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Effect of Serial Administration of Ginsenoside-Rb_2 on Streptozotocin-diabetic Rats

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Abstract

The effect of ginsenoside-Rb_2 purified from ginseng was examined in rats with streptozotocin-induced diabetes. The rats of the ginsenoside-Rb_2-treated group showed a significant decrease in blood glucose level as well as a significant decrease of glucose-6-phosphatase in the liver, whereas a significants rise was observed in the activity of glucokinase. Furthermore, the rats treated with ginsenoside-Rb_2 showed a significant decrease of glucose and a slight increase of glycogen in the hepatic tissue. The glucose-6-phosphate level tended to increase, the pyruvate level was unchanged and the lactate level tended to decrease. There was, however, no accumulation of total lipid in hepatic tissue. The serum levels of triglyceride, non-esterified fatty acid, 3-hydroxybutyrate and acetoacetate were markedly decreased, showing a trend toward restoration of the normal state and inducing an increase in lipids in the adipose tissue. Additional experiments involving long-term administration of ginsenoside-Rb_2 produced results suggesting that ginsenoside-Rb_2 may improve diabetic symptoms such as overeating, overdrinking, polyuria and glycosuria.

Introduction

Metabolic disorders occurring in diabetes mellitus include general abnormalities of metabolism as a whole, involving lipids, proteins and carbohydrates. Through this disorder, the metabolic pattern in the body comes to resemble that in starvation, due to insulin deficiency, despite the fact that food is ingested. Therefore, the starvation-type regulation mechanism, which would normally act to maintain the homeostasis of the body, conversely gives rise to a vicious cycle.[1] The action of ginsenoside-Rb_2 in normalizing this kind of metabolic disorder has been observed in some cases. Consecutive intraperitoneal administration of ginsenoside-Rb_2 to diabetic rats resulted in an obvious, persistent decrease in blood glucose through increased glycolytic metabolism, with evidence of improvement in diabetic symptoms such as body weight loss, polyphagia, polyposia, polyuria and glucosuria. The present paper described the findings obtained in our experiments.

Materials and Methods

Animals : Male rats of the Wistar strain, weighing 150-160g, were employed in this experiment. The animals were maintained in an air-conditioned room with lighting from 6 a.m to 6 p.m. The room temperature (about 23°C) and humidity (about 60%) were controlled automatically.

A laboratory pellet chow (obtained from CLEA Japan Inc., Tokyo; protein 24%, lipid 3.5%, carbohydrate 60.5 %) and water were made freely available. Six rats were used for each experimental group. Values were expressed as mean± S.E.

Streptozotocin-induced diabetic rats: Streptozotocin (50 mg/kg body weight) dissolved in 10 mM citrate buffer (pH 4.5) was injected intraperitoneally.[2] Several days after the injection, the blood glucose level was determined and rats with a level of 350-550 mg/dl were used as diabetic rats.

Saponin: Ginsenoside-Rb_2 was isolated and purified from a root extract of Panax ginseng C.A. Meyer produced in Kumsan, Korea. The structure of ginsenoside-Rb_2 was previously established by Sanada et al.[3] as 20S-protopanaxadiol-3-[O-β-D-glucopyranosyl(1→2)-β-D-glucopyranoside]-20-[O-α-L-arabinopyranosyl (1→6)-β-D-glucopyranoside].

Treatment with ginsenoside-Rb_2: Ginsenoside-Rb_2 (10 mg/rat/day) in saline was administered intraperitoneally to rats every day, while control rats were treated with an equal volum of saline. At 8 h after the last treatment, rats were sacrificed by means of a blow on the head, and exsanguinated. Rats were killed between 3 and 4 p.m to avoid the effect of circadian variation. The blood was collected in a conical centrifuge tube. The serum was separated by centrifugation immediately after collection of the blood. The liver and epididymal adipose tissue were removed quickly. The liver was placed in liquid nitrogen, while the adipose tissue was cooled on ice.

