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Received: 2017 November – Accepted: 2018 February

Human biological characteristics of fructose

Keywords: dietary sources of fructose, intake, metabolism, health consequences

1. Summary

Fructose is a natural ingredient of human nutrition, and it comes mainly from fruits and honey, and to a certain extent, from vegetables. In these sources, it is found partially in the free form of the sugar, and partially as one of the components of the disaccharide sucrose. In recent decades, the use of corn syrup, based on decomposed corn starch and containing large amounts of free fructose, and of enzymatically treated sucrose, also known as invert sugar, for the sweetening of various foods has been spreading rapidly, leading to the excessive intake of fructose. Due to the complex nature of the diet, it is very difficult to examine its consequences on the health of the consumer, transposition of the results of animal experiments to humans requires careful consideration, and is not always feasible. Despite these difficulties, it is worthwhile and important to review previous studies. There is no doubt that fructose participates in metabolism in a unique way, its behavior differs from that of glucose, which has an essential function in humans. Therefore, different physiological consequences have to be considered. Diseases of the cardiovascular system, obesity, symptoms of the metabolic syndrome, and even malignant tumors may be related to excessive fructose intake. Epidemiological studies and research on the correlations do not always present a consistent picture, there are differing results. Resolving contradictions still requires a great amount of analysis. However, the power of science lies exactly in the fact that it can provide a clear picture through evidence and counter-arguments.

2. Introduction

Fructose (formerly known as levulose) is present in our everyday diet, on the one hand, as an ingredient of complex sugars (e.g., sucrose, fructo-oligosaccharide), and on the other hand, as a free monosaccharide. Since there has been an upward trend in the intake of fructose, and since its absorption and involvement in metabolic processes in the body is quite unique, and differs from those of another monosaccharide, glucose, which has a similar intake, it is necessary to overview its effect on human physiological processes separately.

It should be noted here that a significant portion of the studies on fructose report carried out on animals, mainly rodents, and the transposition of the conclusions of these experiments to humans has many uncertainties. The fact that, in human studies, the sugar is never consumed by the subjects in an isolated way requires further considerations. The nutritional matrix and its composition can cause significant changes in physiological reactions and, in addition, the quantity consumed cannot always be regulated with adequate precision, as opposed to animal experiments. In animal models, high fructose intake caused clearly observable insulin resistance, impaired glucose tolerance and high blood pressure, however, human observations are often inconsistent **[1]**, **[2]**.

Results of animal studies conducted with pure fructose and glucose are certainly interesting and valuable from a scientific point of view, but they can be directly adopted to human nutrition only with reservations, and require careful consideration. The relationship between fructose, corn syrup

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and cardiovascular diseases, metabolic syndrome and fatty liver is still the subject of discussion, even more so, because studies carried out using different methods have led to different conclusions. To resolve the contradictions, further investigation and observations are needed, revealing the details **[3]**. The open-chain and cyclic structural formula of glucose (aldohexose) are shown in ***Figure 1***. For comparison, ***Figure 2*** shows the open-chain and cyclic structural formula of fructose (ketohexose).

3. Sources of fructose and the amount consumed

Natural sources of free fructose are fruits and honey, and to a lesser extent, vegetables. 100 g of apples contains approximately 6 g of fructose, the same amount of honey contains 40 g of fructose. The same sources provide also sucrose containing fructose and glucose in a 1:1 ratio. From the sixties and seventies of the last century, the amount of syrup produced from corn flour in an enzymatic way and containing 42 or 55 percent (sometimes less, sometimes more) fructose has grown rapidly, and it has been used for the sweetening of foods, at a price level more favorable than that of traditional sugar. Less often used is invert sugar produced from enzymatically decomposed sucrose, which is marketed as a solution or as a syrup. Its fructose content is 1.5 to 25% **[4]**, **[5]**. Sugar alcohols (e.g., sorbitol) are also a source of fructose **[6]**.

