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Assessment of Total Sugar and Glucose Concentrations in Commonly Consumed Beverages in Japan

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Abstract

The intake of added sugars, such as high-fructose corn syrup and sucrose, has markedly increased in the last hundred years and is closely associated with the increased prevalence of obesity, metabolic syndrome, and type 2 diabetes. We recently reported that the glucose- and fructose-induced generation of glyceraldehyde (GA) caused GA-derived advanced glycation end-products (GA-AGEs), which may be used biomarkers to predict lifestyle-related diseases. Therefore, we assessed total sugar and glucose concentrations in 885 and 298 commonly consumed beverages, respectively, in Japan. Our results revealed that total sugar concentrations were markedly higher in some carbonated drinks, sugar-sweetened fruit drinks, milk beverages, fruit mix juices, milk, cocoa, black tea, fruit juices, and other beverages. Total glucose concentrations were also higher in some carbonated drinks, sugar-sweetened fruit drinks, fruit mix juices, and fruit juices. About 40% of the beverages contained 25 g or more sugar per bottle based on standard serving sizes. This is the upper limit of daily sugar intake, recommended in the guidelines by the American Heart Association and the World Health Organization to prevent health problems in women and adults/ children, respectively. This study has provided potentially useful data on the presence of sugars in commonly consumed beverages.

Keywords: High-Fructose Corn Syrup (HFCS); Sugar-Sweetened Beverages (SSB); Advanced Glycation End-products (AGEs); Glyceraldehyde (GA); Toxic AGEs (TAGE); Metabolic Syndrome (MetS); Lifestyle-related Diseases

Abbreviations: AGEs: Advanced Glycation End-products; AHA: American Heart Association; CML: *N*ε-(Carboxymethyl)lysine; CRF: Chronic Renal Failure; CVD: Cardiovascular Diseases; GA: Glyceraldehyde; GA-AGEs: GA-derived AGEs; GAPDH: G-3-P dehydrogenase; GFCS: Glucose-Fructose Corn Syrup; Glu-AGEs: Glucose-derived AGEs; G-3-P: GA-3-phosphate; HbA1c: Hemoglobin A1c; HFCS: High-Fructose Corn Syrup; HMG-CoA: 3-Hydroxy-3methylglutaryl-CoA; HOMA-IR: Homeostatic Model Assessment of Insulin Resistance; IR: Insulin Resistance; JAS: Japanese Agricultural Standard; MetS: Metabolic Syndrome; NAFLD: Nonalcoholic Fatty Liver Disease; NASH: Nonalcoholic Steatohepatitis; RAGE: Receptor for AGEs; SSB: Sugar-Sweetened Beverages; TAGE: Toxic AGEs; T2D: Type 2 Diabetes; WHO: World Health Organization

Introduction

The combination of two simple sugars, High-Fructose Corn Syrup (HFCS) and sucrose, which are used in many Sugar-Sweetened Beverages (SSB) and commercial products, is commonly consumed worldwide. A growing body of epidemiological and mechanistic evidence argues that excessive sugar consumption affects human health beyond the simple addition of calories [1]. Sugar has been implicated in the development of all diseases associated with Metabolic Syndrome (MetS) [2,3], including hypertension, Cardio Vascular Diseases (CVD), Nonalcoholic Fatty Liver Disease (NAFLD)/Nonalcoholic Steatohepatitis (NASH), Type 2 Diabetes (T2D) and the ageing process, which is promoted by damage to proteins due to the non-enzymatic binding of sugars (socalled glycation) [4-8]. Two major sources of Advanced Glycation Endproducts (AGEs), exogenous and endogenous AGEs, have been identified in humans [4-7]. AGEs are formed by the Maillard reaction, a nonenzymatic reaction between the terminal α-amino group or ε-amino group of the lysine residues of proteins and the aldehyde or ketone groups of reducing sugars, such as glucose, fructose, and glyceraldehyde (GA) [4-7]. We recently demonstrated that interactions between GAderived AGEs (Toxic AGEs, TAGE) and the Receptor for AGEs (RAGE) altered intracellular signaling, gene expression, and the release of proinflammatory molecules and also elicited oxidative stress in numerous types of cells, all of which may contribute to the pathological changes observed in lifestyle-related diseases, such as T2D, diabetic vascular complications, hypertension, Alzheimer's disease, CVD, NAFLD/NASH, and cancer growth and metastasis [8-13].

Two different pathways are responsible for the *in vivo* generation of GA, which is the precursor of TAGE: i) the glycolytic pathway (glycolysis) and ii) the fructose metabolic pathway (fructolysis) [10-14]. In pathway i) the enzyme GA-3-phosphate (G-3-P) dehydrogenase (GAPDH) generally breaks down the glycolytic intermediate G-3-P. However, reductions in GAPDH activity lead to the intracellular accumulation of G-3-P. Therefore, G-3-P starts to be metabolized *via* an alternative pathway, causing increases in the concentration of GA and, as a result, promoting the synthesis of TAGE. Therefore, a positive feedback mechanism is in operation; namely, the inhibition of GAPDH activity by GA promotes the synthesis of TAGE. In pathway ii), an increase in intracellular glucose concentrations under hyperglycemic conditions stimulates the production of fructose *via* the polyol pathway in insulinindependent tissues, such as nerve tissues, the kidneys, the lens of the



eyes, red blood cells, and the brain [15,16]. Fructose is a constituent of HFCS and sucrose, and, hence, is commonly included in the human diet [17,18]. Fructokinase phosphorylates fructose to fructose-1-phosphate, which is then broken down into GA and dihydroxyacetone phosphate by aldolase B [19,20]. The resultant GA is transported (or leaks passively) across the cell membrane. GA induces the synthesis of TAGE in the intracellular and extracellular compartments.

