

Evaluation of Antidiabetic Activity of Novel Diarylsulfonylurea-Chalcone Hybrids in Streptozotocin-Induced Diabetic Models in Rats

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Abstract

Introduction: The aim of the study was to evaluate the diabetic activity of diarylsulfonylurea-chalcone hybrids on streptozotocin (STZ)-induced diabetic male albino rats. **Materials and Methods:** Diabetic activity of diarylsulfonylurea-chalcone hybrids at a dose of 10, 30, and 50 mg/kg body weight was evaluated. Adult male Swiss albino rats of six numbers in each group were undertaken for study and evaluated. **Results:** The results of *in vivo* hypoglycemic and antihyperglycemic activity of the synthesized diarylsulfonylurea-chalcone hybrid molecules (II.1-28) showed that all the compounds were found to possess moderate to potential ability to reduce blood glucose levels in normoglycemic and STZ-induced type 2 diabetic rats. **Conclusions:** The diarylsulfonylurea-chalcone hybrids have potent diabetic activity in the male albino rat.

Key words: Chalcone, diabetes, diarylsulfonylurea, glucose, glycemic, insulin

INTRODUCTION

Diabetes is a chronic disease that is relatively common throughout the world. Diabetes mellitus is a group of metabolic disorders with one common manifestation of hyperglycemia.^[1] The disease crosses many boundaries, from physicians to geneticist, and represents a major health problem. Diabetes means chronic excretion of an excessive volume of the urine and mellitus means honey. Hence, the word diabetes mellitus refers to chronic excretion of large volume of urine containing glucose. Diabetes mellitus is a syndrome resulting from a variable interaction and environmental factors and is characterized by depleted insulin secretion, hyperglycemia and altered metabolism of lipids, carbohydrates, and proteins, in addition to damaged β -cells of pancreas and increased risk of complications of vascular diseases.^[2] It affected about 171 million people worldwide in 2000, and the number is projected to increase to at least 366 million by 2030.^[3] One therapeutic approach for treating diabetes is to decrease the post-prandial hyperglycemia. This is done by inhibiting the glucose absorption in the small intestine.^[4-6]

Diabetes mellitus is a syndrome, initially characterized by loss of glucose homeostasis resulting from deficiencies in insulin secretion, insulin action or both resulting in impaired metabolism of glucose and other energy-yielding fuels such as lipids and proteins.^[7] Diabetes is a major degenerative disease, characterized by hyperglycemia, lipoprotein abnormalities, defect in reactive oxygen species scavenging enzymes, and altered intermediary metabolism.^[8] It is accepted that oxidative stress results from an imbalance between the generation of oxygen-derived radicals and the organism's antioxidant potential. Various studies have shown that diabetes mellitus is associated with the augmented formation of free radicals and decline in antioxidant potential.^[9,10] Due to these events, the balance normally present in cells between radical formation and protection

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against them is disturbed. This leads to oxidative damage of cell components such as proteins, lipids, and nucleic acids. In both insulin-dependent (type 1) and non-insulin-dependent diabetes (type 2), an increased oxidative stress has been notified. Conflicting results have been reported for the role of oxidative stress in diabetes. Streptozotocin (STZ) selectively destroy β -cells of the pancreas by generating excess reactive oxygen species and carbonium ion (CH_3^+) leading to DNA breaks by alkylating DNA bases.^[11] The N nitroso-N methyl urea portion of the molecule exhibits diabetogenic activity. STZ is a naturally occurring nitrosourea product of *Streptomyces achromogenes*.^[12] Usually, the intraperitoneal injection of a single dose (60 mg/kg body weight) of it exerts direct toxicity on β -cells resulting in necrosis within 48–72 h and causes permanent hyperglycemia. Diarylsulfonylureas are the structural analogs of urea (NH_2CONH_2) with aromatic sulfonyl group in the position 3 and an aromatic or heteroaromatic ring at the position 1. Diarylsulfonylureas became widely available since 1955 as popular antidiabetic drugs in clinical practice for the treatment of type 2 diabetes, by virtue of their insulin secretagogue properties. These compounds also exhibit a wide range of biological activities such as antifungal activity,^[13] antimicrobial,^[14] anticancer, or cytotoxic.^[15] In the present study, diarylsulfonylurea-chalcone hybrid molecules have been selected for the hypoglycemic and antihyperglycemic study.

MATERIALS AND METHODS

Chemicals and reagents

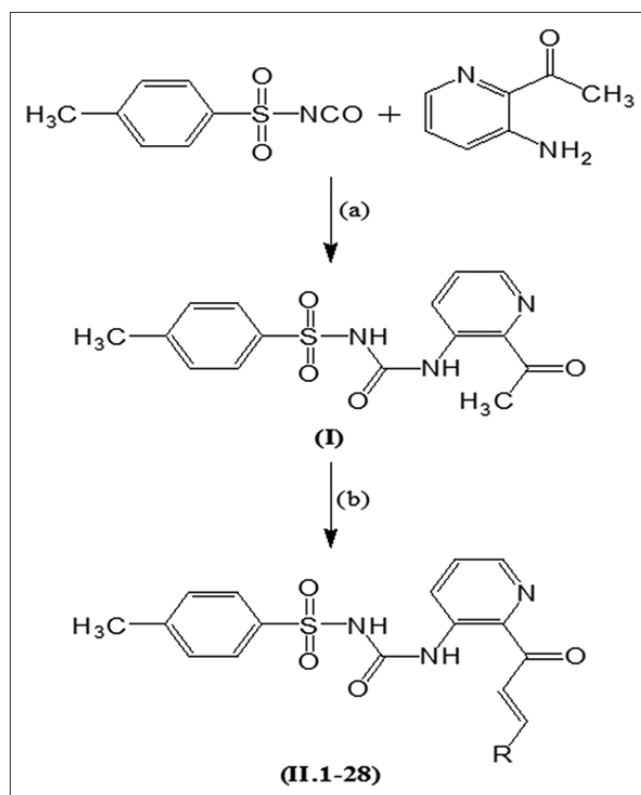
The chemicals used in all experiments were obtained from Sigma (Bangalore, India) and Merck (Mumbai, India). All of other chemicals and reagents were obtained from Sigma-Aldrich, Mumbai.

Chemistry

The reaction sequence employed in the synthesis of diarylsulfonylurea-chalcone conjugates (II.1-28) is shown in Scheme 1, and their physical properties are depicted individually. The key intermediate in the present study 1-(2-acetyl-3-pyridinyl)-3-tosyl urea (I) was synthesized by reaction of tosyl isocyanate with 2-acetyl-3-aminopyridine and subsequent Claisen-Schmidt condensation of the intermediate (I) with appropriate aromatic/heteroaromatic aldehydes under basic conditions to give the corresponding diarylsulfonylurea-chalcone conjugates II.1-28 in good yield.

Acute toxicity

As a general rule, the acute toxicological study of diarylsulfonylurea-chalcone hybrid molecules (II.1-28) was performed as per the OECD 425 guidelines in rats. Healthy and adult female albino Swiss rats weighing between 150 and



Scheme 1: The key intermediate in the present study 1-(2-acetyl-3-pyridinyl)-3-tosylurea

200 g were used in this investigation. Animals were fasted for 24 h and divided into groups of six animals each. The test compounds suspended in sodium carboxymethyl cellulose (sodium CMC) solution (1%) were administered orally in doses of 100 mg to 2000 mg per kg body weight. The control group of animals received only the vehicle (1% sodium CMC).^[16]

Selection of animals

With respect to the antidiabetic activity (hypoglycemic and antihyperglycemic activity), Wistar albino rats of either sex weighing 150–200 g were used for this study. All animals were maintained under 12 h light and 12 h dark cycle at $25^\circ\text{C} \pm 1^\circ\text{C}$. All animals were fed with standard pellet diet and water *ad libitum*. Animals were fasted for 16 h before drug administration, allowing access only to water and were deprived of both food and water during the experiment. The animal housing and handling were in accordance with Committee for the Purpose of Control and Supervision of Experiments on Animals guidelines, and the experimental protocol has been approved by the Institutional Animal Ethics Committee (IAEC) (Proceedings No. 005/Ph.D/2009/IAEC/MIP/MANSAUR).^[17]

Induction of type 2 diabetes

To induce type 2 diabetes, the acclimatized animals were fasted overnight before injecting with STZ. STZ was

dissolved in citrate buffer pH 4.5, and a dose of 65 mg/kg was given after the administration of 150 mg/kg dose of nicotinamide which is helpful to produce partial destruction of the pancreas. The blood glucose levels were estimated after 48 h for the confirmation of diabetes induction.^[18]

Hypoglycemic activity

The euglycemic rats were divided into four groups of six rats each: Control animals received distilled water only (Group I), euglycemic animals received vehicle (Group II), euglycemic animals orally fed with standard drug Gliclazide (dose 2 mg/kg b.w) as 0.25% sodium CMC suspension (Group III), and the euglycemic rats orally fed with synthesized diarylsulfonylurea-chalcone hybrid molecules as 0.25% sodium CMC suspension at doses 10, 30, and 50 mg/kg (Group IV).

Antihyperglycemic activity

The diabetic rats were divided into four groups of six rats each: Control diabetic animals received distilled water only (Group I), diabetic animals received vehicle (Group II), diabetic animals orally fed with standard drug gliclazide (dose 2 mg/kg b.w) as 0.25% sodium CMC suspension (Group III), and the diabetic rats orally fed with synthesized diarylsulfonylurea-chalcone hybrid molecules as 0.25% sodium CMC suspension at doses 10, 30, and 50 mg/kg (Group IV).

For antidiabetic (hypoglycemic and antihyperglycemic) single dose study (acute study) the fasting blood glucose samples were taken before the administration of the test compounds at doses 10, 30, and 50 mg/kg for one day, the blood samples were collected from the retro-orbital plexus periodically at 1, 2, 4, 6, 8, 12, and 24 h and were analyzed for plasma glucose content. Levels of plasmatic glucose were analyzed using commercially available glucometer kits (ACCU-CHEK ACTIVE), based on enzymatic methods.

Statistics

All the data were statistically analyzed for variance and significance, by one-way ANOVA followed by Student's *t*-test and Dunnett's test. All results are expressed as mean \pm standard error of the mean and observed $P < 0.05$.

RESULTS

The animals were observed for 14 days from the time of administration of test compounds to record the mortality. All the compounds synthesized in the present study and employed in the pharmacological screening have been found to be free from toxicity as well as toxic symptoms even at a

high doses of 500–2000 mg/kg body weight and hence they were considered safe. The experimental protocol has been approved by the IAEC (Regd. No. 005/Ph.D/2009/IAEC/MIP/MANSAUR) and by the Animal Regulatory Body of the Government. The direct comparison of the hypoglycemic and antihyperglycemic effect of the diarylsulfonylurea-chalcone hybrid molecules II.1-28 is made rather difficult by the fact that not only the maximal decrease of the blood glucose level produced by the standard dose of a compound but also the dose-response curves vary from compound to compound. The results of *in vivo* hypoglycemic and antihyperglycemic activity of the synthesized diarylsulfonylurea-chalcone hybrid molecules (II.1-28) showed that all the compounds were found to possess moderate to potential ability to reduce blood glucose levels in normoglycemic and STZ-induced type 2 diabetic rats. We consequently found that the blood glucose reduction ability of the titled compounds (II.1-28) was followed a dose-dependent manner in both hypoglycemic and antihyperglycemic activity. Among all the tested compounds, compound II.21 showed significant hypoglycemic and antihyperglycemic activity at various doses such as 10, 30, and 50 mg/kg b.w with percentage blood glucose reduction values $9.64\% \pm 0.39\%$ and $12.86\% \pm 0.07\%$, $13.84\% \pm 0.09\%$ and $14.66\% \pm 0.27\%$, and $20.18\% \pm 1.34\%$ and $21.78\% \pm 2.61\%$, respectively, at 4 h. Similarly, compound II.5 also showed promising hypoglycemic and antihyperglycemic activity. In the same way, compounds such as II.13, II.19, II.4, II.3, II.11, II.27, II.1, II.22, II.9, II.10, II.10, II.26, II.20, II.23, and II.8 exhibited moderate range of hypoglycemic and antihyperglycemic activity at all the doses. The other compounds such as II.12, II.24, II.7, II.6, II.15, II.2, II.25, II.16, II.14, II.17, II.28, and II.18 showed lower level of hypoglycemic and antihyperglycemic activity when compared to that of the reference drug gliclazide with percentage blood glucose reduction values $40.51\% \pm 1.46\%$ and $45.34\% \pm 3.02\%$ at dose 2 mg/kg b.w. However, the hypoglycemic and antihyperglycemic activity produced by diarylsulfonylurea-chalcone hybrid molecules II.1-28 synthesized in the present study was better than that of the standard drug gliclazide in most of the compounds but not at the identical dose level (i.e. gliclazide 2 mg/kg b.w.). The detailed results of the blood glucose reduction value with respect to the hypoglycemic and antihyperglycemic activity of diarylsulfonylureas II.1-28 at various doses such as 10, 30, and 50 mg/kg b.w. are summarized in Tables 1-29.