Determination of serum constituents and urinary glucose : Glucose, triglyceride, non-esterified fatty acid and total cholesterol were determined using commercial reagents (Glucose B-Test Wako obtained from Wako Pure Chemical Industries, Ltd., Osaka, Japan; TG-Five Kainos obtained from Kainos Laboratories, Inc., Tokyo, Japan; NEFA Kainos obtained from Kainos Laboratories, Inc.; Cholesterol B-Test Wako obtained from Wako Pure Chemical Industries, Ltd.). 3-Hydroxybutyrate was determined spectrophotometrically by measuring the increase of optical density at 340 nm resulting from the oxidation of 3-hydroxybutyrate by 3-hydroxybutyrate dehydrogenase and nicotinamide adenine dinucleotide (NAD).[4] The determination of acetoacetate was based on the decrease in extinction at 340 nm due to the oxidation of reduced nicotinamide adenine dinucleotide (NADH).[5] Lactate was determined by a spectrophotometric method, based on measurement of the increase in optical density at 340nm.[6]

Determination of glucose-6-phosphatase activity in the liver : The liver was homogenized in 9 volumes of 0.25M sucrose. The crude homogenate was centrifuged at 11,000 x*g* for 30 min and the precipitate was discarded. The supernatant fluid was further centrifuged at 105,000 x*g* for 60 min and the supernatant fluid was discarded.

The solid precipitate (microsomes) was suspended in ice-cold sucrose-EDTA solution and stored at -20°C until required. The activity of glucose-6-phosphatase was assayed according to the method of Baginski *et al.* with slight modification.[7] The assay mixture contained 0.25 M sucrose-1 mM EDTA (pH 7.0), 0.1 M glucose-6-phos-

phate and 0.1M cacodylate buffer (pH 6.5) in a total volume of 0.3ml. The reaction was started by the addition of a suitably diluted enzyme solution to the assay mixture. After incubation at 37°C for 5 min, the reaction was terminated by the addition of 2 ml of 2% ascorbic acid-10% TCA solution. The precipitate formed was removed by centrifugation after the mixture had been left to stand in an ice-bath. A 0.5ml aliquot was pipetted off and the liberated inorganic phosphate in the supernatant was determined by using a commercial reagent (Phosphor B-Test Wako obtained from Wako Pure Chemical Industries, Ltd.).

Determination of glucokinase activity in the liver : A homogenate of each liver was prepared in 2 volumes of homogenizing medium (0.15M KCl containing 0.004 M $MgSO_4$, 0.004 M EDTA and 0.004M N-acetylcysteine, pH 7.0). This crude homogenate was centrifuged at 105,000 x*g* for 60 min. The supernatant fraction was used for the enzyme assay of glucokinase by the method of Walker and Parry.[8]

Determination of glycogen in the liver : A portion of the liver was digested with 3 ml of 1 N NaOH in a boiling water bath for 60 min, and glycogen was precipitated by the addition of 2 ml of EtOH followed by purification according to the method of Roe and Dailey.[9] Liver glycogen was determined by the anthrone-H_2SO_4 method, with glucose as the standard.[10]

Determination of glucose in the liver : A liver sample was homogenized with 9 volumes of cold 0.9% NaCl. A portion of the homogenate was deproteinized with equimolar amounts of $ZnSO_4$ and $Ba(OH)_2$,[11] and precipitates were removed by centrifugation. Glucose in the supernatant was determined using a commercial reagent.

Determination of glucose-6-phosphate in the liver : [12] A frozen liver sample was powdered in a porcelain mortar continuously chilled with liquid N_2. Aliquots of the powder were transferred to a chilled glasse homogenizer. Five volumes of 0.6 N PCA were added and the mixture was homogenized. Precipitated proteins were removed by centrifugation at 3,000 x g for 10 min. Aliquots of the supernatant were neutralized to pH 3.5 with K_2CO_3. The solution was allowed to stand in an ice-bath for about 15 min and then the supernatant was pipetted off. A portion of the supernatant was used for the assay. The supernatant fluid (1 ml), triethanolamine buffer (0.4 M; pH 7.6), *nicotinamide adenine dinucleotide phosphate* (NADP) (20mM), $MgCl_2$ (0.5M) and glucose-6-phosphate dehydrogenase (0.25 mg protein/ml) were placed in a cuvette, and the increase of optical density at 340nm was determined with a Hitachi 200-20 spectrophotometer.

