

FRUCTOSE FACTSHEET

Despite sugar being in the news constantly, confusion remains about different sugar types and their metabolism. Health professionals are generally aware that the term 'sugars' includes glucose, fructose, lactose and sucrose, but fructose stands out from this list due to claims that it may have specific detrimental health effects. This factsheet will consider questions about fructose, providing answers supported by peer-reviewed research from high-quality scientific journals.

Q: WHICH FOODS CONTAIN FRUCTOSE?

All fruits naturally contain sugars, including fructose, which is why fructose is also found in 100% fruit juices. If the fructose component of sucrose (glucose + fructose) is also taken into account, the amount of fructose in a portion of fruit varies from 1 to 6 g for citrus fruits, around 7 g for pineapple, and 3 to 10 g for apples and pears depending on the variety.

As expected, the fructose content of fruit juices reflects the composition of whole fruit and, in common juices, varies from 0.5 to 7 g per 100 g. For example, 100 ml of orange juice contains 2.4 g fructose, while 100 g of whole orange contains 2.2 g of fructose. For apples, the fructose content is 6.7 g in whole fruit and 5.5 g in juice.¹

Q: WHAT CONTRIBUTES THE MOST FRUCTOSE TO THE DIET?

Data on fructose intakes are scarce. However, dietary surveys from the UK, France and New Zealand suggest that fructose intakes are around 20 to 40 g compared with 50 to 70 g in the USA. A significant source of fructose in the UK and France is whole fruit, followed by soft drinks containing sucrose (50% fructose).

In general, 100% fruit juice contributes very little fructose to the diet. Based on the fruit juice consumption in 46 different countries², an average daily intake of 1.5 g fructose from fruit juices was calculated which corresponds to less than 0.5% of the calories in a typical 2000 kcal diet. A 200 ml glass of 100% orange juice would provide 5 g of fructose daily.

Q: WHAT IS THE "FRUCTOSE HYPOTHESIS"?

The "Fructose-disease-Hypothesis" maintains that fructose plays a unique and causative role in the risk of chronic conditions such as cardiovascular disease, hypertension, diabetes, cancer and non-alcoholic fatty liver disease.³

However, this view has been challenged by scientists^{3,4} on the basis that: A) fructose intakes at normal population levels and patterns do not cause biochemical outcomes substantially different from other dietary sugars; and B) extreme experimental models that feature

hyper-dosing (> 20% of daily energy intake) or which significantly alter the usual dietary glucose-to-fructose ratio (i.e. ingesting pure fructose) are not predictive of typical human outcomes, nor relevant to public health policy.

Under realistic dietary conditions, fructose is seldom consumed in isolation but is almost always combined with glucose. This induces an insulin response which is absent when fructose is given in isolation.^{5,6} Analysis of the literature clearly shows that, in the case of overfeeding, the effects of fructose and glucose are similar pointing to excess calories being more influential than carbohydrate type.⁷

Q: HOW IS FRUCTOSE METABOLISED?

Unlike glucose, when fructose is absorbed from the gut no insulin is required for its metabolism. Following absorption in the small intestine, around a quarter of the fructose is converted to lactic acid, which is used as an energy substrate by the body or stored in glycogen. Around half of the fructose is converted into glucose, of which only a fraction (1-3%) is converted to fatty acids.⁸ The remainder is taken up by the liver and converted to liver glycogen. Where a positive energy balance exists, as in the case of overfeeding, any excess energy from sugars which has not been oxidised, will be stored either as glycogen or lipid.⁸

Q: ARE THERE NEW LEARNINGS ABOUT FRUCTOSE THAT ARE CAUSING CONCERN?

The current focus on fructose is probably driven by renewed interest in sugar and the search for causes of the obesity crisis. Current research does not reveal connections between habitual fructose consumption and obesity or metabolic conditions. Indeed, studies suggest that modest amounts of fructose (< 50 g per day) can help to lower blood glucose levels⁹, HbA1c (a marker of abnormal blood glucose control)¹⁰, diastolic blood pressure¹¹ and risk of type 2 diabetes.¹²

The EU legislators authorised a health claim for fructose¹³ following a positive opinion by the European Food Safety Authority.¹⁴ The claim states: "Consumption of foods containing fructose leads to a lower blood glucose rise compared to foods containing sucrose or glucose."

