre for Molecular Systematics, St.Joseph's College, Tiruchirappalli (Voucher number of the specimen,001). Plant materials were washed under tap water and dried in shaded condition for two weeks and milled to a fine powder using domestic mixer grinder.

Preparation of aqueous extract

Powdered sample (10g) was taken with 100ml of distilled water and kept for 24 hrs. at room temperature. The extract was then separated using Whatman No. 1 filter paper and used for physicochemical, qualitative and quantitative chemical

examination, i*n vitro* anti-inflammatory and *in vitro* anti-diabetic assays.

LC–MS/MS

For qualitative purpose crude extract was weighed and dissolved in ethanol to get final concentration of 1 mg/ml was then filtered using 0.45 µm syringe filter. 500 µL of this solution was analyzed by LC/ESI/MS/MS using UHPLC+ focused (Ultra high-performance liquid chromatography) RP liquid chromatography coupled to mass spectrometer (micro TOF-Q II, Bruker, Germany). Liquid chromatography separations were carried out on a C18 reverse phase column (120 Å, 2.1 x 150 mm Acclaim 120, UHPLC+ Ultimate 3000 series, Dionex). UV detector was set arbitrarily at 260 nm. A discontinuous gradient elution at a flow rate of 0.2 ml/min was performed using mobile phase A represented by acetonitrile and mobile phase B represented by water (MilliQ) acidified with acetic acid (1%). The gradient started from 95% of B for 10 min, followed by achieving 90% B in 1 min, to 60% B in the next 9 min, next 10 min B reaches 80%, next 10 min to reach 40% B, 5 min to reach 0% B and was maintained for another 10 min until the run ends. Mass spectrometer with ESI ionization at negative mode equipped with HyStar 3.2 software was optimized to detect the exact mass and mass fragmentation pattern of each eluted compound. TIC spectra were acquired and elaborated using the HyStar software Data Analysis module. MS/MS experiments were carried out by means of Auto scanning mode, where the mass spectrometer software made a choice in real time about the selection of ion to fragment based on the intensity of each peaks with a threshold set above 1500 absolute counts. Optimized parameters consisted in collision energy 10 eV, focusing potential of 350 Vpp (Voltage per peak), transfer time of 800 µS, prepulse storage of 5 µS the instrument was operated in the negative ion mode with a capillary voltage of 3.5KV, capillary temperature was 280˚C, sheath gas (N2) flow rate was 6 L/min and the data were acquired in the Auto MSn scanning modes. Scan range was *m/z* 50– 1500; number of micro scans was set at 3.

***In vitro* anti-inflammatory assay**

In vitro anti-inflammatory activity assessed by Inhibition of albumin denaturation, Inhibition of protease denaturation and Membrane stabilization activity [25].

In vitro anti-diabetic assay

In vitro antidiabetic activity evaluated by α-Amylase inhibition activity, α-Glucosidase inhibition activity and determination of glucose uptake by Yeast [26].

RESULTS

Physicochemical Constants

Physicochemical constants such as moisture content, total ash, water extractive value and alcohol extractive value were evaluated, and the results showed in table 1.

Phytochemical screening

Preliminary phytochemical analysis on aqueous extract of *S.torvum* exhibits the presence of proteins, sterols, glycosides, tannins and terpenoids (Table 2).

Major organic constituents

Data obtained on the quantitative estimation of major organic constituents present in the selected plant drug was tabulated in the table 3.

LC-MS/MS

The LC-MS/MS result obtained in the aqueous extract of *S. torvum* fruit such as (Iso)pentyl dihexoside, quinic acid derivative, chlorogenic acid, caffeoylglucaric acid and dicaffeoylquinic acid were identified and tabulated in the table 4.

***In vitro* anti-inflammatory assays**

In the present study, 8 different concentrations of the aqueous extract of *S.torvum* were evaluated for anti-inflammatory activity employing *in vitro* assays and the data of the results obtained were presented in table 5. The aqueous extract of *S.torvum* fruit revealed high anti-inflammatory activity (23.95%) by the method of inhibition of protein denaturation (albumin), 59.00% by the method of protease inhibition and 64.00% by the method of membrane stabilization at 1000µg /ml concentration, which was comparable to that of standard aspirin.

