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Research Article

Anti-hyperglycemic and Anti-hyperlipidemic Effects of *Lupinus albus* in Type 2 Diabetic Patients: A Randomized Double-blind, Placebo-controlled Clinical Trial

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Abstract

Background and Objective: *Lupinus albus* contains ingredients that possess a variety of health enhancing effects including anti-diabetic effects. Therefore, the objective of this study was to evaluate the anti-diabetic and anti-hyperlipidemic effect of *Lupinus albus* dry extract on diabetic patients. **Materials and Methods:** In a double-blinded, placebo controlled, randomized trial, a total of 97 type 2 diabetics randomly were assigned to *Lupinus albus* or placebo group, received 400 mg day^{-1} of *Lupinus albus* dry extract supplement or placebo for 12 weeks. Serum glucose and insulin were measured periodically for 2 h following the meal test at base line (without lupine) at 2 and 12 weeks (with lupine). A chi-square test was performed to determine differences at base line in frequencies of categorized variables between the groups. Paired t-test was used to compare mean of normal distribution variables in the two groups before and after the intervention and student t test was used to compare the mean of variables between the two groups. **Results:** *Lupinus albus* supplementation significantly reduced the levels of fasting and post-prandial glucose at 2 and 12 weeks in the intervention group in comparison to base line as well as placebo group. There was a consistently significant improvement in the glucose area under the curve in the intervention group. Administration of *Lupinus albus* dry extract supplement had no significant effect on improving the insulin level. Homeostasis model assessment insulin resistance index was significantly lower at 2 weeks ($p<0.05$) and it was very significantly lower at 12 weeks ($p<0.01$). Glycated haemoglobin, total cholesterol and triglycerides were decreased in the intervention group in comparison to base line ($p<0.001$, $p<0.001$ and $p<0.05$, respectively), as well as the placebo group ($p<0.001$, $p<0.001$ and $p<0.01$ respectively). **Conclusion:** This study suggests that the *Lupinus albus* has a beneficial effect in controlling diabetes by reducing fasting and post-prandial glucose and enhancing insulin sensitivity. The results of this study indicate that *Lupinus albus* might be a beneficial adjuvant to oral hypoglycemic agents in type 2 diabetic patients.

Key words: *Lupinus albus*, type 2 diabetes mellitus, clinical trial, glycemic control, post-prandial glycemic control, glycated hemoglobin, meal test, serum insulin, insulin sensitivity, lipid profile

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Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Chronic non-communicable diseases such as diabetes are increasing public health problems worldwide[1]. The International Diabetes Federation (IFD) estimates that 32.8 million adults are affected by diabetes in the MENA (Middle East and North Africa) region and by 2030, this number will double to 59.9 million[2]. Diabetes is a metabolic disorder of multiple etiologies characterized by chronic hyperglycemia with disturbance of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both[3].

The overall prevalence of T2D (type 2 diabetes) in Tunisia according to World Health Organization (WHO) criteria was 15.1%, which included 7.4% previously diagnosed T2D and 7.7% newly diagnosed T2D[4]. Many oral antihyperglycemic agents, such as sulfonylurea and biguanides are available along with insulin for the treatment of diabetes, but these agents have significant side effects and some are ineffective in chronic diabetes patients[5]. Traditional medicines derived mainly from plants played an important role in the management of diabetes. Thus, there is an increasing need of new natural anti-hyperglycemic products especially nutraceuticals with less side effects, safe and high anti-hyperglycemic potential. One such plant was lupin (*Lupinus* spp.). It belonged to the Genisteae family, Fabaceae or Leguminosae[6,7]. From the genus *Lupinus* more than 400 species are known, from which only four are of agronomic interest[8]: (*L. albus* L.: White lupin, *L. angustifolius* L.: Blue or narrow-leafed lupin, *L. luteus* L.: Yellow lupin and *L. mutabilis* L.: Pearl or tarrwi lupin)[6,8,9]. These species are known as sweet lupins due to their low levels (0.003%) of bitter-tasting and potentially toxic alkaloids[10] and, therefore, there is no risk of toxicity for animals and humans[11].

