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# Quercetin alleviates activities of intestinal and renal disaccharidases in streptozotocin-induced diabetic rats

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Specific activities of both intestinal and renal dissacharidases, such as sucrase, maltase, and lactase, were altered in diabetic rats. Our study was focused to evaluate the effect of feeding quercetin – a bioflavanoid on intestinal and renal dissacharidases in streptozotocin-induced diabetic rats. The rats were fed with 0.1% quercetin in diet. A reduction in intestinal maltase and sucrase, activities in quercetin-fed diabetic rats was observed in contrast to the increased activities in the starch-fed diabetic rats. A significant amelioration in renal dissacharidase activities in quercetin-fed diabetic rats was observed when compared to decreased activity in starch-fed diabetic rats.

**Keywords:** Diabetes / Disaccharidase / Lactase / Maltase / Quercetin / Sucrase

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## 1 Introduction

Diabetes mellitus is a metabolic disorder characterized by hyperglycemia and insufficient synthesis of endogenous insulin. Prolonged uncontrolled hyperglycemic state leads to complications of diabetes, *viz.*, retinopathy, neuropathy, and nephropathy [1]. Prevention of complications is a key issue due to high premature morbidity and mortality associated with diabetes [2]. Diabetes mellitus is a state of nutrient starvation that frequently results in severe metabolic imbalances and pathological changes in many tissues. In the small intestine this causes significant changes in the morphology and functions of mucosa [3]. During diabetes there is increased glucose absorption in the small intestine [4]. This may be attributed to the increase in intestinal disaccharidase activities. These disaccharidases are essential for terminal absorption of carbohydrate digestion especially in the conversion of disaccharides to readily soluble monosaccharides. Studies have shown that hyperglycemia alters the activities of intestinal disacharidases, such as maltase, sucrase, lactase, *etc.*, in rats and humans [5, 6]. Similar changes to some extent were also seen in renal cortex [5]. Luminal membrane upregulation and larger segment of intestinal villus appears to be responsible for alterations in glucose uptake and transport in streptozotocin-induced diabetic rats [7].

Although exogenous insulin and other medications can control many aspects of diabetes, the management of diabetes is well-established to play a key role in longevity and quality of life. In this aspect, the roles of many traditional practices involving medicinal plants are known to have preventive and therapeutic value in diabetes management. The bioactive principles of medicinal plants and foods of medicinal value are receiving much scientific attention in recent years. In this direction, antioxidants are of considerable interest [8]. Higher oxidative stress is one of the factors implicated in the development and progression of diabetic complications resulting in increased levels of free radicals [9] or impaired antioxidant defense mechanisms [10]. It is also shown that pancreatic β-cells have a lower level of free radical-scavenging potential [11]. Epidemiological evidence has suggested that antioxidant-rich dietary flavanoids have potential health-beneficial effects [12]. Quercetin is a well-documented bioflavonoid occurring in many foods and is known to be present in higher concentrations in onions, apples, broccoli, green tea, and red wine [13, 14]. Hence, the polyphenolic compounds constitute an integral part of human diet though they are considered as non-nutrients. Many studies have focused towards the beneficial properties of quercetin, namely, antiproliferative, antibacterial, antioxidant, antiinflammatory, and anticarcinogenic properties [14]. It is also shown that quercetin modulates key regulatory enzymes like alkaline phosphatase, lens aldose reductase [15, 16], *etc*. Dihydroquercetin is used as an effective antioxidant and as a commercial food additive

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**Abbreviations:** **QFC**, quercetin-fed control; **QFD**, quercetin-fed diabetic; **SFC**, starch-fed control; **SFD**, starch-fed diabetic

[14]. The physiological significance of dietary flavanoids depends upon their bioavailability and their subsequent interaction with target tissues [17]. However, quercetin is absorbed or transported in the intestine as glycosides, aglycones, or glucuronides by the hexose pathway involving sodium glucose transporter (SGLT) and glucose transporter-5 (GLUT 5) and its conjugation involving intestinal enzymes is a prerequisite for its absorption and metabolism [18, 19]. But the antidiabetic property of quercetin is still an unexplored field, though some work has been done on antioxidant defense in diabetic rats [20]. Earlier we have reported the antidiabetic effect of quercetin in streptozotocin-induced diabetic rats [21]. Although the antioxidant activity and its uptake in the intestinal mucosa have been reported earlier, its potential effect on intestinal and renal disaccharidases is not yet investigated. Our present study is focused mainly on the effect of feeding quercetin (0.1%) on intestinal and renal disaccharidases in streptozotocin-induced diabetic rats.

