

Siberian Ginseng Results in Beneficial Effects on Glucose Metabolism in Diabetes Type 2 Patients: A Double Blind Placebo-Controlled Study in Comparison to Panax Ginseng

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Abstract Although new antidiabetic agents are introduced, alternative medicine with natural compounds such as ginseng offer a potential benefit, as they have a wide margin of safety with no side-effects. Following informed consent patients with type 2 diabetes (oral medication 80%, insulin therapy 20%) were randomly assigned to receive an extract of Siberian (480 mg/day; n = 27) American (Panax) ginseng (480 mg/day; n = 27), or a placebo preparation over a period of three months. Patients and physician were blinded as to the kind of ginseng being administered. Fasting (BZfast) and postprandial blood glucose level (BZpp), HbA1c, total cholesterol (TC) and triglyceride (TG) levels were determined each week and at the end of each month. In addition, the degree of peripheral neuropathy was evaluated by an electrical stimulus at 5 Hz determining threshold levels for feeling of sensation and pain at both lower extremities at start and after each month of treatment. Contrary to placebo and Panax ginseng, Siberian ginseng intake resulted in a highly significant decline ($p < 0.001$) of fasting blood sugar, and postprandial blood sugar level at the end of the three-month period. Also, Siberian ginseng lowered significantly ($p < 0.001$) HbA1c, TC and TG levels after the 12-week period. Patients taking Siberian ginseng demonstrated some recovery of sensory to an electrical stimulus. Since eleutherosides are only found in Siberian ginseng, they seem to contribute to the observed therapeutic effect, which may be due to their ability to blockade of P-glycoprotein, an ATP-dependent drug efflux pump, which is responsible for an increase in insulin resistance. Since Siberian ginseng induced no adverse side effects, its additional intake is able to fine-tune the pathological glucose metabolism, also reducing symptoms of peripheral polyneuropathy.

Keywords: diabetes type 2, Siberian ginseng, American ginseng, HbA1c, total cholesterol, triglycerides, peripheral neuropathy

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1. Introduction

Diabetes type 2 accounts for 90-95% of all diabetes and exhibits a worldwide prevalence of 150 million. It increase to 225 million by 2010 and is predicted to reach endemic proportions to 340 million by 2025 [1,2,3,4]. This astounding increase results mainly from the massive rise in the number of overweight or obese people. Obesity is one of the main causes of the debilitating pathologies associated with type 2 diabetes. It is therefore that diabetes type 2 accounts for greater than \$ 100 billion in healthcare costs annually in the US [4]. Because of the high morbidity of diabetes and the increasing costs in the treatment of type 2 diabetes using oral prescription medication, or insulin, it therefore is imperative to

continue to evaluate alternatives in the treatment of type 2 diabetes. For example, often-cited remedies such as magnesium, vanadium, gymnema sylvestre, or fanugreel, have been shown to reduce elevated glucose blood levels [5,6,7,8]. Also, chromium [9], or cinnamon are touted as one of the major alimentary alternatives, which purportedly are able to correct the unbalanced carbohydrate metabolism resulting in a reduction of elevated glucose level [10]. However, due to the lack of adequate double-blind studies, general acceptance of these alternative treatments by the medical establishment has not occurred.

Unproven or untested efficacy of these natural-based treatments over a long-range period is questioned. Especially, since alternative therapeutics lack sufficient evidence in double blind, placebo controlled clinical trials, general use of some of the alternative treatments by the medical establishment, inspite their low side-effect potential has not increased.

We therefore set out to evaluate and compare the management of patients with type 2 diabetes, using Siberian ginseng and Panax ginseng respectively. The rationale for their use in diabetic's stems from previous positive preclinical results [11,12] and in alloxan-induced diabetes [13]. In addition, clinical studies with extracts from the roots of Siberian ginseng have demonstrated a better utilization of glucose with lowering of elevated glucose plasma levels in patients [14,15]. Similarly, standardized American (Panax) ginseng extracts have been shown in newly diagnosed non-insulin-dependent diabetes to improve fasting blood glucose levels, elevate mood, and improve HbA1c values and psychophysical performance [16]. Because of the increasing costs in the management of type 2 diabetes with oral prescription medication or the use of insulin, it therefore is necessary to look into alternative kinds of treatment in a disease with epidemic proportions.

