A simple perspective of carbohydrates in food and nutrition (Review)

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Abstract. Carbohydrates are considered as one of the three primary macronutrients in the realm of food and nutrition in the daily human diet. In addition to being a source of food, they encompass a vast category of natural products, along with synthetic bio-mimics, which have found suitable applications in therapeutics and drug design. The present review discusses the importance of carbohydrates for a healthy diet, their sources from plants and animals, and their classification. Information on the biological and chemical changes in carbohydrates in the human body, as well as their therapeutic and drug-design applications, is also provided. The present review provides a narrative review and perspective, integrating nutritional, biochemical and therapeutic perspectives on carbohydrates. The objective was to provide an updated, interdisciplinary overview that connects dietary carbohydrate intake with metabolic processes and emerging medicinal applications.

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Abbreviations: acetyl CoA, acetyl coenzyme A; ADP, adenosine diphosphate; ATP, adenosine triphosphate; BPG, 1,3-bisphosphoglycerate; CD, cyclodextrin; DHAP, dihydroxyacetone phosphate; DNL, *de novo* lipogenesis; FADH2, flavin adenine dinucleotide; G-3-P, D-glyceraldehyde-3-phosphate; HR, hazard ratio; NADH2, nicotinamide adenine dinucleotide; NAFLD, non-alcoholic fatty liver disease; PURE, Prospective Urban Rural Epidemiology; succinyl-CoA, succinyl coenzyme A; TCA, tricarboxylic acid

Key words: food, nutrients, health, carbohydrates, glycolysis, monosaccharides, drug design

1. Introduction

Food is essential for survival and maintaining the overall well-being of all living organisms, and the method of food consumption has evolved throughout history. In order to survive, the diet of an individual requires a balance of both nutritious and antinutritional factors. The diet provides nutrients that serve as raw materials for metabolic processes (1,2), and health is greatly influenced by genetics, diet, lifestyle and nutrition. The gastrointestinal system of the human body processes carbohydrates, dietary fats and proteins that are consumed into monosaccharides, fatty acids and amino acids, respectively, fueling organ function and supporting cellular growth (3,4).

In the 21st century, factors such as climate change, water scarcity, rising food prices and population growth challenge agriculture and food security, particularly in arid and semi-arid regions. Scientists and nutritionists need to explore alternative food sources to address hunger and poverty. Cereal grains are the global primary food source and are central to the human diet (5).

Carbohydrates are a major macronutrient, vital for energy production and organ function. The majority of carbohydrates are biodegradable and biocompatible, thus rendering them suitable for both drug delivery and functional foods. Nanostructured carbohydrates, with self-assembling abilities, provide diverse applications in food and therapeutics. Different saccharide structures enable various self-assembly methods, thereby expanding their functions in food (6). Carbohydrates are unique among macronutrients in not having a minimum dietary requirement.

Increase in global health risks, such as type 2 diabetes, obesity, non-alcoholic fatty liver disease (NAFLD) and

other cardiovascular health issues, have compelled the scientific community to re-evaluate carbohydrate intake (7). Large-scale epidemiological studies and controlled human trials are increasingly demonstrating that, rather than quantity alone, carbohydrate quality may be the cause of health risks (8). Rapidly digestible starches and heavily processed foods containing refined sugar increase the risk of developing hyperinsulinemia, hepatic *de novo* lipogenesis (DNL) and postprandial glycemic excursions, whereas fiber-rich sugars reduce the risks of developing these disorders and support metabolic flexibility (9-11). This has opened views on carbohydrate toxicity, which depicts excessive intake of certain digestible carbohydrates, particularly fructose-rich sugars, as a metabolic stressor capable of disrupting hepatic and systemic homeostasis (12,13). Non-digestible carbohydrates, such as resistant starches and oligosaccharides selectively nourish beneficial gut microbes, leading to the production of bioactive metabolites, such as short-chain fatty acids, that help regulate glucose and support immune function (14,15).

Carbohydrates also contribute greatly to medicine development. Both natural and synthetic sugar-based polymers and glycoconjugates exhibit excellent biocompatibility, molecular and biological recognition, and structural tunability, facilitating a wide range of applications in biological evaluations, such as anticancer and antiviral therapies (16). Technical utilities, such as automated glycan assembly, have further improved the access to complex sugar structure (17), speeding up translational research connecting chemistry, biology and medicine.

The present narrative review presents a comprehensive perspective on carbohydrates, focusing on their physicochemical characteristics, nutritional values and chemical and metabolic functions. Furthermore, contemporary topics, such as carbotoxicity and fructose-induced lipogenesis are also discussed. Unlike the highly specialized reviews, the present review aimed to connect carbohydrate chemistry with food science and nutritional values, providing an interdisciplinary overview relevant to students, researchers, health professionals and nutritionists.

2. Physicochemical properties of carbohydrates and their biological significance in food matrices

The structural hierarchy and complex structural features of carbohydrates influence their nutritional values to a great extent. Monosaccharides, such as glucose and fructose, are the simplest monomeric forms of sugar. Through the formation of glycosidic bonds, these units assemble into disaccharides (for example, sucrose) and eventually into polysaccharides with vast, complex chains that define the texture and energy profile of the human diet. A few common examples of carbohydrates are illustrated in Fig. 1 (18,19). Furthermore, polysaccharides are utilized in various functions, including energy storage in plants (primarily starch) and as structural support for plant cells (primarily cellulose). They function as a gelling component of the intercellular matrix to help hold ions, such as sodium, calcium and magnesium. Polysaccharides, such as cellulose, starch, chitin and seaweed polysaccharides have high commercial value across various industries, from paper manufacturing to food processing (20).

The physicochemical properties of carbohydrates are fundamental factors that affect their functions in food matrices and biological evaluation. These properties, ranging from solubility and hygroscopicity to gelation capacity and reactivity, arise directly from molecular structure, including monomer composition, glycosidic linkage stereochemistry (α vs. β), branching density and molecular weight (21). Such structural features influence not only the texture, stability and sensory properties of foods, but also the rate and extent of their digestion, thus affecting glycemic response and interactions with the gut microbiota (22).

Solubility and hygroscopicity are vital properties influencing food quality and shelf life. Monosaccharides, such as glucose and fructose exhibit high water solubility due to their multiple hydroxyl groups, thereby reducing the reactivity of water with food and inhibiting microbial growth (23), which is utilized in confectionery and baked goods to maintain softness and moisture. However, polysaccharides, such as cellulose are insoluble due to $\beta(1\rightarrow4)$ linkages that result in extensive intermolecular hydrogen bonding, which contributes to dietary fiber content and textural bulk without significantly affecting water activity (24). The solubility of carbohydrates also affects phase behavior in complex matrices; for instance, during the preparation of gummy sweets, incompatibility between gelatin and long-chain polysaccharides in glucose syrups can lead to phase separation, which is modulated by moisture content and the presence of small-molecule additives, such as citric acid or allulose (25).

Carbohydrate physicochemistry is also controlled by viscosity and gelation. Starch, composed of amylose [linear glucan connected through $\alpha(1\rightarrow4)$-linkage] and amylopectin [branched with $\alpha(1\rightarrow6)$ linkages], undergoes gelation upon heating in aqueous media, leading to swelling of the system, loss of crystallinity and formation of a viscoelastic network (26). The ratio of amylose to amylopectin critically influences the gel strength and retrogradation kinetics; a higher amylose content improves gelation but also increases the risk of staling in bakery products (27). Similarly, pectin, a heteropolysaccharide rich in galacturonic acid, forms gels in acidic, high-sugar environments through charge neutralization and water loss, a mechanism essential for jam and jelly preparation. Recent research has demonstrated that processing technologies, including ultrasound-assisted heat-moisture treatment, can modify starch crystallinity and reduce rapidly digestible starch content, thereby lowering glycemic potential while preserving functional properties (28).

Carbohydrate reactivity, particularly through the Maillard reaction, markedly affects both food quality and nutritional outcomes. This non-enzymatic browning reaction occurs between reducing sugars (e.g., glucose, fructose) and the amino groups of proteins at elevated temperatures and in the presence of moisture, generating flavor compounds, brown pigments and advanced glycation end-products (29). While it improves the flavor in roasted coffee or seared meat, etc., uncontrolled Maillard reactions in processed foods can produce potentially harmful compounds and decrease protein bioavailability (30). On the contrary, controlled Maillard reactions between proteins and prebiotic fibers can enhance emulsifying properties, solubility and antioxidant activity, thereby enhancing the functionality of plant-based products (31). Non-reducing sugars

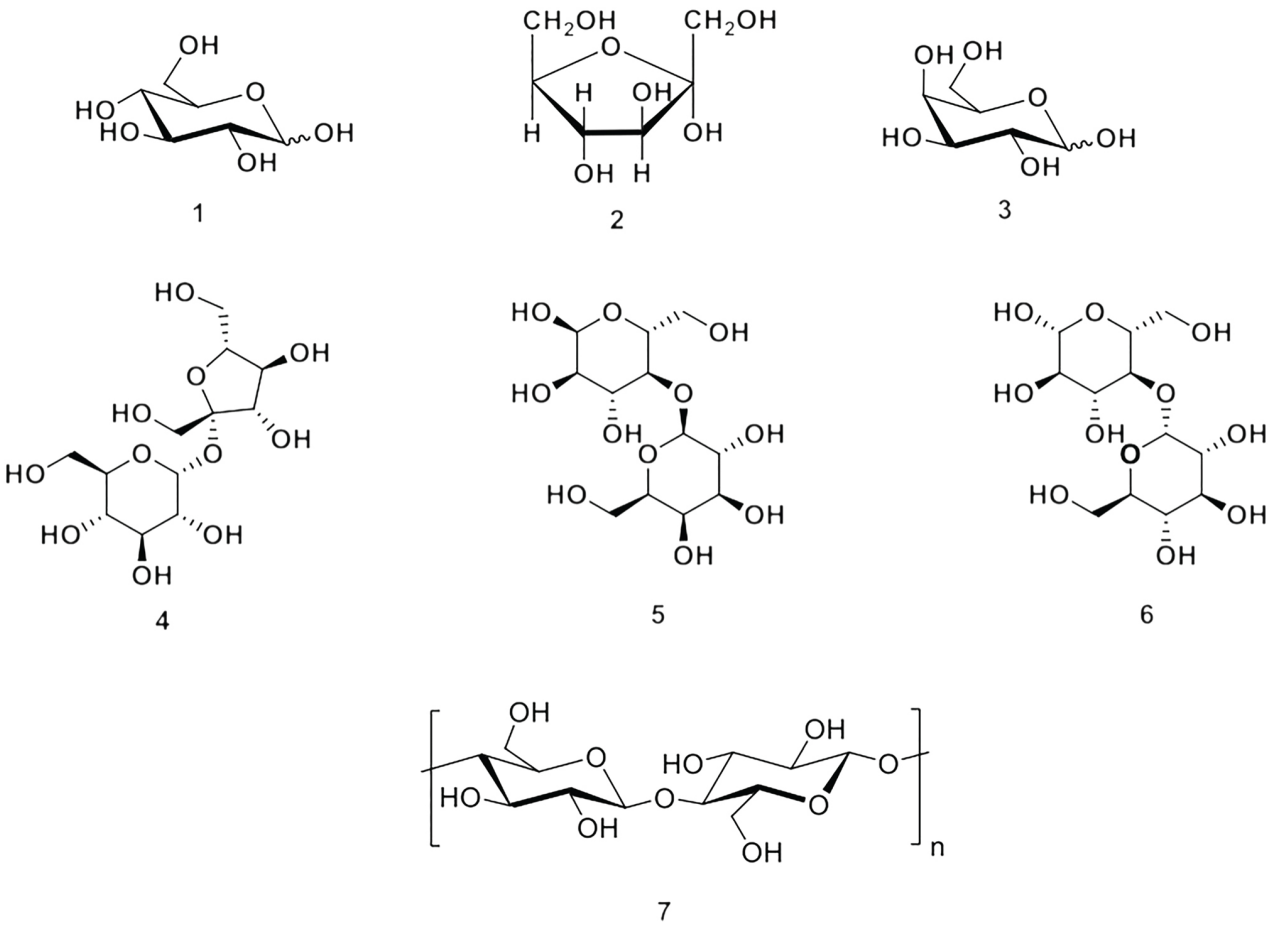

Figure 1. Molecular structure of representative monosaccharides (panels 1-3), disaccharides (panels 4-6) and polysaccharides (panel 7).

such as sucrose do not participate in the Maillard reaction if not hydrolyzed first to glucose and fructose, emphasizing how glycosidic bond affects reactivity.

The biological significance of these physicochemical traits becomes evident in their modulation of carbohydrate bioavailability and gut health. Rapidly digestible starches, often resulting from extensive gelatinization and low amylose content, elicit sharp postprandial glucose spikes, which can contribute to metabolic disorders when consumed chronically (24). By contrast, resistant starches and non-digestible oligosaccharides, characterized by β-linkages or complex branching that are inaccessible to human amylases, reach the colon intact, where they serve as prebiotics, selectively stimulating beneficial bacteria such as *Lactobacilli* and *Bifidobacteria* (32,33). The fermentation of these fibers produces short-chain fatty acids (SCFAs), such as butyrate, which nourish colonocytes, regulate immune function and improve insulin sensitivity (34). The efficacy of prebiotic action is highly dependent on physicochemical parameters: Molecular weight, solubility and glycosidic bond type determine fermentability rates and microbial selectivity (35).

Moreover, the food matrix itself modulates carbohydrate bioaccessibility. Encapsulation within cell walls (as in whole grains) or complexation with proteins and lipids can attenuate enzymatic hydrolysis, reducing glycemic impact (36). Processing methods, both thermal (e.g., baking and extrusion) and non-thermal (e.g., high-pressure processing), can disrupt these matrices, increasing starch digestibility, or they can promote retrogradation and resistant starch formation, depending on conditions (37). Thus, the interplay between intrinsic carbohydrate properties and extrinsic matrix factors ultimately shapes nutritional outcomes.

The physicochemical properties of carbohydrates are not only technical aspects for food formulation but are crucial to their biological outcomes. These properties influence texture and stability in food products, regulate glycemic response and modulate the gut microbiota, thereby connecting food science and human physiology (9,11). The strategic manipulation of carbohydrate structure through breeding, enzymatic modification, or customized processing provides promising opportunities to create foods that meet sensory expectations while enhancing metabolic health (38).

3. Nutritional aspects of carbohydrates in the human diet

Dietary sources and bioavailability. The bioavailability of carbohydrates, the rate and extent to which they are absorbed and utilized, is intrinsically linked to their structural hierarchy and the food matrix in which they reside (9). Dietary carbohydrates range from simple monosaccharides to complex polysaccharides. Monosaccharides, such as glucose and fructose are present in their free form in honey, fruits and corn syrups, providing immediate bioavailability. Disaccharides, such as the lactose found in mammalian milk or the sucrose

Table I. Source of various carbohydrates and diseases related to excess intake.

