organ weight of liver and kidney of diabetic animals were summarized in Table 6.

Prediction of biological activity and toxicity profile of constituents of *Ocimum tenuiflorum*

The biological activity prediction at 70% levels showed various biological actions which were summarized in Table 7 and some activities are scientifically proven for *O. tenuiflorum* phytoconstituents. Most of the *O. tenuiflorum* phytoconstituents showed anti-inflammatory and anti-diabetic activities at various Pa: Pi levels. Toxicity prediction of the phytoconstituents of *O. tenuiflorum* did not show any major toxicity, carcinogenicity and mutagenicity [Table 8].

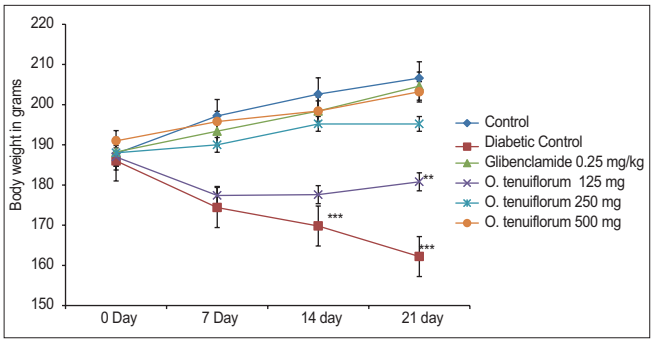

Figure 1: The effect of hydroalcoholic extract of leaves of *O. tenuiflorum* on body weight in streptozotocin-and nicotimanide induced diabetic rats (*O. tenuiflorum*: Hydroalcoholic extract of leaves of *O. tenuiflorum*. All the values are mean ± standard error of the mean [$N = 5$]. $^{*}P < 0.05$, $^{**}P < 0.05$, $^{**}P < 0.05$ when compared with control; one-way analysis of variance, followed by Bonferroni *post-hoc* test) *O. tenuiflorum* = *Ocimum tenuiflorum*

DISCUSSION

In the present study, an anti-diabetic and hyperlipidemic effects of *O. tenuiflorum* was studied against chemical (STZ– and NIC–) induced diabetes mellitus model. STZ is a glucosamine-nitrosourea derived from *Streptomyces achromogenes* (Gram-positive bacterium) and, it is used for the treatment of pancreatic beta cell carcinoma and to induce diabetes mellitus in rodents.[10] NIC was administered, followed by STZ injection to produce stable, moderate hyperglycemia and to prevent early inhibition of beta cell function by STZ, which may be helpful to reduce/prevent the incidence of diabetic coma caused by STZ.[48] STZ causes hyperglycemia after 2 h of injection, hypoglycemia in 6 h and finally hyperglycemia by decreasing the insulin levels through the inhibition/ destruction of pancreatic beta cell function.[9,49]

The hydroalcoholic extract of *O. tenuiflorum* exhibited significant anti-diabetic and anti-hyperlipidemic activities against STZ– and NIC– induced diabetic rats at the dose levels of 250 and 500 mg/kg BW. The effect was comparable with glibenclamide but not superior to it. At the end of this study, glibenclamide reduced the glucose

Table 4: Effect of hydroalcoholic extract of leaves of *O. tenuiflorum* on lipid profile in STZ induced diabetes

Treatment	TCs (mg/dl)	TG (mg/dl)	HDL cholesterol (mg/dl)	LDL cholestero (mg/dl)	VLDL cholesterol (mg/dl)	HDL ratio
Control	91.60±4.45	66.20±4.57	23.60±3.31	52.36±4.89	10.47±0.98	39.61±11.82
Diabetic control	178.60±8.55***	154.40±10.87***	13.20±2.42*	181.35±11.94***	36.27±2.39***	8.00±1.40**
Glibenclamide (0.25 mg/kg)	98.00±6.32$^{\$\$\$}$	74.40±4.12$^{\$\$\$}$	20.00±2.00	65.33±5.86$^{\$\$\$}$	13.07±1.17$^{\$\$\$}$	25.74±2.29
O. tenuiflorum (125 mg/kg)	166.00±9.12***	134.80±8.80***	10.80±1.62**	162.62±7.35***	32.52±1.47***	7.12±1.24**
O. tenuiflorum (250 mg/kg)	138.00±10.08$^{\$}$	100.00±4.38$^{\$\$\$}$	17.80±1.28	114.42±7.94$^{\$\$\$}$	22.88±1.59$^{\$\$\$}$	15.54±2.34
O. tenuiflorum (500 mg/kg)	101.20±6.28$^{\$\$\$}$	77.20±4.50$^{\$\$\$}$	22.80±1.85	66.95±7.12$^{\$\$\$}$	13.39±1.42$^{\$\$\$}$	29.88±3.37

