Hepatology and Pancreatic Science

Review Article Open Access

Resolving the Sugar and Health Controversy with Special Reference to Malaysia

Meer Ahmad AM[1]*, Yadav H[1], Balabaskaran S[2], Suresh L[3] and Savithri NV[4]

[1]*Department of Community Medicine, MAHSA University, Malaysia*
[2]*Department of Biochemistry, MAHSA University, Malaysia*
[3]*Consultant Physician and Gastroenterologist, Assunta Hospital, Petaling Jaya, Malaysia*
[4]*Department of Dental Public Health, MAHSA University, Malaysia*

Abstract

Background: It is alleged that the incidence of obesity, type 2 diabetes mellitus (T2DM), and metabolic syndrome (MetS) have sharply increased throughout the world. It is generally argued that increased consumption of a calorie-rich/high-fat diet, lack of exercise, and sedentary-lifestyles are responsible, besides increasing age, gender, and obesity itself. But, certain authors argue that increased consumption of a carbohydrate-rich diet high in sucrose, fructose, and/or glucose is responsible for the increasing incidence of obesity, T2DM, and MetS. The same proponents also claim that these sugars cause cancers and other chronic diseases through 'chronic low-grade inflammation', besides directly. Some yet argue against these claims, causing an on-going raging international controversy, with strong implications for Malaysia.

Objective: The aim is to resolve this controversy through an appropriate literature-review.

Methodology: Literature from both sides, such as journal-articles, systematic-reviews, meta-analyses and book-summaries were reviewed, besides videos of lectures uploaded onto YouTube.

Results: Although here is observed for and against claims that sugar, especially sucrose and fructose, is an addictive, toxic-substance capable of causing chronic-diseases and, being the main cause of obesity, the evidence is overwhelmingly against such claims. Almost all of the studies for appear to have been done on rats and cell-lines, and not of an epidemiological-study nature. Even the nature of the metabolism of sugars claimed as conclusions from these studies is doubted by different studies/articles. The ACGIH categorizes sucrose as not classifiable as human or animal carcinogen. Current existing guidelines on dietary-sugar do not seem to meet criteria for trustworthy recommendations.

Conclusion: The evidence is overwhelmingly against claims that sugar causes chronic diseases, and that sugar is the main cause of obesity. There is a need for more epidemiological-studies.

Keywords: Obesity; Type-2 diabetes mellitus; Metabolic syndrome; Calorie-rich/high-fat diet; Sedentary lifestyles; Age; Gender; Carbohydrate-rich diet; Sucrose; Fructose

Introduction

It is alleged that the incidences of obesity, type 2 diabetes mellitus (T2DM), and metabolic syndrome (MetS) have sharply increased throughout the world [1]. It is generally argued that increased consumption of a calorie-rich/high-fat diet, lack of exercise, and sedentary-lifestyles are responsible for obesity, besides gender and increasing age–while obesity itself caused the T2DM and MetS. But, certain authors argue that increased consumption of a carbohydrate-rich diet high in sucrose, fructose, and/or glucose is responsible for the increasing incidence of obesity, T2DM, and MetS [1-3].

The same proponents also claim that these sugars cause cancers and other chronic diseases through 'chronic low-grade inflammation', besides directly. While some yet argue against these claims, causing an on-going raging international controversy, with strong-implications for Malaysia [4-11].

Method

With the aim of resolving this controversy through an appropriate literature-review, we reviewed literature from both sides, such as journal-articles, systematic-reviews, meta-analyses and book-summaries, besides videos of lectures uploaded onto YouTube.

Sugars

Sugars are found plenty in nature, and are components of carbohydrates – monosaccharide's, disaccharides, and polysaccharides. The simple sugars convert to energy, but contain little other nutrients [3].

Glucose and fructose are found plenty in fruits, honey, and processed foods. Disaccharides are a combination two simple sugars, and include sucrose, lactose, and maltose. Sucrose (table-sugar), from sugar-cane, is the most plentiful sugar that is found, and is found naturally along with fructose in numerous food-plants [3].

The polysaccharides include starch, cellulose, and pectin found in plants - while, glycogen is the animal storage-form of glucose [3].

Corn syrup and high-fructose corn syrups (HFCS)

Corn syrup is a glucose-derivative derived from corn starch. High-

***Corresponding author:** Meer Ahmad AM, Lecturer in Community Medicine and Convenor MAHSA Cricket Club Faculty of Medicine MAHSA University, Level 7, Main Building, Bandar Saujana Putra, 42610 Jenjarom, Selangor. Malaysia, Tel: +6014-7368183, +603-51022200; E-mail: meerahmad@mahsa.edu.my, drahmadmy3@gmail.com

Received November 15, 2018; **Accepted** December 12, 2018; **Published** December 28, 2018

Citation: Meer Ahmad AM, Yadav H, Balabaskaran S, Suresh L, Savithri NV (2018) Resolving the Sugar and Health Controversy with Special Reference to Malaysia. Hepatol Pancreat Sci 2: 115.

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fructose corn syrup (HFCS) contains plenty of fructose and is sweeter than sucrose. HFCS is probably the main nutritive-sweetener found in the soft-drink industry [3]. The raw-material is hydrolyzed corn-starch [2,3].

There are three types of HFCS, each with a different percentage of fructose: HFCS-42, HFCS-55, and HFCS-90–the number denoting the proportion of synthesized-fructose. HFCS-55 is used in sugar-sweetened beverages (soft drinks), while HFCS-42 in numerous processed-foods and baked-goods [3].

HFCS was developed in the 1970s – and then came a significant-shift in the type of sweetener consumed. HFCS consumption has increased, but the total fructose-intake has not dramatically changed, contrary to popular-belief [3].

The explanation is the commonly used form of HFCS, i.e., HFCS-42 and HFCS-55 has about equal ratios of fructose to glucose. Thus, despite HFCS displacing sucrose, the ratio of glucose to fructose intake has not changed much [3,12,13].

A cross-sectional study that used data from the National Health And Nutrition Examination Survey (NHANES), 2001/02, showed that sweetened carbonated-beverages was responsible for providing 37% of added-sugars (rich in HFCS) for most of Americans [3,14]. But, it should be realized that there are distinct differences in the way glucose and fructose are broken down and used in the body [3,15].

Lustig's (2013) claim is that the normal intake of fructose from fruits and vegetables is only 15 gm/day – and, prior to the Second World War the total-intake was not more than 16 to 24 gm/day [16].

He claims that from 1977 to 1988 in the USA, it shot up to 37 gm/day (or 8% of total calorie-intake), after HFCS was first found in 1975 – and that, in 1994 it increased to 54.7 gm/day (or, 10.2%), and currently in adolescents (only), it was 72.8 gm/day (or, 12.1%) [16].

Sugar-alcohols

Sugar-alcohols are sometimes used as a substitute for sucrose – and, these add bulk and texture to products. Such alcohols are mannitol, sorbitol, maltitol, and xylitol [3].