1.1. Patients and Methods

Following informed consent and after explaining the goal of the study, a total of 75 patients were recruited and randomly allocated to receive either a purified solution of *Eleutherococcus senticosus* (Siberian ginseng) or a solution of *Panax quinquefolius* (American ginseng) in addition to their regular oral antidiabetic medication. Patients with clinically significant liver disease, renal impairment, unstable or severe angina, congestive heart failure, or uncontrolled hypertension were excluded. All patients had a history of type 2 diabetes for at least seven years; they were taking oral antidiabetic medication (80%) or were on insulin (30%). Diet control was not a variable. In comparison a group of 25 patients were randomly allocated to receive a placebo preparation.

The solution of Siberian ginseng consisted of a standardized dried extract of 9% *Eleutherococcus senticosus sicc.* diluted in 36.99% distilled water with 0.07% NaCl mixed together in 54% of a 70% sorbit solution. To this solution 0.27% of agar-agar was given. An additional 0.03% of an apple extract was added for taste purposes. Purity was ascertained by HPLC analysis from Alpinamed Company, Freidorf/Switzerland, where the active ingredients eleutheroside E and B were found to be in a concentration of 1.12% in the *Eleutherococcus* preparation. No toxic concentrations of heavy metal and/or residues of diluents exceeding the official daily allowance of > 20 ppm and > 50 ppm respectively were detected. In addition, no remainders of the poisonous alfatoxins were present. Each day 30 min prior to breakfast, the subjects took a total 450 mg of the extract of *Eleutherococcus senticosus* orally. Such high dose deemed necessary in order to make certain that a therapeutic sufficient high concentration of the active ingredients were reabsorbed resulting in sufficient bioavailability. Due to the lack of side effect in over 200.000 patients and volunteers having taken *Eleutherococcus senticosus* in the past [17,18,19], such high dosages were considered to be safe, especially since the oral LD₅₀ of a fluid extract is > 20 ml/kg body weight in mice. Similarly, a dried preparation of 450 mg of *Panax quinquefolius* (American ginseng) was diluted and given to the other group of patients with type 2 diabetes, while the control population took a solution, which looked alike consisting only of a fiber mixture.

Because of the underlying disease, patients in all three groups were under close ambulatory surveillance. Aside from their daily routine glucose check at home, additional parameters at an interval of 4 weeks were measured in order to demonstrate a beneficial effect of either one of the ginseng preparations. Aside from body weight, and cardiovascular data (systolic, diastolic blood pressure, heart rate), the following parameters were recorded at regular interval at the end of four weeks, totaling 12 weeks:

1. Fasting blood glucose level (BZfast)
2. Postprandial glucose level (BZpp)
3. HbA1c concentration (glycated hemoglobin)
4. Total cholesterol (TC)
5. Triglyceride (TG) level

In addition, individual tolerance to an electrical rectangular stimulus of 0.3 ms duration was evaluated in order to detect changes in the underlying subclinical peripheral neuropathy (loss of vibration senses). For these purpose, two Ag/AgCl stick-on electrodes were applied over the lower tibia region. Electrical current (mA; Digi Stim IITM, Neuro Technology, Houston, USA) was applied at 5 Hz frequencies to a point where the patient reported some tingling (threshold for sensation), and the intensity where he/she reported painful sensations (threshold for pain). It is estimated that the prevalence of distal polyneuropathy with or without autonomic neuropathy increases in relation to the duration of diabetes and to pathological blood glucose level [20]. Since long-lasting diabetes is regularly accompanied by peripheral distal neuropathy resulting in a reduced propagation of nociceptive sensations with an elevated threshold for pain mainly in the distal part of the lower extremities, such measurements seemed of importance to demonstrate efficacy of the ginseng treatment.

1.2. Statistical Analysis

Before starting the study, a priori statistical power analysis was done.

This was necessary in order to calculate the sample size (number to treat) to demonstrate a statistical significance among the three groups of patients. Power analysis demonstrated pragmatic constraints for the investigation and in order to detect the maximum possible sample size and compromised power analysis was performed. Power was calculated using the standard deviations of pain and sensitivity threshold levels to electrical current in patients of a previous study undergoing alternative treatment with amino acids for reversal fibromyalgia [21] Computation of sample size for unpaired t-test yielded a number 25 subjects necessary for having a 95 % power to detect a before-after difference at a significance level (alpha) of 0.05 (one-tailed) between the three groups.