In traditional medicine the lupin seed is used as an anti-helminthic and anti-parasitic agent as well as an anti-diabetic agent[12,13]. *Lupinus* species and their derivates are good candidates to be used as hypoglycemic agents[14].

Most studies were done in normal and experimentally diabetes-induced animals and cultured cells, mainly testing the effect of lupin derivatives, especially the γ-conglutin protein on insulin secretion[15-18]. Effects of prolonged lupine extract administration in humans and its impact on insulin sensitivity and overall diabetes control are rarely investigated[15,19]. Notably, the effect of lupine on insulin secretion and peripheral sensitivity remains controversial. In this study, the *Lupinus albus* seeds anti-diabetic propriety was evaluated in Tunisian patients with type 2 diabetes. Plasma glucose and insulin concentration have been monitored upon a standardized meal test before, after 2 and 12 weeks of *Lupinus albus* administration. Glycated haemoglobin and plasma lipids were evaluated.

MATERIALS AND METHODS

Experimental: The present study was a 12 week long, randomized, double-blind, placebo-controlled clinical trial performed on type 2 diabetic patients. Participants were recruited from the Endocrinology Unit in Rabta hospital in Tunisia.

The Rabta Ethical Committee approved the study. All subjects gave written, informed consent after reviewing the study procedures.

Subjects and study design: A total of 97 diabetic male and female subjects agreed to participate in the study.

The characteristics of those who withdrew were similar to those who participate. Subjects were excluded based on the following criteria: Insulin use, hemoglobin A1c>9%, documented allergy to peanuts, abnormal hepatic liver function or renal disease (acute/chronic renal failure or nephrotic syndrome), any disease or condition that the enrolling physician considered making the subject unsuitable for participation to this trial, pregnant women, change in regular prescription medications in the previous 3 months.

Neither the investigators nor the subjects knew the randomization code or the results of the blood glucose levels until after statistical analysis was complete. The enrolled subjects were scheduled for their first visit and subjects were randomly assigned to one of two groups, either the *Lupinus albus* (n = 47) or placebo group (n = 50). Eligible individuals were matched for body mass index, glycated haemoglobin and randomly assigned (1:1). *Lupinus albus* dry extract (LADE) is manufactured by Vital laboratory (Ben Arous, Tunisia) and originated from France with a ratio plant/extract of 4-1.

Subjects received either *Lupinus albus* or starch, as placebo capsules every month and all subjects were instructed to take either tow lupin capsules or tow placebo capsules per day (400 mg day^{-1}) according to the previous trial[15]. One capsule was administered 30 min before breakfast and dinner. Subjects were asked to visit the hospital once every month for a total five visits (0, 2, 4, 8 and 12 weeks).

At the present trial LADE and placebo were administered per os 30 min before a carbohydrate meal, consisting in one

serving of 60 g bread, an egg, a sweet yoghurt, 25 g jam and 10 g butter which corresponded to an intake of 75 g carbohydrate and 500 kcal.

During the intervention period of 12 weeks, subjects were asked to continue their usual diets and activity and to not ingest any other functional foods or dietary supplements. Information on socio-economic status of participants and the rapport of daily dietary intake were collected by means of a questionnaire. Anthropometric and biochemical parameters and vital signs were measured before and after the intervention period. Every month, the subjects were asked to report any adverse events or changes in training, lifestyle or eating pattern and to assess capsule-dosing compliance. Finally, compliance was assessed by the number of returned capsules.

Volunteers were asked to skip the morning dose the day of the study and to come to the hospital at 8:00 am, in a fasting state.

Anthropometric measurements: Body weight was recorded with the volunteers dressed in only underclothing and after having urinated; the same balance, accurate to ±0.1 g was used for all measurements. The BMI was calculated as weight (kg) divided by height squared (m^2). Fat-free mass, fat mass and percentage body fat estimated with BIA (bioelectrical impedance analysis).

Blood samples: Plasma glucose and serum insulin concentrations were evaluated before and every 30 min after consumption of a standardized meal (500 kcal, 12% proteins, 33% fat and 55% carbohydrates containing 75 g of available carbohydrate) at base line, 2 and 12 weeks.