Sucrose

Sucrose is a white, crystalline, powdery-disaccharide combining the mono-saccharides glucose and fructose, which is odourless [3]. In 2013, about 175 million metric-tons of sucrose was manufactured world-wide [3, 17]. Hydrolysis removes the glycosidic-bond, converting sucrose into glucose and fructose – and, this is enhanced by the enzyme sucrase. Gastric-acidity also transforms (converts) sucrose to glucose and fructose during digestion [3].

Fructose

Fructose occurs in numerous plants, where it often bonds with glucose to form sucrose - a disaccharide.

Pure dry fructose is a very sweet, white crystalline-solid that is odourless – and, is very water-soluble. Fructose is 1.73 times sweeter than sucrose – and, it also enhances other flavours [3, 18, 19].

In general, in foods that contain free-fructose, glucose and fructose are approximately 1:1 ratio [3, 20].

Fructose is seen in honey, fruits (both tree and vine) and berries, flowers, and most root-vegetables. The largest dietary-sources of fructose, besides pure crystalline-fructose, are foods that include table-sugar (sucrose), HFCS, agave-nectar, honey, molasses, maple-syrup, and fruit-juices [3, 20].

In industry, fructose is frequently obtained from sugar-cane, sugar-beets, and corn. Approximately, 240,000 tons of crystalline-fructose is manufactured every year [3, 21].

Obesity, Insulin Resistance, T2DM, and METS

Sugars

Lustig says that the increased prevalence of obesity, insulin-resistance, MetS, and T2DM is due to the increased consumption of fructose [16]

Gary Taubes writing in his book "The Case Against Sugar", quotes only one study that apparently found that "gross per capita consumption of sugar correlates with diabetes prevalence" [22]. But, in that study by Weeratunga et al. the authors themselves admit that their estimates for per capita sugar-consumption (PCSC) In 165 countries "were relatively crude". And although their findings only found a correlation in Asia, South America and the Upper Middle-income Countries, Weeratunga et al. further conclude that "these results show independent associations between Diabetes prevalence and PCSC worldwide" [23].

While their own study does not appear corroborated, Weeratunga et al. further proposed prospective cohort-studies, which Taubes does not say whether started on or not. Besides that, ecological-studies such as these are subject to their intrinsic-fallacies.

Taubes claims that, after reviewing the scientific-literature, Taubes feels that "high consumption of sugar" is a cause of insulin-resistance. But, the only reference which he offers does not list "high consumption of sugar" as a cause of insulin-resistance. Without any evidence, Taubes suggests that "T2DM is rare until Annual Consumption of Sugar exceeds 70 pounds per capita" [22]. Taubes concludes that "enough evidence exists for us to consider sugar very likely to be a toxic-substance and to make an informed-decision about how best to balance the likely risks with the benefits". He admits though, that his case "is not definitive, but many readers will come away agreeing that sugar is a likely suspect in a great many modern-maladies" [22].

Gary Taubes studied Applied Physics at Harvard (1977), and Aerospace Engineering at Stanford University (1978). He obtained a degree in Journalism from Columbia University in 1981. Originally focusing on physics-issues, his interests have more recently turned to Medicine and Nutrition, particularly after he published an article in the Time Magazine on sugar and health [24]. We are unable to find any reference on Taubes' education in Medicine, Biochemistry and Nutrition.

Das says, glucose, sucrose, and fructose (fructose > sucrose > glucose) seem to interfere metabolism of essential fatty acids (EFAs) and thus the production of related-acids - and then, subsequently the formation of certain enzymes, which are found to induce an EFA-deficiency state [25-34].

The result is, those reduced plasma and tissue levels may subject these individuals to become more susceptible to developing Insulin Resistance, T2DM, and MetS, Das says. More confirmatory studies are required, Das says, to support this claim [3].

Rippe and Angelopaulos conclude, based on high-quality evidence

from randomized controlled trials (RCT), systematic reviews and meta-analyses of cohort-studies, that singling out added-sugars as unique-culprits for metabolically-based diseases such as obesity, diabetes and cardiovascular disease appears not consistent with modern, high-quality evidence, and is very likely not to yield health-benefits [35]. While it is wise to consume added-sugars to moderation, the reduction in such parts of the diet without concomitant reductions of different caloric-sources is not likely to achieve any real benefit, say both of them [34].

The current WHO Guidelines do not provide evidence for a correlation between sugar-intake and diabetes mellitus, except through obesity, and say these about sugar and obesity (and, over-weight-ness) [35].

One: "A high level of free-sugar intake is of concern, because of its association with poor dietary-quality, obesity and risk towards non-communicable diseases (NCDs). Free-sugars contribute to the overall energy-density of diets, and may promote a positive energy-balance. Sustaining energy-balance is critical to maintaining healthy body-weight and ensuring optimal nutrient-intake. [35].

Two: "There is increasing concern that intake of free-sugars, particularly in the form of sugar-sweetened beverages, increases overall energy-intake and may reduce the intake of foods containing more nutritionally-adequate calories, leading to an unhealthy diet, weight-gain and increased risk of NCDs" [35,36].

What the WHO Guidelines say is very much what most nutritionists have maintained all along - that a calorie is a calorie; no doubt that calories which come from refined-sugar (sucrose) do not come with vital-fibres, and other nutrients such as vitamins (but, neither do most of processed, refined carbohydrates).

Stanhope KL states that recent reports conclude that there aren't any adverse-effects of consuming beverages containing up to 30% of daily energy-requirement (EReq) from sucrose or HFCS. And, that the conclusions from several meta-analyses seem to say that fructose does not have any specific adverse-effects relative to any of the carbohydrates [37]. Stanhope also states that consumption of excess-sugar may also promote the development of CVD and T2DM indirectly by causing increased body-weight and fat-gain, "but this again is a topic of controversy" [36].

She states though that, based on metabolism, it is possible that fructose-consumption causes increased energy-intake and reduced energy-expenditure due to reduced leptin-production [36]. Klok et al. state that leptin is produced and secreted mostly in adipose-tissue, while ghrelin in the stomach - leptin suppressing appetite in the long-term, while ghrelin increasing it in the short-term [38]. In their article, the authors tabulate and discuss the factors which increase/decrease leptin-levels and also increase/decrease ghrelin levels. While glucose features prominently in this, fructose does not - neither sucrose [37].

These authors also discuss how diet affects leptin and ghrelin, but once again fructose and sucrose do not appear to feature [37]. Peptide-hormones, including leptin and ghrelin, do not cross the blood-brain barrier (BBB). Although it is acknowledged that they act on receptors in the BBB, the secondary-stage from the BBB to brain-receptors has not yet been understood and explained. Stanhope further states that some epidemiological-studies show that sugar-consumption is associated with body-weight gain, and there are interventional-studies in which consumption of (unlimited) high-sugar diets promoted increased body-weight gain compared with consumption of (unlimited) low-sugar diets [36]. But, she states that there are no studies seen in which energy-intake and weight-gain were compared in subjects consuming high or low sugar, blinded, (*ad libitum*) diets that ensured both groups consumed a similar macronutrient-distribution, and the same amounts of fibre [36]. She further states that there is also little data to determine the form in which added-sugar is consumed, whether as liquid (beverage) or as solid-food, determines its ability to promote weight-gain [36]. And that, finding the answers to these evidence-gaps may be vital for supporting the policy-changes that would allow the nutrition-environment become one that does not promote the causation of obesity and metabolic-disease [36].