There are no detailed data available on domestic fructose intake. According to a summary compiled in 2012, among the 42 countries involved in the study, Hungary was second, behind the United States, in the consumption of high-fructose syrup, with an annual per capita consumption of 16.85 kg, which is equivalent to roughly 8 kg of fructose. In Europe, the lowest fructose intake, 11 to 20 g per day or 3.5 to 7.0 kg per year, was found in the case of Finish adolescents, the latter value being close to the Hungarian data **[7]**, **[8]**. In the United States, about 40% of the total sugar consumption comes from sweetened drinks in which fructose corn syrup is used **[9]**. Its consumption grew by 1000% between 1970 and 1990, while its share among sweeteners rose from 16% to 42% between 1978 and 1998 **[10]**, **[11]**! During the third National Health and Nutrition Examination Survey (NHANES) conducted in the United States between 1988 and 1994, involving 21483 children and adults, the average fructose intake was found to be 54.7 g (10.2% of the total energy intake), with extreme values of 38.4 and 72.8 g. The largest amount of fructose was in the diet of adolescents, with an average energy percentage value of 12.1, but in the case of one quarter of them, the value was 15%**[12]**.

4. The absorption of fructose

Fructose is absorbed from the small intestine, mainly from the jejunum, depending on the concentration gradient, without the use of energy and without direct regulation. Therefore, an excessive amount of fructose is not absorbed, it remains in the intestine, and causes diarrhea because of its osmotic effect. Fructose is fermented by the bacterial flora of the colon, and short-chain fatty acids (acetic acid, propionic acid, butyric acid) and gases (hydrogen, methane, carbon dioxide) are produced. The latter cause abdominal pain and bloating, and also contribute to increased bowel movement. The presence of glucose promotes the absorption of fructose **[13]**. The passage of fructose through the intestinal wall, regardless of its source, is assisted by the GLUT5 glucose transporter protein of the cells (enterocytes). It is then transmitted from the enterocytes to the blood vessel leading to the liver by the GLUT2 transporter. Further metabolic processes take place in the liver. GLUT5 is independent of the Na^+ ion, its kinetics (Michaelis-Menten constant, K_m) for fructose is ten times slower than that of GLUT2. GLUT5 is found in the kidney, heart, brain, skeletal muscles and the membrane of fat cells. For the fructose uptake of the cells, no insulin is required. As a result of chemical transformations in the liver, fructose, similarly to glucose, enters the process of glycolysis, and serves as a substrate for gluconeogenesis, glucogenolysis, the lactate/Cori cycle, pentose phosphate and lipid synthesis. A significant part of the fructose is converted to glucose in the liver, the degree of which is directly proportional to physical activity. In the case of excessive fructose intake, the synthesis of glyceraldehyde-3-phosphate and dihydroxyacetone phosphate increases, resulting in an increased amount of acetyl-CoA, which promotes lipogenesis **[1]**, **[14]**. Fructose feeding changes gene expression in rats, as well as the sense of satiety in the brain, increases the risk of inflammation and the amount of reactive oxygen species, and increases the bacterial endotoxin (lipopolysaccharide) concentration of the portal vein in mice **[1]**, **[15]**. Adverse effects accumulate in the case of an excessive energy input **[16]**.

5. The path of fructose in metabolism

According to various studies, the energy required for the metabolising of fructose as a nutrient is one and a half to three times higher than that of glucose, but this basically does not influence basic metabolism **[17]**. Fructose, as was outlined above, is predominantly metabolized in the liver, but the kidneys are also able to use a significant amount of it, although there is only a slight chance of this, because very little fructose enters the bloodstream and so it cannot reach the kidneys. In the liver, fructolysis, similarly to glycolysis, is accompanied by phosphorylation (fructose 1 phosphate), with the involvement of the fructokinase enzyme. The enzyme is not regulated, and operates until the exhaustion of the available adenosine triphosphate. After this, the aldolase B enzyme is activated and the resulting glyceraldehyde, after several modifications, finally joins the glycolysis step **[13]**.

According to several respiratory quotient (RQ, the ratio of the carbon dioxide produced by the body to the oxygen consumed by the body) measurement results, fructose reduces the oxidation of fats and increases the oxidation of carbohydrates (higher RQ), however, since concomitant lipogenesis is accompanied by carbon dioxide release even in the absence of oxidation, this conclusion could be erroneous **[13]**. The working group of Cox carried out a 10-week-long study with the involvement of a small number of people of both sexes, aged 40 to 72, having them consume fructose- or glucose-containing drinks so that the energy provided by the sugars reached 25% of the total energy intake. Resting energy expenditure and fat oxidation decreased significantly, while that of carbohydrates increased as a result of fructose **[18]**.