Five blood samples at 0, 30, 60, 90 and 120 min were obtained. Serum lipid profile and HbA1c were determined before and after 12 weeks of treatment.

Fasting blood was drawn in the morning (around 8 AM) from an antecubital vein. The samples were centrifuged at 2000×g for 25 min and plasma was frozen at -40°C until analysis (within 3 months). Plasma insulin concentrations were measured by chemiluminescence immuno-assay using a Liaison analyzer and the respective reagents kit (DiaSorin Inc., Stillwater, MN) with an intra-assay CV below 5%. Haemoglobin A1c was assessed by a competitive turbidimetric inhibition immunoassay method (Tina-quant HbA1c Gen. 2) using a Cobas 400 plus analyzer (Roche Diagnostics Ltd., Rotkreuz, Switzerland). Plasma glucose, total cholesterol, HDL cholesterol and triglyceride were assessed by colorimetric methods using an architect C8000 analyzer and the respective reagents kits (Abbott Laboratories, Abbott Park, IL). The LDL cholesterol was calculated using the Friedwald formula[20]. Insulin resistance was estimated by the homeostasis model assessment (HOMA-IR) index as[16]:

$$\text{HOMA-IR} = \frac{\text{Fasting insulin (mU L}^{-1}) \times \text{Fasting glucose (mmol L}^{-1})}{22.5}$$

The total area under the curve (AUC) of the glucose response during the meal tolerance test was determined using the trapezoid method.

Statistical analysis: Calculations and statistical analysis were performed using the Systat ver. 19 software for Windows from SPSS. Data are shown as the mean values and standard deviation. A chi-square test was performed to determine differences at baseline in frequencies of categorized variables between the groups. Paired t-test was used to compare mean of normal distribution variables in the two groups before and after the intervention and student t test was used to compare the mean of variables between the two groups. The significance level was set at p-value equal or less than 0.05. Graphical methods were used to show glucose changes over time (minutes).

RESULTS

Of 110 patients initially recruited, 97 persons (47 in the intervention group and 50 in the control group) completed the study and 13 persons were excluded because of treatment drug stop, personal reasons and refusing to continue. Mean±SD age of participants was 51±9 years, BMI was 30.6±4.7 and M/F ratio was 43/54. Randomization was successful, as the two groups generated were comparable for most variables, with no significant differences in the base line demographic, anthropometric and biochemical data between the intervention and control groups. Table 1 showed that there were no significant differences in sex, age, disease duration, type of consumed oral hypoglycemic drugs, weight, body mass index, hemoglobin (HbA1c), fasting glucose levels, fasting insulin or serum lipids between the two groups at the start of the study. The mean and standard deviation of HOMA-IR from previous studies were used in development of the statistical power for this study[16,21]. No statistically significant differences in HOMA-IR were observed between the groups at baseline (Table 1). After the 12 week intervention no statistically significant differences in BMI, body weight, waist circumference, fat mass, fat-free mass

percentages were observed between the groups (Table 2). Regarding glucose concentrations, data show that at 2 and 12 week there was a statistically significant decrease in glucose concentration in the intervention group compared with the placebo. The LADE supplementation, lowered fasting serum glucose ($p<0.001$) in the *Lupinus albus* supplemented group, 150±44 to 137±32.2 mg dL^{-1} at 2 weeks, to 139±27 mg dL^{-1} at 12 weeks compared with 162±47 to 166±57.2 mg dL^{-1} at 2 weeks, to 177±69 mg dL^{-1} at 12 weeks in the placebo control group. Serum glucose 2 h after a 75 g carbohydrate load also decreased significantly ($p<0.001$) in the intervention group, 244±71 to 215±53.8 at 2 weeks, to 214±55 mg dL^{-1} at 12 weeks, compared with non-significant differences in the placebo group, 257±68 to 260±79.3 at 2 weeks, to 274±95 mg dL^{-1} at 12 weeks (Table 3). Consistent with the significant change in the 2 h postprandial glucose level ($p<0.001$), there was a significant difference in the AUC of the glucose response between the placebo and LADE groups at both 2 and 12 weeks (Table 3). Insulin sensitivity, assessed by HOMA-IR was significantly improved by LADE at 2 ($p<0.05$) and 12 weeks ($p<0.01$) (Table 3).

