Naunyn-Schmiedeberg's Archives of Pharmacology (2018) 391:235–245
https://doi.org/10.1007/s00210-017-1453-5

REVIEW

Impact of diet restriction in the management of diabetes: evidences from preclinical studies

Pawan Krishan[1] · Onkar Bedi[2] · Monika Rani[3]

Received: 27 July 2017 / Accepted: 11 December 2017 / Published online: 16 December 2017

Abstract

The inappropriate dietary habits lead to the onset of age-related pathologies which include diabetes and cardiovascular ailments. Dietary restriction and nutritional therapy play an important role in the prevention of these chronic ailments. Preclinical research provides a basis for the therapeutic exploration of new dietary interventions for the clinical trials to potentiate the scientific management of diabetes and its related complications which further help in translating these nutritional improvements from bench to bedside. Within the same context, numerous therapeutically proved preclinical dietary interventions like high-fiber diet, caloric restriction, soy isoflavone-containing diets, etc., have shown the promising results for the management of diabetes and the associated complications. The focus of the present review is to highlight the various preclinical evidences of diet restriction for the management of diabetes and which will be helpful for enlightening the new ideas of nutritional therapy for future research exploration. In addition, some potential approaches are also discussed which are associated with various nutritional interventions to combat progressive diabetes and the associated disorders.

Keywords Dietary restriction (DR) · Hyperinsulinemia · Nutrition therapy · Caloric restriction (CR)

Abbreviations

AGES Advanced glycation end products

Chemical compounds studied in this article Streptozotocin (PubChem CID:29327)

Highlights

- Diet restriction has beneficial effects on insulin action and glycemic control in obesity and mild T2DM
- Soy diet shown to produce anti-diabetic effect by acting through the estrogen receptors.
- Preclinical evidences of diet restriction and dietary approaches in the management of diabetes and their associated complications.
- Other highlight of this review is about nutritional interventions which combat progressive diabetes and the associated disorders.

✉ Pawan Krishan
pawankrishan@rediffmail.com

[1] Department of Pharmaceutical Sciences and Drug Research, Punjabi University, Patiala, India

[2] JRF, DST-SERB, New Delhi, Department of Pharmaceutical Sciences and Drug Research, Punjabi University, Patiala, Punjab, India

[3] Department of Pharmaceutical Sciences and Drug Research, Punjabi University, Patiala, Punjab, India

AMPK	AMP-activated protein kinase
CR	Caloric restriction
DN	Diabetic nephropathy
DNA	Deoxyribonucleic acid
DR	Dietary restriction
ET	Exercise training
GLUT2	Glucose transporter 2
HbAIC	Hemoglobin A1c or glycated hemoglobin
HDL	High-density lipoprotein
HFD	High-fat diet
IGF-1	Insulin-like growth factor 1
KD	Ketogenic diet
LCKD	Low-carbohydrate ketogenic diet
LDL	Low-density lipoprotein
LFSMP	Low-fat soy milk powder
MDA	Malondialdehyde
MNT	Medical nutrition therapy
mTORC1	Mammalian target of rapamycin complex 1
NAD+	Nicotinamide adenine dinucleotide
OLETF	Otsuka-Long-Evans-Tokushima fatty
PPAR	Peroxisome proliferator-activated receptor
SIRT	Sirtuins
STZ	Streptozotocin
T2DM	Type 2 diabetes mellitus
TG	Triglyceride
WHO	World Health Organization

Introduction

Diabetes results in vascular changes and other associated complications which are the major cause of morbidity and mortality in diabetic patients. As per the latest reports of the World Health Organization (WHO 2016), there are about 422 million adults suffering from diabetes mellitus (DM) and its associated complications globally. Diabetes is a metabolic disorder which is strongly associated with increased oxidative stress, inflammatory mediators, altered GFR, abnormal insulin secretion, insulin sensitivity, and proteinuria. Dietary restriction (DR) is considered a good treatment paradigm for the management of various metabolic disorders such as diabetes and associated cardiovascular diseases (Colman et al. 2009; Fontana et al. 2010). Numerous scientific reviews demonstrated the effectiveness of medical nutrition therapy (MNT) in the management of diabetes (Franz et al. 2008, 2010; American Diabetes Association 2008).

High-carbohydrate and high-fat diets and improper dietary habits are the major factors for the development and progression of various metabolic disorders. Proper diet management, i.e., diet composition, distribution, and timing of food intake plays an important role in the improvement of these disorders. So, the diet should be designed to supply an adequate amount of nutrients without causing malnutrition to the patient. It is reported that a diabetic diet should contain 60% carbohydrate, 20–25% fats, and 15–20% protein. A high-carbohydrate diet increases the sensitivity of peripheral tissues to both endogenous and exogenous insulin. Such diet improves glucose tolerance and lowers the level of serum insulin. In addition, the liberalization of carbohydrate might facilitate the reduction of saturated fatty acids and cholesterol in the diabetic conditions (Collier et al. 1985; Jenkins and Josse 1985).

Scientific evidence suggested that diet restriction (i.e., modification of the nutrient intake, lifestyle, and eating habits) tries to prevent chronic complications of diabetes by maintaining the optimal blood glucose levels, lipid profile levels, and blood pressure (Bantle et al. 2008). Recently, Azar et al. (2016) reviewed the benefits of ketogenic diet for the management of type 2 diabetes (T2DM) by demonstrating numerous scientific evidences which proved that there is a significant weight loss, improvement of HbA1c levels, reversal of nephropathy, and cardiac benefits via ketogenic diet. Caloric restriction without malnutrition reduces the incidence of diabetes, cancer, cardiovascular disease, and brain atrophy and slows aging in a primate species. Similarly, it is effective in controlling the diabetes mellitus by stabilizing glucose homeostasis and enhancing glycemic control in mild and severe streptozotocin-induced diabetic rats (Ugochukwu et al. 2004; Colman et al. 2009).

Basically, there are three broad aims of dietary restriction for people with diabetes, first, to abolish the primary symptoms, second to minimize the risks of hypoglycemia, and third to minimize the long-term macro- and micro-vascular complications which together result in the improvement of diabetes and their related complications. The present review focused on various preclinical evidences which support the therapeutic effect of diet restriction or diet therapy for the management of diabetes.