If glucose/sucrose is replaced by fructose in the diet, the rise in blood sugar and insulin levels after a meal are significantly lower and triglyceride levels in the blood are not increased by isocaloric substitution, however, due to excessive intake, there is a marked rise after a meal **[19]**, **[20]**. In the case of a persistent replacement, fasting blood sugar and the level of glucose hemoglobin (HbA1c) decrease, while the titers of triglycerides and insulin remain almost unchanged **[21]**, **[22]**.

Outside the liver (typically in the Leydig cells of the testicles) fructose may be transformed into glucose. During the process, sorbitol is formed. In the case of diabetic patients, due to the comprehensive metabolic disorder, sorbitol accumulates in the eye and can cause cataracts **[10]**.

It was observed by Aeberli et al. in young adults that after consuming, for 3 weeks, 600 ml of a beverage containing 40 g/day fructose (MF), 80 g/day fructose (HF), glucose (HG) or sucrose (HS) the amount of free fatty acids increased significantly for the MF group, while the total cholesterol and LDL cholesterol increased for the MF, HF and HS groups, compared to the HG group. Insulin resistance was increased in the liver by HF **[23]**.

There is an interesting relationship between fructose and the level of the hormone fibroblast growth factor 21 (FGF21). FGF21 is a hormone that performs multiple functions, the properties of which have been studied in rodents, and it seems that it plays a critical role in the adaptation to starvation. In humans, as a result of fructose, its level in the blood serum increases rapidly and pronouncedly, while the increase is much less pronounced and slower due to glucose. Patients with metabolic syndrome react with a higher level. Presumably, FGF21 plays an important role in fructose metabolism **[24]**. The hormone contributes to the reduction of body weight, and to the favorable development of sugar and fat metabolism. Based on the results of animal experiments, there seems to be a contradiction: fructose itself is metabolically unfavorable, however, its intake causes an increase in the level of a beneficial hormone, furthermore, in the case of metabolic syndrome, basic levels are higher. Therefore, it is likely that in these cases a resistance to FGF21 develops, but the exact nature of the process is still to be clarified **[25]**.

6. Fructose and cardiovascular disorders, with special emphasis on lipids

According to epidemiological observations, the consumption of a high energy diet containing fructose increases the blood triglyceride level, which is the result of the increased lipogenesis in the liver. It is difficult to determine accurately the dose-response relationship, however, the phenomenon cannot be observed with fructose doses of less than 50 g per day. It still needs to be clarified, whether lipogenesis is attributable to the abundant energy intake, or it is the *per se* effect of fructose or other sugars. Lipid overload of the liver may lead to the formation of non-alcoholic fatty liver, but the mechanism of this is still unknown. According to animal experiments, oxidative stress may be in the background **[17[**, **[26]**. A unique relationship is indicated by the study, according to which the ratio of Enterobacteriaceae strains in the intestinal microbiota increases due to excessive fructose levels in mice, resulting in the liver in the increased expression of the genes that play a key role in inflammation. Inflammation and its markers (in the liver and systematically) may be suppressed by the administration of small grain size wheat bran which favorably modifies the intestinal flora **[27]**.

Also according to human epidemiological and intervention studies, excessive intake of fructose increases cardiovascular mortality. This fact was confirmed by experiments carried out in cell cultures and animals **[28]**. In adolescents, abdominal obesity mediates cardiometabolic risk **[29]**.

During lipogenesis, mainly palmitic acid is formed, which is related to atherosclerosis. Fatty acids are incorporated into very low-density lipoprotein (VLDL) molecules, which turn into low density lipoprotein (LDL), increasing blood atherogenic triglyceride and LDL levels. Several studies have shown that fructose consumption below 50 g/day does not increase cardiovascular risk **[13]**.