Determination of pyruvate in the liver:[13] A liver sample was homogenized with 4 volumes of 5% TCA and then centrifuged at 3,000 x g for 10 min. The supernatant fluid obtained was used for the estimation of pyruvate by the 2.4-dinitrophenylhydrazone method.

Determination of lactate in the liver[6] : A portion of the liver was homogenized with 5 volumes of 1 N PCA and precipitates were removed by centrifugation at 3,000 x*g* for 10 min. Aliquots of the supernatant were neutralized to pH 3.5 with K_2CO_3. The solution was allowed to stand in an ice-bath for about 10 min and then precipitated $KClO_4$ was filtered off. Lactate in the supernatant was determined by a spectrophotometric method, based on measurement of the increase in optical density at 340 nm.

Determination of total lipid, triglyceride, total cholesterol, phospholipid and non-esterified fatty acid in the liver and adipose tissue : A liver sample was homogenized with 3 volumes of ice-cold 0.9 % NaCl solution. The homogenate was filtered through 4 layers of gauze and 1 ml of the filtrate was mixed with 20 ml of $CHCl_3$-MeOH (2:1, v/v). Epididymal adipose tissue was placed immediately in 20ml of $CHCl_3$ MeOH mixture (2 : 1, v/v). Total lipid was extracted from both tissues by shaking. The residue tissues were then removed and the $CHCl_3$-MeOH solution was partitioned and washed by the method of Folch *et al.*[14] The organic solution was evaporated and the residue was dried over P_2O_5 overnight. The concentration of total lipid was determined by gravimetry. A portion of the $CHCl_3$-MeOH solution extracted from both tissues was used for the estimation of triglyceride, total cholesterol, phospholipid and non-esterified fatty acid. Determinations were performed using commercial reagents.

Statistics : The significance of differences between the non-diabetic and diabetic rats (control or ginsenoside-Rb_2-treated group) was tested by means of Student's *t* test.

Results

Effect of ginsenoside-Rb_2 on carbohydrate and lipid metabolism : When ginsenoside-Rb_2 at a dose of 10mg/day was administered for 6 consecutive days, as shown in Fig. 1, the blood glucose level exhibited a significant decrease from 425 to 150 mg/dl. Even in rats given a dose of 2 mg once a day for 6 days, the blood glucose level fell to 400mg/dl, a significant decrease of 15% from the control value. However, the blood glucose level of normal rats hardly changed.

As part of our research on the mechanism responsible for the decrease of blood glucose level in diabetic rats,

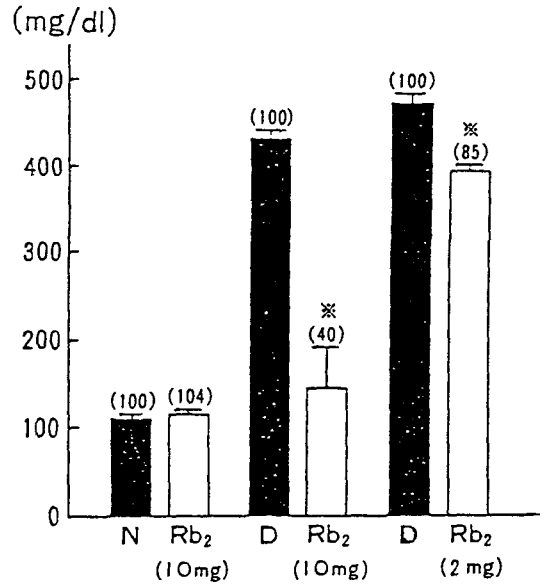

Fig. 1. Effect of Ginsenoside-Rb_2 on Blood Glucose Level

N, non-diabetic rat (control group); D, diabetic rat (control group); Rb_2, non-diabetic or diabetic rat (group treated with ginsenoside-Rb_2 for 6 days). Figures in parentheses are percentages of the non-diabetic or diabetic control value. *Significantly different from the control value, $p<0.001$.

