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Role of *Spirulina* in the Control of Glycemia and Lipidemia in Type 2 Diabetes Mellitus

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ABSTRACT

***Spirulina*, with its high concentration of functional nutrients, is emerging as an important therapeutic food. This study aimed to evaluate the hypoglycemic and hypolipidemic role of *Spirulina*. Twenty-five subjects with type 2 diabetes mellitus were randomly assigned to receive *Spirulina* (study group) or to form the control group. At baseline, the control and study groups were matched for various variables. The efficacy of *Spirulina* supplementation (2 g/day for 2 months) was determined using the preintervention and postintervention blood glucose levels, glycosylated hemoglobin (HbA_{1c}) levels, and lipid profiles of the diabetic subjects. Two-month supplementation with *Spirulina* resulted in an appreciable lowering of fasting blood glucose and postprandial blood glucose levels. A significant reduction in the HbA_{1c} level was also observed, indicating improved long-term glucose regulation. With regard to lipids, triglyceride levels were significantly lowered. Total cholesterol (TC) and its fraction, low-density lipoprotein cholesterol (LDL-C), exhibited a fall coupled with a marginal increase in the level of high-density lipoprotein cholesterol (HDL-C). As a result, a significant reduction in the atherogenic indices, TC:HDL-C and LDL-C: HDL-C, was observed. The level of apolipoprotein B registered a significant fall together with a significant increment in the level of apolipoprotein A1. Therefore, a significant and favorable increase in the ratio of A1:B was also noted. These findings suggest the beneficial effect of *Spirulina* supplementation in controlling blood glucose levels and in improving the lipid profile of subjects with type 2 diabetes mellitus.**

INTRODUCTION

THE CLINICAL EXPRESSION of absolute or relative insulin deficiency, diabetes mellitus is manifested in its fully developed form by hyperglycemia.[1] Epidemiological and prospective studies in non–insulin-dependent diabetes mellitus (type 2 diabetes) have suggested a relationship between hyperglycemia or the degree of metabolic control and the pathophysiology and risk of coronary heart disease.[2,4] For each increase of 1% in glycosylated hemoglobin (HbA_{1c}) concentration, the risk of coronary heart disease increases by 11%.[4,5]

Hyperglycemia and insulin resistance affect each lipid and lipoprotein fraction.[6–8] Lipid abnormality exists in 30% of diabetic patients and is presumed to be responsible for the increased risk of macrovascular disease in patients with diabetes mellitus.[4,9] The common pattern of lipoprotein abnormalities found in type 2 diabetes mellitus consists of an increase in very-low-density lipoprotein cholesterol (VLDL-C), an increase in low-density lipoprotein choles-

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terol (LDL-C) that is more prominent with worsening metabolic control, and a decrease in high-density lipoprotein cholesterol (HDL-C).[8–11] Hypertriglyceridemia often is rather modest but seems to be an independent risk factor for the development of macrovascular disease.[8,9]

Normalization of blood sugar levels and improvements in dyslipidemia form the cornerstone of effective therapy for diabetes management. Adequate metabolic control is best achieved with appropriate dietary intervention. *Spirulina*, a genus of blue-green algae, with high concentrations of functional nutrients, is a subject of extensive research interest. *Spirulina* is a rich source of protein, containing more than 60% digestible vegetable protein. It also has high concentrations of β-carotene, vitamin B_{12} (mainly pseudo-B_{12}), iron, trace minerals, and the essential fatty acid, γ-linolenic acid. These make *Spirulina* a good whole food alternative to isolated vitamin and minerals. With its multiple nutritional properties, *Spirulina* may be used as a therapeutic supplement for the management of various nutritional and metabolic disorders.[12,13]

Earlier work from this laboratory involved studying the effect of *Spirulina* supplementation on the glycemic indices of foods and in subjects with type 2 diabetes. The results indicated a significantly lower 2-hour postprandial glycemic and lipemic response to the recipes supplemented with *Spirulina* (at the 2.5 g level).[14,15] In another study, *Spirulina* supplementation (2 g/day for 21 days) resulted in a significant reduction in fasting blood sugar concentration and improvement in the lipid profile of subjects with type 2 diabetes.[16]

These preliminary findings suggested the hypoglycemic and hypolipidemic properties of *Spirulina*. The present study was designed to study the effect of *Spirulina* supplementation on the fasting and postprandial blood sugar levels and on the long-term indicator of glycemic control, HbA_{1c}. The efficacy of *Spirulina* supplementation on lipid and lipoprotein levels was also evaluated.

