Aspects of chrono-nourishment in diabetes care

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Chrono-nutrition: an emergent discipline, builds on the relationship between eating habits and time, circadian loops and the dynamics of the metabolism in humans. Chrono-nutrition balances circadian rhythms, improving metabolic well-being, and lowering the incidence of type 2 diabetes (T2D). An expanding corpus of studies demonstrates that eating low-glycemic index (GI) meals can reduce the risk of T2D, and eating low-GI foods at dawn improves glycemic response more than eating after dusk. The utility of the GI in the avoidance and treatment of T2D is discussed in this article, along with a critical evaluation of the scientific data on chrono-nutrition taking physiological homeostasis into account hopefully treating diabetes with a specific nutrition formulation (NUC-RDM).

Introduction:

Chrono-nutrition study focuses on how the schedule of food consumption impacts human health including T2D, which is classified as metabolically unhealthy. It is predicated on the assumption that our bodies have an internal clock that manages our metabolism, sleep-wake cycle, and other physical activities. Human health has long been recognised to be influenced by the schedule of food intake, i.e., chrono-nutrition; when we eat in accordance with our bodies' natural cycles, we can boost both our physical and mental health. Chrono-nutrition can significantly affect obesity, metabolic health, sleep, aging, and other aspects of health. The effects of chrono-nutrition on various populations, such as those with chronic diseases or the elderly, their long-term effects, and the mechanisms by which chrono-nutrition operates are all areas of chrono-nutrition research that are still in their infancy [1].

There are still significant knowledge gaps in the following areas: (a) the relationship between peripheral tissue clocks and the brain in metabolic regulation (b) the interaction of circadian rhythm and energetics (c) the connection between circadian homeostasis and nutritional state and (d) human physiology and circadian clock [2].

One area of significant advancement in the management of diabetes is in the field of chrono-nutrition. Chrono-nutrition is a dietary approach that aims to optimize nutrient timing based on the body's natural circadian rhythms. This approach recognizes that the timing of meals can have a profound impact on metabolic health, particularly in individuals with obesity and/or diabetes. There is an increasing amount of affirmation indicating that chrono-nutrition can be particularly relevant for individuals with diabetes, as it may help improve glycemic control and lower the

possibility of issues arising from the disease [3]. For individuals with diabetes, several studies have shown that chrono-nutrition can positively influence blood sugar control and metabolic outcomes. For instance, the schedule of carbohydrate consumption has been found to be paramount in managing postprandial glucose levels in individuals with diabetes. Consuming carbohydrates earlier in the day, when insulin sensitivity is higher, and reducing carbohydrate intake in the evening may help boost glycemic management and insulin sensitivity. In addition to timing of carbohydrate intake, chrono-nutrition also highlights the significance of regular meal patterns and avoiding midnight and substantial large dinners. Late and heavy dinners, as well as nocturnal eating and insomnia, have been shown to contribute to obesity and deterioration of the blood sugar management in individuals with T2D [4]. Furthermore, chrono-nutrition may also have a positive impact on weight management in individuals with diabetes. Studies have proved that eating most of calories earlier in the day, rather than later, can promote slenderize and enhance metabolic markers in individuals with diabetes [5]. Overall, chrono-nutrition offers a promising approach for the dietary management of diabetes [6].
Present day ways of living incorporate eating late around evening time, skipping dinners, being stationary for broadened timeframes, being presented to awful food sources, being even more habitually in the postprandial state, and being stationary with delayed sitting [7,8]. Thus, the propensities for the cutting-edge way of life set off an endless loop by which an undesirable way of life that advances heftiness causes sporadic circadian rhythms, which then advance corpulence. Various examinations have shown the medical advantages of eating plans that permit admittance to food during explicit times during the day [9]. A developing collection of exploration shows how these strategies can further develop glucose resilience and reduce insulin obstruction [10,11]. Through the control of the fasting cycle, these dietary methodologies can incorporate supported times of persistent energy limitation, which are distinguished by a decrease in day-to-day energy admission of up to 40%, but feast recurrence and timing remain unaltered; (ii) discontinuous fasting, which consolidates at least one day of fasting with customary eating examples; and (iii) chrono-nourishment, which confines food use to specific times.Taking care of feeding time limitation (FTR), which requires a standard everyday dinner window, is alluded to in this setting as a kind of chrono-nourishment. In FTR, the daily eating duration, or the interval between the first and last energy consumption, is frequently reduced from 12-14 hours to less than 10 hours.
[11]. A feeding game plan reflects changes in assimilation that occur during the day, which are separate by our natural clock [12]. In general, chrono-nutrition has the potential to influence the outcomes of sleep patterns, dietary habits, and the impact of urban living. Further investigation is warranted to clarify the significance of chrono-nutrition in managing diabetes and its broader implications for public health. [13].

