Nutraceuticals, Glycemic Health & Type 2 Diabetes

EDITORS

Vijai K. Pasupuleti • James W. Anderson

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Preface

The discovery of insulin by Banting and Best in 1921 and its subsequent commercialization moved diabetes from a death sentence to a chronic disease often associated with complications such as neuropathy, nephropathy, retinopathy, and cardiovascular problems. Subsequently there have remarkable improvements in types of insulin—moving from porcine sources to human insulin produced by recombinant microbial cultures—with development of fast, intermediate, and slow-acting forms. Many new pharmacological agents have been developed and approved by the FDA, but some have been discontinued or required serious warning labels. Recently, the outstanding prevention research results from the Diabetes Prevention Program studies from the United States and other countries across the world have ushered in a new era for the prevention and management of prediabetes and type 2 diabetes simply by lifestyle changes, diet, and exercise.

Despite all the advances in knowledge and progress in therapy, diabetes poses a greater challenge than ever. Fueled by the upsurge in overweight/obesity, the diabetes rates continue to rise all over the world. The most recent CDC study (2005) reports that diabetes has risen by over 14% in the last two years (2003 to 2005). Conservative projections suggest that by 2008, 24 million Americans—7.9% of the U.S. population will have diabetes. A combined total of approximately 94 million (70 prediabetic and 24 million diabetic) puts almost one in three as either prediabetic or diabetic (CDC 2005). In addition to these alarming prevalence projections, the cost of diabetes was estimated to be $132 billion in 2002 (CDC 2005) and will escalate to an estimated $167 billion by 2008.

Preventing and controlling prediabetes and type 2 diabetes are important for improving the quality of life and reducing the economic burden. To illustrate the economics of using nutraceutical supplements, one study projected that use of its particular supplement would save $52.9 billion for diabetic patients and public healthcare system when that supplement was used as an adjunct to nutritional therapy. This clearly demonstrates that there is a great opportunity for using nutraceuticals to better control and manage diabetes. At the same time it also illustrates that there is a gap in understanding between consumers, physicians, and researchers from academia and industry as how nutraceuticals can assist in preventing and managing prediabetes and type 2 diabetes. As consumers navigate

the ever-changing health-related nutrition messages promising lasting weight control and good health, they have discovered that good nutrition is not as simple as avoiding carbohydrates. The amount and type of carbohydrates in the diet are of vital importance when trying to combat the global epidemics of overweight, obesity, and type 2 diabetes. This book *Nutraceuticals, Glycemic Health and Type 2 Diabetes* draws experts from academia and industry to highlight the epidemiology, glycemia, and nutraceuticals from scientific/clinical and functional foods points of view to benefit type 2 diabetic patients.

Type 2 diabetes is a growing problem for the developed and developing countries, and it is a burden on healthcare systems as well as individuals. This book primarily focuses on the nutraceuticals that assist in preventing and managing prediabetes and type 2 diabetes. It provides an overview of glycemic health and highlights the use of novel and upcoming nutraceutical ingredients such as bioactive peptides, soy, fiber, traditional herbs from India, China, and Mexico, American ginseng, resistant starches, cinnamon, chromium, novel antioxidants, and others.

This book is a compilation and assessment on emerging concepts and nutraceuticals in the prevention and management of diabetes by the experts who presented valid, accurate, latest, and useful data based on evidence.

The book starts off with an introduction followed by epidemiology of diabetes around the world. In the first section, the glycemic concept is explored from physicians and scientific points of view. In the second section, emerging nutraceuticals including herbs are discussed in detail. The book ends with "Future Trends and Directions" and appendix with a comprehensive list of ingredients for diabetes.

The book is intended to bring out the latest concepts and nutraceuticals based on scientific evidence for the prevention and management of diabetes. We hope that we fulfilled these objectives for all those concerned with the role of nutraceuticals and glycemic health in the prevention and management of type 2 diabetes.

We hope that this book will fill a gap in providing an up-to-date reference from scientific point of view on the nutraceuticals and glycemic concept in the prevention and management of type 2 diabetes.