We recently indicated that serum levels of TAGE, but not those of hemoglobin A1c (HbA1c), glucose-derived AGEs (Glu-AGEs), or Nɛ-(carboxymethyl)lysine (CML), a representative AGE compound found in food, may be used as a biomarker to predict the progression of lifestyle-related diseases [21-25]. We also reported an increase in the expression of hepatic RAGE and the enhanced production/ accumulation of TAGE in normal rats administered Glu-AGE-rich beverages [26]. These findings indicated that Glu-AGEs, which are normally contained in beverages and foods [27], and are taken orally into the body, enhance the production/ accumulation of TAGE, leading to TAGE-RAGE interactions. Therefore, the aim of the present study was to assess the concentrations of total sugars and glucose, which was metabolized to GA as a precursor of TAGE in the liver, in commonly consumed beverages in Japan.

Methods

Measurement of total sugar content

Commonly consumed beverages in Japan were purchased from vending machines, convenience stores, or supermarkets in Kanazawa city. We classified beverages according to the Japanese Agricultural Standard (JAS). The contents of total sugars were analyzed in 885 different commercially available beverages using a digital refractometer (ATAGO Palette PR-201 α). The contents of sugar in each beverage were based on the mean value of at least three measurements per sample and expressed as sugar content (g). These beverages were undiluted or diluted 2- to 10-fold (after controlling for dilution) with distilled water. The contents of the total sugars were calculated based on standard serving sizes (65 mL-500 mL/bottle) in beverages.

Measurement of glucose content

Glucose contents were analyzed in 298 different commercially available beverages by the Glucose C II-Test kit Wako (Wako Pure Chemical Industries, Osaka, Japan) after they were undiluted or diluted 2- to 10-fold (after controlling for dilution) with distilled water. The contents of glucose in each beverage were based on the mean value of at least three measurements per sample and expressed as glucose content (g). The contents of total glucose were calculated based on standard serving sizes (65 mL-500 mL/bottle) in beverages.

Results

Total sugar content in common beverages

The average total sugar content in each type of beverage is shown in (Figure 1). The numbers of beverages in each category that contained \geq 50; 25-49.9; 12.5-24.9 and <12.5 g/bottle of total sugars are shown in (Table 1). The amount of total sugars was \geq 25 g/bottle in *ca.* 40% of the beverages examined. These results suggested the excessive consumption of beverages, especially carbonated drinks, sugar-sweetened fruit drinks, milk beverages, fruit mix juices, milk, cocoa, black tea, fruit juices, and other beverages, needs to be avoided because they contain large amounts of sugars. On the other hand, oolong tea and tea had low sugar content. Moreover, products that used an artificial sweetener (such as aspartame, acesulfame potassium, and sucralose), also in carbonated drinks, also had a low sugar content.

Glucose content in common beverages

The average total glucose content in each type of beverage is shown in Figure 2. The numbers of beverages in each category that contained \geq 20; 10-19.9; 5-9.9; and <5 g/bottle of total glucose are shown in Table 2. The amount of glucose was \geq 10 g/bottle in *ca.* 32% of the beverages examined. These results suggested that the excessive consumption of beverages, especially carbonated drinks, sugar-sweetened fruit drinks, fruit mix juices, and fruit juices, needs to be avoided because they contain large amounts of glucose. On the other hand, black coffee, coffee, cocoa, health drinks, and soy milk had low glucose content. Moreover, products that used an artificial sweetener, also in carbonated drink, had low glucose content. Tea and oolong tea did not contain any glucose (data not shown).

Calculation of fructose and sucrose contents in common beverages

Tables 3 and 4 shows the amount of total sugars and free glucose as well as the calculated fructose/sucrose in a typical beverage in Japan, among drinks with total sugars over 50 g/bottle. The highest total sugar and free glucose contents were observed in carbonated drinks with the commercial names shown in Table 3, followed by sugar-sweetened fruit drinks with the commercial names shown in Table 4. The other highest total sugar contents were detected in fruit juices (Max-Min: 61-53 g, 4 kinds), other beverages (60-51 g, 9 kinds), coffee (GEORGIA MAX COFFEE-X, COCA-COLA, 60 g), fruit mix juices (Oishii 100% mix juice, SANGARIA, 57 g; Orange-blend 100%, SANGARIA, 55 g), and lactic acid bacteria beverages (THE PREMIUM CALPIS, CALPIS, 56 g), which were identified as beverages containing more than 50 g/bottle of total sugar. The other highest total glucose contents were detected in other beverages (Calpis water and CALPIS, 21 g/57 g sugar), fruit juices (Minute Maid Asano-kenkou-kazoku Cassis & Grape 100%, COCA-COLA, 20 g/42 g sugar), and fruit mix juices (Vitamin-fruit, Maturegrape, sugar content 12°C, ITOEN, 20 g/45 g sugar), which were identified as beverages containing more than 20 g/bottle of total glucose.