Ocimum tenuiflorum: Hydroalcoholic extract of leaves of *Ocimum tenuiflorum*. All the values are mean±SEM (n=5). *P<0.05, **P<0.01, ***P<0.001as compared to control; $^{\$}P$<0.05, $^{\$\$\$}P$<0.01 compare to diabetic control, One-way ANOVA followed by Bonferroni *post-hoc* test. SEM=Standard error of mean; *O. tenuiflorum=Ocimum tenuiflorum* STZ=Streptozotocin; TG=Triglyceride; TC=Total cholesterol; HDL=High-density lipoprotein; LDL=Low-density lipoprotein; VLDL=Very-low-density lipoprotein

Table 5: The effect of hydroalcoholic extract of leaves of *O. tenuiflorum* on biochemical parameters in STZ–and NIC–induced diabetic rats

Treatment	SGOT (IU/l)	SGPT (IU/l)	Total protein (g/dl)	Albumin (g/dl)	Creatinine (mg/dl)	Urea (mg/dl)	Serum albumin: Creatinine ratio (g/mg)
Control	123.60±7.42	48.60±5.03	7.58±0.29	4.80±0.29	0.76±0.02	22.40±1.63	6.36±0.48
Diabetic control	165.20±7.22**	116.60±6.98***	4.38±0.62**	2.80±0.21**	1.38±0.06***	52.20±4.00***	2.03±0.15***
Glibenclamide (0.25 mg/kg)	131.40±5.38	50.40±5.54$^{\$\$\$}$	8.32±0.76$^{\$\$\$}$	4.68±0.34$^{\$\$}$	1.18±0.09*	28.80±2.71$^{\$\$}$	4.04±0.42
Ocimum tenuiflorum (125 mg/kg)	157.20±7.42	110.40±10.01***	5.62±0.57	2.88±0.30**	1.32±0.08***	44.40±6.49**	2.25±0.34***
Ocimum tenuiflorum (250 mg/kg)	132.40±7.09	59.20±6.58$^{\$\$\$}$	7.12±0.42$^{\$}$	4.34±0.35$^{\$}$	0.98±0.10$^{\$}$	29.20±3.62$^{\$\$}$	4.48±0.21$^{\$}$
Ocimum tenuiflorum (500 mg/kg)	117.00±9.55$^{\$\$}$	42.40±4.08$^{\$\$\$}$	8.96±0.53$^{\$\$\$}$	4.98±0.31$^{\$\$\$}$	0.80±0.09$^{\$\$\$}$	23.60±2.44$^{\$\$\$}$	6.68±1.00$^{\$\$\$}$

Ocimum tenuiflorum: Hydroalcoholic extract of leaves of *Ocimum tenuiflorum*. All the values are mean±SEM (n=5). **P<0.01, ***P<0.001 as compared to control; $^{\$}P$<0.05, $^{\$\$}P$<0.01, $^{\$\$\$}P$<0.01 compare to diabetic control, One-way ANOVA followed by Bonferroni *post-hoc* test. SEM=Standard error of mean; STZ=Streptozotocin; NIC=Nicotimanide; SGOT=Serum glutamic oxaloacetic transaminase; SGPT=Serum glutamic pyruvate transaminase; *O. tenuiflorum=Ocimum tenuiflorum*

Table 6: The effect of hydroalcoholic extract of leaves of *O. tenuiflorum* on relative, absolute organ weight and kidney weight: Body ratio in STZ– and NIC– induced diabetic rats

Treatment	Relative organ weight		Absolute organ weight		Kidney weight: Body weight ratio (mg/g)
	Liver (g)	Kidney (g)	Liver (g)	Kidney (g)	
Control	6.20±0.26	0.84±0.02	3.00±0.10	0.41±0.01	4.09±0.13
Diabetic control	5.76±0.13	0.72±0.03	3.56±0.11*	0.44±0.01	4.41±0.15
Glibenclamide (0.25 mg/kg)	6.12±0.12	0.80±0.03	3.00±0.12	0.39±0.02	3.94±0.18
O. tenuiflorum (125 mg/kg)	5.82±0.21	0.74±0.02	3.23±0.16	0.41±0.02	4.09±0.16
O. tenuiflorum (250 mg/kg)	6.24±0.10	0.82±0.03	3.20±0.04	0.42±0.01	4.18±0.10
O. tenuiflorum (500 mg/kg)	6.30±0.13	0.81±0.04	3.10±0.06	0.40±0.03	4.01±0.26

Ocimum tenuiflorum: Hydroalcoholic extract of leaves of *Ocimum tenuiflorum*. All the values are mean±SEM (n=5). *P<0.05 as compared to control; One-way ANOVA followed by Bonferroni *post-hoc* test. SEM=Standard error of mean; STZ=Streptozotocin; NIC=Nicotimanide; *O. tenuiflorum=Ocimum tenuiflorum*

