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Fructose, High Fructose Corn Syrup, Sucrose and Health

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*To my beautiful wife, Stephanie Hart Rippe,
and our wonderful children Hart, Jaelin, Devon,
and Jamie.*

Foreword

Sugar, Sugar-Sweetened Beverages, and Obesity: Separating Supposition from Demonstrated Fact, from Misinformation

The word *science* derives from the Latin *scientia*, meaning “to have knowledge.” So science is about knowing. As stated in a maxim often attributed to the French mathematician Henri Poincaré, “Science is built up with facts, as a house is with stones. But a collection of facts is no more a science than a heap of stones is a house” [1] (p. 127). Therefore, science is not merely about the accumulation of facts we know, it is about how we come to know these facts. What distinguishes knowing in science from knowing (or belief) in other domains is that the confidence in one’s knowledge derives not from the strength of one’s convictions but from the strength of one’s evidence. In the fields of biology, medicine, and behavioral science, we generally do not have strong enough theories to derive our evidence mathematically through deductive reasoning and must instead depend on empirical evidence. Thus, almost all of our knowledge is dependent on empirical data. For this reason, the integrity of the generation and communication of collected data must be sacrosanct.

But scientists are humans first and susceptible to the passions of any human. Many scientists in the realms of nutrition, medicine, and public health feel a passion for their duty to beneficence and see a key role for the profession as protecting the public from harm—noble passions in any accounting. In their passion, some scientists come to view themselves as being at war with the presumed enemies of health, which then drives them to rally the troops. We have all heard of the “war on drugs” [2], the “war on tobacco” [3], and the “war on drunk driving” [4]. Now, many are using similar language to describe a war on obesity [5]. We are told that obesity is a “public health threat” [6] and a “crisis” [7, 8]. Obesity is indeed a serious and prevalent problem, and we do need to prioritize finding ways to reduce obesity and the suffering it creates. But the war and crisis mentalities may have a downside. As Aeschylus is said to have told us, “the first casualty of war is truth,” and just as in war where demonizing and dehumanizing the enemy may lead to atrocities, there is a concern that the war metaphor in obesity, while mobilizing, may have the result of demonizing certain industries, persons, and foods and consequently lead to oversimplifying messages, relying on ad hominem reasoning, and distorting information [9].

Now, a growing number of authors [10–19] are pointing out that the fever pitch reached about certain obesity issues, especially sugar-sweetened beverages and sugar in general, appears to be leading to exaggerations and distortions of the evidence base and dialogue around these issues in the scientific and public health literature. In that light, the authors of the current book deserve praise for stepping forward in an attempt to offer a reasoned and balanced view of the health consequences of sugar in general, of specific sugars (e.g., fructose), and of sugars in specific forms (e.g., sugar-sweetened beverages).

The story of sugar’s health effects is complex. Today, sugar is demonized by many [20], whereas at some points in history, it was viewed as an elixir of good health [21]. Today, we are often told that it will promote weight gain because sugar consumption, especially in liquid form, will not be sufficiently compensated for by lesser subsequent energy intake. Ironically, in 1942, when national

sentiment in the United States was also against sugar, perhaps in part due to the desire to ration it for the war effort, the *Science News-Letter* stated, “Sugar rationing certainly will harm no one. *People will meet the restriction on sugar by adding calories from other sources* [emphasis added]” [22]. The opinion offered in this 1942 quotation stands in stark opposition to the modern statements about individuals being incapable of reducing their caloric intake to compensate for calories consumed as sugar or sugar-sweetened beverages. Another publication from that era [23] addressed concerns that the addition of cocoa to milk (i.e., chocolate milk), which provided additional calories in liquid form, led to *less* weight gain for the same energy consumed than did milk without the addition of chocolate. Similarly, *Science* published a paper showing that rats could indeed grow adequately on a diet composed only of chocolate milk and gained no less (and no more) weight on such a diet than did control rats fed non-chocolate milk [24]. In 1980, scientists again studying rats wrote, “Rats decrease total caloric intake, sometimes to the point of starvation, when sugar solutions are offered in conjunction with a daily pellet meal. This phenomenon appears to be based on a tendency to behave as if overestimating the caloric value of simple sugars” [25]. The researchers further showed that this *overcompensation* for sugar-sweetened beverages in rats was relatively impervious to elimination, in other words, the complete opposite of today’s belief that sugar-sweetened beverages are not compensated for. Research today is exploring why simply tasting sugar (even if one does not swallow it) leads to benefits in terms of cognitive, social, and athletic performance [26].

Now, let us not be Pollyannaish about sugar. Sugar consumption is not necessary for human life. It does have metabolizable energy, and many in our modern societies could do well with less energy intake. So, most people in most situations are unlikely to experience much if any harm by decreasing their sugar intake. Furthermore, it would be wise that those struggling to control their weight and who consume a great deal of sugar try decreasing their sugar intake (just as it would be wise for them to decrease their intake of any nonessential foods). Sugar consumption may also have deleterious effects on health other than as a source of unneeded calories for many people. Though dental caries is perhaps the most commonly cited ill effect of sugar, speculation abounds that sugar is addicting [27], a gateway drug to violence [28], a cause of hyperactivity [29], and a cause of diabetes [30]; that sugar reduces fertility, evolutionary fitness, and life-span [31]; and that sugar promotes cognitive decline [32]. For each of these effects, there is (or at least at one point was) a legitimate basis for speculation. But a basis for speculation is not a basis for conclusion.