Impact of inappropriate diet in the progression of diabetes

The fat-enriched diet and a sedentary life style are the major causes of the great prevalence of obesity and type 2 diabetes in the world-wide population (Kahn et al. 2006). One of the preclinical study reported that high-fat, high-simple-carbohydrate and low-fiber diet produce obesity in A/J and C57BL/6 J mice. In this study, obesity was found to be associated with only moderate glucose intolerance and insulin resistance in A/J mice whereas there is a development of clear-cut diabetes with fasting blood glucose levels of > 240 mg/dl and blood insulin levels of > 150 μU/ml in obese C57BL/6J mice (Surwit et al. 1988). The pathway which plays an important role in the pathogenesis of diabetes is a nutrient-sensing pathway which includes the cells' ability to recognize and respond to glucose fuel substrates. Nutrient-sensing pathways help in cell survival and growth, activation of autophagy, and in DNA repairing of mammalian cells, but during hyperglycemia, hyperlipidemia, and hyperinsulinemia as consequences of dietary changes, these nutrient-sensing pathways are affected and play a potential role in the pathogenesis of diabetic complications. Kume et al. (2012) demonstrated that nutrient-sensing pathways have been implicated in the pathogenesis of obesity and diabetes, by acting on β cells, adipocytes, and hepatic and skeletal muscle metabolism, and also play a role in the central regulation of nutrition.

Nutrient-sensing pathways involved mammalian target of rapamycin (mTOR), AMP-activated protein kinase (AMPK), and sirtuins (SIRT). Under low-energy conditions, AMPK and SIRT are activated due to increases in intracellular AMP and NAD+ levels, respectively (Steinberg and Kemp 2009; Imai and Guarente 2010). In excessive nutrient conditions, mTOR is activated and leads to activation of inflammatory mediators, fibrosis, apoptosis, renal hypertrophy, etc. (Wellen and Thompson 2010; Zoncu et al. 2011). So, from the above evidences, it is clearly stated that improper and irregular dietary habits can cause devastating effects on the progression of diabetes and other metabolic disorders.

Role of caloric restriction and dietary approaches for the management of diabetes

Knowing the devastating effects of inappropriate diet in the initiation and progression of metabolic disorders, the main

emphasis is on the various dietary approaches for the management of diabetes which are discussed as below with suitable preclinical evidences.

Caloric restriction and diabetes

Diet restriction has beneficial effects on insulin action and glycemic control in obesity and mild T2DM (Markovic et al. 1998). Lee and Bressler (1981) demonstrated that diet restriction prevents the obesity in the db/db mouse which further helps in the deterrence of diabetic nephropathy by preventing mesangial immunoglobulin deposition and mesangial matrix expansion. One of the scientific evidences of preclinical trial suggested that caloric restriction prevents beta-cell depletion, loss of beta-cell GLUT 2, and glucose incompetence in obese male Zucker diabetic fatty rats (Ohneda et al. 1995). Caloric restriction has a therapeutic effect by regulating neurogranin-associated calcium signaling which is an important factor of high-fat diet-induced memory deficits. One of the recent scientific preclinical trials proved that high-fat diet-fed mice exhibited insulin resistance, glial activation, blood–brain barrier leakage, and memory deficits through neurogranin regulation of Ca2+/calmodulin-dependent synaptic function which was reversed with the help of caloric restriction in C57BL/6 mice (Kim et al. 2016). Moreover, caloric restriction (CR) and regular exercise training (ET) also proved to be front-line strategies in the treatment of type 2 diabetes mellitus and reducing the cardiometabolic risk. CR (reducing food intake by 30%) in the db/db mice for a period of 8 weeks may improve coronary endothelial vasodilator dysfunction in type 2 diabetes (Broderick et al. 2017).

Furthermore, it is also demonstrated that short-term moderate CR (20%) not only normalized the body weight in mice but also improved metabolic programming and reversed oxidative and cardiac dysfunction induced by postnatal overfeeding (Li et al. 2016). From the above discussion, it is concluded that caloric restriction plays an important role in regulating diabetes and their associated complication by exhibiting various therapeutic effects.

High-fiber diet and diabetes

High- and soluble-fiber diets help to lower the cholesterol, regulate blood sugar levels, guard against cancer and heart disease and help to support a healthy digestive tract. There are numerous scientific evidences which show the beneficial and therapeutic role of high-fiber diet for the management of diabetes and its associated complications. One of the scientific evidences demonstrated that administration of brown rice and soybean dietary fiber improved the glucose and lipid metabolism in diabetic rats (Madar 1983). Similarly, scientific results indicated that both wheat and maize bran as fiber diet exert anti-diabetic effects on the alloxan-induced diabetes and therefore, can be a part of a diet-based therapy for the management of diabetes (Hamid et al. 2017).

Li et al. (2003) demonstrated that long-term intake of high dietary fiber has beneficial effects in controlling blood glucose, glucose tolerance, and lipid metabolism in GK rats. The soluble dietary fiber fraction of *Trigonella foenum graecum* has been shown to reduce the postprandial hyperglycemia in type 2 model diabetic rats by delaying the digestion of sucrose (Hannan et al. 2003). High-fiber Okara and soybean bran diets have been proven to act as functional supplements for mice for the management of experimentally induced T2DM (Ismaiel et al. 2017). Within the same context, it is concluded that high-fiber diet could be a new dietary approach for the management of T2DM and required more exploration in clinical trial.

Soy isoflavone-containing diets and diabetes

The long-term consumption of low-fat soy milk powder (LFSMP) hinders diabetic nephropathy progression via suppressing renal injury, myofibroblast differentiation, and renal macrophage infiltration in KKAy diabetic mice (Jheng et al. 2017). Lu et al. (2008) demonstrated that high-isoflavone soy protein lowers blood glucose levels and reduces the incidence of cataracts in streptozotocin-induced diabetic rats. Isoflavones may influence insulin action by means of their well-known receptor-mediated estrogenic activity. However, isoflavones also bind to PPARs which are strongly associated with insulin action. It is also demonstrated that soya diet helps in preventing the progression of DM by regulating the functioning of aquaporin (AQP) and osteopontin (OPN) which were found to be involved in the pathogenesis of diabetic complications and especially in renal disease (Choi et al. 2010).

Wagner et al. (2008) reported that consumption of isoflavone-containing soy protein in a dose-dependent manner increased insulin responses to the hyperglycemic rodents. Isoflavonoids are phytoestrogens that naturally occur with soy proteins and are structurally and functionally similar to estradiol. It is reported that isoflavonoids may improve anti-diabetic actions through estrogen receptors, which are key molecules involved in glucose and lipid metabolism (Knight and Eden 1996). The role of estrogen receptor β is still unknown, but estrogen receptor α plays an important role in the regulation of insulin biosynthesis, insulin secretion, and β cell survival (Kuiper et al. 1998). Soy protein and genistein, which are the main isoflavones in soybeans, help to lower blood glucose and lipid profile and regulates anti-oxidant enzyme activities in streptozotocin (STZ)-induced diabetic rats (Lee,2006). Besides this, still there is a need of extensive clinical and preclinical research for exploring the mechanistic approaches of soy diet with reference to diabetic disorder.

