Lysulin®: A double-blind placebo controlled pilot study of daily oral supplementation in people with type 2 diabetes

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ABSTRACT

Objective: This Pilot Study is aimed at evaluating the effect of daily oral supplementation with Lysulin® on glycemic control as assessed by measurement of Hemoglobin A1c (A1c), cardiometabolic and anthropometric parameters as compared to Placebo in people with Type 2 diabetes. This is a Pilot Study and it is intended to be used to design a further confirmatory clinical study by providing information on the feasibility of recruitment, randomization, sample size, retention, and assessment of procedures, methods and implementation of a novel intervention: Lysulin. Methods: A randomized, double-blind placebo-controlled pilot study was conducted over a 12-week period in 67 subjects. Subjects enrolled in the study had average an A1c 8.5 (2.2) and range 5.1%-12.9% at baseline. The inclusive range of low, medium and high in A1c levels was chosen to evaluate if there was a biased response to a specific A1c level. Subjects of ages 49 (9) years with a range of 33-74 years and both sexes (31 women and 36 men) were included in the study. Subjects were randomized 1:1:1 into groups based on oral supplementation: Group A Placebo, Group B 2.22 g/day Lysulin Group, Group C 3.33 g/day Lysulin. Subjects were evaluated at Baseline and at 4, 8 and 12 weeks. The primary endpoint of this pilot study changed in A1c from baseline to week 12. For observation purposes, Groups B and C were followed to 26 weeks. The data will be presented as Average followed by Standard Deviation in parenthesis where appropriate. Results: The results revealed a statistically significant reduction in A1c in the two groups taking Lysulin (Group B $p<0.02$ and Group C $p<0.004$) as compared to the placebo group. Changes in A1c were observed for some subjects in as little as 4 weeks after initiation of Lysulin supplementation. At 12 weeks, the change in A1c for Group A was 0.03%, the change for Group B was -0.30% and the change for Group C was -0.97%. For Group C, 65% of the subjects responded to Lysulin with a change of -1.64% A1c in 12 weeks and change of -1.91% in 26 weeks. The results also revealed a statistically significant reduction in Systolic ($p<0.04$) and Diastolic ($p<0.05$) Blood Pressure for study subjects in Group C. Clinically significant improvement was also seen in triglycerides in Group C. Conclusion: Daily oral supplementation with Lysulin has a statistically significant reduction in A1c in subjects diagnosed with Type 2 diabetes. Statistically significant improvement in systolic/diastolic blood pressure was also observed. The study revealed that the optimum dose of Lysulin is 3.33 g/day. Further confirmatory clinical studies are planned to verify the results observed in this study.

Introduction

Diabetes and its associated health complications are an increasing global health problem [1,2]. Maintaining good glycemic control is an essential part of routine diabetes care and a major contributor to minimizing future complications [3]. The current clinical practice uses the A1c test to monitor how well diabetes is being managed. The National Institute for Health and Clinical

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KEYWORDS

- type 2 diabetes
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- glycemic control
- pilot study
- blood pressure
- triglycerides