***In vitro* antidiabetic assays**

In the present study, aqueous extract of *S.torvum* was screened for anti-diabetic activity using inhibiting the α-amylase, α-glucosidases activity and glucose uptake by yeast cells and the data of the results obtained were shown in table 6. These results clearly suggest that the extract is capable of effectively inhibiting the α-amylase activity (72.00%) and α- Glucosidases activity (63.00%). The plant extract shows maximum potential 78.00% on glucose uptake by yeast cells at 1000 µg compared with that of acarbose.

Table 1: Physicochemical constants

Physicochemical Constants	Value % (W/W)
Moisture content	20.00
Total ash	2.25
Water extractive value	16.60
Alcohol extractive value	25.00

Table 2: Preliminary phytochemical screening

Tests for	Aqueous extract
Carbohydrates	-
Proteins	+
Tannins	+
Saponins	-
Flavonoids	-
Terpenoids	+
Glycosides	+
Sterols	+
Phenols	-
Alkaloids	-

+ Presence; - Absence

Table 3: Major organic constituents

Organic constituents	Quantity (mg/g)
Total alkaloids	1.525
Total flavonoids	0.503
Total phenols	0.17
Total proteins	1.6
Total carbohydrates	0.53
Total fats	0.27
Total crude fibres	3.93

Table 4: Compounds identified by LC-MS/MS in the aqueous extract of *S.torvum*

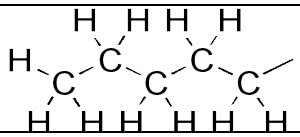
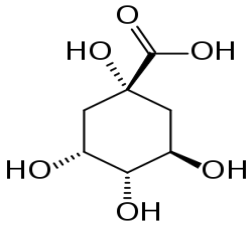
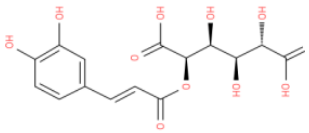
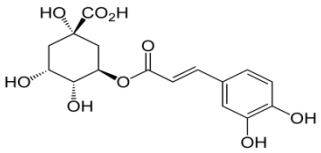
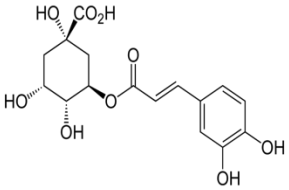
S. No.	R.T (min)	Compound	[M _ H]	Structure	MS/MS (product ion)
1.	2.2-2.3	(Iso)pentyl dihexoside	411.2		249.1, 261.2
2.	2.5-2.7	Quinic acid derivative	533.2		191.1, 449.4
3.	2.7-2.9	Chlorogenic acid	353.1		191.1, 114.7
4.	2.8-3.0	Caffeoylglucaric acid	371.1		191
5.	3.2-3.4	Dicaffeoylquinic acid	515.2		191.1, 341.1, 323.1

Table 5: Anti-inflammatory activity of fruit aqueous extract of *S. torvum*

S.No.	Concentration of sample(µg/ml)	Inhibition of albumin denaturation (%)	Inhibition of Protease denaturation(%)	HRBC Membrane stabilization (%)
1.	1000	23.95±0.04	59±0.02	64±0.02
2.	500	21.87±0.02	46±0.04	57±0.05
3.	250	19.70±0.03	40±0.05	55±0.03
4.	125	16.60±0.08	34±0.01	44±0.06
5.	62.5	14.50±0.05	26±0.03	37±0.04
6.	31.2	12.50±0.09	22±0.07	30±0.05
7.	15.5	07.29±0.10	15±0.10	21±0.01
8.	7.5	03.12±0.12	10±0.11	11±0.07
9.	Aspirin(100)	68.33±0.07	55±0.08	89±0.08