Ketogenic diet and diabetes

Low-carbohydrate ketogenic diet (LCKD) is effective in the amelioration of many of the deleterious consequences of diabetes. However, its role in preventing the onset of diabetes is not explored. Al-Khalifa et al. (2011) suggested that LCKD prevents the development of diabetes in streptozotocin (55 mg/kg), inducing diabetes in rats. Furthermore, low-carbohydrate ketogenic diet proved to be therapeutic in the management of the diabetic state and for stabilizing the hyperglycemia in STZ-induced (55 mg/kg) diabetic rodents (Al-Khalifa et al. 2009). Within the same context, histological studies showed a significant decrease in the islet size and number of β cells in diabetic rodents (Hussain et al. 2012). It is suggested that ketogenic diet significantly produces prolonged elevation of 3-OHB, which reverses pathological changes in rodent models of types 1 (Akita) and 2 (db/db) diabetes (Poplawski et al. 2011). Still, there is a need to explore more in the field of ketogenic diet with respect to pharmacological interventions as there are very less scientific reports in support of the therapeutic use of KD in the management of diabetes.

Low-protein diet and diabetes

Kitada et al. (2016) demonstrated that very-low-protein diet ameliorates advanced diabetic nephropathy through autophagy induction by suppression of the mTORC1 pathway in Wistar fatty rats, an animal model of T2DM and obesity. Protein overload increases insulin-like growth factor 1 (IGF-1) secretion from the liver (Fontana et al. 2008), and this IGF-1 is a potent vasodilator of the renal vessels and causes damage to kidney cells (Tonshoff et al. 1998; Tsukahara et al. 1994). The modulation of intraglomerular pressure achieved with an LPD mainly protects against the progression of kidney disease including DN (Otoda et al. 2014). Recently, Cappelli et al. (2017) demonstrated that low-protein-fed rats are associated with altered pancreatic islets redox status with reduced glucose-induced insulin secretion. So, these clinical evidences provide a brief beneficial history of LPD for the management of diabetes and give a new insight for the same.

Carbohydrate-free diet and diabetes

It is suggested that carbohydrate-restricted diet provides a therapeutic effect by preventing beta cell destruction in diabetic rodent models (Leiter et al. 1983; Mirhashemi et al. 2008). One of the scientific studies by Kluth et al. (2011) revealed that carbohydrate-rich diet causes deleterious effect in New Zealand Obese (NZO) mice by increasing glucose level which further leads to the dephosphorylation of forkhead box O1 protein (FOXO1) and progressive depletion of insulin stores. In the same study, it was concluded that carbohydrate-restricted diet helps to reverse the above-mentioned devastating conditions of diabetes in NZO mice (Kluth et al. 2011). Similarly, it is documented that rich carbohydrate diet is responsible for the β cell destruction and decreased GLUT2 expression and low plasma insulin levels in genetically different mouse models of obesity-associated diabetes (Mirhashemi et al. 2008). It is reported that a high-fat, carbohydrate-free diet fully prevented β cell destruction in NZO mice with a marked inflammatory state of adipose tissue (Jürgens et al. 2007). So, from the above discussion, it is concluded that carbohydrate-deprived diet is a useful tool for the management of diabetes.

Preclinical evidences of diet restriction and dietary approaches in the management of diabetes and their associated complications

Diet restriction acts predominantly via reducing the oxidative stress, through reduction of cholesterol and fat level which is directly or indirectly concerned with improvement in obesity and insulin resistance. Besides numerous effects of diet restriction, various preclinical studies have been conducted to determine the therapeutic and clinical benefits of diet therapy. The available evidence of preclinical studies can truly be envisaged that diet restriction provides promising results in the treatment of diabetes and their associated complications. The major preclinical studies describing the diet restriction as intervention, along with the scientific evidences are summarized in Table 1.

Clinical scenario of diet restriction

Recent study by Gower and Goss (2015) has reported the beneficial effect of low-carbohydrate and high-fat diet on insulin resistance and obesity and prevents further risk of type 2 diabetes. Similarly, it is demonstrated that there is a significant decrease (8.1 to 7.3%, $p < 0.05$) in glycosylated hemoglobin (HbA1c) in weight-stable diabetic patients with carbohydrate restriction as compared with a high-carbohydrate-controlled diet (Sheard et al. 2004). Furthermore, protein-rich diet provides a beneficial effect in type 2 diabetic patients by reducing body weight and postprandial hyperglycemia by replacing carbohydrate-rich foods with protein-rich foods (Campbell and Rains 2015). However, intake of high-protein diets may increase the risk of developing impaired renal function in diabetic patients (Friedman 2004). Existing literature indicates that omega-3 and omega-6 polyunsaturated fatty acids (PUFAs) and monounsaturated fatty acids (MUFAs) were found to have a beneficial impact on diabetic kidney disease (Shapiro et al. 2011). It is interestingly noted that ketogenic

Table 1 List of preclinical evidences of diet restriction in the management of diabetes

Serial no.	Animal model	Intervention and treatment	Observation	Outcomes	Biomarkers targeted	References
1	C57BL/KsJ (db/db) mouse	Diet restriction	• The diet-restricted diabetics have shown enhanced metabolic efficiency. • Results indicated that diabetic control achieved by prevention of obesity in the db/db mouse prevents the development of diabetic nephropathy.	Diet restriction prevents the development of diabetic nephropathy.	• Diet-restricted diabetic rodents showed complete prevention of mesangial immunoglobulin deposition and mesangial matrix expansion. • Significant decreased blood glucose levels.	Lee and Bressler (1981)
2	Diabetic mice (C57 BLKsJ db/db). Fiber-enriched diet, but their absolute caloric intake was 6% less than control diabetic mice.	High-fiber diet	• It is concluded that addition of non-absorbable fiber to the diet of genetically diabetic mice improves glycemic control and retards the development of diabetic nephropathy.	Improves glycemic control and retards the development of diabetic nephropathy.	• High-fiber diet showed prevention of mesangial immunoglobulin deposition and mesangial matrix expansion • Significant lowered blood glucose levels.	Lee and Bressler (1982)
3	Wistar rats; streptozotocin 65 mg/kg, intraperitoneal (i.p.)	Dietary fat derived from four sources: beef tallow (BT; rich in saturated fatty acids), evening primrose oil (EPO; rich in gamma linolenic (GLA) and linoleic acids (LA)), safflower oil (SO; rich in LA), and fish oil (FO; rich in eicosapentaenoic (EPA) and docosahexaenoic (DHA) acids).	• It is concluded that high-LA diets are protective in this model of diabetic nephropathy. • Diets containing FO have a beneficial effect on plasma lipids in this model.	Prevents diabetic nephropathy.	• The diets prepared with EPO and SO had a clear beneficial effect on proteinuria, glomerular sclerosis, and tubular abnormalities, as compared with BT. • The FO diet did not have an effect on renal disease, but decreased plasma lipids, inhibits the eicosanoid synthesis and lowered 6-keto-PGF1α/TXB2 ratio.	Barcelli et al. (1990)
4	Otsuka-Long-Evans-Tokushima fatty (OLETF)) with non-insulin-dependent diabetes mellitus (NIDDM).	Caloric restriction	• Results of this study demonstrate that caloric restriction is effective in preventing NIDDM in diabetes-prone rats.	Caloric restriction prevents the NIDDM.	• Plasma immunoreactive insulin (IRI) levels were significantly lowered.	Okauchi et al. (1995)
5	OLETF rat which develops NIDDM spontaneously after 25–30 weeks of age.	30% restricted diet	• Diet restriction have shown the complete suppression of spontaneous diabetes up to 40 weeks of age and showed milder histopathological change of pancreatic islets • Diet therapy after 70 weeks of age, however, had little or no effect.	30% restricted diet try in the suppression of spontaneous diabetes.	• Urinary protein content decreased in diet restricted animals. • Decreased glomerular damages shown through histological studies in diet restricted group.	Mori et al. (1996)
6	6- and 24-month-old male Fischer 344 (F 344) rats	30% diet restriction	• Expression of Heat Shock Protein 47 (HSP47) is suppressed. • Renal damage was remarkably less than those noted in 24-month-old freely fed rat kidneys.	Renal damage was remarkably less.	• Dietary restriction significantly reduces renal accumulation of types I, III, and IV collagens in areas of glomerulosclerosis and interstitial fibrosis in old rat kidneys in old age. • Dietary restriction significantly diminished phenotypic alterations	Razzaque et al. (1999)