For intragroup comparison, before and 3 months after intake of the ginseng preparation, one-way analysis of variance (ANOVA) with Bonferroni correction for multiple measurements was used. In order to demonstrate any significant difference between the two groups and not assuming equal variances, the unpaired t-test with Welch's correction was used. Significance is defined if p equals or is less than 0.05.

2. Results

Group 1 (Siberian ginseng) consisted of 19 male and 6 female, group 2 (Panax ginseng) incorporated 15 male and 10 female subjects and group 3 (placebo) had 14 male and 11 females [Table 1](#). There was no statistical difference regarding the demographics, the glucose levels, the

glycated hemoglobin concentrations (HbA_{1c}) as well as total cholesterol and triglyceride levels between the three groups of patients at start of the study. And although the mean control values in the Panax ginseng group were lower when compared to the Siberian group, statistically there is no significant difference.

Table 1. Demographic data of patients with type 2 diabetes, their glucose and glycated hemoglobin concentrations as well as total cholesterol and triglyceride levels at start of study using either Eleutherococcus senticosus, Panax quinquefolius or placebo (mean ± SD)

Variables	Siberian Ginseng n = 25	Panax Ginseng n = 25	Placebo n = 25
Age (years)	61.8 ± 10	63.8 ± 10	66.9 ± 11.2
Weight (kg)	89.8 ± 14	88.8 ± 16.3	85.8 ± 18.3
Height (cm)	174 ± 8.7	174 ± 19.0	170.5 ± 9.7
Gender male/female	19/6	15/10	14/11
BMI	29.7 ± 3.5	29.4 ± 3.7	29.3 ± 4.6
Fasting BS (mg/dl)	166 ± 35	154 ± 33	131 ± 34
Postprandial BS (mg/dl)	214 ± 52	210 ± 34	186 ± 56
HbA _{1c} (%)	7.4 ± 1.0	7.2 ± 1.3	6.9 ± 1.0
Total Cholesterol (mg/dl)	227 ± 52	223 ± 54	237 ± 50
Triglycerides (mg/dl)	278 ± 123	229 ± 129	233 ± 84

As shown in [Table 1](#), patients in all three groups had a BMI above the recommended range of the American Diabetes Association and the International Diabetes Federation, reflecting an overweight of grade 2, which suggests a high risk of diabetes related ailments. In addition, pathological findings are also present in other variables, such as the fasting, the postprandial plasma glucose levels, and HbA_{1c} concentration, which are in excess of the normal levels of 100 mg/dl (= 3.8 mmol/l), 135 mg/dl (= 7.5 mmol/L) and 7% respectively [\[22,23\]](#).

2.1. Ginseng on Blood Glucose Level

The fasting and the postprandial blood glucose level began to decline after the second, and considerably after the third month only in the group taking Siberian ginseng [Figure 1](#). This decline was highly significant ($p < 0.001$) when compared to the placebo and to the group taking Panax ginseng extract. Intragroup comparison of fasting blood glucose values before and after the third month, decreased from a mean of 166 to a mean of 130 mg/dl in the Siberian group [Figure 1](#). More important, at the end of study period, fasting glucose level in all three groups differed significantly ($p < 0.05$).

fastening blood glucose level (BSfast) before and after siberian versus panax ginseng following three months of intake (mean ±SD)

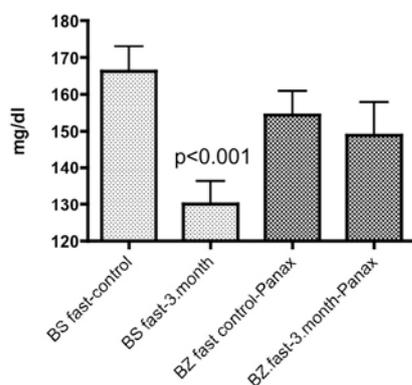


Figure 1. Fasting glucose level in patients with type 2 diabetes before and after additional treatment with Siberian and Panax ginseng respectively