Category of carbohydrates	Type of carbohydrate	Sweetness (relative to sucrose=1)	Food source	Daily amount	Amount of energy (caloric value kcal/g)	Activity on the body parts	Carbohydrate toxicity or diseases	(Refs.)
Monosaccharides	Glucose	0.75	Dates, currants, figs, grapes, dried apricot, sweet corn, and honey	25 g	4	Blood	Hyperglycemia, diabetes	(44-48)
	fructose	1.74	Honey, dates, fruit jams, grapes, apples, pear, kiwi and banana	≤50 g	4	Liver	non-alcoholic fatty liver disease (NAFLD)	(45,47,49-51)
	Galactose	0.32	Flavored yogurts, lactose free milk, ground black peppers	5-20 g	4	ovaries	Ovarian cancer	(44,47,52)
Disaccharides	Sucrose	1	Cakes, cookies, and dark chocolate, beetroot, carrots, sugar cane and sugar beet	20-32 g	4	Heart, breast	heart disease, breast cancer	(47,53-55)
	lactose	0.2	Milk, buttermilk, yogurt, sour cream, condensed milk, Frozen, cottage cheese, evaporated milk, goats milk and ice creams	12 g	4	intestine	Lactose intolerance	(47,54,56,41)
	maltose	0.4	Malted wheat and barley, Breads, bagels, Malt extract, molasses Beer	75 mg	4	Digestive system	Chronic diarrhea	(47,54,55,4)
Oligosaccharide	Fructo-oligosaccharide	0.3-0.6	Legumes, cabbage, broccoli, Onion, fennel, peas, wheat, bananas, asparagus, garlic	10-2 0 g	4	NA	Not specific toxicity	(47,57,58)

Table I. Continued.

Category of carbohydrates	Type of carbohydrate	Sweetness (relative to sucrose=1)	Food source	Daily amount	Amount of energy (caloric value kcal/g)	Activity on the body parts	Carbohydrate toxicity or diseases	(Refs.)
	Galacto-oligosaccharides	0.3-0.6	Cow milk, yogurt, beans.	12-15 g	4	NA	NA	(47,59)
Polysaccharides	Starch	Not sweet	Oats, rice, chickpeas, potato, pasta, corn, flours.	NA	4	NA	NA	(47)
	Fiber	Not sweet	Cereal grains, legumes, nuts, seeds.	28-36 g	2	NA	NA	(60,61)

NA, not available.

concentrated in sugar beets and cane, require minimal enzymatic cleavage prior to absorption (39). While animal-derived foods are generally carbohydrate-poor, dairy products are a unique exception, providing the essential disaccharide lactose, which accounts for almost 40% of the energy in human breast milk and is vital for neonatal development (40,41).

Contemporary nutritional science emphasizes that the health impact of these sugars is heavily dictated by their source. For instance, while refined sucrose and fructose in high-fructose corn syrup are associated with rapid glycemic spikes, the same sugars found within the fibrous matrix of whole fruits such as grapes or kiwi exhibit different kinetic profiles (42,43). As the structural complexity of polysaccharides, such as the starches found in legumes, tubers and cereal grains, increases, the pace of digestion typically slows. However, modern processing techniques have challenged the traditional dichotomy between simple and complex. Current evidence indicates that highly processed complex carbohydrates, such as white bread or instant rice, can have a glycemic index (GI) equal to or higher than that of simple table sugar, leading to significant insulin demand and increasing the risk of metabolic syndromes, obesity and ovulatory infertility (44). The role of carbohydrates in the diet is presented in Table I (41,44-61). Table I provides an overview of dietary carbohydrates, which are vital macronutrients; their types, quantity and metabolic fate critically influence health outcomes.

The interaction between dietary carbohydrates, the gut microbiome, and host health constitutes a dynamic and reciprocal relationship that is fundamental to modern nutritional frameworks. Dietary fibers and other indigestible carbohydrates serve as pivotal environmental factors influencing the composition and metabolic output of the gut microbial ecosystem (62). Subsequently, the gut microbiota converts these dietary elements into bioactive metabolites that affect host metabolism, immune function and even neurological processes (63). This relationship is increasingly recognized in the prevention and management of chronic diseases, including obesity, cardiometabolic disorders and certain types of cancer (62). The notion of carbohydrate quality currently includes not only its glycemic effects, but also its capacity to support a beneficial gut microbiota, thereby enhancing overall health (9,11). This integrated viewpoint emphasizes that the simplistic perception of carbohydrates as mere caloric sources is outdated; they should be regarded as information-rich molecules whose chemical language is deciphered by both human enzymes and the trillions of microbial entities in the gut, ultimately defining their significant biological roles in food and nutrition sciences (34,64).

Role as a primary energy substrate. Carbohydrates are the main source of oxidative fuel for the human body, providing with ~4 kcal/g (17 kJ/g) of energy. Glucose is particularly critical as it is the only metabolic substrate for the central nervous system and red blood cells, which lack the enzymes to efficiently oxidize other fuels under normal physiological conditions (65,66). In the fed state, dietary carbohydrates maintain blood glucose homeostasis and replenish glycogen stores in the liver and skeletal muscle. Under restricted exogenous intake, the body demonstrates metabolic flexibility by activating gluconeogenesis and ketogenesis to maintain brain

function. This change indicates that the quality of carbohydrates is critical for overall health. A balanced intake (usually 45-65% of daily calories) maintains a stable metabolism; however, consuming high-GI foods continuously break down these homeostatic mechanisms (67-70).

Non-digestible polysaccharides, or dietary fiber, have become an integral part of modern preventive medicine. Unlike starch, which is broken down by enzymes in the small intestine, fibers such as cellulose and hemicellulose remain whole until they reach the colon. There, they add bulk to the stool and serve as fermentable substrates for the gut microbiota (71). The SCFAs produced by this process serve as an alternative energy source for colonocytes and exert systemic anti-inflammatory effects (72). Current clinical guidelines suggest that individuals should consume ~30 g of fiber per day, which is linked to lower rates of coronary heart disease, type 2 diabetes and colorectal cancer (73). This indicates that carbohydrate chemistry can affect long-term health outcomes.

Despite the extensive understanding of carbohydrate metabolism, a significant knowledge gap persists regarding inter-individual variability in glycemic response. While tools such as the GI and glycemic load provide a standardized framework for ranking foods, contemporary big data nutrition studies (74) have revealed that two individuals consuming the identical carbohydrate source can exhibit vastly different postprandial glucose excursions. This variability is deemed to be driven by a complex interplay between host genetics, sleep patterns, physical activity, and most crucially the unique composition of the gut microbiome of an individual (74,75).

Furthermore, a vigorous scientific debate remains unresolved concerning the carbohydrate-insulin model (CIM) of obesity. Proponents of the CIM argue that high-carbohydrate diets drive obesity by promoting insulin secretion, which partitions energy toward fat storage rather than oxidation, whereas critics maintain that total energy balance (calories in vs. calories out) remains the primary driver (76,77). Resolving these questions is essential for moving beyond one-size-fits-all dietary guidelines and toward personalized nutritional interventions that can effectively combat the global rise in metabolic disease.

Authoritative international dietary guidelines and the disadvantages of the overconsumption of refined carbohydrates. Authoritative international dietary guidelines consistently identify refined carbohydrates as a key dietary component to limit due to their well-established association with chronic disease risk. The World Health Organization (WHO), in its global recommendations, explicitly advises that the intake of free sugars, which encompass added sugars and those naturally present in honey, syrups and fruit juices, should be limited to <10% of total energy intake for both adults and children, with a further conditional recommendation to reduce this to <5% for additional health benefits (78,79). This guidance is grounded in extensive epidemiological evidence linking a high sugar consumption to weight gain, dental caries and metabolic dysfunction. Similarly, the Dietary Guidelines for Americans (DGA), jointly issued by the US Department of Health and Human Services and the US Department of Agriculture, emphasize minimizing the intake of refined grains and added sugars, recommending that <10% of daily calories should be derived from added sugars and that at least half of all grain consumption should be whole grains (80). The European Food Safety Authority (EFSA) and national bodies such as the UK Scientific Advisory Committee on Nutrition (SACN) echo these principles, advocating for a shift from refined to whole-grain carbohydrate sources to improve long-term health outcomes (81).

The scientific foundation for these guidelines rests on a robust body of epidemiological research. The landmark Prospective Urban Rural Epidemiology (PURE) study, which followed >135,000 individuals across 18 countries, provided critical population-level evidence that high carbohydrate intake, particularly from refined sources, is associated with an increased total mortality (82). This finding challenged older paradigms that focused primarily on fat reduction and highlighted the importance of carbohydrate quality over mere quantity. Further analysis from the PURE cohort specifically linked the higher consumption of refined grains (median intake of 350 g/day in the highest quintile) to a significantly elevated risk of developing major cardiovascular events and total mortality. By contrast, whole grain intake exhibited neutral or protective associations (83). These results underscore the differential health impacts of carbohydrate subtypes, a nuance increasingly emphasized in modern nutritional science.

Longitudinal cohort studies from the USA have provided granular insights into specific refined carbohydrate sources. Data from the Nurses' Health Study and the Health Professionals Follow-Up Study (84) demonstrate a clear dose-response association between the consumption of sugar-sweetened beverages (SSBs) and the incidence of type 2 diabetes and cardiovascular disease. A meta-analysis of prospective cohort studies confirmed that each daily serving of SSBs is associated with an 18% higher risk of coronary heart disease (85). Similarly, a previous systematic review and meta-analysis found that the higher intake of refined carbohydrates predicts a significantly increased risk of developing type 2 diabetes, with the association persisting even after adjustment for body mass index and other confounders (86). The mechanisms underlying these associations are multifactorial: Refined carbohydrates drive rapid postprandial glycemia and hyperinsulinemia, promote hepatic DNL leading to dyslipidemia (elevated triglycerides and reduced high-density lipoprotein cholesterol) and induce systemic inflammation, all key pathways in the development of cardiometabolic diseases (87).

The concept of ultra-processed foods (UPFs), as defined by the NOVA classification system, has further refined the understanding of the risks associated with the consumption of refined carbohydrates. UPFs are industrial formulations that typically contain high levels of refined starches, added sugars and unhealthy fats, while being low in fiber and phytonutrients. A recent umbrella review of epidemiological meta-analyses concluded that a higher consumption of UPFs is consistently associated with increased risks of obesity, type 2 diabetes, cardiovascular disease and all-cause mortality (88). The Framingham Offspring Study reported that for every 10% increase in the proportion of UPFs in the diet, there was a 12% higher risk of overall cardiovascular disease and a 13% higher risk of cerebrovascular disease (89). These findings suggest that the health risks of consuming refined carbohydrates may be amplified in the context of ultra-processing, where the food

matrix is degraded and hyper-palatable combinations override natural satiety signals, leading to excess energy intake and metabolic stress (87).

Despite this strong consensus, some nuances and ongoing debates exist. For instance, not all refined carbohydrate sources carry equal risk; the consumption of white rice in Asian populations exhibits complex associations that may be modified by the overall dietary pattern and glycemic load (83). Furthermore, the focus is shifting from isolated nutrients to holistic dietary patterns. The Mediterranean diet, rich in whole grains, legumes, fruits and vegetables, has been shown in randomized trials, such as the PREDIMED study, to significantly reduce cardiovascular events, demonstrating that the adverse effects of the consumption of refined carbohydrates can be mitigated by replacing them with high-quality carbohydrate sources within a balanced dietary pattern (90). Overall, authoritative guidelines and contemporary epidemiological evidence converge on a clear message that reducing the intake of refined carbohydrates, particularly in the form of added sugars and UPFs, is a critical public health strategy for preventing chronic diseases globally.

4. Metabolic processes and bioenergetics involving carbohydrates

The transition from the structural complexity of dietary carbohydrates to systemic energy requires a highly coordinated sequence of enzymatic transformations. For the human body, the critical connection between food and health is realized through these metabolic pathways, which determine whether a carbohydrate is partitioned toward immediate adenosine triphosphate (ATP) production, biosynthetic precursors, or long-term energy storage. Cells use different enzymatic activities in different phases to convert ingested glucose into carbon dioxide and water. Two metabolic pathways, glycolysis and the tricarboxylic acid (TCA) cycle, also known as the Krebs or citric acid cycle, are involved in the breakdown of glucose (91).

Glycolysis. Glycolysis is a catalytic process that converts glucose into pyruvate via 10 enzyme steps. These highly regulated processes of glycolysis have two stages: The energy input for Step 1 requires two ATPs per glucose molecule, followed by the energy release as four ATPs, two for each glyceraldehyde molecule, which is described as Step 2 (90). Glycolysis, a process in living cells, can also be used in the citric acid cycle or fermentation, and is the primary source of acetyl coenzyme A (acetyl-CoA), the primary energy source. The structures of glycolysis intermediates are depicted in Fig. 2 (92).

The initial stage of glycolysis requires energy in the form of ATP. ATP phosphorylates D-glucose at the six carbons via the enzyme hexokinase to produce D-glucose-6-phosphate (G-6-P). This regulatory process is inhibited by the presence of glucose-6-phosphate. Phosphoglucoisomerase (class: Isomerase) then converts it to D-fructose-6-phosphate (F-6-P), which is phosphorylated again by ATP, this time at the one-carbon position, by the enzyme phosphofructokinase (class: Transferase) to produce D-fructose-1,6-bisphosphate. Owing to its high G value, this is the committed stage of glycolysis. The enzyme, fructose bisphosphate aldolase, then cleaves D-fructose-1,6-bisphosphate into two three-carbon molecules, dihydroxyacetone phosphate (DHAP) and D-glyceraldehyde-3-phosphate (G-3-P). DHAP is transformed into G-3-P as the following step in glycolysis requires the molecule G-3-P by the enzyme triose phosphate isomerase (93).

The second stage involves producing four ATP molecules for each glucose molecule. The glyceraldehyde-3-phosphate dehydrogenase enzyme phosphorylates G-3-P at the one carbon to produce the high-energy molecule, 1,3-bisphosphoglycerate (BPG). Phosphoglycerate kinase then phosphorylates adenosine diphosphate (ADP) at the expense of BPG to produce ATP and 3-phosphoglycerate. Phosphoglycerate mutase then converts 3-phosphoglycerate to 2-phosphoglycerate to produce another high-energy molecule. Enolase then converts 2-phosphoglycerate to phosphoenolpyruvate, releasing water, potassium and manganese ions. Pyruvate kinase phosphorylates ADP to produce ATP and pyruvate, and cellular energy controls this reaction. High energy levels indicate inhibited pyruvate kinase. Stage 2 occurs twice due to glucose division (93).

In parallel, G-6-P can be diverted into the hexose monophosphate shunt (pentose phosphate pathway). Unlike glycolysis, this pathway is not primarily concerned with ATP production. Instead, it serves two vital biosynthetic roles: Generating nicotinamide adenine dinucleotide phosphate, which provides reducing power for fatty acid synthesis and antioxidant defense (reducing glutathione), and producing ribose-5-phosphate, a precursor for nucleotide synthesis (94). In the context of nutrition, the balance between these two pathways is essential; for instance, a diet chronically high in refined sugars can over-activate these shunt pathways, potentially fueling DNL and contributing to metabolic dysfunction (95).

Krebs cycle. The citric acid cycle is the ultimate oxidative process in which carbs, lipids and amino acids interact. It is the most significant metabolic pathway for the energy source of the body. TCA is the most essential core metabolic pathway, connecting nearly all metabolic processes. The Krebs cycle (Fig. 3) is an aerobic biodegradation process that begins with acetyl-CoA and ends with CO_2. Patients with diabetes have lower oxaloacetic acid and Krebs cycle activity due to reduced glucose and pyruvate levels (96).

At higher energy levels, the citrate synthesis rate increases, while the flux through the Krebs cycle decreases. This excess citrate is subsequently transported to the cytosol and degraded to acetyl-CoA. Acetyl-CoA can then be used to produce fatty acids and cholesterol. Citrate has a positive regulatory effect on lipogenic enzymes (e.g., acetyl-CoA carboxylase) and a negative regulatory effect on phosphofructokinase-1 (a glycolytic enzyme). Citrate is also necessary for ketogenesis in non-hepatic tissues (96).