Discussion

The increasing number of patients with T2D in Asian countries including Japan is an important public health problem [28]. One welldocumented change that may contribute to the risk of T2D in Asia and elsewhere is the consumption of SSB [29,30]. The increased consumption of SSB has been observed not only in Western, but also in Asian countries [31], and has been extensively associated with an increased risk of T2D and also with weight gain, obesity, MetS, hypertriglyceridemia, coronary heart disease, and hypertension [32-38]. In the setting of a pandemic of obesity and T2D, the American Heart Association (AHA) has recently released scientific recommendations to reduce added-sugar intake to no more than 100 (for women)-150 (for men) kcal (25-37.5 g sugar)/day for most Americans [39]. A new World Health Organization (WHO) [40] guideline has recommended that adults and children reduce their daily intake of added sugars to less than 10% of their total energy intake (50 g sugar for a 2,000 kcal/day diet). An additional reduction to below 5% of the total energy intake or roughly 25 g sugar/day may provide additional health benefits. This limited is markedly exceeded by today's society [41]. About 40% of the beverages contained 25 g or more sugar per bottle based on standard serving sizes. This is the upper limit of daily sugar intake, recommended in the guidelines by the AHA (2009) and the WHO (2015) to prevent health problems in women and adults/children, respectively (Table 1). A 500-mL bottle of a carbonated drink (Coke, Sprite, or Fanta) contains approximately 50-60 g of added sugars; therefore, the consumption of one bottle equals



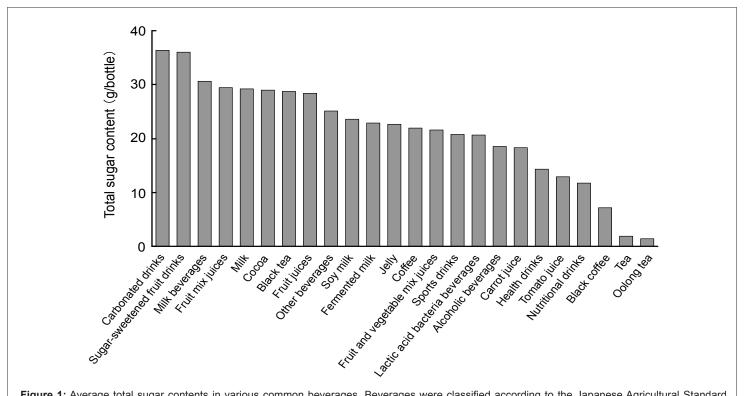


Figure 1: Average total sugar contents in various common beverages. Beverages were classified according to the Japanese Agricultural Standard (JAS). The average total sugar content in each beverage was based on the mean value and expressed as total sugar content (g) per bottle of beverage for a standardized serving size.

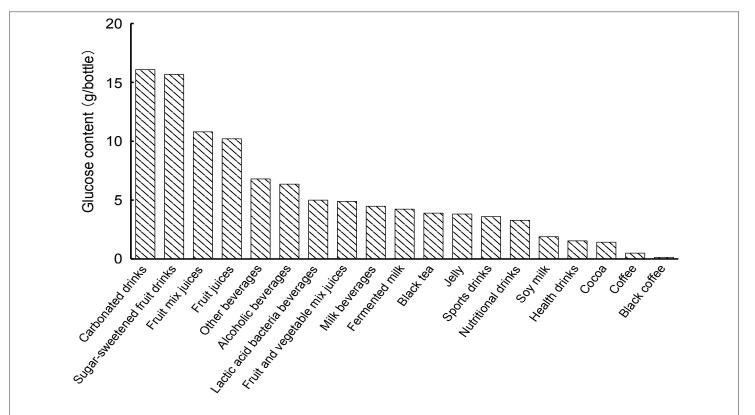


Figure 2: Average glucose contents in various common beverages. The total glucose content in each beverage was based on the mean value and expressed as glucose content (g) per bottle of beverage for a standardized serving size.



| | Average sugar content | | ≥ 50 25-49.9 | | 12.5-24.9 | <12.5 |
|-------------------------------------|-----------------------|-------------|--------------|-------|------------|-------|
| | (g/bottle) | (Min-Max) | | | (g/bottle) | |
| Beverages (660): | ' | | | | | |
| Carbonated drinks (70) | 36.4 | (1.5-65.5) | 25 | 21 | 17 | 7 |
| Oolong tea (7) | 1.4 | (1.0-1.5) | | | | 7 |
| Black tea (24) | 28.7 | (0.9-48.3) | | 15 | 7 | 2 |
| Fruit juices (184): | | | | | | |
| Fruit juices (64) | 28.3 | (9.5-60.5) | 4 | 27 | 32 | 1 |
| Fruit mix juices (27) | 29.5 | (13.5-57.0) | 2 | 10 | 15 | |
| Fruit and vegetable mix juices (28) | 21.6 | (12.1-40.5) | | 5 | 22 | 1 |
| Sugar-sweetened fruit drinks (65) | 36.0 | (5.6-60.5) | 11 | 42 | 9 | 3 |
| Tomato juice (16) | 12.9 | (8.7-15.5) | | | 11 | 5 |
| Carrot juice (5) | 18.2 | (15.4-24.3) | | | 5 | |
| Coffee (65): | | | | | | |
| Black coffee (23) | 7.2 | (2.0-17.8) | | | 2 | 21 |
| Coffee (42) | 21.9 | (12.7-59.5) | 1 | 8 | 33 | |
| Soy milk (22) | 23.6 | (11.2-30.2) | | 6 | 15 | 1 |
| Other beverages (267): | | | | | | |
| Sports drinks (14) | 20.8 | (1.0-33.0) | | 3 | 9 | 2 |
| Health drinks (13) | 14.4 | (3.5-28.5) | | 2 | 5 | 6 |
| Nutritional drinks (35) | 11.7 | (3.1-20.7) | | | 14 | 21 |
| Cocoa (10) | 29.0 | (20.3-35.4) | | 7 | 3 | |
| Jelly (53) | 22.6 | (5.6-49.0) | | 21 | 24 | 8 |
| Tea (36) | 1.9 | (0.7-11.0) | | | | 36 |
| Other beverages (106) | 25.1 | (2.0-59.5) | 9 | 38 | 35 | 24 |
| Milk and Dairy products (90): | 1 | | | | | |
| Milk (11) | 29.2 | (25.0-33.8) | | 11 | | |
| Dairy products (79): | | | | | | 1 |
| Fermented milk (18) | 22.9 | (10.8-44.5) | | 6 | 11 | 1 |
| Milk beverages (35) | 30.6 | (19.8-45.5) | | 30 | 5 | |
| Lactic acid bacteria beverages (26) | 20.6 | (5.4-56.4) | 1 | 8 | 7 | 10 |
| Alcoholic beverages (135) | 18.5 | (2.9-43.8) | | 32 | 59 | 44 |
| | | | (53) | (292) | (340) | (200) |