Table 7: Predicted biological activity of phytoconstituents of *O. tenuiflorum*

Compound	Selective predicted activity with (Pa: Pi)
Ursolic acid	Insulin promoting, hepatoprotecting, chemoprotecting, antiprotozoal, hypoglycemic, anti-inflammatory, wound healing, antiulcer, nitric oxide antagonistic, antinociceptive and analeptic properties.
Eugenol	Antimutagenic, mucomembranous protecting, beta-adrenergic receptor kinase inhibiting, general anesthetic, cardiovascular and analeptic properties.
Carvacrol	Antiseptic, mucomembranous protecting, membrane permeability inhibiting, anti-infective, anthelmintic, beta-adrenergic receptor kinase inhibiting properties and used in phobic disorders treatment.
Linalool	Mucomembranous protector, fatty-acyl-coenzyme synthase inhibitor, beta-adrenergic receptor kinase inhibitor, G-protein-coupled receptor kinase inhibitor, lipid metabolism regulator, antisecretoric, anti-inflammatory, gastrin inhibitor, membrane permeability inhibitor, sugar-phosphatase inhibitor and antiviral properties.
Caryophyllene	Antineoplastic, antieczematic, antineoplastic, anti-inflammatory and antipsoriatic properties.
Estragole	Gluconate 2-dehydrogenase inhibitor, beta-adrenergic receptor kinase inhibitor, G-protein-coupled receptor kinase inhibitor, mucomembranous protector, antimutagenic, general anesthetic, fatty-acyl-coenzyme synthase inhibitor, saccharopepsin inhibitor, polyporopepsin inhibitor, nicotinic receptor antagonist and membrane permeability inhibitor properties.
Rosmarinic acid	Antidiabetic, membrane permeability inhibitor, mucomembranous protector, free radical scavenger and lipid peroxidase inhibitor properties.
Apigenin	Membrane permeability inhibitor, NADP+ inhibitor, aldehyde oxidase inhibitor, anaphylatoxin receptor antagonist, vasoprotector, antihemorrhagic, leukotriene-B420-monooxygenase inhibitor, histamine release inhibitor, mucomembranous protector, antineoplastic, alcohol dehydrogenase inhibitor, free radical scavenger, thioredoxin inhibitor and sugar-phosphatase inhibitor properties.
Cirsimaritin	Membrane permeability inhibitor, anaphylatoxin receptor antagonist, apoptosis agonist, peroxidase inhibitor, vasoprotector, antineoplastic NADP+inhibitor, cytoprotectant, free radical scavenger, lipid peroxidase inhibitor, antineoplastic and histamine release inhibitor properties.

The predicted activities are listed based on descending order of its Pa: Pi ratio at 70% levels. NADP=Dihydrouracil Dehydrogenase; *O. tenuiflorum=Ocimum tenuiflorum*

levels from 226.40 ± 8.33 to 112.80 ± 5.75, whereas *O. tenuiflorum* 500 mg/kg reduced the glucose levels form 229.80 ± 10.00 to 129.00 ± 13.20. *O. tenuiflorum* exhibited significant anti-diabetic effect but the effect was not superior than glibenclamide. This may be due to the amount of active phytoconstituents present in the plant. However, the individual phytoconstituents of *O. tenuiflorum* such as ursolic acid (derivatives) and rosmarinic acid are known to have anti-diabetic activities.[40,50]

Severe hyperlipidemia was observed with STZ– and NIC– induced diabetic animals, and this may be due to exogenous fat loading, an abnormal increase in small intestinal acyl-coenzyme A: Cholesterol acyltransferase activity and enhancement of intestinal CoA-dependent esterification.[51,52] Both glibenclamide and *O. tenuiflorum* (at 250 and 500 mg/kg) reversed the STZ– and NIC– induced hyperlipidemia. However, the exact mechanism of action of anti-hyperlipidemic effect of *O. tenuiflorum* is unclear.

In diabetes mellitus control animals, liver and renal dysfunctions were observed. The increase in aminotransferase level may be due to the destruction of hepatocytes caused by STZ.[53] Decrease in serum albumin levels was observed in diabetes mellitus animals and this may be due to deterioration of kidney function.[54] Park *et al.* also reported that decreased levels of albumin in peripheral blood of STZ-induced diabetic rats.[55] Alteration in serum albumin: creatinine ratio was observed in diabetes mellitus control animal and *O. tenuiflorum* 150 mg/kg treated animals, and this may be due to the alteration in renal functions.