The fibre in plant foods has been known for more than two centuries by nutritionists to have significant effects on digestion. Its role in human nutrition was started research on towards the end of the 19th century. But, between 1966 and 1972, Denis Burkitt, a surgeon returning from Africa, conceived concepts based on a range of disciplines together with his own observations to propose a new view of the role of fibre in human health. Burkitt built on the work of three physicians (Peter Cleave, G. D. Campbell and Hugh Trowell), a surgeon (Neil Painter) and a biochemist (Alec Walker) to convey that diets low in fibre increase the risk of CHD, obesity, diabetes, dental caries, various vascular disorders and large bowel conditions such as cancer, appendicitis and diverticulosis.

Proposing fibre as the key, stimulated much research but also controversy. Basic studies of the laxative action of wheat-bran were done in the United States in the early decades of the 20th century. Walker in South Africa added to these studies among African blacks and subsequently propounded that cereal-fiber protected them against certain metabolic-disorders. Trowell in Uganda extended this concept with concern upon the rarity of common non-infective diseases of the colon. Another school of inquiry arose from the hypothesis of Cleave who conceptualized that the presence of refined-sugar, and to lower extent white-flour, caused many metabolic-diseases - while the loss of fiber caused certain colonic-disorders. In 1972, Trowell proposed a new physiological definition of fiber as "the residue of plant foods that resisted digestion by alimentary enzymes". Southgate then proposed chemical-methods to analyze that which composed dietary-fiber: cellulose, hemicellulose, and lignin. But, this Review is unable to find more on Cleave's work with refined-sugar on metabolic diseases.

A 5-year Prospective-study in South Africa (Vorster HH et al.), comparing those who consumed more added sugars (>10% energy) with those who consumed less only found very minimally- higher waist-circumference and Body Mass Index (BMI), while there was no reduction in HDL-Cholesterol (higher bound of 95% CI >0) [38,39].

Fructose

Lustig claims fructose causes the production of 'junk1 enzyme' in the liver……which in turn causes insulin-resistance and insulin-resistance enhancement [16].

Conversely, this is what Sun and Empie say in a MedScape endorsed review-article (review of 34 papers) titled "Fructose metabolism in Humans: What isotope tracer-studies tell us": "During the last several decades, the prevalence of obesity and metabolic-syndrome has risen dramatically on a global-basis, but more so in the U.S. population" [40]. They state that because the prevalence is correlated in statistics and in time with the increase of added-sugar intakes, particularly concerning HFCS in the U.S., some want to conclude that the intake of HFCS or fructose as a free simple-sugar may be the reason for various adverse health-consequences [39]. Conventional clinical-trials and ecological-

studies have been carried out to study these hypotheses, but not all findings are found to be supportive, the authors further state [39].

Conventional-studies frequently cannot reveal details of (interconnecting) metabolic-pathways when testing fructose or fructose-containing sugars, and such studies also cannot clearly observe a metabolic (mechanistic) cause associated with an observed physiological-consequence linked to the sugar consumed, they state [39]. This is because the usual diets contain many forms of saccharides which are related (inter-convertible) in the body and share many phases of the carbohydrate-metabolism pathways [39]. They both further say, that over the last decade a series of controversies have arisen concerning the consumption of fructose. In 2004, a commentary had been written hypothesizing that the "high" fructose content in HFCS was the cause of the obesity rise in America. Such concern was based on the association of the obesity prevalence-rise with the replacement of cane and beet sugar by HFCS–such although here the fructose-content of these two sweeteners is basically the same [39].

Subsequently it is said, several dietary-studies using calorically high-doses of fructose were published to study fructose-modulation of leptin hormone-status, in a hypothesis that chronic-changes in this hormone-level could lead to weight-gain. But, additional studies and evidence-based reviews do not always back these findings [39].

Recently, Welsh et al reported that the intake of added-sugar has conspicuously decreased between 1999 and 2008 but the obesity-prevalence has continued to rise [40]. The present view is that obesity is a matter of energy-balance [40]. Next, the fructose-moiety in sugars was hypothesized to cause high serum uric-acid which apparently could lead to the development of type-2 diabetes [39,41]. There is presently no direct evidence that uric acid has a causative-relationship with diabetes. Besides, NHANES-data shows no relationship between serum uric acid and fructose-intake at normal dietary consumption-levels [39,42].

Additionally, it is vital to realize the practical-significance of testing the relationship of a sugar using an unrepresentative-dose compared to the true population sugar-intake, a question which is presently under debate [39,43-46]. In several of the interventional-studies involved with studying the various hypotheses above, very high-doses of sugars over the short-term were often applied-the study-designs were much like toxicological-studies [39]. And, the studies were not more than able to come to associative-conclusions between applied-dose and observed health-related outcomes. The observed biological-changes, although here statistically significant by p-value ruling, were frequently not more than fluctuations within normal-ranges [39]. These studies rarely measured actual development of disease or the intermediate-metabolites that characterize mechanism-based reactions. In beginning to prove true-effect of a diet-component, it is imperative to study the component-disposal through the common central-pathways at the molecular-level, Sun and Empie state [39].

Such studies need to be facilitated and detailed by the use of isotope tracer-labelled precursors, and this concept is being reviewed by Sun and Empie here below. Glucose and fructose enter the metabolic-pathways differently, with glucose-conversion to 1,6-diphosphorylated fructose happening before the new-molecule being broken into the three-carbon metabolic-intermediates, dihydroxy-acetone phosphate and glyceraldehyde 3-phosphate. Absorbed-fructose is only mono-phosphorylated before being cleaved [47]. Glucose-utilization can be regulated before being broken down, while fructose is not that much regulated. This initial difference has prompted some to hypothesize that, because fructose-cleavage bypasses key feedback-regulatory phases (steps) in the glucose metabolic-pathway, this bypass may lead to increases in fatty-acid synthesis, which may then contribute to causes of obesity [39,47]. Such (a hypothesis) relies on a rather simplified metabolic-pathway analysis, and on studies using pure-fructose compared with pure-glucose - a situation which rarely happens in the American diet [48,49]. The use of mixed-sugars is more metabolically-predictive of dietary-consequences than that from single monosaccharide's studied individually, as metabolism of each type of sugar is not independent from the different sugars [39].

Metabolic-interactions between glucose and fructose very much impact general sugar-metabolism [39]. Because of the complexity of fructose and glucose metabolism, conventional feeding-study approaches do not usually provide as much information as isotope tracer-studies for obtaining a true picture of mechanisms of the manner dietary-fructose or glucose are used [39,50]. It is known that carbon-moieties in fructose and glucose can be moved about (inter-converted) in the liver, [39,50,51] and thus studying the disposal and metabolic-outcomes of these dietary-sugars with respect to one another is best conducted using isotope-labelled sugars as tracers [39].