Excellence (NICE) in the United Kingdom (UK) currently recommend monitoring of glycated haemoglobin (HbA1c) every 2-6 months in people with type 2 diabetes [4]. The American Diabetes Association (ADA) guidelines [5,6] recommend performing the HbA1c test at least two times a year in subjects who are meeting treatment goals (and who have stable glycemic control) and performing HbA1c tests quarterly in subjects whose therapy has changed or who are not meeting glycemic goals. The causes of type-2 diabetes are multi-factorial, and the diet plays an important role in it's incidence, severity and management [7]. Hence studies have frequently focused on dietary components beneficial in the prevention and treatment of diabetes. Recent studies have demonstrated that numerous herbal and nutraceutical products have beneficial effects in subjects by improving glucose and lipid metabolism, antioxidant status, disease progression and capillary function [8]. Lysulin is a unique nutritional supplement that contains three carefully balanced essential nutrients: Lysine, Zinc and Vitamin C [9]. In over 20 years of independent research, these three essential nutrients have shown to reduce blood glucose and Hemoglobin A1c (A1c) levels while improving the lipid profile. Lysulin is manufactured in the US (Lysulin, Inc., San Diego, CA) and is characterized as a dietary supplement under Dietary Supplement Health and Education Act of 1994 of the US National Institute of Health (NIH) Food and Drug Regulatory Authority (FDA) [10]. This Pilot Study is aimed at evaluating the effect of daily oral supplementation with Lysulin™ on glycemic control as assessed by measurement of Hemoglobin A1c (A1c), cardiometabolic and anthropometric parameters when compared to Placebo in people with Type 2 diabetes. This is a Pilot Study and it is intended to be used to design a further confirmatory clinical study by providing information on the feasibility of recruitment, randomization, sample size, retention, and assessment of procedures, methods and implementation of a novel intervention: Lysulin. Lysine is an essential amino acid that plays a major role in calcium absorption, building muscle protein, and the body's production of hormones, enzymes, and antibodies. It has also shown numerous beneficial effects in the treatment/prevention of diabetes and/or it's complications in *in vivo* animal and human studies. In diabetes-induced animal models, Lysine has shown a beneficial effect in lowering blood glucose as well as acting as an inhibitor of protein glycation [11]. Furthermore, the ability of Lysine to reduce the formation of glycated proteins in diabetes-induced rats, have also shown to delay the appearance of the late pathologies associated with protein glycation [12]. Lysine is known to react with glucose with the glycated amino acid being excreted in urine and it has been shown to markedly attenuate the glucose response to ingested glucose without a change in insulin response in humans [11]. Glycated proteins are known to be involved in the pathogenesis of several chronic diabetes complications, including nephropathy leading to chronic kidney disease, neuropathy, and retinopathy, as well as in other macrovascular complications [13]. Hence, it is evident that Lysine may have the potentially beneficial effect on the reduction of blood glucose as well as on the progression of diabetes and its complications [14,15]. Zinc is involved in numerous metabolic pathways as a cofactor for more than 300 enzymes [16]. Insulin, which contains a variable number of Zinc atoms, are stored in β-cells of the pancreas and released into the portal venous system at the time of β-cells degranulation. It is evident that Zinc plays an important role in insulin action, carbohydrate and protein metabolism [15]. In addition, there is particular interest in the idea that oxidative stress is relevant in the pathogenesis of diabetes and its' complications. Impaired synthesis of enzymes, such as superoxide dismutase and glutathione peroxidase, where Zinc is a part of these enzymes' structures and its deficiency may impair their synthesis and associated with increased oxidative stress [16]. It has been long known that diabetes is accompanied by hypozincemia [17] and hyperzincuria [18]. In Korea, 76 diabetic subjects and 72 normal subjects were supplemented with 50 mg Zinc daily as Zinc gluconate for 4 weeks. The results showed that significant improvement of fasting glucose, as well as HbA1c, was observed in zinc supplemented diabetic subjects with shorter diabetic duration, poorer glycemic control, and marginal Zinc status [19]. A recent double-blind placebo-controlled on 200 patients with prediabetes demonstrated that zinc supplementation helped to reduce blood glucose and insulin resistance while improving beta-cell function [20]. Furthermore, disease progression to Type 2 diabetes was also reduced and beneficial effects of zinc supplementation were also noted on total and LDL cholesterol [20]. Ascorbic acid (vitamin C), an antioxidant vitamin, plays an

important role in protecting free radical-induced damage. Previous studies have shown a decrease in basal vitamin C level in type 2 diabetes [21]. Furthermore, randomized controlled studies have shown that supplementation of Vitamin C reduces blood glucose, serum lipids and improves HbA1c in type 2 diabetes [22]. Hence, we postulate that Lysulin which contains an optimized formulation of Lysine, Zinc and Vitamin C will have beneficial effects on glycemic control in those with diabetes and help to reduce disease progression in subjects with pre-diabetes, and those at risk of developing diabetes.

