Glycemic Carbohydrate and Health: Background and Synopsis of the Symposium
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Carbohydrates are global foodstuffs and important energy sources. They also influence many physiologic functions, including brain function and physical performance and are ultimately related to human health. In 1998, ILSI Japan formed a team to conduct research on “The Medical and Nutritional Aspects of Sugars.” The research included studies of several new aspects of the metabolic characteristics and physiologic effects of sugars. This paper presents some highlights of our research, including the background of the project, the metabolic characteristics of sugars, and the effect of sugars on glycemic response, memory, and appetite and food intake in humans, etc.

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Introduction and Background
Carbohydrates are bio-molecules abundantly available in nature. Dietary energy for animals and humans comes primarily from glycemic carbohydrates and fats. Carbohydrate energy comes mainly from starches and sugars, which influence many physiologic and metabolic systems.

Throughout human history, starches have been important main sources of energy in the diet. Prior to the discovery of fire and processing of starchy foods, however, our ancestors probably ingested uncooked raw starches with low digestibility. In 1976, Fukuba and Mori reported the in vivo starch digestibility of several starches. They found that the digestibility of raw corn starch was practically the same as that of cooked starch, but the digestibility of raw potato starch was only 20% of cooked starch because the percentage of remaining raw starch in feces was found to be 80% (Table 1). In broiler chickens the ileal starch digestion rate varied from 33% (potato starch) to 99% (tapioca) in 12 different feeds, and the starch digestion rates of potato starch and legume seeds were lower than those of cereal grains and tapioca.

With the discovery that fire could be used to cook foods, the utility of carbohydrates as an energy source was advanced. Whereas cooking and processing resulted in greater digestibility of starchy foods, however, other aspects of starch and their digestibility have gained interest. The level of glycemia from starch depends on many factors, one of which is the degree of gelatinization, the extent to which water has been able to enter the molecular structure.

Recently resistant starch has attracted interest because of its remarkable influence on the glycemic response to carbohydrate foods. There are three types of resistant starch: type 1 resistant starch is physically enclosed within intact cell structures, type 2 resistant starch is composed of raw starch granules, and type 3 resistant starch is retrograded starch. Furthermore, their physiologic effects are key because these carbohydrates are substrates for intestinal fermentation, which affects various nutritional and physiologic states.

One should also refer to the most important nutritional and/or physiologic functions of carbohydrates. Regulation of blood glucose concentration is essential to maintain the homeostasis of the physiologic state, especially in brain. Many mechanisms function in this regulation. Therefore, research on carbohydrates is fundamental and important for health.

In 1994, ILSI North America organized an expert panel to review all the available literature on dietary sugars and health, and an ILSI workshop entitled “Nutritional and Health Aspects of Sugars” was held in Washington, DC. ILSI Japan translated this journal supplement issue into Japanese. Because there are many myths in Japan about the role of sugar in health, however, we felt that further research on sugar was necessary.

Fortunately, a three-year research grant was provided from 1998 to 2000 by Agriculture & Livestock Industries Corporation of Japan, allowing ILSI Japan to initiate research on the medical and nutritional aspects of sugars. The research program included studies of the effects of sugars on brain function, food intake, stress resistance, the immune system, activity, and muscle.

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function. Studies were conducted as appropriate in experimental animals or humans. The results of many of the research projects were presented in this symposium.

Because 2001 was the 20th anniversary of ILSI Japan, our symposium was originally planned as a report of the results of the research projects supported under this initiative. However, our plans for the symposium became broader in order to put our studies in the context of other knowledge on sugars and glycemic carbohydrates, which is why we held this international symposium entitled “Glycemic Carbohydrate and Health.”

In this paper, I would like to present comments on the results of the research supported by ILSI Japan and share my opinion about this research of sugars.

**Metabolic Characteristics of Sugars**

In Japan, as in many other countries, there are many misunderstandings about the effect of sugars on health. For example, many people believe that the intake of sucrose leads to extreme elevations of blood glucose levels, which cause diabetes and other metabolic problems. These misunderstandings may be overcome by scientific study. In cooperation with Hashizume et al., we determined the glycemic index values of some Japanese foods, including sucrose and rice. White bread was used as the standard of glycemic index (100), as described by Wolever et al. in these proceedings. The results of our studies have revealed some interesting facts. The blood-glucose response curve of white bread shows an identical curve for Canadian and Japanese populations. We also confirmed that the sensitivity of sucrose ingestion to insulin was lower than that of the staple food items. We still need more analysis of Japanese foods and the glycemic values of these complex foodstuffs.

**Effect of Sucrose on the Central Nervous System**

Sucrose is a sweet and very palatable source of energy. Mechanisms for the sensations of sweetness and palatability were investigated by Yamamoto. In these studies, the levels of the endogenous opioid, \( \beta \)-endorphin, in both the cerebrospinal fluid and plasma of Wistar rats were measured after free access to either drinking water or sweet solutions. The \( \beta \)-endorphins were higher in the cerebrospinal fluid after the intake of sucrose and saccharin compared with water. Sucrose is more efficient in establishing conditioned taste preference because of its postingestive caloric effects.