## 2 Materials and methods

### 2.1 Materials and animals

Streptozotocin, quercetin, maltose, sucrose, and lactose were purchased from Sigma-Aldrich (St. Louis, MO, USA), the GOD/POD kit was from Span Diagnostics Ltd (Surat, India). All other chemicals used were of analytical grade. The study had the consensus of the Institutional Animal Ethical Committee. Six-week-old male Wistar rats (OUTB-Wistar IND cftri), weighing around 110 – 120 g, were taken for the study from the institute animal house facility. Diabetes was induced in fed rats by a single intraperitoneal injection of streptozotocin (55 mg/kg body weight) in freshly prepared citrate buffer (0.1 M, pH 4.5). The control rats were injected with citrate buffer (0.1 M, pH 4.5) only. To streptozotocin-injected rats, glucose water (5%) was given for two days, while control rats injected with citrate buffer received only water [22]. The rats were divided into control groups, each consisting of six rats (SFC-6; QFC-6) and diabetic groups, with 14 rats each (SFD-14; QFD-14). The experimental groups contained starch-fed controls and diabetic rats (SFC/SFD) and quercetin-fed control and diabetic rats (QFC/QFD). The rats were maintained on AIN-76 diet (Table 1) [23]. Water and diet were given *ad libitum*. The starch-fed groups received a starch-based diet. Quercetin was given at 0.1% level in AIN-76-based diet. Fresh diet was given every day.

### 2.2 Collection of urine and blood

Urine was collected (at around 11 o'clock) under a layer of toluene for a period of 24 h by keeping the rats in metabolic cages. At the end of the experiment eight rats were surviving in each of the diabetic groups (SFD/QFD). Both control and diabetic rats were fasted overnight, and the blood was drawn by the retro-orbital plexus during the experiment or from the heart at the time of sacrificing the rats, both at around 9 o'clock in the morning, and collected in tubes containing heparin (20 U/mL blood) to measure the fasting blood glucose. Plasma was separated from the blood and used for the analysis.

**Table 1.** Composition of the basal diet

| Components | SFC/SFD | QFC/QFD |
|---|---|---|
| | (g/kg diet) | |
| Casein | 200 | 200 |
| AIN-76 vitamin mixture | 10 | 10 |
| AIN-76 mineral mixture | 35 | 35 |
| Choline chloride | 2 | 2 |
| Fat | 100 | 100 |
| Corn starch | 653 | 652 |
| Quercetin | – | 1 |

### 2.3 Measurement of urine sugar and fasting blood glucose

The reducing sugar present in the urine was measured by the dinitrosalicylic acid method [24]. The blood glucose level in rats fasted over night was measured by the glucose oxidase method [25] in the plasma using a commercially available kit.

### 2.4 Intestinal and kidney homogenate

The intestinal lumen was cut open after a prior wash with ice-cold saline to remove food particles. The mucosa from the whole intestine was scraped using a glass slide and homogenized in 0.9% saline. Similarly the kidney was homogenized in 0.9% saline and centrifuged at 3000 rpm for 10 min at 4°C. The supernatant obtained was used for the disacharidase assay.

### 2.5 Disaccharidase assay

The amount of glucose released from sucrose, maltose, and lactose was determined by measuring specific activities of sucrase, maltase, and lactase, respectively at 37°C in maleate buffer (0.2 M, pH 6.0) for different time intervals as described by Dahlquist [26]. The amount of protein in the samples was determined by Lowry's method [27].

 

### 2.6 Statistical analysis

The results are represented as mean ± SEM. Student's *t*-test was used for comparison between control, diabetic, and treated groups [28]. *p*-Values of less then 0.05 were considered significant.