The α-ketoglutarate dehydrogenase complex converts α-KG to succinyl coenzyme A (succinyl-CoA) through multiple steps (Fig. 3). Succinyl-CoA is a highly energetic molecule that generates the only guanosine triphosphate molecule in this pathway when succinate thiokinase is present (96). Nicotinamide adenine dinucleotide ($NADH_2$) and flavin adenine dinucleotide ($FADH_2$) are the energy molecules created during this oxidative decarboxylation cycle. These molecules release energy during the oxidative phosphorylation reaction; thus, their power is retained in ATP as high-energy

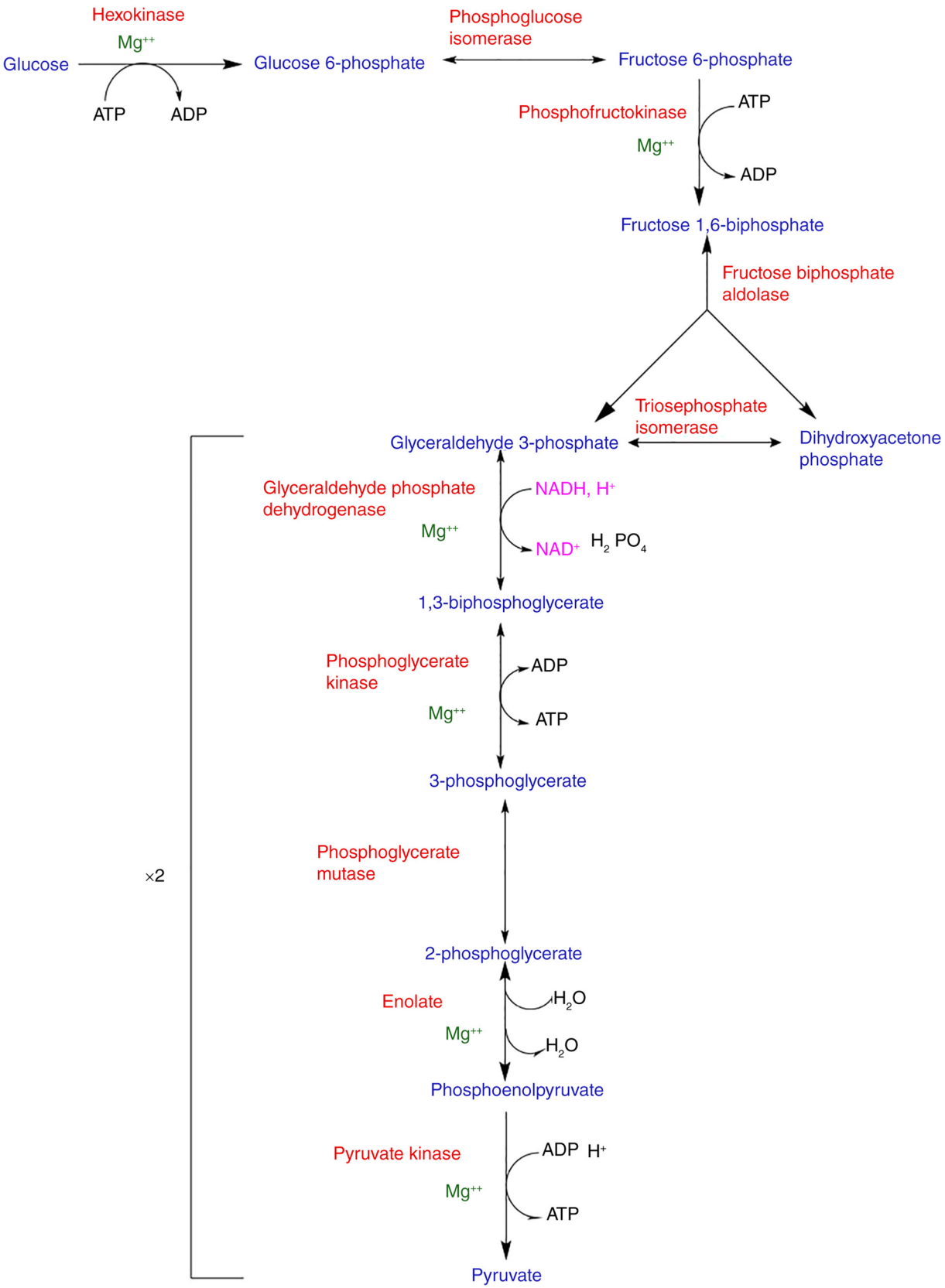

Figure 2. Simple schematic representation of glycolysis pathway. ADP, adenosine diphosphate; ATP, adenosine triphosphate; NAD, nicotinamide adenine dinucleotide; NADH, nicotinamide adenine dinucleotide + hydrogen.

phosphate (97). Contemporary biochemical evidence suggests that the total aerobic yield from a single glucose molecule is ~30-32 ATP. This efficiency highlights why carbohydrates remain the preferred primary energy substrate of the human body. However, this high-efficiency system is also sensitive to nutrient overload. When carbohydrate intake exceeds

the capacity for oxidation and glycogen storage, the excess acetyl-CoA is redirected toward triglyceride synthesis, reinforcing the link between high-glycemic diets and adipose tissue expansion (98).

Energy balance and glycemic response. One glucose molecule is transformed into 38 ATP molecules during cellular respiration. One glucose molecule is broken up to produce two molecules of pyruvate, producing eight ATP directly from anaerobic glycolysis. Each three-carbon pyruvate yields one $NADH_2$ (equivalent to three ATP) during the pyruvate decarboxylation reaction. As a result, each six-carbon glucose molecule in this process generates six ATP. The total energy produced by each three-carbon pyruvate in the Krebs cycle is 12 ATP (91).

This quantity is generated by isocitrate dehydrogenase (+$NADH_2$ 3ATP), alpha-ketoglutarate dehydrogenase (+$NADH_2$=3ATP), malate dehydrogenase (+$NADH_2$=3 ATP), succinate dehydrogenase (+$FADH_2$=2 ATP) and succinate thiokinase (+GTP). As each six-carbon glucose molecule generates two three-carbon pyruvate molecules, the total quantity produced by one glucose molecule is 24 ATP. The glycolysis 8 ATP, the pyruvate dehydrogenase complex 6 ATP, and the Krebs cycle 24 ATP combine to yield 38 ATP (91).

The systemic health impact of carbohydrate metabolism is best observed through the glycemic response, the postprandial rise and fall of blood glucose. This response is governed by a delicate hormonal 'tug-of-war' between insulin and glucagon (99). High-bioavailability carbohydrates (simple sugars and refined starches) elicit a rapid insulin spike, which promotes glucose uptake via GLUT4 transporters in muscle and adipose tissue, while simultaneously suppressing lipolysis (99,100).

The connection here involves metabolic flexibility. In a healthy individual, the body can switch seamlessly between carbohydrate oxidation in the fed state and fat oxidation in the fasted state. However, a diet dominated by high-GI foods can lead to chronic hyperinsulinemia and eventual insulin resistance. This state represents a breakdown in systemic energy balance: Cells become starved of glucose despite elevated blood glucose levels, leading to increased hunger and a cycle of metabolic stress (44). Understanding these pathways emphasizes that the nutritional value of a carbohydrate is defined not only by its caloric content, but by its kinetic interaction with the body's metabolic machinery.

Divergent hepatic kinetics: Fructose vs. glucose metabolism. While glucose and fructose are structural isomers sharing the same caloric density, their metabolic destinies in the human body are fundamentally different due to divergent hepatic processing (101). Glucose metabolism is systemic; although the liver is a primary site for its regulation, glucose is utilized by nearly every cell in the body, and its entry into glycolysis is strictly governed by the energy status of the cell. By contrast, fructose is almost exclusively metabolized by the liver, and its entry into central metabolic pathways bypasses the most critical regulatory checkpoints (101,102).

The primary kinetic distinction lies in the first steps of phosphorylation. Glucose is converted to G-6-P by hexokinase or glucokinase. Fructose, however, is phosphorylated by fructokinase (ketohexokinase or KHK) to form fructose-1-phosphate (F-1-P). This enzyme is not inhibited by ATP or citrate. Furthermore, F-1-P is cleaved by aldolase B into DHAP and glyceraldehyde. These triose phosphates enter the glycolytic sequence downstream of the phosphofructokinase-1 (PFK-1) regulatory step (103,104). Essentially, the excess of fructose in the metabolic machinery provides a continuous supply of carbon precursors, such as acetyl-CoA, regardless of the actual energy requirements of the cell (105). Additionally, the subsequent conversion of fructose-6-phosphate to fructose-1,6-bisphosphate by PFK-1 is the rate-limiting step of glycolysis. When cellular ATP levels are high, PFK-1 is inhibited, decelerating glucose oxidation to prevent an unnecessary surplus of metabolic intermediates (103).

This unregulated flux has profound implications for metabolic health. As the liver is suddenly presented with an abundance of acetyl-CoA that it cannot oxidize in the TCA cycle, it must divert these carbons toward DNL. This leads to the synthesis of palmitate and other fatty acids, contributing to the accumulation of intrahepatic fat (non-alcoholic fatty liver disease, NAFLD) and the secretion of very-low-density lipoprotein, which raises blood triglyceride levels (106).

Furthermore, the rapid, uncontrolled phosphorylation of fructose by KHK leads to transient intracellular ATP depletion. As ATP is rapidly consumed to phosphorylate fructose without the brake of feedback inhibition, the resulting rise in AMP triggers the purine degradation pathway, leading to the production of uric acid. Elevated uric acid is not only a risk factor for gout, but also functions as a pro-oxidant within the hepatocyte, potentially inducing mitochondrial oxidative stress and further impairing insulin sensitivity (107,108). This kinetic reality explains why high-fructose diets, particularly those rich in refined syrups, are uniquely linked to metabolic syndrome, independent of total caloric intake.

Role of resistant starches and oligosaccharides in shaping the gut microbiota and the risk of metabolic disease. Resistant starches and oligosaccharides represent two critical classes of non-digestible carbohydrates that exert profound influence on gut microbial ecology and, consequently, on the risk of developing metabolic diseases, such as obesity, type 2 diabetes and cardiovascular disorders. Their biological significance stems not from caloric contribution, since they largely escape digestion in the small intestine, but from their role as selective substrates for beneficial gut commensals, thereby modulating microbial composition, metabolic output and host physiology (15).

Resistant starch is a form of starch that resists enzymatic hydrolysis by human amylases and reaches the colon intact, where it serves as a fermentable substrate for specific members of the gut microbiota. Primary degraders of resistant starch include *Ruminococcus bromii* and *Bifidobacterium adolescentis*, with emerging evidence identifying additional specialists such as *Ruminococcoides bili* (109). These bacteria initiate the breakdown of complex resistant starch granules through specialized carbohydrate-active enzymes (CAZymes), enabling secondary fermenters to access the resulting oligosaccharides and monosaccharides. This hierarchical degradation process fosters cross-feeding networks, thereby enhancing microbial diversity and stability. The fermentation of resistant starch predominantly yields SCFAs, notably butyrate, acetate and propionate, which serve as key mediators

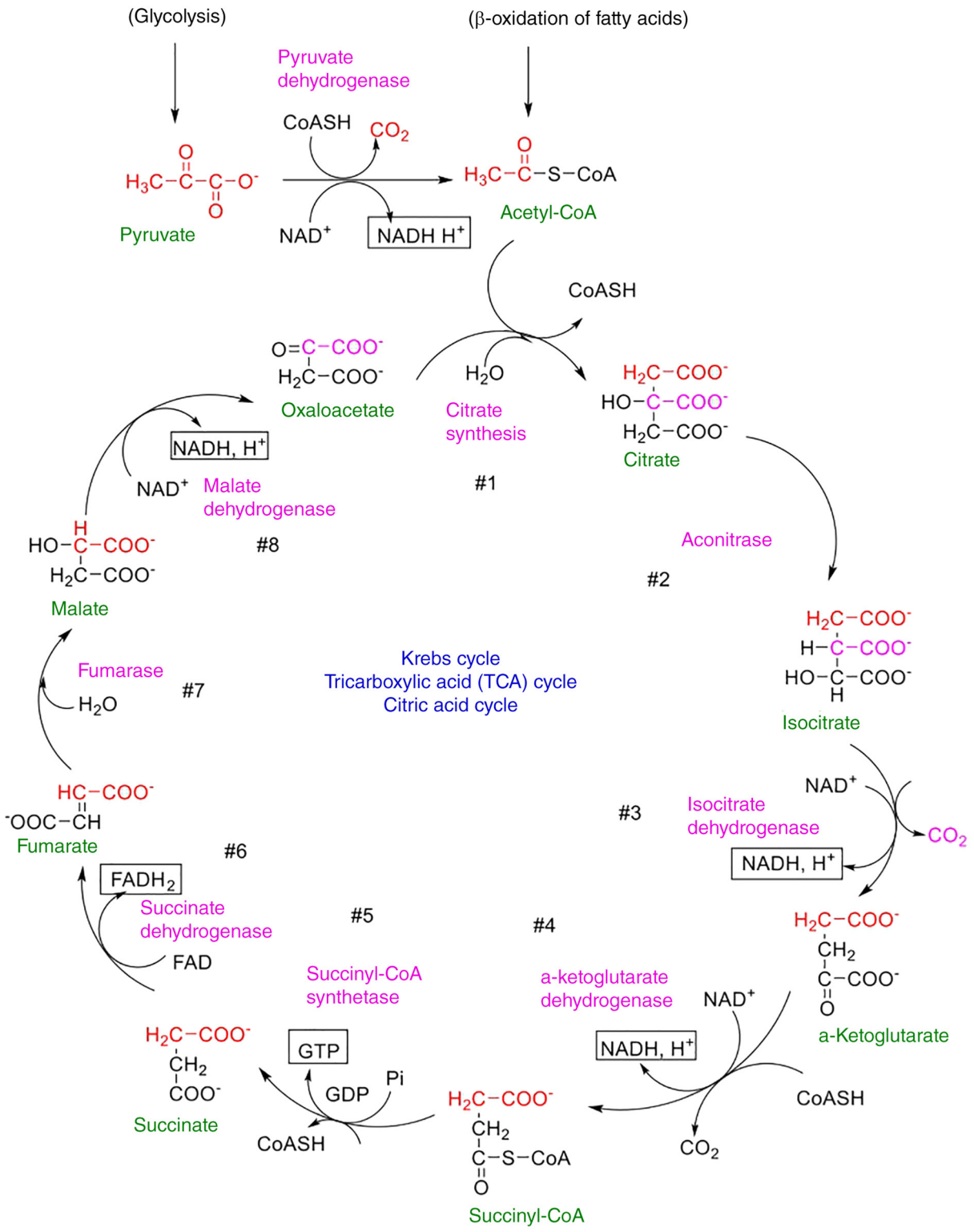

Figure 3. Schematic representation of the Krebs cycle. NAD, nicotinamide adenine dinucleotide; NADH, nicotinamide adenine dinucleotide + hydrogen; CoASH, coenzyme A; GTP, guanosine triphosphate.

of metabolic health. Butyrate, in particular, is the preferred energy source for colonocytes, strengthens the gut barrier by upregulating tight junction proteins, and exerts anti-inflammatory effects by inhibiting histone deacetylases and activating G-protein-coupled receptors (e.g., GPR109A). Clinical and preclinical studies consistently link higher a intake of resistant starch with improved insulin sensitivity, reduced adiposity and lower systemic inflammation, all of which are protective against cardiometabolic diseases (24,62).