Table 1. Effect of Ginsenoside-Rb_2 on Ezyme Activities in the Liver

	Glucose-6-phosphatase (μmol/min/mg protein)	Glucokinase (△OD/h/mg protein)
Non-diabetic rat	16.7± 0.7 (100)	201.7± 12.0 (100)
Diabetic rat		
Control	40.4± 3.3 (242)*** [100]	15.9± 2.9 (8)*** [100]
Rb_2	27.9± 1.3 (167)*** [69]**	25.3± 1.9 (13)*** [159]*

Ginsenoside-Rb_2(10 mg/rat/day) was administered intraperitoneally to diabetic rats for 6 days, while the control group received an equal volum of saline. Figures in parentheses are percentages of the non-diabetic or diabetic control value. * Significantly different from the non-diabetic or diabetic control value, $p<0.05$; **$p<0.01$; ***$p<0.001$.

further studies were performed from the viewpoint of enzyms activities, carbohydrate metabolites and lipid constituents in the liver, adipose tissue and serum.

The effects of ginsenoside-Rb_2 on hepatic enzyme activities are shown in Table 1. These enzymes play an important role in the maintenance of blood glucose. In diabetic control rats, glucose-6-phosphatase activity was increased about 2.4-fold in comparison with that of normal rats. The change in glucokinase activity was inversely related to that of glucose-6-phosphotase activity and its activity was markedly low. Six days of ginsenoside-Rb_2 administration resulted in a singnificant decrease of glucose-6-phosphatase activity, while the glucokinase activity of rats treated with ginsenoside-Rb_2 showed a significant elevation. The glucose-6-phosphatase/glucokinase activity ratio was improved by ginsenoside-Rb_2 adiminstration. Thus, it may be considered that ginsenoside-Rb_2 produces its hypoglycemic activity by changing the levels of gluconeogenic and glycolytic enzymes.

Furthermore, diabetic rats exhibited a significant elevation of hepatic glucose, and a tendency toward an increase of pyruvate and lactate as compared with non-diabetic normal rats. The contents of glycogen and glucose-6-phosphate behaved differently from those of the other carbohydrate metabolites, decreasing by approximately 20% and 12%, respectively. When ginsenoside-Rb_2 was successively given at a dose of 10 mg once a day for 6 days, the hepatic glucose content fell to 9.42 mg/tissue (significantly decreased by 27% of the control value). In contrast, administration of ginsenoside-Rb_2 to rats slightly increased the amounts of glycogen and glucose-6-phosphate. These changes were inversely related to that of hepatic glucose content. However, pyruvate and lactate contents showed no appreciable changes when ginsenoside-Rb_2 was administered (Table 2).

Table 3 shows the contents of hepatic lipid constituents. A slight increase of the total lipid content was seen in diabefic rats as compared with the non-diabetic normal rats. This change was reflected in the triglyceride content, which was increased to 36.6 mg/tissue compared with 26.0 mg/tissue in normal rats. This table further indicates that the amount of phospholipid was decreased significantly as compared with non-diabetic rats, while the level was remarkably hight in the ginsenoside-Rb_2 administered group. On the other hand, hepatic triglyceride was extremely low, at a near-normal level, in the ginsenoside-Rb_2-administered group. Administration of ginsenoside-Rb_2 to rats caused no appreciable changes in the total lipid and total cholesterol contents of the liver.

The contents of lipid constituents in adipose tissue were significantly decreased in diabetic rats as compared with the non-diabetic normal rats: total lipid 40%, triglyceride 37% and phospholipid 26%. A striking increase in total lipid and triglyceride contents was observed after 6 administrations of ginsenoside-Rb_2. The phospholipid content was also increased by 24% by ginsenoside-Rb_2, but non-esterified fatty acid showed no appreciable change (Table 4).