Methods

Reporting on this study is done in accordance with the NIH Policy on Good Clinical Practice (GCP) [22,23]. The data will be presented as Average followed by Standard Deviation in parenthesis where appropriate. Subjects were recruited to the present randomized (1:1:1) double-blind placebo-controlled Pilot Study between April 2018 and November 2018. The duration of the intervention was 12 weeks in Part 1 of this study. At the end of Part 1 of the study, subjects in groups B and C could volunteer to continue the intervention to 26 weeks (Part 2). We recruited subjects with a medical diagnosis of type 2 diabetes of at least 3 months duration who had not had a change in diabetes treatment or medication in the prior 2 months as deemed necessary by their General Practitioner (GP). All subjects gave written informed consent prior to enrollment in the study. Enrolled subjects were randomized 1:1:1 into groups based on oral supplementation: Group A Placebo, Group B 2.22 g/day Lysulin, and Group C 3.33 g/day Lysulin. Subjects were provided with white bottles labelled A, B and C, representing the three groups and instructed to start taking their supplement the following day. Subjects were instructed to report any change in lifestyle, diet or diabetes medication or therapy. At the baseline visit, subjects were evaluated by demographics and anthropometry parameters including measurement of height, weight, waist circumference, BMI and Blood Pressure **TABLE 1**. At the baseline visit, all subjects provided a non-fasting urine sample and venous blood sample for measurement of A1c and thirty chemistry tests including but not limited to lipids panel, liver panel, and cardiovascular biomarkers. A summary of these tests is provided in **TABLE 2**. Non-fasting venous blood samples were taken for A1c measurement at four, eight and twelve weeks after the introduction of either Lysulin or Placebo intervention. All Laboratory testing was done at an independent ISO/IEC 17025 and ISO 9001 accredited laboratory (CERTUS Lab). A1c was measured by High-Performance Liquid Chromatography (HPLC) Bio-Rad A1c System.

■ Study sample size

Though sample size statistical criteria are not required in a Pilot Study, the sample size was calculated to meet the requirement of demonstrating binary outcome superiority of the treatment groups as compared to the placebo group with a 90% power and 95% confidence interval. The sample size requirement was 16 subjects per group or a total sample size of 48 subjects. The drop-out rate was estimated to be around 35%-40%. Thus, a total of 67 subjects were recruited to ensure that there would be at least 16 subjects in each group at the completion of Part 1 of the study (12 weeks). The drop-out rate for Group A was largest at 24% but still within the estimated 34%-40%.

■ Inclusion and exclusion criteria

Subjects were eligible if they had previously been diagnosed as having Type 2 Diabetes by their healthcare professional (>3 months) and that had no changes to diabetes medication or therapy for at least 2 months prior to enrolling. The inclusive range of low, medium and high in A1c levels was chosen to evaluate if there was a biased response at a specific A1c level. Subjects enrolled in the study had average an A1c 8.5 (2.2) and range 5.1%-12.9% at baseline. The baseline A1c levels for each group were within 1 SD of the average A1c (6.3%-10.7%) for the total enrolled subjects: Group A 7.5%, Group B 8.1% and C 9.4%. Subjects of ages 49 (9) years with a range of 33-74 years and both sexes (31 women and 36 men) were included in the study. Subjects were excluded from the study if they were pregnant or breastfeeding had a life-threatening illness or were unable to give informed consent. Additional exclusion criteria were people with Type 1 diabetes, advanced kidney or liver disease, any known medical condition that in the judgement of the principal investigator might interfere with the completion of the study.