Table 1 (continued)

Serial no.	Animal model	Intervention and treatment	Observation	Outcomes	Biomarkers targeted	References
					of mesangial and interstitial cells and glomerular epithelial and tubular epithelial cells in 24-month-old rats.	
7	C57/BL/KsJ db/db mice	Diet with either a low-AGE content (LAD) or a 3.4-fold higher content of AGE (high-AGE diet (HAD)), including ε*N*-carboxymethyllysine (CML) and methylglyoxal (MG).	• Reduced AGE intake leads to lower levels of circulating AGE and improve insulin sensitivity in db/db mice as compared with diet with high-AGE content.	Improved insulin sensitivity.	• LAD-treated rats show significantly lowered serum AGEs levels.	Hofmann et al. (2002)
8	Non-obese diabetic mice (NOD) with type 1 diabetes (T1D) and db/db mice with type 2 diabetes (T2D)	Diet contained 6-fold lower content of advanced glycation end products (L-AGE), but equal calories, macronutrients, and micronutrients	• Dietary AGEs provides sustained protection against DN in mice • And exhibited low levels of renal cortex TGFβ-1	Protection against diabetic nephropathy	• L-AGE-fed NOD and db/db mice exhibited low levels of renal cortex TGFβ-1, laminin B1 mRNA and α1 IV collagen mRNA, and protein with reduced serum and kidney AGEs.	Zheng et al. (2002)
9	Wistar rats (35 and 65 mg/kg) streptozotocin i.p.	40% caloric restriction (CR) and ad libitum feeding for 9 weeks	• CR significantly reduces the body weight, blood glucose, HbAIC, and TG concentrations in mild diabetic rats and non-significantly improving the plasma HDL-cholesterol concentrations. • CR did not produce any significant effect on the antioxidant enzyme activities and MDA concentrations.	Anti-diabetic and antioxidant effect.	• Reducing body weight, blood glucose, HbAIC, and TG concentrations.	Ugochukwu et al. (2004)
10	Spontaneously hypertensive/NIH-corpulent rats (SHR/ND mcr-cp (cp/cp)) established in Disease Model Cooperative Research Association (Kyoto, Japan), and Wistar-Kyoto rats (WKY)	Low-calorie diet	• Reduces oxidative/carbonyl stress and prevents diabetic nephropathy	Prevents diabetic nephropathy.	• Blood glucose, total cholesterol, triglycerides, creatinine, and urea nitrogen • (BUN) concentrations were lowered in plasma of low-calorie diet-treated rats.	Nangaku et al. (2005)
11	Diabetes was induced by a single intraperitoneal injection of 35 mg/kg body weight of streptozotocin in Wistar rats	30% caloric restriction	• Caloric restriction was found to ameliorate the oxidative and inflammatory effects of diabetes in the brain.	Improves diabetes.	• Caloric restriction was able to significantly reduce triglyceride, ROS, IL6, and TNF-α levels.	Ugochukwu et al. (2006)
12	Type II diabetic OLETF rats.	Restricted diets (30% reduction from free intake)	• Caloric restriction may prevent cardiovascular tissues from oxidative stress provoked by diabetes mellitus.	Improves diabetes	• CR decrease the blood glucose, hemoglobin A1c, plasma levels of free fatty acid, triacylglycerol, and plasminogen activator inhibitor-1. • CR significantly improved the nitric oxide (NO)-cGMP pathway via normalizing ROS generation in OLETF rats.	Minamiyama et al. (2007)

Table 1 (continued)

Serial no.	Animal model	Intervention and treatment	Observation	Outcomes	Biomarkers targeted	References
13	Sprague-Dawley rats; streptozotocin (STZ) (55 mg/kg, i.p. dissolved in ice cold sodium citrate buffer, 0.01 M, pH 4.4).	Intermittent fasting	• Intermittent fasting significantly improves biochemical parameters associated with development of DN and changes the expression of Sir2 and p53.	Improves diabetes nephropathy	• Intermittent fasting produces antioxidant effect and • Intermittent fasting reduces the expression of p38 which gets induced under diabetic condition.	Tikoo et al. (2007)
14	Sprague-Dawley rats by intraperitoneal injection of 100 mg/kg STZ	Soy isoflavone-containing diets	• Ingestion of high-isoflavone soy protein not only lowers glucose levels but also reduces the incidence of cataracts in diabetic rats. The beneficial effects of soy isoflavone are attributed to increased insulin secretion, glycemic control, and providing antioxidant protection.	Soy isoflavone--containing diets produce anti-diabetic effect by lowering blood glucose levels and by providing antioxidant effect.	• High-isoflavone-containing diet showed significant increases of body weight and serum insulin levels and reduced serum glucose and methylglyoxal levels.	Lu et al. (2008)
15	Diabetes was induced by a single intraperitoneal injection of streptozotocin (STZ, 50 mg/kg); Sprague-Dawley rats	Soybean diet	• Control of blood glucose levels by using a soybean diet could prevent the progression of diabetes mellitus, and therefore, prevent the diabetic nephropathy. • Dysfunctioning of aquaporin (AQP) and osteopontin (OPN) leads to diabetic complications and renal disease.	Improves diabetes and blood glucose.	• In the soybean-administered diabetic rats, AQP-1 expression was greatly reduced in the glomerular endothelium and the OPN expression was decreased in the renal cortex.	Choi et al. (2010)
16	Types 1 (Akita) and 2 (db/db) rodent models of diabetes	Ketogenic diet	• Diabetic nephropathy which is indicated by albumin/creatinine ratios as well as expression of stress-induced genes was completely reversed by 2 months maintenance on a ketogenic diet. However, histological evidence of nephropathy was only partly reversed.	Diabetic nephropathy was completely reversed.	• Ketogenic diet significantly produces prolonged elevation of 3-OHB, which reverse pathological processes caused by diabetes.	Poplawski et al. (2011)
17	Insulin resistance induced by high-fructose diet in Wistar rats	Dietary salt depletion	• The low-salt diet improved insulin sensitivity and prevented kidney damage. • The beneficial effects of sodium depletion was associated with a decrease in renal inflammation (macrophage infiltration, IL-6, TNF-α) and oxidative stress (NADPH oxidase activity).	Improve insulin sensitivity and inflammation.	• Dietary salt deletion produces anti-inflammatory and antioxidant effect.	Oudot et al. (2013)
18	db/db mouse model of diabetic nephropathy	Dietary iron restriction	• Dietary iron restriction exerts a preventive effect on the progression of diabetic	Prevent the progression of diabetic nephropathy.	• The level of ferroportin, an iron exporter, increased in the kidneys	Ikeda et al. (2013)