As you read the reasoned reviews of evidence compiled in this book, you may wonder why the authors’ conclusions seem so tempered and circumspect compared to more dramatic statements in the literature. There are many factors involved, and these have been discussed elsewhere. In brief, we believe that, perhaps because of the zeal to achieve public health benefits and the mentality of war described above, the evidence has been distorted and exaggerated. We delineate some of these distortions and exaggerations, cite examples, and quantify evidence elsewhere [10, 11]. In brief, some of the distorting factors include the following:

- Investigators describing studies demonstrating associations as having demonstrated causation [11, 33].
- Press releases that markedly distort the evidence in studies [10, 11].
- Statements in abstracts that do not accord with the results in the same papers [11].
- Incorrect citations of past studies in ways that exaggerate their findings [10].
- Publication bias in which studies with supportive results seem more likely to be published than are those with negative results [10].
- Mathematically unverifiable statements in public health media advertisements [11, 34].
- Revision of the primary outcomes of a study when a significant result is not obtained with the original primary outcome [11].

As scientists, we can rely on only data and logic as a basis for our conclusions. Doing otherwise vitiates any claims we may have to knowledge as scientists in a way that is distinct from intuition, superstition, tradition, ad hominem arguments, appeals to authority, and other nonscientific ways of

coming to beliefs. In understanding the effects of sugars and sugar-sweetened beverages on health, the scientific community seems to have occasionally lost its compass, but fortunately the trend may be reversing. The current book offers a thoughtful guide to the challenging and complex evidence about sugar's effects on health. Readers will hopefully bring the combination of open-mindedness and skepticism that this discussion, and all scientific discussions, is due. And as individual scientists working in this domain, it is paramount to recognize that with academic freedom comes the responsibility to exercise this freedom with integrity when communicating the knowledge we obtain from our results. As has been wisely stated, both the buck and the "spin" must stop with us [35].

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Preface

The metabolic and health effects of both nutritive and non-nutritive sweeteners are controversial and subjects of intense scientific debate. These potential effects span not only important scientific questions but are also of great interest to the media, the public, and potentially even regulatory bodies.

Over the past 30 years, the amount of sweeteners consumed in the United States and worldwide has increased along with other major sources of calories in the diet including added fats, flour, and cereal products. Recent epidemiologic studies have suggested possible associations between the consumption of sugar-sweetened beverages (SSBs) and an increased risk of obesity, heart disease, hypertension, and possible inflammatory responses and a decrease in dietary quality—although other studies have disputed these findings resulting in an ongoing, intense scientific debate. Furthermore, it is clear that epidemiologic studies do not establish cause and effect. Randomized clinical trials have provided conflicting evidence on these issues. The American Heart Association has recommended limiting consumption of added sugars to no more than 150 kcal/day for the average adult man and 100 kcal/day for the average adult woman, recommendations that are different and much more restrictive than those of the Institute of Medicine and Dietary Guidelines for Americans, 2010.

Non-nutritive sweetened beverages have recently been associated with increased risk of high blood pressure, heart disease, and preeclampsia. The effects of non-nutritive sweeteners on appetite and food consumption remain controversial. The physiologic and neurologic responses to “sweetness” per se remain areas of intense scientific inquiry.

Several investigators have asserted that both added sugars and non-nutritive sweeteners may be addictive, leading to overconsumption of calories, citing both human and animal data. Other researchers strongly dispute the assertion that sugars are addictive, citing other studies that provide contradictory evidence and the failure of consuming sugar to meet medical criteria for the diagnosis of addiction. Several recent papers have utilized functional MRI (fMRI) findings to suggest that sweeteners may stimulate reward pathways in the brain; other fMRI studies have not supported these findings. More papers are anticipated in this emerging area in the next few years.

Interest in sweeteners has extended far beyond the scientific community. For example, some schools have eliminated chocolate milk from their lunch menus because of a concern over added sugar. Mayor Bloomberg from New York City proposed the prohibition of certain sizes of SSBs from restaurants regulated by the Department of Public Health in New York City based on his belief that this would be a meaningful approach to obesity prevention. The state Supreme Court of New York struck down this proposed ban. Several prominent scientists have suggested increased taxation or other regulatory measures to limit consumption of SSBs. All of these findings and recommendations have been disputed by other scientists and organizations.

With all the interest in sweeteners, what is the current state of science in this area? When are we acting on insufficient knowledge, political correctness, or emotion rather than scientific evidence?

The goal of this book is to provide an evidence-based reference for nutrition professionals, other health care workers, and other interested individuals based on current scientific understandings on the interaction between both nutritive and non-nutritive sweeteners and health.

It has been my pleasure to serve as the editor of this volume. In this effort I have been honored to be joined by an internationally prominent group of scientists and investigators in diverse areas related to sugars and health. What has emerged is an evidence-based, comprehensive textbook covering multiple issues related to sugars and their putative health effects.