Table 6: Antidiabetic activity of aqueous extract of fruit of S. *torvum*

S.No.	Concentration of sample(µg/ml)	Inhibition of α–amylase activity (%)	Inhibition of α –glucosidases activity (%)	Glucose uptake by yeast cells (%)
1.	1000	72 ± 0.02	63±0.01	78±0.03
2.	500	68 ± 0.04	59±0.04	68±0.07
3.	250	59 ± 0.03	55±0.06	57±0.05
4.	125	45 ±0.05	45±0.08	47±0.06
5.	62.5	18 ± 0.07	41±0.02	31±0.10
6.	31.2	22 ± 0.09	36±0.09	20±0.13
7.	15.5	14 ± 0.11	23±0.05	26±0.15
8.	7.5	31 ± 0.13	11±0.01	15±0.17
9.	Acarbose (100)	89 ± 0.16	76±0.03	89±0.19

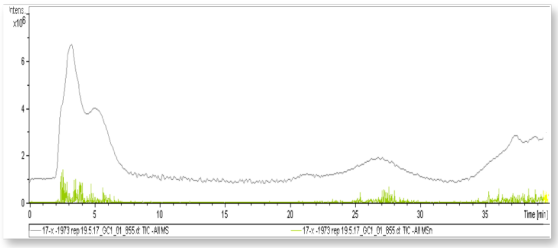


Figure 1: Total Ion Chromatogram (Negative mode) obtained from LC- MS/MS

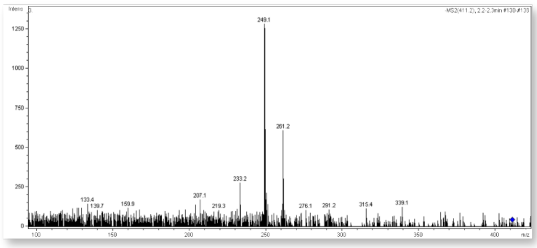


Figure 2: MSMS obtained from LC-MS/MS - (Iso)Pentyl Dihexoside

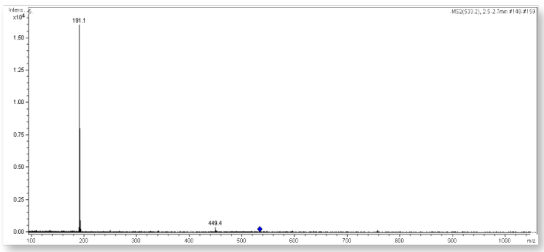


Figure 3: MSMS obtained from LC-MS/MS – Quinic acid Derivative

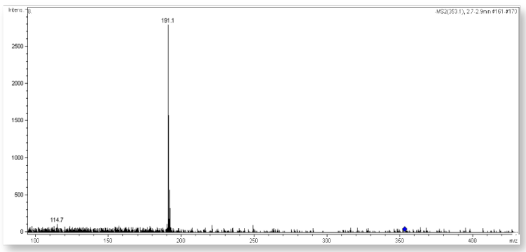


Figure 4: MSMS obtained from LC-MS/MS - Chlorogenic acid

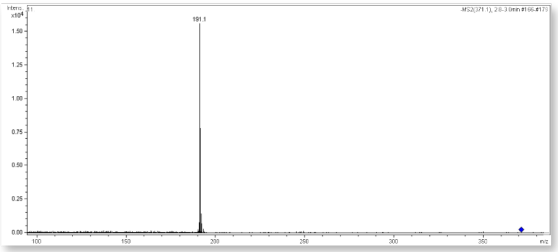


Figure 5: MSMS obtained from LC-MS/MS - Caffeoylglucaric acid

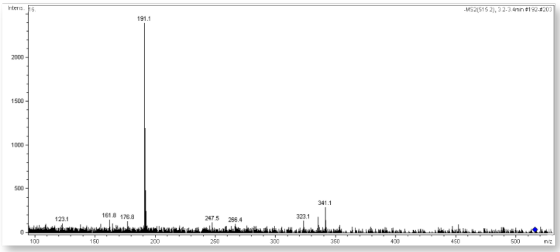


Figure 6: MSMS obtained from LC-MS/MS - Dicaffeoylquinic acid

DISCUSSION

The data obtained on the moisture content of *S. torvum* is (20.00%), which implies that the shelf life is longer. Ash content (2.25%) reveals that the sample is rich in mineral contents. Solubility in water (16.0%) is lesser than that of alcohol (25.0%). The extractive value suggests that the sample satisfies purity standard and is also rich in high polar compounds. Successful predication of natural compounds from plant material depends on the type of solvents used in the extraction process. Traditional healers use mostly water as the solvent [25].

