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Role of Carbohydrates and Herbal Plants in the Management of Diabetes Mellitus

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Abstract

This extensive review explores the intricate relationship between carbohydrates and diabetes mellitus, integrating historical perspectives, biochemical foundations, and modern therapeutic approaches. The article delves into the chemistry of carbohydrates, elucidating their structural diversity and metabolic significance in relation to diabetes pathophysiology. It traces the evolution of diabetes, understanding from ancient civilizations to contemporary molecular insights, highlighting pivotal discoveries such as insulin's identification. They critically examined various forms of diabetes, including Type 1, Type 2, and rarer variants like LADA and MODY, emphasizing their distinct etiologies and clinical presentations. A significant focus is placed on carbohydrate metabolism in diabetic states, exploring concepts such as the glycemic index, carbohydrate counting, and their implications for blood glucose management. Furthermore, the article investigates cutting-edge approaches in diabetes management, including the potential of medicinal plants and their bioactive compounds. It outlines six primary antidiabetic mechanisms, providing a comprehensive framework for understanding current and prospective therapeutic strategies. The review also addresses the complex interplay between lipid metabolism and carbohydrate homeostasis in diabetes, offering insights into the multifaceted nature of metabolic regulation. Another approach can also be employed by means of various phytoconstituents used for the treatment and management of the disease. The major anti-diabetic potential is seen within plants like White Mulberry, Fenugreek, Ceylon cinnamon, and Ginger. This comprehensive analysis synthesizes current knowledge and identifies critical areas for future research, making it an invaluable resource for healthcare professionals, researchers, and individuals seeking a deeper understanding of carbohydrate metabolism in the context of diabetes mellitus.

Keywords: Carbs and carbohydrates, diabetes mellitus, type I & type II diabetes, ginger, fenugreek

INTRODUCTION

Carbohydrates, often called carbs, are a major group of natural molecules found in living things. Back in the early 1800s, scientists discovered that materials like wood, starch, and linen were mostly made up of these carb molecules. These molecules share some key features. They all contain carbon, hydrogen, and oxygen atoms, and often have a simple ratio of hydrogen to oxygen (like 2:1). Because of this ratio, carbs are sometimes nicknamed "watered carbon" ($C_x(H_2O)_y$).

Importantly, carbs are the most abundant organic matter on Earth, and they are essential for all living things. Plants are the rockstars here – they use sunlight, water, and carbon dioxide to create carbs through a process called photosynthesis. These carbs then become the fuel that keeps all living things going, including us humans! [1].

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Carbs, short name for carbohydrates, are essential molecules that power our bodies. They are not just fuel, though! They also act as building blocks for important structures within us. Amazingly, even some of our genetic material, like DNA, contains carbohydrates! Along with protein and fat, carbs are one of the three main types of nutrients that humans need to stay healthy [2]. It is already known that carbs are superstars when it comes to giving our bodies energy. They are like tiny building blocks too. Made from a mix of carbon, hydrogen, and oxygen atoms, carbs come in a variety of shapes and sizes found in many foods.

TYPES OF CARBOHYDRATES

Two Main Types of Carbs

Simple Carbs

These carbs are the “sugar rush”. They are single or double sugar molecules, giving a quick burst of energy. Fruits, table sugar, and honey are all good examples [3, 4].

The body’s main source of fuel is carbs. When digested, they transform into glucose, the body’s primary cellular fuel. This glucose serves dual purposes: immediate energy production or storage within muscular tissue and hepatic cells for future metabolic needs. However, as a vehicle requires precise fuel management, carbohydrate intake demands careful consideration. Excessive consumption may contribute to adipose tissue accumulation and various metabolic disruptions, highlighting the importance of nutritional balance [2].

Uses

- *Quick energy source:* simple carbohydrates are quickly absorbed and can provide a quick energy boost.
- *Sports performance:* athletes may use simple carbohydrates as a quick source of energy during intense exercise [5].
- *Flavoring:* simple carbohydrates are often used to sweeten food and beverages.

Complex Carbs

These are the “slow and steady” carbs. Complex carbohydrates, conversely, consist of extended saccharide chains that undergo gradual enzymatic breakdown, facilitating sustained energy release throughout daily activities. Bread, pasta, and potatoes are full of these complex carbs [1].

Uses

- *Long-lasting energy source:* complex carbohydrates are broken down more slowly and provide a steady source of energy [6].
- *Satiety:* complex carbohydrates can help you feel fuller for longer periods, reducing the urge to snack on unhealthy foods [7].
- *Essential micronutrient reservoirs:* Complex carbohydrate-rich foods, particularly unrefined whole grain varieties, serve as vital repositories of essential nutrients, delivering a comprehensive spectrum of vitamins, minerals, and dietary fiber crucial for optimal physiological function. Overall, it is important to consume a balanced mix of simple and complex carbohydrates to maintain a healthy diet and provide the body with the energy and nutrients it needs.

As carbohydrate categorization, scientists have developed multiple taxonomic frameworks, with one prominent system delineating these biomolecules into four distinct classifications [8–15].

Types of Carbohydrates Based on Their Functional Group Composition

Most monosaccharide carbohydrates naturally occur in fruits, particularly grapes, and honey. While their molecular structure can incorporate between three to nine carbon atoms, the predominant forms typically feature five or six carbon atoms arranged in a linear molecular configuration. These fundamental sugar units can be further categorized based on two distinct chemical properties.

Aldoses

These represent monosaccharides featuring an aldehyde group (CHO) in their structure, with prominent examples including glucose, galactose, and ribose, essential in various biological processes.

Ketoses

These encompass monosaccharides containing a ketone group (C=O), with notable representatives including fructose, ribulose, and xylulose, each serving unique biochemical roles.

Disaccharides

These compounds represent the union of two monosaccharide units joined through glycosidic bonding:

- Sucrose emerges from the combination of one glucose and one fructose molecule.
- Lactose forms through the union of one glucose and one galactose molecule.
- Maltose results from the binding of two glucose molecules.
- Additional variants include trehalose, isomaltose, and cellobiose.

Oligosaccharides

These structures incorporate between three to ten monomeric units linked via glycosidic bonds.

- Maltotriose exemplifies a trisaccharide structure.
- Raffinose represents another trisaccharide configuration.
- Stachyose demonstrates a tetra-saccharide arrangement.
- Verbascose illustrates a penta-saccharide formation.

These compounds play crucial roles in cellular membrane composition and determine blood group antigens.

Polysaccharides

These complex structures contain more than ten monomeric units connected through glycosidic bonds, subdivided into two primary categories:

Homopolysaccharides

Composed exclusively of identical monosaccharide units. Starch serves as the primary energy storage molecule in plants. Glycogen functions as the animal equivalent for energy storage. Cellulose provides structural support in plant tissues. Inulin represents a fructose-based plant polysaccharide.

Heteropolysaccharides (Heteroglycans)

Incorporate multiple distinct monosaccharide units. Agar exemplifies this category-Glycosaminoglycans, including hyaluronic acid, heparin, heparan sulphate, dermatan sulphate, chondroitin sulphate, and keratan sulphate, demonstrates biological significance in various tissues.

Biological Relevance

The importance of carbohydrates for life cannot be overstated. Like most organisms, humans utilize both lipids (fats) and carbohydrates for energy storage. Lipids serve as a long-term energy source, while carbohydrates act as a readily available source for immediate energy needs. Cellular function hinges on the constant supply of glucose, the primary non-complex sugar circulating in the bloodstream. Maintaining proper glucose metabolism is therefore critical for survival [16].

The remarkable digestive capabilities of ruminant animals – cattle, sheep, and goats – serve as humanity's vital protein gateway, transforming grass-based polysaccharides into bioavailable protein sources.

In the realm of pharmaceutical science, carbohydrate derivatives have revolutionized medical treatment, with streptomycin emerging as a prime example of their therapeutic potential. Plants contain cellulose, which is used to create textiles, paper, and wood for building [17].

Like the body's dependence on various carbohydrates for energy, individual calorie requirements vary depending on factors like age and activity level. This daily energy need typically falls within a range of 2,000 to 4,000 calories (For context, the nutritional calorie measurement represents the energy expenditure required to elevate one kilogram of water's temperature by one degree Celsius.). Carbohydrates stand out as a preferred fuel source, offering 4 calories per gram compared to 9 calories per gram for fat. This metabolic conversion holds particular significance in geographical regions facing nutritional scarcity. In such settings, carbohydrates often contribute a significant portion of daily energy intake (around 1–2 pounds worth), with fats filling in the remaining energy gap [18].