Although here, all pathways are still to be completely studied for fructose disposal and metabolism, given different physiological conditions, a conspicuous number of reports on fructose-isotope tracer-studies are published [39]. In their work, Sun and Empie have looked at fructose disposal and metabolism in humans based on isotope tracer-studies to better fathom from a molecular view, fructose-oxidation, fructose-conversion to glucose, fructose-conversion to lipids, and fructose-conversion to lactate [40].

In contrast, Das says, "most, if not all, of the fructose that is consumed gets converted to fat" [3]. Tsilas et al. through systematic-review and meta-analysis showed that existing evidence does not allow them to conclude that fructose-containing sugars, independent of food-form, are associated with greater risk of type-2 diabetes, but "further research is likely to affect our estimates" [52].

Khan and Sievenpiper, through systematic-reviews and meta-analyses, say that "fructose-containing sugars are a focus of attention as a public-health target for their putative-role in obesity and cardio-metabolic disease including diabetes" [53]. The fructose- moiety is singled-out to be the primary-driver for the harms of sugars due to its characteristic endocrine-signal and pathophysiological-role. But, such is only supported by ecological-studies, animal-models of overfeeding and select human interventional-studies with supra- physiological doses or lack of control for energy [52]. The best evidence from systematic-reviews and meta-analyses of controlled-trials has not shown that fructose-containing sugars are any different in their behavior compared with different forms of digestible-carbohydrates [52].

Fructose-containing sugars only lead to weight-gain and various unintended adversity on cardio-metabolic risk-factors only as far as the excess calories they produce [52]. Also, prospective cohort-studies which provide the strongest observational-evidence, have shown an association between fructose-containing sugars and cardio-metabolic risk including weight-gain, cardiovascular disease-outcomes and diabetes only with sugar-sweetened beverages, and not for sugars from different sources [52]. In truth, sugar-sweetened beverages are a marker for unhealthy-lifestyle-their drinkers consume more calories in general, exercise insufficiently, smoke more and have an unacceptable dietary-pattern [52].

Khan and Sivenpiper further state that the possibility of

overconsumption of sugars in the form of sugar-rich foods and drinks makes focusing on sugars as a source of excess-calories, a wise strategy. But, these authors state that sugar-content should not be the sole deciding-factor of a healthy-diet. There are several different factors in the diet-some providing excess-calories while some yet provide beneficial-nutrients [53]. Instead of just focusing on one energy-source, the whole-diet should be looked at for health-benefits, these authors state [52].

Lipids and Cardiovascular Disease

Sugars

Lustig says that the increased prevalence of obesity, MetS, and T2DM is due to increased consumption of fructose. Lustig also claims that the increased intake of fructose also causes hypertension, heart disease, and incessant unsatiated-eating [16]. Taubes wishes to debunk nutrition-science which implicate fat as a cause of atherosclerosis [22]. But, many studies in numerous countries, of an epidemiological-nature, have found that increased blood LDL-cholesterol (with or without hypertriglyceridemia), and even total-cholesterol, is a cause of atherosclerosis [53-76]. In this matter, the various types of familial hyperlipidemias are of concern–and, those with familial hyperlipidemias (especially Type IIa and type IV by Frederickson's classification) may not handle well high dietary-fats. DiNicholantonio JJ et al. discussing sugar and coronary-risk factors, place much emphasis on very early questionable work [78].

In one study (1969) Szantos and Yudkin studied high or low intake of sucrose for periods of 14 days in a group of 19 healthy-men [77]. Szantos and Yudkin does not define what he means by high and low intake [78].

Yudkin claims that, in all of the 19 subjects, there was a significant-rise in triglycerides (TG) , while in six of the 19 subjects "there was a rise in serum immune-reactive insulin, considerable increase in weight, and a significant increase in (percentage) platelet-adhesiveness" [78]. Yet, Yudkin's own results show an observable overlap in the 95% CI of all those variables [77].

In a subsequent article (1980), Szantos and Yudkin states that 14 young men had their average daily-intake of sugar for 3 weeks increased from 115 gm to 260 gm. (1 teaspoon =5 grams) [78].

Yudkin states that 10 out of the 14 showed a significant decrease in HDL-Cholesterol (HDLc) level, while TG-level remained the same. While the reduction in mean HDLc was only 0.20 mmol/L, Yudkin does not say either as to what statistical-test was done which could allow him such a result in just these 14 subjects [78,79].

Fructose

Taubes also unfairly accuses the sugar-industry of having funded much research on fats and health–which is not real reasonable basis to make conclusions on the matter [22]. Taubes claims eating sugars boosts both cholesterol and triglyceride-levels in the blood. It is true that some of glucose is metabolized to acetyl-coA which feeds the formation of fatty-acids, some of which do form triglycerides, but not cholesterol [22].

Further, Taubes says all of fructose from digestion of sucrose (refined-sugar) is converted to fat in the liver [22] but, this would include fructose from HFCS and fruits/vegetables, which are a rich-source of fructose. Then, the hypothesis would be that obesity and hyperlipidemia would tend to be commoner in vegetarians than non-vegetarians.

Although the systematic-review/meta-analysis of randomized controlled-trials by Te Morenga et al does strongly implicate that dietary-sugars influence blood-pressure and serum-lipids (which are strong risk-factors in the causation of coronary heart-disease, CHD), the study is not without short-comings [80].

First, the study does not clearly define "higher sugar-intake" from "lower sugar-intake". Second, the minimum trial-duration of the trials selected for the review/meta-analysis was only 2 weeks, when CHD risk-factors actually need to be sustained. Third, the increase in Total Cholesterol (TC) and LDL was only minimal: TG–0.11 mmol/L (95% CI: 0.07, 0.15 mmol/L), Total Cholesterol (TC) 0.16 mmol/L (95% CI: 0.10, 0.24 mmol/L), LDLc 0.12 mmol/L (95% CI: 0.05, 0.19 mmol/L).

Systolic blood pressure (SBP) 6.9 mmHg (95% CI : 3.4, 10.3 mmHg) and Diastolic blood pressure (DBP) 5.6 mmHg (95% CI: 2.5, 8.8 mmHg). In contrast, there was a very small but significant concomitant increase in HDLc at 0.02 mmol/L (95% CI: 0.00, 0.03 mmol/L). Fourth, the study does not throw light on whether it is the fructose or glucose fraction of sugar which is the cause of the changes in those CHD risk-factors. In view of these findings and the short-comings of Te Morenga's study, besides the fact that basic biochemistry-studies do not support these findings, nor the biochemical cause ascertained, a well-designed prospective-study (and biochemical studies) may be needed to validate the findings of Te Morenga's review/meta-analysis in relation to CHD risk-factors–without confounding for energy-balance and weight-gain.