Table 1: The number of common beverages tested for sugar content (Total 885).

the recommended amount of added sugars for 1 day. Imamura et al. [42] prospectively examined the relationship between consumption of SSB and risk of T2D from 17 cohorts (38,253 cases/10,126,754 person years). They repeated meta-analysis to estimate the relative risk for each 250 mL/day. Higher consumption of SSB was associated with a greater incidence of T2D, by 18% per one serving/day (95% confidence interval 9% to 28%) and 13% (6% to 21%) before and after adjustment for adiposity. Habitual consumption of SSB was associated with a greater incidence of T2D, independently of adiposity. These findings suggested that the continued intake of negligible amounts of SSB increased the risk of T2D. The consumption of SSB has been directly and indirectly linked to an

increased risk of T2D. Extensive and lasting changes in public policies are needed to curb the worldwide obesity and T2D epidemics, and limiting the consumption of SSB may be an important strategy to achieve this.

We herein showed the amount of total sugar and free glucose and calculated fructose plus sucrose in a typical beverage in Japan (Tables 1-4). The amount of glucose was ≥ 10 g/bottle (the amount of glucose that is prescribed during hypoglycemia to diabetic patients in Japan) in ca. 32% of the beverages examined (Table 2). The highest total sugar and free glucose contents were observed in carbonated drinks, followed by sugar-sweetened fruit drinks with the commercial names shown in Tables 3 and 4, among drinks with total sugars over 50 g/bottle. In



| | Average glucose content | | ≥ 20 | 10-19.9 | 5-9.9 | <5 |
|-------------------------------------|-------------------------|------------|------|------------|-------|-------|
| | (g/bottle) | (Min-Max) | | (g/bottle) | | |
| Beverages (232): | | | | | | |
| Carbonated drinks (40) | 16.1 | (0- 4.7) | 19 | 14 | 2 | 5 |
| Black tea (11) | 3.9 | (0-11.0) | | 3 | | 8 |
| Fruit juices (67): | | | | ' | ' | |
| Fruit juices (17) | 10.2 | (4.8-20.3) | 1 | 8 | 7 | 1 |
| Fruit mix juices (15) | 10.8 | (5.0-19.6) | 1 | 8 | 6 | |
| Fruit and vegetable mix juices (8) | 4.9 | (3.1-6.9) | | | 5 | 3 |
| Sugar-sweetened fruit drinks (27) | 15.7 | (0.4-32.8) | 11 | 10 | 4 | 2 |
| Coffee (26): | | | | | | |
| Black coffee (7) | 0.1 | (0.1-0.3) | | | | 7 |
| Coffee (19) | 0.5 | (0.1-2.6) | | | | 19 |
| Soy milk (9) | 1.9 | (0.4-6.9) | | | 2 | 7 |
| Other beverages (79): | | | | | | |
| Sports drinks (11) | 3.6 | (0-10.9) | | 1 | 3 | 7 |
| Health drinks (3) | 1.5 | (0-4.1) | | | | 3 |
| Nutritional drinks (21) | 3.3 | (0-8.1) | | | 7 | 14 |
| Cocoa (5) | 1.4 | (0.3-5.3) | | | | 5 |
| Jelly (13) | 3.8 | (0.5-9.3) | | | 3 | 10 |
| Other beverages (26) | 6.8 | (0.2-20.5) | 1 | 5 | 8 | 12 |
| Milk and Dairy products (31): | | | | | | |
| Dairy products (31): | | | | | | |
| Fermented milk (5) | 4.2 | (0.2-8.8) | | | 3 | 2 |
| Milk beverages (16) | 4.5 | (0.3-12.5) | | 1 | 8 | 7 |
| Lactic acid bacteria beverages (10) | 5.0 | (1.4-9.5) | | 1 | 4 | 5 |
| Alcoholic beverages (35) | 6.4 | (0-15.1) | | 10 | 13 | 12 |
| | | | (33) | (61) | (75) | (129) |

Table 2: The number of common beverages tested for glucose content (Total 298).

these tables, most SSB (especially those containing HFCS) contained more fructose than glucose, while glucose-fructose corn syrup (GFCS) contains more glucose than fructose. Fructose has several metabolic properties that make it more toxic than glucose. It is a potent stimulant of *de novo* lipogenesis, leading to ectopic fat deposition and Insulin Resistance (IR) [43]. It does not stimulate insulin or the subsequent secretion of leptin, thereby failing to induce satiety signals [44,45]. Recent studies showed that the excess consumption of SSB was associated with obesity, a cardio metabolic risk, CVD, and NAFLD [46-49]. SSB have been targeted as one of the primary culprits in the escalating rates of obesity and T2D, and reductions in added sugars have been considered necessary in order to promote cardiovascular health and reduce deaths from cardiovascular causes.