Carbohydrates can make up a significant portion of human dietary intake, with some individuals consuming up to 80% of their daily calories from these energy sources. However, the specific types of carbohydrates consumed vary greatly depending on regional dietary customs. In regions of East Asia and Africa, where rice or starchy tubers like cassava (manioc) are staple foods, starch can contribute a substantial amount – as much as 80% – of total calorie intake. In contrast, Western diets typically feature a lower overall carbohydrate intake (around 33–50% of calories), with starch comprising roughly half of that (17–25%). Within Western diets, other carbohydrates play a role as well. Within human dietary patterns, disaccharides – specifically sucrose from table sugar and lactose from dairy – constitute approximately one-third of total carbohydrate consumption. Additionally, smaller amounts of simple sugars, such as glucose and fructose, are found in fruits, honey, syrups, and even some vegetables like artichokes, onions, and sugar beets [19]. The minimal amount that is left over is bulk, or indigestible carbohydrates, mostly found on the vegetable stalks and leaves as well as the cellulose coating on seeds.

ENERGY STORAGE ROLE

Starches, the primary polysaccharide energy source used by humans, are stored in plants in nearly spherical granules that have a size that ranges from 3–100 micrometers (or around 0.0001 to 0.004 inches). The two substances that make up most plant starches are amylose and amylopectin [20].

Amylose is made up of glucose molecules with a straight-chain, or linear, structure. Amylopectin is a compact molecule with a branched-chain structure. The molecular complexity of starch is remarkable, with individual molecules potentially incorporating thousands of interconnected glucose units within their structure. (In the illustration, each tiny circle stands for a single glucose molecule) (Figure 1) [21].

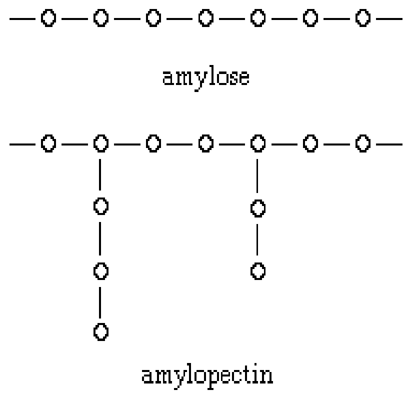

Figure 1. Amylopectin.

Within plant tissues, specialized cells known as parenchyma act as energy storehouses. These abundant cells are particularly prevalent in root crops and tubers, which serve as energy reserves for the plant during dormancy or growth spurts.

Starch, a complex carbohydrate, comes in various forms within plants. Seeds and cereal grains are champions in starch storage, containing up to 80% of their total carbohydrates in this form. Interestingly, the composition of starch itself differs between plant species. Starch is a combination of two main molecules: amylose and amylopectin.

Plant Amylose-Amylopectin Composition

The predominant starch storage mechanism in plants maintains a characteristic molecular ratio – approximately one-quarter amylose to three-quarters amylopectin. However, scientists have utilized selective breeding to create maize varieties with a starch composition that is up to 70% amylose. This is significant because amylose may be absorbed more quickly by the human body compared to amylopectin [22].

Alternative Plant Energy Storage

Certain plant species, notably the Jerusalem artichoke and select grass varieties including rye grass, synthesize fructose-based storage polysaccharides rather than glucose-based compounds. While these fructose polymers can undergo industrial processing into syrup formulations, they remain metabolically inaccessible to higher organisms [23].

While plants starch for energy storage, animals have their champion: glycogen. This complex carbohydrate, structurally like starch, serves as the primary energy reserve molecule in animals. Glycogen has a wider reach than starch in the animal kingdom. It is present in most vertebrates and invertebrates, as well as in many fungi and protozoans. However, the highest concentrations of glycogen are found in the liver and muscle cells of higher animals. These tissues act as a readily accessible energy reservoir for critical functions [24].

While structurally distinct from starch, glycogen shares a similar overall layout: a highly branched molecule composed of glucose units. This resemblance is particularly evident when compared to amylopectin, a major component of starch. For animals, glycogen serves as a critically readily available source of carbohydrates. During times of stress or exercise, the body rapidly converts glycogen stored in muscles to glucose, the body’s preferred fuel source. Hepatic glycogen as metabolic indicator: The quantitative presence of glycogen within hepatic tissue serves as a precise biological marker of an organism's overall nutritional equilibrium. Under conditions of adequate food intake, both glycogen and fat reserves within the body increase. However, during periods of limited food intake or when energy demand exceed consumption, these reserves are depleted. Unlike fat reserves, which are utilized at a slower rate, glycogen stores are broken down much quicker to meet immediate energy needs [25].

The Structural Importance of Polysaccharides in Plants and Animals

As starch and glycogen are the primary reserve polysaccharides in living organisms, most carbohydrates in nature play a structural role. Plant cell walls, for instance, are intricate structures composed of multiple carbohydrate layers. Notably, one of these layers boasts a significantly higher concentration of cellulose compared to the others. Cellulose, a key structural component of plant cell walls, exhibits stark physical and chemical differences when compared to amylose, the component of starch responsible for linear structure.

Carbohydrate Functional Diversity

Recognizing the structural and functional variations among carbohydrate molecules proves essential for comprehending their multifaceted biological roles across living systems [26].

A mixture of cellulose, pentose-containing polysaccharides (pentosans), and an inert (chemically unreactive) substance referred to as lignin make up most plants' cell walls, which are roughly 0.5 micrometers thick. Pentosan and cellulose content can range, although most plants contain between 40 and 60 percent of each, with higher concentrations seen in cotton fiber. In animals, polysaccharides serve as important structural elements. Insects and other arthropods contain chitin, a substance related to cellulose. The structural tissues of higher animals are dominated by other complex polysaccharides [23].

DIABETES MELLITUS

Diabetes mellitus represents a complex spectrum of metabolic disorders unified by the hallmark feature of chronic hyperglycemia. This hyperglycemia can arise due to two main mechanisms: either insufficient insulin production by the pancreas or impaired cellular response to insulin. In some cases, both factors can contribute. Individuals with uncontrolled diabetes often experience a constellation of symptoms, including frequent urination (polyuria), excessive thirst (polydipsia), and increased hunger (polyphagia). The etymology of this condition reflects its classical presentation - the term derives from ancient Greek, referencing a siphon, an apt metaphor for the characteristic symptom of excessive urination [27].

History of Diabetes Mellitus

The historical documentation of this metabolic disorder spans millennia, with initial medical recognition dating to the second century CE. This hyperglycemia can stem from two primary causes: a lack of insulin production (Type 1 diabetes) or the body's inability to effectively utilize insulin (Type 2 diabetes). Both forms of diabetes affect millions of people globally and, if left unmanaged, can lead to serious health complications. Ancient medical manuscripts from Mediterranean civilizations – Egyptian, Greek, and Roman – provided detailed clinical observations of diabetic manifestations. Greek physician Aretus, the Cappadocian coined the term "diabainein" to describe the condition, referencing the excessive urination (polyuria) experienced by patients. This historical term aptly reflects a key symptom of uncontrolled diabetes, where the body essentially loses fluids through frequent urination, mimicking the action of a siphon [28].

The term "diabetes" has a long and well-traveled path. English speakers adopted it from the Medieval Latin term for the condition, highlighting the enduring nature of this disease throughout history. Contemporary epidemiological data reveals the substantial global impact of this condition. The International Diabetes Federation identifies 463 million affected adults worldwide, significantly increasing from the 382 million cases recorded in 2013.

Type 1 diabetes, distinguished as insulin-dependent or early-onset diabetes, represents a distinct clinical entity within this broader spectrum. This variant typically manifests before age 40, with peak incidence during adolescence and young adulthood. Comprising approximately 10% of total diabetes diagnoses, Type 1 diabetes necessitates lifelong therapeutic intervention through insulin replacement. Management protocols demand rigorous glycemic monitoring and dietary modification to maintain metabolic homeostasis. He recognized the condition by its key symptoms: excessive urination and thirst. However, during the Middle Ages, a more descriptive, albeit less polite, term, "pissing evil," gained traction due to the prominent symptom of polyuria (excessive urination) [29].

From centuries, diabetes remained an enigmatic condition. It was not until the 17th century that English physician Thomas Willis distinguished diabetes as a separate disease entity. A key diagnostic tool at the time was the identification of a sweet taste in diabetic patients' urine. Fast forward to the early 20th century, a breakthrough discovery revolutionized diabetes management: the identification of insulin. Frederick Banting and Charles Best are credited with this landmark achievement, paving the way for the development of life-saving insulin therapy. The field of diabetes research continues to flourish. Since the discovery of insulin, advancements have included the development of new medications, improved monitoring devices, and a broader spectrum of treatment options. Despite these advancements, diabetes remains a significant global health concern. Contemporary epidemiological data from the International Diabetes Federation reveals a striking global prevalence, with 463 million adults affected by this metabolic disorder [30].