Figure 2 shows the effect of ginsenoside-Rb_2 on lipid constituents in the serum. The levels of triglyceride, non-esterified fatty acid, 3-hydroxybutyrate and acetoacetate were significantly increased in diabetic rats as compared with the non-diabetic rats. The ginsenoside-Rb_2 treated rats showed a significant decrease in triglyceride level; as shown in Fig. 2, the triglyceride level was about 50% less at the 6th day in the ginsenoside-Rb_2-treated group than that in the control group. Similarly, administration of ginsenoside-Rb_2 produced a significant decrease in

Table. 2. Effect of Ginsenoside-Rb_2 on Carbohydrate Metabolites in the Liver

	Glycogen (mg/tissue)	Glucose (mg/tissue)	Glucose-6-phosphate (mg/tissue)	Pyruvate (mg/tissue)	Lactate (mg/tissue)
Non-diabetic rat	168.9± 17.8 (100)	8.89± 0.51 (100)	0.41± 0.06 (100)	0.19± 0.04 (100)	11.58± 0.96 (100)
Diabetic rat					
Control	134.5± 14.9 (80) [100]	12.97± 1.00 (146)* [100]	0.36± 0.02 (88) [100]	0.25± 0.03 (132) [100]	13.63± 1.61 (118) [100]
Rb_2	152.1± 7.7 (90) [113]	9.42± 0.52 (106) [73]*	0.44± 0.04 (107) [122]	0.25± 0.01 (132) [100]	11.20± 1.14 (97) [82]

Details are the same as in the legend to Table 1. *Significantly different from the non-diabetic or diabetic control value, $p<0.05$

Table. 3. Effect of Ginsenoside-Rb_2 on Lipid Constituents in Liver

	Total lipid (mg/tissue)	Triglyceride (mg/tissue)	T. cholesterol (mg/tissue)	Phospholipid (mg/tissue)
Non-diabetic rat	188.4± 4.9	26.0± 2.0	8.9± 0.5	91.3± 1.2
	(100)	(100)	(100)	(100)
Diabetic rat				
Control	201.3± 5.1	36.6± 2.5	8.8± 0.6	82.5± 1.3
	(107)	(141)*	(99)	(90)***
	[100]	[100]	[100]	[100]
Rb_2	192.3± 6.3	27.8± 3.6	9.2± 0.2	98.5± 1.6
	(102)	(107)	(103)	(108)*
	[96]	[76]*	[105]	[119]**

Details are the same as in the legend to Table 1. *. * Significantly different from the non-diabetic or diabetic control value, $p<0.05$; **.**$p<0.01$.

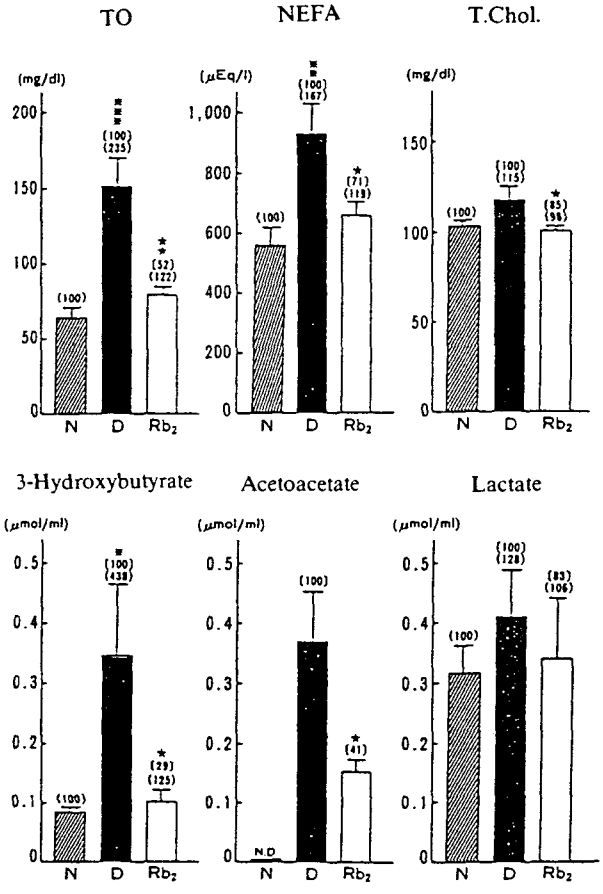

Fig. 2. Effect of Ginsenoside-Rb_2 on the Lipid Constituents in the Serum

N, non-diabetic rat; D, diabetic rat (control group); Rb_2, diabetic rat (group treated with ginsenoside-Rb_2 10mg/rat/day for 6 days). Figures in parentheses are percentages of the non-diabetic or diabetic control value. *. * Significantly different from the non-diabetic or diabetic control value, $p<0.05$; **.**, $p<0.01$; *** $p<0.001$. Abbreviations: TG, triglyceride; NEFA, non-esterified fatty acid; T. Chol., total cholesterol.