The beneficial effect of Siberian ginseng is also observed in the postprandial blood glucose level. This parameter is of major significance in diagnosing diabetes and is of utmost importance in showing an effective therapeutic regimen. Postprandial glucose level in diabetic patients dropped from a mean of 214 to a mean of 179 mg/dl ($p < 0.001$) at the end of the observation period in the group receiving Siberian ginseng [Figure 2](#). In patients taking Panax ginseng there was only a decline from a mean of 210 mg/dl to a mean of 202 mg/dl at the end of the observation period while the placebo group stayed at high levels over the whole observation period (186 ± 56 SD). Although there is some decrease in postprandial glucose level in Panax group at the end of the third month, the decline greater in the Siberian group, resulting in a significant difference ($p < 0.05$) between the two groups [Figure 2](#).

Comparison of postprandial glucose level (BSpp) after siberian versus panax ginseng in type 2 diabetics (mean ±SD)

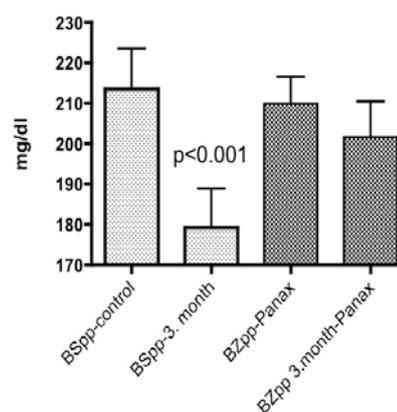


Figure 2. Effect of Siberian and Panax ginseng respectively on postprandial glucose level before and after three months of intake in patients with type 2 diabetes

2.2. Ginseng on Glycated Hemoglobin (HbA_{1c})

Lastly, the long-lasting beneficial effect of Siberian ginseng on the pathological carbohydrate metabolism in type 2 diabetic patients is also mirrored in the glycated hemoglobin concentration. Intragroup difference before

and after three months of ginseng intake was highly significant ($p < 0.005$) only in the Siberian group [Figure 3](#). In addition, intergroup differences at the end of the third month shows a significant difference ($p < 0.05$) in comparison to the Panax and the placebo group [Figure 3](#).

comparison of siberain versus panax ginseng on glycolated hemoglobin (HbA1c) in type 2 diabetics before and after three months (mean \pm SD)

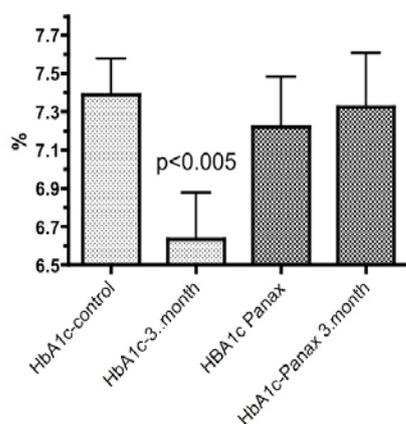


Figure 3. Differences in concentration of glycated hemoglobin (HbA1c) within the erythrocyte in type 2 diabetic patients before and after three months of intake of Siberian versus Panax ginseng

2.3. Ginseng on Lipid Metabolism

Aside from the significant beneficial effect of a regular intake of Siberian ginseng on the unbalanced carbohydrate metabolism, there is also a beneficial effect on lipid metabolism. This is reflected in the concentrations of total cholesterol and triglyceride. While the official accepted total cholesterol and triglyceride levels greatly exceed the normal range of 185 mg/dl (= 4.8 mmol/L) and 150 mg/dl (= 1.7 mmol/L) respectively in all three groups at the start of the study [Table 1](#), daily intake of both ginseng preparations resulted in a gradual reduction within the two groups. This decline, however, is significant only in the Siberian ginseng group [Figure 4](#). Starting off with mean total cholesterol level at 227 (± 52 SD) mg/dl it slowly

declined to a mean of 206 (± 47 SD) mg/dl at the end of the study. The difference between the three groups is highly significant ($p < 0.01$) in favor of Siberian ginseng. Similar effects were noted on the triglyceride level, which dropped from a mean of 278 (± 122 SD) mg/dl to a mean of 172 (± 83 SD) mg/dl, which statistically is significant at the $p < 0.001$ level. No such significant differences were noted following the intake of Panax ginseng or placebo, as high total cholesterol showed no improvement at the end of the study when compared to control values. Starting of at 223 (± 54.3 SD) mg/dl, total cholesterol even slightly rose to 229 (± 57.8 SD) mg/dl after intake of Panax ginseng while it stayed at a high level in the placebo group (239 ± 50 SD). Only triglyceride concentration demonstrated some decline from a mean of 229 (± 129 SD) mg/dl to a mean of 220 (± 119 SD) mg/dl in the Panax group, which however, was not statistically significant.

