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Fruit Sugar (Fructose) A Principal Driver for Reversing Type-2-Diabetes

[1]Dillip Kumar Mohapatra, [2]Deepika Rani Panigrahi, [3]Geetanjali Amat

[1,2,3]Department of Pharma Analysis, Gayatri College of Pharmacy, Sambalpur, Odisha

ABSTRACT

Effects of fructose on long-term glucose metabolism (glycosylated haemoglobin) in type 2 diabetes more insulin is needed than the pancreas can produce. Therefore, foods that need lower secretion of insulin, i.e. foods that have a lower glycemic index, are known to be beneficial for glucose metabolism.

AIM-The aim of this research study is to elucidate the role of fructose metabolism in type 2 diabetes and other metabolic diseases.

Objective: The objective of this study was to review to show some evidence that the short term replacement of other carbohydrate sources in the diabetic diet with fructose is known to improve short-term glycemic control, but there is also evidence of more prolonged improvement in glucose metabolism.

Design: We searched the e- Library; a literature search was performed as appropriate for narrative reviews, including electronic databases and clinicaltrials.gov databases with no time or language restrictions.

Results: Most people think of fructose as a natural fruit sugar. After all, it's one of the main sugars (along with glucose and sucrose) in fruits. In fact, the amount of fructose in most fruits is relatively small, compared with other sources. Fruit also contains a host of great nutrients, including fiber, which slows the absorption of sugars. The fructose found in processed foods, however, is another story. Between 1980 and 2000, Americans decreased their intake of sucrose (table sugar), but the amount of fructose consumption more than tripled. The reason for this was that food makers replaced sucrose (table sugar) with high-fructose corn syrup (HFCS) to sweeten foods and beverages. Also, people with diabetes were told that because fructose doesn't raise blood glucose levels, it was a good alternative to sugar. Therefore, they began using fructose-rich agave nectar under the mistaken assumption that it posed no diabetes-related risk.

Conclusions: Therefore, the available studies show some evidence that the replacement of other carbohydrate sources in the diabetic diet with fructose may improve the prolonged glycaemic control, although more research is needed to reach more precise conclusions.

KEY WORDS: *- Glycosylated haemoglobin, Glycemic index, HFCS*

INTRODUCTION

Most people think of fructose as a natural fruit sugar. After all, it's one of the main sugars (along with glucose and sucrose) in fruits. In fact, the amount of fructose in most fruits is relatively small, compared with other sources. Fruit also contains a host of great nutrients, including fiber, which slows the absorption of sugars.[1] General context this review investigates the role of fructose in metabolism of type 2 diabetes, and other metabolic diseases. Diabetes is associated with various factors such as dietary intake, genetics, physical activity and obesity, Type 2 diabetes is determined by measuring the amount of glucose in our blood. A reference range between 60-100 mg/ dL shows a normal range while 101-125 mg/dL is considered prediabetes and 126 mg/dL or higher shows you have diabetes. There is very little scientific literature on how fructose may also affect type 2 diabetes. Very few human studies on fructose and type 2 diabetes are present and the exact mechanism on how fructose affects insulin secretion is still under speculation. Only evidence from animal studies have shown the relationship between fructose and type 2 diabetes. Human studies have shown fructose in conjunction with another nutrient or compound to increase likelihood of type 2 diabetes. After absorption of fructose, it is transported to the liver where it is effectively absorbed by liver cells. In the liver, fructose can enter metabolic pathways: it can be oxidized, converted to glucose (and glycogen) or converted to lactic acid, or enter de novo lipogenesis (DNL). After an overnight fast, approximately 50% of fructose eaten as an oral dose of approximately 30-70g is converted to glucose via gluconeogenesis. The daily intake of fructose has been as high as 110 g, approximately 250 g, 80 g and 138 g. This indicates that fructose intake must be high to potentially cause insulin resistance [2].

Despite early considerations for the use of fructose as an alternative sweetener in people with diabetes, owing to its observed potential to lower postprandial glycaemic excursions when compared with isocaloric amounts of starch[3]increasing evidence has suggested that fructose could be particularly detrimental to metabolic health, and even more so than other sugars[4]. This view has received support from ecological evidence [5] as well as animal studies [6, 7, 8] and select human intervention studies [9, 10, 11].

As dietary guidelines shift from nutrient based recommendations to more food and dietary pattern based recommendations [12, 13], it is important to understand the role of the food matrix in modifying the effect of fructose-containing sugars. Current recommendations from the World Health Organization, United States, and United Kingdom have focused on the reduction of added or free sugars (added sugars plus sugars contained in fruit juices) to less than 5-10% energy[14,15,16], especially free fructose-containing sugars from SSBs[17]. Fructose also encourages food intake due to stimulation of dopamine in the mesolimbic system and effects on the hypothalamus [18, 19]. Food intake is also stimulated by hepatic ATP depletion [20], which occurs in animals and humans administered fructose [21]. Fructose may also affect metabolic rate. A recent study in humans documented a reduction in resting energy expenditure in overweight and obese subjects fed fructose but not glucose [22]. In this paper we aim to present a review on studies show some evidence that the replacement of other carbohydrate sources in the diabetic diet with fructose may improve the prolonged glycaemic control.