As with any editorial project, some decisions had to be made from the onset. While there are numerous sweeteners, we made the decision to focus on the ones that were most prominent in the debate about sugars and health; therefore, we have focused our efforts almost entirely on fructose, high fructose corn syrup, and sucrose. Since non-nutritive sweeteners have also been prominent in scientific debates and public discussions, we also included a chapter on non-nutritive sweeteners.

The book consists of 21 chapters divided into five sections. The first section contains overviews related to such topics as a general discussion of sweeteners and health and a historical perspective on the manufacture, composition, and applications of these three sugars. Also discussed are the metabolism of nutritive sweeteners in humans, current understandings of solid versus liquid calories, and a separate chapter on non-nutritive sweeteners.

The second section moves on from these general considerations to issues related to global perspectives on sweeteners. The section starts with a chapter on most recent trends of worldwide consumption of sweeteners. The following chapter explores evidence from prospective cohort studies and controlled trials. The third chapter examines public policy issues related to fructose-containing sugars, while the fourth chapter provides an industry perspective focusing specifically on high fructose corn syrup.

The third section delves into functional effects of fructose, high fructose corn syrup, and sucrose. This section includes a chapter on sweeteners and dietary quality as well as a chapter on energy regulating hormones and sweeteners. The ensuing chapter on sweeteners and the brain highlights emerging science in this area. The section concludes with a chapter on the important topic of whether or not sugars are addictive.

The fourth section summarizes issues related to sweeteners in healthy populations. The opening chapter of this section elucidates the health effects of sweeteners in children and adolescents. The second chapter provides a case study exploring flavored milk and dietary quality. The section concludes with chapters on sugar-sweetened beverages and hydration and one on sugars, sports drinks, and performance.

The final section explores issues related to sweeteners in chronic disease and includes chapters on diabetes, nonalcoholic fatty liver disease, fruit juice and childhood obesity, and sugars and cardiovascular disease.

I challenged every chapter author to deliver state-of-the-art science based on objective evidence to provide information that would be useful to not only nutrition professionals and other health care practitioners but also public policy experts, the media, and the public at large. All chapter authors have risen admirably to this challenge.

Editing an academic textbook is the ultimate exercise in collaboration. I am grateful to all of the chapter authors who have done a magnificent job in sorting through an enormous body of scientific literature to provide expert scientific summaries of key topics in an emotional area where considerable misinformation exists.

In addition to my scientific colleagues, I also want to acknowledge the expert editorial work of my Editorial Director, Beth Grady, who has helped coordinate the entire process and keep this project moving forward. My Executive Assistant, Carol Moreau, deftly handles my complex schedule to free time for such large editorial projects. My editor at Springer Publishing, Amanda Quinn, was an early and strong supporter of this project. Our Series Editor, Dr. Adrienne Bendich, also strongly endorsed this effort and has made numerous, helpful suggestions concerning its organization. Our Development

Editor, Kevin Wright, has done an excellent work in coordinating all aspects of the publication process. To these individuals, I am grateful. If credit is due for this book it rests with the chapter authors and all of the other individuals I have mentioned.

As always, my family including my loving wife Stephanie and our four great daughters Hart, Jaelin, Devon, and Jamie provide the love and support which makes it all worthwhile. I hope that that which has emerged is a useful, authoritative book that will help advance a sound, scientific discussion of fructose, high fructose corn syrup, sucrose, and health.

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Series Editor Page

The great success of the Nutrition and Health Series is the result of the consistent overriding mission of providing health professionals with texts that are essential because each includes (1) a synthesis of the state of the science; (2) timely, in-depth reviews by the leading researchers in their respective fields; (3) extensive, up-to-date fully annotated reference lists; (4) a detailed index; (5) relevant tables and figures; (6) identification of paradigm shifts and the consequences; (7) virtually no overlap of information between chapters, but targeted, interchapter referrals; (8) suggestions of areas for future research; and (9) balanced, data-driven answers to patients' as well as health professionals' questions which are based upon the totality of evidence rather than the findings of any single study.

The Series volumes are not the outcome of a symposium. Rather, each editor has the potential to examine a chosen area with a broad perspective, both in subject matter as well as in the choice of chapter authors. The editor(s), whose training(s) is (are) both research and practice oriented, has the opportunity to develop a primary objective for his or her book, define the scope and focus, and then invite the leading authorities to be part of his or her initiative. The authors are encouraged to provide an overview of the field, discuss their own research, and relate the research findings to potential human health consequences. Because each book is developed *de novo*, the chapters are coordinated so that the resulting volume imparts greater knowledge than the sum of the information contained in the individual chapters.

“Fructose, High Fructose Corn Syrup, Sucrose and Health” edited by James M. Rippe, MD, clearly exemplifies the goals of the Nutrition and Health Series. The major driver of this unique and timely volume is to provide the reader with an objective, data-driven summary of the current scientific understanding of the relationships, both biochemical as well as physiological and pathological, between three sugars found in the diet (fructose, high fructose corn syrup (HFCS), and sucrose) as well as non-nutritive sweeteners and health outcomes. As we are all aware, there has been intensive media interest in the obesity epidemic and numerous stories in the lay press as well as commentary in scientific publications have linked the increased risk of obesity with the increased consumption of these sweeteners. Thus, it is of great value to the scientific community, health practitioners, and graduate and medical students to now have a volume that examines the totality of the evidence and also suggests avenues where future clinical studies can provide more definitive answers to questions concerning the roles of sweeteners in human health.