2.4. Ginseng on Peripheral Neuropathy

In addition to the advantageous effect of Siberian ginseng on carbohydrate and lipid metabolism, there is also some favorable effect on peripheral neuropathy, being determined by the threshold for sensitivity and pain to an applied electrical stimulus. As demonstrated in [Table 2](#) both thresholds significantly decreased ($p < 0.01$) only in the group taking Siberian ginseng. This beneficial effect is seen on both sides of the lower extremities, suggesting a recovery in the mediation of sensory impulses, which in general are impaired in long-lasting diabetes. While there is no change in the placebo group, there seems to be some recovery in sensitivity and an earlier feeling for pain to the applied electrical stimulus after intake of Panax ginseng. However, these changes are not statistically significant [Table 2](#). This is due to the wide standard deviation, especially when determining the threshold for pain, as patients demonstrate no real difference in their previous loss of sensory peripheral nociception following three months of treatment.

Table 2. Increase in thresholds to an electrical stimulus (mA), in regard to sensitivity and feeling of pain in patients with type 2 diabetes and peripheral neuropathy at start and following intake of Siberian ginseng, Panax ginseng or placebo before and after 3 months (mean \pm SD; * $p < 0.01$)

Group	Threshold right leg for sensitivity	Threshold left leg for sensitivity	Threshold right leg for pain	Threshold left leg for pain
Siberian Ginseng	3.1 \pm 1.9 to 2.3 \pm 1.4*	3.3 \pm 1.8 to 2.8 \pm 1.5*	13.6 \pm 6.1 to 11.1 \pm 4.5*	13.5 \pm 7.0 to 10.8 \pm 5.0*
Panax Ginseng	4.2 \pm 2.3 to 3.8 \pm 2.7	4.6 \pm 2.8 to 4.1 \pm 3.1	18.5 \pm 14.0 to 12.9 \pm 8.0	20.5 \pm 15.2 to 15.8 \pm 13.7
Placebo	4.9 \pm 2.4 to 4.7 \pm 2.4	4.8 \pm 3.1 to 4.7 \pm 2.1	22.9 \pm 12.7 to 21.7 \pm 10.7	22.5 \pm 11.9 to 22.0 \pm 12.2

3. Discussion

Ginseng preparations in general have been reported as having some glucose lowering effect [\[24\]](#). However, it has not been clarified, which if the various ginseng plants exhibit a major benefit, and whether other effects may also result from these agents [\[17\]](#). We therefore undertook the study to compare two well characterized ginseng

preparations, not only for their effect on glucose homeostasis, but also on lipid metabolism and peripheral neuropathy in type 2 diabetes.

3.1. Ingredients in Different Ginseng Preparations

The main active substances in Panax ginseng are ginsenosides, which are triterpene saponins. It is because of these ginsenosides that the majority of published

research on the medicinal activity of *Panax ginseng* has been focused [25]. These substances are used to standardize other ginseng products. Reviews [24,26] have postulated that extracts of *Panax ginseng* affect the hypothalamus-pituitary-adrenal axis and the immune system, which could account for many of the documented effects. Animal models and in vitro studies mentioned in these reviews [24,26] indicate that *Panax ginseng* enhances phagocytosis, natural killer cell activity, and the production of interferon, thus improving physical and mental performance in mice and rats. In addition, it supposedly causes vasodilatation, and increases resistance to exogenous stress factors.