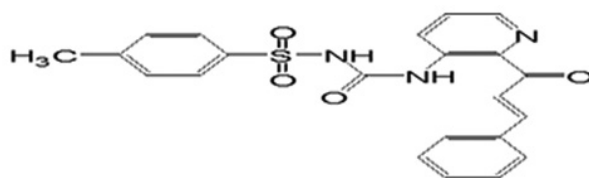
In the present investigation, it is noteworthy to establish the structure-activity relationships for observed hypoglycemic and antihyperglycemic activity of diarylsulfonylurea-chalcone hybrid molecules II.1-28. It is clear from the results of hypoglycemic and antihyperglycemic activity that the structural requirements for retaining (or enhancing) antihyperglycemic property in diarylsulfonylurea-chalcone hybrid molecules II.1-28 are not inflexible.

As such, following are the conventional structure-activity relationships: The α, β -unsaturated ketone and diarylsulfonylurea

Table 1: Antidiabetic activity of Group I, Group II, and Group III

Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	(Group-I) Control	(Group-II) Vehicle	(Group-III) Gliclazide 2 mg/kg b.w	(Group-I) Control	(Group-II) Vehicle	(Group-III) Gliclazide 2 mg/kg b.w
0 h	93.6±3.02 0%	94.32±1.28 0%	93.12±0.52 0%	299.12±0.52 0%	286.94±0.52 0%	295.81±2.11 0%
1 h	92.5±0.52 1.17±0.73%	92.09±0.52 2.36±0.73%	71.47±1.28 23.24±2.11%	300.11±1.97 0.33±1.33%	282.46±1.28 1.56±2.11%	206.32±0.52 30.25±0.73%
2 h	90.6±0.52 3.20±0.73%	89.74±2.21 4.85±1.46%	55.39±2.21 40.51±1.46%	299.08±3.02 0%	276.0±0.52 3.81±0.73%	161.68±1.02 45.34±3.02%
3 h	92.18±0.52 1.51±2.11%	89.41±1.46 5.20±2.20%	68.84±1.46 26.07±2.20%	297.15±1.97 0.66±1.33%	274.77±1.97 4.24±1.33%	200.14±1.28 32.34±2.21%
4h	91.1±3.02 2.67±1.02%	88.98±0.52 5.66±1.46%	84.26±1.25 9.51±1.69%	298.18±0.52 0.31±0.73%	271.24±1.46 5.47±2.20%	242.41±1.46 18.05±1.28%
6 h	92.5±2.21 1.17±1.46%	88.55±1.02 6.11±1.25%	74.62±2.11 19.86±0.52%	296.76±2.11 0.78±0.73%	266.02±3.02 7.29±1.02%	222.30±2.11 24.85±1.02%
12 h	89.8±2.66 4.05±0.02%	87.89±1.69 6.81±1.25%	75.01±0.73 19.44±0.52%	296.73±0.52 0.79±0.73%	260.79±1.25 9.11±1.69%	232.71±3.02 21.33±0.52%
18 h	90.2±3.02 3.63±1.02%	87.69±1.69 7.02±1.02%	88.16±1.97 5.32±1.33%	293.61±1.97 1.84±1.33%	257.90±1.46 10.12±2.20%	271.25±3.02 8.30±1.69%
24 h	90.0±1.46 3.84±2.20%	89.40±1.97 5.21±1.33%	91.15±2.21 2.11±1.46%	288.90±2.21 3.41±1.46%	267.82±1.28 6.66±0.52%	292.14±2.11 1.24±0.52%

STZ: Streptozotocin. All values are expressed as mean±SEM, n=6, Values given with % indicate percentage blood glucose reduction when compared to "0 h" value (s). SEM: Standard error of mean

Table 2: Antidiabetic activity of diarylsulfonylurea-chalcone hybrid II.1

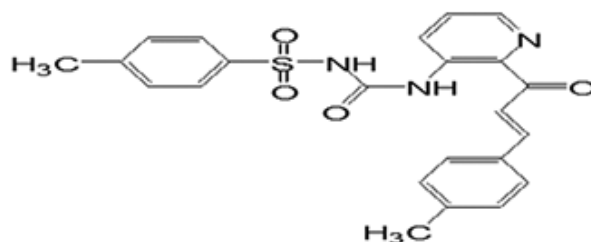
Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
0 h	95.12±0.11 0%	88.33±0.42 0%	87.28±0.74 0%	285.16±0.66 0%	281.78±0.11 0%	282.64±0.51 0%
1 h	87.24±0.57 8.16±0.39%	75.14±0.89 14.61±0.11%	72.45±0.34 16.72±0.37%	271.46±0.69 4.71±0.94%	253.37±0.36 9.83±0.25%	220.83±0.22 21.69±0.52%
2 h	81.56±0.66 14.14±0.86%	70.09±0.51 20.32±0.91%	66.±0.73 24.13±0.06%	256.84±0.06 9.88±0.73%	221.48±0.91 11.76±0.51%	212.28±0.86 24.72±0.66%
3 h	77.20±0.88 18.73±0.02%	67.92±0.37 22.81±0.34%	64.21±0.72 26.19±0.77%	240.48±0.23 15.62±0.42%	232.98±0.52 16.73±0.65%	186.51±0.97 33.86±0.72%
4h	82.25±0.38 13.42±0.22%	68.88±0.11 21.72±0.36%	59.53±0.41 31.57±0.52%	232.21±0.65 18.52±0.23%	221.±0.65 21.35±0.72%	221.58±0.17 21.78±0.37%

(Contd...)

Table 2: (Continued)

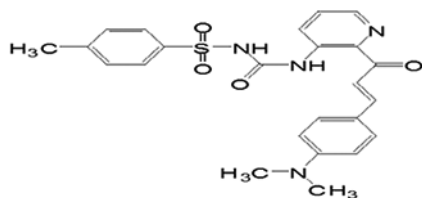
Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
6 h	84.01±0.94	70.95±0.86	64.05±0.34	245.78±0.02	238.51±0.72	229.49±0.17
	11.56±0.51%	19.37±0.42	26.37±0.74%	13.76±0.65	15.12±0.42%	18.62±0.17%
12 h	89.±0.97	80.56±0.23	77.01±0.72	254.41±0.37	258.96±0.88	254.30±0.86
	6.31±0.65%	8.45±0.72%	11.48±0.02%	10.73±0.34%	7.84±0.88%	9.82±0.39%
18 h	92.41±0.73	86.07±0.66	84.80±0.36	274.71±0.51	277.31±0.82	281.09±0.73
	2.72±0.23%	2.19±0.29%	2.52±0.31%	3.61±0.73%	1.31±0.82%	4.32±0.98%
24 h	93.44±0.29	86.87±0.52	85.35±0.88	279.58±0.06	279.81±0.22	278.92±0.39
	1.64±0.97%	1.28±0.38%	1.89±0.41%	1.90±0.94%	0.42±0.86%	1.09±0.77%

STZ: Streptozotocin, all values are expressed as mean±SEM, *n*=6, values given with % indicate percentage blood glucose reduction when compared to "0 h" value (s), *P*<0.5. SEM: Standard error of the mean

Table 3: Antidiabetic activity of diarylsulfonylurea-chalcone hybrid II.2

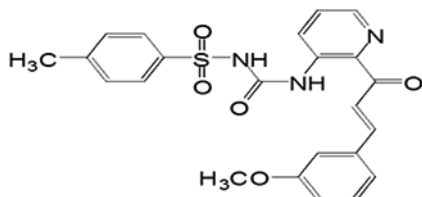
Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
0 h	96.12±0.02 0%	88.43±0.06 0%	88.52±0.51 0%	286.11±0.34 0%	282.24±0.88 0%	281.98±0.23 0%
1 h	89.93±0.36	71.46±0.51	75.09±0.39	275.36±0.39	221.09±0.22	292.74±0.72
	6.32±0.39%	18.78±0.86%	14.66±0.86%	3.72±0.36%	21.32±0.37%	21.80±0.51%
2 h	83.82±0.41	64.38±0.02	67.90±0.51	255.62±0.31	200.32±0.66	192.11±0.54
	12.56±0.82%	26.83±0.73%	22.84±0.91%	10.62±0.72%	28.71±0.74%	31.63±0.36%
3 h	82.24±0.97	55.22±0.41	60.05±0.94	235.±0.29	186.79±0.45	188.46±0.22
	14.33±0.73%	27.36±0.22%	31.76±0.06%	17.83±0.72%	36.76±0.42%	32.93±0.74%
4 h	76.84±0.74	66.60±0.36	55.25±0.41	226.36±0.23	170.63±0.54	163.93±0.51
	19.95±0.23%	24.31±0.52%	37.21±0.51%	20.85±0.34%	39.49±0.65%	41.66±0.37%
6 h	84.27±0.23	71.86±0.72	62.99±0.34	243.75±1.84	192.26±2.13	191.58±0.22
	12.21±0.86%	18.33±0.51%	28.42±0.22%	14.77±0.39%	31.82±0.34%	31.82±0.34%
12 h	87.69±0.86	74.87±0.94	76.07±0.88	257.80±0.82	240.34±0.73	200.57±0.54
	8.65±2.46%	14.92±0.72%	13.55±0.37%	9.86±0.73%	14.77±0.73%	28.62±2.02%
18 h	93.56±0.73	81.29±0.52	86.75±0.86	278.16±0.22	262.76±0.98	255.28±0.88
	2.54±0.34%	7.62±0.39%	1.42±0.42%	2.74±0.31%	6.82±0.88%	93.15±0.11%
24 h	94.63±0.23	87.83±0.94	87.89±0.02	281.85±0.22	275.42±0.39	2788.78±0.45
	1.42±2.02%	0.19±0.97%	0.22±0.34%	1.45±0.23%	2.33±0.51%	0.97±0.52%

STZ: Streptozotocin, all values are expressed as mean±SEM, *n*=6, values given with % indicate percentage blood glucose reduction when compared to "0 h" value (s), *P*<0.5. SEM: Standard error of the mean

Table 4: Antidiabetic activity of diarylsulfonylurea-chalcone hybrid II.3

Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
0 h	95.32±0.73 0%	87.21±0.22 0%	89.14±0.32 0%	285.25±0.31 0%	283.21±0.54 0%	285.27±0.45 0%
1 h	87.27±0.81 8.13±0.66%	69.75±0.73 19.82±0.74%	73.97±0.81 16.88±0.91%	262.99±0.39 7.72±0.23%	218.24±0.58 22.88±0.52%	208.67±0.91 26.78±0.37%
2 h	83.±0.32 12.42±0.36%	61.19±0.73 29.66±0.73%	67.07±0.73 24.63±0.06%	243.04±0.81 14.72±0.82%	193.06±0.39 31.78±0.52%	185.76±0.81 34.82±0.73%
3 h	73.±0.86 16.84±0.52%	59.±0.22 32.189±0.74%	56.23±0.86 36.81±0.73%	229.08±0.39 19.62±0.73%	161.50±0.72 42.93±0.23%	151.87±0.58 46.71±0.52%
4h	76.73±0.73 19.23±0.51%	45.83±1.84 47.32±0.73%	50.45±0.45 43.31±0.51%	217.25±0.58 23.77±0.72%	141.01±0.37 50.17±0.72%	123.73±0.58 55.81±0.52%
6 h	82.54±0.81 13.11±0.17%	60.31±0.39 30.67±0.23%	62.60±0.22 29.66±0.66%	226.23±0.37 20.62±0.52%	170.48±0.81 39.82±0.73%	162.82±0.91 42.87±0.52%
12 h	89.16±0.73 6.14±0.88%	61.38±0.58 29.44±0.36%	75.±0.86 15.72±0.22%	252.79±0.39 11.63±0.52%	201.97±0.58 28.63±0.52%	194.59±0.37 31.72±0.82%
18 h	92.32±0.66 2.82±0.17%	75.84±0.72 12.82±0.23%	87.31±0.45 1.89±0.23%	274.42±0.91 3.71±0.37%	250.03±0.91 11.65±0.17%	240.20±0.91 12.54±0.82%
24 h	94.29±0.22 0.74±0.72%	84.69±0.73 2.65±0.36%	88.87±0.81 0.14±0.74%	281.95±0.45 1.07±0.36%	277.93±0.45 1.79±0.37%	279.75±0.45 1.84±0.82%