“Fructose, High Fructose Corn Syrup, Sucrose and Health” represents the most comprehensive compilation of recent data on the critical drivers of caloric intakes in children and adults from foods containing these sweeteners. Consumption is compared with the potential consequences to the heart, kidneys, brain, and overall body weight, strength, and endurance. The expertise of the volume's editor, Dr. James M. Rippe, MD, and his in-depth knowledge and widely acknowledged expertise in this field help the reader to understand the value of sweeteners in our daily diets. Dr. Rippe, MD, is board certified both in Internal Medicine and its subspecialty of Cardiology, is Founder and Director of the

Rippe Lifestyle Institute, serves as Editor in Chief in American Journal of Lifestyle Medicine, is Professor of Biomedical Sciences at the University of Central Florida, and serves on the Scientific Advisory Board of WebMD. Dr. Rippe has authored more than 100 peer-reviewed scientific journal articles and over 250 medically related abstracts and has written over 40 books for health professionals and knowledgeable consumers. His excellent communication skills have been acknowledged by his peers, and he has made numerous appearances on television and radio programs that discussed dieting, exercise, and nutritional requirements for optimal health.

The volume contains a most relevant Foreword written by Drs. Mark B. Cope, Mallory Koenings and Dr. David B. Allison, three of the leading researchers in the field of obesity and its consequences who state: “The current book offers a thoughtful guide to the challenging and complex evidence about sugar’s effects on health.” This 21-chapter volume is organized into five sections including five chapters within the Overviews section; four chapters in the section on Global Perspectives; four chapters on Functional Effects; five chapters on the role of Sweeteners in Healthy Populations; and a final Section V that includes three chapters that review the effects of sweeteners in populations with chronic metabolic diseases. There is also a comprehensive Appendix that includes relevant recent journal articles, conferences, and symposia. Also included is a collection of scientific statements concerning sugars and health from leading scientific and medical organizations. Relevant websites and videos are also listed.

The overview section begins with a chapter that places the data within the volume in perspective with regard to the important consistent findings and provides a comprehensive list of over 100 critical references. The second chapter reviews the history, manufacture, composition, applications, and consumption of the primary fructose-based sweeteners: sucrose and HFCS. It is pointed out to the reader that HFCS contains 55 % fructose and 45 % glucose which does not differ greatly from sucrose that contains 50 % fructose and 50 % glucose. The author explains that sugar is derived from sugarcane or sugar beets and is produced in 123 countries and is still used at ten times the level of high fructose syrups worldwide. The excellent historical timeline reminds us that HFCS was only developed in the 1900s. The historic perspective of the development and commercialization of HFCS documents its use in carbonated beverages by the major manufacturers beginning in the mid-1980s. With regard to manufacturing, sugar and HFCS/crystalline fructose manufacturing processes are similar. The author uses both excellent tables and figures to compare the chemical composition of sugar from sugarcane and beet sugar with HFCS from corn following digestion and states that sucrose and HFCS deliver the same sugars (free glucose and free fructose) in similar ratios to the same tissues within the same time frame to the same metabolic pathways. The physical differences between the sweeteners are described, and their uses in food manufacture, in addition to adding sweetness, are reviewed.

Chapter 3 describes the metabolism of nutritive sweeteners with a special emphasis on the differences between glucose and fructose digestion and metabolism post-absorption. The enzymes, glucose transporters, and organs involved in these processes are reviewed in detail, and it indicates that these differences can affect human energy utilization and storage. There is a discussion of the metabolism of fructose when given intravenously as well as a review of the genetic condition whereby fructose cannot be metabolized. The unique chapter on the behavioral and metabolic responses to the intake of solid versus liquid calories adds yet another perspective on the potential role of HFCS in the increased risk of obesity. The chapter contains reviews of the epidemiological data, short-term appetite and feeding studies, randomized controlled trials, and mechanistic findings that strongly suggest that energy-yielding beverage consumption, currently containing either HFCS or sucrose, may be directly related to the risk of weight gain. The last chapter in the overview section examines the role of non-nutritive sweeteners and their potential impact on the obesity epidemic. The author reviews the biological responses to non-nutritive sweeteners compared to caloric sweeteners and discusses the metabolism of the six non-nutritive sweeteners currently approved for use in the United States: acesulfame-K, aspartame, neotame, saccharin, sucralose, and stevia glycosides. The review of the epidemiological survey as well as intervention study data in both children and adults suggests that non-nutritive sweeteners are not consistently associated with increased risk of weight gain and/or

obesity and decreased loss of weight during dieting nor increases in weight regain following dieting. The chapter includes over 100 references and important figures.