Vijai K Pasupuleti and James W Anderson

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Nutraceuticals, Glycemic Health and Type 2 Diabetes

Chapter 1

Nutraceuticals and Diabetes Prevention and Management

James W Anderson, MD, and Vijai K Pasupuleti, PhD

Introduction

Individual bioactive chemicals or foods claimed to have health promoting, disease preventing, or medicinal effect on human health are called nutraceuticals. Such foods are also called functional foods. The impact of these nutraceuticals in diabetes prevention and management will be briefly discussed in this chapter and throughout the book.

Every nation on this planet at some stage in their history has adapted to new lifestyles in search of comfort, convenience, and taste. These changes appear to be the direct result of overweight, obesity, and related diseases such as type 2 diabetes. Ironically, in order to prevent, manage, or reverse diabetes the first step is the lifestyle change to eat healthy foods and exercise regularly (Diabetes Prevention Program 2002).

Diabetes is increasing in prevalence worldwide at an alarming rate. This is closely linked to the emergence of obesity in developed and developing countries. Zimmet (2007) has recently stated that this is the largest epidemic the world has ever faced. The estimated number of persons with diabetes in the world is projected to grow from present 246 million to 380 million in 2025. Because of frightening consequences of diabetes on individuals and national economies, on December 21, 2006, the United Nations General Assembly unanimously passed a resolution declaring diabetes as an international public health issue; after HIV/AIDS, diabetes is only the second disease to attain this unenviable designation.

Unfortunately, populations in developing areas have a greater genetic propensity for diabetes than populations in northern Europe. Consequently, African, Southern European, South American, and Asian populations are at a significantly greater risk for developing type 2 diabetes at lower body masses and with less weight gain than are indigenous populations, for example, England (Chapman-Novakofski 2008). Some believe that the risk for diabetes is much higher in these countries as well

as in Pima Indians (prevalence and incidence rates of diabetes in Pima Indians are the highest in the world (Bogardus and Tataranni 2002), Nauruans are only next to Pima Indians and rank as the second highest incidence rates of type 2 diabetes in the world with 45% having type 2 diabetes and >75% of the adult population are overweight or obese (King and Rewers 1993)) and Australian aborigines (Guest and O'Dea 1992) because of thrifty genes (Neel 1962). However, the fundamental basis of the thrifty gene hypothesis has recently been challenged by Speakman (Speakman 2007).

Approximately half of all the individuals in the United States have diabetes, prediabetes, or are at a substantial risk for developing diabetes because of the presence of the metabolic syndrome. For 2008 the estimated prevalence of diabetes and related conditions for all ages in the U.S. population are: diabetes 7.9% or 24.1 million; prediabetes 23% or 70.3 million; and the metabolic syndrome 20.3% or 62.0 million. These estimates were derived from firm estimates in the literature (CDC 2005; Ford et al. 2002; Nathan 2007 and Weiss et al. 2004). Of those with diagnosed diabetes, approximately 90% have type 2 diabetes and ~80% of these are obese (Anderson et al. 2003).

Prediabetes precedes type 2 diabetes and the term prediabetes was introduced in 2002 by Department of Health and Human Services and American Diabetes Association to bring awareness among physicians and general population. One of the reasons for renaming prediabetes from its former clinical name of impaired glucose tolerance (IGT) was to highlight the seriousness of the condition and to motivate people to get appropriate help. As the name suggests, prediabetes is defined as condition that precedes type 2 diabetes. Both IGT or impaired fasting glucose (IFG) are included in the term prediabetes. People with prediabetes have higher than normal blood glucose levels, but they are not elevated enough to be diagnosed as diabetes. A fasting plasma glucose value between 100 and 125 mg/dL or more indicates IFG. In an oral glucose tolerance test, plasma glucose values between 140 and 199 mg/dL at 2 h postglucose load indicates impaired glucose tolerance.

Prevention of type 2 diabetes should begin before or during the IFG and/or IGT stage. Both prevention and management of diabetes can be achieved by lifestyle changes, nutraceuticals, and/or drugs. In this short review, we cover the nutraceuticals and briefly touch upon the lifestyle and pharmacological approaches and how they can be potentially used to prevent and manage diabetes.

The main causative factors of diabetes are a genetic disposition, overweight or obesity, lack of physical activity, consumption of high-fat, low-fiber diets, oxidative stress, and possibly deficiencies in certain minerals (Figure 1.1).