The liver is very sensitive to changes in nutrient delivery and is uniquely suited to metabolize ingested simple sugars, such as fructose and glucose. Fructose and glucose are metabolized to GA, a precursor of TAGE in the liver (Figure 3). The findings of our recent studies revealed that i) the formation of TAGE was enhanced during NASH, and serum and hepatic TAGE levels, but not Glu-AGEs and CML, were significantly higher in patients with NASH than in healthy controls or patients with simple steatosis [50], ii) atorvastatin, a 3-hydroxy-

3-methylglutaryl (HMG)-CoA reductase inhibitor, reduced serum TAGE levels in NASH patients with dyslipidemia [51], iii) the serum level of TAGE, but not CML, was one of the independent correlates in the homeostatic model assessment of IR (HOMA-IR) in non-diabetic subjects [21], iv) TAGE, but not HbA1c or Glu-AGEs, may be used as a biomarker to reflect cumulative postprandial hyperglycemia in T2D patients [22], v) the level of TAGE, but not HbA1c or CML, was independently associated with vascular inflammation, as evaluated by [18F] fluorodeoxyglucose-positron emission tomography (FDG-PET) in outpatients [23], vi) TAGE levels were one of the independent correlates of the decreased cell number and impaired migratory activity of circulating endothelial progenitor cells in apparently healthy subjects [24], and vii) high baseline TAGE levels were associated with plaque progression in an assessment of pitavastatin and atorvastatin in an acute coronary syndrome trial (The JAPAN-ACS Sub-study) in Japan [25]. These findings indicated that the serum level of TAGE, but not HbA1c, CML, or Glu-AGEs, may be used as a biomarker to predict the development and progression of lifestyle-related diseases. SSB need to be taken into consideration for disease prevention, particularly in individuals at high risk of developing lifestyle-related diseases.



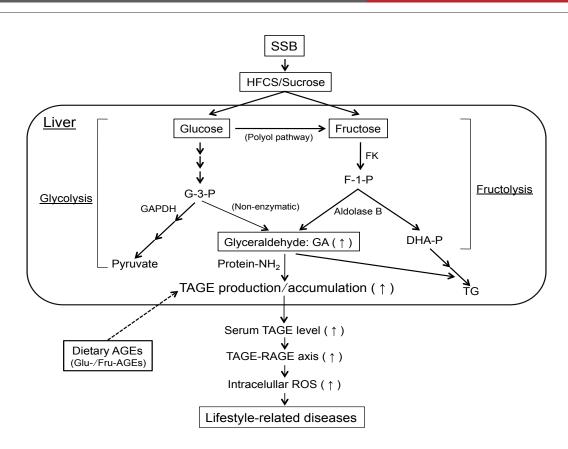


Figure 3: Effects of the commonly consumed dietary sugar metabolite, glyceraldehyde (GA). The chronic ingestion of excessive amounts of SSB (HFCS/sucrose) increases the levels of the sugar metabolite, GA in the liver. GA is known to react non-enzymatically with the amino groups of proteins to form GA-AGEs (TAGE). The interaction between TAGE and RAGE alters intracellular signaling, gene expression and the release of pro-inflammatory molecules and also elicits the generation of ROS in numerous types of cells, all of which may contribute to the pathological changes observed in lifestyle-related diseases [8-13]. Furthermore, the chronic ingestion of excessive dietary AGEs (mainly Glu-/Fru-AGEs) increases the expression of RAGE and the enhanced production/accumulation of TAGE, thereby leading to TAGE-RAGE interactions.

AGEs: Advanced Glycation End-products; DHA-P: Dihydroxyacetone-phosphate; F-1-P: Fructose-1-phosphate; FK: Fructokinase; G-3-P: Glyceraldehyde-3-phosphate; GA: Glyceraldehyde; GA-AGEs: Glyceraldehyde-derived AGEs; GAPDH: Glyceraldehyde-3-phosphate dehydrogenase; HFCS: High-Fructose Corn Syrup; RAGE: Receptor for AGEs; ROS: Reactive Oxygen Species; SSB: Sugar-Sweetened Beverages; TAGE: Toxic AGEs; TG: Triglyceride; Protein-NH2: Free Amino Acids of Proteins.

We previously reported that the hepatic expression of RAGE was elevated in normal rats that had been given a Glu-AGE-rich beverage [26]. In addition, hepatic cells were found to contain TAGE and Glu-AGEs even though the beverage administered to these rats did not contain TAGE. These findings suggest that the synthesis and hepatic accumulation of TAGE are promoted by Glu-AGEs, which are often found in SSB and foods [27], resulting in increased TAGE-RAGE interactions [26,52]. In another study, Kremezin, an oral adsorbent that slows the development of chronic renal failure (CRF) by promoting the removal of uremic toxins, reduced serum Glu-AGE and TAGE concentrations in non-diabetic CRF patients [52]. The chronic ingestion of excessive amounts of SSB, which contained HFCS, sucrose, and dietary AGEs, increased the levels of the sugar metabolite, GA in the liver. GA is known to react non-enzymatically with the amino groups of proteins to form TAGE, enhance the production/accumulation of TAGE, up-regulate RAGE mRNA levels, and increase serum TAGE levels, leading to TAGE-RAGE interactions. The interaction between TAGE and RAGE has been shown to alter intracellular signaling, gene expression and the release of pro-inflammatory molecules and also elicit the generation of reactive oxygen species in numerous types of cells, all of which may contribute to the pathological changes observed in lifestyle-related diseases (Figure 3) [8-13]. The results of the present and previous studies suggest that sugars (glucose, fructose, and sucrose) are present in appreciable levels in common beverages, and exogenous, dietary Glu-AGEs [27] may contribute to the accumulation of TAGE in the body. The contents of HFCS/sucrose and dietary AGEs in beverages/foods need to be taken into consideration for disease prevention, particularly in individuals at high risk of developing lifestyle-related diseases.