Taubes still yet claims that fat-cells release factors that increase inflammation, "contributing to all sorts of chronic-maladies including arthritis, high blood pressure, heart disease, kidney-disease and dementia" [22]. Das UN says, "in the liver, however, fructose by-passes that whole machinery of glucose-metabolism because it does not need phospho-fructokinase (PFK)" [3]. Das says, fructose gets phosphorylated to become fructose-1-phosphate and, consequently becomes a substrate for aldolase, thus producing higher-levels of ATP and citrate–and, from these fatty-acids are synthesized. "Thus most, if not all, of the fructose that is consumed gets converted to fat" [3] and Das quotes Collison et al. [81] and Parks et al. [82].

Das also states that all of the fructose consumed is brought to the liver and without delay converted to fat, while "glucose stays in the blood-stream for some period of time, either for energy-source or conversion to glycogen." [3]. Yet still, Das says that only after the energy-demands are met, are glucose converted to fat [3].

Das also states that fructose cannot provide energy-source in the brain, nor does it supply energy for use by muscles. "Fructose gets stored only as fat" [3].

In other words Das says, one has to eat exactly twice as much fructose as starch to get the same amount of energy-supplied to both muscle and brain compared to glucose - resulting in the brain relaying a feedback such that one needs to consume more fructose to meet the energy-demands, which could lead to addiction to sweetness [3]. Nevertheless, tracer-studies with C13 have refuted all these.

Lustig (2013) says 100% of fructose goes to the liver (as opposed to only 24% of glucose), where all of it is converted to Fructose-1-phosphate [16]. Lustig also claims phosphorylation and de-phosphorylation of fructose produces uric acid as waste product "which inhibits the action of nitrous oxide in the endothelial-cells of the blood-vessels, leading to hypertension" [16]. He also claims that fructose-1-phosphate is metabolized to xylulose-5-phosphate, which

induces 'fat-storing enzymes'. And yet still, he claims that fructose-1-phosphate, just like glucose-6-phosphate, is also converted to pyruvate in the liver, which subsequently converts to acetyl-coA, the left-over of what (that is very much more than when compared to glucose-uptake in the liver) converts to citrate, which citrate then induces fat-storing enzymes and converts into large amounts of VLDL and stored-fat [16]. Tracer C13-studies also refute Lustig's claims, proving that with both fructose and glucose, lactate-conversion plays a vital role in conveying carbohydrate potential-energy between gluconeogenesis and acetyl-CoA, with entry into the TCA-cycle or use in lipid-synthesis [39].

In addition, Culleton et al. in a community-based prospective observational-study showed that uric acid does not have a causal-role in the development of coronary heart disease, death from cardiovascular-disease, or death from all causes–and, any apparent association with these outcomes was likely due to the association of uric acid with other risk factors [83]. Lecoultre et al conducted a tracer-study in 7 men exercising [84].

The researchers found that 28% of fructose-ingested was converted to lactate (35 micromol/kg-bw/min). Most of the converted-lactate (89.3%) from fructose was oxidized - mainly by working skeletal-muscles (31 micromol/kg-bw/min) [83].

Lecoultre et al. also state that a conspicuous number of clinical-studies have been carried out to investigate the influence of fructose-intake on blood-triglyceride (TG) concentrations. But, tracer-studies with the objective of showing metabolic-conversion from labelled fructose-carbons to TG are scarce. In contrast with conversion from fructose to glucose, the metabolic-pathway from fructose to TG conversion is much more complicated due to the complex distribution and diversity of blood-lipid compositions in the body, they state [84].

These authors further state that de novo lipogenesis (DNL) from sugars can be observed in the liver and end up as packaged-VLDL TG and/or as intrahepatocellular lipids. Here presently is found no convenient method to quantitate overall DNL and intrahepatic lipid-deposition. The proportionate-contribution of sugars to de novo lipogenesis and VLDL TG are usually determined using tracer-enrichment data of blood-samples. The time-required for liver de novo lipogenesis from sugars, and the factors influencing it, are not completely realized yet [83].

De novo lipogenesis may also take place in adipose-tissue or muscles, but there are not any acceptable methods available to quantitate this. A more detailed discussion of de novo lipogenesis and methodological-considerations is an appropriate topic for a separate review, they state [83].

The authors cite Chong et al who studied fructose and postprandial lipidemia in 14 adults (8 men) who were given (orally) ^{13}C-labeled fructose or 13C-labeled glucose at required doses [85].

Blood lipid-changes were checked along a 6-hour period [85].

Plasma TG-concentration was observed to rise more significantly after fructose-ingestion (from baseline 1240 μmol/L (≈110 mg/dl) to its plateau of 2350 μmol/L (≈208 mg/dl)) than that after glucose-ingestion (from baseline 1240 μmol/L to its plateau of 1700 μmol/L(≈150 mg/dl)) [85].

But, the increases of 13C-enriched TG-fatty acids and TG-glycerol from the labelled-fructose in the Sf 20–400 lipid fraction (including VLDL) were very small (0.05% fatty-acids and 0.15% TG-glycerol) [85].

In a different study, Tran et al reported that 13C-labeled fructose-consumption at 3 × 0.3 g/kg body-weight caused a small but significant increase of 13C-enrichment in VLDL-palmitate in 8 men compared with that found in 9 women (no increase) over 6 hours [86].

But compared to baselines, plasma-TG and non-esterified fatty-acid decreased 5.3% and 32.9% in men and 3.3% and 24.4% in women, respectively [86].

The findings indicate that the conversion from fructose to fatty-acid happened – but not blood-lipid concentrations increase. The findings also suggest that the increase in blood-TG frequently observed in men compared with women after high-dose fructose-ingestion could be attributed to fat-sparing during energy-utilization [61].

There are several studies which used labelled-acetate as a precursor of lipid-synthesis and administered by intravenous-infusion, to assess the fructose-stimulation of de novo lipogenesis (DNL) [39].

Compared to glucose, more palmitate-synthesis within triglyceride-rich lipoprotein (TRL) TG was noted after fructose-containing drinks, but not after solid-food consumption [87]. And, no significant difference was observed for TRL-TG concentrations between glucose and fructose-containing drinks after baseline-correction [39].

David Wang et al showed by pooled-analyses that fructose in iso-caloric exchange with a different carbohydrate does not increase postprandial-TG, "although an effect cannot be excluded under all conditions, fructose providing excess energy does increase postprandial triglycerides" [87].

"Larger, longer, and higher-quality trials are needed", the authors state [87-91].

Stanhope KL states that, most recently, her group has reported that supplementing the unlimited (*ad libitum*) diets of young adults with beverages containing 0%, 10%, 17.5% or 25% of daily energy-requirement (Ereq) as HFCS, increased lipid/lipoprotein risk-factors for CVD and uric acid in a dose-response manner [36].

But Stanhope also states that, un-confounded studies carried out in healthy-humans under a controlled, energy-balanced diet-protocol that enables determination of the relationship of sugar with diets that are controlled for body-weight gain are mostly unavailable [36].