Major organic constituents (secondary metabolites) were estimated. Today food industries are very much interested in using the plant extracts having good number of secondary metabolites such as flavonoids, phenolic acids and tannins as they are known anti-oxidants. Diverse biological activities, such as anti-inflammatory, anti-atherosclerotic and anti-carcinogenic activities are also possessed by these anti-oxidant compounds[26]. Alkaloid recorded higher percentage of yield (1.525mg), when compared to flavonoids (0.503mg), and phenols (0.17mg) in the fruits of *S.torvum*. Alkaloids are also known for decreasing blood pressure, balancing the nervous system in case of mental illness and also possess anti-malarial properties [27]. The flavonoids are a prominent group of secondary metabolites in citrus fruits that may possess biological activity and have beneficial effects on human health as antimicrobial, anti-inflammatory, antidiabetic, anticholesterolemic, antioxidant and anti-cancer agents. This indicated that higher flavonoid content was associated with a higher total phenolic content. Phenolic compounds are one of the largest and most ubiquitous groups of plant metabolic. It possesses the ideal chemistry for free radical scavenging activity due to the presence of high reactivity as hydrogen or electron donors and metal chelating activity. So, the regular consumption of phenolic rich vegetables along with foods will inhibit carcinogenesis and mutagenesis in humans [25]. According to our

results, the sample contained significant amount of total phenolic that may increase antioxidant intake in human diet. Some major organic constituents total protein (1.6mg), fats (0.27mg), crude fiber (3.93mg) and total carbohydrates (0.53mg) of *S.torvum* is clearly depicted in the (Table 3).

LC-MS/MS Analysis

Herbal products can be considered only when it is scientifically validated. Ingredients in the final products must be characterized and authenticated in order to ensure reproducibility and quality of the product. Lack of this leads to many side effects like direct poisonous effects, allergic reactions, effect from contaminants upon interaction with herbal medicines have been reported in recent times. Remedial measure for those side effects depends on its phytochemical constituents. The progress of valid analytical methods which can reliably profile the phytochemical composition is a main tool for scientists [28]. The chemical constituent along with their chemical name, molecular weight, retention time (RT) and structure were tabulated. The chromatogram and the double mass spectrum of the extract were shown. The result obtained in the aqueous extract of *S. torvum* fruit such as (Iso)pentyl dihexoside, quinic acid derivative, chlorogenic acid, caffeoylglucaric acid and dicaffeoylquinic acid were identified.

Anti- inflammatory assays

Inflammation is complex process, very often associated with pain. Anti-inflammatory compounds can act on various level of pathophysiological process by blocking the biosynthesis of pro-inflammatory mediators, by decreasing the enzymes expression or by reducing substrate levels or by inhibiting the releases of performed stored mediators, by blocking-receptor interaction on target cells, mediator and immune stimulation, which result in less aggressive response to allergen challenge [25]. Inflammation is described as the succession of change in a living tissue, when it is injured provided that the injury is not such a degree as to at once destroy its structure and vitality, as well injure living microcirculation and related tissue. Inflammatory response to tissue injury involves a complex array of enzyme activation, mediator release, fluids extravasations, cell in migration, tissue breakdown and repair [29]. Inflammation can be classified as either acute or chronic. Acute inflammation is the initial response of the body to harmful stimuli and is achieved by the increased movement of plasma and leukocytes (especially granlocytes) from the blood in to the injured tissues. A cascade of biochemical events propagates and matures the inflammatory response, involving the local vascular system, the immune system and various cells within the injured tissues. Prolonged inflammation, known as chronic inflammation leads to a progressive shift in the type of cells present at the site of inflammation and is characterized by simultaneous destruction [30].

Denaturation of protein is a well-documented cause of inflammation. Since during inflammation condition, protein of the cell gets denatured, albumin protein is used as a model, whose protection by the plant extract during heat-induced denaturation was evaluated [25]. Inhibition of protein denaturation (albumin) activity of aqueous extract *S.torvum* fruit (Table 5) revealed high anti-inflammatory activity (23.95%) at 1000µg/ml concentration, which is lower than that of standard aspirin. Thus, the aqueous extract of *S.torvum* fruit may possibly inhibit the protein denaturation caused by the release of lysosomal content of neutrophils at the site of inflammation.