STZ: Streptozotocin, all values are expressed as mean±SEM, $n=6$, values given with % indicate percentage blood glucose reduction when compared to "0 h" value (s), $P<0.5$. SEM: Standard error of the mean

Table 5: Antidiabetic activity of diarylsulfonylurea-chalcone hybrid II.4

Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
0 h	98.31±0.73 0%	89.11±0.21 0%	85.23±0.68 0%	288.54±0.92 0%	285.43±0.34 0%	284.78±0.17 0%
1 h	83.66±0.17 14.63±0.73%	81.02±0.21 8.96±0.17%	66.53±0.34 21.72±0.17%	269.79±0.34 6.32±0.17%	256.75±0.17 9.91±0.92%	213.45±0.73 24.84±0.92%
2 h	78.29±0.34 20.11±0.73%	75.65±0.68 13.87±0.34%	55.58±0.68 34.61±0.17%	236.62±0.34 17.84±0.73%	248.46±0.21 12.81±0.92%	182.38±0.73 35.78±0.68%

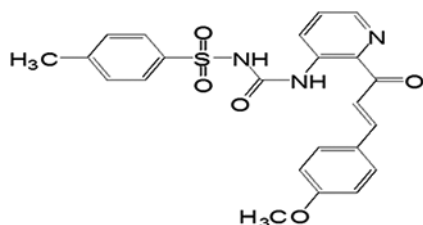
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Table 5: (Continued)

Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
3 h	71.30±0.73	75.11±0.68	48.52±0.17	226.48±0.73	235.68±0.92	148.73±0.92
	27.24±0.17%	16.77±0.17%	42.91±0.73%	21.36±0.68%	163.72±0.34%	47.63±0.34%
4h	74.16±0.73	70.61±0.21	41.79±0.34	213.95±0.17	221.75±0.17	132.17±0.73
	24.32±0.92%	20.66±0.92%	50.83±0.17%	25.71±0.21%	22.19±0.68%	53.46±0.92%
6 h	77.07±0.34	73.56±0.21	49.36±0.17	206.95±0.68	238.51±0.17	151.82±0.21
	21.35±0.68%	17.45±0.17%	41.92±0.68%	28.14±0.73%	16.31±0.68%	46.54±0.92%
12 h	80.09±0.21	78.62±0.34	53.91±0.68	251.02±0.17	260.14±0.21	185.56±0.73
	18.27±0.92%	11.66±0.68%	36.57±0.17%	12.84±0.68%	8.72±0.68%	34.66±0.92%
18 h	88.54±0.17	80.61±0.73	70.47±0.34	274.29±0.92	281.26±0.17	253.49±0.34
	9.65±0.92%	9.42±0.21%	17.09±0.21%	4.76±0.17%	1.31±0.73%	10.74±0.17%
24 h	96.87±0.17	87.94±0.34	75.96±0.92	285.86±0.21	282.69±0.92	253.82±0.68
	1.15±0.73%	1.19±0.17%	10.63±0.17%	0.74±0.17%	0.18±0.17%	0.06±0.92%

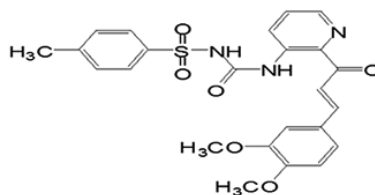
STZ: Streptozotocin, all values are expressed as mean±SEM, *n*=6, values given with % indicate percentage blood glucose reduction when compared to "0 h" value (s), *P*<0.5. SEM: Standard error of the mean

Table 6: Antidiabetic activity of diarylsulfonylurea-chalcone hybrid II.5



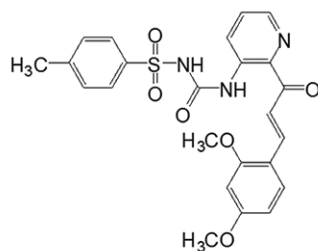
Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
0 h	97.12±0.18	90.32±0.63	87.47±0.39	286.71±0.71	284.97±0.44	286.88±0.44
	0%	0%	0%	0%	0%	0%
1 h	85.19±0.44	79.22±0.63	76.17±0.82	261.08±0.39	242.19±0.18	248.47±0.44
	12.17±0.63%	11.97±0.82%	12.44±0.63%	8.71±0.71%	14.72±0.82%	13.12±0.63%
2 h	80.10±0.63	72.60±0.18	69.48±0.82	241.29±0.44	225.18±0.63	227.25±0.39
	17.42±0.39%	19.33±0.39%	20.13±0.18%	15.63±0.71%	20.79±0.18%	20.54±0.82%
3 h	75.83±0.71	65.14±0.82	67.23±0.71	236.17±0.82	216.18±0.44	222.53±0.82
	21.82±0.18%	27.62±0.71%	22.72±0.44%	17.42±0.18%	23.88±0.71%	22.19±0.18%
4h	82.76±0.71	58.85±0.18	62.52±0.18	229.28±0.82	193.91±0.39	193.64±0.39
	14.68±0.63%	34.61±0.63%	28.13±0.71%	19.83±0.63%	31.72±0.18%	32.46±0.18%
6 h	89.08±0.82	67.12±0.71	67.98±0.71	237.92±0.39	208.37±0.44	212.41±0.44
	8.16±0.18%	25.42±0.39%	21.86±0.63%	16.81±0.63%	26.63±0.63%	25.73±0.44%
12 h	93.77±0.39	74.83±0.18	77.63±0.44	258.20±0.39	230.06±0.82	234.83±0.82
	3.32±0.63%	16.85±0.39%	10.77±0.71%	9.72±0.71%	18.99±0.63%	17.89±0.63%
18 h	95.86±0.44	83.57±0.71	85.57±0.71	282.45±0.71	262.33±0.39	267.41±0.44
	1.17±0.39%	7.14±0.18%	1.64±0.63%	1.24±0.39%	7.63±0.82%	6.55±0.18%
24 h	96.92±0.82	88.10±0.44	86.83±0.82	283.25±0.39	277.04±0.71	281.76±0.39
	0.08±0.18%	2.11±0.71%	0.19±0.18%	0.96±0.82%	2.45±0.44%	1.48±0.82%

STZ: Streptozotocin, all values are expressed as mean±SEM, *n*=6, values given with % indicate percentage blood glucose reduction when compared to "0 h" value (s), *P*<0.5. SEM: Standard error of the mean

Table 7: Antidiabetic activity of diarylsulfonylurea-chalcone hybrid II.6

Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
0 h	96.16 0%	92.44 0%	91.82 0%	287.29 0%	284.33 0%	286.64 0%
1 h	93.39±1.22 2.71±1.37%	88.94±1.56 3.32±0.09%	85.05±1.56 6.523±0.09%	280.31±1.56 2.33±0.09%	263.21±0.07 7.32±1.32%	265.60±0.23 7.13±0.17%
2 h	90.02±1.88 6.22±0.92%	81.22±1.22 11.71±1.37%	78.55±1.22 13.68±1.37%	267.45±1.22 6.81±1.37%	245.23±0.66 13.65±0.14%	249.54±1.87 12.64±0.64%
3 h	87.72±1.56 8.64±0.09%	79.26±0.66 13.84±0.14%	76.32±0.66 16.13±0.14%	256.26±0.66 10.71±0.14%	240.34±0.09 15.37±1.56%	241.29±0.66 15.63±0.14%
4 h	84.73±0.23 11.73±0.17%	76.49±0.23 16.85±0.17%	74.04±0.23 18.63±0.17%	251.35±1.88 12.42±0.92%	228.02±1.87 19.71±0.64%	226.91±1.22 20.66±1.37%
6 h	86.76±1.87 9.62±0.64%	79.65±0.64 13.42±1.87%	80.79±1.23 11.21±1.69%	262.69±0.23 8.47±0.17%	242.22±1.88 14.22±0.92%	248.47±0.92 13.12±1.88%
12 h	91.84±0.66 4.33±0.14%	88.66±1.88 3.62±0.92%	84.03±1.88 7.65±0.92%	280.74±1.23 2.18±1.69%	256.42±1.37 9.71±1.22%	268.81±1.22 6.01±1.37%
18 h	94.43±1.69 1.63±1.23%	90.96±1.23 1.12±1.69%	88.79±1.23 2.42±1.69%	282.86±0.64 1.44±1.87%	279.34±0.23 1.64±0.17%	279.76±0.07 2.18±1.32%
24 h	95.12±0.07 0.91±1.32%	91.82±0.07 0.19±1.32%	89.92±0.07 1.18±1.32%	284.21±0.07 0.97±1.32%	281.21±1.23 0.98±1.69%	285.54±1.69 0.16±1.23%

STZ: Streptozotocin, all values are expressed as mean±SEM, $n=6$, values given with % indicate percentage blood glucose reduction when compared to "0 h" value (s), $P<0.5$. SEM: Standard error of the mean

Table 8: Antidiabetic activity of diarylsulfonylurea-chalcone hybrid II.7

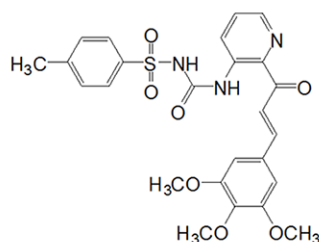
Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
0 h	101.12±1.17 0%	94.56±1.88 0%	92.78±1.71 0%	286.23±1.32 0%	283.76±0.06 0%	284.24±0.19 0%
1 h	96.63±0.23 4.32±0.17%	88.99±0.33 5.32±1.41%	83.24±1.29 9.52±1.78%	272.70±0.47 4.65±0.34%	250.68±1.72 11.42±1.21%	243.30±0.54 14.33±0.27%
2 h	88.16±0.64 12.71±1.87%	82.79±1.34 11.92±1.66%	79.46±0.62 13.63±0.44%	260.51±0.14 8.91±1.34%	241.22±1.84 14.76±1.36%	224.01±0.32 21.12±0.41%

(Contd...)

Table 8: (Continued)

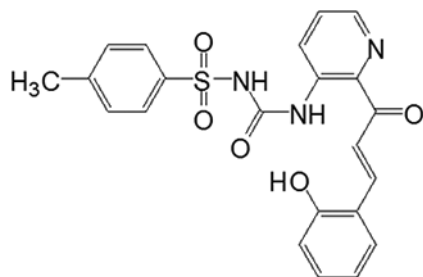
Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
3 h	84.47±0.07	76.45±0.03	69.22±0.31	243.78±1.83	229.71±1.22	212.65±0.33
	16.36±1.32%	18.66±0.11%	17.82±0.12%	14.76±1.64%	18.83±1.11%	25.12±0.55%
4 h	87.45±1.56	72.52±1.82	69.22±0.71	236.15±2.11	207.32±0.37	199.19±1.03
	13.41±0.09%	22.85±1.98%	24.76±0.97%	17.43±0.07%	26.74±0.27%	29.86±2.61%
6 h	91.66±1.22	78.57±0.88	72.38±0.73	243.50±1.36	241.14±1.22	251.44±0.64
	9.24±1.37%	16.41±0.64%	21.32±0.88%	14.86±2.84%	14.79±1.11%	24.14±0.77%
12 h	97.24±1.23	82.09±1.98	80.20±0.93	258.20±3.61	265.65±0.12	229.55±2.37
	3.72±1.69%	12.66±1.82%	12.82±0.39%	9.72±1.97%	6.13±0.33%	19.17±1.04%
18 h	99.75±1.22	92.86±0.21	87.74±2.11	273.04±2.11	272.64±0.25	279.08±0.29
	1.23±1.37%	1.21±0.73%	4.62±1.55%	4.53±0.07%	3.66±0.24%	1.73±0.65%
24 h	100.87±0.66	93.84±1.26	90.93±2.31	282.48±0.03	277.96±0.11	281.12±0.64
	0.12±0.14%	0.17±1.39%	1.16±0.02%	1.23±1.42%	1.98±0.56%	0.73±0.77%

STZ: Streptozotocin, all values are expressed as mean±SEM, *n*=6, values given with % indicate percentage blood glucose reduction when compared to "0 h" value (s), *P*<0.5. SEM: Standard error of the mean