In the case of overweight people, consequences differing from the above have been found by Johnston et al. after the consumption of fructose or glucose. If either fructose or glucose was administered while maintaining the energy value of the diet, there was no change in liver enzymes or in triglyceride levels. However, in the case of excessive energy intake, both parameters increased for both sugars, indicating the energy dependence of the effect, rather than the specific effect of the macronutrient **[30]**. Similar changes in triglyceride, glucose, insulin, leptin, ghrelin and uric acid levels have been found by Yu et

al. in the case of daily fructose or glucose intakes of 40, 90 or 150 g, so the metabolic consequences of these two sugars did not differ in these respects **[31]**.

Fructose-induced uric acid in physiological concentrations protects the cell membrane from oxidative effects, but under certain inflammatory conditions, such as atheromatous plaque formation (a fatty degeneration of the artery wall), it can be prooxidative. Oxidative stress contributes to the dysfunction of the endothelial cells that form the inner walls of the arteries, to atherosclerosis, to myocardial energy disorder, and also to insulin resistance. Evaluation of the cardiometabolic significance of uric acid is not a closed question yet, although the relationships outlined above rely on scientific evidence **[32]**. Experimental results show that hyperuricaemia (the high blood serum level of uric acid) is related to higher systolic blood pressure, because the formation of vasodilatory nitric oxide in the internal vascular wall is inhibited by uric acid **[1]**.

However, according to the meta-analysis of three prospective studies involving more than 220,000 individuals, no correlation could be demonstrated between fructose of no more than 14 energy% and the incidence of hypertension. The spline curve is negative under ~10 energy%, while above this value it is positive, U-shaped **[33]**.

In their overview, Malik and his working group attach special importance drinks sweetened by sugars, the fructose content of which is derived from corn syrup and/or sucrose. The risk of cardiovascular diseases (and of obesity and diabetes) is increased by these drinks due to the special metabolic effects of fructose (*de novo* lipogenesis, abdominal obesity, uric acid formation) **[34]**, **[35]**.

7. Fructose and uric acid

Uric acid is the end product of purine metabolism, a commonly known consequence of its accumulation in the body is gout. Fructose intake is closely related to high blood pressure, metabolic syndrome and cardiovascular diseases, and it is also an independent risk factor for chronic kidney disease, type 2 diabetes and advanced age dementia. The phenomena can already be observed near the upper limit of the normal blood serum uric acid range. Phosphorylation of fructose to fructose-1-phosphate is a rapid process, leading to a decrease the phosphate and adenosine triphosphate (ATP) levels within the cell. As a result, AMP deaminase degrading adenosine monophosphate (AMP) is stimulated, together with purine (xanthine) degradation, which results in the formation of uric acid and mitochondrial oxidants, and even fructose itself can induce oxidative stress. The latter process leads to *de novo* lipogenesis in the liver through the Krebs cycle, and to the accumulation of fatty acids **[32]**. The increase in triglyceride levels leads to the formation of non-alcoholic fatty liver **[1]**. Fructose promotes fat accumulation in fat cells from the mesenchyme (a tissue group originating from the mesoderm), and this process is mediated by uric acid **[36]**.

The lack of ATP was already observed when consuming 15 g of fructose per day, as well as the disturbance in its substitution following intravenous fructose provocation. People with high uric acid levels had lower ATP levels in the liver after fructose injection. A high fructose intake and a high uric acid level both indicate the lack of ATP as a response to fructose, and it is a risk factor for the development and progression of fatty liver. No adverse changes are caused by isoenergetic fructose intake **[37]**, **[38]**, **[39]**, **[40]**.

In children, isoenergetic reduction of fructose intake improves blood pressure, as well as triglyceride, LDL cholesterol and insulin levels, and glucose tolerance **[41]**. Fructose and uric acid are still independent risk factors for fatty liver in adolescence, overweight people being particularly at risk in this respect **[42]**, **[43]**.

It was supported by the observation of more than 125,000 people for 17 years, during which 1533 cases of gout were registered, that high fructose intake is associated with this disease, apparently because of increased uric acid levels **[44]**. However, according to certain literature data, the antioxidant capacity of blood may be increased by uric acid by up to 50% **[6]**.