Figure 1 shows the time-course changes in the plasma glucose levels during the meal tolerance test. The fasting and postprandial blood glucose level in the placebo group was not significantly changed after 2 and 12 weeks of the study (Fig. 1a, b). The LADE supplementation significantly reduced the levels of fasting and postprandial blood glucose in the intervention group in comparison to the baseline ($p<0.05$) (Fig. 1c, d).Insulin plasma levels are concerned, no statistically significant difference was observed upon the treatment (Table 4). Glycated haemoglobin was also determined at theend of 12th week. A significant reduction was observed as compared to placebo group ($p<0.001$) (Table 5). Lipid profile changes after twelve weeks of supplementation, there were significant differences in total cholesterol ($p<0.001$), or triglyceride ($p<0.01$) levels between the intervention group and placebo groups (Table 5).

No clinical subjective side effects were observed, nor any adverse events recorded upon administration and during the time course of this study.

Table 1: Base line anthropometric and demographic characteristics of participants

	Intervention group (n = 47)	Placebo (n = 50)	*p-value
Age (years)	51.02±8.82	52.0±8.85	0.58
Male (n (%))	21 (45)	22 (44)	0.94**
Female (n (%))	26 (55)	28 (56)	
Diabetes medications (n (%))	41 (87.5)	46 (92)	0.44**
Class of anti-diabetic medication			
Biguanides (Metformin) (n (%))	24 (51)	23 (46)	
Sulfonyluea (Glibenclamide) (n (%))	3 (6.5)	6 (12)	0.65
Combination (n (%))	14 (30)	17 (34)	
Duration of diabetes (months)	24.42±18.16	23.24±18.27	0.75
Weight (kg)	82.65±14.23	82.44±11.89	0.93
Body mass index (kg m^{-2})	30.62±4.71	31.26±4.32	0.48
Excess weight (kg)	22.35±12.32	23.34±10.42	0.66
Fasting plasma glucose (mg dL^{-1})	150±44	162±47	0.19
2 h plasma glucose (mg dL^{-1})	244±71	257±68	0.36
HbA1c (%)	7.18±0.76	7.43±0.89	0.12
Fasting insulin (mIU L^{-1})	11.97±6.58	11.84±5.55	0.91
HOMA-IR	4.40±2.80	4.74±2.59	0.53
Total cholesterol (mg dL^{-1})	197±34.2	204±30.1	0.28
HDL cholesterol (mg dL^{-1})	41±9.5	43±9.3	0.49
Triglycerides (mg dL^{-1})	152±85	172±94	0.31

Data are presented as Mean±SD. *Analyzed by independent t-tests and the p-value represents the comparison to the placebo group. **Analyzed by chi-square tests. BMI: Body mass index, HbA1c: Glycated haemoglobin, HOMA-IR: Index of insulin resistance

Table 2: Mean and standard deviation (Mean±SD) of anthropometric characteristics and body composition at the end of the study

	Lupin (n = 47)	Placebo (n = 50)	p-value
Weight (kg)	81.60±13.8	81.70±11.9	0.97
Body mass index (kg m^{-2})	30.20±4.65	31.00±4.38	0.41
Waist (cm)	98.00±8.99	99.40±8.62	0.43
Hip (cm)	104.00±8.38	105.00±8.21	0.66
WHR (cm)	0.93±0.07	0.94±0.06	0.64
Body fat (%)	30.60±7.56	32.00±6.33	0.33
Fat-free mass (%)	68.80±6.44	68.00±6.33	0.53
Excess weight (kg)	21.60±11.8	22.60±10.6	0.66

Data are presented as Mean±SD, n: Effective, WHR: Waist to hip ratio

Table 3: Comparison of blood glucose in volunteers with type 2 diabetes treated with LADE or placebo at 2 and 12 weeks