Table 9: Antidiabetic activity of diarylsulfonylurea-chalcone hybrid II.8

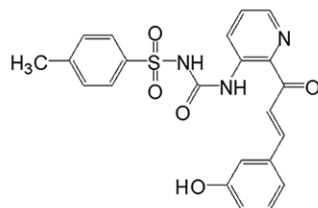
Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
0 h	94.45±0.06 0%	89.34±0.19 0%	89.67±1.17 0%	286.23±1.88 0%	284.45±1.71 0%	282.56±1.32 0%
1 h	83.49±1.29	79.53±1.72	79.69±0.23	268.44±0.47	233.10±0.54	236.37±0.33
	11.18±1.78%	10.63±1.21%	10.46±0.17%	5.81±0.34%	17.92±0.27%	16.18±1.41%
2 h	78.65±0.31	73.65±1.84	69.75±1.87	258.42±1.83	220.58±0.32	221.59±1.34
	16.32±0.12%	17.24±1.36%	21.62±0.64%	9.64±1.64%	22.33±0.41%	21.42±1.66%
3 h	73.94±0.93	67.47±1.22	63.42±1.22	245.47±0.14	208.05±0.64	203.51±0.03
	21.34±0.39%	24.18±1.11%	28.74±1.37%	13.87±1.34%	26.74±0.77%	27.83±0.11%
4h	79.39±0.71	63.43±0.37	59.95±1.56	226.11±3.61	192.60±0.33	183.92±0.88
	15.54±0.97%	28.72±0.27%	32.63±0.09%	20.66±1.97%	32.18±0.55%	34.78±0.64%
6 h	85.38±0.73	69.13±0.11	71.03±1.22	235.41±0.07	209.42±3.57	214.99±1.82
	9.17±0.88%	22.32±0.56%	20.18±1.37%	17.54±2.11%	26.19±2.54%	23.76±1.98%
12 h	91.72±2.11	75.36±0.37	80.39±0.66	249.22±1.36	233.30±2.37	240.99±1.26
	2.42±1.55%	15.32±0.27%	9.67±0.14%	12.63±2.84%	17.85±1.04%	14.54±1.39%
18 h	92.19±0.62	87.23±0.02	87.38±1.23	266.81±0.03	267.92±0.64	275.20±1.49
	1.92±0.44%	1.98±0.16%	1.82±1.69%	6.38±1.42%	5.66±0.77%	2.41±1.67%
24 h	93.75±2.31	88.87±0.25	88.87±0.07	278.18±1.55	279.91±0.29	279.65±1.98
	0.26±0.02%	0.14±0.24%	0.14±1.32%	2.39±1.33%	1.44±0.65%	0.89±1.82%

STZ: Streptozotocin, all values are expressed as mean±SEM, *n*=6, values given with % indicate percentage blood glucose reduction when compared to "0 h" value (s), *P*<0.5. SEM: Standard error of the mean

Table 10: Antidiabetic activity of diarylsulfonylurea-chalcone hybrid II.9

Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
0 h	92.34±1.71 0%	87.54±1.32 0%	90.56±1.17 0%	284.34±1.88 0%	285.68±0.06 0%	281.33±0.19 0%
1 h	88.63±0.33 3.66±1.41%	81.10±0.23 6.78±0.17%	76.74±1.29 14.73±1.78%	278.13±0.47 2.41±0.34%	240.14±1.72 15.74±1.21%	244.02±0.54 13.16±0.27%
2 h	85.36±1.34 7.21±1.66%	75.82±0.64 12.84±1.87%	67.12±0.44 25.55±0.62%	268.69±0.14 5.72±1.34%	227.68±1.84 20.11±1.36%	220.21±0.32 21.63±0.41%
3 h	83.529±0.03 9.14±0.11%	69.33±0.09 20.31±1.56%	58.75±0.31 34.72±0.12%	258.38±1.83 9.34±1.64%	215.68±1.22 24.32±1.11%	211.42±0.33 24.76±0.55%
4 h	78.25±0.88 14.94±0.64%	62.88±1.22 27.72±1.37%	53.19±0.93 40.89±0.39%	251.59±3.61 11.72±1.97%	199.84±0.25 29.88±0.24%	188.85±0.64 32.78±0.77%
6 h	84.74±1.82 7.89±1.98%	55.79±1.88 35.87±0.92%	63.34±0.73 29.62±0.88%	254.64±1.36 10.65±2.84%	208.56±0.37 26.82±0.27%	210.38±1.03 25.13±2.61%
12 h	89.12±0.21 3.12±0.73%	64.88±0.07 25.42±1.32%	76.67±2.11 14.81±1.55%	265.84±1.55 6.72±1.33%	232.93±0.12 18.27±0.33%	226.96±0.33 19.23±0.55%
18 h	90.58±1.26 1.54±1.39%	72.35±1.69 16.83±1.23%	86.65±0.73 3.72±0.88%	273.22±1.36 4.13±2.84%	257.21±0.11 9.75±0.56%	275.97±2.37 1.79±1.04%
24 h	91.23±1.49 1.08±1.67%	85.13±0.66 2.14±0.14%	88.11±2.31 2.10±0.02%	279.38±0.03 1.97±1.42%	278.55±1.84 2.26±1.36%	275.54±0.29 0.97±0.65%

STZ: Streptozotocin, all values are expressed as mean±SEM, *n*=6, values given with % indicate percentage blood glucose reduction when compared to "0 h" value (s), *P*<0.5. SEM: Standard error of the mean

Table 11: Antidiabetic activity of diarylsulfonylurea-chalcone hybrid II.10

Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
0 h	93.34±1.32 0%	88.34±1.71 0%	95.76±0.06 0%	285.65±0.19 0%	283.76±1.17 0%	282.87±1.88 0%
1 h	91.24±1.72 1.89±1.21%	80.15±1.29 8.92±1.78%	86.20±0.23 9.26±0.17%	273.23±0.33 4.21±1.41%	234.23±0.47 17.23±0.34%	247.56±0.54 12.21±0.27%

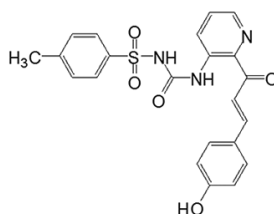
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Table 11: (Continued)

Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
2 h	90.47±1.84	75.49±0.62	73.35±0.64	256.84±1.34	225.72±0.03	221.14±0.32
	2.71±1.36%	14.21±0.44%	22.78±1.87%	9.88±1.66%	20.24±1.42%	21.82±0.41%
3 h	87.11±1.22	70.69±0.31	70.19±1.22	251.74±0.03	210.38±1.83	217.76±0.29
	6.33±1.11%	19.66±0.12%	26.11±1.37%	11.67±0.11%	25.66±1.64%	22.78±0.65%
4 h	84.28±0.37	67.03±0.73	66.28±0.92	241.33±0.88	202.85±3.61	192.54±0.33
	9.37±0.27%	23.82±0.88%	30.23±1.88%	15.32±0.64%	28.42±1.97%	31.72±0.55%
6 h	87.68±0.37	63.61±2.11	76.81±0.66	243.74±0.21	222.38±1.55	207.15±0.64
	5.72±0.27%	27.71±1.55%	19.14±0.14%	12.72±0.73%	21.42±1.33%	26.54±0.77%
12 h	90.22±0.11	68.84±0.93	86.69±1.56	251.34±1.98	230.19±1.36	234.59±2.37
	3.22±0.56%	21.77±0.39%	8.74±0.09%	11.81±1.82%	18.66±2.84%	16.81±1.04%
18 h	91.19±0.12	80.36±2.11	92.88±1.69	266.70±1.67	250.31±0.14	278.50±3.57
	1.94±0.33%	8.68±1.55%	2.23±1.23%	6.42±1.49%	11.55±1.34%	1.24±2.54%
24 h	92.98±0.25	86.27±2.31	93.88±0.07	282.34±0.21	278.95±2.11	281.30±0.64
	0.02±0.24%	1.96±0.02%	1.17±1.32%	0.93±0.73%	1.43±0.07%	0.06±0.77%

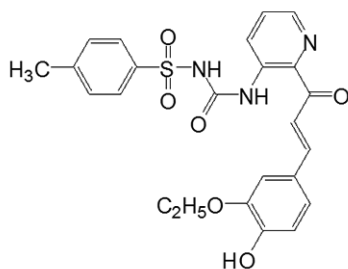
STZ: Streptozotocin, all values are expressed as mean±SEM, *n*=6, values given with % indicate percentage blood glucose reduction when compared to "0 h" value (s), *P*<0.5. SEM: Standard error of the mean

Table 12: Antidiabetic activity of diarylsulfonylurea-chalcone hybrid II.11



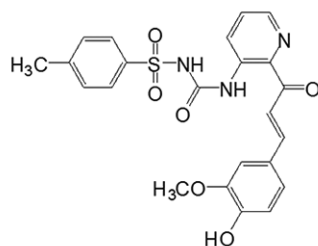
Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
0 h	87.34±0.19	89.54±0.06	95.65±1.88	286.45±1.17	282.35±1.71	282.75±1.32
	0%	0%	0%	0%	0%	0%
1 h	85.41±1.29	85.76±1.72	91.53±0.47	269.66±0.54	266.94±0.23	257.11±0.33
	1.82±1.78%	3.64±1.21%	3.65±0.34%	5.71±0.27%	5.34±0.17%	8.82±1.41%
2 h	84.39±0.62	84.33±1.84	88.16±0.14	260.48±0.32	257.15±0.64	248.52±1.66
	2.99±0.44%	5.24±1.36%	7.20±1.34%	8.92±0.41%	8.81±1.87%	11.87±1.34%
3 h	82.81±0.31	80.50±1.22	86.33±1.83	253.02±0.64	249.17±1.88	223.59±1.26
	4.81±0.12%	9.55±1.11%	9.12±1.64%	11.53±0.77%	11.64±0.92%	20.71±1.39%
4 h	81.41±0.93	78.62±0.25	82.15±1.36	249.50±0.33	237.31±1.22	234.84±0.03
	6.42±0.39%	11.66±0.24%	13.52±2.84%	12.76±0.55%	15.88±1.37%	16.82±0.11%
6 h	79.93±0.73	81.50±0.37	88.54±1.55	262.74±1.03	256.08±1.56	239.36±0.88
	8.12±0.88%	8.42±0.27%	6.79±1.33%	8.13±2.61%	9.19±0.09%	15.12±0.64%
12 h	82.93±2.11	83.98±0.02	93.93±1.83	276.61±0.33	263.89±0.66	257.66±1.82
	4.67±1.55%	5.63±0.16%	1.12±1.64%	3.28±0.55%	6.42±0.14%	8.63±1.98%
18 h	85.10±0.93	86.65±0.12	94.81±0.03	281.08±1.03	275.85±0.07	279.69±0.21
	2.18±0.39%	2.63±0.33%	0.19±1.42%	1.72±2.61%	2.14±1.32%	2.31±0.73%
24 h	86.02±2.31	88.83±0.11	94.89±1.55	283.62±0.29	279.68±1.69	281.06±1.67
	1.12±0.02%	0.19±0.56%	0.11±1.33%	0.83±0.65%	0.82±1.23%	0.33±1.49%

STZ: Streptozotocin, all values are expressed as mean±SEM, *n*=6, values given with % indicate percentage blood glucose reduction when compared to "0 h" value (s), *P*<0.5. SEM: Standard error of the mean

Table 13: Antidiabetic activity of diarylsulfonylurea-chalcone hybrid II.12

Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
0 h	88.54±1.71 0%	90.64±1.32 0%	97.65±0.19 0%	287.67±0.06 0%	282.53±1.17 0%	283.23±1.88 0%
1 h	86.64±0.23 1.54±0.17%	81.34±1.29 9.62±1.78%	88.83±0.33 8.42±1.41%	276.06±0.47 3.81±0.34%	263.89±1.72 6.42±1.21%	258.60±0.54 8.62±0.27%
2 h	85.67±0.64 2.64±1.87%	75.31±0.62 16.32±0.44%	83.09±1.34 14.33±1.66%	270.61±0.03 5.71±1.42%	256.08±1.22 9.19±1.11%	249.54±0.32 11.92±0.41%
3 h	85.19±0.92 3.19±1.88%	74.08±0.31 17.68±0.12%	77.94±0.03 19.64±0.11%	264.26±1.83 7.92±1.64%	251.71±0.25 10.74±0.24%	233.13±0.64 17.62±0.77%
4h	84.19±1.22 4.32±1.37%	75.79±0.93 15.78±0.39%	71.62±0.88 26.16±0.64%	262.±1.36 8.71±2.84%	234.84±0.25 16.72±1.22%	218.53±0.33 22.78±0.55%
6 h	83.04±1.56 5.63±0.09%	78.55±0.73 12.72±0.88%	75.87±1.82 21.78±1.98%	268.57±3.61 6.42±1.97%	257.35±0.02 8.75±0.16%	240.15±3.57 15.13±2.54%
12 h	85.92±0.14 2.36±0.66%	81.98±2.11 8.91±1.55%	83.74±0.21 13.66±0.73%	279.22±1.36 2.71±2.84%	265.61±0.37 5.81±0.27%	255.77±1.03 9.62±2.61%
18 h	86.43±0.07 1.78±1.32%	87.19±0.71 3.12±0.97%	92.36±1.49 4.78±1.67%	284.58±1.55 0.84±1.33%	278.22±0.11 1.34±0.56%	276.46±0.29 2.31±0.65%
24 h	87.98±1.69 0.02±1.23%	89.87±2.31 0.17±0.02%	96.30±1.26 0.72±1.39%	286.59±0.14 0.14±1.34%	281.68±1.84 0.11±1.36%	280.19±0.32 0.99±0.41%