Contrary to the above, it was found in a study United States, involving nearly 9,400 individuals aged 20 to 80 years, that dietary fructose was not related to serum uric acid, however, alcohol consumption showed a significant positive and fiber intake showed a negative correlation **[45]**.

8. Fructose and obesity

The unique metabolism of fructose promotes obesity and, according to the data gathered so far, the fetus developing in the womb, the newborn and the infant are not immune to this either. Therefore, fructose exposure, which is not part of the infant's natural diet, together with the active transport of fructose in the uterus through the placenta, is likely to enable fructose to cause a malfunction in metabolism and development. Fructose effects in the critical period are obesogenic, and cause life-long changes in the neuroendocrine system, in hunger control, eating habits, *de novo* fat formation, fat distribution and metabolic processes and their systems **[46]**.

If a mother consumes a diet rich in fructose during pregnancy, it leads to obesity, as well as metabolic dysfunction, high blood pressure, i.e., cardiovascular risk in the offspring in adulthood, through fetal "programming". Consequences are more pronounced in the case of female offspring. It is definitely justified

to create the diet plan of a pregnant women by taking into consideration the risks of fructose, and limit its amount **[47]**.

The question still remains whether the ability of fructose to cause satiety is lower or higher than that of other sugars, i.e., whether it contributes to the consumption of more food. The modern imaging process, nuclear magnetic resonance spectroscopy makes it possible to observe the activities of certain brain areas by studying the blood supply of the areas in question. It turned out that the activity of the hypothalamus, playing an important role in energy regulation, lower in the case of fructose than in the case of glucose, and this is probably an indicator of a lack of satiety **[48]**, **[49]**, **[50]**. Fructose also influences other hormones that regulate food consumption **[51]**. There are also contrasting observations: fructose decreases appetite to the same extent, or even better than glucose, if consumed before a meal. Even if the causal role of fructose in obesity could be accepted because of a lack of the sense of satiety in the brain, there are still other results that raise doubts. One of these is the limited absorption of fructose, as a result of which not much sugar can enter the metabolism and so it cannot cause weight gain. Another one: the thermogenic heat of fructose is higher than that of glucose. Moreover, fructose is sweeter than glucose, therefore, less of it is needed to achieve the same sweetness **[13]**.

The conclusion was drawn by Tappy et al. from 17 studies dealing exclusively with obesity that, according to the experiences gained while examining the consumption of drinks sweetened with corn syrup, fructose does not reduce the use of energy, weight gain is more likely to be due to the higher energy intake **[52]**. Particularly unfavorable from a weight gain point of view is the long-term consumption of drinks sweetened with fructose-containing syrup in large amounts **[14]**.

In rats, fructose causes a more pronounced weight gain than glucose or sucrose, although the latter ones also cause obesity, as a function of the energy intake. In addition, fructose intake produces less brown adipose tissue, which turns excess energy intake into heat (and not into spare fat). The phenomenon is more pronounced in males than in females **[10]**.

According to other researchers, the role of fructose or corn syrup in obesity is insufficiently corroborated scientifically, several other factors should be investigated, excess energy intake could be more important, the discussion is not yet over **[53]**, **[54]**. White concludes in his summary article that dietary fructose is safe in proportionate amounts, it can cause metabolic disturbances in the case of an abuse (excess intake), but this is also true for other nutrients in similar cases **[55]**. The same applies to the relationship between childhood obesity and the consumption of corn syrup **[56]**.

9. Fructose and metabolic syndrome

Animal experiments and human studies both support the fact that added sugar contributes to the risk of diabetes and related metabolic disorders (cardiovascular risk). Added fructose (either as an ingredient of sucrose or in the form of corn syrup) is particularly important in this regard. Another disadvantage: isolated fructose causes kidney damage in rodents, in humans this can be observed after long-term consumption of drinks sweetened with corn syrup. It is important to note that food containing natural fructose (fruits, vegetables) do not pose a health risk, they even have a protective effect. A typical data is that while about one half of the weight of corn syrup used for sweetening is fructose, in the case of sweet peaches the value is 1%. Ideally, there is no need to add fructose to foods. It is desirable that the proportion of all added sugar remains below the 5% recently recommended by the World Health Organization, with respect to the total energy intake **[57]**.