Conclusion

We here presented useful information regarding the sugar concentrations of numerous beverages that are commonly consumed in Japan. Much of the sugars consumed today are "hidden" in processed foods that are not regarded as sweets. Added sugars refer to HFCS and sucrose added to drinks and foods by the manufacturer, cook, or consumer, and sugars naturally present in honey, syrups, and fruit juices. Current social and environmental factors have been linked to the purchase and consumption of SSB, including advertising and promotions, increased portion sizes, fast food consumption (at convenience stores, supermarkets (food markets), restaurants, and vending machines), television watching,





| Name | Total sugars | Free glucose | Fructose +Sucrose | Kinds of sugars |
|---|--------------|--------------|----------------------|-----------------|
| | | | | |
| Ambasa Sour-white | 66 | 12 | 54 | sucrose/HFCS |
| Fanta Fruit Punch | 60 | 25 | 35 | HFCS |
| Mountain Dew | 60 | 24 | 36 | HFCS |
| MITSUYA CIDER Muscat | 60 | 24 | 36 | (Muscat)/HFCS |
| Swilling Melon-cream-soda | 59 | 20 | 39 | HFCS/sucrose |
| condensed milk containing MITSUYA CIDER | 58 | 20 | 38 | sucrose/HFCS |
| natchan! Soda Fruity-grape | 58 | 21 | 37 | fructose/HFCS |
| natchan! Soda Sukkiri-orange | 58 | 21 | 37 | fructose/HFCS |
| natchan! Soda Refreshing-orange | 58 | 21 | 37 | fructose/HFCS |
| Fanta Grape | 58 | 23 | 35 | HFCS |
| Fanta Orange | 58 | 22 | 36 | HFCS |
| Skatto-shiroi MITSUYA CIDER | 58 | 16 | 42 | HFCS/sucrose |
| Coca-Cola | 56 | 20 | 36 | HFCS/sucrose |
| Fanta Green-apple | 55 | 23 | 32 | HFCS |
| Fanta Pineapple | 55 | 23 | 32 | HFCS |
| Melon-cream-soda | 55 | 22 | 33 | HFCS/sucrose |
| Small-plum soda | 55 | 23 | 32 | HFCS/sucrose |
| COCA-COLA Refreshing & Uplifting | 55 | 23 | 32 | sucrose/HFCS |
| Fanta Grapefruit | 53 | 22 | 31 | HFCS |
| Sprite | 52 | 22 | 30 | HFCS |
| CALPIS soda | 52 | 17 | 35 | sucrose/HFCS |
| TOPVALU Cider | 52 | 19 | 33 | sucrose/HFCS |
| White-peach-cream-soda | 51 | 18 | 33 | HFCS/sucrose |
| ASAHI MITSUYA CIDER | 50 | 20 | 30 | sucrose/HFCS |
| C.C. Lemon | 50 | 13 | 37 | sucrose/HFCS |

Table 3: List of carbonated drinks containing total sugar, free glucose, and fructose plus sucrose HFCS: High-Fructose Corn Syrup

| Name | Total sugars | Free glucose | Fructose +Sucrose | Kinds of sugars | |
|--------------------------------|--------------|--------------|----------------------|-----------------------|--|
| | | (g/bottle) | | | |
| KOIWAI Pure-apple | 57 | 18 | 39 | HFCS/fructose/sucrose | |
| KOIWAI Pure-green-apple | 57 | 20 | 37 | HFCS/sucrose | |
| KOIWAI Pure-grape | 56 | 20 | 36 | sucrose/HFCS | |
| FUJIYA Nectar Sparkling-peach | 55 | 20 | 35 | sucrose/HFCS | |
| natchan! Peach-party | 55 | 20 | 35 | HFCS/sucrose | |
| TOPVALU Orange | 54 | 20 | 34 | HFCS/fructose | |
| Qoo Tottemo-apple | 54 | 21 | 33 | HFCS | |
| KOIWAI Pure-orange | 53 | 20 | 33 | HFCS | |
| KOIWAI Pure-water-fruit | 53 | 13 | 40 | HFCS/sucrose | |
| Qoo Tottemo-orange | 51 | 20 | 31 | HFCS | |
| natchan! Nomigoro-apple | 50 | 3 | 47 | fructose | |
| Fruit-village grape-blend | 45 | 33 | 12 | GFCS* | |
| Fruit-village peach-blend | 43 | 30 | 13 | GFCS* | |
| Fruit-village grapefruit-blend | 41 | 30 | 11 | GFCS* | |

Table 4: List of sugar-sweetened fruit drinks containing total sugar, free glucose, and fructose plus sucrose

^{*}GFCS: Glucose-Fructose Corn Syrup



permissive parenting practices, parental SSB consumption, sneaking away-from-home meals, and increased access to SSB in the home and school [53]. Thus, free fructose consumption may be mainly responsible for the cardiovascular risk associated with SSB worldwide, and their adverse metabolic effects may also be related to their fructose over glucose fraction [54]. Additional clinical investigations may provide us with more information as to whether the restriction of dietary sugars and Glu-AGEs is beneficial for the prevention and progression of lifestyle-related diseases and may be a novel therapeutic target to prevent these diseases.

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Conflict of interests

The authors declare no potential conflicts of interest.