The second section of the volume examines the global consumption of sweeteners and their impact on diets and health. Chapter 6 provides an overview of dietary intake of sweeteners and their consumption in the United States and worldwide. We learn that currently the US consumes more sweeteners than any other country in the world although consumption appears to be decreasing. The authors point out the methodologies used to estimate intakes and the differences between nations in assessing and calculating intakes. There appears to be a small increase in fructose intake as % of daily calories from the 1980s to present. The detailed discussion of the difficulties in determining the intake of added sugars versus naturally occurring sugars and the inability of differentiating these with biochemical assays attests further to accurate assessments. However, the 14 tables and figures included in the chapter provide important information concerning current intakes in adults, children, and teens, and data from a number of European countries are also included. The next chapter carefully examines the data from prospective cohort studies and controlled intake studies to help clarify the role of fructose and sweetener intake and health risks. Prospective cohort studies have failed to show a consistent relationship between total fructose-containing sugars in the diet and body weight and incidence of metabolic diseases including diabetes, hypertension, or coronary heart disease. There does appear to be a direct relationship between fructose intake and incidence of gout. A meta-analysis of 30+ studies has reported a significant association between sugary beverages and risk of overweight/obesity in children and weight gain in adults. With regard to the controlled clinical trials, several meta-analyses have consistently reported a lack of effect of either added sucrose or added HFCS in isocaloric exchange with other carbohydrates on cardiovascular indicators, insulin responses, and other related biomarkers. In contrast with the results of these data, intervention studies in which individuals were supplemented with baseline diets with excess energy from sucrose or HFCS-sweetened beverages compared to individuals consuming only the baseline diet showed that the supplemented group had the expected significant weight gain over short term as well as studies lasting 24 months.

The next insightful chapter reviews and tabulates the global recommendations from government and national health organizations with regard to consumption of added sugars and sugar-sweetened beverages (SSBs). Although the scientific data that form the bases of the recommendations is equivalent between nations, there are wide variations in the scope and intent of the public health responses including a tax on SSBs and the banning of their sale in schools and other public places; these are discussed. The last chapter in this section examines the development of HFCS as a sweetener from historic and industry perspectives. We learn that this sweetener is known as HFCS in the United States, isoglucose in Europe, and dextrose/fructose and fructose/dextrose syrup in other parts of the world. We are reminded that in the 1970s HFCS was initially used in food industries such as canning, jam, and jelly manufacture, condiments, and baking not only for its sweetness but also for its promotion of browning of baked goods, various texture components, and mouthfeel. The corn refining industry was able to compete with cane and beet sugar. However, as HFCS was not used commercially in the major soft drink beverages until the mid-1980s when sucrose was also at high demand, it is difficult to explain the association of HFCS alone with the rise in obesity rates. The US regulations on sugars are described in detail.

The third section contains four chapters that examine the effects of sweeteners on the quality of the overall diet and their effects on energy regulating hormones and brain function and ends with a novel chapter that provides some clarity to the question of whether sugars are addictive. Chapter 10 describes the techniques used to measure diet quality, includes informative tables and figures, and examines how sweeteners may affect diet quality in both children and adults. The chapter reviews the critical lifestyle factors as well as relevant foods that have significant impacts on the quality of the diet including socioeconomic status and consumption of sweetened beverages especially in children. The next chapter reviews the data linking the effects of sucrose, glucose, HFCS, and pure fructose on the signaling of the synthesis and release of insulin, leptin, ghrelin, and other regulatory

hormones and peptides and describes how these affect energy homeostasis. The roles of these hormones in obesity are explained in detail, and the author points out areas where further research is needed. The chapter includes over 100 up-to-date references and valuable figures. Well-controlled clinical trials using relevant concentrations of sugars in balanced diets as well as hypocaloric diets have shown no differences between HFCS and sucrose on weight maintenance, weight loss or lipid profiles, risk of type 2 diabetes or metabolic syndrome, and risk of hypertension. The chapter on the interactions between dietary intakes of sources of glucose and the function of the brain is of great interest. There is a detailed discussion of the brain–endocrine pancreatic axis that maintains the constant and optimal level of glucose in the brain. The neurological and hormonal interplays within the brain that monitor glucose concentrations and communication with the gastrointestinal system are reviewed, and areas for future research are noted. Taste and flavor perceptions and the measurement of brain activities are included. The links between sweetness and reward messages in the brain are described in detail. Yet, the authors wisely remind us that the integration of neuroscience and sweetener intake is still at an early stage of research. The final chapter in this section explores the question of whether sugars are addictive and includes over 100 relevant references. The authors provide the details of the medical bases for the term addiction and indicate that currently there are no compelling data to suggest that dietary sugars fulfill these definitions. There is also a lengthy discussion of the Yale Food Addiction Scale, which is similar to the overall substance addiction scales, and its inconsistent association with obesity. Binge eating and binge eating disorder are described as are the use of MRI and PET to examine brain functions in obese lab animals and human subjects during food consumption.