## 3 Results

Type 1 diabetes mellitus was induced in male Wistar rats by intraperitoneal injection of streptozotocin. The rats were sacrificed under ether anesthesia when mortality was set in about 6 weeks after injection of streptozotocin which was initially in the starch-fed diabetic group. The diabetic status was assessed by fasting blood glucose (Fig. 1) and urine sugar (Table 2). Quercetin (0.1%) feeding significantly reduced the fasting blood glucose to ~25% compared to starch feeding in diabetic rats (SFD). Quercetin supplementation to the diet showed amelioration in urine excretion of ~42%. Both the control groups (SFC and QFC) gained weight (around 130 – 140 g) during the course of the experiment. The starch-fed diabetic rats (SFD) lost weight

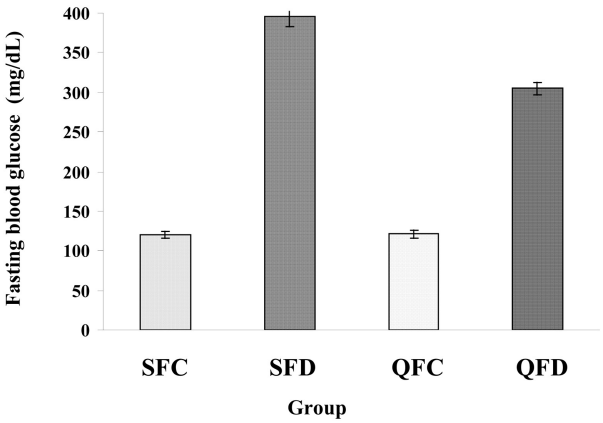


**Figure 1.** Effect of quercetin on fasting blood sugar (mg/dL) in control and diabetic rats.

**Table 2.** Effect of quercetin on urine sugar and urine output in control and diabetic rats

| Group | Urine sugar (g /day) | Urine output (mL/day) |
|---|---|---|
| SFC | 0.08 ± 0.04 | 16.89 ± 3.6 |
| SFD | 6.35 ± 1.31[a)] | 86.83 ± 14.4[a)] |
| QFC | 0.16 ± 0.007 | 14.66 ± 2.7 |
| QFD | 2.94 ± 0.34[b)] | 55.00 ± 4.0[b)] |

Abbreviations as in Table 1. Values are mean ± SEM of six rats in the control groups and eight rats in diabetic groups.
a) Statistically significant when compared to SFC at $p < 0.05$.
b) Statistically significant when compared to SFD at $p < 0.05$.

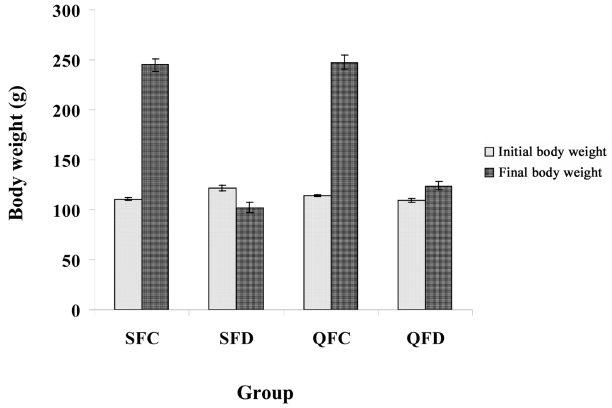


**Figure 2.** Effect of quercetin on body weight (g) in control and diabetic rats. Left column: initial body weight of control and diabetic rats; right column: final body weight of control and diabetic rats.

**Table 3.** Effect of quercetin on activities of intestinal maltase, sucrase, and lactase in control and diabetic rats

| Groups | Maltase | Sucrase | Lactase |
|---|---|---|---|
| | nmol of product formed/mg protein/min | | |
| SFC | 437.66 ± 17.99 | 68.24 ± 10.32 | 32.14 ± 4.17 |
| SFD | 1004.16 ± 72.75[a)] | 93.37 ± 8.29[a)] | 24.17 ± 1.35 |
| QFC | 407.16 ± 52.00 | 64.64 ± 6.97 | 29.67 ± 1.80 |
| QFD | 754.16 ± 38.11[b)] | 78.63 ± 5.11[b)] | 27.57 ± 1.45 |

Abbreviations and footnotes as in Tables 1 and 2.

(Fig. 2), around ~19 g over a period of time when compared to their initial weight, while quercetin-fed diabetic rats (QFD) did not loose weight compared to the starch-fed diabetic group [21].

Disaccharidase activity was tested in the intestine where a twofold increase in maltase activity was observed in starch-fed diabetic rats (SFD) when compared to control rats (SFC). Quercetin in the diet proved to be beneficial in decreasing the maltase activity when compared to starch-fed diabetic rats (SFD). There was a significant increase in sucrase activity in SFD rats compared to the control rats. An effective reduction in the intestinal sucrase activity with quercetin feeding was observed indicating a beneficial role of quercetin in the diet. Our studies did not show significant alteration in lactase activity. Hence, in the intestine, quercetin feeding at 0.1% concentration showed a significant improvement of ~33% and 18% in maltase and sucrase activity, respectively, while lactase activity did not change to a lesser extent (Table 3).