■ Study masking

The study was blinded to the principal investigator, the independent laboratory, and to the subjects. The subjects received their assigned supplement in white plastic bottles

Table 1. Baseline anthropometric summary					
	Group A	**Group B**	**Group C**	**All per Group**	**Each Group**
	Average (SD)	Average (SD)	Average (SD)	Average (SD)	Within 1 SD
n baseline	25	23	19	22 (3)	Yes
n Completed	19	20	17	19 (2)	Yes
% Dropout	24%	13%	11%	16% (7)	No*
Age	48 (10)	48 (8)	49 (10)	49 (9)	Yes
Female	15	8	8	8	NA
Male	10	15	11	13	NA
Weight	186 (48)	214 (62)	188 (40)	196 (52)	Yes
Height	5.3 (0.4)	5.5 (0.4)	5.5 (0.3)	5.4 (0.4)	Yes
Waist	41 (7)	44 (8)	40 (5)	42 (7)	Yes
Hip	43 (5)	43 (5)	42 (3)	43 (4)	Yes
Waist/Hip Ratio	0.96 (0.08)	1.01 (0.09)	0.96 (0.08)	0.98 (0.08)	Yes
BMI	32 (8)	34 (8)	31 (5)	32 (7)	Yes

*The placebo had the largest drop-out rate. But still within the estimated 34-40%. Reason unknown.

Table 2. Baseline clinical chemistry results summary				
Parameter	**Average at Baseline**	**SD**	**Normal lab values**	**Units**
Hematocrit	40.6	-4.1	>36F >41M	%
CRP*	7.2	-11	<5	mg/L
Glucose**	195	-116	70-100	mg/dL
BUN	14	-5.7	7-18.7	mg/dL
Creatinine	0.72	-0.24	0.4-1.2	mg/dL
Total protein	7.25	-0.52	6.3-8.3	g/dL
Albumin	4.3	-0.4	3.5-5	g/dL
AST	23.2	-11.7	Feb-50	U/L
ALT	33.6	-23.8	Feb-60	U/L
ALP	79.5	-35.4	40-150	U/L
Bilirubin	0.48	-0.2	0.1-1.4	mg/dL
Triglycerides**	236	-168	50-150	mg/dL
Cholesterol	197	-47	50-200	mg/dL
HDL	44.5	-11.3	>40	mg/dL
LDL	124	-31.5	<129	mg/dL
Ur-Protein**	20.4	-71.4	0-10	mg/dL
Ur- Glucose**	348.5	-456.9	0-15	mg/dL

*Above Normal Lab Values ** Above Normal Lab Values may be due to non-fasting sample

designated as Group A, B or C representing the three groups. Randomization was performed by the study sponsor. The treatment code for any subject could be broken in a medical emergency; however, the treatment code was not broken for any subject during this study.

■ Study intervention and monitoring

The subjects were given uniform instructions regarding their scheduled visits, how to take the supplements and how to contact the study administrator with any questions or concern. The visit schedule was provided in writing plus the study administrator contacted each of the subjects a few days prior to the day of the visit **(TABLE 3)**. The subjects were informed that they could chew, swallow or crush the supplement tablets and that they could take the tablets altogether or spread out during the day. All Laboratory and Anthropometric analysis were performed by licensed laboratory or medical technologist at an independent ISO/IEC 17025 and ISO 9001 accredited laboratory (CERTUS Lab)

■ Statistical analysis

Data were analyzed using parametric and nonparametric tests in SPSS version 16 (SPSS Inc., Chicago, IL, USA) and Microsoft® Excel® MSO Version 1810 Statistical Analysis Tool Pac and XLSTAT 365. Summary statistics were calculated and are presented as the Average (SD). Baseline and end-of-study characteristics, as well as laboratory findings, were compared using two-sample and paired t-tests, with one-sided $P<0.05$ considered significant.

Table 3. Study schedule					
	Base line	4 Weeks	8 Weeks	12 Weeks	26 Weeks
Informed consent form	☒				
Socio-demographic data	☒				
Clinical/Anthropometric Parameters[1]	☒			☒	☒
A1C	☒	☒	☒	☒	☒
Lipid Biochemical Parameters[2]	☒			☒	☒
Liver Biochemical Parameters[3]	☒			☒	☒
Blood pressure	☒			☒	☒

Body weight, height, waist circumference and hip circumference;
Total cholesterol, triglyceride, LDL cholesterol, and HDL cholesterol;
Creatinine and blood urea nitrogen (BUN)