Table 1 (continued)

Serial no.	Animal model	Intervention and treatment	Observation	Outcomes	Biomarkers targeted	References
			nephropathy partly due to the reduction of oxidative stress.		of the db/db mice and reversed in dietary iron restricted animals. • Urinary albumin excretion was suppressed in db/db mice with LID.	
19	Diabetic male Wistar fatty (fa/fa) rats (WFRs)	Low-protein diet (LPD)	• A very-low-protein diet improved advanced diabetic renal injuries, including tubulointerstitial damage, by restoring autophagy through the suppression of the mTORC1 pathway.	Improves advanced diabetic renal injuries.	• LPD act through improving advanced diabetic renal injuries and by restoring autophagy through the suppression of the mTORC1 pathway.	Kitada et al. (2016)
20	Wistar rats; HFD—25% fat, 48% carbohydrates, and 20% protein for 28 days and low dose of STZ (35 mg/kg)	Exercise and beta-glucan (fibers diet)	• Both beta-glucan and exercise improved metabolic parameters in type 2 (HFD/STZ) diabetic rats.	Improves diabetes and blood glucose levels.	• Beta-glucan decreases glucose levels in fasting, glycated hemoglobin (HbA1c), triglycerides (TAG), total cholesterol (TC), low-density lipoprotein (LDL-C), and the atherogenic index of plasma in diabetic rats.	Andrade et al. (2016)
21	Male Sprague-Dawley (SD) rats; STZ (60 mg/kg) in 10 mM citrate buffer (pH 4.5) was injected into the i.p. cavity for induction of T2DM.	Dietary-resistant starch	• Resistant starch normalized growth patterns in T1D rats after diabetes. • Induction in a dose-dependent manner despite having no effect on blood glucose and vitamin D balances.	Improves diabetes	Renal health and glucose metabolism were not improved by resistant starch diet.	Koh et al. (2016)

diet plays an important role in the management of diabetes as well as its complication. One of the clinical studies has demonstrated that intake of well-formulated ketogenic diet in obese diabetic patients for 56 weeks have shown significant improvements in blood glucose levels and in various metabolic parameters (Dashti et al. 2006). Similarly, soy protein diet also has shown beneficial effect in diabetic patients by improving the blood glucose level and lipid profile (Azadbakht et al. 2008). Moreover, numerous clinical studies also revealed that increased intake of dietary fiber (soluble type) improved glycemic control and decreased hyperinsulinemia in type 2 diabetes mellitus patients (Holman et al. 1987; Uusitupa et al. 1989; Chandalia et al. 2000). Thus, from the above clinical evidences, it is suggested that various dietary approaches are beneficial for the management of diabetes which is also supported by various preclinical studies as discussed earlier, suggesting a close relationship between diabetic animal models and human diabetic studies.

Summarized discussion and conclusion

From the above scientific evidences, it is concluded that CR and various dietary approaches such as the inclusion of HFD, soy isoflavone diet, low-protein diet, ketogenic diet, etc., may be proved as promising tools for the management of diabetes and its associated disorders. These dietary approaches try to manage the complications of diabetes through various nutrient-sensing mechanistic pathways. Caloric restriction maintains the glucose homeostasis by preventing the beta cell destruction and glucose incompetence. Diet with soy isoflavone content has shown to produce anti-diabetic effect by acting through the estrogen receptor and plays an important role in the regulation of insulin secretion and their biosynthesis. Similarly, high-fiber diet, low ketogenic, low-protein diet, and carbohydrate-restricted diet have shown to lower the blood glucose and cholesterol levels, but the exact mechanism of action is still controversial. Some scientific reports suggested that low-protein diet helps to reduce the mTORC1 pathway and ameliorates the diabetic-related complications. Dietary-resistant starch, low-protein diet, dietary salt depletion and restricted diets (30% reduction from free intake), etc., proved to be beneficial in various preclinical studies for the treatment of diabetes and its associated disorders. Thus, diet restriction and other dietary approaches will generate new insights into the therapeutic basis for the management of diabetes. Preclinical evidences of diet restriction provide a new direction in the field of metabolic disorders, which emphasize its further exploration in the development of new and effective therapeutic approaches for the treatment of diabetes and associated disorder.

Acknowledgements We want to acknowledge the Department of Pharmaceutical Sciences and Drug Research, Punjabi University, Patiala and UGC, New Delhi for extending the necessary research facilities for our work. We also want to acknowledge Elegant Foreign Language Institute (EFLI) IELTS Institute Sunam, Punjab, India for English writing and editing.