Type 1 Diabetes

This variant, alternatively designated as insulin-dependent or early-onset diabetes, manifests predominantly before the fourth decade of life, with peak incidence during adolescence and young adulthood. Within the diabetes spectrum, Type 1 represents a distinct minority, accounting for approximately one-tenth of total diagnoses. The therapeutic management necessitates perpetual insulin replacement therapy, coupled with systematic blood glucose monitoring and adherence to specific nutritional protocols [31].

Type 2 Diabetes

The pathophysiological basis of diabetes mellitus centers on dual metabolic disruptions: either insufficient pancreatic insulin production or compromised cellular insulin sensitivity, termed insulin resistance. These mechanisms fundamentally alter glucose homeostasis, leading to characteristic metabolic perturbations. Most diabetes cases, exceeding 90% globally, fall under the category of type 2 diabetes. For individuals with type 2 diabetes, managing blood sugar levels often involves a multi-pronged approach, including weight management, a balanced diet, regular exercise, and blood glucose monitoring. In some cases, these lifestyle modifications can effectively manage symptoms. The natural progression of Type 2 diabetes frequently demonstrates a temporal deterioration of metabolic control. This progression may necessitate therapeutic escalation to insulin supplementation, traditionally administered orally. Adiposity presents a significant risk modifier, with individuals exhibiting elevated body mass indices demonstrating markedly increased susceptibility compared to those maintaining normative weight parameters [32].

The link between sugary drinks and weight gain is well-established, researchers posit a more direct effect on diabetes risk. Contemporary research suggests that sugar-sweetened beverage consumption may independently influence Type 2 diabetes pathogenesis, operating through mechanisms distinct from adiposity-mediated pathways.

The temporal relationship between aging and Type 2 diabetes risk demonstrates a positive correlation. While the precise mechanistic underpinnings remain incompletely elucidated, current hypotheses implicate age-associated factors including progressive weight accumulation and declining physical activity patterns. Additionally, genetic predisposition, particularly evident in individuals of Middle Eastern, African, or South Asian ancestry, represents a significant non-modifiable risk factor, highlighting the complex interplay between genetic and environmental influences in disease development [33].

Different Variations of Type-2 Diabetes

Type 2 Diabetes

This most prevalent form of diabetes is either insufficient insulin production or impaired cellular response to insulin (insulin resistance). While typically diagnosed in adults, type 2 diabetes can also affect children.

Prediabetes

This condition serves as a precursor to type 2 diabetes. Individuals with prediabetes have blood sugar levels exceeding normal levels but not yet high enough to warrant a diagnosis of type 2 diabetes [34].

Diabetes Type 1

Type 2 diabetes represents an autoimmune pathology characterized by immunological destruction of pancreatic β-cells. While the precise etiology of this immunological dysregulation remains elusive, clinical manifestation can occur across the age spectrum, with predominant presentation in pediatric and young adult populations. A distinct form of diabetes, gestational diabetes, can develop during pregnancy in some women. This condition typically resolves after childbirth. Gestational diabetes warrants particular attention as it significantly amplifies a woman's subsequent risk for Type 2 diabetes development. This temporal relationship highlights the importance of long-term metabolic monitoring in affected individuals [35].

Other forms of diabetes include.

Diabetes Type 3c

In addition to the primary classifications of diabetes, a category known as secondary diabetes mellitus exists. Secondary diabetes emerges through non-autoimmune pancreatic injury, resulting in compromised insulin production capacity. This distinct pathophysiological mechanism differentiates it from primary diabetic conditions. Several conditions can contribute to pancreatic damage and subsequent secondary diabetes mellitus.

These include,

Pancreatitis

Pancreatitis represents a complex inflammatory pathology of the pancreatic tissue, manifesting in both acute and chronic forms, each capable of compromising endocrine function. This inflammatory process initiates a cascade of pathophysiological events that can significantly impair insulin production and secretion.

In acute manifestations, pancreatic inflammation typically triggers temporary metabolic disruptions. However, recurrent inflammatory episodes or chronic progression can lead to irreversible structural alterations within pancreatic tissue. These changes often result in permanent compromise of β-cell function, the specialized cellular units responsible for insulin synthesis and secretion.

The pathogenic mechanism involves progressive fibrotic transformation of functional pancreatic tissue, particularly affecting the insulin-producing islets of Langerhans. This fibrosclerotic process diminishes the pancreatic endocrine capacity, potentially culminating in pancreatogenesis diabetes, a distinct form of secondary diabetes mellitus.

Clinical significance extends beyond immediate metabolic derangements. Chronic pancreatitis patients face an elevated risk of developing diabetes, with epidemiological studies suggesting incidence rates between 30–50% among affected individuals. This risk is amplified with disease duration and severity, particularly in cases involving extensive tissue destruction or recurrent inflammatory episodes.

The therapeutic approach necessitates dual consideration of both the underlying pancreatic inflammation and potential metabolic complications. Management strategies must address both the primary inflammatory process and any resultant diabetic manifestations, often requiring a multifaceted treatment protocol to maintain optimal glycemic control.

Pancreatic Cancer

Pancreatic neoplasms represent a particularly aggressive form of malignancy with profound implications for endocrine function. Malignant cells' anatomical infiltration of pancreatic tissue creates a complex pathophysiological cascade that disrupts normal insulin biosynthesis and secretion mechanisms.

Neoplastic lesions within pancreatic tissue can compromise endocrine function through multiple pathways. Tumoral invasion directly destroys insulin-producing β-cells, while indirect effects manifest through altered pancreatic architecture and compromised cellular signaling networks. This dual mechanism of injury frequently results in disturbed glucose homeostasis.

The relationship between pancreatic malignancy and metabolic dysfunction often presents bidirectionally. New-onset diabetes mellitus may serve as an early clinical indicator of pancreatic neoplasia, particularly in individuals without traditional risk factors. Conversely, longstanding diabetes may predispose individuals to pancreatic cancer development, suggesting a complex interplay between metabolic dysfunction and oncogenesis.

Clinical manifestations often include progressive deterioration of glycemic control, potentially preceding other classical symptoms of pancreatic malignancy. This temporal relationship underscores the importance of vigilant monitoring for metabolic derangements in patients with pancreatic lesions, as early recognition may facilitate timely therapeutic intervention.

Management strategies must address both the underlying malignancy and resultant metabolic complications, often requiring an integrated approach to maintain optimal glycemic control while treating the primary neoplastic process.

Cystic Fibrosis

Cystic fibrosis represents an autosomal recessive genetic disorder characterized by mutations in the CFTR (Cystic Fibrosis Transmembrane Conductance Regulator) gene, manifesting with profound implications for pancreatic structure and function. The pathophysiological cascade initiated by defective chloride channels leads to progressive pancreatic tissue remodeling and subsequent endocrine dysfunction.

The mechanism of pancreatic injury in cystic fibrosis follows a distinct pattern: abnormal mucus secretion triggers obstruction of pancreatic ducts, leading to recurrent inflammation and progressive fibrotic transformation. This structural deterioration particularly affects the insulin-producing islets of Langerhans, culminating in compromised endocrine function and insulin deficiency, a condition termed cystic fibrosis-related diabetes (CFRD).

The temporal progression of pancreatic dysfunction typically manifests initially through exocrine insufficiency, followed by gradual deterioration of endocrine function. This sequential pattern reflects the differential vulnerability of pancreatic tissue components to CFTR-mediated damage. The prevalence of insulin deficiency increases with age in affected individuals, with approximately 40-50% of adult cystic fibrosis patients developing significant glucose homeostasis abnormalities.

Management strategies must address both the underlying genetic disorder and its metabolic complications, necessitating an integrated therapeutic approach encompassing both pancreatic enzyme replacement and careful glycemic control protocols.

Hemochromatosis: Hemochromatosis and Its Potential Link to Type 2 Diabetes

Hemochromatosis is a medical condition characterized by the excessive accumulation of iron in the body. This abnormal iron buildup can affect multiple organs, including the pancreas, which plays a crucial role in insulin production and blood sugar regulation.

In individuals with hemochromatosis, excess iron deposits in the pancreas can lead to cellular damage, impairing the function of insulin-producing beta cells. Over time, this disruption in insulin production and secretion can contribute to insulin resistance, a hallmark of type 2 diabetes. This connection highlights a potential variation in the development of type 2 diabetes, where the underlying cause is linked to iron overload rather than traditional risk factors like obesity or poor dietary habits.

The progression of iron-related damage in the pancreas emphasizes the importance of early detection and management of hemochromatosis. Regular monitoring of iron levels and timely interventions, such as therapeutic phlebotomy (removal of blood to reduce iron stores), can help mitigate the risk of complications, including diabetes.

Type 3c diabetes can potentially arise after having the affected pancreas removed (pancreatectomy).