3.2. *Panax* and Siberian Ginseng in Diabetics

Aside from such diverse effects, *Panax ginseng* purportedly also influences hyperglycemic activity in patients. Previous data with *Panax ginseng*, given in a dosage of 100 or 200 mg per day for eight weeks in 36 patients with newly diagnosed non-insulin-dependent diabetes showed little improvement on fasting blood glucose levels, elevated mood, and improved psychophysical performance. *Panax ginseng* 200-mg also resulted in some improvement of elevated HbA1c, but no consequence on fasting glucose levels [16]. However, this and another study [27] was done on a short-term basis, the latter evaluating the efficacy of *Panax ginseng* on a glucose test meal. In our group of patients, *Panax* was compared with Siberian ginseng given over a 12-week period and their efficacy was rated not only in regard to fastening and postprandial glucose level but also to HbA1c concentration. This is of importance as high blood glucose levels have been associated with a higher risk of ischemic heart disease, and glycated hemoglobin (HbA1c) mirrors the blood-glucose concentration in the preceding months, also acts as a marker of atherosclerosis risk [28].

Contrary to *Panax ginseng*, Siberian ginseng demonstrated a number of beneficial effects in diabetic patients over a long period of time. Such difference in effects may be due to several factors: In contrast to ginsenosides in *Panax ginseng* preparation, Siberian ginseng (*Eleutherococcus senticosus*) has different chemical compositions. Among saponins and polysaccharides it mainly consists of oleonolacid glycoside, β -stosterol glycoside (eleutheroside A), isofaxidin glycoside (a coumarin derivative), syringaresinol glycoside (eleutheroside E) and chlorogenic acid [18], the latter being considered a key compound for standardization [29]. Its glucose-lowering effect, however, reportedly is due to the specific glycoside-like elements, also termed eleutherosides, which are not a common constituent of *Panax ginseng* [30]. It therefore is reasonable to assume that because of this difference in the composition there is also a difference in the glucose-lowering effect, as demonstrated between the two groups of patients in our study. Only administration of Siberian ginseng induced a constant and steady glucose lowering result, which was highly significant after three months of intake.

3.3. Putative Mode of Action of Siberian Ginseng in Diabetics

As to the mode of action of such glucose lowering appearance, and in spite the fact that type 2 diabetic

patients demonstrate a selective resistance of the receptor to its endogenous ligand insulin, different mechanisms of action can be discussed to account for the observed beneficial result. First, eleutherosides induce an increase in the kinetics of insulin acting on its receptor. This would result in a higher inflow of glucose molecules into target cells. Evidence for such mode of action is the fact that the blood glucose lowering effect of Siberian ginseng is only observed as long as there is a daily intake of the preparation to maintain adequate blood levels. In addition, it had been demonstrated, that the components β -sitosterol as well as β -sitosterol-3- β -D-glucosid increased glucose-induced secretion of insulin resulting in lower plasma glucose levels following an oral glucose test meal [31].

Second, independent of the insulin receptor, the eleutherosides, especially the eleutherosides E and B, induce an insuline-independant transfer of glucose into the cell. There are several reasons to believe that eleutherosides induce such activation within the anabolic process, which is similar to insulin and other anabolic hormones, resulting in an increase of activity of hexokinase and glucose-6-phosphatdehydrogenase, as demonstrated in isolated cell cultures [32]. In addition, eleutherosides may selectively neutralize the β -lipoprotein-induced block of transfer of glucose through cellular membranes. Such anabolic actions have been demonstrated in vivo and in vitro tissue studies [30,33,34]. Thirdly, extracts of Siberian ginseng, due to their steroidal activity, have been shown to bind to mineralocorticoid, glucocorticoid and estrogen receptor sites [35], triggering off an anabolic process. This very well may result in an increased metabolism of glucose with a glucose-lowering result. There is some evidence for such a physiological effect on the insulin-glucagon-epinephrine-axis, as the extracts of Siberian ginseng induce hyperglycemia in the early stage of stress and a hypoglycemic action in the "post adaptation" phase of a general stress response [36].

And lastly, Siberian ginseng may interfere with the way the body processes certain drugs, herbs, or supplements using the liver's cytochrome P450 enzyme system, p-glycoprotein, or SULT1A3. As a result, the levels of these agents may change in the blood and may cause increased or decreased effects or potentially serious adverse reactions. Patients taking any medications should check the package insert and speak with a qualified healthcare professional, including a pharmacist, about possible interactions. This is corroborated by data demonstrating that, *eleutherococcus* selectively inhibits p-glycoprotein (PGP) drug efflux pump [37] which are the mainstay of a pump-off mechanism of cellular structures. Such mechanism of action results in an increase of the intracellular accumulation of insulin through direct interaction with PGP at the azidopine site [38].