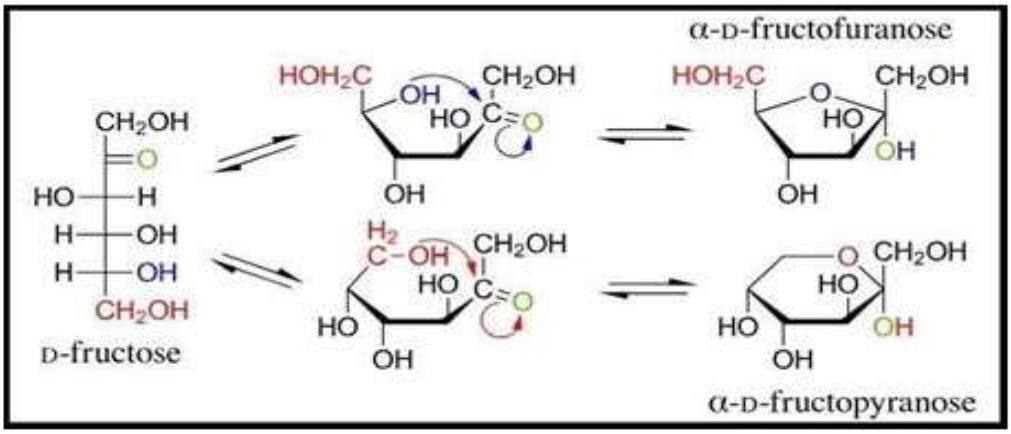
Data sources and searches

We searched the e- Library; a literature search was performed as appropriate for narrative reviews, including electronic databases and clinicaltrials govt databases with no time or language restrictions. References of the identified publications were searched for more research articles to include in this review. Selected studies were reviewed and evaluated for eligibility for inclusion in this review based on their relevance for diabetes reversal.

Study selection

We examined the full-text articles from all included abstracts, Blinded inclusion or exclusion of full-text articles was carried out independently.

Fructose is an important ketohexose. The molecular formula of fructose is $C_6H_{12}O_6$ and contains ketonic functional group at carbon number 2 and has six carbon atoms in a straight chain. The ring member of fructose is in analogy to the compound Furan and is named as furanose. The cyclic structure of fructose is shown below:



Carbohydrate Classification – Fructose

In the past several years traditional and social media caught up with the scientific debate and have now published numerous popular books, mainstream documentaries and newspaper headlines portraying fructose containing sugars as being toxic [23-24].

Fructose is a naturally occurring sugar with a pleasant taste. Fructose produces a smaller postprandial rise in plasma glucose than other common carbohydrates and thus might be a useful sweetening agent in the diabetic diet. However, dietary fructose appears to have adverse effects on plasma lipids in both diabetic and healthy populations. There is also concern that dietary fructose may stimulate energy intake and promote weight gain and obesity. However, there is no compelling evidence that this is true. Nevertheless, adding large amounts of fructose to the diet may be undesirable because of adverse effects on lipemia. Glucose may be a suitable replacement sugar. Concern about fructose should not extend to the naturally occurring fructose in fruits and vegetables. These are healthy foods that provide only a modest amount of fructose in most people's diets. [25] Fructose metabolism and its relation to type 2 diabetes and other metabolic diseases has been examined. Based on studies conducted, fructose can cause obesity, type 2 diabetes, increase hypertension and induce insulin resistance. Foods such as juices and pastries which are known to be plentiful in HFCS should be avoided. Regulating the consumption of fructose and consuming it minimally (only 25-40 g daily) is the best solution to prevent these metabolic diseases.

Commercially, fructose is derived from sugar cane, sugar beets, and maize. Crystalline fructose is the monosaccharide, dried, ground, and of high purity. High-fructose corn syrup is a mixture of glucose and fructose as monosaccharide. Sucrose is a compound with one molecule of glucose covalently linked to one molecule of fructose. All forms of fructose, including fruits and juices, are commonly added to foods and drinks for palatability and taste enhancement, and for browning of some foods, such as baked goods. About 240,000 tones of crystalline fructose are produced annually.

Sweetness of fructose

The primary reason that fructose is used commercially in foods and beverages, besides its low cost, is its high relative sweetness. It is the sweetest of all naturally occurring carbohydrates. The relative sweetness of fructose has been reported in the range of 1.2–1.8 times that of sucrose. However, it is the 6-membered ring form of fructose that is sweeter; the 5-membered ring form tastes about the same as usual table sugar. Warming fructose leads to formation of the 5-membered ring form. Therefore, the relative sweetness decreases with increasing temperature. However it has been observed that the absolute sweetness of fructose is identical at 5 °C as 50 °C and thus the relative sweetness to sucrose is not due to anomeric distribution but a decrease in the absolute sweetness of sucrose at lower temperatures.[26] Regular consumption of SSBs indicates that it can lead to weight gain and substantially increase risk of developing cardiometabolic diseases[27] .