The results of more and more research suggest that fructose intake greater than 50 g is associated with metabolic syndrome, which presents the group of obesity, blood fat dysfunctions (dyslipidaemia: high LDL cholesterol level and decreased HDL cholesterol level[1]), high blood pressure and insulin resistance/high fasting blood sugar/diabetes as a complex concept, as well as the associated disposition to inflammation and thrombosis (prothrombosis). In animal experiments, glucose or starch do not produce similar symptoms **[58]**. This is the consequence of the lack of adenosine triphosphate due to the rapid metabolism of fructose, associated with mitochondrial and endothelial dysfunction, making people predisposed to obesity, diabetes and hypertension. This unfavorable phenomenon can be averted to a great extent by physical activity requiring large energy consumption (e.g., in the case of athletes) **[59]**, **[60]**. Fructose poses a particular risk for the development of metabolic syndrome in the case of overweight, obese people **[61]**.

Fructose in amounts of less than 50 g or 10 energy% does not effect a change in lipid and glucose metabolism **[62]**, however, long-term intake of even small amounts causes kidney damage **[63]**, **[64]**.

Fructose does not induce insulin secretion and does not increase leptin production. The latter factor points toward an increased food consumption, however, excess energy leads to a clear increase in body weight **[9]**.

[1] High-density lipoprotein, it transports cholesterol deposited in the blood vessels back to the liver. Its popular name is „good" cholesterol.

Extreme increase in the intake of fructose (up to 80 g/day) moderately reduces the sensitivity of the liver to insulin, but this does not affect blood sugar levels, normal amounts of fructose do not increase the risk of diabetes **[17]**, **[65]**. For decades, fructose had been a staple in the diet of diabetic patients because of its low glycemic index. However, experiments on rodents demonstrated insulin resistance and weight gain caused by long-term consumption of significant amounts, and similar consequences of drinks sweetened with fructose and large amounts of dietary fructose, therefore, fructose has been removed from the treatment scheme **[1]**.

According to some low-volume studies, the intake of small amounts of fructose (no more than 10 g per meal, no more than 36 g per day, as a substitute for other carbohydrates) may improve the glycemic index of the diet and, thus, fasting blood glucose, uric acid and triglyceride levels, as may reduce obesity **[66]**.

The role of fructose in the development of type 2 diabetes:

- It increases fat accumulation in the liver and, as a consequence, the insulin resistance of liver cells.
- Free fatty acids are released from VLDL and they induce insulin resistance by deposition in the skeletal muscle cells.
- The decrease in the amount of ATP also decreases the insulin-binding capacity of the cells and presumably the number of insulin receptors as well.
- Inflammation and oxidative stress damage the insulin production capacity of the pancreas **[57]**.

In countries where fructose intake is high and corn syrup is regularly used for sweetening (with a significant amount of free fructose), the incidence of type 2 diabetes, regardless of obesity, is almost 20% higher than in places where there is no such use: the average prevalence of diabetes is 8% compared to 6.7%. However, many researchers argue that fructose alone is responsible for this difference, that this monosaccharide is so different from other sugars **[8]**, **[67]**, **[68]**. The same view is reflected in the official statement of the United States Department of Agriculture (USDA) **[69]**. According to other researchers, drinks sweetened with syrup are directly linked to the causes of metabolic diseases **[14]**.

Uric acid can contribute to the insulin resistance of the liver by inducing mitochondrial oxidative stress and fatty liver. It inhibits the vasodilating effect of insulin, which is important for the delivery of glucose to skeletal muscle. It inhibits the production of the hormone adiponectin in fat cells and thus causes local inflammation. Through oxidative stress, uric acid directly damages the insulin-producing islet cells of the pancreas, causing dysfunction and diabetes **[58]**, **[70]**.

Although there is little research data regarding the physiological effects of fructose in humans, it can be concluded that an intake not exceeding 50 to 60 g/day does not increase the risk of atherosclerosis, type 2 diabetes and obesity more than other sugars. However, if the intake exceeds this value, especially together with a high energy intake from glucose/ starch, the negative health consequences of *de novo* lipogenesis have to be considered **[13]**.