Oligosaccharides, such as fructooligosaccharides (FOS), galactooligosaccharides and human milk oligosaccharides, function similarly as prebiotics by selectively stimulating the growth and activity of beneficial bacteria, especially *Bifidobacteria* and certain *Lactobacilli*. Their structural

complexity, defined by glycosidic linkage types [e.g., β(2→1) in inulin-type FOS] and the degree of polymerization, determines their resistance to host enzymes and specificity for microbial utilization. Research profiling the metabolic capacities of 17 gut commensal strains has revealed marked strain-specific differences in oligosaccharide fermentation, underscoring that prebiotic efficacy is contingent on both substrate structure and the recipient's microbial repertoire (110). This individualized response explains the variable outcomes observed in dietary interventions and highlights the need for personalized nutrition approaches. The SCFAs produced from oligosaccharide fermentation regulate host metabolism through multiple pathways: propionate reduces hepatic lipogenesis and gluconeogenesis, while acetate influences appetite regulation via central nervous system signaling (62). Moreover, oligosaccharides can directly inhibit pathogen adhesion by acting as decoy receptors, thereby enhancing gut defense mechanisms.

The interplay between these carbohydrates and the gut microbiome has significant implications for the prevention of chronic disease. Dietary fibers, including RS and oligosaccharides, are associated with a reduced risk of obesity, type 2 diabetes and types of certain cancer, largely through microbiota-dependent mechanisms (62,111). For instance, low-carbohydrate diets that inadvertently reduce fiber intake may diminish SCFA production, potentially compromising gut barrier integrity and promoting endotoxemia, a known driver of insulin resistance (111). Conversely, the strategic inclusion of high-quality, fermentable carbohydrates supports a resilient microbial ecosystem that buffers against dysbiosis induced by Western diets high in refined sugars and saturated fats (112). Notably, the concept of 'carbohydrate quality' now supersedes mere quantity; slowly digestible or non-digestible forms such as resistant starch and oligosaccharides are favored for their ability to modulate postprandial glycemia and sustain microbial health without contributing to hyperinsulinemia or DNL (24,112). Hence, resistant starches and oligosaccharides function as keystone dietary components that shape a health-promoting gut microbiota, drive beneficial metabolic signaling via SCFAs, and mitigate risk factors for major chronic diseases, positioning them at the nexus of food science, microbiome research and precision nutrition.

Despite these advances however, challenges remain in translating findings into universal dietary recommendations due to inter-individual variability in gut microbiota composition, host genetics and baseline metabolic status. Furthermore, the structural heterogeneity of dietary carbohydrates complicates analytical characterization and standardization. Emerging glycomic platforms combining chromatography and mass spectrometry are beginning to address these gaps by enabling precise mapping of carbohydrate structures to microbial responses (34).

5. The global intake trends of dietary fiber

In the 1970s, Burkitt's research (113,114) led to a resurgence of scientific interest in dietary fiber (97). Subsequent research has demonstrated a connection between the consumption of dietary fiber, body weight, metabolic processes and overall health. The consumption of dietary fiber is associated with a favorable body weight, a healthy gut microbiota and a lower risk of cardiovascular disease and mortality. It also enhances intestinal health and lowers the riss of developing cancer. The primary health benefits of dietary fiber and the risks of deficiency are discussed in this synopsis, with particular attention to the effects of abdominal obesity and overall metabolic health (61).

Global dietary fiber intake trends reveal a persistent and concerning gap between recommended levels and actual consumption across most populations worldwide. Current evidence indicates that median intake values typically range from 15 to 20 g per day, substantially below the widely accepted recommendations of 25-38 g per day for adults (8,115). This deficit is particularly pronounced in high- and middle-income countries where dietary patterns have markedly shifted toward energy-dense, nutrient-poor options. Recent global macrotrend analyses demonstrated that while some middle-income countries have experienced modest increases in fiber consumption over the past three decades, these improvements are often offset by concurrent rises in sodium intake and the consumption of UPFs (116). The Swiss National Nutrition Survey provides a compelling case study, demonstrating that a higher consumption of UPFs is significantly associated with a lower dietary fiber intake, highlighting the inverse association between industrial food processing and fiber adequacy (117). Similarly, data from the USA spanning 1999=2017 reveal only minimal increases in fiber consumption, with persistent racial disparities; African Americans consistently exhibit a lower fiber intake compared to other demographic groups, potentially contributing to elevated colorectal cancer rates in this population (118). In Chile, national surveys indicate that fiber intake remains suboptimal despite public health initiatives, with primary sources being traditional staples rather than diverse plant-based foods (119,120).

For example, according to a previous analysis, adults in the USA and Europe ingest 18-24 g of dietary fiber daily for men and 16-20 g for women, with grain products as the main source. This is approximately one-third of what is advised; the majority of Western populations wish to increase their intake by ~50%. According to the NHANES (National Health and Nutrition Examination Survey), dietary fiber intake was higher in European nations than in North American nations (97).

An emerging scientific debate centers on the differential physiological effects of various fiber types and sources, challenging the traditional view of fiber as a homogeneous nutrient category. Contemporary research increasingly distinguishes between isolated and intrinsic fiber, fermentable and non-fermentable varieties, and the impact of fiber across different dietary contexts, including low-carbohydrate and ultra-processed food frameworks. The controversy extends to regulatory definitions, particularly regarding low-molecular-weight carbohydrates, such as oligosaccharides and inulin, which are accepted as dietary fiber in many jurisdictions, but remain optional in the Codex Alimentarius definition, creating inconsistencies in nutritional labeling and research interpretation (121). This debate is further complicated by the recognition that the health benefits of fiber are not merely mechanical, but are profoundly mediated through interactions with the gut microbiome. Different fiber types serve as selective substrates for specific microbial taxa, leading to varied production profiles of SCFAs, such as acetate, propionate and

butyrate, which function as critical signaling molecules influencing immune regulation, metabolic homeostasis and even neurocognitive function (62,122,123).

Contemporary evidence from large-scale prospective cohort studies and comprehensive meta-analyses robustly supports the protective role of higher total fiber intake against major chronic diseases. The landmark Lancet systematic review established that every 8-g increase in daily fiber consumption is associated with a 5-27% reduction in mortality and the incidence of coronary heart disease, stroke, type 2 diabetes and colorectal cancer (8). This finding has been reinforced by more recent umbrella reviews encompassing millions of individuals, which confirm strong, credible associations between adequate fiber intake and reduced risk across diverse health outcomes (115). The mechanisms underlying these benefits extend beyond the traditional understanding of the role of fiber in gastrointestinal health to include modulation of the gut-brain axis, the enhancement of gut barrier integrity and the epigenetic regulation of immune function through SCFA-mediated histone deacetylase inhibition (123-125). Furthermore, fiber consumption has demonstrated specific protective effects in vulnerable populations, including the reduced risk of surgery for inflammatory bowel disease (126), improved metabolic parameters in obesity (127,128) and improved glycemic control in diabetes (129,130).

Despite this substantial body of evidence, several critical scientific questions remain unresolved. First, the causal vs. the associative nature of fiber-microbiome-host interactions requires further elucidation through well-designed intervention trials that account for interindividual variability in baseline microbiota composition and host genetics, such as the FUT2 secretor status, which influences microbial niche availability (62,122). Second, optimal dose-response associations for specific fiber types and distinct health endpoints have not been definitively established, rendering precise dietary recommendations challenging (115). Third, the relative efficacy of whole food vs. supplements or fortified foods in promoting long-term adherence and sustained health benefits remains unclear, particularly given the complex food matrix effects that may enhance fiber bioactivity (131,132). Fourth, the impact of modern food processing methods on fiber structure and functionality requires systematic investigation, as industrial processing may alter the physicochemical properties of fiber and, consequently, its biological effects (133,134). Finally, the development of personalized nutrition approaches necessitates a better understanding of how individual factors, including age, sex, metabolic status and existing disease conditions, influence responses to different fiber interventions, which could revolutionize dietary guidance from population-based to precision-based recommendations (135).

6. Medicinal aspects of carbohydrates

Among the bioactive glycosides that have been naturally extracted or derived, *O*- and *N*-glycosides are abundant, while *C*-glycosides (both naturally occurring and laboratory synthesized) make more stable bio-mimics than native *O*-glycosides as they are not prone to catalytic or enzymatic cleavage (136). These widespread classes of biomolecules play vital roles in immune system function and the stimulation of the immune response, which have yet to be properly explored by researchers. Several such carbohydrate-based drugs developed with potential biological activities are illustrated in Fig. 4 (137,138). Additionally, they have inherent chiral complexity, high bioavailability and excellent biocompatibility, rendering this class of compounds an excellent option for the development of prodrugs (139). Depending on the evidence, some carbohydrate-based medicines are given in Table II (140-157). It underscores the versatility of carbohydrates in drug design, delivery and therapeutic function, while emphasizing the importance of dosage control to minimize adverse effects.

Natural sources. Carbohydrates have not only been a major source of food and nutrition but also have excellent pharmaceutical applications. Carbohydrates derived from natural sources have been studied as therapeutic agents for a number of years. Among all carbohydrate-based drugs developed between 2000 and 2021, the majority have been derived from naturally occurring carbohydrate moieties, of which 37% are nucleosides. Furthermore, 60% of all carbohydrate-based drugs have broad applications in the preparation of antiviral, antibacterial/antiparasitic, anticancer and antidiabetic drugs (156). For instance, saponins, a diverse family of glycosides having brilliant adjuvant activity, such as *Quillaja brasiliensis* saponins (triterpene glycosides). Its source is the Chilean tree *Quillaja saponaria* bark. It has been reported to have >20 water-soluble *Quillaja saponaria* saponins, from which several led to the eliciting of humoral and cell-mediated responses (158). Similarly, in Asian countries, *Coriolus versicolor* polysaccharides (polysaccharides Krestin and Lentinan) have been used for >40 years as antitumor adjuvants (159). Pectin, a family of polysaccharides, is a fine source of dietary fiber. It has been reported to exhibit inhibitory activity against various cancer cell lines (160-164).

Synthetic carbohydrate-based materials. Structures of naturally occurring carbohydrates are often very complex due to their complex biosynthetic pathway. Hence, isolating structurally defined pure compounds from natural sources becomes cumbersome. To better address demands in glycobiology, synthetic carbohydrate derivatives or glycoconjugates comprise a fascinating alternative. Synthetic or non-natural glycoconjugates can aid in understanding structure-activity associations in biological responses and mimic the functions of native saccharide derivatives (165).

Some of the advantages of these synthetic carbohydrate-based materials stem from their biocompatibility and intrinsic biological functionality, resulting in generally low toxicity and excellent biodegradability, which are crucial for clinical translation (166). Their most significant asset is their ability to engage in specific, high-affinity interactions with carbohydrate-binding proteins (lectins, selectins and siglecs) that are central to numerous disease processes, including cancer, inflammation and infection This allows for the rational design of therapeutics that can modulate immune responses; for instance, synthetic glycopolymers can be engineered to mimic the multivalent presentation of glycans on cell surfaces, amplifying binding avidity through the 'glycocluster effect' to either activate or suppress immune cells for applications

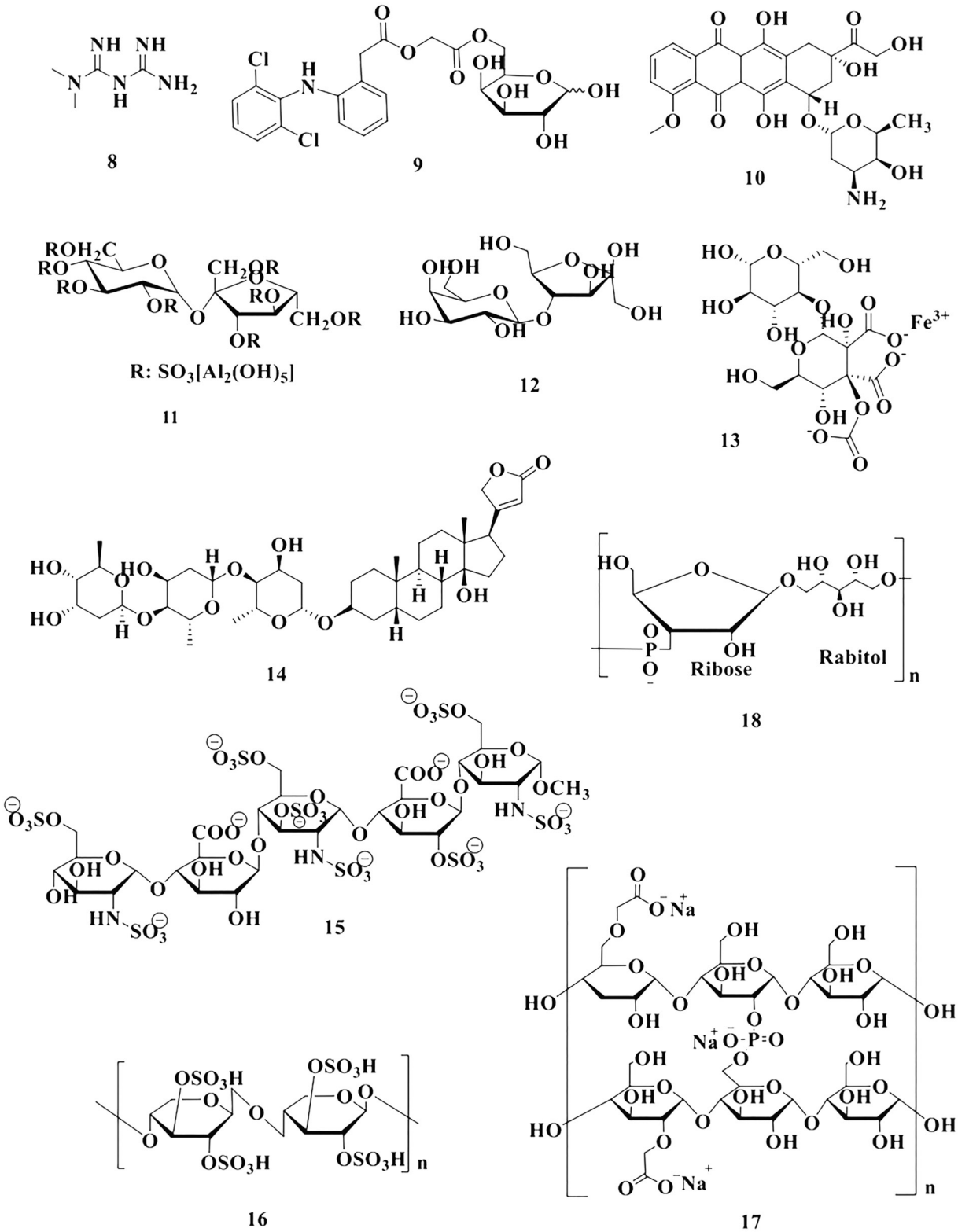

Figure 4. Molecular structures of carbohydrate-based medicines: Monosaccharides (panels 8, 9 and 10), disaccharides (panels 11, 12 and 13), tri-saccharides (panel 14), oligosaccharides (panels 15 and 16), and polysaccharides (panels 17 and 18).

in tumor immunotherapy (167,168). Furthermore, carbohydrate polymers, such as chitosan, alginate and hyaluronic acid serve as excellent scaffolds for targeted drug delivery, particularly for colon-specific release, as they can be degraded by colonic microflora enzymes, thereby minimizing systemic side-effects (169,170). The structural diversity of the sugar scaffold also provides multiple points for chemical modification, enabling fine-tuning of pharmacokinetic properties such as solubility and half-life (171).