The claim can be made when at least 30% of sucrose or glucose in a food is replaced by fructose.

Q: HOW MUCH FRUIT JUICE WOULD NEED TO BE CONSUMED TO SEE ANY POTENTIAL NEGATIVE EFFECTS?

To get to even the most stringent threshold amounts advocated in the current literature, an individual would theoretically have to consume at least 1 litre of fruit juice per day. This is highly unlikely in the overall population given that the average consumption of 100% fruit juice in the EU28 is 12.7 litres per person per year. Fruit juice recommendations, where stated, are in the region of 150 ml to 200 ml per day.

Q: IS THERE GUIDANCE OF HOW MUCH FRUCTOSE CAN BE CONSUMED?

Fructose, as a simple sugar, falls within general sugar targets which vary across different countries. The World Health Organisation and several national food authorities recommend that added or free sugars are limited to 10% of daily energy intake.¹⁵ The European Food Safety Authority is currently reviewing the literature on free/added sugar and health, and will publish guidelines in due course.

Q: DOES FRUCTOSE CONSUMPTION INFLUENCE DISEASE RISK?

Intervention studies on moderate fructose intakes (< 50 g per day) have reported statistically lower blood glucose levels¹⁶, HbA1c (a marker of abnormal blood glucose control)¹⁰, diastolic blood pressure¹¹ and reduced diabetes risk.¹² In general, studies of modest fructose intake, in line with current European intakes, find either neutral or positive effects of fructose in the diet. The mechanism for these effects is most likely related to improved glucose tolerance via stimulation of net liver and muscle uptake of glucose.

As mentioned before, the EU legislators have authorised a health claim for fructose which states that it leads to a lower blood glucose rise compared to foods containing sucrose or glucose.¹³

Q: CAN FRUCTOSE BE PART OF AN ENERGY-RESTRICTED DIET?

Yes, since overall energy intake matters more than individual carbohydrates. In one intervention trial, 131 patients were randomised to one of two energy-restricted diets in order to investigate effects on weight loss and metabolic syndrome. The first diet was low in fructose (< 20 g/day) while the second contained 50-70 g/day from fruit supplements. After six weeks, more weight was lost on the moderate fructose diet compared with the low fructose diet (4.2 vs. 2.8 kg; P = 0.0016).¹⁷

In a recent intervention study¹⁸, individuals following a low-calorie diet were randomised to include either water or 750 ml of 100% orange juice daily. Despite the additional energy intake from fruit sugars, which included a significant proportion of fructose, weight loss over the eight weeks was similar after the two diets, and

significant improvements in metabolic risk factors were noted after the diet which included orange juice.

Q: IS THERE ANY ASSOCIATION BETWEEN DIABETES RISK AND FRUIT JUICE OR FRUCTOSE CONSUMPTION?

As evidenced by several systematic reviews and meta-analyses, there is no statistical association between fructose consumption and risk of type 2 diabetes¹⁹, nor between habitual 100% fruit juice consumption and risk of type 2 diabetes²⁰. Regular fruit juice consumption does not result in poor glycaemic control nor reduced insulin sensitivity²¹, and significant changes have not been observed for fasting blood glucose and insulin levels in randomised controlled trials where intakes of 100% fruit juice were 400 ml per day and above.²² It is likely that consumption of fructose in moderation improves glucose tolerance by modulating insulin sensitivity.¹²

Q: IS FRUCTOSE AN ISSUE FOR PEOPLE WITH DIABETES?

It does not appear to be so. A systematic review and meta-analysis of controlled feeding trials (typically less than 12 weeks in duration) examined the effect of fructose on glycaemic control in individuals with diabetes.²³ This revealed that isocaloric exchange of fructose for other carbohydrates improves long-term glycaemic control, as assessed by glycated blood proteins, without affecting insulin production. This fits with the observation that low to moderate amounts of fructose with meals have positive effects on insulin sensitivity.¹² As mentioned, there is an authorised health claim in Europe¹³ that states: "Consumption of foods containing fructose leads to a lower blood glucose rise compared to foods containing sucrose or glucose."

Q: IS THERE ANY ASSOCIATION BETWEEN FRUCTOSE CONSUMPTION AND HYPERTENSION?