STZ: Streptozotocin, all values are expressed as mean±SEM, *n*=6, values given with % indicate percentage blood glucose reduction when compared to "0 h" value (s), *P*<0.5. SEM: Standard error of the mean

Table 14: Antidiabetic activity of diarylsulfonylurea-chalcone hybrid II.13

Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
0 h	90.53±1.17 0%	91.35±1.88 0%	91.45±1.71 0%	285.34±1.32 0%	281.34±0.06 0%	284.45±0.19 0%
1 h	83.93±0.33 6.74±1.41%	83.13±1.29 8.64±1.78%	80.40±1.72 11.64±1.21%	259.54±0.23 8.93±0.17%	249.75±0.47 11.12±0.34%	261.53±0.54 7.91±0.27%

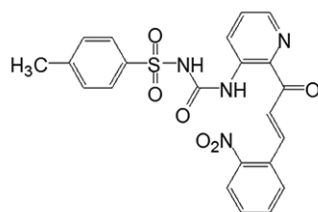
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Table 14: (Continued)

Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
2 h	81.13±1.34	80.38±0.62	74.01±1.84	248.89±0.64	242.33±0.03	250.43±0.32
	9.85±1.66%	11.78±0.44%	18.66±1.36%	12.69±1.87%	13.63±1.42%	11.82±0.41%
3 h	78.47±0.03	75.78±0.31	71.12±1.22	237.09±1.37	225.58±0.14	241.05±0.33
	12.81±0.11%	16.72±0.12%	21.62±1.11%	16.81±1.22%	19.72±1.34%	15.12±0.55%
4 h	75.20±1.26	67.17±0.73	65.78±0.37	227.54±1.56	208.72±1.83	199.25±0.64
	16.44±1.39%	26.18±0.88%	27.71±0.27%	20.16±0.09%	25.72±1.64%	29.84±0.77%
6 h	73.14±1.82	68.86±0.93	72.96±0.02	244.21±0.66	242.75±3.61	220.98±1.03
	18.73±1.98%	24.32±0.39%	19.82±0.16%	14.31±0.14%	13.61±1.97%	22.19±2.61%
12 h	78.47±0.88	76.19±2.11	79.57±0.12	265.79±1.69	263.63±2.11	243.35±2.37
	12.81±0.64%	16.27±1.55%	12.55±0.33%	6.74±1.23%	6.18±0.07%	14.31±1.04%
18 h	79.50±0.21	88.10±0.71	87.96±0.11	278.41±0.07	277.17±1.83	266.05±3.57
	11.66±0.73%	3.18±0.97%	3.33±0.56%	2.31±1.32%	1.36±1.64%	6.32±2.54%
24 h	86.10±1.49	89.97±2.31	89.48±0.12	283.43±1.88	278.97±1.55	280.64±0.29
	4.33±1.67%	1.13±0.02%	1.66±0.33%	0.55±0.92%	0.72±1.33%	1.18±0.65%

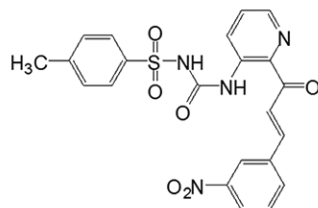
STZ: Streptozotocin, all values are expressed as mean±SEM, *n*=6, values given with % indicate percentage blood glucose reduction when compared to "0 h" value (s), *P*<0.5. SEM: Standard error of the mean

Table 15: Antidiabetic activity of diarylsulfonylurea-chalcone hybrid II.14



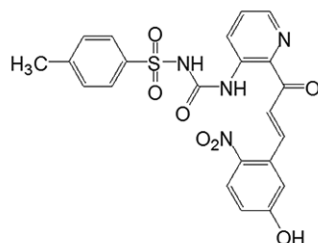
Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
0 h	92.54±0.19	92.45±0.06	89.56±1.17	285.45±1.88	283.46±1.71	284.34±1.32
	0%	0%	0%	0%	0%	0%
1 h	86.61±1.29	84.87±0.23	77.08±0.33	266.93±1.42	261.97±1.72	247.90±0.54
	5.85±1.78%	7.74±0.17%	13.39±1.41%	6.34±0.03%	7.43±1.21%	12.71±0.27%
2 h	88.02±0.62	79.32±0.64	69.73±0.03	257.01±0.47	255.10±1.84	224.87±0.32
	4.02±0.44%	13.78±1.87%	21.65±0.11%	9.82±0.34%	10.12±1.36%	20.82±0.41%
3 h	81.31±0.31	73.94±1.22	65.28±1.26	251.39±1.83	238.25±1.22	190.90±0.33
	11.61±0.12%	19.62±1.37%	26.65±1.39%	11.79±1.64%	15.81±1.11%	32.78±2.61%
4 h	77.39±0.62	70.11±0.66	60.64±1.82	248.91±1.36	224.02±0.37	213.99±0.33
	15.88±0.44%	23.79±0.14%	31.86±1.98%	12.66±2.84%	20.84±0.27%	24.65±0.55%
6 h	75.51±0.93	78.49±1.88	67.74±0.88	255.95±1.55	248.55±0.25	219.75±2.37
	17.92±0.39%	14.68±0.92%	23.88±0.64%	10.19±1.33%	12.17±0.24%	22.62±1.04%
12 h	81.15±2.11	83.96±1.32	76.06±1.49	263.95±3.61	255.46±1.22	230.29±1.03
	11.79±1.55%	8.73±0.07%	14.53±1.67%	7.42±1.97%	9.73±1.11%	18.91±2.61%
18 h	87.58±0.71	90.04±1.56	87.05±1.26	275.90±2.11	276.77±0.11	265.22±3.57
	4.80±0.97%	2.12±0.09%	2.19±1.39%	3.19±0.07%	20.20±0.56%	6.61±2.54%
24 h	90.96±2.31	91.83±1.69	87.98±0.88	284.45±0.14	281.44±0.12	280.90±0.29
	1.13±0.02%	0.18±1.23%	1.14±0.64%	0.19±1.34%	0.55±0.33%	1.09±0.65%

STZ: Streptozotocin, all values are expressed as mean±SEM, *n*=6, values given with % indicate percentage blood glucose reduction when compared to "0 h" value (s), *P*<0.5. SEM: Standard error of the mean

Table 16: Antidiabetic activity of diarylsulfonylurea-chalcone hybrid II.15

Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
0 h	95.34±1.32 0%	90.34±1.71 0%	90.46±0.06 0%	284.54±0.19 0%	284.87±1.17 0%	285.83±1.88 0%
1 h	85.76±0.47 9.72±0.34%	81.72±1.72 9.19±1.21%	79.10±0.54 12.11±0.27%	236.77±1.29 16.92±1.78%	243.35±0.33 14.31±1.41%	227.60±0.23 20.14±0.17%
2 h	82.05±0.14 13.63±1.34%	75.90±1.84 15.66±1.36%	71.83±0.32 20.18±0.41%	223.45±0.62 21.32±0.44%	224.87±1.34 20.82±1.66%	191.49±1.87 32.81±0.64%
3 h	78.08±1.83 17.81±1.64%	68.59±1.22 23.78±1.11%	67.69±0.33 24.78±0.55%	213.36±0.31 24.87±0.12%	205.53±0.03 27.63±0.11%	167.20±1.22 41.33±1.37%
4 h	74.74±1.36 21.32±2.84%	62.21±0.37 30.87±0.27%	59.74±2.37 33.62±1.04%	198.28±0.88 30.18±0.73%	173.86±1.26 38.78±1.39%	140.61±0.09 50.66±1.56%
6 h	70.62±3.61 25.66±1.97%	70.34±0.11 21.84±0.56%	51.55±3.57 42.72±2.54%	205.27±0.97 27.72±0.71%	193.63±1.82 31.82±1.98%	177.21±1.88 37.82±0.92%
12 h	82.82±2.11 12.82±0.07%	73.14±0.12 18.73±0.33%	64.20±0.64 28.66±0.77%	229.27±2.11 19.27±1.55%	232.25±0.88 18.22±0.64%	206.85±1.23 27.42±1.69%
18 h	90.61±1.42 4.62±0.03%	82.21±1.84 8.65±1.36%	76.72±0.65 17.75±0.54%	259.15±0.93 8.75±0.39%	262.35±0.21 7.62±0.73%	255.01±1.32 10.52±0.07%
24 h	93.90±1.55 1.15±1.33%	88.93±0.25 1.18±0.24%	83.87±0.29 6.81±0.65%	275.62±2.31 2.73±0.02%	276.84±1.49 2.52±1.67%	278.01±0.66 2.45±0.14%

STZ: Streptozotocin, all values are expressed as mean±SEM, $n=6$, values given with % indicate percentage blood glucose reduction when compared to "0 h" value (s), $P<0.5$. SEM: Standard error of the mean

Table 17: Antidiabetic activity of diarylsulfonylurea-chalcone hybrid II.16

Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
0 h	96.23±0.06 0%	88.55±0.19 0%	85.24±1.17 0%	283.65±1.88 0%	282.56±1.71 0%	285.32±1.32 0%
1 h	90.42±1.72 5.81±1.21%	79.91±0.23 9.19±0.17%	75.29±0.54 11.42±0.27%	255.15±1.29 9.84±1.78%	260.51±0.47 7.62±0.34%	231.81±0.33 18.66±1.41%
2 h	85.74±1.84 10.68±1.36%	75.39±1.87 14.32±0.64%	65.93±0.64 22.43±0.77%	250.68±0.62 11.42±0.44%	249.37±0.14 11.57±1.34%	207.70±0.03 27.12±0.11%

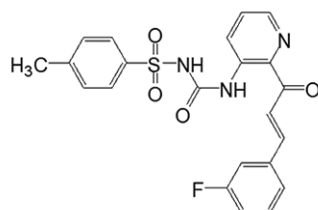
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Table 17: (Continued)

Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
3 h	83.33±0.25	71.65±1.88	60.56±0.33	239.67±2.11	241.64±1.83	195.33±1.26
	13.19±0.24%	18.57±0.92%	28.75±0.55%	15.31±1.55%	14.31±1.64%	31.76±1.39%
4 h	79.36±1.22	67.33±1.37	59.35±1.03	230.02±0.93	220.63±1.36	189.61±0.88
	17.33±1.11%	23.48±1.22%	30.17±2.61%	18.72±0.39%	21.76±2.84%	33.47±0.64%
6 h	76.15±0.02	73.44±0.66	63.98±0.64	247.99±0.73	233.04±3.61	203.31±1.82
	20.67±0.16%	16.54±0.14%	24.72±0.77%	12.37±0.88%	17.36±1.97%	28.66±1.98%
12 h	83.35±0.37	79.78±1.23	73.59±3.57	266.81±0.31	246.15±0.07	246.63±1.49
	13.17±0.27%	9.33±1.69%	13.42±2.54%	5.72±0.12%	12.71±2.11%	13.46±1.67%
18 h	83.96±0.11	87.01±1.32	83.99±0.29	276.80±0.71	275.90±0.03	268.98±1.34
	12.54±0.56%	1.12±0.07%	1.18±0.65%	2.19±0.97%	2.16±1.42%	5.62±1.66%
24 h	93.44±1.36	87.26±1.56	84.84±0.32	281.24±2.31	281.09±1.34	284.45±0.21
	2.66±1.84%	0.83±0.09%	0.18±0.41%	0.62±0.02%	0.32±1.64%	0.19±0.73%

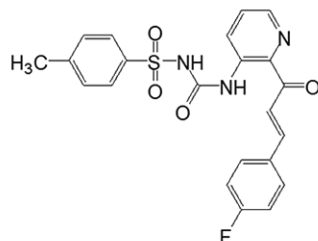
STZ: Streptozotocin, all values are expressed as mean±SEM, $n=6$, values given with % indicate percentage blood glucose reduction when compared to "0 h" value (s), $P<0.5$. SEM: Standard error of the mean