The increased absolute organ weight of liver was observed in diabetic animals, and this may be due to cellular damage in the liver because of increasing resistance to insulin signaling pathways in hepatocytes.[56] There was increased kidney weight: BW ratio (results were not significant) found in diabetes mellitus animals. This may be due to glomerular damage, changes in bradykinin system and increased

Table 8: Predicted toxicological properties of phytoconstituents of *O. tenuiflorum*

Compound	Prediction (confidence)				
	EPA v4b Fathead Minnow acute toxicity LC_{50}_mmol (fist lethality)	Carcinogenic potency in DBS hamster	Carcinogenic potency in DBS mouse	Kazius-Bursi Salmonella mutagenicity	FDA v3b maximum recommended daily dose_mmol
Ursolic acid	Not predicted	Noncarcinogen	Carcinogen (0.699)	Nonmutagenic	0.0050 (0.276)
Eugenol	0.1411 (0.381)	Noncarcinogen	Noncarcinogen	Nonmutagenic	0.0092 (0.212)
Carvacrol	0.0145 (0.332)	Noncarcinogen	Noncarcinogen	Nonmutagenic	0.0231 (0.156)
Linalool	0.04988 (0.129)	Noncarcinogen	Noncarcinogen	Nonmutagenic	0.1118 (0.129)
Caryophyllene	0.01247 (0.106)	Noncarcinogen	Noncarcinogen	Nonmutagenic	0.00645 (0.205)
Estragole	0.075259 (0.431)	Noncarcinogen	Carcinogen (measured activity)	Nonmutagenic	0.020585 (0.218)
Rosmarinic acid	0.00436 (0.173)	Noncarcinogen	Noncarcinogen	Nonmutagenic	0.012936 (0.109)
Apigenin	0.005571 (0.235)	Noncarcinogen	Noncarcinogen	Nonmutagenic	Not predicted
Cirsimaritin	0.006595 (0.23)	Noncarcinogen	Noncarcinogen	Mutagenic (0.0235)	Not predicted

DBS=Deep brain stimulation; FDA=Food and Drug Administration; EPA=Environmental Protection Agency; *O. tenuiflorum=Ocimum tenuiflorum*

gene expression of fibronectin and collagen I.[57,58] *In vivo* study revealed that hydroalcoholic extract of *O. tenuiflorum* possesses the anti-diabetic and anti-hyperlipidemic activities but not superior to it., but the effect was not dose dependently. This may be due to the time of collection of the plant parts, and the amount of phytoconstituents present in the plant.

Ocimum tenuiflorum is known to have many pharmacological activities and it is traditionally used as an anti-tussive agent. In this present investigation, we predicted the biological activities of phytoconstituents of *O. tenuiflorum* which indicated pharmacological actions as insulin promotor activity, anti-oxidant activity, free radical scavenging property, anti-neoplastic effect, hypolipidemic effect, etc., This plant is known to have anti-diabetic, cardioprotective, wound healing, anti-oxidant, hypolipidemic, anti-microbial, gastroprotective, immunomodulatory, anti-nociceptive and anti-cancer effects.[17] The whole plant may have different pharmacological effects at different doses, due to the variation in phytoconstituents and plant geographical location. Some of the individual phytoconstituents of *O. tenuiflorum* have anti-diabetic, anti-microbial, anti-cancer, gastroprotective, mucoprotective effects. Many of the listed predicted activities for the various phytoconstituents are under investigation. Hence further *in silico*, *in vitro* and *in vivo* pharmacological studies on *O. tenuiflorum* phytoconstituents may give new lead to the biomedical researchers.

CONCLUSION

Hydroalcoholic extract of leaves of *O. tenuiflorum* has significant anti-diabetic and anti-hyperlipidemic activities at 250 and 500 mg/kg BW against STZ and NIC – induced diabetes mellitus in rats. The anti-diabetic effect of hydroalcoholic extract of leaves of *O. tenuiflorum* is not dose dependent. The biological activity prediction of phytoconstituents of *O. tenuiflorum* showed "n" of biological activities which include anti-diabetic and anti-hyperlipidemic properties at 70% Pa: Pi level and toxicological effect prediction did not show any major harmful effects. Further studies are required to confirm the anti-diabetic and anti-hyperlipidemic activities of individual phytoconstituents of *O. tenuiflorum*, which showed the mentioned properties in computer aided prediction.

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Cite this article as: Parasuraman S, Balamurugan S, Christapher PV, Petchi RR, Yeng WY, Sujithra J, *et al*. Evaluation of Antidiabetic and Antihyperlipidemic Effects of Hydroalcoholic Extract of Leaves of *Ocimum tenuiflorum* (Lamiaceae) and Prediction of Biological Activity of its Phytoconstituents. Phcog Res 2015;7:156-65.

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