MATERIALS AND METHODS

Subjects

Of the 25 type 2 diabetic subjects enrolled for the study, 15 subjects (9 men and 6 women) were randomly allocated to the study group for supplementation with *Spirulina*. The mean age of the subjects in the study group was 67.2 ± 11.5 years, and the duration of disease was 12.9 ± 5.5 years. The control group comprised 10 subjects with type 2 diabetes (6 men and 4 women) matched for age, duration of disease, body mass index, waist-to-hip ratio, blood glucose level, and blood lipid levels with the study group. Clinical characteristics of the subjects are given in Table 1. None of the subjects had diabetic complications, and none were receiving treatment with lipid-lowering drugs.

TABLE 1. CLINICAL DATA (MEAN ± SD) OF TYPE 2 DIABETIC PATIENTS IN THE CONTROL AND STUDY GROUPS

Parameter	*Control group* (n = *10)*	*Study group* (n = *15)*
No. men/women	6/4	9/6
Age (yr)	54.6 ± 5.4	53.8 ± 7.2
Weight (kg)	67.1 ± 13.1	67.2 ± 11.5
Body mass index (kg/m^2)	25.1 ± 2.7	25.2 ± 5.4
Waist circumference (cm)	96.8 ± 11.8	99.4 ± 18.8
Waist-to-hip ratio	0.94 ± 0.11	0.95 ± 0.13
Duration of disease (yr)	12.6 ± 4.2	12.9 ± 5.5
Fasting blood glucose (mg %)	164.3 ± 59.4	161.7 ± 48.6
Total cholesterol (mg %)	201.8 ± 32.5	201.3 ± 27.0
Triglyceride (mg %)	155.6 ± 46.6	163.9 ± 55.2
Treatment	Oral hypoglycemic agents	

[a]Oral hypoglycemic agents: Glide, Glynase, Glyciphage, Diamicron

Supplementation

Spirulina (Sunova *Spirulina*, Sanat Products Ltd., Sikandrabad, India) supplementation at 2 g/day for 2 months was done in the study group. The patients were asked to take two tablets along with lunch and two tablets with dinner. The typical nutrition profile of *Spirulina* is given in Table 2. Subjects were asked to maintain their habitual diet, medication regimen, and level of physical activity throughout the study period.

Assay methods

A venous blood sample was collected after an overnight fast before the study and after a period of 2 months for both the control and the study groups. The blood sample collected with fluoride and ethylenediamine tetraacetic acid (EDTA) preservatives was used for analysis of blood glucose and glycosylated hemoglobin (HbA_{1c}). The serum was used for the estimation of lipid profile. Blood glucose was estimated using a Bayer diagnostic kit (Bayer, Gujarat, India). The HbA_{1c} levels were determined by the variant hemoglobin A_{1c} program through the high performance liquid chromatography technique.[17] Randox diagnostic kits procured from Randox Laboratories Ltd., Antrim, United Kingdom were used to estimate total cholesterol (TC) and HDL-C (direct method). LDL-C and VLDL-C levels were obtained by calculation. Apolipoproteins (apo) A1 and B were measured on the Array Protein Systems (Beckman Instruments, Brea, California) following the principle of antigen-antibody reaction by rate nephelometry. Triglyceride estimations were made with the use of the Randox diagnostic kits.

TABLE 2. *SPIRULINA*[a]—TYPICAL NUTRITION PROFILE

Nutrients	*Amount per 100 g*	*Amount per 2 g*
Moisture, g	7.0	0.14
Ash, g	9.0	0.18
Protein, g	71.0	1.42
Crude fiber, g	0.9	0.018
Xanthophylls, mg	180.0	3.6
Carotene, mg	190.0	3.8
Chlorophyll, mg	760.0	15.2
Thiamine (B_1), mg	5.5	0.11
Riboflavin (B_2), mg	4.0	0.08
Nicotinic acid, mg	11.8	0.236
Inositol, mg	35.0	0.7
Pyridoxine (B_6), mg	0.3	0.006
Cyanocobalamine (B_{12}), mg	0.2	0.004
Tocopherol, mg	19.0	0.38
Biotin, g	0.04	0.0008
γ-linolenic acid, g	1.3	0.026
Calcium, mg	132.0	2.64
Phosphorous, mg	894.0	17.88
Iron, mg	58.0	1.16
Zinc, mg	3.9	0.078

[a]Sunova Spirulina, Sanat Products Ltd., Sikandrabad, India.