Fructose absorption and metabolism in the GIT

Fructose enters cells by facilitated diffusion on the GLUT5 transporter. Expression of GLUT5 in the intestine is up regulated by fructose and not sucrose. As it enters the enterocyte, fructose difuses into the blood vessels through a transport mediated by GLUT2 at the basolateral pole of the enterocyte . GLUT8 has also been shown to regulate enterocyte fructose transport. The study tested the hypothesis that GLUT8 regulates intestinal hexose uptake and metabolic homeostasis in vivo. In addition, mice lacking GLUT8 rapidly developed significantly higher serum fructose concentration after oral glucose. GLUT8 is not involved in fructose uptake. In addition, mice lacking GLUT8 rapidly developed significantly higher serum fructose concentration after oral glucose. Therefore, GLUT8 is not involved in fructose uptake.

Hepatic metabolism

Fructose can be found in equimolar amounts with glucose from sucrose. Its metabolism takes place in the liver, where fructose is converted to pyruvate, or under fasting conditions to glucose. It is then metabolized to intermediates of glycolysis. For fructose to enter the pathways of intermediary metabolism, it must be phosphorylated. This can be done by hexokinase or fructokinase. It then becomes fructose 1-phosphate and is cleaved by aldolase B to form dihydroxyacetone phosphate (DHAP) and glyceraldehyde, which is phosphorylated by ATP to form glyceraldehyde 3-phosphate. Both of them are intermediates of glycolysis. Alternatively, the fructose can be converted to glucose by gluconeogenesis. Fructose metabolism parallels that of glycolysis. When it becomes pyruvate, it enters the tricarboxylic acid cycle and fatty acid synthesis. This is the reason why excess fructose can cause obesity, thereby affecting type 2 diabetes.

Carbohydrate intake, particularly intake of sucrose (glucose and fructose), has been directly correlated with fasting insulin levels and insulin concentrations 2 hours after a glucose load[28] But correlations were not as strong when looking solely at starch. The observational study that produced these findings used a 7-day weighed-food assessment, which provides a relatively robust method to estimate nutrient intake, giving more credence and relevance to the findings.

Exercise has a positive effect on fructose content in the body. Studies show that exercise performed immediately after fructose ingestion increases fructose oxidation and decreases fructose storage.

As diabetes rates have risen to unprecedented levels, the number of studies examining diabetes reversal using non-surgical techniques has increased. A handful of studies have reported successful weight loss with decreased insulin resistance, plasma glucose, and medication use following a low calorie diet.

Additional evidence has become available in recent years suggesting that diabetes reversal is a possible alternative to consider in place of traditional diabetes treatment and management.

Fructose-containing sugars and weight

A criticism that can be levelled on the systematic reviews and meta-analyses of controlled trials of fructose described above is that in diet pure fructose is not consumed in isolation but is commonly consumed together with glucose, either in form of HFCS or honey, or as part of the sucrose molecule. In other words, it can be argued that the above studies do not represent real-world situations for the vast majority of people. For this reason, we investigated the trials of fructose-containing sugars (HFCS, sucrose, honey, etc.) found normally in the diet and examined their effects on cardiometabolic outcomes. [28]

Conclusion

Fructose has been regarded as an acceptable caloric sweetener for diabetic subjects for two decades, but recently some important mechanisms of the effects of fructose have been documented. Small, catalytic amounts of fructose seem to improve glucose tolerance in healthy and especially in diabetic patients. The replacement of other carbohydrate sources in the diabetic diet with fructose may also improve prolonged glycaemic control, measured by HbA1c. All of these results were obtained with a small or moderate amount of fructose. High-fructose diets have been postulated to cause hypertension, insulin resistance, hyperlipidaemia and hyperinsuliaemia, but small and moderate amounts of fructose seem to have a favorable effect on glucose metabolism. Therefore, the available studies show some evidence that the replacement of other carbohydrate sources in the diabetic diet with fructose

may improve the prolonged glycaemic control, although more research is needed to reach more precise conclusions. Fructose metabolism and its relation to type 2 diabetes and other metabolic diseases has been examined. Based on studies conducted, fructose can cause obesity, type 2 diabetes, increase hypertension and induce insulin resistance. Foods such as juices and pastries which are known to be plentiful in HFCS should be avoided. Regulating the consumption of fructose and consuming it minimally (only 25-40 g daily) is the best solution to prevent these metabolic diseases. At an individual level, limiting consumption of foods and beverages that contain added sugars, particularly added fructose, may be one of the most effective strategies for ensuring one's robust future health.

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