		At 2 weeks			At 12 weeks		
Parameters	Time (min)	Lupin (n = 47)	Placebo (n = 50)	p-value	Lupin (n = 47)	Placebo (n = 50)	p-value
Glucose (mg dL^{-1})	0	137±32.2	166±57.2	0.003	139±27.2	177±69.7	0.001
	30	176±33.0	210±66.7	0.002	180±40.1	225±80.9	0.001
	60	219±38.6	248±72.2	0.015	217±50.4	268±95.9	0.002
	90	229±49.1	264±72.2	0.009	230±54.2	279±95.8	0.003
	120	215±53.8	260±79.3	0.002	214±55.3	274±95.6	0.000
AUC		24071±4354	28134±8261	0.003	24189±5285	30003±1038	0.001
HOMA-IR		3.69± 2.00	5.53± 4.64	0.016	3.50±2.01	5.10±3.43	0.007

Data are presented as Mean±SD, AUC (mg dL^{-1} min^{-1}): Area under the curve, n: Effective

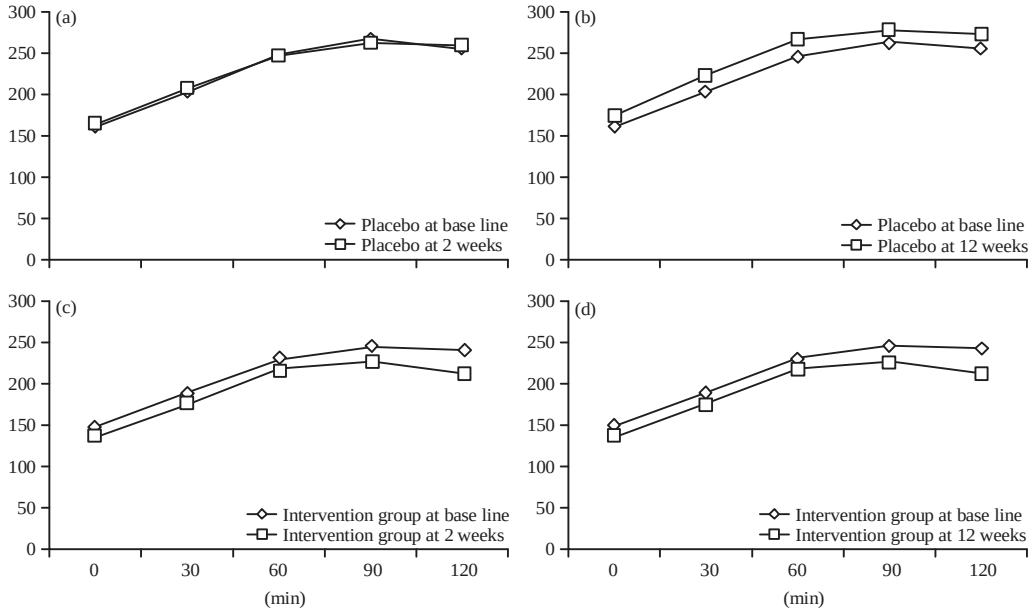

Fig. 1(a-d): Effect of LASE supplementation on glucose levels during meal tolerance tests. (a-b) Placebo after 2 and 12 weeks and (c-d) Intervention group after 2 and 12 weeks

Table 4: Comparison of insulin concentrations in volunteers with type 2 diabetes treated with LADE or placebo at 2 and 12 weeks

		At 2 weeks			At 12 weeks		
Parameters	Time (min)	Lupin (n = 47)	Placebo (n = 50)	p-value	Lupin (n = 47)	Placebo (n = 50)	p-value
Serum insulin (mIU L^{-1})	0	11.1±5.59	13.5±9.10	0.22	10.3±5.34	11.8±6.07	0.20
	30	23.2±13.7	27.5±14.3	0.13	23.7±11.0	27.2±13.4	0.16
	60	35.8±21.0	39.2±19.4	0.41	33.6±15.6	37.4±17.7	0.28
	90	42.8±19.3	46.2±25.7	0.47	41.4±21.4	42.3±21.6	0.83
	120	42.8±18.5	42.1±21.6	0.92	41.7±21.3	41.3±21.6	0.91
AUC		3851±1805	4226±2066	0.35	3747±1669	4008±1822	0.46