The kidney also showed significant disaccharidase activity in diabetic rats. Renal disaccharidases showed a considerable amelioratory effect in their activities by feeding of quercetin during diabetes (Table 4). A significant decrease

 

**Table 4.** Effect of quercetin on activities of renal maltase, sucrase, and lactase in control and diabetic rats

| Groups | Maltase | Sucrase | Lactase |
|---|---|---|---|
| | nmol of product formed/mg protein/min | | |
| SFC | 151.16 ± 6.07 | 1.32 ± 0.08 | 2.48 ± 0.11 |
| SFD | 96.71 ± 5.39[a)] | 0.70 ± 0.03[a)] | 1.45 ± 0.02[a)] |
| QFC | 165.00 ± 8.72 | 1.42 ± 0.10 | 2.40 ± 0.16 |
| QFD | 117.83 ± 2.46[b)] | 0.93 ± 0.02[b)] | 1.71 ± 0.06[b)] |

Abbreviations and footnotes as in Tables 1 and 2.

during diabetes in all three enzymatic activities is observed when compared to their controls. Quercetin was effective in controlling this decrement. The renal maltase activity in starch-fed diabetic rats (SFD) was decreased when compared to the control. An increase in the maltase activity was observed by quercetin feeding in the diabetic rats (QFD) when compared to the control diabetic rats (SFD). The specific activities of renal sucrase and lactase were decreased during diabetes compared to their control. The decrement in sucrase activity was significantly alleviated in diabetic rats by quercetin feeding. These results showed amelioration in renal disacharidase activities of ~21% in maltase, 33% in sucrase, and 17% in lactase in quercetin-fed diabetic rats (QFD) when compared to the starch-fed diabetic rats (SFD).

## 4 Discussion

The diabetic status was assessed by measuring fasting blood glucose and urine sugar. The blood sugar level in diabetic rats was higher when compared to control rats. Our studies clearly demonstrated an improvement in blood sugar level in quercetin-fed diabetic rats (Fig. 1) [21]. Diabetes is characterized by polyurea. During diabetes sugar is excreted in urine. Our earlier studies showed a substantial decrease in sugar excretion in the quercetin-fed diabetic groups when compared to starch-fed diabetic groups over a period of time, hence showing a two fold improvement [21]. Body weight is an important parameter under diabetic condition. Diabetic rats showed a decrease in body weight. The starch-fed diabetic group lost weight over a period of time, while quercetin-fed rats did not loose weight [21].

Diabetes mellitus is a state of nutrient starvation that frequently results in severe metabolic imbalances and pathological changes in many tissues. During diabetes, metabolic changes in digestion and enhanced sugar transport have been reported [29]. Therefore, studies on alteration in the activities of disacharidases during diabetes and their modulation by feeding quercetin play a key role in understanding the mechanism regulating the progression of the diabetic status. Our present experimental studies showed significant changes in the intestinal and renal disaccharidases, *viz.*, maltase, sucrase, and lactase in streptozotocin-induced diabetic rats fed with quercetin at 0.1% concentration in the AIN-76 diet.

Management of diabetes by dietary treatment is receiving much attention in recent years. Several studies on the effect of diets on intestinal and renal disaccharidases have been reported. Enhanced sugar transport in high-carbohydrate diet and effect of phlorizin and other phenolic glycosides during diabetes has been studied [29, 30]. Insulin has been shown to suppress the intestinal sucrase-isomaltase activity in diabetic rats [31]. Modulatory effects of dietary fiber and butyric acid on intestinal and renal disaccharidases in control and diabetic rats have been reported [32, 33]. Earlier studies have shown that the restriction of food intake increases the total and specific activities of intestinal disaccharidases [34].

Many studies have shown effects of different dietary constituents on intestinal disaccharidases activity during diabetes. Dietary spices or their active principles have been shown to have a positive influence on activities of intestinal disaccharidases [35]. Maltose and sucrose in diets showed increased intestinal maltase and sucrase activities in rats [36]. Our studies have shown a significant improvement in intestinal disaccharidases, *viz.*, maltase and sucrase activity in quercetin-fed diabetic groups (QFD) when compared to starch fed-diabetic groups (SFD), which is in accordance with the studies reported. It has been observed that increased lactase activity in insulin-dependent diabetes mellitus (IDDM) was suppressed by insulin administration [37]. Lactase activity did not change significantly by quercetin feeding during diabetes. This supports the hypothesis that lactose feeding did not show significant alteration in lactase activity in rats [38].