Funding information The authors are thankful to DST-SERB, New Delhi for providing financial assistance under project no. EMR/2014/000438 to accomplish this research work.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

Al-Khalifa A, Mathew TC, Al-Zaid NS, Mathew E, Dashti H (2011) Low carbohydrate ketogenic diet prevents the induction of diabetes using streptozotocin in rats. Exp Toxicol Pathol 63(7):663–669. https://doi.org/10.1016/j.etp.2010.05.008

Al-Khalifa A, Mathew TC, Al-Zaid NS, Mathew E, Dashti HM (2009) Therapeutic role of low-carbohydrate ketogenic diet in diabetes. Nutrition 25(11):1177–1185. https://doi.org/10.1016/j.nut.2009.04.004

American Dietetic Association (2008) Diabetes type 1 and 2 evidence-based nutrition practice guidelines for adults Chicago, IL. http://wwwadaevidencelibrary.com/topiccfm?=3252. Accessed 12 Aug 2017

Andrade EF, Lima AR, Nunes IE, Orlando DR, Gondim PN, Zangeronimo MG, Alves FH, Pereira LJ (2016) Exercise and beta-glucan consumption (Saccharomyces cerevisiae) improve the metabolic profile and reduce the Atherogenic Index in type 2 diabetic rats (HFD/STZ). Nutrients 8(12):792. https://doi.org/10.3390/nu8120792

Azadbakht L, Atabak S, Esmaillzadeh A (2008) Soy protein intake, cardiorenal indices, and C-reactive protein in type 2 diabetes with nephropathy. Diabetes Care 31(4):648–654. https://doi.org/10.2337/dc07-2065

Azar ST, Beydoun HM, Albadri MR (2016) Benefits of ketogenic diet for management of type two diabetes: a review. J Obes Eat Disord 2:1–3

Bantle JP, Wylie-Rosett J, Albright AL, Apovian CM, Clark NG, Franz MJ, Hoogwerf BJ, Lichtenstein AH, Mayer-Davis E, Mooradian AD, Wheeler ML, American Diabetes Association (2008) Nutrition recommendations and interventions for diabetes: a position statement of the American Diabetes Association. Diabetes Care 31(Suppl. 1):S61–S78

Barcelli UO, Weiss M, Beach D, Motz A, Thompson B (1990) High linoleic acid diets ameliorate diabetic nephropathy in rats. Am J Kidney Dis 16(3):244–251. https://doi.org/10.1016/S0272-6386(12)81024-9

Broderick TL, Jankowski M, Gutkowska J (2017) The effects of exercise training and caloric restriction on the cardiac oxytocin natriuretic peptide system in the diabetic mouse. Diabetes Metab Syndr Obes 10:27–36. https://doi.org/10.2147/DMSO.S115453

Campbell AP, Rains TM (2015) Dietary protein is important in the practical management of prediabetes and type 2 diabetes. J Nutr 145(1):164S–169S. https://doi.org/10.3945/jn.114.194878

Cappelli AP, Zoppi CC, Silveira LR, Batista TM, Paula FM, da Silva PM, Rafacho A, Barbosa-Sampaio HC, Boschero AC, Carneiro EM (2017) Reduced glucose-induced insulin secretion in low-protein-

fed rats is associated with altered pancreatic islets redox status. J Cell Physiol

Chandalia M, Garg A, Lutjohann D, von Bergmann K, Grundy SM, Brinkley LJ (2000) Beneficial effects of high dietary fiber intake in patients with type 2 diabetes mellitus. N Engl J Med 342(19): 1392–1398. https://doi.org/10.1056/NEJM200005113421903

Choi YE, Ahn SK, Lee WT, Lee JE, Park SH, Yoon BB, Park KA (2010) Soybeans ameliolate diabetic nephropathy in rats. Evid Based Complement Alternat Med 7(4):433–440. https://doi.org/10.1093/ecam/nen021

Collier GR, Kalmusky J, Guidici S (1985) Effect of slowly digested carbohydrates in type I diabetic children. Diabetes 32:33A

Colman RJ, Anderson RM, Johnson SC, Kastman EK, Kosmatka KJ, Beasley TM, Allison DB, Cruzen C, Simmons HA, Kemnitz JW, Weindruch R (2009) Caloric restriction delays disease onset and mortality in rhesus monkeys. Science 325(5937):201–204. https://doi.org/10.1126/science.1173635

Dashti HM, Al-Zaid NS, Mathew TC, Al-Mousawi M, Talib H, Asfar SK, Behbahani AI (2006) Long term effects of ketogenic diet in obese subjects with high cholesterol level. Mol Cell Biochem 286(1-2):1–9. https://doi.org/10.1007/s11010-005-9001-x

Fontana L, Partridge L, Longo VD (2010) Extending healthy life span-from yeast to humans. Science 328(5976):321–326. https://doi.org/10.1126/science.1172539

Fontana L, Weiss EP, Villareal DT, Klein S, Holloszy JO (2008) Long-term effects of calorie or protein restriction on serum IGF-1 and IGFBP-3 concentration in humans. Aging Cell 7(5):681–687. https://doi.org/10.1111/j.1474-9726.2008.00417.x

Franz MJ, Boucher JL, Green-Pastors J, Powers MA (2008) Evidence-based nutrition practice guidelines for diabetes and scope and standards of practice. J Am Diet Assoc 108(1):S52–S58. https://doi.org/10.1016/j.jada.2008.01.021

Franz MJ, Powers MA, Leontos C, Holzmeister LA, Kulkarni K, Monk A, Wedel N, Gradwell E (2010) The evidence for medical nutrition therapy for type 1 and type 2 diabetes in adults. J Am Diet Assoc 110(12):1852–1889. https://doi.org/10.1016/j.jada.2010.09.014

Friedman AN (2004) High-protein diets: potential effects on the kidney in renal health and disease. Am J Kidney Dis 44(6):950–962. https://doi.org/10.1053/j.ajkd.2004.08.020

Gower BA, Goss AM (2015) A lower-carbohydrate, higher-fat diet reduces abdominal and intermuscular fat and increases insulin sensitivity in adults at risk of type 2 diabetes. J Nutr 145(1):177S–183S. https://doi.org/10.3945/jn.114.195065

Hamid A, Ilyas M, Kalsoom S, Bhatty N (2017) Effects of wheat bran diet and maize bran diet on the random blood glucose and weight of alloxan induced diabetic rats. J Anim Plant Sci 27(1):325–330

Hannan JM, Rokeya B, Faruque O, Nahar N, Mosihuzzaman M, Khan AA, Ali L (2003) Effect of soluble dietary fibre fraction of Trigonella foenum graecum on glycemic, insulinemic, lipidemic and platelet aggregation status of type 2 diabetic model rats. J Ethnopharmacol 88(1):73–77. https://doi.org/10.1016/S0378-8741(03)00190-9

Hofmann SM, Dong HJ, Li Z, Cai W, Altomonte J, Thung SN, Zeng F, Fisher EA, Vlassara H (2002) Improved insulin sensitivity is associated with restricted intake of dietary glycoxidation products in the db/db mouse. Diabetes 51(7):2082–2089. https://doi.org/10.2337/diabetes.51.7.2082

Holman RR, Steemson J, Darling P, Turner RC (1987) No glycemic benefit from guar administration in NIDDM. Diabetes Care 10(1): 68–71. https://doi.org/10.2337/diacare.10.1.68