This, Stanhope states in response to the study by Yang et al. [92], (that is the only study of its conclusion), which was reflected in the American Heart Association statement on the matter that "those who got 17 to 21 percent of calories from added sugar had a 38 percent higher risk of dying from cardiovascular disease compared to those who consumed 8 percent of their calories from added-sugar. And that the relative-risk was more than double for those who consumed 21 percent or more of their calories from added sugar". Among those in Johnson's panel was Lustig.

Further, Stanhope states that recent-reports conclude that there aren't any adverse effects of consuming beverages containing as much as 30% EReq sucrose or HFCS, and that the conclusions from several meta-analyses suggest that fructose hasn't any specific adverse cause (effects) relative to any other carbohydrate [36].

Stanhope also states that consumption of excess-sugar may also promote the development of CVD and T2DM indirectly by causing increased body-weight and fat-gain, but such is "also a topic of controversy" [37].

Cancers

Fructose and sucrose

Das says, phosphatidylinositol-4,5-biphosphate 3-kinase (PI3Ks) are a family of enzymes involved in cellular-functions such as cell-growth, proliferation, differentiation, motility, survival, and intra-cellular trafficking, which could cause cancer [3,89-91]. Das says PI3K activity contributes conspicuously to cellular-transformation and the development of cancer and that certain oncoproteins activate PI3K [3]. He further states, when experimental animals were fed a diet containing 60% glucose or fructose for 7 days, a significant increase was noted in the activities of certain enzymes which Das identifies. These changes in enzyme-activities are similar to mutated tumor-suppressor PTEN, which causes a hyperactivation of PI3K-signaling that results in enhanced cell-proliferation, he states [3,92-96]. Thus he states, high fructose and even high glucose and sucrose consumption could lead to an increase in cancer-incidence. Similarly, cancer-proliferation can be enhanced by these sugars, he states [3,38]. But, Das' claims here and his supporting referenced-studies, appear entirely be based on studies on rats and cell-lines, and a search of PubMed reveals no epidemiological (observational)-studies on the matter except for one study by Fuchs et al. [97]. Also, Das does not discuss a dose-response relationship in this so-called causation of cancer and thus, since fructose and sucrose are found abundantly and naturally in most fruits and vegetables, it does come about to mean that these foods are carcinogenic. This can be easily proven or disproven in a well-designed nutritional/epidemiological cohort-study over even a short-period of one year, using such foods in their content of these sugars as exposure, and the enzyme-changes which Das claims as carcinogenic to be biomarkers pointing to an outcome of cancer subsequently. The hypothesis being that, cancer is caused by these sugars.

The American Conference of Governmental Industrial Hygienists (ACGIH) categorizes sucrose as a Category A4 Carcinogen i.e., Not classifiable as human or animal carcinogen (while no data is available for fructose per se)–which is reflected in the current existing Chemical Safety Data Sheets (CSDS). These CSDS' also state that sugar is not toxic, but a slight health-hazard as a respiratory, skin and eye irritant. Similarly, fructose.

Cancer Research UK (2017) states that a high-sugar diet could be undesirable when it comes to cancer-risk, but not for the reasons that frequently cited in the news. And it states that this thought that sugar is responsible for initiating or fuelling a cancer's growth is "an over-simplification of some complicated biology" [94,95].

The article states the myth that sugar fuels cancer was born from the argument that because cancer-cells need plenty of glucose, then cutting sugar out of our diet would help stop cancer from growing, and could even stop cancers establishing in the first place. Unfortunately it's not that simple, states the article. Our healthy-cells require glucose also, and there isn't any way for our bodies to allow healthy-cells have the glucose they need, but not give it to cancer-cells [94,95]. There isn't any proof that following a sugar-free diet lowers the risk of getting cancer, or boosts the chances of surviving if one is diagnosed with cancer. And, following severely restrictive-diets with very low amounts of carbohydrate could damage health in the long-term by eliminating foods that are good-sources of fibre and vitamins [94,95].

This is particularly vital for cancer-patients, because some treatments can result in weight-loss and put the body under a lot of stress. Thus, inadequate-nutrition from restrictive-diets could hamper recovery, or even be life-threatening [94,95].

Although this won't proof that cutting carbohydrates from our diet will help treat cancer, vital-research has shown that fathoming the abnormal ways that cancer-cells make energy could lead to new treatment-modalities." [94,95]. Healthy-cells use a series of chemical-reactions in mitochondria. The Warburg Phenomenon describes how cancer-cells bypass the mitochondria to generate energy more rapidly to meet demand [94,95].

Such shortcut for making energy might be a weakness for some cancers that gives researchers an advantage for developing new treatment-modalities [94,95]. But, we don't know yet whether treatment-modalities that starve cancer-cells are safe or whether such ever work [94,95].

It's certainly does not justify cancer-patients trying to do it themselves by restricting their diet during treatment - they could be endangering themselves [94,95].

Cutting out sugar doesn't help treat cancer, and sugar doesn't directly cause cancer. Why then do we encourage people to cut down on sugary-foods in our diet-advice?

That is because there exists an indirect-link between cancer-risk and sugar. Eating plenty of sugar can cause someone to gain weight over time–and, scientific-evidence shows that being obese (or overweight) increases the risk of 13 different-types of cancer. In fact, obesity is the single biggest preventable-cause of cancer after smoking [94,95]. Also, evidence does not reveal that adopting a diet very low in carbohydrates will lower one's cancer-risk, or help as a treatment. And for patients, getting adequate-nutrition is vital for helping their bodies cope with treatment [94,95].

But, in a case-control study of 816 of colorectal-patients and 815 community-controls, Wang Z et al. using the consumption of 29 food-items to determine sugars and sucrose intake, showed that sugars-intake was associated with increased-risk of colorectal-cancer among smokers and those who do not drink alcohol, in men selectively - although here overall, intakes of sugars and sucrose were not related to colorectal cancer-risk either in men or women. These researchers had made statistical-adjustments for confounding-factors. Body Mass Index did not modify the association with sugars-intake in either men or women [96].

In a contrasting study, Fuchs MA et al. in assessing the association between sugar-sweetened beverage consumption on cancer-recurrence and mortality in 1,011 stage III colon-cancer patients who completed food-frequency questionnaires as part of a U.S. National Cancer Institute-sponsored adjuvant-chemotherapy trial, showed that "higher sugar-sweetened beverage (SSB) -intake was associated with a significantly increased-risk of cancer recurrence and mortality in stage III colon-cancer patients" [93].

Patients consuming ≥ 2 servings of SSBs per day experienced an adjusted Hazard Ratio for disease recurrence or mortality of 1.67 (95% CI, 1.04-2.68), compared with those consuming <2 servings per day. This association of sugar-sweetened beverages on cancer recurrence or mortality was found greater among patients who were both overweight (body mass index ≥ 2 5 kg/m (2)) and physically-inactive (metabolic-equivalence task-hours per week <18) (HR = 2.22; 95% CI, 1.29-3.81) [93].

Thus, this issue of sugar being a cancer-risk, causing higher cancer-recurrence, causing cancer-proliferation, and causing increased cancer-mortality needs to be studied further in well-designed observational-studies (controlled for BMI and energy-balance) and basic medical-science studies, preferably in various types of cancer and its stage.