Many reports show an irreversible decline in taste and smell acuity with aging. Interestingly, it was suggested that the decline in the senses of taste and smell may result in the decline of the immune functions. The effect of activity-stress in animal models was first described by Hall and Hanford in 1954. The original...
methodology provided rats with access to running wheels all day and they were fed for only 1 to 2 hours per day. Activity-stressed rats reduce food consumption, lose body weight, increase wheel running, and die within 3 to 12 days. The animals also develop severe gastric ulcers and exhibit abnormal behavior, such as anorexia nervosa and compulsive behavior similar to that observed in humans.

Using this methodology, we investigated the effects of glucose on activity-stress. In these experiments, the extended duration of stressful conditions induced hypertrophy of the adrenals, atrophy of the thymus and spleen, increased ulcer index, decreased blood glucose, decreased rectal temperature, and increased anxiety. On the other hand, rats fed ad libitum 0.25, 0.5, or 1 M glucose solutions showed dose-dependent reversal of the stress responses. Our findings suggest that the decrease in plasma glucose concentration is one of the important factors determining the behavioral and physical stress responses induced by the activity-stress paradigm.

Recent reports stated that heat-shock proteins might be involved in the defense against stress. We therefore determined heat-shock protein mRNA levels in the hypothalamus, cerebellum, and cerebral cortex after restraint stress in sucrose diet–fed rats. The results suggested that sucrose facilitates the gene expression of heat-shock protein 27 (in cerebral cortex and cerebellum) and heat-shock protein 70 (cerebral cortex, hypothalamus, and cerebellum) in brain after restricted stress, which may attenuate stress.

Effects of Sucrose on Appetite, Mood, and Memory

In humans, the brain is the most metabolically active organ in the body, accounting for approximately 20% of the basal metabolic rate and a mere 2% of body weight. Unlike other organs in the body, the brain uses glucose almost exclusively as its source of energy. The energy reserves in the brain are extremely small, and the brain requires a continuous glucose supply. Without replenishment, the glucose reserves in the brain will be used up in approximately ten minutes.

Dietary carbohydrates are important regulators of the nervous system and positively affect several human behaviors, including appetite, mood, and memory. The effects of carbohydrates on the mechanisms controlling food intake and satiety in humans are poorly understood.

Carbohydrate food ingestion leads to decreased appetite, but no systematic investigation has been undertaken to determine the effect of size and timing of preload of different forms of carbohydrates on subsequent food intake. For this reason, ILSI Japan supported studies of the effect of size and timing of sucrose preload on subjective appetite, food intake, mood, and memory in young healthy males. The findings indicated that sucrose suppresses appetite and food intake in a dose-dependent manner. In these studies, the effects of sucrose were compared with those of other carbohydrates and to safflower oil; results revealed that sucrose is more effective than lower glycemic carbohydrates and safflower oil.

Studies of the effect of sugars on memory were also supported. Benton et al. gave 21-year-old women drinks containing 0, 10, 30, 50, or 70 g of glucose after one overnight fast to investigate the role of different doses on the improvement in memory and other aspects of cognition. The appropriate dose of sugars, a drink containing 10 g of glucose, showed good effects on the memory of subjects who had low blood glucose levels in the morning. Those who had low baseline blood glucose had better memories if their blood glucose levels increased rapidly after a drink, irrespective of the amount of glucose it contained. It was concluded that individual differences in control blood glucose levels influence the effect that a glucose-containing drink has on memory.

The Effect of Sucrose on Physical Performance

The timing of food intake in relation to activity is an important factor affecting physical performance. Feeding sucrose with amino acids to rats immediately after exercise enhanced muscle protein synthesis, compared with feeding a few hours after exercise. Insulin response was found to be important in these effects.

Sucrose and amino acids fed immediately after exercise resulted in higher gastrocnemius and quadriceps muscle mass (% of BW), higher bone mineral density and greater strength in lumbar vertebra than when fructose was given with the amino acids.

The Effect of Sugars on Immune System Response

Adaptation to stress includes atrophy of the thymus, increased stomach and duodenal ulcers, and hypertrophy of adrenals. The thymus is an important organ in the immune system response. Atrophy of the thymus influences immune activity thought to influence infectious disease, allergy, autoimmune disease, and cancer because the immune responses regulate the resistance to these complaints. Because we showed that glucose moderated the stress-induced damages, we investigated the effect of sugar intake on the immune system response under stress (Sato M, Nishimura T, Kimura S, 1999, unpublished data).

There are two types of T cell subsets, T helper 1 (Th1) and T helper 2 (Th2), and the balance of these cells (Th1/Th2 balance) plays an important role in immunoregulation. Sugar consumption by rats reduced the influence of restraint stress on immune activity.

Conclusion

Research supported by ILSI Japan has led to several new investigations and knowledge of the effect of sugars and glycemic carbohydrate on physiologic and metabolic
systems in rats and on memory and food intake in humans. Also included in this symposium were presentations by several researchers not supported by ILSI Japan. They presented reviews of the current status and application of the glycemic index, the determinants of body weight and the role of sugars, the effect of ethnicity on the relationship between body mass index and risk of chronic disease, and the effect of sugars and other foods on memory of older persons. As a result, discussions at the symposium covered a broad range of the current knowledge of the effects of sugars and glycemic carbohydrate on body systems and on health. Through publication of the presentations, the goal of ILSI Japan is to have a permanent record of its 20th anniversary.