Proteases have been implicated in arthritic reaction. Neutrophiles contain natural serine protease in their liposomal granules. Leukocyte protease plays an important role in the development of tissue damage during inflammatory reactions and significant level of protection is provided by proteases inhibitors. Protease inhibition study revealed that the aqueous extract of fruits of *S.torvum* shower moderate activity of (59.00%) inhibition at 1000µg/ ml concentration (Table 5). However, this value is higher than that of standard aspirin (55.00%).

Stabilization of liposomal membrane is important in limiting the inflammatory response by inhibiting the release of liposomal constituents of activated neutrophil such as bactericidal enzymes and protease, which cause further tissue inflammation and damage upon extracellular release [31]. Human Red Blood Cell Membrane and its stabilization implies that the extract may stabilize liposomal membrane. Hypo-tonicity induced HRBC membrane damage can be taken as an *in vitro* measure of anti-inflammatory activity of the extract [39]. Membrance stabilization method revealed significant membrane stabilizing activity of aqueous extract of *S.torvum* fruits (64.00%) inhibition at 1000 µg/ml concentration (Table 5), which was comparable to that of standard aspirin (89.00%). The aqueous extract of *S.torvum* fruits was effectively inhibiting the hypo-tonicity induced hemolysis of erythrocyte membrane. This property provides evidence for membrane stabilization as an additional mechanism of anti-inflammatory effect of *S.torvum* fruit extract.

Anti-diabetic assays

Diabetes is characterized by high concentrations of blood sugar which can cause serious complications in the kidneys, eyes and cardiovascular system. Insulin is a key player in the control of glucose homeostasis. Lack of insulin affects carbohydrate, fat and protein metabolism[32]. The treatment of diabetes therefore mainly focuses on reducing fluctuations in blood sugar and subsequent complications. Among the different antidiabetic therapeutic approaches one major strategy is dropping gastro intestine absorption of glucose by inhibition of carbohydrate metabolizing enzymes α-amylase and α glucosidase. The recent advances in understanding the activity of intestinal enzymes (α-amylase and α glucosidase) have led to the development of newer pharmacological agents. A high postprandial blood glucose response is associated with micro and macro vascular complications in diabetes and more strongly associated with the risk for cardiovascular diseases. Pancreatic and intestinal glucosidases are the key enzymes of dietary carbohydrate digestion and inhibitors of these enzymes may be effective in retarding glucose absorption. This is because only monosaccharide is readily taken up from the intestine and all other carbohydrate has to be broken down enzymatically before they can be absorbed [33].

Natural antioxidants from fruits and vegetables offer an alternative source of dietary ingredients to promote healthy life. For example, α-amylase, α-glucosidase inhibitors are considered as one of the effective measures for regulating type II diabetes by controlling glucose uptake[34]. The digestion of starch by human undergoes several stages. Partial digestion of starch by the salivary α amylase produces shorter oligomers. On complete digestion of starch produces maltose, maltotriose and glucose. Inhibition of α -amylase leads to reduction in post prandial hyperglycemia[35]. The α-amylase inhibitors are currently used for diabetic treatment as oral hypoglycemic agents. Acarbose is a commercially available enzyme inhibitor for type II diabetes. However, it is reported to cause various side effects such as abdominal distention, flatulence and possibly diarrhea[36]. Searching for safe and effective inhibitors from natural sources is of emerging interest. The inhibitory effects of the *Solanum torvum* and acarbose on α-amylase and are shown in Table 6.

From the following data obtained, result suggested that aqueous extract showed significant inhibitory activity. The percentage inhibition varied from 31.00% to 72.00%. These results clearly suggest that the aqueous of selected plant is capable of effectively inhibiting the α-amylase activity. Plant extract shows maximum α-amylase inhibition (72.00%) at 1000µg. However, the extract showed lower inhibitory activities compared with that of acarbose (89.00%).