3.4. Mode of Action of Beneficial Effects on Lipid Metabolism

Aside from a beneficial effect on the carbohydrate metabolism, there is also a favorable effect on the lipid metabolism. Not being metabolically inert, fat cells possess a very active glucose transport system, a well-developed hexokinase and glycolyte activity and a very intense rate of fatty acids formation from glucose. It is because of because of glucose deficiency within the cell,

that via acetyl coenzyme A, fatty acids and its components triglyceride and cholesterol from glucose are formed in excess. As a consequence of the correction of glucose transfer, the pathologic lipid metabolism is normalized with an ensuing decline in the previously high cholesterol and triglyceride levels. The present results demonstrate such gradual decline of elevated cholesterol and triglyceride levels, which goes in hand with a correction of glucose metabolism. Such beneficial effects are of clinical relevance, since a 1% reduction in total cholesterol has been associated with a risk reduction for ischemic heart disease by 2-3% [39], 76, a 10% reduction in cholesterol leads to a 20% reduction in ischemic heart disease [40], and a reduction of only 0.6 mmol/l at any point on the scale to a 50% reduction at the age of 40 [41]. Thus, the present results corroborate others, who also documented a significant lowering effect on total cholesterol and triglyceride level of Siberian ginseng in man [42].

3.5. Putative Mode of Action of Siberian Ginseng on Periheral Neuropathy

In addition to the beneficial effects on carbohydrate and lipid metabolism, subclinical signs of diabetic peripheral neuropathy improved with Siberian ginseng, especially small nerve fiber mediated pain. Although in the present patient population no signs of large fiber dysfunction with motor and/or neuropathic ulcerations were evident, the abnormal increase in measured thresholds to an electrical stimulus suggests latent neuropathological changes. While in a normal population, the threshold of pain to an electrical stimulus is around 7.5 mA [43,44,45], the present patient population with type 2 diabetes identified the stimulus as pain at a mean intensity of 18 mA. This twofold increase is indicative for sensory peripheral neuropathy with a damage of sensory nerves. Since peripheral neuropathy begins gradually and therapeutically can effectively only be managed by a strict control of the elevated blood glucose level, the present data support such an advantageous property of Siberian ginseng. Its additional intake seems to be able to modulate the pathologically deranged carbohydrate metabolism to such a degree, that chronically developing complications such as peripheral neuropathy gradually declines. This is clearly demonstrated by the present data, where the previous subclinical but abnormal sensory and pain threshold levels to an electrical stimulus after a long-term intake of Siberian ginseng gradually normalizes. Patients responded to sensation at lower threshold levels and develop an earlier feeling of pain, suggesting a recovery on the previously deteriorated afferent sensory nervous function.

3.6. Conclusion of Study

Panax ginseng has different pharmacodynamic properties when compared to Siberian ginseng (*Eleutherococcus senticosus*). What has now been demonstrated is that in contrast to *Panax ginseng* and placebo, Siberian ginseng is able to lower elevated blood sugar levels in patients with type 2 diabetes, both at fasting states and after eating. This is also the first report demonstrating a favorable long-term effect on lipid metabolism and on peripheral neuropathy. The doses taken at regular interval were safe and effective, and they did not carry a significant risk of causing dangerously low

blood sugar levels (hypoglycemia) in diabetes patients, which otherwise took standard prescription drug medication. In addition, because of the lack in developing hypoglycemia in any of our patients, Siberian ginseng can be considered an agent for assisting in the correction of an abnormal carbohydrate and lipid metabolism in people with type 2 diabetes. However, from the results of this study one cannot draw the conclusion, that Siberian ginseng is a substitute for any oral antidiabetic medication. It should be considered an adjunct to diabetic therapy and may act additively or possibly synergistically with standard oral antidiabetic agents. This seems a rational approach as a premiss of insulin is advocated in patients, which otherwise are failing to reach glycemetic targets on basal insulin [46]. Because if the favorable results, a follow-up study with Siberian ginseng should be undertaken, where the preparation is given for a period of at least a year.

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