Statistical analysis

Results are expressed as mean ± standard deviation. Analysis of differences between the means (within groups) was performed using a paired *t* test. All tests were considered significant at the $P < .05$ level.

RESULTS

Patient characteristics

Table 1 shows the main baseline characteristics of the subjects. There were no significant differences in clinical characteristics between the two groups, indicating that the groups were well matched.

Changes in blood glucose levels

The blood glucose levels of the subjects in the control group exhibited a trend contrary to that of the study group. The fasting blood glucose levels of the subjects in the control group remained unaltered during the intervention period, and the 2-hour postprandial blood glucose levels were marginally decreased. Moreover, no change was noted in the HbA_{1c} levels of the control group. In contrast, a 19.3 mg reduction in fasting blood glucose and a 16.1 mg reduction in 2-hour postprandial blood glucose were observed in the study group. The significant lowering of HbA_{1c} levels (1.0%, $P < .05$) compared with baseline concentrations in the study group further supported these results. Blood glucose values and HbA_{1c} levels of the control and the study groups are given in Tables 3 and 4.

TABLE 3. BLOOD GLUCOSE LEVELS (MEAN ± SD, mg/dl) OF TYPE 2 DIABETIC PATIENTS IN THE CONTROL AND STUDY GROUPS

Patient group	*Fasting blood glucose concentration*	*2-Hour postprandial blood glucose concentration*
Control group (n = 10)		
Baseline	164.3 ± 59.4	215.2 ± 67.3
2 Months	165.1 ± 44.3	212.3 ± 57.6
Study group (n = 15)		
Baseline	161.7 ± 48.6	264.9 ± 65.2
2 Months	142.4 ± 27.4	248.8 ± 68.9

Changes in lipid profile

Two-month *Spirulina* supplementation resulted in an appreciable reduction in the levels of TC (6.4 mg) and LDL-C (7.1 mg) in the study group. Also, a marginal increase of 1.4% in the HDL-C level was noted. These favorable alterations in the lipid profile resulted in a significant reduction ($P < .05$) in the levels of the atherogenic indices (i.e., TC:HDL-C and LDL-C:HDL-C ratios) in the study group. A significant reduction was noticed in the level of apo B (16.1 mg, $P < .001$), coupled with a significant increase (11.4 mg, $P < .05$) in the level of apo A1. Concomitantly, a significant increment ($P < .01$) in the apo A1:B ratio was also observed. The triglyceride levels of the study group also registered a significant fall (21.3 mg, $P < .05$), suggesting a beneficial effect of *Spirulina*.

A contrary trend was observed in the lipid profile of the control group, with increases in the triglyceride, TC, and VLDL-C concentrations (17.5 mg, 13.2 mg, and 3.5 mg, respectively). Moreover, the LDL-C level of the control group exhibited a significant increase (9.4 mg, $P < .05$). Coupled with a reduction in the level of HDL-C (1.7 mg), these changes caused appreciable increases in the TC:HDL-C and LDL-C:HDL-C ratios, further tilting the lipid profile to the unfavorable. A significant increase (18.8%, $P < .05$) in the apo B level of the control group was also observed, along with a marginal reduction (8.1 mg) in the apo A1 level. As a result, the ratio of apo A1:B was significantly lowered ($P < .05$). A summary of the lipid levels of the control and study groups is presented in Table 5.