The next section in the volume examines the importance of sweeteners in healthy populations. There are five chapters that examine the carbohydrate requirements in infancy, growing children, teens, amateur athletes, and sports professionals. Chapters include reviews of topical issues including flavored milks and 100 % fruit juices. The first chapter in this section, Chap. 14, provides a biological explanation for the higher consumption of sweet-tasting foods during infancy and childhood. We learn that specialized taste cells are discernable as early as 7–8 weeks of fetal development, and mature receptors are found at weeks 13–15 of pregnancy. The preference for sweet-tasting foods has been seen in children throughout the world and provides compelling evidence for the genetic component of these preferences. The potential for sugar and/or SSBs to impact childhood behaviors negatively or increase the risk of obesity is reviewed, and it concludes that there are little data to support this hypothesis. In contrast, there are overwhelming data that directly link sugar intake to risk of dental caries. One of the most nutrient-dense foods in children’s diets is milk, and the next chapter examines the value of flavored milks in children’s diets. The author points out that the Dietary Guidelines for Americans, 2010, emphasize that four nutrients are of particular concern due to their low level of consumption in children and young adults. The four are calcium, potassium, vitamin D, and fiber, and milk is the leading source of the first three out of these four nutrients of concern. The additional nutrients found in milk are reviewed. Studies of the preferences of flavored milks in both children and adults as well as data from research on the negative effects on milk consumption when flavored milks are removed from schools are reviewed, and relevant figures and tables are included. Another beverage that has gotten a great deal of scrutiny is 100 % fruit juices, and the next chapter, containing over 130 references and six valuable tables and figures, examines the data concerning consumption of 100 % fruit juices and risk of childhood obesity. The chapter includes an extensive discussion of the regulatory status of beverages that may include the word juice in the name but are juice drinks that are not 100 % juice; the effects of such distinctions in the scientific literature, professional association recommendations, and food program allotments are included.

The next informative chapter examines the hydration potential of SSB. SSB and similar beverages used during endurance exercise can spare liver glycogen, maintain blood glucose levels, and increase water absorption. Importantly, SSB and water are equally effective in maintaining normal thermoregulatory and cardiovascular function during exercise. During rehydration, SSB can be more

effective in restoring fluid balance to normal compared to water as these can aid in fluid retention and minimize urinary losses. There is a discussion of the potential gastrointestinal effects of the added low-to-moderate caffeine levels in most SSB. The use of sports drinks in exercise programs is carefully reviewed in the next chapter. The author indicates that sports drinks represent a convenient way to ingest water, sugar, and salt during physical activity, three nutrients that have been shown to provide physiological and performance benefits. Sugar ingestion during exercise improves various aspects of physical and cognitive performance and enhances voluntary fluid consumption, blunts the stress hormone response to intense and prolonged exercise, and reduces subjective ratings of perceived exertion. During strenuous physical activity, consuming a sports drink can replace the water and salts lost in sweat and supply sugars to fuel active skeletal muscles and the central nervous system.

The last section in this comprehensive volume contains three chapters that review the potential associations between sweeteners and serious chronic metabolic diseases. The first chapter examines the clinical research to determine whether the totality of the evidence points to an association between sweetener intake and risk of type 2 diabetes. The authors indicate that high-quality studies (compared to ecological survey studies) from longer term randomized, controlled trials, prospective cohorts, and systematic reviews and meta-analyses do not support the link between fructose alone and fructose-containing sugars and the development or the aggravation of type 2 diabetes. The next chapter examines the associations between sweeteners, obesity, and nonalcoholic fatty liver disease (NAFLD). In order to confirm the diagnosis of NAFLD a liver biopsy may be required. If there is lipid accumulation in the liver cells (hepatocytes) and greater than 5 % of the hepatocytes contain detectable triglyceride, this is considered a positive finding. Currently, the systematic review of published studies related to NAFLD prevalence and incidence finds that definitions for the diagnosis of NAFLD are heterogeneous and cautions that the estimated prevalence varies on the basis of diagnostic technique. Clinical researches using well-controlled studies concerning dietary intakes of sweeteners and NAFLD progression and/or risk reduction are in their infancy, and therefore the authors are unable to make definitive cause-and-effect conclusions. The final chapter in the volume looks at the critical issue of sugars and cardiovascular disease risk factors including triglyceride, total cholesterol, LDL and HDL cholesterol levels, blood pressure, certain hormones, and inflammation biomarkers. The chapter includes an extensive discussion of clinical studies that indicate that under some circumstances increased sugar consumption may be associated with increased triglyceride levels; however, the effects of sugar intake on total cholesterol, LDL, and HDL are not clear. Similar inconsistent data are reviewed for other risk factors, whereas a link between sweetener intakes and risk of hypertension has not been found to date. Over 130 relevant references are included in this comprehensive and informative chapter.

The logical sequence of the sections enhances the understanding of the latest clinical studies of dietary sweetener intakes and their functional effects on human metabolism, growth, and weight maintenance. This unique volume serves as a critical resource for practice-oriented physicians, integrative health care practitioners, academicians involved in the education of graduate students and postdoctoral fellows, and medical students, interns, and residents, allied health professionals, and public health nutritionists who are actively involved in providing data-driven recommendations on the role of sucrose, HFCS, glucose, fructose, and non-nutritive sweeteners in the health of their students, patients, and clients. The volume is of great importance as it contains balanced objective evaluations of the value of carbohydrates for the pediatric population, athletes, and adult individuals who consume sweetened foods as part of a healthy diet.