Chronic Low-Grade Inflammation

Das says obesity, T2DM, and MetS are considered low-grade systemic-inflammatory conditions due to the presence of increased amounts of circulating-fats and adipose-tissue, interleukin (IL)-6, and tumor-necrosis factor (TNF), and various different pro-inflammatory markers [3,97-104]. Das says, because fructose is believed to enhance the risk for obesity, T2DM, and MetS, it follows that fructose will have pro-inflammatory actions [3].

He states, this assumption was supported by a study that demonstrated that male C57 Bl6/J mice treated for 30wk with HFCS showed hyperlipidemia; hyperinsulinemia; hyperleptinemia; hypoadiponectinemia; reduced GLUT-4 and GLUT-5 expression and membrane-translocation; activation of nuclear factor-kB; and expression of inducible nitric oxide synthase and intercellular adhesion-molecule-1, which he concludes are not only characteristics of obesity, peripheral insulin-resistance (IR), and T2DM, but also of inflammation [3,105]. In addition, he states that similar pro-inflammatory actions, including an increase in plasma IL-6 and TNF-A concentrations following high-fructose supplemented-diets, were reported by several different studies. 3, 81-83.

"These results emphasize that fructose has pro-inflammatory actions similar to high glucose, since hyperglycemia has pro-inflammatory actions" [3,106-108]. "These results emphasize that fructose has pro-inflammatory actions similar to high glucose, since hyperglycemia has pro-inflammatory actions" [3,109-111].

West Washington University states that low-grade inflammation is an immune-system response, and that clinically, low-grade inflammation is defined as a two to four-fold increase in circulating-levels of pro-inflammatory and anti-inflammatory cytokines, as well as numerous other markers of immune-system activity, such as interleukins, C-reactive protein and tumor-necrosis factor-alpha.

Straub RH says that according to the theory of chronic low-grade inflammation, disease-sequelae can be explained based on redirection of energy-rich fuels from storage-organs to the activated immune-system. These disease-sequelae, he states, are highly diverse and include the following: sickness-behaviour, anorexia, malnutrition, muscle wasting–cachexia, cachectic obesity, insulin resistance with hyperinsulinemia, dyslipidemia, increase of adipose-tissue near inflamed-tissue, alterations of steroid-hormone axes, elevated sympathetic-tone and local sympathetic-nerve fiber-loss, decreased parasympathetic-tone, hypertension, inflammation-related anemia, and osteopenia. Since these disease-sequelae can be found in many animal-models of chronic inflammatory-diseases with mammals (e.g., monkeys, mice, rats, rabbits, etc.), he states, "the evolutionary time-line goes back at least 70 million years" [112].

A lot of the hypothesis in low-grade chronic inflammatory states goes to support treatment in alternative-medicine such as very many detoxification methods, anti-oxidant treatment, and a variety of unsubstantiated-diets. Thus, the hypotheses on chronic inflammatory-states need to be studied and verified at length also vitally in this, we have already resolved earlier that sucrose and fructose do not cause obesity (other than through overall energy balance), MetS and T2DM - thus nullifying this hypothesis about the causation of such inflammation. The prospective study that we propose can go on to prove this stand of ours.

Dental caries

The World Sugar Research Organization states that the relationship between the amount of sugar-consumed and the levels of (tooth) decay in individuals is actually very weak. The frequency of consumption of sugar is a better, but still inadequate, predictor. The relationship between sugar-consumption and caries is much weaker in this modern age of fluoride exposure than it used to be. It states that the most effective-means of preventing caries is through the routine-use of fluoride-toothpaste in conjunction with acceptable oral-hygiene practices [113].

But, controlling the consumption of sugar remains a justifiable part of caries prevention, if not always the most important aspect. WHO recommends a reduced intake of free sugars, and that in both children and adults the intake of free sugars should not exceed 10% of total energy intake. An intake of free sugars of ≤10% of energy is associated with lower risk of dental caries, but this threshold does not eliminate dental caries as dental caries is a progressive cumulative lifelong disease [114].

Digestion, absorption and metabolism

Sun and Empie state that in nature, fructose is frequently found together with glucose, and the composition-values for some foods have been tabulated by the USDA on its website [115].

In one study, type-2 diabetic patients were fed sucrose or HFCS with a background-diet, resulting in plasma-glucose concentrations not being different between sucrose and the HFCS, nor were mean plasma-insulin values. [39,116-120]. Thus, the body appears to handle ingested free glucose-fructose mixtures or HFCS similarly as sucrose and that hydrolysis of sucrose does not appear to be rate-limiting by uptake. Once absorbed, glucose is transported to the liver and then to peripheral organs for use–and, its entrance into muscle and fat cells is insulin-dependent [39,116-120].

Fructose is primarily transported to and metabolized in the liver for energy and for two and three carbon precursor-production without dependence on insulin. Although here little dietary-fructose appears in the circulation, it could bring about changes in plasma-glucose concentrations via sugar (inter)conversions [116-120].

In man, studies indicate fructose to glucose conversion may be possible to a highly-conspicuous extent, and that this conversion comes about via the 3-carbon intermediate-pathways [39,116-120].

Most absorbed-fructose is broken in the liver into glyceraldehyde and dihydroxy-acetone phosphate, and these further go to glycerol-phosphate and pyruvate-metabolism pathways, respectively. In the case of fructose and glucose, lactate-conversion plays a vital-role in distributing potential-energy of carbohydrate-origin between gluconeogenesis and acetyl CoA, with entry into the TCA-cycle or use in lipid-synthesis [39,121,122].

Lactate-discharge is also a way for fructose-carbons to avoid the liver and be brought to peripheral-tissues. Fructose-cleavage to glyceraldehyde could bring about the synthesis of glycerol via reduction [39,123-125].

It was observed that blood-glycerol concentration increased after fructose-ingestion among exercising-subjects. The observed glycerol-increases after fructose-ingestion are either greater or the same compared with the values after glucose-ingestion, and the produced-glycerol can be oxidized for energy [39,123-125].

Thus, according to the authors, Sun and Empie, fructose-assimilated does get oxidized, and does become converted to glucose, lactate, and lipids–thus, not entirely become converted to lipids as Das, Lustig and Taubes claim.

Prevention of Related Diseases, and Dietary Guidelines

Sugars

Primary Prevention of obesity should mainly focus on the Community Education aspect of Health Promotion.

And all, including children, should be taught their daily calorie-requirement by age, sex, weight and activity-level. And, before we venture into imposing higher-taxes on sugar-sweetened beverages (SSBs), we should venture into educating the public to count their calories on everything that we eat and drink, and those of their children. Higher-taxes on cigarettes never really brought down the smoking-prevalence. By legislation, places where SSB's are displayed for sale, should also display the daily calorie-requirement chart by age, weight, sex and activity-level. SSB's should prominently display their sugar and calorie content.