Latent Autoimmune Diabetes in Adults (LADA): A Stealthy Form of Autoimmune Diabetes

Latent Autoimmune Diabetes in Adults (LADA) is a unique and often underdiagnosed form of autoimmune diabetes. Unlike classic type 1 diabetes, which typically manifests in childhood or adolescence, LADA develops more gradually and commonly occurs in adults over the age of 30. Its progression and clinical presentation often overlap with type 2 diabetes, leading to frequent misdiagnosis.

The hallmark of LADA lies in its autoimmune nature. The condition is caused by the immune system's attack on the insulin-producing beta cells in the pancreas. This autoimmune response is like type 1 diabetes; however, in LADA, the destruction of beta cells occurs at a slower pace. As a result, individuals with LADA initially retain some capacity to produce insulin, delaying the onset of symptoms and the need for insulin therapy compared to classic type 1 diabetes.

Clinical Features and Diagnosis

Patients with LADA often present with mild hyperglycemia that is manageable with oral antidiabetic medications initially, leading to confusion with type 2 diabetes. However, over time, as beta-cell function deteriorates, insulin dependency becomes inevitable. Key diagnostic markers include:

- The presence of autoantibodies (e.g., GAD antibodies) is commonly seen in type 1 diabetes.
- Reduced C-peptide levels, indicating diminished insulin production. There is a progressive need for insulin therapy despite lifestyle modifications and oral medications.

Implications and Management

The delayed recognition of LADA can lead to suboptimal treatment strategies. Early identification is crucial to tailor therapy, prevent complications, and preserve residual beta-cell function. Treatment often includes insulin therapy alongside lifestyle interventions to maintain blood sugar control [36].

Maturity-Onset Diabetes of the Young (MODY): A Genetic Form of Diabetes

Maturity-Onset Diabetes of the Young (MODY) is a rare, hereditary form of diabetes caused by mutations in a single gene, distinguishing it from the more common multifactorial types of diabetes, such as type 1 and type 2. Often referred to as monogenic diabetes, MODY primarily affects insulin production and utilization, leading to early onset hyperglycemia.

Unlike type 1 or type 2 diabetes, MODY does not typically involve autoimmune destruction of beta cells or insulin resistance. It usually develops in adolescence or early adulthood, hence the term "maturity-onset”. To date, over ten genetic subtypes of MODY have been identified, with each subtype linked to a specific gene mutation. Some of the most common gene mutations involve HNF1A, HNF4A, and GCK.

Prevalence and Familial Patterns

Although MODY accounts for only 1–5% of all diabetes cases, it often runs in families, exhibiting an autosomal dominant inheritance pattern. This familial tendency means that an affected individual has a 50% chance of passing the condition to their offspring.

Clinical and Diagnostic Considerations

MODY is frequently misdiagnosed as type 1 or type 2 diabetes due to overlapping symptoms. However, its unique genetic basis and milder disease course, in some cases, require tailored management. Genetic testing is crucial for accurate diagnosis, guiding treatment, and identifying affected family members [37].

Neonatal Diabetes Mellitus (NDM): A Rare Monogenic Diabetes in Infants

Neonatal diabetes mellitus (NDM) is a rare form of diabetes that appears within the first six months of life. As with Maturity-Onset Diabetes of the Young (MODY), NDM is classified as monogenic diabetes, meaning it arises from mutations in a single gene. This condition disrupts the body's ability to produce or regulate insulin, leading to hyperglycemia early in life.

Classification of NDM

NDM is categorized into two subtypes: persistent and transient**.**

Persistent Neonatal Diabetes Mellitus (PNDM)

This subtype accounts for approximately half of NDM cases and is lifelong. Infants with PNDM require ongoing management to control blood sugar levels and prevent complications.

Transient Neonatal Diabetes Mellitus (TNDM)

The other half of NDM cases is classified as TNDM, where hyperglycemia resolves spontaneously within a few months after diagnosis. However, TNDM is not always permanently resolved, as it can recur later in life, often during adolescence or adulthood.

Genetic Basis and Clinical Relevance

Common gene mutations associated with NDM include those in KCNJ11, ABCC8, and INS, among others. Genetic testing is critical for accurate diagnosis and personalized treatment strategies. For example, patients with specific mutations may benefit from sulfonylurea therapy instead of insulin injections, dramatically improving their quality of life [38].

Brittle Diabetes: A Severe and Unstable Form of Type 1 Diabetes

Brittle diabetes, also known as labile diabetes, is a rare and challenging subtype of type 1 diabetes. This condition is marked by extreme and unpredictable fluctuations in blood sugar levels, with patients experiencing rapid swings between hyperglycemia (elevated blood sugar) and hypoglycemia (low blood sugar). These dramatic variations can lead to significant physical and emotional strain, requiring careful and frequent medical attention.

Clinical Features and Challenges

The hallmark of brittle diabetes is its instability, which often results in recurrent hospitalizations. Managing this form of diabetes is particularly complex, as standard insulin regimens and dietary adjustments may prove insufficient to stabilize blood sugar levels. Episodes of severe hypoglycemia can cause confusion, seizures, or loss of consciousness, while persistent hyperglycemia increases the risk of long-term complications like cardiovascular disease and kidney damage.

Underlying Causes

While the exact mechanisms behind brittle diabetes remain unclear, contributing factors may include psychological stress, gastrointestinal disorders affecting insulin absorption, hormonal imbalances, and variability in insulin sensitivity. Poor adherence to treatment regimens and advanced complications of diabetes can also exacerbate the condition.

Treatment Approaches

Managing brittle diabetes requires a multidisciplinary approach, often involving continuous glucose monitoring (CGM), insulin pumps, and intensive patient education. In some severe and refractory cases, a pancreas transplant may be considered to provide long-term glycemic stability. Advances in closed-loop insulin delivery systems (artificial pancreas) offer promising solutions for better glucose regulation in such patients [39].

Symptom Severity Across Diabetes Types

The presentation of symptoms in diabetes can vary significantly depending on the underlying type. Individuals with type 1 diabetes typically experience a more severe manifestation of symptoms compared to those with type 2 diabetes (Figure 2) [40].

Diabetes symptoms include,

- Dry mouth and increased thirst (polydipsia).
- A lot of urine.
- Fatigue.
- Cloudy vision.
- Unaccounted-for weight reduction.
- Tingling or numbness in your hands or feet.
- Cuts and sores heal slowly.
- Recurrent yeast infections of the skin or vagina [41].

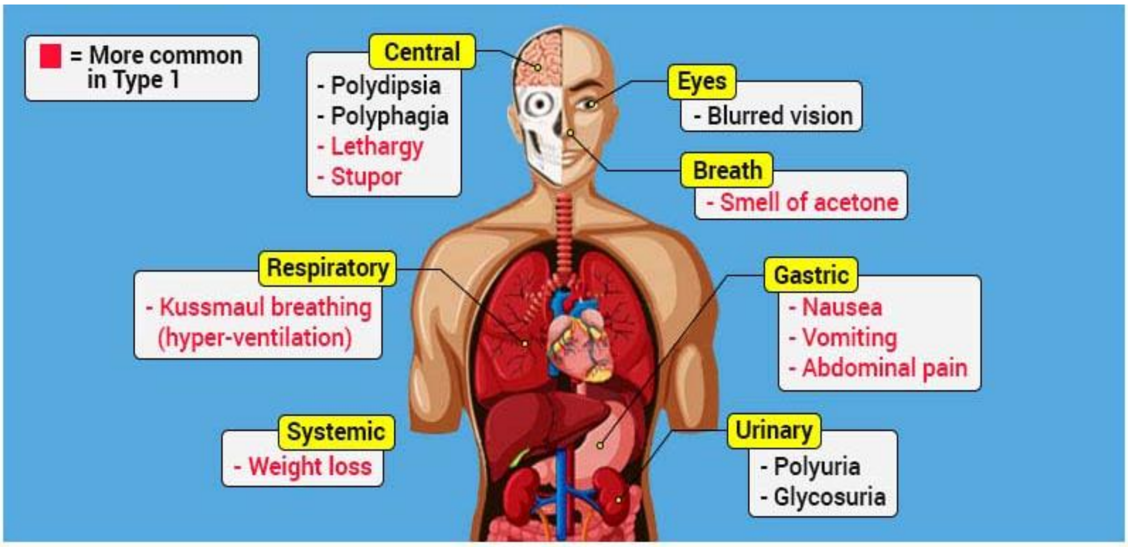

Figure 2. Symptoms of diabetes.

If any person or child exhibits these symptoms, it is crucial to speak with the healthcare professional.