Table 18: Antidiabetic activity of diarylsulfonylurea-chalcone hybrid II.17



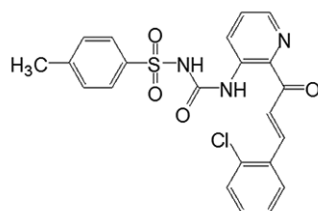
Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
0 h	96.64±1.71	87.34±1.32	88.65±1.17	287.46±1.88	281.46±0.06	284.36±0.19
	0%	0%	0%	0%	0%	0%
1 h	90.41±1.72	80.53±1.29	75.39±0.33	263.72±0.23	256.29±0.47	237.36±0.54
	5.82±1.21%	7.43±1.78%	14.32±1.41%	8.11±0.17%	15.91±0.34%	16.42±0.27%
2 h	87.69±1.22	72.36±0.62	68.15±1.34	250.72±0.64	222.74±1.83	215.32±0.33
	8.65±1.11%	16.82±0.44%	22.55±1.66%	12.64±1.87%	20.73±1.64%	24.18±0.55%
3 h	85.25±1.84	69.02±0.31	63.07±0.03	240.16±1.22	211.81±3.61	197.06±0.64
	11.19±1.36%	20.66±0.12%	28.32±0.11%	16.32±1.37%	24.62±1.97%	30.61±0.77%
4 h	80.32±1.22	62.47±0.73	59.47±1.26	231.26±1.56	189.36±1.36	181.27±2.37
	16.33±1.11%	28.19±0.88%	32.42±1.39%	19.42±0.09%	32.61±2.84%	36.17±1.04%
6 h	79.04±0.37	68.04±0.71	68.54±0.21	237.40±0.66	201.81±2.11	199.68±1.03
	17.66±0.27%	21.79±0.97%	22.11±0.73%	17.28±0.14%	28.18±0.07%	29.69±2.61%
12 h	85.65±0.11	79.76±0.93	77.53±0.88	253.10±1.88	234.24±1.36	241.91±0.64
	10.78±0.56%	8.32±0.39%	11.89±0.64%	11.81±0.92%	16.64±2.84%	14.82±0.77%
18 h	92.76±0.12	85.09±2.11	85.19±1.98	283.58±1.32	267.45±0.14	259.54±1.03
	3.79±0.33%	2.19±1.55%	3.19±1.82%	1.19±0.07%	4.82±1.34%	8.61±2.61%
24 h	94.82±0.02	86.09±2.31	86.36±1.49	285.16±1.69	279.11±0.03	280.25±0.29
	1.22±0.16%	1.04±0.02%	1.36±1.67%	0.14±1.23%	0.17±1.42%	1.32±0.65%

STZ: Streptozotocin, all values are expressed as mean ± SEM, $n = 6$, values given with % indicate percentage blood glucose reduction when compared to "0 h" value (s), $P < 0.5$. SEM: Standard error of the mean

Table 19: Antidiabetic activity of diarylsulfonylurea-chalcone hybrid II.18

Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
0 h	96.56±1.71 0%	85.66±1.32 0%	87.64±0.06 0%	286.24±0.19 0%	283.34±1.88 0%	285.54±1.17 0%
1 h	94.14±0.23 1.93±0.17%	80.84±0.33 4.89±1.41%	72.71±1.29 16.42±1.78%	266.95±0.47 6.66±0.34%	255.79±1.72 8.97±1.21%	243.37±0.54 14.64±0.27%
2 h	92.46±0.64 3.68±1.87%	74.98±1.34 11.78±1.66%	65.45±0.62 24.77±0.44%	264.80±0.14 7.41±1.34%	235.51±1.84 16.78±1.36%	208.81±0.32 26.73±0.41%
3 h	86.57±1.22 9.82±1.37%	68.58±0.03 19.31±0.11%	61.05±0.93 29.82±0.39%	258.48±1.83 9.62±1.64%	226.76±1.22 19.87±1.11%	194.82±0.64 31.64±0.77%
4 h	84.85±1.56 11.61±0.09%	63.59±1.26 25.18±1.39%	59.35±0.31 31.78±0.12%	252.33±1.36 11.77±2.84%	219.52±0.25 22.43±0.24%	185.62±0.33 34.87±0.55%
6 h	81.76±0.66 14.83±0.14%	69.97±1.82 17.68±1.98%	65.57±0.73 24.63±0.88%	260.34±2.11 8.97±0.07%	247.25±0.37 12.63±0.27%	203.63±2.37 28.55±1.04%
12 h	89.03±1.69 7.26±1.23%	76.99±0.88 9.42±0.64%	75.527±2.11 13.13±1.55%	276.90±3.61 3.18±1.97%	263.78±0.24 6.79±0.25%	249.03±3.57 12.62±2.54%
18 h	93.74±1.88 2.35±0.92%	84.01±0.21 1.16±0.73%	85.96±0.02 1.19±2.31%	280.50±1.55 1.92±1.33%	273.63±0.11 3.31±0.56%	263.51±2.37 7.54±1.04%
24 h	94.95±0.07 1.09±1.32%	84.84±1.49 0.18±1.67%	86.89±0.71 0.12±0.97%	285.37±0.03 0.22±1.42%	280.56±1.84 0.86±1.36%	278.69±0.29 2.22±0.65%

STZ: Streptozotocin, all values are expressed as mean±SEM, *n*=6, values given with % indicate percentage blood glucose reduction when compared to "0 h" value (s), *P*<0.5. SEM: Standard error of the mean

Table 20: Antidiabetic activity of diarylsulfonylurea-chalcone hybrid II.19

Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
0 h	97.56±1.32 0%	84.43±1.71 0%	90.42±0.19 0%	285.54±0.06 0%	284.23±1.88 0%	284.24±1.17 0%
1 h	91.25±0.47 5.92±0.34%	79.60±0.23 5.23±0.17%	80.50±1.29 10.55±1.78%	250.76±0.33 12.32±1.41%	233.41±1.72 17.81±1.21%	247.59±0.54 12.82±0.27%
2 h	85.54±1.83 11.81±1.64%	73.89±0.64 12.03±1.87%	72.44±0.62 19.51±0.44%	243.84±1.34 14.74±1.66%	226.54±1.84 20.23±1.36%	214.07±0.41 24.62±0.32%

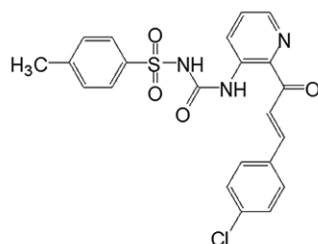
(Contd...)

Table 20: (Continued)

Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
3 h	82.77±1.36	68.76±1.22	70.80±0.31	232.17±0.03	212.48±1.22	199.82±0.33
	14.66±2.84%	18.14±1.37%	21.33±0.12%	18.82±0.11%	25.18±1.11%	29.64±0.55%
4 h	78.84±2.11	62.36±1.56	64.62±0.93	214.40±1.39	199.42±0.37	182.64±0.64
	18.72±0.07%	25.76±0.09%	28.19±0.39%	24.77±1.26%	29.78±0.27%	35.69±0.77%
6 h	76.45±3.61	69.95±0.66	72.25±2.11	248.69±1.82	208.28±1.22	212.63±3.57
	21.18±1.97%	16.72±0.14%	19.72±1.55%	12.74±1.98%	26.66±1.11%	25.13±2.54%
12 h	85.68±1.55	76.75±1.88	79.62±0.71	269.83±0.88	226.66±0.25	250.99±0.29
	11.66±1.33%	8.62±0.92%	11.53±0.97%	5.32±0.64%	20.19±0.24%	11.62±0.65%
18 h	90.99±1.36	82.92±1.32	86.56±2.11	277.41±0.21	262.30±0.12	270.22±0.64
	6.19±2.84%	1.28±0.07%	3.82±1.55%	2.66±0.73%	7.64±0.33%	4.85±0.77%
24 h	95.81±0.03	83.89±1.69	88.54±2.31	284.82±1.67	274.99±0.11	280.62±0.32
	1.22±1.42%	0.12±1.23%	1.64±0.02%	0.18±1.49%	3.17±0.56%	1.19±0.41%

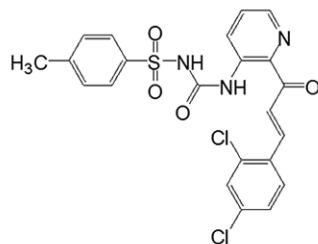
STZ: Streptozotocin, all values are expressed as mean±SEM, *n*=6, values given with % indicate percentage blood glucose reduction when compared to "0 h" value (s), *P*<0.5. SEM: Standard error of the mean

Table 21: Antidiabetic activity of diarylsulfonylurea-chalcone hybrid II.20



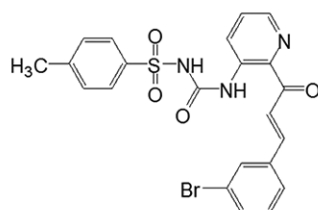
Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
0 h	95.65±0.06	88.45±0.19	91.36±1.17	284.32±1.88	285.53±1.71	283.78±1.32
	0%	0%	0%	0%	0%	0%
1 h	86.81±0.47	81.67±1.29	80.18±0.23	250.11±1.72	252.73±0.33	230.19±0.54
	8.62±0.34%	7.19±1.78%	11.88±0.17%	11.93±1.21%	11.32±1.41%	18.66±0.27%
2 h	83.09±0.03	73.18±0.62	71.72±0.64	233.33±0.12	225.66±1.34	185.05±0.33
	12.53±1.42%	16.18±0.44%	21.18±1.87%	17.84±0.33%	20.82±1.66%	34.61±0.55%
3 h	77.13±1.83	63.92±0.31	67.46±1.22	222.31±0.25	212.01±0.03	166.06±0.33
	18.81±1.64%	27.36±0.12%	25.86±1.37%	21.72±0.24%	25.61±0.11%	41.32±0.55%
4 h	75.69±1.36	56.17±0.73	55.12±1.88	209.64±1.22	182.±1.26	146.62±0.64
	20.32±2.84%	36.17±0.88%	39.42±0.92%	26.18±1.11%	36.14±1.39%	48.12±0.77%
6 h	72.69±3.61	66.57±2.11	45.70±1.56	216.49±0.25	170.48±1.82	133.97±0.32
	23.48±1.97%	24.32±1.55%	49.77±0.09%	23.77±0.24%	40.18±1.98%	52.66±0.41%
12 h	81.05±1.55	72.31±0.93	64.87±0.66	231.06±1.84	231.64±0.88	193.58±0.29
	14.68±1.33%	17.82±0.39%	28.71±0.14%	18.64±1.36%	18.74±0.64%	31.64±0.65%
18 h	87.73±0.14	81.45±2.31	79.47±0.07	264.74±0.11	260.43±0.21	247.59±2.54
	7.65±1.34%	7.44±0.02%	12.66±1.32%	6.78±0.56%	8.63±0.73%	12.51±3.57%
24 h	93.91±0.03	86.12±0.73	86.58±1.69	281.75±1.22	281.60±1.49	279.54±1.03
	1.14±1.42%	2.13±0.88%	4.85±1.23%	0.79±1.11%	1.19±1.67%	1.12±2.61%

STZ: Streptozotocin, all values are expressed as mean±SEM, *n*=6, values given with % indicate percentage blood glucose reduction when compared to "0 h" value (s), *P*<0.5. SEM: Standard error of the mean