Suggested Daily Dietary Intake for Malaysians has already been prepared by the Institute for Medical Research (IMR) Malaysia since 1973, including Energy (Calorie) Requirement by age, gender, weight and activity-level–besides for those pregnant/lactating, infants (by age in months), children (by age 1–9 years), boys (by age 10–19 years) and girls (by age 10–19 years).

Signages must teach that excess calorie-intake leads to obesity, and its consequent diseases. Restaurants and confectionaries should be required to display the calorie-content of every one of the items on their menu. Similarly, snacks in packets.

Parents should weigh their food, and their children's, and estimate the calorie-content before dining. This should be part of the objectives of the Family Health Development Division of the Health Ministry.

Only then, will over-weightiness and obesity (and the consequences) become not so prevalent in Malaysia. Calorie-counting in Developed-countries is a well-established, well-accepted, and well-adhered to cultural-practice. In Malaysia, the Calorie-content of common food (and drink) items have already been worked out by the IMR, and the Kuala Lumpur City Council Health Department.

In comparison, 100 grams of sugar (20 teaspoonfuls) amount to 387 Calories.

Erickson et al. in a systematic-review, reviewed guidelines on sugar-intake and assessed consistency of recommendations, methodological-quality of guidelines, and the quality of evidence supporting each recommendation - guidelines addressing sugar-intake that reported their methods of development and were published in English between 1995 and 2016, using the Appraisal of Guidelines for Research and Evaluation, 2nd edition (AGREE II), instrument [125].

To assess evidence quality, articles supporting recommendations were independently reviewed and their quality was determined by using GRADE (Grading of Recommendations Assessment, Development and Evaluation) methods [125].

They concluded that guidelines on dietary-sugar do not meet criteria for trustworthy recommendations, and are based on low-quality evidence [125].

They say that Public Health officials (when promulgating these recommendations) and their public audience (when considering dietary behavior) should be aware of these limitations [125].

Conclusion

Although here, we find for and against claims that sugar, especially sucrose and fructose, is an addictive, toxic-substance capable of causing (and, being the main cause) of obesity, type-2 diabetes mellitus, metabolic syndrome, heart disease, hypertension, insulin-resistance, non-alcoholic fatty liver disease, cancer, and unsatiated-eating, the evidence (including from meta-analyses and systematic-reviews) are overwhelmingly against such claims. Most of the studies for appear to have been done on rats and cell-lines, and not of an epidemiological (observational) study nature.

Even the nature of the metabolism of sugars, in particular fructose, claimed as conclusions from these studies are doubted by other studies/articles.

Much of the pathophysiology of sugar causing disease, importantly cancer and cardio-vascular disease, is attributable to its alleged link to the causation of the so-called low-grade chronic systemic inflammatory state–which appear to be the founding principle for the alternative medicine treatment-modalities such as detox, scores of anti-oxidants, and novo nutritional therapies.

Certainly, some Knowledge Gap exists which need to be filled in by conducting appropriately-designed research, particularly of observational and interventional nature, besides systematic-reviews and meta-analysis. Results and Conclusions from stand-alone research need to be validated by repeated-research which are appropriately designed.

The American Conference of Governmental Industrial Hygienists (ACGIH) categorizes sucrose as an Category A4 Carcinogen i.e., Not classifiable as human or animal carcinogen (while no data is available for fructose per se) – which is reflected in the current existing Chemical Safety Data Sheets (CSDS), which also say that sugar is not toxic, but a slight health-hazard as a respiratory, skin and eye irritant; similarly, fructose.

Even the advice that substantially cutting down on sugar-intake is the most vital preventive step against dental caries is disputed.

The WHO Guidelines categorically say that there is no evidence for a correlation between sugar-intake and diabetes-mellitus, except through obesity.

One prominent very recent systematic-review concluded that current existing guidelines on dietary-sugar do not meet criteria for trustworthy recommendations, and are based on low-quality evidence, and that Public Health Officials and their public audience, should be aware of these limitations.

More studies of an epidemiological-nature, including longitudinal cohort-studies, may be needed. An immediate short cohort-study in Malaysia may be necessary and useful.

This is particularly necessary and not difficult to perform, because sucrose, fructose and glucose occur abundantly in fruits, vegetables and other food of plant origin–and, refined-sugar is no more than crystallized from sucrose in cane-sugar in which it is found in its free-molecular form.

For example, at this website http://dietgrail.com/sugars/, the total sugar-content of 7000 different foods are listed–and, so are the total content of fructose, sucrose, glucose, lactose, galactose and maltose.

Is obesity and over-weightiness more common among vegetarians than non-vegetarians then? And, other similar Research Questions are of concern.

In such short cohort-studies, actual development of disease, or the metabolites characterizing mechanism-based outcomes, could be made the outcome(s) in relation to the exposure.

Also, the proponents of "the case against sugar", sugar and fructose in particular, need to explain why there is a dearth of literature and research on the other sugars, lactose and galactose (which occur abundantly in milk and milk-products) and maltose (which occurs abundantly in many beverages) in relation to the diseases which they discuss in their case. They do not even touch on these sugars in passing in discussing their case. Until then, their case would need to be viewed with skepticism in this light.

In the meantime, Primary Prevention of obesity should mainly focus on the Community Education aspect of Health Promotion. And all, including children, should be taught their daily calorie-requirement by age, sex, weight and activity-level. We should venture into educating the public to count their calories on everything that we eat and drink, and those of their children.

By legislation, places where sugar-sweetened beverages (SSBs) are displayed for sale, should also display the daily calorie-requirement chart by age, weight, sex and activity-level. SSBs should prominently display their sugar and calorie content. Signages must teach that excess calorie-intake leads to obesity, and its consequent diseases.

Restaurants and confectionaries should be required to display the calorie-content of every one of the items on their menu. Similarly, snacks in packets. Parents should weigh their food, and their children's, and estimate the calorie-content before dining.

Only then, will over-weightiness and obesity (and the consequences) be no so prevalent in Malaysia.

The National Plan of Action for Nutrition Malaysia (NPANM) is the framework for action to address food and nutrition challenges in the country. The NPANM series are Malaysia's commitment towards the Rome Declaration on Nutrition arising from the International Conference on Nutrition (ICN 2) held in 1992 and 2014 [125].

The development of the NPANM III, 2016-2025 is spearheaded by the Ministry of Health under the purview of the National Coordinating Committee of Food and Nutrition (NCCFN), with active participation and consensus from all stakeholders in food and nutrition in the country. These include relevant ministries and government agencies, research institutions, academia, professional bodies, non-government organizations including consumer-groups and food-industries [125].

The Plan has identified (46) nutrition-indicators and set targets to be achieved by 2025 under following specific areas; Promoting Maternal, Infant and Young Child Nutrition (10); Promoting Healthy Eating and Active Living (11); Preventing and Controlling Nutritional Deficiencies (9) and Preventing and Controlling Obesity and Diet-related NCDs (16) [125].

To achieve the targets, the Plan has proposed 3 main strategies, namely Foundation Strategy; Enabling Strategies and Facilitating Strategies [125].

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