Automated glycan assembly (AGA) has expedited access to synthetic glycans up to 50-mers (172), while other automated platforms based on electrochemical assembly (173),

Table II. Medicines derived from carbohydrate sources and their functions.

Category of carbohydrates	Types of carbohydrate	Medicine derived from the carbohydrate (Fig. 4)[a]	Activity on the body parts	Function of the medicine	Diseases caused by overdosage of the medicine (side-effects)	(Refs.)
Monosaccharides	Glucose	Metformin (no. 8)	Liver	To balance the production of glucose in the liver.	Induces gastrointestinal disturbance, lactic acidosis, hepatotoxicity, vitamin B12 deficiency, acute pancreatitis, hypoglycemia	(140,141)
	Galactose	ACEgal anti-inflammatory drug (aceclofenac with D-galactose) (no. 9)	Inflammatory tissues	Aceclofenac works by blocking the enzyme called cyclooxygenase (COX) which generates prostaglandins that causes pain, fever and inflammation	NA	(142)
	3-amino-2,3,6-trideoxy-L-lyxo-hexopyranose	Doxorubicin (no. 10)	Cancer cells	It regulates the growth of cancer cells by intercalating into DNA and inhibits the topoisomerase II and further it blocks DNA and RNA synthesis.	Cardiotoxicity, neuropathy, hepatotoxicity, nephrotoxicity, alopecia, typhlitis, myelosuppression, neutropenia, anemia, thrombocytopenia, nausea, and diarrhea	(143,144)
Disaccharides	Sucrose	Sucralfate (no. 11)	gastrointestinal (GI) tract	It stimulates the healing of duodenal ulcers by reducing pepsin activity in gastric juice in the stomach.	Constipation, aluminium toxicity, dry mouth & skin, headaches, nausea, vomiting, flatulence, low phosphate levels (hypophosphatemia)	(143,145)
	lactose	Lactulose (no. 12)	colon	It enhances the growth of beneficial bacteria such as *Lactobacilli*. It draws the water into colon and reduces constipation. It promotes gut health.	Lactulose affects the intestine, plasma metabolomes, and nitrogen metabolism.	(146,147)
	maltose	Ferric carboxymaltose (FCM)-Medication (no. 13)	Bone marrow	It promotes ferric iron into the bloodstream then utilized for the production of red blood cells in the bone marrow and it will be stored in the liver and spleen.	Acute renal failure, headache and aseptic meningitis, blood clots	(148,149)

Table II. Continued.

Category of carbohydrates	Types of carbohydrate	Medicine derived from the carbohydrate (Fig. 4)[a]	Activity on the body parts	Function of the medicine	Diseases caused by overdosage of the medicine (side-effects)	(Refs.)
Trisaccharides	A trisaccharide moiety attached to a steroidal aglycone	Digoxin (no. 14)	Heart	It inhibits sodium-potassium ATPase which leads to the increase of intracellular concentration of sodium and calcium. This leads to a chain of biochemical reactions that show multiple effects on cardiac muscle and the cardiovascular system.	Irregular heart rhythms, visual disturbances, confusion, dizziness, nausea and vomiting	(143,150)
Oligosaccharides	Heparin-derived pentasaccharide	Fondaparinu x-Injection (prefilled syringe) (no. 15)	Blood	It stimulates the action of antithrombin III against Factor Xa and it prevents blood clotting.	Headache and gastrointestinal disorders, including diarrhea, nausea and vomiting.	(151,152)
	Multiple β-D-xylopyranose units are chemically sulfated and linked together	Pentosan polysulfate (no. 16)	Blood	It works on the blood where it functions as a heparin-like anticoagulant & reduces the risk of blood clotting and intensifies the process of fibrinolysis.	Headache, Nausea,	(143,153)
Polysaccharides	Starch	Sodium starch glycolate (SSG)-pharmaceutical excipient (no. 17)	Stomach and small intestine.	It induces the effectiveness of medicines and by speeding up the process of tablet disintegration and drug release.	NA	(154)
	Ribosylribitol phosphate-carbohydrate-containing medication	*Haemophilus influenzae* type b (Hib) Vaccine (no. 18)	Immune cells in the bloodstream and lymphoid tissues.	It is a preventive vaccine protect the infections of the blood.	Redness, swelling or pain at the injection site, Low-grade fever, Fatigue.	(155-157)

[a]The numbers in parentheses correspond to the compound numbers presented in Fig. 4. NA, not available.

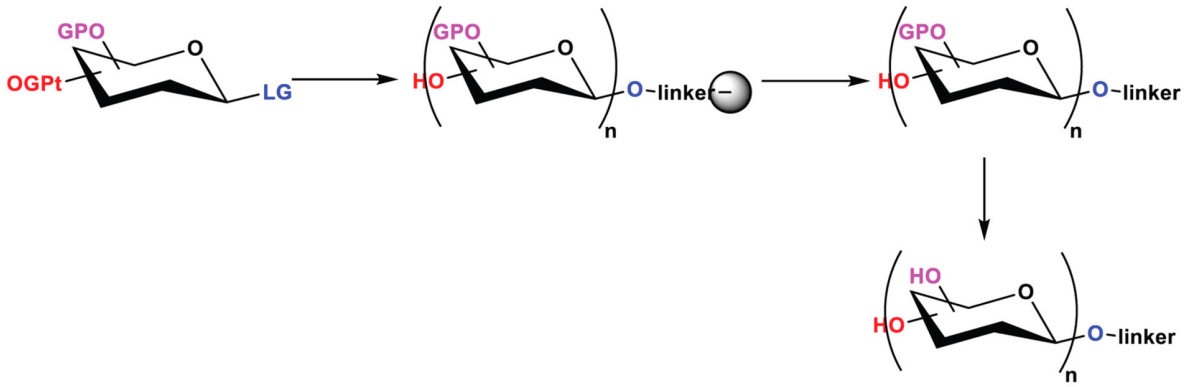

Figure 5. A general schematic representation of AGA oligosaccharide synthesis workflow.

fluorous-assisted solution-phase (174) and HPLC-assisted synthesis (175) have been limited to a few examples not exceeding hexasaccharides (176). From the proof-of-concept using a modified peptide synthesizer in 2001 to the first commercial Glyconeer 2.1 synthesizer (177), AGA has been developed using glycans of mammalian, bacterial and plant origin as a precursor (178,179).

The AGA oligosaccharide synthesis workflow is designed to minimize the number of purification steps and manipulations (Fig. 5). Inside the reaction vessel of the synthesizer, a resin-bound linker serves as an anchor for sequentially attaching monosaccharide building blocks. In this manner, excess reagents can be washed away, and time-consuming intermediate purification steps can be avoided. Following synthesis, the resin-bound oligosaccharide is removed from the synthesizer and cleaved from the solid support. Analytical normal-phase high-performance liquid chromatography (NP-HPLC) and MALDI analysis of the crude product after cleavage are used to assess the success of the synthesis qualitatively. The protected glycan is purified using preparative NP-HPLC. Global deprotection removes all permanent protecting groups and following reverse-phase HPLC (RP-HPLC), the unprotected glycan is obtained (177,178,180,181). This enhanced accessibility has directly fueled progress in glycomimetic design, in which natural carbohydrate leads are modified to overcome inherent limitations such as poor metabolic stability and low bioavailability (182). Common strategies include replacing the endocyclic oxygen with carbon (carbasugars) or sulfur (thiosugars), or substituting the glycosidic oxygen with a methylene group to form C-glycosides, all of which confer resistance to enzymatic hydrolysis by glycosidases (183).

Cyclodextrin (CD)-based materials have garnered applications in the food and pharmaceutical industries since the 1980s. For example, Sugammadex (Bridion), a modified γ-CD, has been used in anesthesia since 2008 and also functions as an antidote to some curare-like muscle relaxants (184). The electrostatic interaction and complex formation of CD with drugs can significantly alter the pharmacokinetic profile of a drug, and CD inclusion complex-based nanofibers have great applications in drug discovery and delivery, as they tend to increase the bioavailability of the drugs (185-187). For instance, the oral delivery of insulin is difficult owing to its instability in the gastric conditions of patients. However, reports suggest that carboxymethyl-β-CD-grafted chitosan (CMCD-g-CS) leads to the more effective oral delivery of insulin at pH 7.4 due to increased insulin bioavailability after pH-triggered complexation with CMCD-g-CS (188).

Other saccharide derivatives, such as imine sugars, have been suggested to function as potent inhibitors to several glycosidases, such as glycogen phosphorylases, glycoside hydrolases and glycosyltransferases. Their inhibitory potency against these carbohydrate-processing enzymes is suggested to depend on structural and electronic similarity to the oxocarbenium transition state of the natural substrate at a physiological pH (189,190).

Additionally, research on carbohydrate-conjugated noble metal-based nanoparticles, such as Au, Ag and Pt, has seen tremendous growth over the past few decades due to their applications in bioimaging, diagnostic imaging, biosensing, gene/drug delivery (targeted/triggered/controlled), targeted therapeutics. Despite their inertness, they can form a stable covalent linkage via facile synthetic methods with compounds containing functional groups, such as thiols and disulfides (16).

7. Carbotoxicity and its relevance to fructose-induced lipogenesis

Even though lipotoxicity (excess of lipids or a specific lipid class) is a more familiar term in the biomedical field, carbotoxicity is gaining increased recognition. The excessive ingestion of carbohydrates has the potential to degrade human health and ultimately cause the development of metabolic syndrome, diabetes, obesity and their multiple co-morbidities. Hence, the concept of 'carbotoxicity' was proposed in 2018, stating that non-cellulose-digestible carbohydrates can be toxic to a certain extent (12). Additionally, the PURE cohort study established a link between excessive carbohydrate consumption and adverse health effects worldwide (82). The study involved human subjects, demonstrating that a high intake of carbohydrates could increase the risk of mortality with a hazard ratio (HR) of 1.28 for highest 77.2% vs. lowest 46.4% quintile carbohydrate energy, which is significantly low with increasing fat intake with a HR of 0.77 (35.3 vs. 10.6% quintile energy) or excess protein consumption with a HR 0.88 (19.7 vs. 10.8% quintile energy) (82,191). Additional research has demonstrated that the excess intake of free sugars (monosaccharides and disaccharides) is associated with the risk of DNL in the liver, leading to the accumulation of a large number of lipids

and finally resulting in NAFLD; an increase in the hepatic DNL following a high-carbohydrate meal was found in ob/ob mice, Western-diet-fed mice and healthy individuals, which may increase the risk of hepatic steatosis (192). Another study with human trials demonstrated that carbohydrate-restricted diets, otherwise known as ketogenic diets, can serve as a good technique for weight loss and the management of type 2 diabetes (193), along with various antidiabetic therapies, including antidiabetic drugs that effectively improve hyperglycemia and hyperinsulinemia (194-196).

The investigation of fructose-induced lipogenesis through human clinical trials has been pivotal in establishing the mechanistic link between excessive dietary fructose consumption and metabolic dysfunction, forming a core component of carbotoxicity. Carbotoxicity posits that the chronic overconsumption of specific carbohydrates, particularly fructose, drives metabolic disease through the substrate overload of hepatic metabolic pathways, leading to ATP depletion, uric acid generation, mitochondrial stress and transcriptional upregulation of lipogenic enzymes (108). Unlike glucose, which is metabolized in a regulated manner under insulin control, fructose bypasses the rate-limiting enzyme phosphofructokinase, enabling unregulated entry into glycolysis and acetyl-CoA production, thereby fueling DNL, independent of insulin signaling. This property renders it uniquely hepatotoxic at high doses (108,197).

Several landmarks and recent clinical trials have provided robust evidence for this pathway. The foundational study by Schwarz *et al* (198) demonstrated that even a moderate increase in fructose intake can significantly affect liver metabolism. In that trial, 40 children with obesity were placed on an isocaloric diet, with fructose restricted to 4% of total calories, for 9 days. This intervention resulted in a marked 56% decrease in DNL, a 22% reduction in liver fat and significant improvements in insulin kinetics, all without any change in body weight. This finding was critical, as it established that the lipogenic effects of fructose are direct and rapid, and that its restriction can reverse key features of NAFLD and insulin resistance, independently of weight loss (198).

Building on this, the 2018 randomized crossover trial by Beysen *et al* (199) provided detailed dose-response data on acute fructose administration in healthy men. The study revealed that fructose feeding acutely and dose-dependently stimulates hepatic fractional DNL, with considerable inter-individual variability in susceptibility. That study quantified the immediate lipogenic potential of fructose and highlighted that not all individuals respond equally, suggesting a role for genetic or metabolic predisposition (199).

More recently, the narrative review by Geidl-Flueck and Gerber (200) and a post-publication peer review (letter to the editor) by Prinz (201) synthesized findings from multiple controlled feeding trials. Their research directly compared beverages sweetened with glucose, fructose and sucrose in healthy men. These studies demonstrated that fructose and sucrose, but not glucose, significantly increased hepatic DNL. These findings were instrumental in differentiating the metabolic effects of monosaccharides, confirming that fructose, as a component of both sucrose and high-fructose corn syrup, is the primary driver of sugar-induced lipogenesis.

The relevance of these trials to carbotoxicity is profound. They provide human experimental evidence validating the biochemical hypothesis: Excess fructose functions as a chronic metabolic stressor. The process begins with fructose metabolism in the liver, which rapidly depletes ATP and generates uric acid, a known inducer of oxidative stress and inflammation (202). Concurrently, the flood of carbon from fructose metabolism provides abundant substrate for DNL. This is further amplified by the activation of key transcription factors, such as carbohydrate-responsive element-binding protein and sterol regulatory element-binding protein-1c, which upregulate the entire lipogenic gene program (203). The resulting increase in the intrahepatic triglyceride content is a hallmark of NAFLD, which is now recognized as the hepatic manifestation of metabolic syndrome (204).

Furthermore, the gut microbiome has emerged as a crucial intermediary in this process. The pivotal study by Zhao *et al* (205) demonstrated that dietary fructose is not only metabolized by the liver, but also by the gut microbiota, which convert it to acetate. This microbiota-derived acetate is then used by the liver as an additional substrate for DNL, effectively creating a second pathway through which fructose promotes fat synthesis. This finding, highlighted in a commentary by Postic (206), underscores the systemic nature of the metabolic impact of fructose.

The cumulative evidence from these trials paints a consistent picture: Fructose is a potent, direct stimulator of hepatic DNL in humans. This mechanism is central to the pathophysiology of NAFLD, dyslipidemia and insulin resistance, all key components of metabolic syndrome. The concept of carbotoxicity integrates these findings, framing high fructose intake not merely as a source of empty calories, but as a specific metabolic toxin that disrupts hepatic homeostasis through defined molecular and physiological pathways. This understanding shifts the focus of dietary recommendations from simple caloric restriction to the quality of carbohydrate intake, emphasizing the need to limit added sugars, particularly those rich in fructose, to mitigate the risk of chronic metabolic diseases. The slow yet optimal strategy to address carbotoxicity, a potential cause of obesity, is to incorporate physical activity, dietary changes and lifestyle modifications, which can help manage body weight and contribute to improving metabolic syndrome, cardiovascular disease and premature mortality.

8. Future perspectives

Carbohydrates and their derivatives play a crucial role in several biological processes. Researchers have been involved in the synthesis, characterization and applications of carbohydrate derivatives for the past two decades. In continuation of the ongoing projects in carbohydrate chemistry (207-210), the present review attempted to elucidate the role of carbohydrates in nutrition, which further broadened our research area. Scientists are likely to focus on precision nutrition, tailoring carbohydrate composition in foods to individual needs based on genetic and metabolic factors. Socially, a growing demand for sustainable, plant-based options is driving the food industry to innovate with alternative carbohydrate sources. Health-conscious consumers may drive the development of functional carbohydrates with specific health benefits. Advances in biotechnology may lead to genetically modified

crops with improved carbohydrate profiles. Additionally, smart packaging technologies could help preserve the freshness and quality of carbohydrate-containing products.