Table 4. Average changes in A1C for group A (Placebo) n=19										
	% A1c	% A1c	% A1c	% A1c	Absolute Change	Absolute Change	Absolute Change	% Change from Day 0	% Change from Day 0	% Change from Day 0
	Week 0	Week 4	Week 8	Week 12	Week 4	Week 8	Week 12	Week 4	Week 8	Week 12
AVERAGE	7.5	7.4	7.0	7.3	-0.07	-0.15	0.04	-1.0%	-2.7%	0.6%
STDEV	1.7	1.8	1.8	1.5	0.25	0.30	0.28	0.03	0.04	0.04

Table 5. Average changes in A1C for group B (2.22 g/day Lysulin)5a. Responders n=14										
	% A1c	% A1c	% A1c	% A1c	Absolute Change	Absolute Change	Absolute Change	% Change from Day 0	% Change from Day 0	% Change from Day 0
	Week 0	Week 4	Week 8	Week 12	Week 4	Week 8	Week 12	Week 4	Week 8	Week 12
AVERAGE	8.6	8.5	8.2	8.1	-0.19	-0.47	-0.56	-2.3%	-5.6%	-6.5%
STDEV	2.3	2.3	2.3	2.2	0.30	0.51	0.52	3.3%	5.9%	5.4%

5b. Non-responders n=6										
AVERAGE	6.9	7.0	7.0	7.2	0.05	0.10	0.30	0.7%	0.6%	3.6%
STDEV	1.9	1.9	2.3	2.3	0.10	0.40	0.46	1.6%	4.1%	4.4%

5c. All n=20										
AVERAGE	8.13	8.02	7.83	7.83	-0.12	-0.30	-0.30	-1.4%	-3.7%	-3.5%
STDEV	2.26	2.24	2.26	2.21	0.27	0.54	0.63	3.2%	6.1%	6.9%

Results

HbA1c test results are presented in % HbA1c as reported in the USA. To convert to the IFCC mmol/mol unit, the following equation can be used: mmol/mol=(% A1c - 2.15) x 10.929. As shown in **TABLES 4-6**, the results revealed a statistically significant reduction in A1c in the

Table 6. Average changes in A1C for group C (3.33g/day Lysulin) 6a. Responders n=11										
	%A1C	%A1C	%A1C	%A1C	Absolute Change	Absolute Change	Absolute Change	% Change from Day 0	% Change from Day 0	% Change from Day 0
	0 Week	4 Weeks	8 Weeks	12 Weeks	4 Weeks	8 Weeks	12 Weeks	4 Weeks	8 Weeks	12 Weeks
AVERAGE	9.51	9.21	8.00	7.87	-0.66	-1.51	-1.64	-7.0%	-15.2%	-16.6%
STDEV	2.0	1.9	1.7	1.8	0.8	1.1	1.2	7.7%	11.0%	11.3%
6b. Non-Responders n=6										
AVERAGE	9.0	8.9	8.1	8.1	0.25	0.15	0.25	-2.9%	-8.5%	-9.0%
STDEV	2.5	2.4	2.4	2.4	0.7	1.0	1.0	8%	13%	14%
6c. All n=17										
AVERAGE	9.41	9.3	8.5	8.44	-0.32	-0.92	-0.97	-3.4%	-9.3%	-9.7%
STDEV	2.0	2.0	1.9	2.0	0.8	1.2	1.4	8.4%	12.4%	13.5%

Table 7. Statistical analysis of average A1C results at 12 weeks					
t-Test: Two-Sample Assuming Unequal Variances			t-Test: Two-Sample Assuming Unequal Variances		
At 12 Weeks	Placebo	2.22 g Lysulin	At 12 Weeks	Placebo	3.33 g Lysulin
Average	0.038889	0.3	Average	0.0388889	-0.9705882
Variance	0.080163	0.4	Variance	0.0801634	1.8459559
Observations	18	20	Observations	18	17
P(T<=t) one-tail	0.019607		P(T<=t) one-tail	0.004006	