DISCUSSION

Hyperglycemia, the characteristic manifestation of diabetes mellitus, is a cardiovascular risk factor possibly because of the nonenzymatic glycosylation of proteins and lipoproteins, which may increase their atherogenic potential.[8,18–20] A two to three times higher risk for coronary heart disease and a four to six times greater cardiovascular mortality rate is seen in diabetic patients.[4,8] Recently, the role of postprandial "hyperglycemic spikes" in the pathophysiology of diabetic complications has been reviewed.[21,22] Various studies have demonstrated that, apart from fasting hyperglycemia, 2-hour postprandial hyperglycemia plays an important role in

TABLE 4. GLYCOSYLATED HEMOGLOBIN (HbA_1C) LEVELS (MEAN ± SD, %) OF TYPE 2 DIABETIC PATIENTS IN THE CONTROL AND STUDY GROUPS

Patient group	*HbA_1 concentration*	*Mean blood glucose concentration (mg/dl)*
Control group (n = 10)		
Baseline	8.7 ± 1.5	206.7 ± 51.4
2 Months	8.7 ± 1.3	202.4 ± 44.0
Study group (n = 15)		
Baseline	9.0 ± 2.3	216.0 ± 56.8
2 Months	8.0 ± 1.3[a]	181.1 ± 44.8[a]

[a]Significantly different from baseline at $p < .05$.

TABLE 5. LIPID PROFILE (MEAN ± SD, mg/dl) OF TYPE 2 DIABETIC PATIENTS IN THE CONTROL AND STUDY GROUPS

	Control group (n = 10)		*Study group* (n = 15)	
Parameter	*Baseline*	*2 Months*	*Baseline*	*2 Months*
Triglyceride	155.6 ± 46.6	173.1 ± 61.1	163.9 ± 55.2	142.6 ± 55.8[a]
TC	201.8 ± 32.5	215.0 ± 28.5	201.3 ± 27.0	194.9 ± 24.6
HDL-C	42.9 ± 6.2	41.2 ± 4.6	37.9 ± 7.7	39.3 ± 9.1
LDL-C	127.8 ± 28.0	137.2 ± 23.2[a]	128.5 ± 23.1	121.4 ± 20.7
VLDL-C	31.1 ± 16.8	34.6 ± 10.0	34.9 ± 14.0	34.1 ± 17.9
Apo A1	126.3 ± 18.1	118.2 ± 21.0	123.4 ± 17.3	134.8 ± 25.8[a]
Apo B	111.3 ± 19.0	130.1 ± 16.6[a]	122.1 ± 22.5	106.0 ± 19.8[c]
TC: HDL-C	4.3 ± 0.9	4.8 ± 1.1	5.4 ± 1.0	5.0 ± 1.0[a]
LDL-C: HDL-C	2.6 ± 0.8	3.1 ± 0.9	3.5 ± 0.8	2.9 ± 0.5[a]
Apo A1:B	1.2 ± 0.3	1.0 ± 0.2[a]	1.2 ± 0.5	1.3 ± 0.5[b]

[a]Significantly different from baseline at $P < .05$.
[b]Significantly different from baseline at $P < .01$.
[c]Significantly different from baseline at $P < .001$.

the development of coronary heart disease.[21–23] Appropriate control of blood glucose, both fasting and postprandial, is therefore important in subjects with diabetes mellitus.

In the present study, *Spirulina* supplementation of 2 g/day for 2 months resulted in a prominent but nonsignificant lowering of not only the fasting but also the postprandial glucose level. Various theories validating the hypoglycemic effect of *Spirulina* have been proposed. One theory attributed this effect to its fiber content, which leads to reduced glucose absorption.[12] Another theory suggested the possible action of peptides and polypeptides generated by the digestion of *Spirulina* proteins.[12] *Spirulina* is a rich source of proteins, and it provides good-quality proteins. It is well established that both protein and amino-acid ingestion stimulate insulin secretion. This effect may be responsible for a reduction in postprandial blood sugar levels.[14–16,24]

This study also demonstrated a significant reduction in HbA_{1c} in diabetic subjects. HbA_{1c} provides a means to objectively assess average glycemia in a diabetic patient; this is an integrated index of blood sugar levels over the past 2 to 3 months.[25] The reduction in HbA_{1c} level of the diabetic subjects in this study therefore indicates an improved long-term glycemic control. Consequently, it can be suggested that the hypoglycemic effect of *Spirulina* is a physiological event and not a transient one.