No. A meta-analysis of prospective cohort studies, involving more than 200,000 adults, found no difference in risk of developing hypertension between the quintiles with the lowest (5-6% energy) versus highest (14% energy) intakes of fructose.²⁴ Indeed, the authors speculated that intakes of fructose up to 10% of daily energy (around 50 g per day) were associated with a lower risk of hypertension.

This finding was confirmed by a 10-week intervention study²⁵ which found that adding fructose-containing sugars to the diet (up to 9% energy) had no significant impact on blood pressure or uric acid levels (a risk factor for gout and endothelial dysfunction). A further meta-analysis of 13 controlled feeding trials²⁶ reported that isocaloric exchange of fructose for other carbohydrates (53-182 g/day of fructose) significantly lowered diastolic blood pressure but had no impact on systolic blood pressure.

Q: IS THERE ANY ASSOCIATION BETWEEN FRUCTOSE CONSUMPTION AND BLOOD LIPIDS?

This depends on the amount consumed and whether over-feeding occurs. A meta-analysis²⁷ looking at post-prandial triglycerides found no effect of fructose intake in 14 isocaloric trials (290

participants), but there was a significant increase in triglycerides in the two hypercaloric trials (33 participants). Nevertheless, fructose intakes in both types of trials were far in excess of current intakes which are in the region of 20-40 g in European countries. In the isocaloric trials, 20% energy from fructose was provided while, in the hypercaloric trials, this was > 25% energy, or 175 g fructose per day.

A meta-analysis of 16 feeding trials (236 participants)²⁸, which focused on the impact of fructose in people with type 2 diabetes, reported that isocaloric exchange of fructose for starch raised triglycerides and lowered total cholesterol but did not influence low-density lipoprotein cholesterol or high-density lipoprotein cholesterol. The effect was seen only at fructose intakes exceeding 60 g per day (equivalent to 120 g of added sugars per day).²⁹

Q: IS THERE ANY ASSOCIATION BETWEEN FRUCTOSE CONSUMPTION AND BODY WEIGHT?

Studies considering the impact of fructose on body composition have not found any consistent evidence of harm when participants remain in energy balance and the fructose comes from natural sources, such as fruit or 100% fruit juice. In contrast, moderate amounts of fructose are associated with reduced risk of overweight¹² and the impacts of fructose and glucose are the same under conditions of overfeeding, suggesting that excess calories are more important than sugar type.⁷

In this respect, a systematic review²⁹ considered 31 isocaloric trials (637 participants) and 10 hypercaloric trials (119 participants) where fructose intakes ranged from an average of 69 g per day (17% energy) in the isocaloric trials to an average of 182 g (38% energy) in the hypercaloric trials. Even at these high intakes, fructose had no significant overall effect on body weight (-0.14 kg) in normal weight participants, nor in people with diabetes in the isocaloric trials. Interestingly, weight reduced in the five trials that recruited overweight/obese participants (-0.55 kg; P = 0.04). However, in the hypercaloric trials, body weight increased (+0.53 kg; P < 0.001), leading the authors to conclude that this effect may be due to the extra calories provided, rather than the fructose per se.

Disclaimer: Every effort has been made to ensure that the information contained in this document is reliable and has been verified. The information is intended for non-commercial communication to health care professionals only. The information given in this dossier does not constitute dietary advice.