“Fructose, High Fructose Corn Syrup, Sucrose and Health” edited by James M. Rippe, MD, contains over 100 detailed tables and figures that assist the reader in comprehending the complexities of nutrient interactions, quantification of intake and availability of essential nutrients, composition of diets, and nutritional needs of normal-weight children, teens, and active adults who have different nutritional requirements compared to obese children, teens, and adults who are at great risk for developing diabetes, nonalcoholic liver disease, as well as cardiovascular diseases. There are in-depth discussions of the genetic aspects of carbohydrate metabolism. Health professionals involved in the care

of the pediatric patients are provided balanced documentation and awareness of the newest research on the critical importance of nutritious sources of sweeteners such as flavored milks and 100 % fruit juices that can reduce the risk of nutrient deficiencies in their young patients. Hallmarks of the 21 chapters include key words and bulleted key points at the beginning of each chapter, complete definitions of terms with the abbreviations fully defined for the reader, and consistent use of terms between chapters. There are over 1,700 up-to-date references; all chapters include a conclusion to highlight major findings. The volume also contains a highly annotated index.

This unique text, with chapters written by well-recognized, practice- and research-oriented nutrition authorities, provides practical, data-driven resources based upon the totality of the evidence to help the reader understand the basics of sucrose and fructose biochemistry and examines the consequences of acute and chronic consumption of these sweeteners in the diets of young children through to adolescence and adulthood. The overarching goal of the editor is to provide fully referenced information to practicing health professionals and educators so that they may have a balanced perspective on the value of assuring the best nutritional quality for their patients and clients.

In conclusion, “Fructose, High Fructose Corn Syrup, Sucrose and Health” edited by James M. Rippe, MD, provides health professionals in many areas of research and practice with the most data-driven, up-to-date, well-referenced, and comprehensive volume on the current state of the science and medical practice guidelines with regard to the nutritional care of patients and clients who have to answer their questions about consuming solid foods and beverages that contain sugars including fructose, sucrose, HFCS, glucose, and/or non-nutrient sweeteners. The volume will serve the reader as the most authoritative resource in the field to date and is a very welcome addition to the Nutrition and Health Series.

Morristown, NJ, USA

Adrienne Bendich, Ph.D., FASN, FACN
Series Editor

About Series Editor



Dr. Adrienne Bendich, Ph.D., FASN, FACN has served as the “Nutrition and Health” Series Editor for over 15 years and has provided leadership and guidance to more than 100 editors that have developed the 50+ well respected and highly recommended volumes in the Series.

In addition to “Fructose, High Fructose Corn Syrup, Sucrose and Health” edited by James M. Rippe, MD—major new editions in 2013–2014 include:

1. *Handbook of Food Fortification and Health, volume I* edited by Dr. Victor R. Preedy, Dr. Rajaventhana Srirajaskanthan, Dr. Vinood B. Patel, 2013
2. *Handbook of Food Fortification and Health, volume II* edited by Dr. Victor R. Preedy, Dr. Rajaventhana Srirajaskanthan, Dr. Vinood B. Patel, 2013
3. *Diet Quality: An Evidence-Based Approach, volume I* edited by Dr. Victor R. Preedy, Dr. Lan-Ahn Hunter and Dr. Vinood B. Patel, 2013
4. *Diet Quality: An Evidence-Based Approach, volume II* edited by Dr. Victor R. Preedy, Dr. Lan-Ahn Hunter and Dr. Vinood B. Patel, 2013
5. *The Handbook of Clinical Nutrition and Stroke*, edited by Mandy L. Corrigan, MPH, RD Arlene A. Escuro, MS, RD, and Donald F. Kirby, MD, FACP, FACN, FACG, 2013
6. *Nutrition in Infancy, volume I* edited by Dr. Ronald Ross Watson, Dr. George Grimbale, Dr. Victor Preedy and Dr. Sherma Zibadi, 2013
7. *Nutrition in Infancy, volume II* edited by Dr. Ronald Ross Watson, Dr. George Grimbale, Dr. Victor Preedy and Dr. Sherma Zibadi, 2013
8. *Carotenoids and Human Health*, edited by Dr. Sherry A. Tanumihardjo, 2013

9. *Bioactive Dietary Factors and Plant Extracts in Dermatology*, edited by Dr. Ronald Ross Watson and Dr. Sherma Zibadi, 2013
10. *Omega 6/3 Fatty Acids*, edited by Dr. Fabien De Meester, Dr. Ronald Ross Watson and Dr. Sherma Zibadi, 2013
11. *Nutrition in Pediatric Pulmonary Disease*, edited by Dr. Robert Dumont and Dr. Youngran Chung, 2013
12. *Magnesium and Health*, edited by Dr. Ronald Ross Watson and Dr. Victor R. Preedy, 2012.
13. *Alcohol, Nutrition and Health Consequences*, edited by Dr. Ronald Ross Watson, Dr. Victor R. Preedy, and Dr. Sherma Zibadi, 2012
14. *Nutritional Health, Strategies for Disease Prevention, Third Edition*, edited by Norman J. Temple, Ted Wilson, and David R. Jacobs, Jr., 2012
15. *Chocolate in Health and Nutrition*, edited by Dr. Ronald Ross Watson, Dr. Victor R. Preedy, and Dr. Sherma Zibadi, 2012
16. *Iron Physiology and Pathophysiology in Humans*, edited by Dr. Gregory J. Anderson and Dr. Gordon D. McLaren, 2012