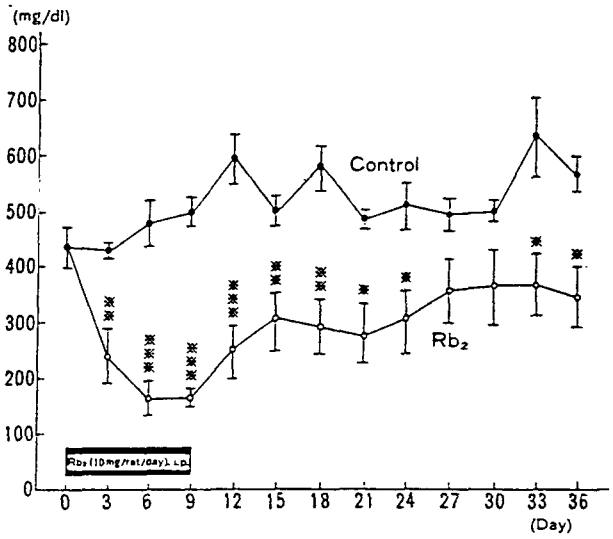

Fig. 3. Effect of Ginsenoside-Rb_2 on Blood Glucose Level

●—●, Control group ; ○—○, group treated with ginsenoside-Rb_2 10 mg/rat/day. * Significantly different from the control value, $p<0.05$; **$p<0.01$; ***$p<0.001$.

non-esterified fatty acid. Furthermore, a conspicuous decrease was observed in the levels of 3-hydroxybutyrate and acetoacetate. The total cholesterol level was also about 15% lower after 6 administrations. Lactate showed no significant change.

Improving effect on diabetic symptoms by long-term administration of ginsenoside-Rb_2: The changes in blood glucose levels are shown in Fig. 3. When ginsenoside-Rb_2 was successively given at a dose of 10 mg once a day, the blood glucose level fell to 240 mg/dl after 3 days of administration and to about 160 mg/dl on the 6th day of administration. The level on the 9th day was similar to that on the 6th day. Administration was stopped after 9 days and subsequently the changes in blood glucose level were followed. Blood glucose levels of about 300 mg/dl persisted up to the 36th day of the experiment. Therefore, a low blood glucose level was maintained for a markedly longer time in rats receiving ginsenoside-Rb_2, in comparison with the control.

Next, during the period when the level of blood glucose remained relatively constant after discontinuation

Table. 4. Effect of Ginsenoside-Rb_2 on Lipid Constituents in the Adipose Tissue

	Total lipid (mg/tissue)	Triglyceride (mg/tissue)	Phospholipid (mg/tissue)	Non-esterified fatty acid (mg/tissue)
Non-diabetic rat	218.4± 15.0	167.3± 12.1	16.0± 1.4	2.47± 0.21
	(100)	(100)	(100)	(100)
Diabetic rat				
Control	131.0± 9.8	105.4± 7.0	11.8± 0.9	2.15± 0.11
	(60)**	(63)**	(74)*	(87)
	[100]	[100]	[100]	[100]
Rb_2	183.7± 10.1	152.6± 11.2	14.6± 1.0	2.13± 0.10
	(84)	(91)	(91)	(91)
	[140]**	[145]**	[124]*	[119]

Details are the same as in the legend to Table 1. *.*Significantly different from the non-diabetic or diabetic control value, $p<0.05$; **, **$p<0.01$.