The meta-analysis of 15 research programs revealed a significant positive correlation between fructose intake and fasting blood glucose, systolic blood pressure and elevated triglyceride levels, a negative relationship with HDL cholesterol, however, after taking into consideration the significant heterogeneity of the individual studies, the significance could only be maintained in the case of blood sugar **[71]**.

10. Fructose intolerance, fructosuria

In the case of essential/benign fructose intolerance, due to the lack of the liver enzyme fructokinase, fructose concentration in blood rises (fruktosemia) and the sugar is secreted by the kidneys, so it appears in the urine (fruktosuria). It occurs in certain ethnic groups, does not cause any symptoms, and treatment is not justified.

Hereditary fructose intolerance is a consequence of the absence of the aldolase B enzyme. It is a rather rare disorder, statistically affecting one person out of every 20,000 to 130,000. The disease is inherited autosomally in a recessive way, that is, both parents must carry the altered gene without them being sick. Already in childhood it causes symptoms such as vomiting, decreased blood sugar levels, because no glucose is produced from glycogen. Fructose 1-phosphate accumulates in the liver, disrupting ATP regeneration, uric acid is produced from AMP, gout may develop. Avoiding fructose-containing foods is the main factor in its treatment **[10]**.

Poor absorption (malabsorption) of fructose, also known as dietary fructose intolerance, is much more common, it is similar to lactose intolerance, and may affect one third of the population. The cause could be the reduced efficiency of GLUT5 transport, or the lack of glucose-1-phosphate aldolase and, as a result, the toxic effect due to the accumulation of fructose-1-phosphate. There are studies that do not support these deficiencies consider an increased individual sensitivity to fructose or the unique role of the gut flora the cause. Its symptoms are similar to the above, and its treatment also **[7]**, **[72]**, **[73]**.

11. Malignant tumors

Because of their increased ability to divide, tumor cells require more cell growth material and protein. Fructose, along with glucose, but more strongly, promotes protein biosynthesis. Observation studies

and experiments indicate that fructose increases the risk of certain malignant processes, probably through oxidative stress and metabolic irregularities. Fructose mainly promotes the development of aggressive pancreatic and small intestine tumors and metastases. To bring to light all the details, much more research is needed **[74]**.

Tumor cells use fructose readily for proliferation, and they prefer this sugar for their nucleic acid synthesis. Dietary fructose contributes to the development of the tumor in several possible ways: through changed cell metabolism, more reactive oxygen species, nucleic acid lesions or inflammation **[75]**.

12. Conclusions

The thought „You are what you eat", based on the traditions of Hippocrates, comes from Feuerbach. It means that the food consumed by humans fundamentally affects their health, including physiological, psychological and mental ability characteristics **[76]**. With this literature overview, my intention was to summarize the results of the scientific works on the effects of one of the most common ingredients of our everyday diet, fructose, a ketose type monosaccharide which has been consumed for decades, on humans. I undertook to collect literature results and opinions, because Hungarian source works lack a detailed discussion of the physiological effects of this long-known food ingredient, which has not been considered the least bit dangerous.

Based on the available literature sources, it can be concluded that regular consumption of fructose raises many questions. From the publications processed in my overview, it is not possible to determine clearly whether fructose has a beneficial or unfavorable physiological effect, but it is indisputable that this natural sweetener, in contrast with its close relative, glucose, participates in completely different biochemical processes. Its glycemic index is lower than that of glucose, yet it is not suitable for the diet of people suffering from type 2 diabetes, because of the indication of uric acid, among other things. Many researchers believe that excessive fructose intake may increase the prevalence of fatty liver and high blood lipid levels. The involvement of fructose is suggested in the development of metabolic syndrome, abdominal obesity, high blood pressure, and in general, cardiovascular diseases, as well as occasionally in the development of tumor diseases.

The development of the above-mentioned abnormalities is linked by several papers to the consumption of significant amounts of fructose (more than 50 g per day). This means that if fructose intake is restricted to fruits and vegetables, and a personalized diet is followed, no adverse human health effects are expected.

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