The presence of disaccharidase activities in subcellular fractions of the kidney cortex, their association with lysosomes [39], and the distribution of lactase activity has been reported [40]. However, during diabetes the significance of other disaccharidase activities in renal tissue remains undefined. Our studies on renal tissue showed an effective reduction in disaccharidase activity in starch-fed diabetic rats (SFD) compared to their controls (Table 4). Previous reports have shown decrease in renal disaccharidase activity during diabetes [41]. Our studies have demonstrated that quercetin in the diet is beneficial in improving activities of dissacharidases in the renal tissue in diabetic rats when compared to starch-fed diabetic rats (SFD). The renoprotective potential of quercetin has been reported in ischemic reperfusion injury [42]. Absorption of dietary flavanols and their appearance in plasma and urine correlate to its uptake [43].

 

We have reported earlier that quercetin feeding (0.1%) ameliorates the diabetic status [21], but its role on intestinal and renal disacharidases was not evalated. Our present study clearly suggests that quercetin at 0.1% level in a diet is effective in modulating disaccharidase activity and thereby controlling further progression of diabetic complications. The potent therapeutic effect of quercetin at 0.1% has been shown to reverse diabetic oxidative stress, normalize the glycemic level, and to reduce glycated hemoglobin and cholesterol concentration [20, 44 – 46]. Hii and Howell [44] reported that quercetin enhanced insulin release in isolated islets of Langerhans in rats by altering the $Ca^{2+}$ metabolism, thus showing an antidiabetic activity. The above results clearly provided experimental evidence that quercetin feeding at 0.1% ameliorates disaccharidase activities both in intestine and kidney. However, the molecular mechanism underlying the modulation by quercetin in diabetic status still remains undefined and work in this aspect is in progress in our laboratory.

In conclusion, the dietary bioflavanoid quercetin shows an effective reduction in postprandial hyperglycemia reflecting its ability of increasing the carbohydrate metabolism in the small intestine. The reduction in glycemic conditions may be attributed to its effective insulin-induced uptake of glucose, galactose, and fructose by SGLT/GLUT5 or alterations in the bioavailability. Our investigation clearly indicated the modulatory effect of quercetin on intestinal and renal disacharidases in diabetic rats. Hence, quercetin ameliorates the diabetic status by reducing the urine sugar and fasting blood glucose, and also modulates intestinal and renal disaccharidase activities, thus making diabetic animals more tolerant to hyperglycemia. A thorough understanding of the underlying mechanisms is a prerequisite for prevention of chronic diseases, such as diabetes, and its management by good dietary habits is essential.

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## 5 References

[1] Report of WHO study group on Diabetes Mellitus. *WHO Techn. Re. Ser.* 1985, *727*, 1 – 113.

[2] Amos, A., Mc Carty, D., Zimmet, P., The raising global burden of diabetes and its complications – estimates and projections to the year 2010. *Diabetic Med.* 1997, *14*, S1 – S85.

[3] Caspary, W. F., Rhein, A. M., Creutzfeldt, W., Increase of intestinal brush border hydrolases in mucosa of streptozotocin induced diabetic rats. *Diabetologia.* 1972, *8*, 412 – 414.

[4] Sheldl, H. P., Wilson, H. D., Effects of diabetes on intestinal growth and hexose transport in the rat. *Am. J. Physiol.* 1971, 1739 – 1745.

[5] Murakami, I., Ikeda, T., Scand, J., Effects of diabetes and hyperglycemia on disaccharidase activities in the rat. *Gastroenterology* 1998, *33*, 1069 – 1073.

[6] Tondon, R. K., Srivastava, M. D. L. M., Pandey, S. C., Increased disaccharidase activity in human diabetics. *Am. J. Clin. Nutr.* 1975, *28*, 621 – 625.

[7] Philpott, D. J., Butzner, J. B., Meddings, J. B., Regulation of intestinal glucose transport. *Can. J. Physiol. Pharmacol.* 1992, *70*, 1201 – 1207.