9. Conclusion

Carbohydrates remain one of the most abundant, versatile and biologically influential macronutrients in the human diet. Far from functioning solely as sources of metabolic energy, carbohydrates operate at the intersection of food structure, digestion kinetics, metabolic regulation, microbial ecology and therapeutic innovation. Developments in glycomimetics, carbohydrate-based polymers and automated glycan assembly highlight their expanding role in therapeutics, immunomodulation and targeted drug delivery. Looking ahead, emerging paradigms, such as precision nutrition, microbiome-informed dietary strategies and structure-guided food processing approaches are poised to redefine carbohydrate functionality in both health and disease. In continuation of the ongoing project in carbohydrate chemistry, the present review attempted to briefly consolidate the roles of carbohydrates in the food industry, their nutritional value and their medicinal aspects, emphasizing their function as a critical macronutrient. Understanding the numerous functions of carbohydrates will aid in humans make better dietary decisions that will support their general well-being with healthier diets, functional foods and innovative therapeutics as aligning carbohydrate intake with physiological needs, while minimizing exposure to refined and ultra-processed forms, remains a central, evidence-based strategy for promoting metabolic health and preventing chronic disease in the modern era. The present review emphasizes the connection between carbohydrate-rich foods and human health, while promoting knowledgeable, sensible eating habits. By adopting a narrative review and perspective-based approach, the present review consolidates the current understanding of carbohydrates across nutrition, metabolism and therapeutics, while highlighting emerging concepts, such as carbotoxicity and precision nutrition.

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Availability of data and materials

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Authors' contributions

SP and TMD conceptualized the review topic and designed the manuscript framework. VA and JV conducted the literature search and screening of suitable literature. SP and VA wrote the initial draft of the manuscript and the figures/tables were prepared by VA and JV. TMD critically revised the manuscript for important intellectual content and supervised the project. All authors have read and approved the final manuscript. Data authentication is not applicable.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. Carocho M, Morales P and Ferreira ICFR: Natural food additives: Quo vadis? Trends Food Sci Technol 45: 284-295, 2015.
2. Chen Y, Michalak M and Agellon LB: Importance of nutrients and nutrient metabolism on human health. Yale J Biol Med 91: 95-103, 2018.
3. Moco S, Martin FPJ and Rezzi S: Metabolomics view on gut microbiome modulation by polyphenol-rich foods. J Proteome Res 11: 4781-4790, 2012.
4. Román S, Sánchez-Siles LM and Siegrist M: The importance of food naturalness for consumers: Results of a systematic review. Trends Food Sci Technol 67: 44-57, 2017.
5. Saleh ASM, Zhang Q, Chen J and Shen Q: Millet grains: Nutritional quality, processing, and potential health benefits. Compr Rev Food Sci Food Saf 12: 281-295, 2013.
6. Lu X, Chen J, Guo Z, Zheng Y, Rea MC, Su H, Zheng X, Zheng B and Miao S: Using polysaccharides for the enhancement of functionality of foods: A review. Trends Food Sci Technol 86: 311-327, 2019.
7. Mozaffarian D: Dietary and policy priorities for cardiovascular disease, diabetes, and obesity: A comprehensive review. Circulation 133: 187-225, 2016.
8. Reynolds A, Mann J, Cummings J, Winter N, Mete E and Te Morenga L: Carbohydrate quality and human health: A series of systematic reviews and meta-analyses. Lancet 393: 434-445, 2019.
9. Razouki AS, Hameed WR, Naeem BA, Falaih HH, Nassar SA and Mashchal MB: Metabolic effects of dietary fiber, carbohydrate, glucose, lipid metabolism on human health and nutritional therapy. Curr Clin Med Educ 3: 11-23, 2025.
10. Svihus B and Hervik AK: Digestion and metabolic fates of starch, and its relation to major nutrition-related health problems: A review. Starch - Stärke 68: 302-313, 2016.
11. Gao Q, Li Y and Wang L: Dietary Carbohydrate modulation in metabolic syndrome: Mechanistic insights, gut microbiota interactions, and precision nutrition approaches. Food Rev Int: 1-29, 2026.

12. Kroemer G, López-Otín C, Madeo F and de Cabo R: Carbotoxicity-noxious effects of carbohydrates. Cell 175: 605-614, 2018.
13. Kushwaha R, Vardhan PS and Kushwaha PP: Chronic kidney disease interplay with comorbidities and carbohydrate metabolism: A review. Life (Basel) 14: 13, 2023.
14. Topping DL and Clifton PM: Short-chain fatty acids and human colonic function: Roles of resistant starch and nonstarch polysaccharides. Physiol Rev 81: 1031-1064, 2001.
15. Liu H, Zhang M, Ma Q, Tian B, Nie C, Chen Z and Li J: Health beneficial effects of resistant starch on diabetes and obesity via regulation of gut microbiota: A review. Food Funct 11: 5749-5767, 2020.
16. Thodikayil AT, Sharma S and Saha S: Engineering carbohydrate-based particles for biomedical applications: Strategies to construct and modify. ACS Appl Bio Mater 4: 2907-2940, 2021.
17. Suri J and Gilmour R: Expediting glycospace exploration: Therapeutic glycans via automated synthesis. Angew Chem Int Ed Engl 64: e202422766, 2025.
18. Barrett JS and Gibson PR: Fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAPs) and nonallergic food intolerance: FODMAPs or food chemicals? Ther Adv Gastroenterol 5: 261-268, 2012.
19. Gilbert RG, Wu AC, Sullivan MA, Sumarriva GE, Ersch N and Hasjim J: Improving human health through understanding the complex structure of glucose polymers. Anal Bioanal Chem 405: 8969-8980, 2013.
20. Qi X and Tester RF: Fructose, galactose and glucose-In health and disease. Clin Nutr ESPEN 33: 18-28, 2019.
21. Duceac IA, Stanciu MC, Nechifor M, Tanasă F and Teacă CA: Insights on some polysaccharide gel type materials and their structural peculiarities. Gels 8: 771, 2022.
22. Tharanathan RN: Food-derived carbohydrates-structural complexity and functional diversity. Crit Rev Biotechnol 22: 65-84, 2002.
23. K R, S VK, Saravanan P, Rajeshkannan R, Rajasimman M, Kamyab H and Vasseghian Y: Exploring the diverse applications of Carbohydrate macromolecules in food, pharmaceutical, and environmental technologies. Environ Res 240: 117521, 2024.
24. Garrido-Romero M, Montilla A and Moreno FJ: Dietary carbohydrates: A trade-off between appealing organoleptic and physicochemical properties and ability to control glucose release and weight management. Curr Opin Food Sci 49: 100976, 2023.
25. Wang R, Hartel RW, Zhai X, Fu W, Sun Y and Wang S: Phase separation and gelation of gelatin-glucose syrup mixtures and gummy confections: Effects of moisture content, sugars, citric acid, and citrates. Food Hydrocoll 153: 110006, 2024.
26. Wang Q and Wood P: Carbohydrates: Physical properties. In: Handbook of Food Science, Technology, and Engineering. Hui YH (Ed). Vol. 1. CRC Press: Taylor & Francis, 2005.
27. Wang Y, Bai Y, Ji H, Dong J, Li X, Liu J and Jin Z: Insights into rice starch degradation by maltogenic α-amylase: Effect of starch structure on its rheological properties. Food Hydrocoll 124: 107289, 2021.
28. Han L, Wei Q, Cao S, Yu Y, Cao X and Chen W: The assisting effects of ultrasound on the multiscale characteristics of heat-moisture treated starch from Agriophyllum squarrosum seeds. Int J Biol Macromol 187: 471-480, 2021.
29. Tr'ân TN: The role of physical chemistry in food and beverage. Int J Sci Res Arch 13: 2959-2968, 2024.
30. Wang R, Zhai X, Hartel RW, Chang Y, Pang W, Han W, Lv H and Wang S: Effects of saccharide type and extended heating on the Maillard reaction and physicochemical properties of high-solid gelatin gels. Food Chem 459: 140249, 2024.
31. Urango ACM, Meireles MAA and Silva EK: Maillard conjugates produced from proteins and prebiotic dietary fibers: Technological properties, health benefits and challenges. Trends Food Sci Technol 147: 104438, 2024.
32. Wang W, Fan Z, Yan Q, Pan T, Luo J, Wei Y, Li B, Fang Z and Lu W: Gut microbiota determines the fate of dietary fiber-targeted interventions in host health. Gut Microbes 16: 2416915, 2024.
33. Lu X, Dai X, He W, Ma S and Gong N: Prebiotic Effects of Polysaccharides and Their Influence on Lactobacilli. In: Exploring Lactobacilli: Biology, Roles and Potential Applications in Food Industry and Human Health. Laranjo M (Ed.), IntechOpen, 2025.
34. Lee H, Song J, Lee B, Cha J and Lee H: Food carbohydrates in the gut: Structural diversity, microbial utilization, and analytical strategies. Food Sci Biotechnol 33: 2123-2140, 2024.
35. Hernandez-Hernandez O, Sabater C, Calvete-Torre I, Doyagüez EG, Muñoz-Labrador AM, Julio-Gonzalez C, de las Rivas B, Muñoz R, Ruiz L, Margolles A, *et al*: Tailoring the natural rare sugars D-tagatose and L-sorbose to produce novel functional carbohydrates. NPJ Sci Food 8: 74, 2024.
36. Sęczyk Ł, Sugier D, Świeca M and Gawlik-Dziki U: The effect of in vitro digestion, food matrix, and hydrothermal treatment on the potential bioaccessibility of selected phenolic compounds. Food Chem 344: 128581, 2021.
37. Song P, Huang Y, Li J, Shan S, Zhou Z, Cao H and Zhao C: The influence of processing technologies on the biological activity of carbohydrates in food. Food Chem X 23: 101590, 2024.
38. Chen X, Zhang W, Quek SY and Zhao L: Flavor-food ingredient interactions in fortified or reformulated novel food: Binding behaviors, manipulation strategies, sensory impacts, and future trends in delicious and healthy food design. Compr Rev Food Sci Food Saf 22: 4004-4029, 2023.
39. Urminská D, Haring N, Fábry V and Urminská J: Fermentable oligosaccharides, disaccharides, monosaccharides and polyols and their role in food digestion. J Microbiol Biotech Food Sci 11: e5521, 2022.
40. Borer KT: Relevance of milk composition to human longitudinal growth from infancy through puberty: Facts and controversies. Nutrients 17: 827, 2025.
41. Romero-Velarde E, Delgado-Franco D, García-Gutiérrez M, Gurrola-Díaz C, Larrosa-Haro A, Montijo-Barrios E Muskiet FAJ, Vargas-Guerrero B and Geurts J: The importance of lactose in the human diet: Outcomes of a Mexican consensus meeting. Nutrients 11: 2737, 2019.
42. Stanhope KL, Griffen SC, Bair BR, Swarbrick MM, Keim NL and Havel PJ: 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, 2008.
43. Khorshidian N, Shadnoush M, Zabihzadeh Khajavi M, Sohrabvandi S, Yousefi M and Mortazavian AM: Fructose and high fructose corn syrup: Are they a two-edged sword? Int J Food Sci Nutr 72: 592-614, 2021.
44. Aghaei B, Moradi F, Soleimani D, Moradinazar M, Khosravy T and Samadi M: Glycemic index, glycemic load, dietary inflammatory index, and risk of infertility in women. Food Sci Nutr 11: 6413-6424, 2023.
45. Grembecka M: Natural sweeteners in a human diet. Rocz Panstw Zakl Hig 66: 195-202, 2015.
46. den Berghe GV: How does blood glucose control with insulin save lives in intensive care? J Clin Invest 114: 1187-1195. 2004.
47. Wirfält E, McTaggart A, Pala V, Gullberg B, Frasca G, Panico S, Bueno-de-Mesquita H, Peeters PHM, Engeset D, Skeie G, *et al*: Food sources of carbohydrates in a European cohort of adults. Public Health Nutr 5: 1197-1215, 2002.
48. Sünram-Lea SI, Foster JK, Durlach P and Perez C: Glucose facilitation of cognitive performance in healthy young adults: Examination of the influence of fast-duration, time of day and pre-consumption plasma glucose levels. Psychopharmacology (Berl) 157: 46-54, 2001.
49. Alwahsh SM and Gebhardt R: Dietary fructose as a risk factor for non-alcoholic fatty liver disease (NAFLD). Arch Toxicol 91: 1545-1563, 2017.
50. Yu S, Li C, Ji G and Zhang L: The contribution of dietary fructose to non-alcoholic fatty liver disease. Front Pharmacol 12: 783393, 2021.
51. Rizkalla SW: Health implications of fructose consumption: A review of recent data. Nutr Metab (Lond) 7: 82, 2010.
52. Liu G, Hale GE and Hughes CL: Galactose metabolism and ovarian toxicity. Reprod Toxicol 14: 377-384, 2000.
53. Jiang Y, Pan Y, Rhea PR, Tan L, Gagea M, Cohen L and Yang P: A sucrose-enriched diet promotes tumorigenesis in mammary gland in part through the 12-lipoxygenase pathway. Cancer Res 76: 24-29, 2016.
54. Qi X and Tester RF: Lactose, maltose, and sucrose in health and disease. Mol Nutr Food Res 64: 1901082, 2020.
55. Misra V, Shrivastava AK, Shukla SP and Ansari MI: Effect of sugar intake towards human health. Saudi J Med 1: 29-36, 2016.
56. Misselwitz B, Butter M, Verbeke K and Fox MR: Update on lactose malabsorption and intolerance: Pathogenesis, diagnosis and clinical management. Gut 68: 2080-2091, 2019.
57. Poothullil JM: Maltose: The primary signal of hunger and satiation in human beings. Physiol Behav 52: 27-31, 1992.
58. Costa GT, Guimarães SB and de Carvalho Sampaio HA: Fructo-oligosaccharide effects on blood glucose: An overview. Acta Cir Bras 27: 279-282, 2012.