Diabetes mellitus remains the most prevalent chronic worldwide, with the number of diabetics having increased rapidly over the preceding three decades [14]. The predominant approach to decreasing the occurrence and seriousness of type 2 diabetes revolves around the selection and nutritional value of the diet. [6].

Our research suggests potential links in the future between the diversity and amount of carbohydrates and proteins consumed from various food sources and diabetes management.

Circadian Rhythms Setup and Misalignments

The circadian system, consisting of a network of interconnected clock oscillators located in the suprachiasmatic nuclei (SCN) of the hypothalamus and in select metabolically active peripheral organs, regulates functions such as body temperature, endocrine activities, and daily patterns of behavior and physiology, including sleep/wake cycles, fasting/feeding rhythms, and catabolic/anabolic processes. While most peripheral organs and tissues can exhibit circadian rhythms independently, the SCN in the hypothalamus is considered the primary regulator of circadian rhythms. [15]. Viewed through a chronobiological lens, human glucose metabolism follows a circadian pattern characterized by fluctuations in glucose tolerance. This tolerance typically reaches its peak during daylight hours, aligning with periods of food intake, and decreases during the nighttime fasting period when darkness prevails. [16]. The link between disturbances in the circadian rhythm and disruptions in metabolic balance or homeostasis manifests in various ways [17]. The circadian clock preserves metabolic equilibrium by regulating daily patterns of eating and fasting, as well as by managing the equilibrium between nutrient availability and cellular stress responses. [10].

Numerous hormones implicated in glucose regulation, including cortisol and insulin, exhibit circadian fluctuations. Research conducted in rodents underscores the critical role of the circadian clock in glucose metabolism, illustrating how alterations in insulin sensitivity and secretion patterns influence blood glucose levels. Consequently, the circadian rhythm profoundly influences the interplay between insulin secretion, sensitivity, and glucose metabolism [18–23]. The link between factors like meal timing and nutrient intake (Chrono-nutrition), which may disrupt circadian rhythms and impact the development of metabolic conditions like T2D, is apparent in how diet affects circadian rhythmicity[24].

A deep understanding of both the light-based and metabolic cues influencing the circadian clock, along with its hormonal and autonomic signals affecting peripheral oscillators that regulate energy metabolism, will enhance our comprehension and management of circadian-related health issues, including cardiometabolic disorders, diabetes, and obesity [25,26]. Cyclic AMP-responsive element binding protein, hepatocyte specific (CREBH) is a liver-specific transcription factor that is tethered to the endoplasmic reticulum. It serves as a circadian transcriptional regulator with significant involvement in preserving glucose balance within the body[27]. Prediabetic individuals experience compromised glycemic regulation during the evening due to various daily circadian patterns [28].

Different ways of circadian misalignment affect glucose tolerance, insulin sensitivity, and insulin secretion [29]. The circadian rhythm serves as a vital link between nutrition and overall homeostasis, highlighting the need for increased focus on the advantageous impacts of chrono-nutrition [9]. Melatonin or its genetic components could disrupt glycemic regulation, particularly in individuals with diabetes, by interfering with circadian rhythm patterns [30]. Disruption of circadian rhythms diminishes glucose tolerance among shift workers, offering an explanation for the heightened diabetes risk observed in this group [31].

Worth of food timing dawn-to-dark and glucose metabolism

Meal timing plays an essential part in managing glucose levels and overseeing diabetes. When carbohydrates are ingested, they undergo breakdown into glucose, which enters the bloodstream. The timing of meals can affect how quickly glucose is released into the bloodstream and how efficiently it is metabolized. Eating at consistent intervals during the day aids in stabilizing blood glucose levels and prevent spikes or drops. This is especially important for individuals with diabetes, because their bodies may have difficulty regulating blood glucose levels on their own [32]. By spacing out meals and avoiding long periods of fasting, people with diabetes can effectively regulate their blood glucose levels.