Hussain TA, Mathew TC, Dashti AA, Asfar S, Al-Zaid N, Dashti HM (2012) Effect of low-calorie versus low-carbohydrate ketogenic diet in type 2 diabetes. Nutrition 28(10):1016–1021. https://doi.org/10.1016/j.nut.2012.01.016

Ikeda Y, Enomoto H, Tajima S, Izawa-Ishizawa Y, Kihira Y, Ishizawa K, Tomita S, Tsuchiya K, Tamaki T (2013) Dietary iron restriction inhibits progression of diabetic nephropathy in db/db mice. Am J Physiol Ren Physiol 304(7):F1028–F1036. https://doi.org/10.1152/ajprenal.00473.2012

Imai S, Guarente L (2010) Ten years of NAD-dependent SIR2 family deacetylases: implications for metabolic diseases. Trends Pharmacol Sci 31(5):212–220. https://doi.org/10.1016/j.tips.2010.02.003

Ismaiel M, Yang H, Cui M (2017) Evaluation of high fibers Okara and soybean bran as functional supplements for mice with experimentally induced type 2 diabetes. PJFNS

Jenkins A, Josse RG (1985) Effects of processing/preparation as the blood glucose response to potatoes in diabetic patients. Diabetes (Suppl) 34:32A

Jheng HF, Hirotsuka M, Goto T, Shibata M, Matsumura Y, Kawada T (2017) Dietary low-fat soy milk powder retards diabetic nephropathy progression via inhibition of renal fibrosis and renal inflammation. Mol Nutr Food Res 61(3)

Jürgens H, Neschen S, Ortmann S, Scherneck S, Schmolz K, Schüler G, Schmidt S, Blüher M, Klaus S, Perez-Tilve D, Tschöp M, Schürmann A, Joost HG (2007) Development of diabetes in obese, insulinresistant mice: essential role of dietary carbohydrate in ß-cell destruction. Diabetologia 50(7):1481–1489. https://doi.org/10.1007/s00125-007-0662-8

Kahn SE, Hull RL, Utzschneider KM (2006) Mechanisms linking obesity to insulin resistance and type 2 diabetes. Nature 444(7121):840–846. https://doi.org/10.1038/nature05482

Kim H, Kang H, Heo RW, Jeon BT, Yi CO, Shin HJ, Kim J, Jeong SY, Kwak W, Kim WH, Kang SS (2016) Caloric restriction improves diabetes-induced cognitive deficits by attenuating neurogranin-associated calcium signaling in high-fat diet-fed mice. J Cereb Blood Flow Metab 6:1098–1110

Kitada M, Ogura Y, Suzuki T, Sen S, Lee SM, Kanasaki K, Kume S, Koya D (2016) A very-low-protein diet ameliorates advanced diabetic nephropathy through autophagy induction by suppression of the mTORC1 pathway in Wistar fatty rats, an animal model of type 2 diabetes and obesity. Diabetologia 59(6):1307–1317. https://doi.org/10.1007/s00125-016-3925-4

Kluth O, Mirhashemi F, Scherneck S, Kaiser D, Kluge R, Neschen S, Joost HG, Schürmann A (2011) Dissociation of lipotoxicity and glucotoxicity in a mouse model of obesity associated diabetes: role of forkhead box O1 (FOXO1) in glucose-induced beta cell failure. Diabetologia 54(3):605–616. https://doi.org/10.1007/s00125-010-1973-8

Knight DC, Eden JA (1996) A review of the clinical effects of phytoestrogens. Obstet Gynecol 87(5):897–904

Koh GY, Rowling MJ, Schalinske KL, Grapentine K, Loo YT (2016) Consumption of dietary resistant starch partially corrected the growth pattern despite hyperglycemia and compromised kidney function in streptozotocin-induced diabetic rats. J Agric Food Chem 64(40):7540–7545. https://doi.org/10.1021/acs.jafc.6b03808

Kuiper GG, Lemmen JG, Carlsson BO, Corton JC, Safe SH, Van Der Saag PT, Van Der Burg B, Gustafsson JA (1998) Interaction of estrogenic chemicals and phytoestrogens with estrogen receptor β. Endocrinology 139(10):4252–4263. https://doi.org/10.1210/endo.139.10.6216

Kume S, Thomas MC, Koya D (2012) Nutrient sensing, autophagy, and diabetic nephropathy. Diabetes 61(1):23–29. https://doi.org/10.2337/db11-0555

Lee JS (2006) Effects of soy protein and genistein on blood glucose, antioxidant enzyme activities, and lipid profile in streptozotocin-induced diabetic rats. Life Sci 79(16):1578–1584. https://doi.org/10.1016/j.lfs.2006.06.030

Lee SM (1982) The effect of a high fibre diet on diabetic nephropathy in the db/db mouse. Diabetologia 22(5):349–353

Lee SM, Bressler R (1981) Prevention of diabetic nephropathy by diet control in the db/db mouse. Diabetes 30(2):106–111. https://doi.org/10.2337/diab.30.2.106

Leiter EH, Coleman DL, Ingram DK, Reynolds MA (1983) Influence of dietary carbohydrate on the induction of diabetes in C57BL/KsJ-db/db diabetes mice. J Nutr 113(1):184–195

Li J, Kaneko T, Qin LQ, Wang J, Wang Y, Sato A (2003) Long-term effects of high dietary fiber intake on glucose tolerance and lipid metabolism in GK rats: comparison among barley, rice, and cornstarch. Metabolism 52(9):1206–1210. https://doi.org/10.1016/S0026-0495(03)00159-8

Li N, Guenancia C, Rigal E, Hachet O, Chollet P, Desmoulins L, Leloup C, Rochette L, Vergely C (2016) Short-term moderate diet restriction in adulthood can reverse oxidative, cardiovascular and metabolic alterations induced by postnatal overfeeding in mice. Sci Rep 6

Lu MP, Wang R, Song X, Chibbar R, Wang X, Wu L, Meng QH (2008) Dietary soy isoflavones increase insulin secretion and prevent the development of diabetic cataracts in streptozotocin-induced diabetic rats. Nutr Res 28(7):464–471

Madar Z (1983) Effect of brown rice and soybean dietary fiber on the control of glucose and lipid metabolism in diabetic rats. Am J Clin Nutr 38(3):388–393

Markovic TP, Jenkins AB, Campbell LV, Furler SM, Kraegen EW, Chisholm DJ (1998) The determinants of glycemic responses to diet restriction and weight loss in obesity and NIDDM. Diabetes Care 21(5):687–694. https://doi.org/10.2337/diacare.21.5.687

Minamiyama Y, Bito Y, Takemura S, Takahashi Y, Kodai S, Mizuguchi S, Nishikawa Y, Suehiro S, Okada S (2007) Calorie restriction improves cardiovascular risk factors via reduction of mitochondrial reactive oxygen species in type II diabetic rats. J Pharmacol Exp Ther 320(2):535–543