Data are presented as Mean±SD, AUC (mg dL^{-1} min^{-1}): Area under the curve, n: Effective

Table 5: Effect of *Lupinus albus* extract on glycated haemoglobin level (HbA1c) percentage and serum lipids after 3 months in volunteers with type 2 diabetics treated with *Lupinus albus* or placebo

	Placebo group (n = 50)			LADE group (n = 47)			
Parameters	Base line	Week 12	*p-value	Base line	Week 12	*p-value	**p-value
HbA1c (%)	7.43±0.89	7.68±1.42	0.18	7.16±0.78	6.77±0.76	0.000	0.000
Total cholesterol (mg dL^{-1})	204±30.2	203±32.5	0.88	197±34.6	181±30.1	0.000	0.001
Triglycerides (mg dL^{-1})	172±104	195±164	0.20	172±149	132±56.0	0.051	0.01
HDL-cholesterol (mg dL^{-1})	43±9.200	42±10.10	0.67	42±9.30	41.0±9.10	0.130	0.44
LDL-cholesterol (mg dL^{-1})	128±27.4	131±29.8	0.49	120±24.4	114±24.9	0.022	0.16

*Analyzed by linear mixed effect model and p-value represents the comparison to the base line visit. **Analyzed by linear mixed effect model and p-value represents the comparison to the placebo group. Data are presented as Mean±SD

DISCUSSION

The present study used a well-controlled and defined parallel study design to carefully characterize the response of plasma glucose metabolism in Tunisia adults with hyperglycemia to daily consumption of a well-defined, dry extract of *Lupinus albus*. The present study is the first well-controlled, randomized clinical study to examine the medium (2 weeks) and long-term (12 weeks) metabolic efficacy of *Lupinus albus* diabetic subjects. The changes of glucose concentrations in the plasma of treated subjects, with respect to placebo were remarkable both at 2 and 12 weeks. In particular, statistically significant and comparable reduction with *Lupius albus* was observed at all time points. Moreover, in the present work the LADE, orally administered to diabetic adults with good tolerability, proved to induce a significant

reduction of fasting and post-prandial plasma glucose concentration upon a standard load of carbohydrates, without a quantitatively significant modification of the insulin secretion response. These findings are in agreement with Magni *et al.*[17] who explained the same result and who showed that γ-conglutina lupin seed glycoprotein can influence glucose metabolism and can reduce postprandial glycaemia in the γ-conglutin-treated rats[17] and healthy human[22]. As a result of measurements of the areas under the curve glucose was significantly decreased compared to placebo. A similar result was reported[15], on the effects of *Lupinus albus* in rats and healthy human, as well as[19] on type 2 diabetes patients. Another studies show that consumption of *L. mutabilis* by normal weight healthy young individuals did not change importantly blood glucose and insulin levels. On the other hand, consumption of similar doses of *Lupinus* by dysglycemic individuals (fasting glucose >100 mg dL^{-1}) decreased significantly blood glucose[14]. In a previous study of non-diabetic adults, postprandial blood glucose was unaffected and insulin was decreased compared with control with lupin[23]. Moreover, Vargas-Guerrero *et al.*[24] demonstrated that γ-conglutin administered rats had increased insulin levels, higher Ins-1 expression and reduced blood glucose levels than the control, although these changes were lower than in the glibenclamide group. There is evidence that particular components of lupin may have anti-hyperglycaemic effects. In previous works, γ-conglutin was shown to display glycaemia-lowering properties in animal[17] glucose overload trials, exerts an insulin-like action[18] and was shown to positively influence glucose uptake by various model cells[16,24,25] which could explain the results of the present study. More recently, a relevant increase of glucose uptake by HepG2 cells, as well as a glucose lowering effect in chronically treated mice, was described by Lovati[16]. As a matter of facts, γ-conglutin cell stimulation resulted in the persistent activation of protein synthetic pathway kinases and increased glucose transport, GLUT4 translocation, as well as muscle-specific gene transcription regulation. A more recent study compared γ-conglutin to the other conglutins in relation to their effect on body and blood parameters of hyperglycemic rats[26]. The researchers reported the advantages of conglutins, in particular γ-conglutin, in controlling body weight gain and glycemia.