Alpha-glucosidase is a membrane bound enzyme which is located in the epithelium of the small intestine. This enzyme catalyses, the conversion of disaccharides to glucose.Hence, inorder to control diabetes there is a need for the inhibition of α-glucosidase enzyme to control the conversion of glucose from disaccharides. Some of the antiviral agents acts on α-Glucosidase which plays a key role in glycoprotein and glycolipid for the assembly of viral capsid [37]. α-Glucosidase is also involved in a variety of metabolic disorders and carcinogenesis [38]. The inhibitory effects of *S. torvum* or and acarbose on α- Glucosidase and are shown in Table 6. The potential inhibition of *S. torvum* against α- Glucosidase ranged from 11.00% to 63.00%. Plant extract shows high α-Glucosidases inhibition 63.00% at 1000µg. However, the extract showed lower inhibitory activities compared with that of acarbose (20.25%).

The amount of glucose lining in the medium after a specific time serves as a marker for the biochemical parameter glucose uptake by the yeast cells. Sugar transport across the yeast cell membrane is mediated by certain specific membrane barriers. The process of uptake of glucose by yeast cells is facilitated diffusion process. Facilitated carriers transport is only attained if there is removal of intracellular glucose [39]. Aqueous extract of *S. torvum* increased the glucose uptake in yeast cells. It increases with increasing concentration and the results are comparable with that of the standard acarbose which was shown in Table6. The potential of *S.torvum* on glucose uptake by yeast cells ranged from 15.00% to 78.00%.The plant extract shows maximum potential 78.00% on glucose uptake by yeast cells at 1000 µg. However, the extract showed lower inhibitory activities compared with that of acarbose (89.00%).

The plant revealed better *in vitro* enzyme inhibitory activities, which are involved in regulation and absorption of carbohydrate, anti-diabetic activity proved by glucose uptake by yeast cells assay and also exhibits good anti-inflammatory activity. This present data illustrates that the aqueous extract of *S. torvum* fruit has medicinal properties and it will be useful in treating various diseases including diabetes.

CONCLUSION

Finally, it can be concluded from the results, the plant reveals better *in vitro* enzyme inhibitory activity which are involved in regulation and absorption of carbohydrate. Antidiabetic activity proved by inhibition of α–amylase, α –glucosidases and influence glucose uptake by yeast cells assay and also exhibits good anti-inflammatory activity. This present data illustrates that the aqueous extract of *S. torvum* fruits has medicinal properties and it will be useful in treating various diseases including diabetes.