Further information on diabetes symptoms per type is as follows. Diabetes type 1 (T1D) symptoms may appear within a few weeks or months. Diabetes-related ketoacidosis (DKA) is a potentially life-threatening complication of diabetes that requires immediate medical attention. It occurs when the body cannot utilize glucose for energy due to insufficient insulin levels, leading to the breakdown of fats and the production of acidic ketones, which accumulate in the bloodstream. Early recognition and prompt treatment of DKA are crucial to prevent severe outcomes. Vomiting, stomach discomfort, fruity breath, and difficulty breathing are all signs of DKA [42].

CHEMISTRY OF CARBOHYDRATES

Carbohydrates, ubiquitous biomolecules essential for life, play a pivotal role in the pathophysiology of Diabetes Mellitus. To comprehend their involvement in this metabolic disorder, it is crucial to first explore their fundamental chemistry.

Carbohydrates are organic compounds composed primarily of carbon, hydrogen, and oxygen atoms, typically in a 2:1 hydrogen to oxygen ratio. Their general formula, $(CH_2O)_n$ where $n \geq 3$, underlies a diverse array of structures and functions in biological systems.

Carbohydrates are the foundation of the body's energy metabolism. The simplest carbohydrates, monosaccharides, act as the basic units for more complex structures. Glucose, a pivotal hexose sugar in diabetes management, exists in both open-chain and cyclic forms in solution, playing a central role in cellular energy supply. Its ability to interconvert between these forms is critical for its metabolism and its role in diabetes.

The formation of glycosidic bonds between monosaccharides leads to more complex carbohydrates. Disaccharides like sucrose (glucose + fructose) and lactose (glucose + galactose) are common dietary components that significantly impact blood glucose levels. Polysaccharides, including glycogen and starch, are essential for energy storage and help maintain glucose homeostasis. Glycogen, stored in the liver and muscles, acts as a readily available energy reserve, especially during periods of fasting or physical activity.

The stereochemistry of carbohydrates, particularly the distinction between D- and L-isomers, is vital in biological systems. Enzymes involved in carbohydrate metabolism are typically specific to certain isomers, a factor that influences their processing in the body.

In biological systems, carbohydrates participate in several chemical reactions, such as oxidation and reduction, which are vital for glucose metabolism. However, in diabetes, these processes can lead to the formation of advanced glycation end-products (AGEs). AGEs are harmful compounds that contribute to the development of diabetic complications, such as vascular and tissue damage.

The reactivity of carbohydrates stems from their functional groups, particularly the hydroxyl (-OH) groups. These groups make carbohydrates hydrophilic, allowing them to form hydrogen bonds and interact with other molecules, which is essential for their biological functions and metabolic pathways. The carbonyl group (aldehyde or ketone) is crucial for many biochemical reactions, including the formation of glycosidic bonds and reactions with amino acids [43].

Monosaccharides: The Fundamental Units of Carbohydrates

Monosaccharides, the simplest form of carbohydrates, are single sugar units (mono- = “one”; sacchar- = “sugar”. Glucose, the most abundant monosaccharide in living organisms, is fundamental to cellular energy production and metabolic processes. These basic building blocks of carbohydrates typically possess a chemical formula of $(CH_2O)_n$ where n ranges from three to seven, indicating the variation in their carbon chain length [40].

Most of the oxygen atoms in monosaccharides are found in hydroxyl, O, and H groups, but one of them is part of a carbonyl (C=OC=O, C, O) group. The position of the carbonyl (C=OC=O, C group can be used to categorize the sugars [44, 45].

A sugar type is referred to as an aldose if it contains an aldehyde group, which indicates that carbonyl C is the last one in the chain.

If the carbonyl C is internal to the chain, meaning there are other carbons on both sides of it, it creates a ketone group, and the sugar is known as a ketose. Structurally, monosaccharides are classified based on the position of their carbonyl group. If the carbonyl carbon is located at the end of the carbon chain, forming an aldehyde group, the sugar is referred to as an aldose. Common sugars are further categorized by the number of carbon atoms they contain, such as trioses (three carbons), pentoses (five carbons), and hexoses (six carbons), with glucose being a prominent example of a hexose (Figure 3) [46].

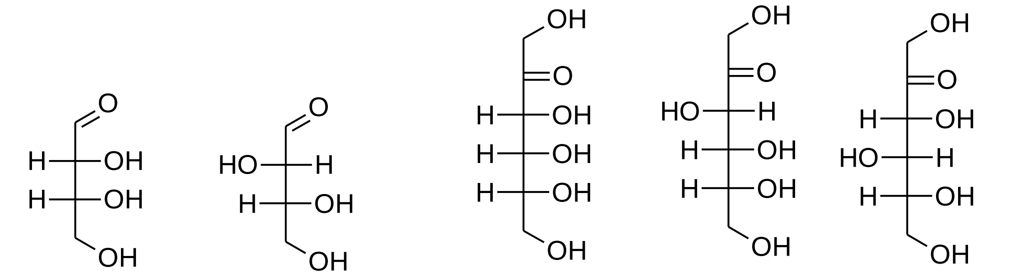

Figure 3. D-Erythrose and D-Threose as aldose, while D-Psicose, D-Fructose and D-Sorbose as ketose.

GENERAL OVERVIEW OF CARBOHYDRATES

In the context of type 1 diabetes mellitus (T1DM), managing blood glucose levels is paramount. One effective dietary strategy for individuals with T1DM is carbohydrate counting. This technique involves monitoring and calculating the amount of carbohydrate consumed during meals to better match insulin doses with the body's glucose needs. By accurately assessing carbohydrate intake, people with T1DM can achieve better glycemic control, minimize blood sugar fluctuations, and reduce the risk of diabetes-related complications. It can be used by people with T1DM who control their diabetes with either numerous daily injections (basal bolus regime) or continuous subcutaneous insulin infusion. It is used to modify insulin dose levels in accordance with the amount of carbohydrates in a meal and concentrates on carbohydrates as the main macronutrient impacting the postprandial glycemic response [47]. By counting carbohydrates, the patient is made aware of how foods high in carbohydrates affect blood sugar levels. Patients are instructed to visualize the amount of carbs by employing teaching aids like plate models or hand portions [48]. They are then instructed on how to administer the appropriate dose of insulin based on the amount of carbohydrate to avoid hyper- and hypoglycemia and maintain normal blood glucose levels. As part of self-management organized education, the National Institute for Health and Care Excellence (NICE) guidelines advise that carbohydrate counting be made available to all people with T1DM [49]. It is advised that it be offered one-on-one to individuals who are unable to participate in such structured education groups [50]. It has been demonstrated that carbohydrate counting can enhance both glycemic management and quality of life, but it must be taught by a professional with clinical knowledge in this area, such as a seasoned registered dietitian [50]. The Diabetes Control and Complications Trial (DCCT) trial's subjects employed carb counting, a nutrition intervention that has been around since the 1920s, in conjunction with aggressive insulin therapy to achieve normoglycemia. This approach worked well for glycemic control and provided flexibility in terms of dietary options. A meta-analysis of the most recent research on the effectiveness of carbohydrate counting in contrast to other diet strategies revealed that it significantly decreased levels of glycosylated hemoglobin (HbA1c) [51].

In the United States of America (USA) and the United Kingdom (UK), carbohydrate counting is suggested as routine medical therapy for the management of T1DM. The American Diabetes Association (ADA) suggests including carbohydrate counting in the standard of care for T1DM patients. The use of carbohydrate counting in T1DM in South Africa (SA) is not well documented. On a six-point Likert scale, when dietitians were asked to rate how much of the following assertions about their education in carbohydrate counting, they agreed with, dietitians substantially disagreed with the claims that their undergraduate education effectively prepared them for educating a patient with T1DM and that they had adequate instruction in carbohydrate counting. Dietitians strongly agreed that they needed additional training or instruction in the use of carbohydrate counting to manage patients with T1DM and significantly disagreed that they had obtained specialized training in the dietary management of diabetes. Dietitians overwhelmingly agreed that they would go to a training or teaching session on using carb counting, if they had access to it. They overwhelmingly concurred that they would find it helpful to use an online tool or resource (such as a mobile app or web-based calorie counting tool) while instructing their patients or clients on carbohydrate tracking [52].

Use of Carb Counting is Hampered by Certain Obstacles

Using a six-point Likert scale, respondents were asked to score their level of agreement about the obstacles to carbohydrate counting as a tool for managing a diabetes diet. The following factors were significantly cited by dietitians as obstacles to their use of carbohydrate counting in the management of diabetes: a lack of financial resources, a lack of dietitians' training or knowledge, a lack of experience using carbohydrate counting, a lack of confidence in using carbohydrate counting, patient illiteracy, a lack of time, a lack of blood glucose records, and a lack of patient motivation [53].

What Exactly Is a Glycemic Index?