The γ-linolenic acid content of *Spirulina* may contribute to its hypocholesterolemic effect. *Spirulina* is a natural whole food source of γ-linolenic acid.[12,26,27] γ-Linolenic acid is an essential fatty acid that may play a role in the prevention of fats and cholesterol in the human body, thereby reducing the serum cholesterol level.[12,26–29] The significant reduction in triglyceride level could be attributed to decreased VLDL triglyceride production and increased peripheral clearance of VLDL due to the high protein and fiber content of *Spirulina*. Apart from all this, the beneficial roles of antioxidants and superoxide dismutase cannot be ruled out. The lipid changes observed included a nonsignificant increase in the HDL-C level coupled with appreciable lowering of the TC and LDL-C levels after 2 months of *Spirulina* supplementation. A resultant significant lowering in the atherogenic indices of TC:HDL-C and LDL-C:HDL-C was consequently noted.[30] Such changes in lipid levels have been associated with a lower incidence of coronary heart disease.[31]

Because apo A1 and B are the major protein components of HDL-C and LDL-C, respectively, they have been most frequently investigated as quantitative risk factors of coronary heart disease. Apo A1 and B measurements are used both independently and as a ratio to assess the risk of coronary heart disease. Studies have demonstrated that the changes as observed in this study with *Spirulina* supplementation (i.e., a highly significant reduction in apo

B and a significant increment in apo A1 causing a significant increase of the A1:B ratio) are well correlated with a lower incidence of coronary heart disease.[32] Furthermore, because apo B is independently associated with cardiovascular disease and identifies high-risk phenotypes in normocholesterolemic type 2 diabetic patients,[33] the 16.1 mg reduction induced by *Spirulina* is noteworthy.

In conclusion, *Spirulina* supplementation may play a beneficial role in improving long-term glycemic control and in favorably altering lipid profiles in the type 2 diabetic patients.

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REFERENCES

1. Ahuja MMS: Prevalence of diabetes mellitus. In: *Practice of Diabetes Mellitus in India.* Vikas Publication House Pvt Ltd, Delhi, 1994, p. 45.
2. Fu CC, Chang CJ, Tseng CH, Chen MS, Kao CS, Wu TJ, Wu HP, Chuang LM, Chen CJ, Tai TY: Development of macrovascular diseases in NIDDM patients in Northern Taiwan. A 4-yr follow-up study. *Diabetes Care* 1993;16:137–143.
3. Kuusisto J, Mykkamen L, Pyorala L, Laakso M: NIDDM and its metabolic control predict coronary heart disease in elderly subjects. *Diabetes* 1994;43: 960–967.
4. Wolffenbuttael BHR, Drzewoski J: Prevention of complications in type 2 diabetes mellitus. *Med Sci Monit* 1999;5:1013–1019.
5. Turner RC, Millns H, Neil HA, Stratton IM, Manley SE, Matthews DR, Holman RR: Risk factors for coronary artery disease in non-insulin dependent diabetes mellitus: United Kingdom Prospective Diabetes Study (UKPDS 23). *BMJ* 1998;316:823–828.
6. Hulley SB: The associations between triglyceride and coronary heart disease. *N Engl J Med* 1980;302: 1383–1389.
7. Jeppesen J, Hein H, Suadicani P, Gyntelberg F: Triglyceride concentration and ischemic heart disease: An eight year follow-up in Copenhagen Male Study. *Circulation* 1998;97:1029–1036.
8. George P, Ludvik B: Lipids and diabetes. *J Clin Basic Cardiol* 2000;3:159–162.
9. Betteridge DJ: Diabetic dyslipidemia. *Am J Med* 1994; 96:25–31.
10. Reaven GM, Greenfield MS: Diabetic hypertriglyceridemia: Evidence from three clinical syndromes. *Diabetes* 1981;30:66–75.
11. Bergman M, Glidez LI, Eder HB: High-density lipoprotein subclasses in diabetes. *Am J Med* 1986;81: 488–492.
12. Henrikson R: *Earth Food: Spirulina*, ed 4. Ronore Enterprises Inc., Kenwood, California, 1997.
13. Mani UV, Sadliwala A, Iyer UM, Parikh PM: The effect of *Spirulina* supplementation on blood haemoglobin levels of anaemic adult girls. *J Food Sci Technol* 2000;37:642–644.
14. Iyer UM, Ahmedi S, Mani UV: Glycemic and lipemic responses of selected *Spirulina* supplemented rice-based recipes in normal subjects. *Int J Diab Dev Countries* 1999;19:17–25.
15. Iyer UM, Deshmukh SM, Mani UV: Glycemic indices of *Spirulina* supplemented meals. *Int J Diab Dev Countries* 1999;19:108–113.
16. Mani UV, Desai S, Iyer UM: Studies on the long-term effect of *Spirulina* supplementation on serum lipid profile and glycated proteins in NIDDM patients. *J Neutraceuticals Functional and Medical Foods* 2000; 2:25–32.
17. Bio-Rad Laboratories: Variant hemoglobin A_{1c} program. In: *Instruction Manual 700: 157-4.* Richmond, California: Bio-Rad Laboratories Diagnostics Group, 2000, pp. 1–21.
18. Balkau B, Shipley M, Jarrett RJ, Pyorala K, Pyorala M, Forhan A, Eschwege E: High blood glucose concentration is a risk factor for mortality in middle-aged nondiabetic men. 20-year follow-up in the Whitehall Study, the Paris Prospective Study, and the Helsinki Policemen Study. *Diabetes Care* 1998;21:360–367.
19. Barret-Connor E, Ferrara A: Isolated post-challenge hyperglycaemia and the risk of fatal cardiovascular disease in older women and men. *Diabetes Care* 1998;21:1236–1239.
20. Wei M, Gaskill SP, Haffner SM, Stern MP: Effects of diabetes and levels of glycaemia on all-case and cardiovascular mortality: The San Antonio Heart Study. *Diabetes Care* 1998;21:1167–1172.
21. Ceriello A: The emerging role of post-prandial hyperglycaemic spikes in the pathogenesis of diabetic complications. *Diabet Med* 1998;15:188–193.
22. Ceriello A: The post-prandial state and cardiovascular disease: Relevance to diabetes mellitus. *Diabetes Metab Res Rev* 2000;16:125–132.
23. Hanefeld M, Schmechel H, Schwanebeck U, Lindner J: Predictors of coronary heart disease and death in NIDDM: The Diabetes Intervention Study experience. *Diabetologia* 1997;40(Suppl 2):S123–S124.
24. Westphal SA, Gannon MC, Nuttal FQ: Metabolic re-