Table 8. Baseline and 12 weeks anthropometric results summary					
Anthropometric Parameters	Baseline Placebo	12 Weeks Placebo	Baseline Group C	12 Weeks Group C	26 Weeks Group C
	Average	Average	Average	Average	Average
Weight (lbs)	185.7 (48)	181.8 (44.3)	187.7 (39.9)	185.3 (38.8)	190.1 (40.2)
Waist (in)	41.1 (7)	40.7 (6.3)	40.3 (4.8)	41.2 (4.8)	42.0 (4.8)
Hip (in)	42.5 (5)	42.7 (5.4)	41.8 (3.3)	43.1 (3.7)	43.1 (3.6)
Waist/ Hip Ratio (NA)	0.96 (0)	0.95 (0.1)	0.96 (0.1)	0.96 (0.1)	0.97 (0.07)
BP Systolic (mmHg)	128.6 (21)	122.5 (15.8)	144.9 (21.5)	134.2 (19.2)	133.3 (10.3)
BP Diastolic (mmHg)	79.8 (14)	74.2 (8.4)	89.7 (14.2)	80.1 (13.6)	78.4 (11.3)
BMI (NA)	31.7 (8)	32.1 (6.9)	30.9 (5.3)	31.6 (5.3)	32.8 (5.2)

two groups taking Lysulin at 12 weeks, Group B p<0.02, Group C p<0.004; 26 weeks, Group B p<0.02, Group C p<0.004) as compared to the placebo group. In **TABLE 7** changes in A1c were observed for some subjects in as little as 4 weeks after initiation of Lysulin supplementation. At 12 weeks the change in A1c for the placebo Group A was 0.03%, the change for Group B was -0.30% and the change for Group C was -0.97%. At 26 weeks the reduction in A1C for Group B was -0.35% and for Group C was -1.44%. In **TABLES 5 and 6**, a responder is defined as a study subject with an observed drop in A1c. For Group B, 14 of 20 subjects responded to Lysulin with a drop of -0.35% A1c in 12 weeks and -0.9 in 26 Weeks. For Group C, 11 of 17 subjects responded to Lysulin with a drop of -1.64% A1c in 12 weeks and -1.91 in 26 Weeks **(FIGURES 1-3).**

The results also revealed a statistically significant reduction in Systolic (p<0.04) and Diastolic (p<0.05) Blood Pressure for study subjects in Group C **(TABLES 8 AND 9)**. In Group C, the moderate improvement was also seen in triglycerides **(TABLE 10)**.

■ Adverse effects and safety

There were no serious adverse effects noted and no subject was hospitalized due to adverse effects during the 6- month follow-up period. Biochemical assessments evaluating potential target organ toxicity (liver enzymes, serum

Table 9. Statistical analysis of diastolic and systolic blood pressure from baseline to 12 Weeks for Placebo and Group C; and from baseline to 26 weeks for group C		
12 Weeks Placebo	**12 Weeks Group C**	**26 Weeks Group C**
Change	**Change**	**Change**
4.79	-2.4	2.39
0.73	0.98	1.71
0	1.32	1.32
0.02	0	0.02
-0.89	-10.76	-11.65
-1.72	-9.56	-11.28
1.19	0.72	t1.91

Table 10. Baseline and 12 weeks clinical chemistry results summary

			Baseline		12 Weeks		12 Weeks	Baseline		12 Weeks		12 Weeks
			Placebo		Placebo		Placebo	Group C		Group C		Group C
Analyte	**Normal Range**	**Units**	**Average**	**±SD**	**Average**	**± SD**	**Change**	**Average**	**± SD**	**Average**	**± SD**	**Change**
Hematocrit	>36F >41M	%	40	5	41	5	1	40	4	40	5	0
CRP	>5	mg/L	8	16	4	4	-4	8	8	5	5	-2
BUN	7-18.7	mg/dL	13	7	15	7	2	15	6	17	6	1
Creatinine	0.4-1.2	mg/dL	1	0	1	0	0	1	0	1	0	0
T-protein	6.3-8.3	g/dL	7	1	7	1	0	7	1	7	0	0
Albumin	3.5-5	g/dL	4	0	4	0	0	4	0	4	0	0
AST	Feb-50	U/L	25	14	24	14	-1	22	13	22	11	0
ALT	Feb-60	U/L	34	31	30	22	-4	36	24	29	19	-7
ALP	40-150	U/L	80	28	92	32	12	76	19	100	30	25
Bilirubin	0.1-1.4	mg/dL	0	0	0	0	0	0	0	0	0	0
Tryglicerides	50-150	mg/dL	248	212	232	92	-15	244	175	197	76	-47
Cholesterol	50-200	mg/dL	195	62	197	33	2	201	41	197	44	-4
HDL	>40	mg/dL	44	15	42	13	-3	43	8	39	9	-3
LDL	<129	mg/dL	117	37	127	23	9	130	28	128	31	-3