Lifestyle

Diabetes prevention program studies in the United States, Europe, and Asia clearly demonstrated that by lifestyle changes one could prevent, manage, and

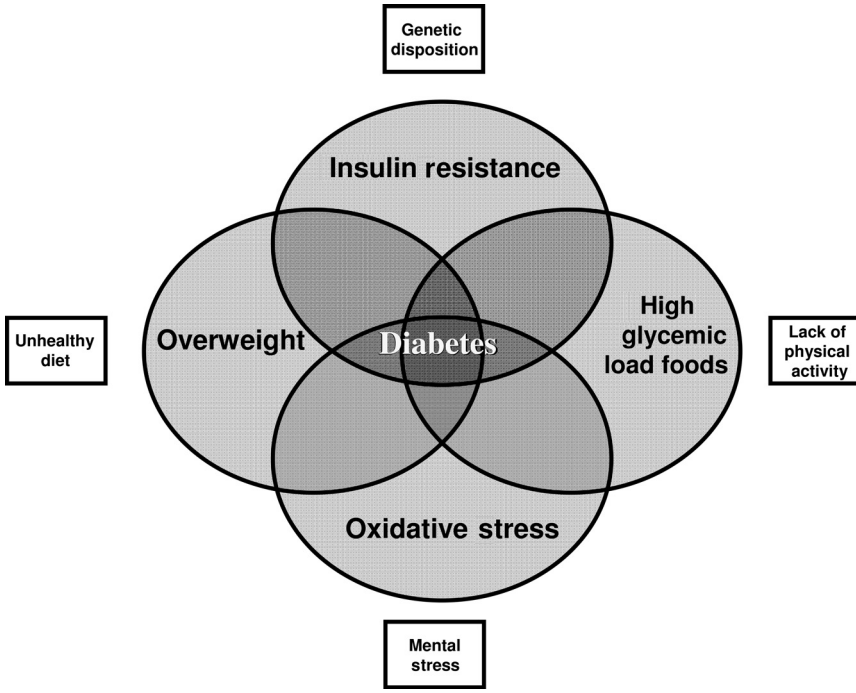

Figure 1.1. Contributing factors to prediabetes and type 2 diabetes.

reverse the prediabetes. U.S. Diabetes Prevention Program studies pointed out that lifestyle changes have achieved better results in prevention of diabetes compared to metformin (58% vs. 31%, respectively). The additional benefit of lifestyle change is that there are no side effects like those associated with the drugs. By adopting the lifestyle changes the human and economic costs of diabetes can be significantly reduced. It was estimated that in 2002 the total annual economic cost of diabetes was $132 billion or $1 for every $10 of healthcare dollars spent in America (French 2007) (ADA 2002). The goals for lifestyle changes are increased physical activity, improving dietary composition with fiber, and reducing the consumption of refined sugars, saturated fats, eliminating trans fats, avoiding smoking and excessive alcohol drinking, and losing body weight to a desirable level (Anderson et al. 2003) or at least 5–7% body weight. Hamman et al. (2006) followed up with DPP participants randomized to the intensive lifestyle intervention had a significantly reduced risk of diabetes compared to placebo participants. Weight loss is the dominant predictor for reduced diabetes incidence rates. Based on their studies it is predicted that patients who lose more weight than the DPP average of 5–7% and who meet physical activity and dietary fat goals could reduce their diabetes risk by greater than 90%. For every kilogram of weight loss, there was a 16% reduction in risk,

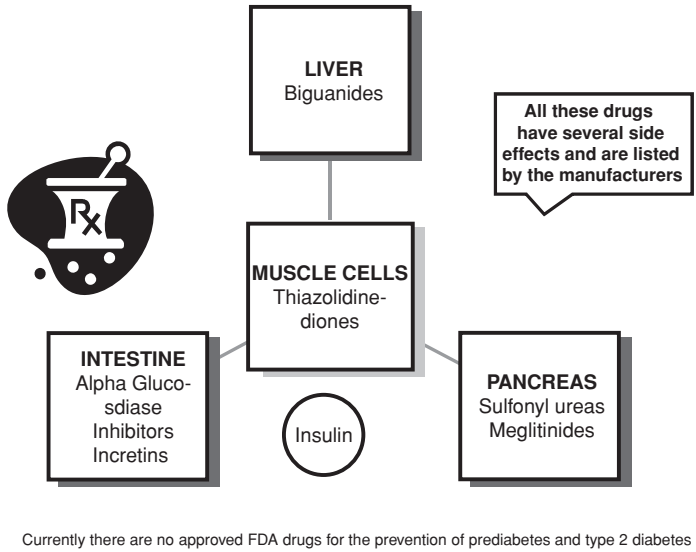

Figure 1.2. Action sites of different FDA approved drugs for type 2 diabetes.