sponse to glucose ingested with various amounts of proteins. *Am J Clin Nutr* 1990;52:262–272.
25. Shamoon H: The relationship between hemoglobin A_{1c} levels and the long-term complications of diabetes. *Drug Benefit Trends* 1996;Suppl 8E:10–17.
26. Grattan RP: *Spirulina*: A source of dietary gamma linolenic acid. *J Sci Food Agric* 1989;47:85–93.
27. Dillon JC, Phan Phuc A, Dubacq JP: Nutritional value of the alga *Spirulina*. *World Rev Nutr Diet* 1995; 77:32–46.
28. Nayaka N, Homma Y, Goto Y: Cholesterol lowering effect of *Spirulina: Nutr Rep Int* 1988;6:1329–1337.
29. Nayaka N: The effect of *Spirulina* on reduction of serum cholesterol. In: *Progress in Medicine*, Vol. 6, Tokai University, Japan, 1986.
30. Shils ME, Young VR: *Modern Nutrition in Health and Disease*. KM Varghese Company, Mumbai, 1988, pp. 1201–1229.
31. Lamarche B, Moorjani S, Lupien PJ, Cantin B, Bernard PM, Dagenais GR, Despres JP: Apolipoprotein A-I and B levels and the risk of ischemic heart disease during a five-year follow-up of men in the Quebec cardiovascular study. *Circulation* 1996;94: 273–278.
32. Niebauer J, Hambrecht R, Velich T, Marburger C, Hauer K, Kreuzer J, Zimmermann R, von Hodenberg E, Schlierf G, Schuler G, Kubler W: Predictive value of lipid profile for salutary coronary angiographic changes in patients on a low-fat diet and physical exercise program. *Am J Cardiol* 1996;78:163–167.
33. Wagner AM, Perez A, Calvo E, Bonet R, Castellvi A, Ordonez J: Apolipoprotein(B) identifies dyslipidemic phenotypes associated with cardiovascular risk in normocholesterolemic type 2 diabetic patients. *Diabetes Care* 1999;22:812–817.

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