REFERENCES

1. UK Department of Health (2013) Nutrient analysis of fruit and vegetables. <https://www.gov.uk/government/publications/nutrient-analysis-of-fruit-and-vegetables>.
2. Singh GM et al. (2015) Global burden of diseases nutrition and chronic diseases expert group (NutriCoDE). Global, regional and national consumption of sugar-sweetened beverages, fruit juices and milk: a systematic assessment of beverage intake in 187 countries. PLoS One 10: e0124845.
3. White JS (2013) Challenging the Fructose Hypothesis: New Perspectives on Fructose Consumption and Metabolism. Adv Nutr 4: 246-256.
4. van Buul VJ et al. (2014) Misconceptions about fructose-containing sugars and their role in the obesity epidemic. Nutr Res Rev 27: 119-30.
5. Sievenpiper JL et al. (2012) 'Catalytic' doses of fructose may benefit glycaemic control without harming cardiometabolic risk factors: a small meta-analysis of randomised controlled feeding trials. Br J Nutr 108: 418-423.
6. Sievenpiper JL et al. (2012) Effect of fructose on body weight in controlled feeding trials: a systematic review and meta-analysis. Ann Intern Med 156: 291-304.
7. Macdonald IA (2016) A review of recent evidence relating to sugars, insulin resistance and diabetes. Eur J Nutr 55 (Suppl 2): S17-S23.
8. Tappy L & Lê KA (2010). Metabolic effects of fructose and the worldwide increase in obesity. Physiol Rev 90: 23-46.
9. Wiebe N et al. (2011) A systematic review on the effect of sweeteners on glycemic response and clinically relevant outcomes. BMC Med 9: 123.
10. Livesey G & Taylor R (2008) Fructose consumption and consequences for glycation, plasma triacylglycerol, and body weight: meta-analyses and meta-regression models of intervention studies. Am J Clin Nutr 88: 1419-37.
11. Ha V et al. (2012) Effect of fructose on blood pressure: a systematic review and meta-analysis of controlled feeding trials. Hypertension 59: 787-795.
12. Livesey G (2009). Fructose ingestion: dose-dependent responses in health research. J Nutr 139: 1246S-1252S.
13. EU health claims register http://ec.europa.eu/food/safety/labelling_nutrition/claims/register/public/?event=register.home.
14. European Food Safety Authority (2011) Scientific Opinion on the substantiation of health claims related to fructose and reduction of post-prandial glycaemic responses (ID 558) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 9(6): 2223.
15. Buyken AE et al. (2018) Dietary carbohydrates: a review of international recommendations and the methods used to derive them. Euro J Clin Nutr doi: 10.1038/s41430-017-0035-4. [Epub ahead of print]
16. Wiebe N et al. (2011) A systematic review on the effect of sweeteners on glycemic response and clinically relevant outcomes. BMC Med 9: 123.
17. Madero M et al. (2011) The effect of two energy-restricted diets, a low-fructose diet versus a moderate natural fructose diet, on weight loss and metabolic syndrome parameters: a randomized controlled trial. Metabolism 60: 1551-9.
18. Ribeiro C et al. (2017) Orange juice allied to a reduced-calorie diet results in weight loss and ameliorates obesity-related biomarkers: A randomized controlled trial. Nutr 38: 13-19.
19. Tsalis CS et al. (2017) Relation of total sugars, fructose and sucrose with incident type 2 diabetes: a systematic review and meta-analysis of prospective cohort studies. CMAJ 189: E711-E720.
20. Xi B et al. (2014) Intake of fruit juice and incidence of type 2 diabetes: a systematic review and meta-analysis. PLoS One 9: e93471.
21. Murphy MM et al. (2017) 100% Fruit juice and measures of glucose control and insulin sensitivity: a systematic review and meta-analysis of randomised controlled trials. J Nutr Sci 6: e59 (15 pages).
22. Wang B et al. (2014) Effect of fruit juice on glucose control and insulin sensitivity in adults: a meta-analysis of 12 randomized controlled trials. PLoS One 9: e95323.
23. Cozma AI et al. (2012) Effect of Fructose on Glycemic Control in Diabetes: A systematic review and meta-analysis of controlled feeding trials. Diabetes Care 35: 1611-1620. <http://care.diabetesjournals.org/content/35/7/1611>.
24. Jayalath VH et al. (2014) Total fructose intake and risk of hypertension: a systematic review and meta-analysis of prospective cohorts. J Am Coll Nutr 33: 328-339.
25. Angelopoulos TJ et al. (2015) Fructose containing sugars do not raise blood pressure or uric acid at normal levels of human consumption. J Clin Hypertens 17: 87-94.
26. Ha V et al. (2012) Effect of fructose on blood pressure: a systematic review and meta-analysis of controlled feeding trials. Hypertension 59: 787-95.
27. Wang DD et al. (2014) Effect of fructose on postprandial triglycerides: A systematic review and meta-analysis of controlled feeding trials. Atherosclerosis 232: 125-133.
28. Sievenpiper JL et al. (2009) Heterogeneous effects of fructose on blood lipids in individuals with type 2 diabetes: systematic review and meta-analysis of experimental trials in humans. Diabetes Care 32: 1930-7.
29. Sievenpiper JL et al. (2012) Effect of fructose on body weight in controlled feeding trials. Ann Intern Med 156: 291-304.