References

- Joint WHO/FAO Expert Consultation (2003) Diet, nutrition and the prevention of chronic diseases. WHO Technical Report Series 916.
- Lustig RH (2010) Fructose: metabolic, hedonic, and societal parallels with ethanol. J Am Diet Assoc 110: 1307-1321.
- Tappy L, Lê KA, Tran C, Paquot N (2010) Fructose and metabolic diseases: new findings, new questions. Nutrition 26: 1044-1049.
- 4. Bucala R, Cerami A (1992) Advanced glycosylation: chemistry, biology, and implications for diabetes and aging. Adv Pharmacol 23: 1-34.
- Vlassara H, Bucala R, Striker L (1994) Pathogenic effects of advanced glycosylation: biochemical, biologic, and clinical implications for diabetes and aging. Lab Invest 70: 138-151.
- Brownlee M (1995) Advanced protein glycosylation in diabetes and aging. Ann Rev Med 46: 223-234.
- Takeuchi M, Makita Z (2001) Alternative routes for the formation of immunochemically distinct advanced glycation end-products in vivo. Curr Mol Med 1: 305-315.
- 8. Takeuchi M, Yamagishi S (2004) TAGE (toxic AGEs) hypothesis in various chronic diseases. Med Hypotheses 63: 449-452.
- Abe R, Yamagishi S (2008) AGE-RAGE system and carcinogenesis. Curr Pharm Des 14: 940-945.
- Sato T, Iwaki M, Shimogaito N, Wu X, Yamagishi S, et al. (2006) TAGE (toxic AGEs) theory in diabetic complications. Curr Mol Med 6: 351-358.
- Takeuchi M, Yamagishi S (2009) Involvement of toxic AGEs (TAGE) in the pathogenesis of diabetic vascular complications and Alzheimer's disease. J Alzheimers Dis 16: 845-858.
- Takeuchi M, Takino J, Yamagishi S (2010) Involvement of the toxic AGEs (TAGE)-RAGE system in the pathogenesis of diabetic vascular complications: A novel therapeutic strategy. Curr Drug Targets 11: 1468-1482.
- Takeuchi M, Takino J, Sakasai-Sakai A, Takata T, Ueda T, et al. (2014) Involvement of the TAGE-RAGE system in NASH: Novel treatment strategies. World J Hepatol 6: 880-893.
- Takeuchi M, Yamagishi S (2004) Alternative routes for the formation of glyceraldehyde-derived AGEs (TAGE) in vivo. Med Hypotheses 63: 453-455.
- Oates PJ (2002) Polyol pathway and diabetic peripheral neuropathy. Int Rev Neurobiol 50: 325-392.

- Maekawa K, Tanimoto T, Okada S (2002) Gene expression of enzymes comprising the polyol pathway in various rat tissues determined by the competitive RT-PCR method. Jpn J Pharmacol 88: 123-126.
- Schalkwijk CG, Stehouwer CD, van Hinsbergh VW (2004) Fructosemediated non-enzymatic glycation: sweet coupling or bad modification. Diabetes Metab Res Rev 20: 369-382.
- Gaby AR (2005) Adverse effects of dietary fructose. Altern Med Rev 10: 294-306.
- Hallfrisch J (1990) Metabolic effects of dietary fructose. FASEB J 4: 2652-2660.
- Mayes PA (1993) Intermediary metabolism of fructose. Am J Clin Nutr 58: 754S-765S.
- Tahara N, Yamagishi S, Matsui T, Takeuchi M, Nitta Y, et al. (2012) Serum levels of advanced glycation end products (AGEs) are independent correlates of insulin resistance in non-diabetic subjects. Cardiovasc Ther 30: 42-48.
- 22. Tsunosue M, Makiko N, Ohta Y, Matsuo Y, Ueda K, et al. (2010) An α-glucosidase inhibitor, acarbose treatment decreases serum levels of glyceraldehyde-derived advanced glycation end products (AGEs) in patients with type 2 diabetes. Clin Exp Med 10: 139-141.
- Tahara N, Yamagishi S, Takeuchi M, Honda A, Tahara A, et al. (2012) Positive association between serum level of glyceraldehyde-derived advanced glycation end products (AGEs) and vascular inflammation evaluated by 18F-fluorodeoxyglucose positron emission tomography (FDG-PET). Diabetes Care 35: 2618-2625.
- Ueda, S, Yamagishi S, Matsui T, Noda Y, Ueda SI, et al. (2012) Serum levels of advanced glycation end products (AGEs) are inversely associated with the number and migratory activity of circulating endothelial progenitor cells in apparently healthy subjects. Cardiovasc Ther 30: 249-254.
- Fukushima, Y, Daida H, Morimoto T, Kasai T, Miyauchi K, et al. (2013) Relationship between advanced glycation end products and plaque progression in patients with acute coronary syndrome: The JAPAN-ACS Sub-study. Cardiovasc Diabetol 12: 5.
- Sato T, Wu X, Shimogaito N, Takino J, Yamagishi S, et al. (2009) Effects of high-AGE beverage on RAGE and VEGF expressions in the liver and kidneys. Eur J Nutr 48: 6-11.
- Takeuchi M, Takino J, Furuno S, Shirai H, Kawakami M, et al. (2015)
 Assessment of the contents of various advanced glycation end-products in commonly consumed beverages and foods in Japanese culture. PLoS One 10: e0118652.
- 28. Yoon KH, Lee JH, Kim JW, Cho JH, Choi YH, et al. (2006) Epidemic obesity and type 2 diabetes in Asia. Lancet 368: 1681-1688.
- Woodward-lopez G, Kao J, Ritchie L (2010) To what extent have sweetened beverages contributed to the obesity epidemic? Public Health Nutr 14: 499-509.
- Malik VS, Popkin BM, Bray GA, Després JP, Willett WC, et al. (2010) Sugar-sweetened beverages and risk of metabolic syndrome and type 2 diabetes: a meta-analysis. Diabetes Care 33: 2477-2483.
- Basu S, McKee M, Galea G, Stuckler D (2013) Relationship of soft drink consumption to global overweight, obesity, and diabetes: A crossnational analysis of 75 countries. Am J Public Health 103: 2071-2077.
- Hu FB, Malik VS (2010) Sugar-sweetened beverages and risk of obesity and type 2 diabetes: epidemiologic evidence. Physiol Behav 100: 47-54.
- Malik VS, Pan A, Willett WC, Hu FB (2013) Sugar-sweetened beverages and weight gain in children and adults: A systematic review and meta-analysis. Am J Clin Nutr 98: 1084-1102.
- 34. Malik VS, Hu FB (2012) Sweeteners and risk of obesity and type 2