REFERENCES

1. Kumar PJ, Clark, M. Textbook of Clinical Medicine. 8th ed. Saunders (London): W.B. Saunders Company Publishers; 2002.
2. Beverley B, Eschwege E. Textbook of Diabetes. 3rd ed. John C Pickup and Gareth Williams (UK): Blackwell Publisher; 2003.
3. Lindberg G, Lindblad U, Melander A. Sulfonylureas for treating type 2 diabetes mellitus. Cochrane Database Systemic Reviews. 2004. 3: 254.
4. Bearse MA, Han T, Schneck ME. Local multifocal oscillatory potential abnormalities in diabetes and early diabetic retinopathy. Investigative ophthalmology and visual science 2004; 45: 3259-3265. https://doi.org/10.1167/iovs.04-0308
5. Hove MN, Kristensen JK, Lauritzen T, Bek T. The prevalence of retinopathy in an unselected population of type 2 diabetes patients from Arhus County, Denmark. Acta ophthalmologica 2004; 82: 443-448. https://doi.org/10.1111/j.1600-0420.2004.00270.x
6. Seki M, Tanaka T, Nawa H. Involvement of brain-derived neurotrophic factor in early retinal neuropathy of streptozotocin-induced diabetes in rats: therapeutic potential of brain-derived neurotrophic factors for dopaminergic amacrine cells. Diabetes, 2004; 53:9-12. https://doi.org/10.2337/diabetes.53.9.2412
7. Moran A, Palmas W, Field L. Cardiovascular autonomic neuropathy is associated with micro albuminuria in older patients with type 2 diabetes. Diabetes care 2004; 27: 972-977. https://doi.org/10.2337/diacare.27.4.972
8. Huang C, Kim Y, Caramori ML. Cellular basis of diabetic nephropathy: II. The transforming growth factor-beta system and diabetic nephropathy lesions in type 1 diabetes. Diabetes 2002; 51: 3577-3581. https://doi.org/10.2337/diabetes.51.12.3577
9. Shukla N, Angelini GD, Jeremy JY. Homocysteine as a risk factor for nephropathy and retinopathy in type 2 diabetes. Diabetologia 2003; 46: 766-772. https://doi.org/10.1007/s00125-003-1104-x
10. Svensson M, Eriksson JW, Dahlquist G. Early glycemic control, age at onset, and development of microvascular Bastaki S 128 complications in childhood-onset type 1 diabetes: a population-based study in northern Sweden. Diabetes Care 2004; 27: 955-962. https://doi.org/10.2337/diacare.27.4.955
11. Saely CH, Aczel S, Marte T. Cardiovascular complications in type 2 diabetes mellitus depend on the coronary angiographic state rather than on the diabetes state. Diabetologia 2004; 47: 145-146. https://doi.org/10.1007/s00125-003-1274-6
12. Wallace C, Reiber GE, LeMaster J. Incidence of falls, risk factors for falls, and fall-related factures in individuals with diabetes and a prior foot ulcer. Diabetes Care 2002; 25: 1983-1986. https://doi.org/10.2337/diacare.25.11.1983
13. Gousset C, Collonnier C, Mulya K, Mariska I, Rotino GL, Besse P, Servaes A, Sihachakr D. Solanum torvum, as a useful source of resistance against bacterial and fungal diseases for improvement of eggplant (*S. melongena* L.). Plant Science 2005; 168: 319-327. https://doi.org/10.1016/j.plantsci.2004.07.034
14. Hawkes JG, Lester RN, Skelding AD. The biology and taxonomy of the Solanaceae. London: Published for the Linnean Society of London by Academic Press; 1979.
15. Sivapriya M, Srinivas L. Isolation and purification of a novel antioxidant protein from the water extract of Sundakai (*Solanum torvum*) seeds. Food Chemistry 2007; 104: 510 - 517. https://doi.org/10.1016/j.foodchem.2006.11.060
16. Bari MA, Islam W, Khan AR Abul Mandal. Antibacterial and antifungal activity of *Solanum torvum* (Solanaceae). International Journal of Agriculture and Biology 2010; 12: 386–390.
17. Israf DA, Lajis NH, Somchit MN, Sulaiman MR. Enhancement of ovalbumin specific IgA responses via oral boosting with antigen co administered with an aqueous *Solanum torvum* extract. Life Science 2004; 75:397 406. https://doi.org/10.1016/j.lfs.2003.10.038