Foods high in carbohydrates are ranked according to how rapidly their blood sugar levels are raised on the Glycemic Index (GI). Low GI foods boost glucose levels gradually while high GI foods elevate glucose levels much faster. It has been demonstrated that eating more nutritious low-GI meals may help people with diabetes lower their HbA1c by 5 mmol/mol.

Fruits and vegetables, nuts, seeds, porridge, muesli, bran-based cereals, multigrain or granary bread, pasta, new potatoes in their skins, sweet potatoes, basmati, long grain, or brown rice are examples of foods that have a lower glycemic index (GI). However, it must be noted that blood glucose will be affected more by the amount of carbohydrates ingested than by altering the GI of the meals [54].

The glycemic index (GI) of a food is a measure of how quickly it raises blood glucose levels after consumption, compared to pure glucose. Foods with a low GI produce a slower and more gradual increase in blood sugar, whereas those with a high GI led to rapid spikes. Understanding the factors that impact a food’s GI can help make informed dietary choices, especially for managing or preventing type 2 diabetes and associated cardiovascular conditions.

Food Processing

The degree of processing significantly affects a food's glycemic index. Whole grains that retain their bran and germ, such as brown rice and quinoa, have a lower GI compared to processed grains where these components are removed. Milling and refining grains make them easier to digest, which increases their GI. For instance, whole wheat berries have a lower GI than whole wheat bread or pasta. Choosing minimally processed grains can help maintain steady blood sugar levels and reduce the risk of metabolic diseases.

Physical Form

The texture and form of a grain also play a crucial role. Finely ground grains digest more quickly than coarsely ground or intact grains, leading to a higher GI. This is why consuming grains in their whole, unaltered form, such as steel-cut oats or whole barley, is more beneficial than consuming highly processed equivalents like instant oatmeal or white bread.

Dietary Fiber

High-fiber foods have a lower glycemic index because fiber slows digestion and the absorption of carbohydrates. This results in a controlled and gradual increase in blood sugar levels. Fiber-rich foods like legumes, vegetables, and whole grains are excellent for managing blood glucose and are linked to better cardiovascular health.

Ripeness of Fruits and Vegetables

As fruits and vegetables ripen, their starch content converts to sugar, increasing their GI. For instance, a ripe banana has a higher GI than a green banana. Being mindful of fruit ripeness can help regulate sugar intake, particularly for individuals needing tighter glucose control.

HEALTH IMPLICATIONS

Epidemiological studies have established a connection between high-GI diets and an increased risk of type 2 diabetes and coronary heart disease. Rapid glucose spikes from high-GI foods can lead to insulin resistance, inflammation, and other metabolic issues over time. Opting for low-GI foods can improve glucose control, reduce the risk of chronic conditions, and promote overall health. The connection between glycemic index and body weight, however, has received less research and is still debatable [55].

Glucose Load

The amount of digestible carbs in food provides, or the overall amount of carbohydrates excluding fiber, is one thing that a product's glycemic index does not reveal. For this reason, researchers created a related system for categorizing foods that considers both the quantity of carbohydrates in the food and how it affects blood sugar levels. The glycemic load is the name of this measurement [54]. Glycemic load (GL) is a more comprehensive measure than glycemic index (GI) as it accounts for both the quality (GI) and quantity of carbohydrates in a food portion. It provides a clearer picture of how a specific food affects blood sugar levels.

Calculating Glycemic Load

The following formula determines the glycemic load of a food:

GL= GI × Carbohydrate Content (grams) / 100

GL = GI × Carbohydrate Content (grams) / 100

This calculation helps to evaluate how a standard portion of food impacts blood sugar levels, not just how quickly it causes a spike.

High Glycemic Load (≥20)

Foods in this category can cause significant blood sugar spikes and are best consumed sparingly. Examples include white bread, sugary snacks, and some processed foods.

***Medium Glycemic Load** (11–19)*

These foods have a moderate impact on blood sugar and can be included in a balanced diet when consumed in moderation.

Low Glycemic Load (≤10)

Foods with a low glycemic load have a minimal effect on blood sugar levels and are ideal for frequent consumption. Examples include non-starchy vegetables, legumes, and certain whole grains.

Dietary Recommendations

For optimal health, particularly for individuals with diabetes or those at risk of developing it, focus on (Table 1).

Low GL Foods

Prioritize foods with a low glycemic load to maintain steady blood sugar levels. Examples include leafy greens, lentils, and whole grains like quinoa or barley.

Moderate GL Foods

Include these in controlled portions to maintain a balanced diet.

Limit High GL Foods

Reduce the intake of high GL foods like sugary drinks, white rice, and processed snacks to prevent blood sugar spikes and reduce the risk of insulin resistance and related complications.

It has been investigated using the glycemic load whether high-glycemic load meals are linked to an increased risk of type 2 diabetes and cardiac events. Researchers concluded that patients with type 2 diabetes were less likely to consume diets rich in higher glycemic load items after conducting a major meta-analysis of 24 prospective cohort studies [55]. Higher-glycemic load diets were similarly linked to an elevated risk for coronary heart disease events, according to a comparable meta-analysis [56–62]. The foods with low, medium, and high glycemic loads are listed below. We need to choose food with a low or medium glycemic load for optimal health and consume fewer items with a high glycemic load [63].

Table 1. Glycemic Index (GI) categories: Foods classified by their impact on blood sugar levels.

Low GI with Below 10 or Less	(11–19) Medium GI	High Glycemic Index (Above 20)
• Grains with bran • Apple Orange • Mung beans • Brown beans • Lentils • Corn tortillas • Lite milk • Cashews • Peanuts • Carrots	• Barley with pearls: 1 cup prepared. • Cooked 3/4 cup of brown rice. • 1 cup cooked oats. • 3/4 cup cooked bulgur. • 3 cakes made of rice. • Slice of whole-grain bread. • Cooked whole-grain pasta, 1 1/4 cups.	• Fried potatoes baked in the oven. • 1 oz. of refined cereal for breakfast. • 12 ounces of beverages with added sugar. • 1 2-oz bar of candy or 3 mini bars. • One cooked cup of couscous. • Cooked white basmati rice, 1 cup. • Cooked white-flour pasta, 1 1/4 cups.

The Role of Carbohydrates in Type 1 Diabetes Management

Carbohydrates play a central role in energy metabolism, as they are broken down into glucose, the body’s primary source of fuel. In individuals without diabetes, this process is seamlessly regulated by insulin, a hormone produced by the pancreas. Insulin facilitates the uptake of glucose by cells, ensuring stable blood sugar levels and efficient energy utilization.

In type 1 diabetes, however, this natural regulation is impaired because the pancreas is unable to produce insulin. As a result, individuals with this condition must rely on external sources of insulin, known as exogenous insulin, to manage their blood glucose levels. This is typically administered via injections or an insulin pump.

The relationship between carbohydrate consumption and blood sugar levels is particularly significant for people with type 1 diabetes. Each meal or snack containing carbohydrates directly influences blood glucose levels, requiring careful monitoring and precise insulin dosing to prevent fluctuations. This delicate balance underscores the importance of understanding carbohydrate intake, portion control, and the timing of insulin administration in managing the condition effectively. This external insulin helps transport glucose from the bloodstream into cells, effectively lowering blood sugar levels after consuming carbohydrate-rich foods. Two common insulin regimens used for type 1 diabetes management include basal-bolus therapy (providing a continuous background level of insulin) and multiple daily injections (mimicking the body’s natural insulin release patterns) [31].

Daily Insulin Shots

It may be advantageous to have roughly the same amounts of carbohydrates at the same times each day if you take fixed doses of insulin twice a day. To get the numbers correct, this entails estimating how many carbohydrates are present in the various foods and meals you consume. Blood glucose levels can become excessively high by eating too much carbohydrate, and a hypo (low blood glucose level) from eating too little [34].

Insulin Bolus Basal

The person can be considerably more flexible with how many carbs they are and when consuming them if we use a basal-bolus insulin regimen, either by utilizing a pump or an injection schedule that occurs numerous times during the day. The majority of those who adhere to this plan will first count the carbohydrates in their food and liquids before determining how much insulin they should take. The amount of insulin will vary based on the amount of carbohydrates consumed. Other elements, such as any physical activity you have engaged in or want to do in, any previous hypos, and any infections, are also crucial [36].

How do People With Type 2 Diabetes React to Carbohydrates?

Calorie Reduction and Weight Management in Type 2 Diabetes

For individuals with type 2 diabetes who are overweight or obese, reducing calorie intake can be a significant factor in weight management. Glucose metabolism can be effectively managed through strategic dietary modifications. Reducing overall carbohydrate intake or following a low-carbohydrate diet has been shown to stabilize blood sugar levels, enhance insulin sensitivity, and support weight management. These approaches limit the postprandial glucose spikes that strain insulin response, fostering better glycemic control.