59. Niittynen L, Kajander K and Korpela R: Galacto-oligosaccharides and bowel function. Scand J Food Nutr 51: 62-66, 2007.
60. Otles S and Ozgoz S: Health effects of dietary fiber. Acta Sci Pol Technol Aliment 13: 191-202, 2014.
61. Anderson JW, Baird P, Davis RH JR, Ferreri S, Knudtson M, Koraym A, Waters V and Williams CL: Health benefits of dietary fiber. Nutr Rev 67: 188-205, 2009.
62. Delzenne NM, Bindels LB, Neyrinck AM and Walter J: The gut microbiome and dietary fibers: implications in obesity, cardiometabolic diseases and cancer. Nat Rev Microbiol 23: 225-238, 2024.
63. Tan Z, Yang C, Zhao Y, Yang X and Li T: Interactional effects of food macronutrients with gut microbiome: Implications for host health and risk. J Agric Food Chem 73: 19109-19132, 2025.
64. Mora-Flores LP, Moreno-Terrazas Casildo R, Fuentes-Cabrera J, Pérez-Vicente HA, de Anda-Jáuregui G and Neri-Torres EE: The role of carbohydrate intake on the gut microbiome: A weight of evidence systematic review. Microorganisms 11: 1728, 2023.
65. Frayn KN: Understanding human metabolism. Cambridge University Press, Cambridge, 2022.
66. Wilkinson JG and Liebman M: Carbohydrate metabolism in sport and exercise. In: Nutrition in Exercise and Sport, third edition. CRC Press, Boca Raton, FL, pp63-99, 2022.
67. Garrido G, Guzmán M and Odriozola JM: Effect of different types of high carbohydrate diets on glycogen metabolism in liver and skeletal muscle of endurance-trained rats. Eur J Appl Physiol Occup Physiol 74: 91-99, 1996.
68. Paoli A, Bosco G, Camporesi EM and Mangar D: Ketosis, ketogenic diet and food intake control: A complex relationship. Front Psychol 6: 27, 2015.
69. Dreher ML: Whole fruits and fruit fiber emerging health effects. Nutrients 10: 1833, 2018.
70. Yu W: Metabolic effects in C57B/6J mice fed a high-fat diet supplemented with chromium picolinate and chromium yeast. Honors College Thesis, 2019. https://ir.library.oregonstate.edu/concern/honors_college_theses/s1784s179.
71. Baky MH, Salah M, Ezzelarab N, Shao P, Elshahed MS and Farag MA: Insoluble dietary fibers: structure, metabolism, interactions with human microbiome, and role in gut homeostasis. Crit Rev Food Sci Nutr 64: 1954-1968, 2024.
72. Yao Y, Cai X, Fei W, Ye Y, Zhao M and Zheng C: The role of short-chain fatty acids in immunity, inflammation and metabolism. Crit Rev Food Sci Nutr 62: 1-12, 2022.
73. Song M, Wu K, Meyerhardt JA, Ogino S, Wang M, Fuchs CS and Chan AT: Fiber intake and survival after colorectal cancer diagnosis. JAMA Oncol 4: 71-79, 2018.
74. Tily H, Patridge E, Cai Y, Gopu V, Gline S, Genkin M, Lindau H, Sjue A, Slavov I, Perlina A,: Gut microbiome activity contributes to prediction of individual variation in glycemic response in adults. Diabetes Ther 13: 89-111, 2022.
75. Carmody RN, Varady K and Turnbaugh PJ: Digesting the complex metabolic effects of diet on the host and microbiome. Cell 187: 3857-3876, 2024.
76. Ludwig DS, Apovian CM, Aronne LJ, Astrup A, Cantley LC, Ebbeling CB, Heymsfield SB, Johnson JD, King JC, Krauss RM, *et al*: Competing paradigms of obesity pathogenesis: Energy balance versus carbohydrate-insulin models. Eur J Clin Nutr 76: 1209-1221, 2022.
77. Ludwig DS: Carbohydrate-insulin model: Does the conventional view of obesity reverse cause and effect? Philos Trans R Soc Lond B Biol Sci 378: 20220212, 2023.
78. World Health Organization: Sugars intake for adults and children. Geneva, 2015. https: //www.who.int/publications/i/item/9789241549028.
79. Ludwig DS, Hu FB, Tappy L and Brand-Miller J: Dietary carbohydrates: Role of quality and quantity in chronic disease. BMJ 361: k2340, 2018.
80. Williams KA, Fughhi I, Fugar S, Mazur M, Gates S, Sawyer S, Patel H, Chambers D, McDaniel R, Reiser JR, *et al*: Nutrition intervention for reduction of cardiovascular risk in african americans using the 2019 American college of cardiology/american heart association primary prevention guidelines. Nutrients 13: 3422, 2021.
81. Singh M, Hung ES, Cullum A, Allen RE, Aggett PJ, Dyson P, Forouhi NG, Greenwood DC, Pryke R, Taylor R, Twenefour D, *et al*: Lower carbohydrate diets for adults with type 2 diabetes. Br J Nutr 127: 1352-1357, 2021.
82. Dehghan M, Mente A, Zhang X, Swaminathan S, Li W, Mohan V, Iqbal R, Kumar R, Wentzel-Viljoen E, Rosengren A, *et al*: Associations of fats and carbohydrate intake with cardiovascular disease and mortality in 18 countries from five continents (PURE): A prospective cohort study. Lancet 390: 2050-2062, 2017.
83. Swaminathan S, Dehghan M, Raj JM, Thomas T, Rangarajan S, Jenkins D, Mony P, Mohan V, Lear SA, Avezum A, *et al*: Associations of cereal grains intake with cardiovascular disease and mortality across 21 countries in prospective urban and rural epidemiology study: Prospective cohort study. BMJ 372: m4948, 2021.
84. Malik VS, Li Y, Pan A, De Koning L, Schernhammer E, Willett WC and Hu FB: Long-term consumption of sugar-sweetened and artificially sweetened beverages and risk of mortality in US adults. Circulation 139: 2113-2125, 2019.
85. Yin J, Zhu Y, Malik V, Li X, Peng X, Zhang FF, Shan Z and Liu L: Intake of sugar-sweetened and low-calorie sweetened beverages and risk of cardiovascular disease: A meta-analysis and systematic review. Adv Nutr 12: 89-101, 2021.
86. Mahzari M and Mamun A: Does consumption of refined carbohydrates predict the incidence of type 2 diabetes mellitus? A systematic review and meta-analysis. Rom J Diabetes Nutr Metab Dis 27: 168-179, 2020.
87. Maffetone P and Laursen PB: Refined carbohydrates and the overfat pandemic: Implications for brain health and public health policy. Front Public Health 13: 1585680, 2025.
88. Lane MM, Gamage E, Du S, Ashtree DN, McGuinness AJ, Gauci S, Baker P, Lawrence M, Rebholz CM, Srour B, *et al*: Ultra-processed food exposure and adverse health outcomes: Umbrella review of epidemiological meta-analyses. BMJ 384: e077310, 2024.
89. Juul F, Vaidean G, Lin Y, Deierlein AL and Parekh N: Ultra-processed foods and incident cardiovascular disease in the framingham offspring study. J Am Coll Cardiol 77: 1520-1531, 2021.
90. Lacroix S, Cantin J and Nigam A: Contemporary issues regarding nutrition in cardiovascular rehabilitation. Ann Phys Rehabil Med 60: 36-42, 2017.
91. Maughan R: Carbohydrate metabolism. Surgery (Oxf) 27: 6-10, 2009.
92. Bolaños JP, Almeida A and Moncada S: Glycolysis: A bioenergetic or a survival pathway? Trends Biochem Sci 35: 145-149, 2010.
93. Chandel NS: Glycolysis. Cold Spring Harb Perspect Biol 13: a040535, 2021.
94. Akram M, Ali Shah SM, Munir N, Daniyal M, Tahir IM, Mahmood Z, Irshad M, Akhlaq M, Sultana S and Zainab R: Hexose monophosphate shunt, the role of its metabolites and associated disorders: A review. J Cell Physiol 234: 14473-14482, 2019.
95. Machado MG: The role of acetate in macrophages response against Streptococcus pneumoniae. Human health and pathology (unpublished thesis). Université de Lille, 2022.
96. Dashty M: A quick look at biochemistry: Carbohydrate metabolism. Clin Biochem 46: 1339-1352, 2013.
97. Stephen AM, Champ MMJ, Cloran SJ, Fleith M, van Lieshout L, Mejborn H and Burley VJ: Dietary fibre in Europe: Current state of knowledge on definitions, sources, recommendations, intakes and relationships to health. Nutr Res Rev 30: 149-190, 2017.
98. Theodorakis N, Kreouzi M, Pappas A and Nikolaou M: Beyond calories: Individual metabolic and hormonal adaptations driving variability in weight management-a state-of-the-art narrative review. Int J Mol Sci 25: 13438, 2024.
99. Vergari E, Knudsen JG, Ramracheya R, Salehi A, Zhang Q, Adam J, Asterholm IW, Benrick A, Briant LJ, Chibalina MV, *et al*: Insulin inhibits glucagon release by SGLT2-induced stimulation of somatostatin secretion. Nat Commun 10: 139, 2019.
100. Tiller NB, Roberts JD, Beasley L, Chapman S, Pinto JM, Smith L, Wiffin M, Russell M, Sparks SA, Duckworth L, *et al*: International society of sports nutrition position stand: Nutritional considerations for single-stage ultra-marathon training and racing. J Int Soc Sports Nutr 16: 50, 2019.
101. Tappy L: Metabolism of sugars: A window to the regulation of glucose and lipid homeostasis by splanchnic organs. Clin Nutr 40: 1691-1698, 2021.
102. Li Z, Fan X, Gao F, Pan S, Ma X, Cheng H, Nakatsukasa H, Zhang W and Zhang D: Fructose metabolism and its roles in metabolic diseases, inflammatory diseases, and cancer. Mol Biomed 6: 43, 2025.
103. Cirillo P, Gersch MS, Mu W, Scherer PM, Kim KM, Gesualdo L, Henderson GN, Johnson RJ and Sautin YY: Ketohexokinase-dependent metabolism of fructose induces proinflammatory mediators in proximal tubular cells. J Am Soc Nephrol 20: 545-553, 2009.

104. Federico A, Rosato V, Masarone M, Torre P, Dallio M, Romeo M and Persico M: The role of fructose in non-alcoholic steatohepatitis: Old relationship and new insights. Nutrients 13: 1314, 2021.
105. Tappy L and Lê KA: Metabolic effects of fructose and the worldwide increase in obesity. Physiol Rev 90: 23-46, 2010.
106. Zhu Z, Zhang X, Pan Q, Zhang L and Chai J: In-depth analysis of de novo lipogenesis in non-alcoholic fatty liver disease: Mechanism and pharmacological interventions. Liver Res 7: 285-295, 2023.
107. Khitan Z and Kim DH: Fructose: A key factor in the development of metabolic syndrome and hypertension. J Nutr Metab 2013: 682673, 2013.
108. Takir M, Kostek O, Ozkok A, Elcioglu OC, Bakan A, Erek A, Mutlu HH, Telci O, Semerci A, Odabas AR, *et al*: Lowering uric acid with allopurinol improves insulin resistance and systemic inflammation in asymptomatic hyperuricemia. J Investig Med 63: 924-929, 2015.
109. Kim YJ, Jung DH and Park CS: Important roles of Ruminococcaceae in the human intestine for resistant starch utilization. Food Sci Biotechnol 33: 2009-2019, 2024.
110. Bedu-Ferrari C, Biscarrat P, Pepke F, Vati S, Chaudemanche C, Castelli F, Chollet C, Rué O, Hennequet-Antier C, Langella P and Cherbuy C: In-depth characterization of a selection of gut commensal bacteria reveals their functional capacities to metabolize dietary carbohydrates with prebiotic potential. mSystems 9: e0140123, 2024.
111. Liu L, Sun T, Liu H, Li J and Tian L: Carbohydrate quality vs quantity on cancer risk: Perspective of microbiome mechanisms. J Funct Foods 118: 106246, 2024.
112. Pavani M, Geethika KV, Ramya D, Patibandla J and Sunitha A: The role of carbohydrate intake in obesity: Implications for diet and weight management. J Integral Sci 8: 16-21, 2025.
113. Burkitt DP and Trowell HC: Dietary fibre and western diseases. Ir Med J 70: 272-277, 1977.
114. Painter NS and Burkitt DP: Diverticular disease of the colon: A deficiency disease of western civilization. Br Med J 2: 450-454, 1971.
115. Veronese N, Gianfredi V, Solmi M, Barbagallo M, Dominguez LJ, Mandalà C, Di Palermo C, Carruba L, Solimando L, Stubbs B, *et al*: The impact of dietary fiber consumption on human health: An umbrella review of evidence from 17,155,277 individuals. Clin Nutr 51: 325-333, 2025.
116. Tao J, Quan J, El Helali A, Lam WWT and Pang H: Global trends indicate increasing consumption of dietary sodium and fiber in middle-income countries: A study of 30-year global macrotrends. Nutr Res 118: 63-69, 2023.
117. Schönenberger KA, Huwiler VV, Reber E, Mühlebach S, Stanga Z, Pestoni G and Faeh D: Dietary fibre intake and its association with ultraprocessed food consumption in the general population of Switzerland: Analysis of a population-based, cross-sectional national nutrition survey. BMJ Nutr Prev Health 7: 26-37, 2024.
118. Cifuentes L and O'Keefe S: Analysis of 1999-2017 NHANES data: Minimal increase and racial disparities in U.S. Fiber consumption over 18 years. Nutr Cancer 76: 345-351, 2024.
119. Guzmán C, Espinoza J and Fuentealba F: Pilot study to estimate dietary fiber intake in adults residing in chile. Nutrients 15: 900, 2023.
120. Guzmán C, Espinoza J, Durán-Agüero S, Obregón AM and Fuentealba F: Dietary fiber intake in chile: 13 years after the last national report. Nutrients 15: 3671, 2023.
121. Stribling P and Ibrahim F: Dietary fibre definition revisited-The case of low molecular weight carbohydrates. Clin Nutr ESPEN 55: 340-356, 2023.
122. Li L, Yan S, Liu S, Wang P, Li W, Yi Y and Qin S: In-depth insight into correlations between gut microbiota and dietary fiber elucidates a dietary causal relationship with host health. Food Res Int 172: 113133, 2023.
123. Xie L, Alam MJ, Marques FZ and Mackay CR: A major mechanism for immunomodulation: Dietary fibres and acid metabolites. Semin Immunol 66: 101737, 2023.
124. Gill SK, Rossi M, Bajka B and Whelan K: Dietary fiber in gastrointestinal health and disease. Nat Rev Gastroenterol Hepatol 18: 101-116, 2020.
125. Schneider E, Balasubramanian R, Ferri A, Cotter PD, Clarke G and Cryan JF: Fiber & fermented foods: Differential effects on the microbiota-gut-brain axis. Proc Nutr Soc 84: 365-380, 2025.
126. Deng M, Dan L, Ye S, Chen X, Wang X, Tian L and Chen J: Higher fiber intake is associated with reduced risk of related surgery among individuals with inflammatory bowel disease in a prospective cohort study. J Nutr 153: 2274-2282, 2023.
127. Deehan EC, Mocanu V and Madsen KL: Effects of dietary fiber on metabolic health and obesity. Nat Rev Gastroenterol Hepatol 21: 301-318, 2024.
128. Sharma D, Sharma L, Banerjee D and Dhama K: Effect of dietary fiber on obese/overweight persons and its mechanism of action: A systematic and meta-analysis on randomized controlled trials. Nutr Clin Métabol 39: 164-179, 2025.
129. Liu M: A review of the effects of dietary fiber on type 2 diabetes. Theor Nat Sci 124: 114-119, 2025.
130. Miketinas DC, Tucker WJ, Douglas CC and Patterson MA: Usual dietary fibre intake according to diabetes status in USA adults-NHANES 2013-2018. Br J Nutr 130: 1056-1064, 2023.
131. Biscarrat P, Bedu-Ferrari C, Langella P and Cherbuy C: Pulses: A way to encourage sustainable fiber consumption. Trends Food Sci Technol 143: 104281, 2024.
132. Sempio R, Segura Godoy C, Nyhan L, Sahin AW, Zannini E, Walter J and Arendt EK: Closing the fibre gap-the impact of combination of soluble and insoluble dietary fibre on bread quality and health benefits. Foods 13: 1980, 2024.
133. Wang Y, Jian C, Salonen A, Dong M and Yang Z: Designing healthier bread through the lens of the gut microbiota. Trends Food Sci Technol 134: 13-28, 2023.
134. Wang J, He S, Tao S, Ma S, Luo Y, Wu M and Zhou M: Structural, physicochemical, prebiotic properties of guava pulp insoluble dietary fiber and its quality enhancement ability on cow/goat yogurt: Impacts of ultrasound-assisted enzyme treatment. Food Biosci 58: 103797, 2024.
135. Aksornkitti V, Visuthranukul C, Leelahavanichkul A, Joyjinda Y and Sriswasdi S: Gut microbiome enterotypes and temporal variations during a six-month inulin-supplemented weight loss randomized controlled trial in Thai children with obesity. Comput Struct Biotechnol J 27: 5007-5019, 2025.
136. Wu X, Li S, Chen L, Ma S, Ma B, Song L and Qian D: Stereoselective construction of multifunctional C-glycosides enabled by nickel-catalyzed tandem borylation/glycosylation. J Am Chem Soc 146: 22413-22423, 2024.
137. van Kooyk Y and Rabinovich GA: Protein-glycan interactions in the control of innate and adaptive immune responses. Nat Immunol 9: 593-601, 2008.
138. Fernández-Tejada A, Cañada FJ and Jiménez Barbero J: Glycans in medicinal chemistry: An underexploited resource. ChemMedChem 10: 1291-1295, 2015.
139. Vasanthan RJ, Pradhan S and Thangamuthu MD: Emerging aspects of triazole in organic synthesis: Exploring its potential as a gelator. Curr Org Synth 21: 456-512, 2024.
140. LaMoia TE and Shulman GI: Cellular and molecular mechanisms of metformin action. Endocr Rev 42: 77-96, 2021.
141. Shurrab NT and Arafa ESA: Metformin: A review of its therapeutic efficacy and adverse effects. Obes Med 17: 100186, 2020.
142. Magliocca S, De Caro C, Lazzarato L, Russo R, Rolando B, Chegaev K, Marini E, Nieddu M, Burrai L, Boatto G, *et al*: Aceclofenac-galactose conjugate: design, synthesis, characterization, and pharmacological and toxicological evaluations. Mol Pharm 15: 3101-3110, 2018.
143. Klyosov AA: Carbohydrates and drug design. ACS Symp Ser 1021: 3-22, 2012.
144. Ajaykumar C: Overview on the side effects of doxorubicin. IntechOpen, 2021.
145. Putri SA, Purnomo RW and Savitri IJ: The potential of sucralfate as adjunctive therapy in the treatment of periodontal disease: A review. World J Adv Res Rev 25: 490-495, 2025.
146. Cao X, Du X, Jiao H, An Q, Chen R, Fang P, Wang J and Yu B: Carbohydrate-based drugs launched during 2000-2021. Acta Pharm Sin B 12: 3783-3821, 2022.
147. Panesar PS and Kumari S: Lactulose: Production, purification and potential applications. Biotechnol Adv 29: 940-948, 2011.
148. Ruszkowski J and Witkowski JM: Lactulose: Patient- and dose-dependent prebiotic properties in humans. Anaerobe 59: 100-106, 2019.
149. Bregman DB and Goodnough LT: Experience with intravenous ferric carboxymaltose in patients with iron deficiency anemia. Ther Adv Hematol 5: 48-60, 2014.
150. Boots JMM and Quax RAM: High-dose intravenous iron with either ferric carboxymaltose or ferric derisomaltose: A benefit-risk assessment. Drug Saf 45: 1019-1036, 2022.
151. Patocka J, Nepovimova E, Wu W and Kuca K: Digoxin: Pharmacology and toxicology-a review. Environ Toxicol Pharmacol 79: 103400, 2020.