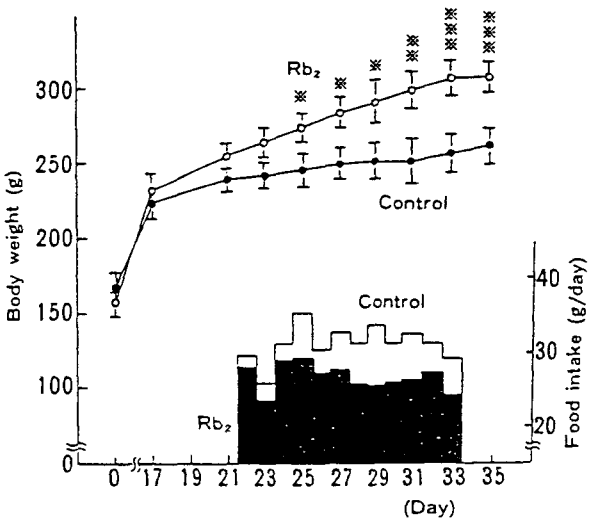

Fig. 4. Effect of Ginsenoside-Rb_2 on Changes in Body Weight and Food Intake

● − ● and □, Control group ; ○ − ○ and ■, group treated with ginsenoside-Rb_2 10 mg/rat/day. * Significantly different from the control value, $p<0.05$; **$p<0.01$; ***$p<0.001$.

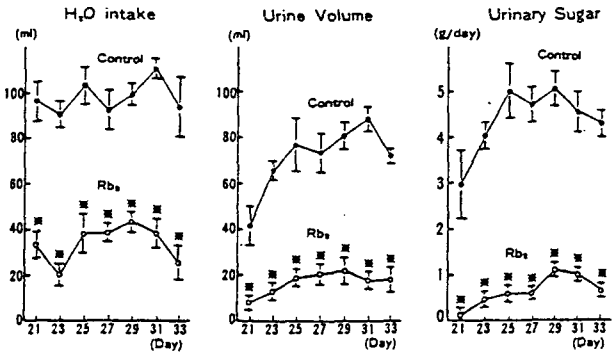

Fig. 5. Effect of Ginsenoside-Rb_2 on H_2O Intake, Urinary Output and the Level of Urinary Glucose

● − ●, Control group ; ○ − ○, group treated with ginsenoside-Rb_2 10 mg/rat/day. *Significantly different from the control value, $p<0.001$.

of ginsenoside-Rb_2 administration, measurement of body weight and food intake was carried out. As shown in Fig. 4, body weight increased to a significantly greater extent in the ginsenoside-Rb_2-treated group. However, the daily intake of food was smaller, despite the larger weight gain.

Figure 5 shows intake of drinking water, urinary output and the level of urinary glucose during the period when the ginsenoside-Rb_2-treated group showed a persistently low relative blood glucose level, that is, from the 21st to 33rd days. Daily intake of drinking water was 90-110 ml in the control group, while it was remarkably low (20-40ml) in the ginsenoside-Rb_2-administered group. Similarly, urinary output was markedly low, close to normal, in the ginsenoside-Rb_2-administered group. The level of urinary glucose was 3-5 g/day in the control group, while it was extremely low (0.1-1.1 g/day) in the ginsenoside-Rb_2-administered group.

Discussion

As reported previously,[15,16] in normal rats, intraperitoneal administration of ginsenoside-Rb_2 caused a decrease in hepatic glycogen content followed by an increase in both the content of glucose-6-phosphate and in the activities of glucose-6-phosphate dehydrogenase, phosphofructokinase, malic enzyme and acetyl-CoA carboxylase in the hepatic tissue. In the adipose tissue, increased lipoprotein lipase activity, decreased hormone-sensitive lipase activity, and an increased triglyceride content were found. A series of effects of ginsenoside-Rb_2 to facilitate carbohydrate and lipid metabolism were observed. That is, in normal rats, increased glycolytic metabolism, starting from the decomposition of hepatic glycogen, led to an increase in the triglyceride content of adipose tissue through very-low-density lipoprotein in the blood.