[8] Yoshikawa, M., Murakami, T., Matsuda, H., in: Ageta H., Aimi, N., Ebiuka, Y., Fujita, T., Honda, G. (Eds.), *Towards Natural Medicine Research in the 21st Century,* Elsevier, Amsterdam 1998, pp. 137 – 147.

[9] Ceriello, A., Oxidative stress and glycemic regulation. *Metabolism.* 2000, *49*, 27s – 29s.

[10] Saxena, A. K., Srivastava, P., Kale, R. K., Baquer, N. Z., Impaired antioxidant status in rat liver – effect of vanadate. *Biochem. Pharmacol.* 1993, *45*, 539 – 542.

[11] Bopana, K. N., Kannan, J., Gadgil, S., Balaraman, R., Rathod, S. D., Free radicals – their role in the development of diabetes and its complications. *Ind. J. Pharmacol.* 1987, *29*, 182 – 187.

[12] Gee, J. M., Dupont, M. S., Rhodes, M. J. C., Johnson, I. T., Quercetin glucosides interact with the intestinal glucose transport pathway. *Free. Radic. Biol. Med.* 1998, *25*, 19 – 25.

[13] Kiviranta, J., Huovinen, K., Hiltunen, R., Variation of phenolic substances in onion. *Acta. Pharm. Fenn.* 1998, *97*, 67 – 72.

[14] Weisburer, J. H., Approaches for chronic disease prevention based on current understanding of underlying mechanisms. *Am. J. Clin. Nutr.* 2000, *71*, 1710s – 1719s.

[15] Schedl, H. P., As-Al-Jurf., Wilson, H. P., Elevated intestinal disaccharidase activity in the streptozotocin diabetic rats is independent of enteral feeding. *Diabetes* 1983, *32*, 265 – 270.

[16] Varma, S. D., Mizuno, A., Kinoshita, J. H., Diabetic cataracts and flavanoids. *Science* 1977, *195*, 205 – 206.

[17] Scalbert, A., Williamson, G., Dietary intake and bioavailability of polyphenols. *J. Nutr.* 2000, *130*, 2073s – 208s.

[18] Gee, J. M., Dupont, M. S., Day, A. J., Plumb, G. W., Williamson, G., Johnson, I. T., Intestinal transport of quercetin glycosides in rats involves both deglycosylation and interaction with hexose transport pathway. *J. Nutr.* 2000, *130*, 2765 – 2771.

[19] Richard, A. W., Lin, J. T., Kinne, R. K. H., Walle, T., Cellular uptake of dietary flavanoid – quercetin 4′-β-glucoside by sodium-dependent glucose trasporter (SGLT). *J. Pharmacol. Exp. Ther.* 2000, *294*, 837 – 843.

[20] Sanders, R. A., Rausher, F. M., Watking, J. B., Effects of quercetin on antioxidant defense in streptozotocin-induced diabetic rats. *J. Biochem. Mol. Toxicol.* 2001, *15*, 143 – 149.

[21] Shetty, A. K., Rashmi, R., Rajan, M. G. R., Sambaiah, K., Salimath, P. V., Antidiabetic influence of quercetin in streptozotocin-induced diabetic rats. *Nutr. Res.* 2004, *24*, 373 – 381.

[22] Hatch, G. M., Cao, S. G., Angel, A., Decrease in cardiac phosphotidyl glycerol in streptozotocin induced diabetic rats does not affect cardiolipin biosynthesis: evidence for distant pools of phosphotidyl glycerol in the heart. *Biochem. J.* 1995, *306*, 759 – 764.

[23] Bieri, J. G., Stoewsand, G. S., Briggs, G. M., Phillips, R. W., Woodard, J. C., Knapka, J. J., Report of the American institute of nutrition. Ad hoc committee on standards for nutritional values. *J. Nutr.* 1977, *107*, 1340 – 1348.

[24] Miller, G. L., Use of DNS reagent for determination of reducing sugar. *Anal. Chem.* 1959, *31*, 426 – 428.

 

[25] Hugget, A.S. G., Nixon, D. A., Use of glucose oxidase, peroxidase and *O*-dianisidine in the determination of blood glucose and urinary glucose. *Lancet* 1957, *273*, 366 – 370.

[26] Dahlquist, A., Assay of intestinal dissacharidases. *Anal. Biochem.* 1968, *22*, 99 – 107.

[27] Lowry, O. H., Rosenbrough, N. J., Far, A. L., Randall, R. J., Protein measurement with folin phenol reagent. *J. Biol. Chem.* 1951, *193*, 265 – 275.