Low-carbohydrate diets have shown promise in promoting weight loss, improved glycemic control in type 2 diabetes, and potentially lower HbA1c, cholesterol, and blood pressure readings. Additionally, these dietary changes may allow for a reduction in diabetes medications.

Blood Glucose Monitoring and Medication Management

Regular blood glucose monitoring is crucial when implementing dietary changes, particularly those that restrict carbohydrate intake. It is essential to discuss any adjustments with your healthcare team to assess potential medication modifications and minimize the risk of hypoglycemia (low blood sugar) associated with certain diabetes medications [40].

Antidiabetic Effect of Carbohydrates

Potential of Medicinal Plants in Diabetes Management

Plants serve as a rich source of bioactive compounds with diverse pharmacological properties that hold promises for diabetes treatment. This is particularly relevant in developing nations, where traditional medicine utilizing medicinal plants remains prevalent due to their affordability and accessibility [56]. However, the interest in exploring these natural remedies is growing in developed nations as well.

Phytochemicals and Anti-diabetic Effects

Many medicinal plants contain phytoconstituents, such as terpenoids, saponins, flavonoids, carotenoids, alkaloids, and glycosides, exhibiting anti-diabetic properties. These bioactive compounds are embedded within a complex plant matrix, which influences their interaction and potential health benefits.

Six Main Antidiabetic Drug Mechanisms

Modulating Glucose Metabolism for Therapeutic Benefit

Glucose metabolism plays a central role in human energy homeostasis, involving intricate pathways and regulatory mechanisms. Targeting these pathways offers promising therapeutic avenues for various metabolic disorders, particularly diabetes mellitus. This review explores current strategies for modifying glucose metabolism, focusing on enzyme inhibition and stimulation of specific metabolic processes.

Inhibiting Starch Digestion and Glucose Absorption

Starch, dietary polysaccharide, is a major source of glucose. Its breakdown into absorbable glucose involves sequential enzymatic steps mediated by salivary and pancreatic amylases, followed by maltase and isomaltose. Here, two main approaches can be employed.

- *α-Amylase Inhibition: Competitive inhibitors like acarbose can impede α-amylase activity, reducing starch degradation into glucose and leading to lower postprandial blood glucose levels.*

- *Dietary Fiber:* Soluble fibers can hinder the enzymatic action on starch, thereby slowing down glucose absorption from the gut.

Targeting α-Galactosidase for Digestive Health

α-Galactosidase is an enzyme responsible for hydrolyzing complex carbohydrates like raffinose and stachyose found in legumes and certain vegetables. Inhibiting the enzyme α-galactosidase can alleviate digestive discomfort, such as bloating, by reducing the breakdown of complex carbohydrates in the gut. This targeted inhibition decreases gas production, improving overall gastrointestinal health and comfort. This strategy reduces the fermentation of undigested carbohydrates by gut microbiota, leading to decreased gas production.

α-Glucosidase Inhibition for Glycemic Control

α-Glucosidase, located in the small intestine's brush border, is critical for the final step of carbohydrate digestion, converting disaccharides into absorbable monosaccharides like glucose. Drugs such as acarbose, miglitol, and voglibose function as α-glucosidase inhibitors, delaying carbohydrate breakdown and subsequent glucose absorption. This approach is particularly valuable in managing postprandial hyperglycemia in diabetic patients.

Stimulating Glycogenesis for Glucose Metabolism

Glycogenesis is a crucial metabolic pathway where excess glucose is converted into glycogen, primarily stored in the liver and muscle tissues. This process is tightly regulated by insulin, which is released by the pancreas in response to elevated blood glucose levels. By promoting glycogenesis, the body effectively disposes off surplus glucose, preventing hyperglycemia and ensuring an energy reserve for future use. Therapeutic strategies aimed at enhancing glycogenesis can be beneficial for diabetes management. These may involve the use of insulin or insulin-mimetic agents to promote glycogen synthesis and storage, thereby lowering circulating blood glucose.

Enhancing Hepatic Glycolysis for Blood Sugar Balance

Hepatic glycolysis, the breakdown of glucose into pyruvate with ATP as a byproduct, plays a pivotal role in blood glucose homeostasis. Insulin enhances this pathway by stimulating glucose uptake and metabolism in liver cells, while glucagon acts as its counter-regulator, inhibiting the process during low glucose states. Maintaining a balance between these hormones ensures stable energy levels and minimizes fluctuations in blood sugar. Therapeutic agents that enhance insulin sensitivity or mimic insulin action can promote hepatic glycolysis, leading to increased glucose utilization and reduced hyperglycemia.

Therapeutic Implications of Glucose Metabolism Modulation

Modulating glucose metabolism presents a multifaceted approach for managing various conditions.

Diabetes Management

α-Amylase and α-glucosidase inhibitors are established therapeutic tools for controlling postprandial hyperglycemia in type 2 diabetes.

Digestive Health

α-Galactosidase inhibitors offer relief from symptoms like bloating and gas associated with certain dietary carbohydrates.

Metabolic Syndrome

Enhancing glycogenesis and glycolysis can help alleviate symptoms of metabolic syndrome, such as insulin resistance and hyperglycemia [56].

Lipid peroxidation

Impact of Hypolipidemic Antidiabetic Drugs on Lipid Peroxidation and Carbohydrate Metabolism

Therapeutic strategies for diabetes often target multiple facets of the disease, including hyperglycemia (elevated blood sugar) and dyslipidemia (abnormal blood lipid levels). Notably, hypolipidemic medications used for diabetes management can also influence lipid peroxidation, a process that damages cellular membranes due to free radical activity.

Mechanism of Lipid Peroxidation Reduction

The exact mechanisms by which hypolipidemic drugs diminish lipid peroxidation remain under investigation. However, some potential explanations include:

- *Reduced Substrate Availability:* Certain hypolipidemic drugs, like statins, primarily target cholesterol synthesis. By lowering circulating low-density lipoprotein (LDL) cholesterol, a major substrate for peroxidation, these drugs may indirectly reduce the formation of oxidized lipids.
- *Enhanced Antioxidant Activity:* Some medications might possess antioxidant properties or induce the body's natural antioxidant defenses. This can help neutralize free radicals and prevent their attack on lipids within cell membranes.

Carbohydrate Metabolism and Lipid Peroxidation

The role of carbohydrates in this context is multifaceted. While excessive refined carbohydrate intake can contribute to hyperglycemia and potentially exacerbate oxidative stress, certain complex carbohydrates might offer some protective benefits:

- *Dietary Fiber:* Soluble fiber intake may be associated with lower lipid peroxidation levels. This could be due to fiber's ability to bind cholesterol and bile acids in the gut, leading to their excretion and potentially reducing the amount of substrates available for oxidation.
- *Glycemic Control:* Chronic hyperglycemia, a hallmark of diabetes, is a known risk factor for increased oxidative stress and lipid peroxidation. Medications that improve glycemic control may indirectly contribute to a reduction in lipid peroxidation by mitigating hyperglycemia-induced oxidative damage.

Overall, the interplay between hypolipidemic drugs, carbohydrate metabolism, and lipid peroxidation is complex. Further research is needed to fully elucidate the precise mechanisms by which these factors interact and how they can be optimized for comprehensive diabetes management.

Pancreatic Effect

It is the impact on cell regeneration/repair, impact on cell protection, impact on increasing number and/or size of cells in Langerhans islets, impact on reducing insulin resistance, impact on stimulating insulin secretion, and impact on inhibiting cell degradative processes.

Oxidative Stress

It is caused by an imbalance between free radicals and antioxidants, contributes to β-cell dysfunction in diabetes. Antioxidants mitigate this damage by neutralizing free radicals, reducing hydrogen peroxide formation, and inhibiting reactive oxygen species (ROS) production. They also regulate key enzymes like NADH oxidase, xanthine oxidase, and lipoxygenase, preserving cellular integrity and maintaining the oxidant-antioxidant balance critical for optimal metabolic function.

Treatment for Diabetes Complications

It includes inhibiting NF-'s pro-inflammatory pathway, which causes vascular problems and has an insulin-like action [29].

PLANTS WITH ANTIDIABETIC ACTIVITY

White Mulberry (*Morus alba* L.)

The mulberry, a rapidly growing deciduous plant from the *Moraceae* family, thrives across diverse climates, ranging from tropical to temperate zones. Its adaptability to various geographic latitudes makes it an important agricultural resource and a valuable component of natural ecosystems (Figure 4).

Figure 4. White mulberry.