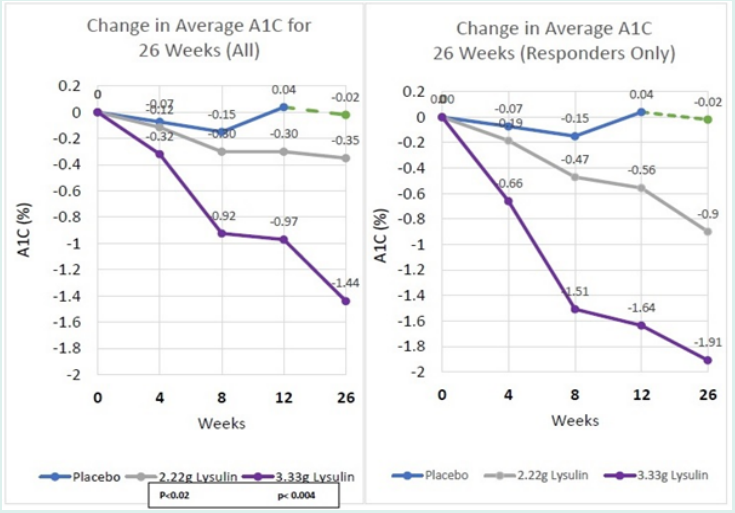

Figure 1. Change in average A1c in 26 weeks. *The 26 Week value for the Placebo Group was calculated by linear regression.

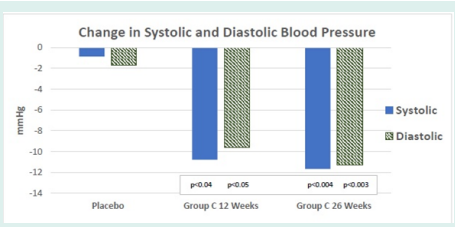

Figure 2. Change in Systolic and Diastolic blood pressure.

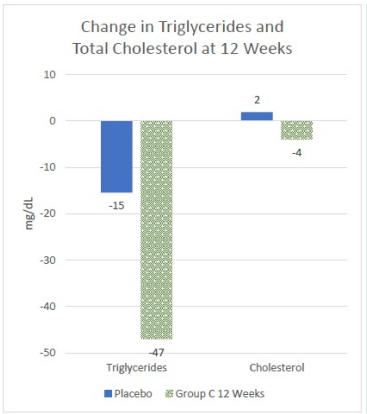

Figure 3. Change in triglycerides and total cholesterol at 12 weeks.

bilirubin, and serum creatinine) remained normal throughout. None of the subjects experienced any form of hypersensitivity during the study (immediate and/or delayed).

Conclusions

This double-blind, placebo-controlled study with people with Type 2 diabetes has clearly shown that Lysulin supplementation has a dramatic improvement in glycemic control. The observed improvement in A1c and blood pressure compared to placebo all meet statistical significance. The optimum dose of Lysulin is 3.33 g/day. Further confirmatory clinical studies are planned to verify the results observed in this study.

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Disclosures

The principal investigator, Dr Francisco Alberto Alvarez Melero and the clinical site and the laboratory had no conflict of interest. The other three authors are employees of Lysulin, Inc. The study was funded by Lysulin, Inc.

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