[28] Snedecor, G. W., Cochran, W. G. (Eds.), *Statistical Methods*, State University Press., 6th ed. Ames, IA, USA 1976, p. 298.

[29] Ferraris, R. P., Casirola, D. M., Vinnakota, R. R., Dietary carbohydrate enhances intestinal sugar transport in diabetic mice. *Diabetes* 1993, *42*, 1579 – 1587.

[30] Ferraris, R. P., Dietary and developmental regulation of intestinal sugar transport. *Biochem. J.* 2001, *360*, 265 – 276.

[31] Takenoshita, M., Yamaji, R., Inui, H., Miyatake, K., Nakano, Y., Suppressive effect of insulin on the synthesis of sucrase-isomaltase complex in small intestinal epithelial cells and abnormal increase in the complex under diabetic conditions. *Biochem. J.* 1998, *329*, 597 – 600.

[32] Nandini, C. D., Sambaiah, K., Salimath, P. V., Effect of dietary fibre on intestinal and renal disaccharidases in diabetic rats. *Nutr. Res.* 2000, *20*, 1301 – 1307.

[33] Chethankumar, M., Salimath, P. V., Sambaiah, K., Butyric acid modulates activities of intestinal and renal disaccharidases in experimentally induced diabetic rats. *Nahrung* 2002, *46*, 345 – 348.

[34] Yamada, K., Goda, T., Sasaki, M., Moriuchi, S., Hosoya, N., Effect of food restriction on intestinal disaccharidases in streptozotocin induced diabetic rats. *J. Nur. Sci. Vitaminol.* 1980, *26*, 599 – 606.

[35] Kalpana, P., Srinivasan, K., Influence of dietary spices or their active principles on digestive enzymes of small intestinal mucosa in rats. *Int. J. Food. Sci. Nutr.* 1996, *47*, 55 – 59.

[36] Deren, J. J., Broitman, S. A., Zamcheck, N., Effect of diet on intestinal disaccharidases and disaccharide absorption. *J. Clin. Invest.* 1967, *46*, 186 – 189.

[37] Meloni, G. F., Colombo, C., La Vecchia, C., Pacifico, A., *et al.*, High prevalence of lactose absorbers in northern Sardinian patients with type 1 and type 2 diabetes mellitus. *Am. J. Clin. Nutr.* 2001, *73*, 582 – 585.

[38] Lee, C. M., Chichester, C. O., Lee, T. C., Effect of Maillard reaction products on disaccharidase activities in the rat. *J. Agric. Food Chem.* 1977, *25*, 775 – 778.

[39] Taylor, D. G., Price, R. G., Robinson, D., The subcellular distribution of some disaccharides in rat renal cortex. *Biochim. Biophys. Acta* 1972, *273*, 237 – 242.

[40] Price, R. G., Dance, N., The cellular distribution of some rat-kidney glycosidases. *Biochem. J.* 1967, *105*, 877 – 883.

[41] Yukisumi, I., Eiichi, S., Noburu, H., Hiroshi, N., Effects of insulin on maltase and N-acetyl β-glucosaminidase activities of serum and kidney in experimental diabetic rats. *Nippon. Yakuvi-gaku. Zasshi.* 1989, *94*, 129 – 135.

[42] Shoskes, D. A., Effect of bioflavanoids – quercetin and curcumin on ischemic renal injury: a new class of renoprotective agents. *Transplantation* 1998, *66*, 147 – 152.

[43] Noroozi, M., Burns, J., Crozier, A., Kelly, I. F., Lean, M. E., Prediction of dietary flavanol consumption from fasting plasma concentration or urinary excretion. *Eur. J. Clin. Nutr.* 2000, *54*, 143 – 149.

[44] Hii, C. S. T., Howell, S. L., Effects of flavanoids on insulin secretion and $Ca^{2+}$ handling in rat islets of Langerhans. *J. Endorcrinol.* 1985, *107*, 1 – 8.

[45] Nuraliev, I. N., Avezov, G. A., The efficacy of quercetin in alloxan diabetes. *Eksp. Klin. Farmakol.* 1992, *55*, 42 – 44.

[46] Asgary, S., Nader, G., Sarrafzadegan, N., Ghassemi, N., *et al.*, Anti-oxidant effect of flavanoids on hemoglobin glycosylation. *Pharm. Acta Helv.* 1999, *73*, 223 – 226.

 