

Eating whole fruit, not drinking fruit juice, may reduce the risk of type 2 diabetes mellitus

Carbohydrates, otherwise known as saccharides, are macronutrients that are found in a wide variety of natural and processed foods. Carbohydrates include sugars, starch, and cellulose (insoluble dietary fiber), and can be categorized as monosaccharides, disaccharides, oligosaccharides, and polysaccharides. Monosaccharides such as glucose and fructose, and disaccharides such as sucrose, are together referred to as sugars.

The effects of carbohydrate consumption on the incidence of type 2 diabetes are dependent on the type of carbohydrate consumed. If fructose is consumed in small quantities, it is slowly absorbed and converted into glucose and lactate in the intestine, which prevents an increase in the plasma glucose concentration^{1,2}. However, when consumed in large amounts, it reaches the colonic microbiota and is delivered to the liver, where it promotes *de novo* lipogenesis and fatty liver^{1,2}. In animal studies, high-sucrose and fructose diets have been shown to cause fatty liver, obesity, and glucose tolerance due to decreased glycogen accumulation caused by decreased glucokinase activity in the liver and decreased glucagon-like peptide 1 (GLP-1) secretion³. However, human studies have provided little direct evidence for a relationship between the consumption of sugars and the onset of type 2 diabetes⁴. However, beverages containing high-fructose corn syrup may present a risk for the development of metabolic syndrome and non-alcoholic fatty liver disease/non-alcoholic steatohepatitis⁵. Conversely, a meta-analysis has shown that high dietary fiber consumption

reduces the risk of developing type 2 diabetes by 20–30%⁶. Therefore, the type and quantity of carbohydrate that is ingested can modify the risk of developing type 2 diabetes.

Recently, Bondonno *et al.*⁷ evaluated the relationship between fruit and fruit juice intake and the risk of type 2 diabetes in the Australian Diabetes, Obesity and Lifestyle Study (AusDiab) study. A total of 7,675 participants of >25 years of age (54 ± 12 years) completed a semi-quantitative food frequency questionnaire to evaluate their dietary intake at baseline, then 4,674 were followed for 5 years and 3,518 were followed for 12 years. The participants were allocated to four groups according to their median total fruit intake at baseline, and this was found to correlate inversely with insulin secretion and positively to correlate with insulin sensitivity. Moreover, the postprandial blood glucose concentration was significantly lower, and insulin sensitivity was considerably higher in the highest intake group than in the lowest intake group⁷.

The authors also investigated the relationship between high fruit consumption and the prevention of type 2 diabetes. One hundred seventy-nine of 4,674 participants developed type 2 diabetes during the 5 year follow-up period, and total fruit intake showed a non-linear, inverse association with the onset of type 2 diabetes (Figure 1). In particular, the moderate fruit intake group (230 g per day) showed a 36% lower incidence of type 2 diabetes after 5 years than the lowest intake group. In addition, 247 of the 3,518 participants developed type 2 diabetes during the 12 year follow-up period, and the incidence of type 2 diabetes was lower in those who ingested moderate-to-high quantities of fruit. The authors also evaluated the relationships

with individual fruits, the intake of which comprised $\geq 10\%$ of the total, and found that a higher intake of apples, bananas, oranges, and other citrus fruits reduced the risk of developing type 2 diabetes during the 5 (Figure 1) and 12 year follow-up periods. In particular, apple consumption inversely correlated with serum insulin, homeostasis model assessment HOMA2-% β , which reflects serum insulin levels and β -cell function, fasting blood glucose level, and postprandial blood glucose level, and showed a positive correlation with HOMA2-% S which reflects insulin sensitivity⁷.

In response to the results of this AusDiab study⁷, we hypothesize that dietary fiber reduces the glycemic load and is associated with a beneficial intestinal microbiota, which promotes satiety through greater production of short-chain fatty acids and GLP-1 secretion (Figure 2). Flavonoids are known to improve insulin sensitivity by causing beta-cell proliferation and reducing muscle inflammation. Moreover, small amounts of fructose do not increase plasma glucose, despite their potent sweetness. Fructose also induces the secretion of two hormones that affect appetite: GLP-1 in the gut and fibroblast growth factor (FGF)-21 in the liver. Fructose induces GLP-1 secretion independent of the closure of the K_{ATP} channel. In addition to causing gastric distension and peripheral vagal nerve activation, GLP-1 induces satiety through effects on the brain regions involved in the regulation of feeding. Furthermore, fructose increases *Fgf21* messenger ribonucleic acid expression through the activation of carbohydrate response element-binding protein². Both fructose and sucrose stimulate FGF21 secretion, which reduces the consumption of simple sugars, and because fruit is rich in fructose, its intake