18. Waghulde H, Kamble S, Patankar P, Jaiswal B, Pattanayak S, Bhagat C, Mohan M. Antioxidant activity, phenol and flavonoid contents of seeds of *Punica granatum* (Punicaceae) and Solanum torvum (Solanaceae). Pharmacology Online 2011; 1: 193–202.
19. Ndebia EJ, Kamga R, Nchunga-Anye Nkeh B. Analgesic and anti- inflammatory properties of aqueous extract from leaves of *Solanum torvum* (Solanaceae). African Journal of Traditional, Complementary and Alternative Medicines 2007; 4: 240 - 4.
20. Télesphore B, Nguelefack S, Catherine B, Feumebo T, Ateufack G, Watcho P et al. Anti-ulcerogenic properties of the aqueous and methanol extracts from the leaves of *Solanum torvum* Swartz (Solanaceae) in rats. Journal of Ethnopharmacology 2008; 119: 135–140. https://doi.org/10.1016/j.jep.2008.06.008
21. Kamble S, Mohan M, Kasture S. Protective Effect of *Solanum torvum* on doxorubicin-induced cardiactoxicity in rats. Pharmacology Online 2009; 2: 1192-1204.
22. Pattanayak P, Parhi PK, Mishra SK, Khandei PK. Screening of anti-diabetic activity of bark extracts of *Gmelina arborea* in streptozotacin induced diabetic rats. International Journal of Pharmaceutical Sciences Review and Research 2011;8:130–132.
23. Gandhi GR, Ignacimuthu S, Paulraj MG, Sasikumar P. Antihyperglycemic activity and antidiabetic effect of methyl caffeate isolated from *Solanum torvum* Swartz. fruit in streptozotocin induced diabetic rats. European Journal of Pharmacology 2011; 670(2-3):623-631. https://doi.org/10.1016/j.ejphar.2011.09.159
24. Jaiswal BS, Mohan M. Effect of *S. torvum* on the contractile response of isolated tissues preparation in fructose fed rat. International Journal of Pharma and Bio Sciences 2012; 3: 161 – 169.
25. Manikandaselvi S, Vadivel V, Brindha P. Studies on nutraceutical properties of *Caesalpinia bonducella* L. An Indian traditional medicinal plant. Research Journal of Medicinal Plant 2016; 10:127-139. https://doi.org/10.3923/rjmp.2016.127.139
26. Cirillo VP. Mechanism of glucose transport across the yeast cell membrane. Journal of Bacteriology 1962; 84:485-91.
27. Batista R, Silva Ade JJ, Oliveira AB. Plant-derived antimalarial agents: new leads and efficient phytomedicines. Part II. Non-alkaloidal natural products. Molecules 2009; 14:3037-3072. https://doi.org/10.3390/molecules14083037
28. Manikandaselvi S, Brindha P. Quality control studies on *Luffa acutangula* L. International Journal of Pharmacy and Pharmaceutical Sciences 2014; 6: 55-62.
29. Vane JR. Botting RM. New insights into mode of action of anti-inflammatory drugs. Inflammation Research 1995; 44:1-10. https://doi.org/10.1007/BF01630479
30. Coussens LM, Werb C. Inflammation and Cancer. Nature 2002; 420: 860-867. https://doi.org/10.1038/nature01322
31. Da Silveira Sa RDC, Andrade LN, De Sousa DP. A review on anti-inflammatory activity of monoterpenes. Molecules 2013; 18:1227-1254. https://doi.org/10.3390/molecules18011227
32. Gandhi GRP, Sasikumar P. Antidiabetic effect of *Merremia emarginata* Burm.F. in Streptozotocin induced diabetic rats. Asian Pacific Journal of Tropical Biomedicine 2012; 2: 281-286. https://doi.org/10.1016/S2221-1691(12)60023-9
33. Nagaraj santhiya, Suriya moorthy priyanga, Subrahamanian Hemmalakshmi , Kanakasabapathi Devaki. Phytochemical analysis, Antiinflammatory activity, invitro antidiabetic activity and GC-MS profile of *Enythrina variegate*; L. bark. Journal of Applied Pharmaceutical Science 2016; 7:147-155. https://doi.org/10.7324/JAPS.2016.60722
34. Singhal AK. Naithani V, Bangar OP. Medicinal plants with a potential to treat Alzheimer and associated symptoms. International Journal of Nutrition, Pharmacology, Neurological Diseases 2012; 2 : 84–91. https://doi.org/10.4103/2231-0738.95927
35. Lonkisch M, Layer P, Rizza RA, Di Magno EP. Acute post prandial gastrointestinal and metabolic effects of wheat amylase inhibitor (WAI) in normal, obsess and diabetic humans. Pancreas 1998; 17: 176-181. https://doi.org/10.1097/00006676-199808000-00011
36. Krentz AJ, Bailey CJ. Oral antidiabetic agents: current role in type 2 diabetes mellitus. Drugs 2005; 65:385-411. https://doi.org/10.2165/00003495-200565030-00005
37. Gruters RA, Neefjes JJ, Tersmette M, De Goede REV, Huisman G, Miedema F et al. Interference with HIV-induced syncytium formation and viral infectivity by inhibitors of trimming glucosidase. Nature 1987; 330: 74-77. https://doi.org/10.1038/330074a0
38. Dennis JW, Laferte S, Waghorne C, Breitman ML, Kerbel RS. Beta 1-6 branching of Asn-linked oligosaccharides is directly associated with metastasis. Science 1987; 236:582–585. https://doi.org/10.1126/science.2953071
39. Wagner H, Bladt S. Plant drug analysis –A thin layer chromatography atlas, 2nd ed, (New delhi), Thompson publisher; 2004.

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