Table 22: Antidiabetic activity of diarylsulfonylurea-chalcone hybrid II.21

Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
0 h	88.54±0.06 0%	89.56±0.19 0%	91.45±1.17 0%	287.34±1.88 0%	282.54±1.71 0%	284.75±1.32 0%
1 h	85.65±1.29 2.66±1.78%	86.16±0.23 3.18±0.17%	84.25±0.33 7.24±1.41%	277.87±0.47 3.18±0.34%	275.82±1.72 2.19±1.21%	259.17±0.54 8.74±0.27%
2 h	84.14±0.62 4.38±0.44%	84.84±0.64 4.64±1.87%	78.67±0.03 13.54±0.11%	273.36±0.14 4.75±1.34%	270.86±1.84 3.95±1.36%	254.32±0.32 10.56±0.41%
3 h	80.28±0.31 8.67±0.12%	81.95±1.22 7.92±1.37%	75.22±1.26 17.33±1.39%	261.97±1.83 8.72±1.64%	254.44±1.22 9.77±1.11%	242.45±0.33 14.63±0.55%
4 h	79.51±0.93 9.64±0.39%	76.68±1.56 13.84±0.09%	72.63±1.66 20.18±1.34%	250.09±2.11 12.86±0.07%	240.65±0.37 14.66±0.27%	222.14±1.03 21.78±2.61%
6 h	77.63±2.11 11.78±1.55%	72.82±0.66 18.17±0.14%	79.97±1.82 12.12±1.98%	260.71±1.83 9.16±1.64%	258.81±0.56 8.22±0.11%	238.21±0.64 16.12±0.77%
12 h	79.84±0.73 9.27±0.88%	74.05±1.88 16.79±0.92%	84.96±0.88 6.63±0.64%	279.22±1.36 2.71±2.84%	272.38±0.25 3.41±0.24%	264.77±0.29 6.77±0.65%
18 h	84.77±0.71 3.67±0.97%	82.04±1.69 7.82±1.23%	89.59±0.21 1.54±0.73%	281.66±1.55 1.86±1.33%	277.91±1.84 1.42±1.36%	277.97±0.55 21.12±0.33%
24 h	87.04±2.31 1.09±0.02%	87.05±1.32 2.19±0.07%	90.82±1.49 0.19±1.67%	286.65±0.03 0.12±1.42%	279.88±0.11 0.75±1.21%	283.46±0.32 0.19±0.41%

STZ: Streptozotocin, all values are expressed as mean±SEM, *n*=6, values given with % indicate percentage blood glucose reduction when compared to "0 h" value (s), *P*<0.5. SEM: Standard error of the mean

Table 23: Antidiabetic activity of diarylsulfonylurea-chalcone hybrid II.22

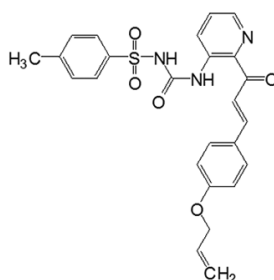
Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
0 h	89.46±1.32 0%	88.34±1.71 0%	92.24±0.19 0%	283.34±0.06 0%	281.23±1.17 0%	282.45±1.88 0%
1 h	83.35±0.47 6.34±0.34%	85.63±0.23 2.66±0.17%	85.99±1.29 6.53±1.78%	255.60±0.33 9.68±1.41%	262.62±1.72 6.54±1.21%	251.62±0.54 10.77±0.27%
2 h	81.23±1.83 8.72±1.64%	82.94±0.07 5.74±1.32%	78.45±0.62 14.72±0.44%	240.94±1.34 14.86±1.66%	267.27±1.84 13.79±1.36%	218.77±0.33 22.42±0.55%

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Table 23: (Continued)

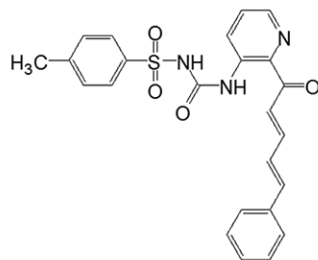
Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
3 h	78.42±1.36	80.79±0.64	74.86±0.31	232.90±0.03	235.70±1.22	213.95±0.64
	11.81±2.84%	8.19±1.87%	18.63±0.12%	17.73±0.11%	16.12±1.11%	24.13±0.77%
4 h	75.22±3.61	76.78±1.22	72.06±0.93	230.27±1.26	219.82±0.02	206.64±0.32
	15.32±1.97%	12.74±1.37%	21.67±0.39%	18.63±1.39%	21.77±0.16%	26.72±0.41%
6 h	74.02±1.55	70.61±0.66	80.28±2.11	242.07±0.21	238.20±0.12	218.15±1.03
	16.83±1.33%	19.76±0.14%	12.73±1.55%	14.46±0.73%	15.23±0.33%	22.64±2.61%
12 h	81.69±2.11	72.45±1.56	86.62±0.73	266.86±0.88	256.66±1.22	232.31±0.33
	8.21±0.07%	17.67±0.09%	5.84±0.88%	5.72±0.64%	8.66±1.11%	17.62±0.55%
18 h	85.11±0.14	79.30±1.69	89.99±0.71	272.21±1.49	273.46±0.25	254.81±2.37
	4.36±1.34%	9.88±1.23%	2.18±0.97%	3.85±1.67%	2.68±0.24%	9.64±1.04%
24 h	87.38±0.03	86.98±1.88	90.96±2.31	281.47±1.82	276.11±0.11	277.37±0.29
	1.82±1.42%	1.15±0.92%	1.12±0.02%	0.54±1.98%	1.74±0.56%	1.64±0.65%

STZ: Streptozotocin, all values are expressed as mean±SEM, *n*=6, values given with % indicate percentage blood glucose reduction when compared to "0 h" value (s), *P*<0.5. SEM: Standard error of the mean

Table 24: Antidiabetic activity of diarylsulfonylurea-chalcone hybrid II.23

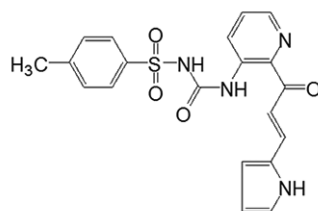
Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
0 h	90.55±1.71	87.35±0.19	94.53±0.06	289.43±1.32	288.65±1.88	282.54±1.17
	0%	0%	0%	0%	0%	0%
1 h	85.59±0.47	80.37±0.23	83.64±1.29	252.21±0.33	234.68±1.72	223.42±0.54
	4.89±0.34%	8.66±0.17%	11.05±1.78%	12.73±1.41%	16.78±1.21%	20.77±0.27%
2 h	81.25±0.14	70.62±0.64	72.24±0.62	231.74±1.34	217.67±1.22	279.59±0.32
	9.72±1.34%	19.74±1.87%	23.14±0.44%	19.81±1.66%	22.81±1.11%	32.41±0.41%
3 h	74.70±1.83	66.12±1.22	58.39±0.93	223.59±0.03	189.92±0.25	161.69±0.33
	16.99±1.64%	24.86±1.37%	37.88±0.39%	22.63±0.11%	32.65±0.24%	42.66±0.55%
4 h	69.56±3.61	57.35±1.56	48.49±0.31	211.60±1.26	174.36±0.37	140.09±0.64
	22.71±1.97%	34.82±0.09%	48.41±0.12%	26.78±1.39%	38.17±0.27%	47.13±0.77%
6 h	73.77±1.36	66.99±0.66	45.43±0.71	229.40±0.88	193.59±0.02	121.88±1.03
	18.03±2.84%	23.87±0.14%	51.67±0.97%	20.62±0.64%	30.66±0.16%	56.78±2.61%
12 h	82.16±1.55	75.31±1.69	56.01±0.73	246.17±1.82	211.58±0.11	173.06±3.57
	8.71±1.33%	14.42±1.23%	40.41±0.88%	14.82±1.98%	24.97±0.56%	38.64±2.54%
18 h	86.01±3.61	83.74±1.88	72.15±0.93	275.21±0.21	248.66±0.25	240.71±2.37
	4.43±1.97%	4.83±0.92%	23.24±0.39%	4.77±0.73%	11.82±0.24%	14.64±1.04%
24 h	89.07±0.03	86.14±0.07	84.71±2.31	283.74±1.49	271.31±0.02	275.45±0.29
	1.03±1.42%	2.11±1.32%	9.88±0.02%	1.82±1.67%	3.79±0.16%	2.32±0.65%

STZ: Streptozotocin, all values are expressed as mean±SEM, *n*=6, values given with % indicate percentage blood glucose reduction when compared to "0 h" value (s), *P*<0.5. SEM: Standard error of the mean

Table 25: Antidiabetic activity of diarylsulfonylurea-chalcone hybrid II.24

Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
0 h	93.32±0.06 0%	89.45±0.19 0%	89.56±1.71 0%	288.67±1.32 0%	283.32±1.17 0%	281.43±1.88 0%
1 h	87.13±0.23 6.31±0.17%	86.63±1.29 2.66±1.78%	81.29±0.47 8.66±0.34%	273.02±0.33 5.12±1.41%	258.52±1.72 8.65±1.21%	248.34±0.54 11.65±0.27%
2 h	83.53±0.64 10.18±1.87%	83.85±0.62 5.78±0.44%	74.12±0.14 16.71±1.34%	262.74±1.34 8.74±1.66%	244.32±1.84 13.78±1.36%	220.24±0.29 21.62±0.65%
3 h	81.17±1.22 12.71±1.37%	81.57±0.31 8.34±0.12%	67.44±1.83 24.22±1.64%	251.59±0.03 12.64±0.11%	231.66±1.22 18.14±0.27%	217.01±0.32 22.77±0.41%
4 h	77.35±1.56 13.82±0.09%	73.68±0.93 16.27±0.39%	63.91±1.36 28.19±2.84%	237.13±1.26 17.66±1.39%	225.23±1.22 20.41±1.11%	196.22±0.33 30.17±0.55%
6 h	76.10±0.66 18.17±0.14%	69.03±2.11 22.43±1.55%	69.53±3.61 21.87±1.97%	255.11±0.88 11.42±0.64%	241.34±0.25 14.72±0.24%	217.69±2.37 22.53±1.04%
12 h	84.94±1.69 8.66±1.23%	77.24±0.71 13.21±0.97%	86.22±1.55 3.12±1.33%	263.03±0.21 8.67±0.73%	259.82±0.12 8.19±0.33%	230.89±0.33 17.83±0.55%
18 h	87.90±1.88 5.48±0.92%	83.54±0.73 6.67±0.88%	88.03±0.03 1.08±1.42%	283.96±1.82 1.74±1.98%	276.88±0.11 2.16±0.56%	262.95±0.64 6.42±0.77%
24 h	91.95±1.32 1.12±0.07%	87.05±2.31 2.18±0.02%	88.87±2.11 0.14±0.07%	285.58±1.49 0.84±1.67%	282.46±1.72 0.19±1.21%	277.65±3.57 1.19±2.54%

STZ: Streptozotocin, all values are expressed as mean±SEM, *n*=6, values given with % indicate percentage blood glucose reduction when compared to "0 h" value (s), *P*<0.5. SEM: Standard error of the mean

Table 26: Antidiabetic activity of diarylsulfonylurea-chalcone hybrid II.25

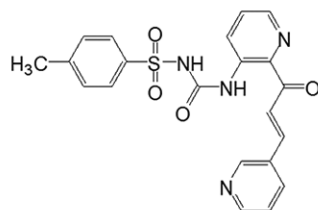
Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
0 h	95.55±1.32 0%	90.53±1.71 0%	88.23±0.06 0%	285.34±0.19 0%	285.22±1.17 0%	285.23±1.88 0%
1 h	93.16±1.29 1.93±1.78%	87.52±0.23 2.75±0.17%	83.23±0.33 5.42±1.41%	274.31±0.47 3.75±0.34%	260.63±1.72 8.55±1.21%	255.55±0.54 10.32±0.27%
2 h	90.89±0.31 4.32±0.12%	84.03±0.64 6.63±1.87%	76.02±1.66 13.61±1.34%	262.74±1.83 7.81±1.64%	246.15±0.24 13.63±0.25%	246.09±0.29 13.65±0.65%

(Contd...)