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increase in both the content of glucose-6-phosphate and in the activities of glucose-6-phosphate dehydrogenase, phosphofructokinase, malic enzyme and acetyl-CoA carboxylase in the hepatic tissue. In the adipose tissue, increased lipoprotein lipase activity, decreased hormone-sensitive lipase activity, and an increased triglyceride content were found. A series of effects of ginsenoside-Rb_2 to facilitate carbohydrate and lipid metabolism were observed. That is, in normal rats, increased glycolytic metabolism, starting from the decomposition of hepatic glycogen, led to an increase in the triglyceride content of adipose tissue through very-low-density lipoprotein in the blood.

On the other hand, whereas no decrease in blood glucose level was found in normal rats, a single administration of ginsenoside-Rb_2 caused a slight decrease of blood glucose in diabetic rats, as reported previously.[17] In addition, when ginsenoside-Rb_2 at a dose of 10 mg/day was administered for 6 consecutive days, the blood glucose level was significantly decreased.[18]

In the present study, the blood glucose-decreasing effect was investigated in terms of carbohydrate and lipid metabolism. A significant decrease in hepatic tissue glucose in proportion to the decrease in blood glucose was found. The contents of hepatic glucose-6-phosphate and glycogen were slightly increased after ginsenoside-Rb_2 administration. However, the rats of the ginsenoside-Rb_2-treated group showed a less marked effect on the content of pyruvate and lactate in the liver. There was also no accumulation of total lipid in hepatic tissue, and the decreased glucose was not accumulated as lipids. In addition, serum triglyceride, non-esterified fatty acid, ketone body and total cholesterol were significantly decreased, showing a trend toward restoration of a normal state and inducing an increase in adipose tissue lipid. On the basis of these findings, it is speculated that, in diabetic rats, ginsenoside-Rb_2 first facilitates the utilization of blood glucose in the liver and consequently leads to an increase in adipose tissue triglyceride. In addition, diabetic rats receiving ginsenoside-Rb_2 showed a significant increase in body weight, even though they took less food than untreated diabetic rats. Moreover, their intake of drinking water, urinary output and urinary glucose level were 1/4 - 1/5 of the respective levels in the control group. It was thus apparent that ginsenoside-Rb_2 has continuous effectiveness for improvement of diabetic symptoms.

In conclusion, the present study revealed that consecutive administration of ginsenoside-Rb_2 to diabetic rats resulted in an obvious, persistent decrease in blood glucose due to increased glycolytic metabolism, with evidence of improvement in diabetic symptoms such as body weight loss, polyphagia, polyposia, polyuria and glucosuria. These actions are very similar to the metabolic alterations produced by insulin. Further study along these lines is planned.

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H. Okuda: Did you estimate catecholamine content after administration of ginsenoside Rb_2 ?

T. Yokozawa: I am sorry I have not determined. However, hormonal behavior in the body is important problem. I would like to determine catecholamine as well as insulin.

B. H. Han: What is SI fraction you used in this experiment and did you separate it clearly ?

K. J. Na: We purified the SI fraction from red ginseng buthanol layer. The physical and chemical properties of it is not yet fully studied.

Streptozotocin 유발 당뇨병성 쥐에대한 Ginsenoside-Rb_2의 연속투여 효과

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Streptozotocin으로 유발시킨 당뇨병성 쥐(혈당수준430± 30 ml/dl)에게 ginsenoside-Rb_2를 연속적으로 복강투여 하였다. Ginsenoside Rb_2 투여군은 현저한 혈당감소를 보였으며 이군들의 혈당수준은 6-9일 투여로 약 160mg/dl로 떨어졌다. 한편 대조군보다 먹이섭취량이 적지만 체중은 ginsenoside-Rb_2를 투여한 당뇨쥐에서 상당히 증가하였다. Ginsenoside-Rb_2투여군은 과식, 다뇨, 당뇨 등과 같은 당뇨병 증상이 개선 되었다. 혈당을 떨어뜨리는 작용기전을 연구하기위한 일환으로 간 및 지방조직 그리고 혈청 등에 있는 탄수화물 대사물질과 지질성분 등에 미치는 ginsenoside-Rb_2의 효과를 조사하였다. 당뇨쥐에서는 ginsenoside-Rb_2가 먼저 정상쥐에서와 같이 간에서 혈당의 이용을 촉진 시키고 그결과 지방조직에 triglyceride 들이 증가되는 것으로 추측된다.