All the white mulberry's parts, including the fruits, leaves, and bark, were first employed in medicine about 3000 B.C., according to historical texts. White mulberries are native to China, Japan, and India. The 11th century saw its introduction to Europe via silkworm caterpillars. Other nations in Asia, Europe, and America also experience high rates of occurrence. Because of its low agro-technical needs, ease of cultivation, low cost, and potential for use in the food business, white mulberry is also grown throughout Europe [57].

Fenugreek

An annual herb from the *Leguminosae family*, fenugreek has beautiful seeds. Fenugreek can be found in the Mediterranean region, India, and China in its natural state. It is mostly grown as a fodder plant. Fenugreek seeds and leaves are mentioned in literature as food and medical ingredients. Germinated fenugreek seeds are highly regarded for their rich nutritional profile, making them an excellent addition to a balanced diet. These seeds are packed with protein, essential vitamins, and minerals (Figure 5).

Figure 5. Fenugreek seeds.

Key components include,

- *Mucous polysaccharides (galactomannans):* 25–45%.
- *Proteins:* 43.8%, rich in amino acids like tryptophan and lysine.
- *Free amino acids:* Primarily 4-hydroxy isoleucine and histidine.
- *Fats:* 7.9%.

- *Bioactive compounds:* Steroid saponins, trigonelline (an alkaloid), coumarins, flavonoids, sterols, and lecithin.

Roasting fenugreek seeds enhance their flavor and results in the breakdown of trigonelline, further enriching their bioactive properties. -carotene (0.019%), ascorbate (0.22%), iron, calcium, and zinc are all found in fenugreek leaves. Rhaponticin and isovitexin are the most bioactive fenugreek polyphenol components (Savych et al., 2021) [58].

Ceylon Cinnamon (*Cinnamomum zeylanicum J. Presl)*

The Lauraceae family includes the Ceylon-born Ceylon cinnamon, which is also grown in different parts of southern Asia and North America. Cinnamon bark, scientifically known as *Cinnamomi cortex,* refers to the primary bark layer stripped of its inner layer. This aromatic raw material has been a staple in traditional medicine and culinary applications for its potent therapeutic properties. Depending on where the raw material came from, the oil content of Ceylon cinnamon bark ranges from 0.5% to 4.0%. Cinnamaldehyde (65–75%), cinnamyl acetate, eugenol (about 5% combined), and -caryophyllene (up to 4%) make up most of the oils. In addition, the bark includes oligomeric proanthocyanidins, diterpenes, phenolic acids (cinnamic acid and its derivatives), polysaccharides (mucilage), and others [57] (Figure 6).

Figure 6. *Cinnamomum zeylanicum.*

***Zingiber officinale Rosc*., or Ginger**

One of the first known medicinal and spice plants is ginger. The herbaceous plant known as common ginger, which is a member of the Zingiberaceae family, has a robust rhizome that is divided into tuberous portions. It has sterile shoots that can reach a height of 1.5 m and uniformly narrow lanceolate leaves that are 5–30 cm long and 8–20 cm broad. It is grown in many tropical countries, including Africa, China, India, and Jamaica. It is most likely a Southeast Asian native. Ginger is widely used in European cuisine and frequently combined with dishes from the Far East. The number of essential oils in ginger's rhizome, which ranges from 1% to 3%, is significant (Figure 7). There are more than 50 known essential oils, however the ones that will be discussed in particularly noteworthy are sesquiterpenes (ar-curcumen and -zingiberene 30–70%, -sesquifelandrene 15–20%, -bisabolene 10–15%, zingiberol) and monoterpenes (felandrene, camphene, 1,8-cineol, geranial, citral, terpineol, and borneol). Fresh ginger's heat is attributed to gingerols, whereas dried ginger's heat is attributed to shoagols, their dehydrated relatives. Diterpenes, monoacyldigalactosylglycerols, and diarylheptones are additional components found in ginger (Savych et al., 2021).


Figure 7. Ginger.

Current Scenario

Carbohydrates themselves are not typically used as antidiabetic agents. However, carbohydrates play a crucial role in the management of diabetes by providing energy and influencing blood sugar levels. Recent advancements highlight the potential of specific carbohydrate types, such as dietary fiber and resistant starch, in diabetes management. These carbohydrates, largely undigested by the body, offer significant metabolic benefits.

Dietary Fiber

Found in plant-based foods, fiber slows glucose absorption, preventing post-meal blood sugar spikes. It also improves insulin sensitivity, aiding in long-term diabetes control [47].

Resistant Starch

Unlike typical carbohydrates, resistant starch bypasses digestion in the small intestine and undergoes fermentation in the colon. This process produces short-chain fatty acids, which enhance insulin sensitivity and support gut health.

Low Glycemic Index (GI) Carbohydrates

Foods with a low GI are digested and absorbed at a slower rate, leading to a gradual rise in blood sugar levels. Incorporating these carbohydrates into a diabetes-friendly diet can improve glycemic control and reduce the risk of complications. Eating a diet that is rich in low GI carbohydrates has been shown to improve blood sugar control in individuals with diabetes [51].

Overall, while carbohydrates themselves are not typically used as antidiabetic agents, certain types of carbohydrates, such as dietary fiber, resistant starch, and low GI carbohydrates, may have potential as part of a comprehensive diabetes management plan. However, further research is needed to fully understand the mechanisms by which these carbohydrates exert their antidiabetic effects, and to develop effective strategies for incorporating them into diabetes treatment plans. Carbohydrates play an important role in the management of diabetes mellitus. The main goal of carbohydrate management in diabetes is to regulate blood sugar levels, as elevated blood sugar levels over time can cause damage to the various organs of the body [49].

Carbohydrate Counting for Blood Sugar Management

Carbohydrate counting is a cornerstone of diabetes management, enabling individuals to better regulate their blood sugar levels. Carbohydrates are the primary macronutrients that influence glucose fluctuations, and tracking their intake allows for more precise meal planning and insulin dose adjustments. This personalized approach helps maintain blood sugar within a target range, reducing the risk of complications [62].

Prioritizing Complex Carbohydrates

The type of carbohydrates consumed plays a crucial role in blood sugar control. Complex carbohydrates, found in whole grains, fruits, and vegetables, are digested more gradually than simple carbohydrates present in refined sugars and processed foods. This slower digestion minimizes sudden blood sugar spikes, providing a more stable energy release and improving overall glycemic control. By prioritizing complex carbohydrates, individuals with diabetes can achieve better long-term blood sugar management [61].

Insulin Therapy: A Lifesaving Necessity for Type 1 Diabetes

For individuals with Type 1 diabetes, insulin therapy is essential for survival and effective glucose regulation. Since their pancreas cannot produce insulin, exogenous insulin must be administered to facilitate glucose uptake by cells. Whether delivered via injections or insulin pumps, this therapy is tailored to align with dietary intake and physical activity, ensuring optimal blood sugar levels and reducing the risk of acute and chronic complications**.** Carbohydrates play a crucial role in determining insulin dosages, as the amount of insulin required depends on the amount and type of carbohydrates consumed [59].

Preventing Hypoglycemia

In some cases, individuals with diabetes may experience low blood sugar levels (hypoglycemia) because of medication or insulin therapy. Consuming carbohydrates can help raise blood sugar levels and prevent hypoglycemia. Overall, carbohydrate management is an important aspect of diabetes treatment. Careful monitoring of carbohydrate intake, coupled with mindful dietary choices, plays a pivotal role in managing diabetes and reducing the risk of associated complications. By keeping track of the quantity and type of carbohydrates consumed, individuals can gain better control over blood sugar fluctuations. Choosing nutrient-dense, low-glycemic carbohydrates such as whole grains, fruits, and vegetables over refined options helps stabilize blood sugar levels, promoting long-term health.

CONCLUSIONS

In conclusion, carbohydrates themselves are not typically used as antidiabetic agents. However, certain types of carbohydrates, such as dietary fiber, resistant starch, and low glycemic index carbohydrates, have been shown to have potential antidiabetic effects. Certain carbohydrates, especially those rich in fiber and resistant starch, have the potential to play a beneficial role in regulating blood sugar levels, enhancing insulin sensitivity, and preventing the long-term complications often associated with diabetes. Incorporating these into a balanced diet can significantly support diabetes management. However, the mechanisms by which these carbohydrates exert their antidiabetic effects are not fully understood, and further research is needed to develop effective strategies for incorporating them into diabetes treatment plans. Overall, while carbohydrates play an important role in diabetes management, their specific effects on blood sugar levels and diabetes outcomes depend on a variety of factors, including the type and amount of carbohydrate consumed, individual dietary needs and preferences, and overall health status. It is crucial for individuals with diabetes to collaborate with their healthcare team to create a personalized management plan tailored to their specific needs, preferences, and lifestyle. This tailored approach ensures that the plan is both effective and sustainable for long-term health.

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