*Corresponding author. Yusuke Seino

Tel: +81(Japan)-56-293-9242

Fax: +81(Japan)-56-295-1879

E-mail address: seinoy@fujita-hu.ac.jp

Received 19 July 2021; revised 23 July 2021;

accepted 26 July 2021

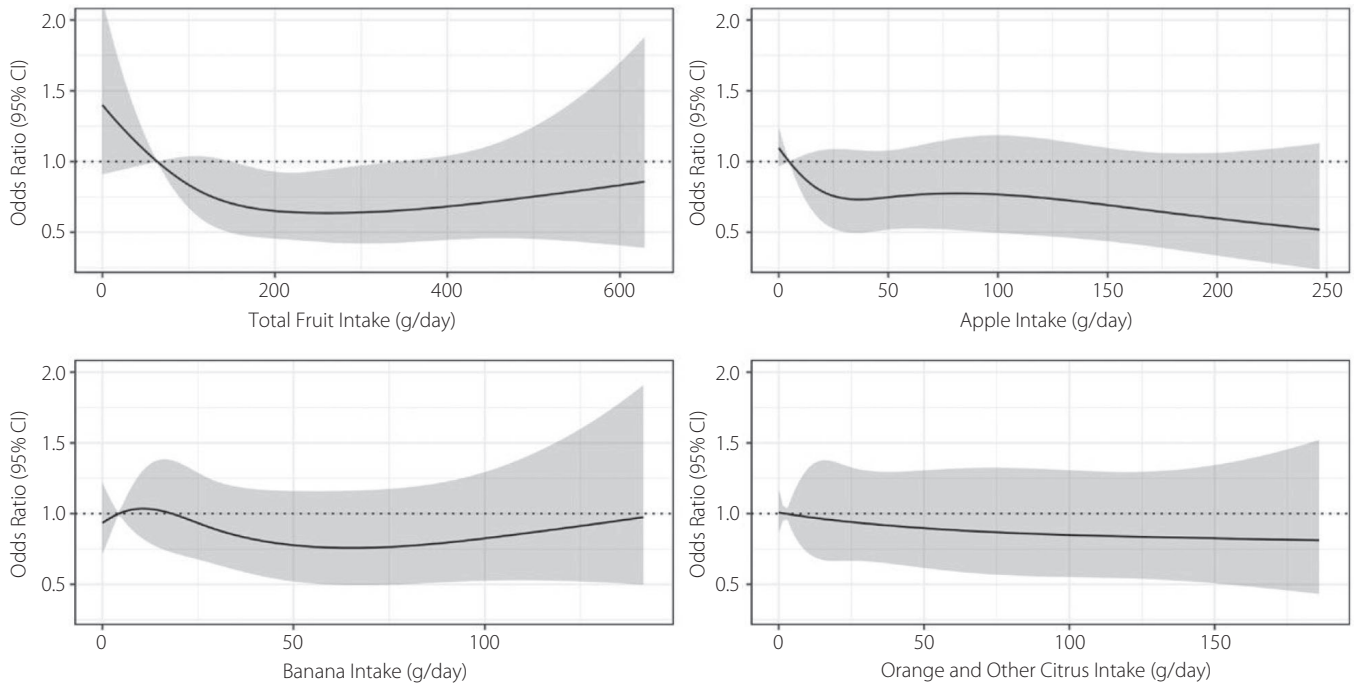


Figure 1 | Association of total fruit and individual fruit intake and the presence of type 2 diabetes. Multivariate analysis investigating the relationship between total fruit and individual fruit intake and presence of type 2 diabetes at 5 years. Values are odds ratios and 95% CI and compare the specific level of fruit intake (horizontal axis) to the median intake for participants in the Q1 group. Cited from Bondonno *et al.*⁷