adjusted for changes in diet and physical activity. Thus far it is evident and very impressive from all the preventive studies across the world that a simple lifestyle change makes a big difference. If this research can be implemented/translated to bring a change in individuals and in the communities we can prevent, manage, and reverse prediabetes, diabetes, and their associated risks in a considerable amount of population. This will not only improve the quality of life but also significantly reduce the financial burden on the individuals and Government. Greenway covers in detail lifestyle changes and its effect on diabetes in Chapter 3.

Pharmacologic Approaches

There are a number of FDA approved drugs for the management of diabetes, and each class of drugs is unique and acts on different sites Figure 1.2.

Active research is focused on new pharmacotherapies for prevention of type 2 diabetes. Some prior pharmacologic agents had serious side effects. An early agent in the biguanide class was withdrawn from the market because of renal toxicity and an association with lactic acidosis; the currently available metformin should not be used in persons with impaired renal failure or persons at risk for lactic acidosis. Troglitazone, a thiazolidinedione, was withdrawn from the market because of an association with liver failure; one of the currently available agents—rosiglitazone—is associated with an increased risk for congestive heart failure and, perhaps, for coronary heart disease.

Greenway (Chapter 3) reviews currently available pharmacologic agents that may have diabetes protective effects. Currently, metformin is the only agent that has documented protective effects related to type 2 diabetes (Diabetes Prevention Program Research Group 2002; Ramachandran et al. 2006). However, its protective effect is not as significant as with the lifestyle changes. To date, there are no FDA-approved drugs for the prevention of insulin resistance, prediabetes, and diabetes. Diet and exercise are the only currently accepted approaches for preventing the progression of prediabetes to type 2 diabetes.

Conventional Nutrition and Medical Nutrition Therapy

It may not be possible to come up with an optimal mix of macronutrients (carbohydrate, protein, and fat) as a universal diet for all the diabetics as the individual requirement varies from person to person (ADA 2006). Conventional or standard nutritional formulas are enriched with high carbohydrates, minerals, and vitamins and are low in fiber (Campbell and Schiller 1991). These may not be suitable to prediabetic and diabetic patients, as they tend to increase the blood glucose levels faster and compromise the glycemic control leading to several complications. Keeping this in mind diabetic specific formulas have been developed for use in conjunction with MNT as the comprehensive nutrition intervention (Coulston 1998). The diabetic specific ingredients may be combined with MNT formulas using a defined nutrient composition to achieve tighter glycemic control. Some of these specific nutrients are fiber, magnesium, soy protein and peptides, mono unsaturated fatty acids, antioxidants, chromium, and so on. Fiber, cinnamon, soy, antioxidants, resistant starch, and bioactive peptides are covered in detail in Chapters 7, 8, 9, 11, 16, and 17, respectively. The specific ingredients in MNT diabetic formulas assists in managing tighter glycemic control by delaying gastric emptying, intestinal absorption, producing smaller rise in glucose levels, increasing insulin sensitivity, and decreasing hepatic glucose output.

In the literature few clinical reviews have been published on the use of nutritional formulas for diabetes patients. Murakami et al. (2006) systematically reviewed published cohort studies on the effect of nutrient and food intake on the incidence of diabetes. They found significant inverse relationship with the intake of vegetable fat, poly unsaturated fat, dietary fiber, magnesium, and caffeine and direct relationship with intake of trans fatty acid and heme-iron, high glycemic index, and glycemic load foods to the incidence of diabetes.

Marinos et al. (2005) have done a systematic review and meta-analysis of diabetic specific formulas versus standard nutritional formulas. They looked at several parameters such as glycemia, lipidemia, nutritional status, medication requirements, quality of life, complications, and mortality. It was evident that the use of diabetes-specific formulas consistently resulted in significantly lower postprandial rise in blood glucose, peak blood glucose concentrations, and glucose area under the curve in diabetic patients.