Table 26: (Continued)

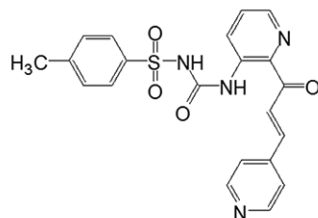
Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
3 h	88.59±0.62	81.25±1.22	72.45±0.03	251.85±0.14	237.60±1.22	234.75±0.32
	6.74±0.44%	9.72±1.37%	17.66±0.11%	11.63±1.34%	16.63±1.11%	17.63±0.41%
4 h	87.28±0.73	79.96±1.56	68.89±1.26	242.90±3.61	233.13±0.37	241.54±0.33
	8.28±0.88%	11.82±0.09%	21.71±1.39%	14.77±1.97%	18.20±0.27%	24.74±0.55%
6 h	84.09±2.11	76.67±0.66	76.79±0.88	255.53±1.36	245.39±0.11	248.71±3.57
	11.48±1.55%	14.81±0.14%	12.73±0.64%	10.34±2.84%	12.63±0.56%	12.76±2.54%
12 h	88.02±0.97	83.99±1.69	83.67±1.82	271.54±2.11	248.31±0.12	266.58±0.64
	7.34±0.71%	6.67±1.23%	4.91±1.98%	4.72±0.07%	6.73±0.33%	6.63±0.77%
18 h	91.96±2.31	88.03±1.88	86.89±0.21	281.92±0.03	248.75±1.22	275.75±0.33
	3.19±0.02%	2.18±0.92%	1.26±0.73%	1.08±1.42%	2.19±1.11%	2.19±0.55%
24 h	93.97±0.93	88.97±1.32	87.84±1.49	284.62±1.34	282.74±0.12	284.60±0.64
	1.08±0.39%	1.17±0.07%	0.18±1.67%	0.13±0.14%	0.79±0.33%	0.14±0.77%

STZ: Streptozotocin, all values are expressed as mean±SEM, *n*=6, values given with % indicate percentage blood glucose reduction when compared to "0 h" value (s), *P*<0.5. SEM: Standard error of the mean

Table 27: Antidiabetic activity of diarylsulfonylurea-chalcone hybrid II.26

Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
0 h	96.45±0.19 0%	91.23±0.06 0%	85.34±1.32 0%	285.45±1.71 0%	285.24±1.88 0%	282.34±1.17 0%
1 h	90.48±1.29	85.84±0.33	76.68±0.23	276.62±0.47	253.87±1.72	248.80±0.54
	5.48±1.78%	5.66±1.41%	9.78±0.17%	2.67±0.34%	10.92±1.21%	11.77±0.27%
2 h	88.16±0.62	83.15±1.34	65.59±0.64	268.69±0.14	227.45±1.84	217.42±0.29
	8.65±0.44%	8.62±1.66%	22.83±1.87%	5.72±1.34%	20.19±1.36%	22.45±0.65%
3 h	84.66±0.31	76.64±0.03	59.61±1.22	257.01±1.83	223.06±1.22	215.33±0.64
	11.81±0.12%	15.78±0.11%	29.87±1.37%	9.82±1.64%	21.73±1.11%	23.64±0.77%
4h	81.92±0.73	71.68±1.26	58.08±1.56	248.60±1.36	208.50±0.25	189.89±0.33
	14.66±0.88%	21.22±1.39%	31.67±0.09%	12.77±2.84%	26.84±0.24%	32.66±0.55%
6 h	81.29±2.11	73.70±1.82	63.37±0.66	260.31±3.61	226.43±0.37	201.88±0.64
	15.32±1.55%	19.01±1.98%	25.44±0.14%	8.66±1.97%	20.55±0.27%	28.41±0.77%
12 h	89.02±0.31	85.04±0.88	70.68±1.88	275.96±0.07	248.43±0.02	240.01±2.37
	7.27±0.12%	6.54±0.64%	16.84±0.92%	3.17±0.07%	12.19±0.16%	14.89±1.04%
18 h	92.75±0.71	88.07±0.21	78.48±1.69	281.92±1.55	274.08±1.72	266.71±3.57
	3.38±0.97%	3.21±0.73%	7.66±1.23%	1.08±1.33%	3.83±1.21%	5.42±2.54%
24 h	93.99±2.31	90.07±1.49	83.95±0.07	284.97±0.03	281.92±0.11	275.45±1.03
	2.09±0.02%	1.02±1.67%	1.23±1.32%	0.01±1.42%	1.08±0.56%	2.32±2.61%

STZ: Streptozotocin, all values are expressed as mean±SEM, *n*=6, values given with % indicate percentage blood glucose reduction when compared to "0 h" value (s), *P*<0.5. SEM: Standard error of the mean

Table 28: Antidiabetic activity of diarylsulfonylurea-chalcone hybrid II.27

Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
0 h	96.54±0.19 0%	92.65±0.06 0%	87.23±1.17 0%	286.45±1.88 0%	286.43±1.71 0%	284.87±1.32 0%
1 h	88.98±2.31 7.31±0.02%	88.02±0.23 4.32±0.17%	76.02±0.33 12.61±1.41%	258.05±0.47 9.77±0.34%	247.07±0.11 13.61±0.56%	246.73±0.54 13.12±0.27%
2 h	87.18±1.29 9.18±1.78%	85.04±0.64 7.56±1.87%	68.01±1.34 21.82±1.66%	243.88±0.14 14.82±1.34%	224.05±1.72 21.66±1.21%	248.64±0.32 12.45±0.41%
3 h	82.67±0.62 13.88±0.44%	78.35±1.22 14.83±1.37%	60.74±0.03 30.18±0.11%	236.52±1.83 17.63±1.64%	216.47±1.22 24.31±1.11%	237.36±0.33 16.42±0.55%
4h	80.90±0.31 15.72±0.12%	69.26±1.56 24.71±0.09%	57.92±1.26 33.42±1.39%	226.74±1.36 20.72±2.84%	203.46±0.25 28.86±0.24%	216.20±0.64 23.87±0.77%
6 h	78.08±0.93 18.66±0.39%	73.59±0.66 20.01±0.14%	63.12±1.82 27.44±1.98%	237.83±3.61 16.84±1.97%	225.45±0.02 21.17±0.16%	248.72±1.04 12.42±2.37%
12 h	86.61±0.71 9.78±0.97%	84.85±1.69 7.77±1.23%	72.41±0.88 14.81±0.64%	258.20±2.11 9.72±0.07%	251.96±0.37 12.11±0.27%	259.26±3.57 8.71±2.54%
18 h	91.55±0.73 4.63±0.88%	87.57±1.88 4.81±0.92%	81.38±0.21 6.45±0.73%	275.18±0.03 3.78±1.42%	275.21±0.25 3.77±0.24%	273.71±0.64 3.62±0.77%
24 h	95.02±2.11 1.02±1.55%	90.15±1.32 2.01±0.07%	85.31±1.49 1.94±1.67%	281.36±1.55 1.62±1.33%	280.88±0.25 1.79±0.24%	283.63±0.29 0.13±0.65%

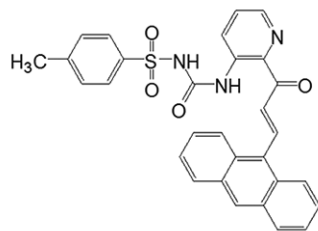
STZ: Streptozotocin, all values are expressed as mean±SEM, $n=6$, values given with % indicate percentage blood glucose reduction when compared to "0 h" value (s), $P<0.5$. SEM: Standard error of the mean

moieties are the vital structural pharmacophores for maintaining the hypoglycemic and antihyperglycemic activity. It is remarkable that enhanced level of activity was observed when the phenyl ring of α,β -unsaturated carbonyl system is substituted with different functional groups and decreased by some other substituents. The order of activity was II.5 (4-OCH₃) > II.13 (3-OCH₃,4-OH) > II.19 (2-Cl) > II.4 (3-OCH₃) > II.3 (N(CH₃)₂) > II.11 (4-OH) > II.22 (3-Br) > II.9 (2-OH) > II.10 (3-OH) > II.20 (4-Cl) > II.23 (4-Allyloxy) > II.8 (3,4,5-triOCH₃) > II.12 (3-C₂H₅,4-OH) > II.24 (phenylethenyl) > II.7 (2,4-diOCH₃) > II.6 (3,4-diOCH₃) > II.15 (3-NO₂) > II.2 (4-CH₃) > II.16 (5-OH,2-NO₂) > II.14 (2-NO₂) > II.17 (3-F) > II.18 (4-F), respectively. An ortho- and para-substitution on the phenyl ring of α,β -unsaturated carbonyl system with less electronegative halogens compared to fluorine, such as chloro may significantly enhance the activity as seen in case of compound II.21. A para-substitution on the phenyl ring of α,β -unsaturated carbonyl system with electron-donating groups possibly will increase the activity. A para-substitution on the phenyl ring of α,β -unsaturated carbonyl system with hydroxyl group relevant for

maintaining activity. The replacement of phenyl ring with a pyridine-4-yl ring as in compound II.27 exhibited a significant increase in activity compared to the compounds possessing other aromatic or heteroaromatic ring systems, the order of activity was II.26 (pyridin-3-yl) > II.25 (pyrrole) > II.28 (anthracen-9-yl), respectively.

DISCUSSION

Diabetes mellitus is one of the major health disorders in developing countries affects people of all age groups. Till date, there is no effective remedy available for effective control and management of diabetes mellitus except administration required dose of insulin. Several enzymes are involved in carbohydrate metabolism, which serves as the target for controlling hyperglycemia.^[19] Alpha-amylase and glucosidase enzymes play a key role in the conversion of complex sugars into simple glucose that gets absorbed into the blood. Thus, these enzymes are responsible for increasing the blood sugar level. Under diabetic condition, the sugar

Table 29: Antidiabetic activity of diarylsulfonylurea-chalcone hybrid II.28

Time (h)	Blood glucose levels in mg/dL (% blood glucose reduction)					
	Hypoglycemic activity (euglycemic rats)			Antihyperglycemic activity (STZ-induced type 2 diabetic rats)		
	10 mg/kg	30 mg/kg	50 mg/kg	10 mg/kg	30 mg/kg	50 mg/kg
0 h	96.65±0.06 0%	94.34±0.19 0%	88.34±1.17 0%	286.34±1.88 0%	287.44±1.71 0%	284.21±1.32 0%
1 h	94.29±0.33 1.78±1.41%	91.82±0.23 2.31±0.17%	79.96±2.31 9.13±0.02%	279.30±0.47 2.34±0.34%	266.39±1.72 7.18±1.21%	246.73±0.54 13.12±0.27%
2 h	93.20±1.34 2.91±1.66%	89.46±0.64 4.82±1.87%	75.09±1.29 14.66±1.78%	268.38±0.14 6.16±1.34%	249.34±0.11 13.12±0.56%	248.64±0.33 12.45±0.55%
3 h	91.84±0.03 4.33±0.11%	86.40±1.22 8.08±1.37%	74.07±0.62 15.82±0.44%	262.46±1.83 8.23±1.64%	240.16±0.12 16.32±0.33%	237.69±0.64 16.42±0.77%
4 h	89.71±1.26 6.55±1.39%	81.15±1.56 13.66±0.09%	72.41±0.31 17.71±0.12%	249.84±2.11 12.64±0.07%	233.10±0.37 18.78±0.27%	216.20±0.32 23.87±0.41%
6 h	86.58±0.88 9.81±0.64%	84.67±0.66 9.92±0.14%	77.33±0.73 12.12±0.88%	264.77±1.36 7.42±2.84%	251.58±0.02 12.34±0.16%	248.72±1.03 12.42±2.61%
12 h	90.55±1.82 5.67±1.98%	87.66±1.69 6.74±1.23%	82.59±2.11 6.14±1.55%	276.90±3.61 3.18±1.97%	267.65±0.25 6.74±0.24%	259.26±3.57 8.71±2.54%
18 h	94.86±0.21 1.18±0.73%	91.94±1.88 2.19±0.92%	86.38±0.71 1.84±0.97%	282.85±0.03 1.91±1.42%	280.71±1.84 2.19±1.36%	273.71±0.29 3.62±0.65%
24 h	95.88±1.49 0.12±1.67%	92.94±1.32 1.12±0.07%	87.87±0.93 0.14±0.39%	285.77±1.34 0.08±1.34%	284.87±0.11 0.74±0.56%	283.63±0.64 0.13±0.77%

STZ: Streptozotocin, all values are expressed as mean±SEM, $n=6$, values given with % indicate percentage blood glucose reduction when compared to "0 h" value (s), $P<0.5$. SEM: Standard error of the mean

level was not controlled by insulin, and thus, the blood sugar level stays high (hyperglycemia) for a prolonged period of time leading to cell damage in specific tissues.^[20,21]

The hypoglycemic studies on the diarylsulfonylurea-chalcone hybrids from 28 compounds revealed significant hypoglycemic effects when compared to that of control animals and diabetic animals models. It was revealed further that elevated glucose lowering effect was recorded in II.28. On the other hand, the hypoglycemic effects of diarylsulfonylurea-chalcone hybrids increased when compared to that of Gliclazide (reference drug), administered indicating the hypoglycemic potency. Similar observation was also made in the STZ induced diabetic rat model.

Studies elsewhere on diarylsulfonylurea-chalcone hybrids revealed antidiabetic potential in STZ induced diabetic rats^[22] and STZ^[23] induced diabetic animals as well as in human subjects.^[24] Sulfonylureas were discovered in 1942, when Janbon *et al.* observed that some sulfonamides generated hypoglycemia in experimental animals. From

this observation, carbutamide (1-butyl-3-sulfonylurea) was synthesized. Carbutamide was the first sulfonylurea used to treat diabetes but was subsequently withdrawn from the market because of its adverse effects on bone marrow.

Further studies were designed to assess the hypoglycemic effect of diarylsulfonylurea-chalcone during hyperglycemia.

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