Mirhashemi F, Kluth O, Scherneck S, Vogel H, Kluge R, Schürmann A, Joost HG, Neschen S (2008) High-fat, carbohydrate-free diet markedly aggravates obesity but prevents beta cell loss and diabetes in the obese, diabetes-susceptible db/db strain. Obes Facts 1(6):292–297. https://doi.org/10.1159/000176064

Mori S, Kawano K, Hirashima T, Natori T (1996) Relationships between diet control and the development of spontaneous type II diabetes and diabetic nephropathy in OLETF rats. Diabetes Res Clin Pract 33(3):145–152. https://doi.org/10.1016/0168-8227(96)01290-9

Nangaku M, Izuhara Y, Usuda N, Inagi R, Shibata T, Sugiyama S, Kurokawa K, de Strihou CV, Miyata T (2005) In a type 2 diabetic nephropathy rat model, the improvement of obesity by a low calorie diet reduces oxidative/carbonyl stress and prevents diabetic nephropathy. Nephrol Dial Transplant 20(12):2661–2669. https://doi.org/10.1093/ndt/gfi096

Ohneda M, Inman LR, Unger RH (1995) Caloric restriction in obese prediabetic rats prevents beta-cell depletion, loss of beta-cell GLUT 2 and glucose incompetence. Diabetologia 38(2):173–179. https://doi.org/10.1007/BF00400091

Okauchi N, Mizuno A, Yoshimoto S, Zhu M, Sano T, Shima K (1995) Is caloric restriction effective in preventing diabetes mellitus in the Otsuka Long Evans Tokushima fatty rat, a model of spontaneous non-insulin-dependent diabetes mellitus? Diabetes Res Clin Pract 27(2):97–106. https://doi.org/10.1016/0168-8227(95)01029-D

Otoda T, Kanasaki K, Koya D (2014) Low-protein diet for diabetic nephropathy. Curr Diab Rep 14(9):523. https://doi.org/10.1007/s11892-014-0523-z

Oudot C, Lajoix AD, Jover B, Rugale C (2013) Dietary sodium restriction prevents kidney damage in high fructose-fed rats. Kidney Int 83(4):674–683. https://doi.org/10.1038/ki.2012.478

Poplawski MM, Mastaitis JW, Isoda F, Grosjean F, Zheng F, Mobbs CV (2011) Reversal of diabetic nephropathy by a ketogenic diet. PLoS One 6(4):e18604. https://doi.org/10.1371/journal.pone.0018604

Razzaque MS, Shimokawa I, Nazneen A, Liu D, Naito T, Higami Y, Taguchi T (1999) Life-long dietary restriction modulates the expression of collagens and collagen-binding heat shock protein 47 in aged Fischer 344 rat kidney. Histochem J 31(2):123–132. https://doi.org/10.1023/A:1003578928487

Shapiro H, Theilla M, Attal-Singer J, Singer P (2011) Effects of polyunsaturated fatty acid consumption in diabetic nephropathy. Nat Rev Nephrol 7(2):110–121. https://doi.org/10.1038/nrneph.2010.156

Sheard NF, Clark NG, Brand-Miller JC, Franz MJ, Pi-Sunyer FX, Mayer-Davis E, Kulkarni K, Geil P (2004) Dietary carbohydrate (amount and type) in the prevention and management of diabetes: a statement by the american diabetes association. Diabetes Care 27(9):2266–2271. https://doi.org/10.2337/diacare.27.9.2266

Steinberg GR, Kemp BE (2009) AMPK in health and disease. Physiol Rev 89(3):1025–1078. https://doi.org/10.1152/physrev.00011.2008

Surwit RS, Kuhn CM, Cochrane C, Mc Cubbin JA, Feinglos MN (1988) Diet-induced type II diabetes in C57BL/6J mice. Diabetes 37(9):1163–1167. https://doi.org/10.2337/diab.37.9.1163

Tikoo K, Tripathi DN, Kabra DG, Sharma V, Gaikwad AB (2007) Intermittent fasting prevents the progression of type I diabetic nephropathy in rats and changes the expression of Sir2 and p53. FEBS Lett 581(5):1071–1078. https://doi.org/10.1016/j.febslet.2007.02.006

Tonshoff B, Kaskel FJ, Moore LC (1998) Effects of insulin-like growth factor I on the renal juxtamedullary microvasculature. Am J Phys 274:F120–F128

Tsukahara H, Gordienko DV, Tonshoff B, Gelato MC, Goligorsky MS (1994) Direct demonstration of insulin-like growth factor-I-induced nitric oxide production by endothelial cells. Kidney Int 45(2):598–604. https://doi.org/10.1038/ki.1994.78

Ugochukwu NH, Bagayoko ND, Antwi ME (2004) The effects of dietary caloric restriction on antioxidant status and lipid peroxidation in mild and severe streptozotocin-induced diabetic rats. Clin Chim Acta 348(1):121–129. https://doi.org/10.1016/j.cccn.2004.05.005

Ugochukwu NH, Mukes JD, Figgers CL (2006) Ameliorative effects of dietary caloric restriction on oxidative stress and inflammation in the brain of streptozotocin-induced diabetic rats. Clin Chim Acta 370(1):165–173. https://doi.org/10.1016/j.cca.2006.02.003

Uusitupa M, Siitonen O, Savolainen K, Silvasti M, Penttila I, Parviainen M (1989) Metabolic and nutritional effects of long-term use of guar gum in the treatment of noninsulin-dependent diabetes of poor metabolic control. Am J Clin Nutr 49(2):345–351

Wagner JD, Zhang L, Shadoan MK, Kavanagh K, Chen H, Tresnasari K, Kaplan JR, Adams MR (2008) Effects of soy protein and isoflavones on insulin resistance and adiponectin in male monkeys. Metabolism 57(7 Suppl 1):S24–S31. https://doi.org/10.1016/j.metabol.2008.04.001

Wellen KE, Thompson CB (2010) Cellular metabolic stress: considering how cells respond to nutrient excess. Mol Cell 40(2):323–332. https://doi.org/10.1016/j.molcel.2010.10.004

World Health Organization (2016) Global report on diabetes. Geneva. Available from http://apps.who.int/iris/bitstream/10665/204871/1/9789241565257_eng.pdf?u. Accessed 5 May 2017

Zheng F, He C, Cai W, Hattori M, Steffes M, Vlassara H (2002) Prevention of diabetic nephropathy in mice by a diet low in glycoxidation products. Diabetes Metab Res Rev 18(3):224–237. https://doi.org/10.1002/dmrr.283

Zoncu R, Efeyan A, Sabatini DM (2011) mTOR: from growth signal integration to cancer, diabetes and ageing. Nat Rev Mol Cell Biol 12(1):21–35. https://doi.org/10.1038/nrm3025