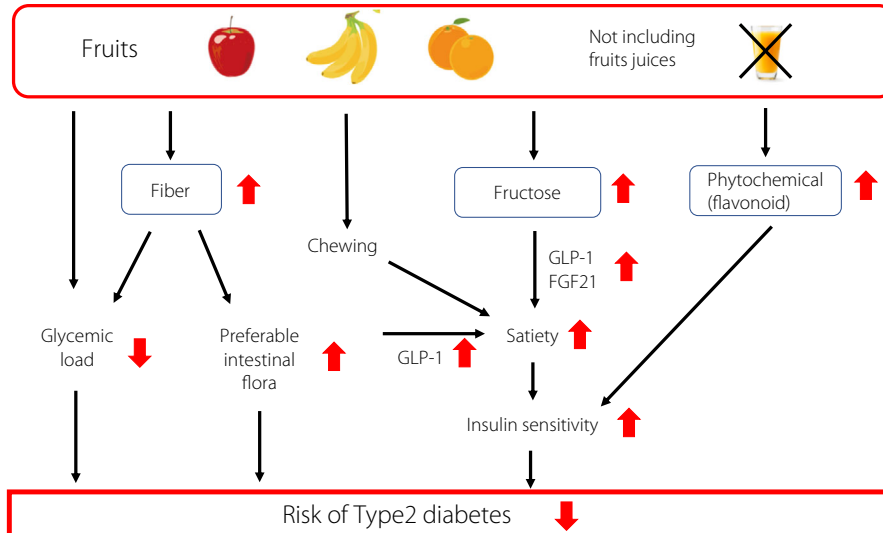


Figure 2 | Association of fruit intake and the risk of type 2 diabetes (hypothesis). Fruit intake may reduce risk of type 2 diabetes by probably four factors: dietary fiber, phytochemicals (flavonoids), fructose, and chewing. FGF-21, fibroblast growth factor-21; GLP-1, glucagon-like peptide 1.

may be associated with fructose-induced GLP-1 and FGF-21 secretion. Finally, chewing food is known to suppress appetite⁸, and given that the consumption of

fruit juice is not associated with the development of type 2 diabetes, chewing whole fruits may be protective against type 2 diabetes. Thus, fruit intake may

reduce the risk of type 2 diabetes through several pathways (Figure 2).

In conclusion, this study has shown that fruit consumption mitigates the risk

of type 2 diabetes. The finding that appropriate fruit intake reduces the risk of type 2 diabetes is useful knowledge for healthy individuals also. A low level of fructose consumption does not affect circulating glucose concentration and dietary fiber prevents postprandial hyperglycemia; therefore, the consumption of dietary fiber and a small amount of fructose may help to prevent type 2 diabetes. Further studies are required to understand why fruit juice does not reduce the risk of type 2 diabetes and to investigate whether fruit intake is useful for maintaining good glycemic control in patients with type 2 diabetes. Biting into an apple may be protective against type 2 diabetes.

DISCLOSURE

The authors declare no conflict of interest.

Yusuke Seino^{1*}, Katsumi Iizuka²,
Atsushi Suzuki¹

¹Departments of Endocrinology, Diabetes and Metabolism, Fujita Health University Graduate School of Medicine, Toyoake, Japan, ²Department of Diabetes and Endocrinology, Graduate School of Medicine, Gifu University, Gifu, Japan

REFERENCES

1. Jang C, Hui S, Lu W, *et al.* The small intestine converts dietary fructose into glucose and organic acids. *Cell Metab* 2018; 27: 351–361.
2. Iizuka K. The role of carbohydrate response element binding protein in intestinal and hepatic fructose metabolism. *Nutrients* 2017; 9: 181.
3. Seino Y, Murase M, Hayashi Y, *et al.* Carbohydrate-induced weight gain models for diabetes research: contribution of incretins and parasympathetic signal. *J Diabetes Investig* 2021; 12: 3–5.
4. Bazzano LA, Li TY, Joshipura KJ, *et al.* intake of fruit, vegetables, fruit juices and risk of diabetes in women. *Diabetes Care* 2008; 31: 1311–1317.
5. Bray GA. Potential health risks from beverages containing fructose found in sugar or high-fructose corn syrup. *Diabetes Care* 2013; 36: 11–12.
6. Weickert MO, Pfeiffer AFH. Impact of dietary fiber consumption on insulin resistance and the prevention of type 2 diabetes. *J Nutr* 2018; 148: 7–12.
7. Bondonno NP, Davey RJ, Murray K, *et al.* Associations between fruit intake and risk of diabetes in the AusDiab cohort. *J Clin Endocrinol Metab* 2021; <https://doi.org/10.1210/clinem/dgab335>
8. Miquel-Kergoat S, Azais-Braesco V, Burton-Freeman B, *et al.* Effects of chewing on appetite, food intake and gut hormones: a systematic review and meta-analysis. *Physiol Behav* 2015; 151: 88–96.

Doi: 10.1111/jdi.13639