The most important practice for diabetic individuals is to make a lifestyle change—eating a healthy diet, regular exercise, and using nutraceuticals to achieve an optimal blood glucose level. When it comes to ingredients in diabetic foods, there is no single magic bullet. However, there are ingredients that will slow down the absorption of glucose to avoid spikes, low glycemic index food ingredients that will yield relatively lower glucose levels, and some other ingredients increase insulin sensitivity and alleviate oxidative stress. The key to a successful diabetic diet is to combine all or some of these ingredients into foods and beverages with a great taste to appeal the consumers' palate (Pasupuleti 2007). Such a product coupled with regular exercise may replace or reduce the dosage of existing drugs without any side effects.

The American Diabetic Association (ADA 2006) issued nutrition recommendations and interventions for diabetes based on the best available scientific evidence. This is to bring awareness of beneficial nutrition intervention to the diabetic patients and healthcare providers for prevention and management of diabetes. The specific goals of MNT vary according to individual situations.

People with Prediabetes

The goal of MNT is to decrease the risk of diabetes and cardiovascular disease by lifestyle changes that include healthy food choices and physical activity leading to weight loss that is maintained. ADA (2006) recommended consumption of a minimum of 14 g fiber/1,000 kcal containing whole grains and other important nutrients. However, according to ADA there is no sufficient, consistent information to conclude that low glycemic load diets reduce risk for diabetes but low glycemic load diets that are rich in fiber and other important nutrients should be encouraged to prevent the progression of prediabetes to type 2 diabetes. Lifestyle changes, glycemia, and fiber have been covered in detail by Greenway, Wong, Reynolds, Foster-Powell, and Anderson in Chapters 3–7.

People with Type 2 Diabetes

The goals of MNT are to achieve and maintain blood glucose levels, lipid, lipoprotein profile, body weight, and blood pressure in the normal range or as close to normal as is safely possible; by changing the lifestyle and nutrition prevent or slow the rate of development of the chronic complications of diabetes; addressing the individual nutrition needs by taking into account personal and cultural preferences and willingness to change and to maintain the pleasure of eating by only limiting food choices when indicated by scientific evidence.

The most important aspect is to monitor blood glucose on a regular basis and, if needed, adjust the medication or diet by discussing with the healthcare professionals.

Minerals

Typically, micronutrient deficiencies are observed in uncontrolled diabetic patients. Therefore, it is essential to consume mineral requirements from natural food sources and if needed obtain from the supplements. There are reports suggesting that chromium, magnesium, zinc, vanadium, calcium, boron, and manganese assist in achieving tighter glycemic control. However, there is no clear evidence of benefit from mineral supplementation in people who do not have underlying deficiencies. Of all the minerals chromium has been extensively studied and it recently won a conditional health claim from FDA. Chromium and other minerals have been extensively reviewed by Domenico in Chapter 10.

Herbals

It is interesting to point out once again that certain ethnic groups such as Native Americans, Hispanics, and Asians are more vulnerable to diabetes and at the same time they have a long history of using traditional folk medicine in the form of herbs. More than 1,200 medicinal plants have been cited from Mexico, China, India, and other countries (Marles and Fransworth 1995). Some of the well-studied herbs like American ginseng, Chinese herbs, fenugreek, nopal, and traditional herbs from India and Mexico have been covered in detail by Sievenpiper, Lankarani-Fard, Srinivasan and Reynoso in Chapters 12, 13, 14, and 15, respectively. A list of all the herbs, and current concepts about their mechanisms and human studies are listed in Appendix.

Conclusions

From all the diabetes preventive studies one thing is evident that type 2 diabetes can be prevented or delayed by lifestyle modification. The screening tools for prediabetes and type 2 diabetes are readily available. However, the challenge is to implement the screening procedures and encourage high-risk individuals to modify their lifestyle. Further research is necessary to translate the excellent findings of DPP studies into practice in the communities to prevent or delay the onset of diabetes. At the same time intensive research efforts are ongoing across the globe to prevent and manage diabetes by nutraceuticals and pharmaceuticals. Anderson discusses future trends and directions in the prevention and management of diabetes in Chapter 18.

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