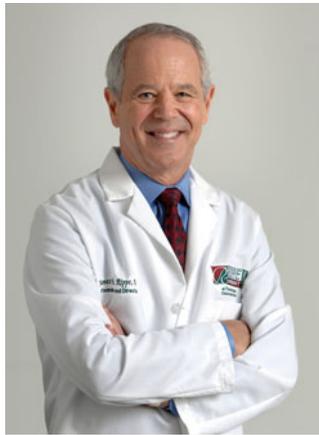
Earlier books included *Vitamin D, Second Edition* edited by Dr. Michael Holick; “Dietary Components and Immune Function” edited by Dr. Ronald Ross Watson, Dr. Sherma Zibadi and Dr. Victor R. Preedy; “Bioactive Compounds and Cancer” edited by Dr. John A. Milner and Dr. Donato F. Romagnolo; “Modern Dietary Fat Intakes in Disease Promotion” edited by Dr. Fabien De Meester, Dr. Sherma Zibadi, and Dr. Ronald Ross Watson; “Iron Deficiency and Overload” edited by Dr. Shlomo Yehuda and Dr. David Mostofsky; “Nutrition Guide for Physicians” edited by Dr. Edward Wilson, Dr. George A. Bray, Dr. Norman Temple and Dr. Mary Struble; “Nutrition and Metabolism” edited by Dr. Christos Mantzoros and “Fluid and Electrolytes in Pediatrics” edited by Leonard Feld and Dr. Frederick Kaskel. Recent volumes include: “Handbook of Drug-Nutrient Interactions” edited by Dr. Joseph Boullata and Dr. Vincent Armenti; “Probiotics in Pediatric Medicine” edited by Dr. Sonia Michail and Dr. Philip Sherman; “Handbook of Nutrition and Pregnancy” edited by Dr. Carol Lammi-Keefe, Dr. Sarah Couch and Dr. Elliot Philipson; “Nutrition and Rheumatic Disease” edited by Dr. Laura Coleman; “Nutrition and Kidney Disease” edited by Dr. Laura Byham-Grey, Dr. Jerrilynn Burrowes and Dr. Glenn Chertow; “Nutrition and Health in Developing Countries” edited by Dr. Richard Semba and Dr. Martin Bloem; “Calcium in Human Health” edited by Dr. Robert Heaney and Dr. Connie Weaver and “Nutrition and Bone Health” edited by Dr. Michael Holick and Dr. Bess Dawson-Hughes.

Dr. Bendich is President of Consultants in Consumer Healthcare LLC, and is the editor of ten books including “Preventive Nutrition: The Comprehensive Guide for Health Professionals, Fourth Edition” co-edited with Dr. Richard Deckelbaum (www.springer.com/series/7659). Dr. Bendich serves on the Editorial Boards of the *Journal of Nutrition in Gerontology and Geriatrics*, and *Antioxidants*, and has served as Associate Editor for “Nutrition” the International Journal; served on the Editorial Board of the *Journal of Women’s Health and Gender-based Medicine*, and served on the Board of Directors of the American College of Nutrition.

Dr. Bendich was Director of Medical Affairs at GlaxoSmithKline (GSK) Consumer Healthcare and provided medical leadership for many well-known brands including TUMS and Os-Cal. Dr. Bendich had primary responsibility for GSK’s support for the Women’s Health Initiative (WHI) intervention study. Prior to joining GSK, Dr. Bendich was at Roche Vitamins Inc. and was involved with the groundbreaking clinical studies showing that folic acid-containing multivitamins significantly reduced major classes of birth defects. Dr. Bendich has co-authored over 100 major clinical research studies in the area of preventive nutrition. She is recognized as a leading authority on antioxidants, nutrition and immunity and pregnancy outcomes, vitamin safety and the cost-effectiveness of vitamin/mineral supplementation.

Dr. Bendich received the Roche Research Award, is a *Tribute to Women and Industry* Awardee and was a recipient of the Burroughs Wellcome Visiting Professorship in Basic Medical Sciences. Dr. Bendich was given the Council for Responsible Nutrition (CRN) Apple Award in recognition of her many contributions to the scientific understanding of dietary supplements. In 2012, she was recognized for her contributions to the field of clinical nutrition by the American Society for Nutrition and was elected a Fellow of ASN. Dr Bendich is Adjunct Professor at Rutgers University. She is listed in Who's Who in American Women.

About Volume Editor



James M. Rippe, M.D. is a graduate of Harvard College and Harvard Medical School with postgraduate training at Massachusetts General Hospital. He is currently the Founder and Director of the Rippe Lifestyle Institute (RLI) and Professor of Biomedical Sciences at the University of Central Florida.

Over the past 25 years Dr. Rippe has established and run the largest research organization in the world exploring how daily habits and actions impact short- and long-term health and quality of life. This organization, RLI, has published hundreds of papers that form the scientific basis for the fields of lifestyle medicine and high-performance health. RLI also conducts numerous studies every year on nutrition and healthy weight management. One recent research interest of the RLI team has been the metabolism and health effects of sugars.

A lifelong and avid athlete Dr. Rippe maintains his personal fitness with a regular walk, jog, swimming, and weight training program. He holds a black belt in karate and is an avid wind surfer, skier, and tennis player. He lives outside of Boston with his wife, television news anchor Stephanie Hart, and their four children, Hart, Jaelin, Devon, and Jamie.

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