On the other hand, *Lupinus albus* contain low levels of quinolizidinealkoloid in vegetation as well as seed[27]. In addition, some studies have also shown that lupanine (alkaloids from *Lupinus*) and its derivatives enhanced glucose-induced insulin secretion *in vitro* conditions[28]. Results of Sgambato *et al.*[29] indicated that the hypoglycemic effect of sparteine sulphate (alkaloids from *Lupinus*) in lupin might be related to its ability to enhance insulin release in pancreatic islets. Paolisso *et al.*[30] have reported that intravenous administration of sparteine sulphate to subjects with type-2 diabetes decreased blood glucose and increased insulin. Chronic treatment with γ-conglutin also improved the state of insulin resistance as determined by the decrease of HOMAS in the treated animals[16]. Present study revealed that the lupin seeds can acutely reduce fasting and postprandial glycaemia. Such effects, if maintained in the longer term 12 weeks, contributed to improved insulin sensitivity. These results are in the same line of the previous studies that demonstrated that *Lupinus mutabilis* decreases blood glucose and improved insulin sensitivity in animals and humans[31]. The amelioration effect of *Lupinus albus* treatment in all previous parameters are in agreement with Farghaly and Hassan[13] who reported that the treatment with *Lupinus albus* improved insulin resistance in dysglycemic subjects, so ameliorates hyperglycemia.

Limited data from human and animal studies suggest that a lupin may benefit HbA1c. In the present study, the group of diabetic subjects supplemented with *Lupinus albus* showed significantly lower values of HbA1c than respective group of placebo. Furthermore, fenugreek has been shown to have a similar hypoglycemic effect than *Lupinus albus*. Intake of hydro-alcoholic extracts of fenugreek seeds resulted in a significant reduction in fasting blood glucose, 2 h glucose and HbA1c[32].

Lipids play an important role in cardiovascular disease, by modifying the composition, structure and stability of cell membranes. Altered lipid metabolism is considered to accelerate the development of atherosclerosis, a major risk factor in myocardial infarction[33]. Several earlier studies confirmed the beneficial effects of lupin on lipid profile[34,35]. Moreover, numerous investigations have shown that lupin provides cholesterol reduction[36-39]. In the current study the lupin treatment resulted in a significant reduction in serum lipid profile (triglyceride and total cholesterol levels). These findings agree with Fontanari *et al.*[40] who indicated that whole lupin seeds supplementation decreases total cholesterol and non-HDL cholesterol in the hamster's plasma as compared with control group. The same author added that, lupin interferes with cholesterol enterohepatic circulation and decrease the accumulation of fat in the liver. Likewise, Marchesi *et al.*[41] established the role of lupin as hypolipidemic and anti-atherosclerotic agent. The present study was the first human research investigating the effects of *Lupinus albus* on post-prandial glucose levels. However, this study had limitations, as well. First, several patients

participating in the intervention were excluded from the study. Moreover, frequent inclusion and exclusion criteria led to further reduction in the number of patients eligible for the study. Finally it is suggested to perform similar studies with longer study period for a better observation of the effects of *Lupinus albus* bioactive compounds in improving diabetic patient status.

CONCLUSION

The present study showed for the first time that *Lupinus albus* supplementation has the potential to improve HOMA-IR, fasting and post-prandial plasma glucose levels as well as to decrease HbA1c, total cholesterol and triglycerides levels with no significant change in insulin. These results suggest that *Lupinus albus* may exert its hypoglycaemic effect, not by stimulation of insulin release from β-cells, but by other mechanisms, such as stimulation of glucose uptake, correction of insulin resistance, inhibition of endogenous glucose production or activation of glycogenogenesis in liver and muscles. *Lupinus albus* may be a good candidate to be used as hypoglycaemic agents.

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