- diabetes: the role of sugar-sweetened beverages. Curr Diab Rep 12: 195-203.
- Dhingra R, Sullivan L, Jacques PF, Wang TJ, Fox CS, et al. (2007) Soft drink consumption and risk of developing cardiometabolic risk factors and the metabolic syndrome in middle-aged adults in the community. Circulation 116: 480-488.
- Nettleton JA, Lutsey PL, Wang Y, Lima JA, Michos ED, et al. (2009) Diet soda intake and risk of incident metabolic syndrome and type 2 diabetes in the Multi-Ethnic Study of Atherosclerosis (MESA). Diabetes Care 32: 688-694.
- Fung TT, Malik V, Rexrode KM, Manson JE, Willett WC, et al. (2009) Sweetened beverage consumption and risk of coronary heart disease in women. Am J Clin Nutr 89: 1037-1042.
- Chen L, Caballero B, Mitchell DC, Loria C, Lin PH, et al. (2010) Reducing consumption of sugar-sweetened beverages is associated with reduced blood pressure: a prospective study among United States adults. Circulation 121: 2398-2406.
- Johnson RK, Appel LJ, Brands M, Howard BV, Lefevre M, et al. (2009)
 Dietary sugars intake and cardiovascular health: a scientific statement from the American Heart Association. Circulation 120: 1011-1020.
- 40. WHO guideline (2015) Sugars intake for adults and children.
- Welsh JA, Sharma AJ, Grellinger L, Vos MB (2011) Consumption of added sugars is decreasing in the United States. Am J Clin Nutr 94: 726-734.
- 42. Imamura F, O'Connor L, Ye Z, Mursu J, Hayashino Y, et al. (2015) Consumption of sugar sweetened beverages, artificially sweetened beverages, and fruit juice and incidence of type 2 diabetes: systematic review, meta-analysis, and estimation of population attributable fraction. BMJ 351: h3576.
- Lustig RH (2013) Fructose: it's "alcohol without the buzz". Adv Nutr 4: 226-235.
- 44. Elliott SS, Keim NL, Stern JS, Teff K, Havel PJ (2002) Fructose, weight gain, and the insulin resistance syndrome. Am J Clin Nutr 76: 911-922.

- Bray GA (2010) Fructose: pure, white, and deadly? Fructose, by any other name, is a health hazard. J Diabetes Sci Technol 4: 1003-1007.
- Te Morenga L, Mallard S, Mann J (2013) Dietary sugars and body weight: systematic review and meta-analyses of randomised controlled trials and cohort studies. BMJ 346: e7492.
- Te Morenga LA, Howatson AJ, Jones RM, Mann J (2014) Dietary sugars and cardiometabolic risk: systematic review and meta-analyses of randomized controlled trials of the effects on blood pressure and lipids. Am J Clin Nutr 100: 65-79.
- 48. Yang Q, Zhang Z, Gregg EW, Flanders WD, Merritt R, et al. (2014) Added sugar intake and cardiovascular diseases mortality among us adults. JAMA Int Med 174: 516-524.
- Vos MB, Lavine JE (2013) Dietary fructose in nonalcoholic fatty liver disease. Hepatology 57: 2525-2531.
- Hyogo H, Yamagishi S, Iwamoto K, Arihiro K, Takeuchi M, et al. (2007) Elevated levels of serum advanced glycation end products in patients with non-alcoholic steatohepatitis. J Gastroenterol Hepatol 22: 1112-1119
- 51. Kimura Y, Hyogo H, Yamagishi S, Takeuchi M, Ishitobi T, et al. (2010) Atorvastatin decreases serum levels of advanced glycation endproducts (AGEs) in nonalcoholic steatohepatitis (NASH) patients with dyslipidemia: clinical usefulness of AGEs as a biomarker for the attenuation of NASH. J Gastroenterol 45: 750-757.
- 52. Ueda S, Yamagishi S, Takeuchi M, Kohno K, Shibata R, et al. (2006) Oral adsorbent AST-120 decreases serum levels of AGEs in patients with chronic renal failure. Mol Med 12: 180-184.
- Haerens L, Craeynest M, Deforche B, Maes L, Cardon G, et al. (2008)
 The contribution of psychosocial and home environmental factors in explaining eating behaviours in adolescents. Eur J Clin Nutr 62: 51-59.
- 54. Stanhope KL, Griffen SC, Bair BR, Swarbrick MM, Keim NL, et al. (2008) Twenty-four-hour endocrine and metabolic profiles following consumption of high-fructose corn syrup-, sucrose-, fructose-, and glucose-sweetened beverages with meals. Am J Clin Nutr 87: 1194-1203.