152. Hricovíni M: Structural aspects of carbohydrates and the relation with their biological properties. Curr Med Chem 11: 2565-2583, 2004.
153. Donat F, Duret JP, Santoni A, Cariou R, Necciari J, Magnani H and de Greef R: The pharmacokinetics of fondaparinux sodium in healthy volunteers. Clin Pharmacokinet 41 (Suppl 2): S1-S9, 2002.
154. Anderson VR and Perry CM: Pentosan polysulfate: A review of its use in the relief of bladder pain or discomfort in interstitial cystitis. Drugs 66: 821-835, 2006.
155. Putra ON, Musfiroh I, Elisa S, Musa M, Ikram EHK, Chaidir C and Muchtaridi M: Sodium starch glycolate (SSG) from sago starch (metroxylon sago) as a superdisintegrant: Synthesis and characterization. Molecules 29: 151, 2023.
156. Stallforth P, Lepenies B, Adibekian A and Seeberger PH: 2009 Claude S. Hudson award in carbohydrate chemistry. Carbohydrates: A frontier in medicinal chemistry. J Med Chem 52: 5561-5577, 2009.
157. Campbell H and Carter H: Rational use of haemophilus influenzae type b vaccine. Drugs 46: 378-383, 1993.
158. Pifferi C, Fuentes R and Fernández-Tejada A: Natural and synthetic carbohydrate-based vaccine adjuvants and their mechanisms of action. Nat Rev Chem 5: 197-216, 2021.
159. Pan L, Cai C, Liu C, Liu D, Li G, Linhardt RJ and Yu G: Recent progress and advanced technology in carbohydrate-based drug development. Curr Opin Biotechnol 69: 191-198, 2021.
160. Maxwell EG, Colquhoun IJ, Chau HK, Hotchkiss AT, Waldron KW, Morris VJ and Belshaw NJ: Modified sugar beet pectin induces apoptosis of colon cancer cells via an interaction with the neutral sugar side-chains. Carbohydr Polym 136: 923-929, 2016.
161. Ji X, Peng Q, Yuan Y, Shen J, Xie X and Wang M: Isolation, structures and bioactivities of the polysaccharides from jujube fruit (Ziziphus jujuba Mill.): A review. Food Chem 227: 349-357, 2017.
162. Shao P, Chen X and Sun P: Chemical characterization, antioxidant and antitumor activity of sulfated polysaccharide from Sargassum horneri. Carbohydr Polym 105: 260-269, 2014.
163. Shao P, Pei Y, Fang Z and Sun P: Effects of partial desulfation on antioxidant and inhibition of DLD cancer cell of Ulva fasciata polysaccharide. Int J Biol Macromol 65: 307-313, 2014.
164. Yu Y, Shen M, Song Q and Xie J: Biological activities and pharmaceutical applications of polysaccharide from natural resources: A review. Carbohydr Polym 183: 91-101, 2018.
165. Bhavya PV, Rabecca Jenifer V, Ahmad Y and Mohan Das T: A simple perspective of glycosciences. J Indian Chem Soc 97: 157-176, 2020.
166. Lalhmangaihzuala S, Vanlaldinpuia K, Khiangte V, Laldinpuii Z, Liana T, Lalhriatpuia C and Pachuau Z: Therapeutic applications of carbohydrate-based compounds: A sweet solution for medical advancement. Mol Divers 28: 4553-4579, 2024.
167. Chen Y, Song J, Chen X and Chen G: Synthetic glycopolymers in tumor immunotherapy. Macromol Rapid Commun 46: e2401089, 2025.
168. Hulugalla K, Abodunrin OD, Anderson J, Smith AE and Werfel T: A 'sweeter' approach to cancer immunotherapy: Glycopolymers as diverse tools for immune modulation. J Control Release 388: 114372, 2025.
169. Bhirud D, Bhattacharya S and Prajapati BG: Bioengineered carbohydrate polymers for colon-specific drug release: Current trends and future prospects. J Biomed Mater Res A 112: 1860-1872, 2024.
170. Udaipuria N and Bhattacharya S: Novel carbohydrate polymer-based systems for precise drug delivery in colon cancer: Improving treatment effectiveness with intelligent biodegradable materials. Biopolymers 116: e23632, 2025.
171. Mishra VK, Khanna A, Tiwari G, Tyagi R and Sagar R: Recent developments on the synthesis of biologically active glycohybrids. Bioorg Chem 145: 107172, 2024.
172. Plante OJ, Palmacci ER and Seeberger PH: Automated solid-phase synthesis of oligosaccharides. Science 291: 1523-1527, 2001.
173. Nokami T, Hayashi R, Saigusa Y, Shimizu A, Liu CY, Mong KKT and Yoshida JI: Automated solution-phase synthesis of oligosaccharides via iterative electrochemical assembly of thioglycosides. Org Lett 15: 4520-4523, 2013.
174. Tang SL, Linz LB, Bonning BC and Pohl NLB: Automated solution-phase synthesis of insect glycans to probe the binding affinity of pea enation mosaic virus. J Org Chem 80: 10482-10489, 2015.
175. Ganesh NV, Fujikawa K, Tan YH, Stine KJ and Demchenko AV: HPLC-assisted automated oligosaccharide synthesis. Org Lett 14: 3036-3039, 2012.
176. Panza M, Pistorio SG, Stine KJ and Demchenko AV: Automated chemical oligosaccharide synthesis: Novel approach to traditional challenges. Chem Rev 118: 8105-8150, 2018.
177. Hahm HS, Schlegel MK, Hurevich M, Eller S, Schuhmacher F, Hofmann J, Pagel K and Seeberger PH: Automated glycan assembly using the glyconeer 2.1 synthesizer. Proc Natl Acad Sci USA 114: E3385-E3389, 2017.
178. Seeberger PH: The logic of automated glycan assembly. Acc Chem Res 48: 1450-1463, 2015.
179. Naresh K, Schumacher F, Hahm HS and Seeberger PH: Pushing the limits of automated glycan assembly: Synthesis of a 50mer polymannoside. Chem Commun (Camb) 53: 9085-9088, 2017.
180. Guberman M and Seeberger PH: Automated glycan assembly: A perspective. J Am Chem Soc 141: 5581-5592, 2019.
181. Niggemeyer GB, Danglad-Flores JA and Seeberger PH: Automated synthesis of C1-functionalized oligosaccharides. J Am Chem Soc 147: 1649-1655, 2024.
182. Yuan L, Hua Y and Wang X: Recent progress of glycomimetics in drug development. Org Biomol Chem 23: 7671-7680, 2025.
183. Martínez-Pascual R, Valera-Zaragoza M, Fernández-Bolaños JG and López Ó: Exploring the chemistry and applications of Thio-, Seleno-, and tellurosugars. Molecules 30: 2053, 2025.
184. Brandariz I and Iglesias E: Local anesthetics: Acid base behaviour and inclusion with cyclodextrin. Curr Org Chem 17: 3050-3063, 2013.
185. Jacob S and Nair AB: Cyclodextrin complexes: Perspective from drug delivery and formulation. Drug Dev Res 79: 201-217, 2018.
186. Jansook P, Ogawa N and Loftsson T: Cyclodextrins: Structure, physicochemical properties and pharmaceutical applications. Int J Pharm 535: 272-284, 2018.
187. Gadade DD and Pekamwar SS: Cyclodextrin based nanoparticles for drug delivery and theranostics. Adv Pharm Bull 10: 166-183, 2020.
188. Mansourpour M, Mahjub R, Amini M, Ostad SN, Shamsa ES, Rafiee-Tehrani M and Dorkoosh FA: Development of acid-resistant alginate/trimethyl chitosan nanoparticles containing cationic β-cyclodextrin polymers for insulin oral delivery. AAPS PharmSciTech 16: 952-962, 2015.
189. Lahiri R, Ansari AA and Vankar YD: Recent developments in design and synthesis of bicyclic azasugars, carbasugars and related molecules as glycosidase inhibitors. Chem Soc Rev 42: 5102-5118, 2013.
190. Tamburrini A, Colombo C and Bernardi A: Design and synthesis of glycomimetics: Recent advances. Med Res Rev 40: 495-531, 2020.
191. Wali JA, Raubenheimer D, Senior AM, Le Couteur DG and Simpson SJ: Cardio-metabolic consequences of dietary carbohydrates: Reconciling contradictions using nutritional geometry. Cardiovasc Dis 117: 386-401, 2021.
192. Gao Y, Hua R, Hu K and Wang Z: Carbohydrates deteriorate fatty liver by activating the inflammatory response. Nutr Res Rev 35: 252-267, 2022.
193. Webster C: Preliminary investigations for studying the effects of low carbohydrate high fat diets on gluconeogenesis in type 2 diabetes patients (unpublished thesis). University of Cape Town, 2020.
194. Bray GA, Fruhbeck G, Ryan DH and Wilding JPH: Management of obesity. Lancet 387: 1947-1956, 2016.
195. Patnode CD, Evans CV, Senger CA, Redmond N and Lin JS: Behavioral counseling to promote a healthful diet and physical activity for cardiovascular disease prevention in adults without known cardiovascular disease risk factors: Updated evidence report and systematic review for the US preventive services task force. JAMA 318: 175-193, 2017.
196. Nakamura M and Sadoshima J: Cardiomyopathy in obesity, insulin resistance and diabetes. J Physiol 598: 2977-2993, 2020.
197. Liao Y: Computational modelling of fructose metabolism and lipid deposition in non-alcoholic fatty liver disease (unpublished thesis). University College London, 2021.
198. Schwarz JM, Noworolski SM, Erkin-Cakmak A, Korn NJ, Wen MJ, Tai VW, Jones GM, Palii SP, Velasco-Alin M, Pan K, *et al*: Effects of dietary fructose restriction on liver fat, de novo lipogenesis, and insulin kinetics in children with obesity. Gastroenterology 153: 743-752, 2017.
199. Beysen C, Ruddy M, Stoch A, Mixson L, Rosko K, Riiff T, Turner SM, Hellerstein MK and Murphy EJ: Dose-dependent quantitative effects of acute fructose administration on hepatic de novo lipogenesis in healthy humans. Am J Physiol Endocrinol Metab 315: E126-E132, 2018.

200. Geidl-Flueck B and Gerber PA: Fructose drives de novo lipogenesis affecting metabolic health. J Endocrinol 257: e220270, 2023.
201. Prinz P: Comments on 'Fructose- and sucrose- but not glucose-sweetened beverages promote hepatic de novo lipogenesis-a randomized controlled trial'. J Hepatol 75: 753-754, 2021.
202. Brouwers MCGJ: Fructose 1-phosphate, an evolutionary signaling molecule of abundancy. Trends Endocrinol Metab 33: 680-689, 2022.
203. Iizuka K: The roles of carbohydrate response element binding protein in the relationship between carbohydrate intake and diseases. Int J Mol Sci 22: 12058, 2021.
204. Coronati M, Baratta F, Pastori D, Ferro D, Angelico F and Del Ben M: Added fructose in non-alcoholic fatty liver disease and in metabolic syndrome: A narrative review. Nutrients 14: 1127, 2022.
205. Zhao S, Jang C, Liu J, Uehara K, Gilbert M, Izzo L, Zeng X, Trefely S, Fernandez S, Carrer A, *et al*: Dietary fructose feeds hepatic lipogenesis via microbiota-derived acetate. Nature 579: 586-591, 2020.
206. Postic C: Conversion of a dietary fructose: New clues from the gut microbiome. Nat Metab 2: 217-218, 2020.
207. Pradhan S, Małecki JG and Mohan Das T: Highly selective iodide detection in solution and gel state using tuneable benzoate N-glucosides. Anal Sens 6: e202500083, 2026.
208. V RJ, Malecki JG and Thangamuthu MD: Photo-responsive organogelator based on cholesterol incorporated sugar-azobenzene derivatives. Carbohydr Res 549: 109356, 2025.
209. Bhavya PV, Malecki JG and Mohan Das T: Isoniazid-sugar-triazole-based fluorescent 'turn-on' chemosensor for Zn^{2+} and Mn^{2+} detection with potential biological applications. ChemistrySelect 10: e202405443, 2025.
210. Pradhan S, Hussain F, Małecki JG and Mohan Das T: Pyridine hydrazide glycoconjugate-based gelators: Facile synthesis and exploring their application in iodide sensing. J Mol Liq 416: 126529, 2024.