This is because regular meal timing allows for a steady release of glucose into the bloodstream, which can be more easily managed by the body's insulin or medication. For example, individuals with Type 1 diabetes must adjust their insulin dosage based on the timing of meals to align with the variations in insulin levels correspond to the light-dark cycle and meal timings [33]. Furthermore, meal timing can also help to prevent postprandial hyperglycemia, which is a spike in blood glucose levels after meals. By timing meals appropriately and avoiding larger meals that can cause a rapid rise in blood glucose, individuals with diabetes can better control their glucose levels and prevent complications [34].

Chrono-nutrition aims to enhance metabolism by aligning nutrient consumption with the peak phases of metabolic rhythms. This strategy improves overall insulin sensitivity and blood sugar management, leading to beneficial effects on diabetic health [34]. From this perspective, examining how meal timing aligns with findings from both nutritional studies and chrono-biology, known as chrono-nutrition, could greatly influence personalized nutrition approaches. This has the potential to significantly reduce the occurrence and impact of diabetes [1]. The interconnectedness of the circadian system, metabolism, and behavior highlights the critical role of chronobiology in preventing and treating conditions such as T2D, obesity, and hyperlipidemia [35].

Nowadays, after 6 p.m., more than one-third of calories are ingested, indicating a change in eating patterns since the midpoint of the 20th century. This late-eating behavior, which is a common part of modern living, may result in circadian desynchronization and have adverse effects on glucose regulation. A significant body of epidemiological data indicates that the biological circadian rhythm is inversely linked to various metabolic disorders, including obesity, heart disease, gastrointestinal issues, and diabetes [6].

Additionally, recent research indicates that a person's "chronotype" may influence their nutritional needs. An individual's chronotype, which can be used to classify them as preferring the morning or evening, is an outward behavioral expression of their internal circadian rhythm system. People with a "evening chronotype," often referred to as a "later chronotype," are biologically inclined to eat in the afternoon [36–38]. According to certain studies, skipping breakfast is significantly associated with type 2 diabetes mellitus or insulin resistance. In a 16-year follow-up cohort study, American males who skipped breakfast were found to have a 21% greater likelihood of developing type 2 diabetes compared to those who consumed breakfast. This was true even after accounting

for known T2D risk variables including BMI. People with later chronotypes, who typically eat dinner later in the evening, may tend to forgo breakfast the following morning. This can be due to a lack of time during the day to eat or a lack of appetite in the morning. After correcting for body mass index (BMI), significant cross-sectional research of healthy Japanese suggested that eating dinner late at night was also a source of hyperglycemia. This was not merely caused by skipping breakfast. Another investigation found that in healthy men who skipped breakfast but had substantial lunches and dinners, post-meal glucose levels were elevated, particularly following dinner. In a brief examination, individuals with type 2 diabetes who skipped breakfast, exhibited later sleep-wake cycles, and showed elevated HbA1c levels experienced poorer management of blood sugar levels[38–43].

Conversely, maintaining comparable durations of overnight fasting, regardless of meal timing, could lead to similar metabolic outcomes. Consistent with the previous instance, routine observations indicated that omitting breakfast was associated with a higher BMI and increased energy expenditure later in the day, yet a direct cause-and-effect relationship has not been established. Given that caloric limitation can significantly affect metabolic health and that suppressing appetite may result in voluntary calorie reduction, the potential indirect advantages of skipping breakfast in the context of intermittent fasting have been anticipated.[44,45].

Diurnal intake of nutrition and glucose metabolism

The link between timing of food consumption and diabetes, raises the question of when you eat it matters more than whether what and how much you eat. A late or irregular meal time represents a circadian chronodisruption that, results in metabolic deficits, according to the new definition of diabetes as a chronobiological disease [46]. Enhanced comprehension regarding how circadian gene networks influence nutrient equilibrium across molecular, cellular, and systemic dimensions will illuminate the growing correlation between conditions like diabetes, obesity, sleep disorders, and circadian rhythms [47] . Even with just a 3-hour disparity, consuming dinner early (at 18:00) demonstrates a favorable impact on fluctuations in blood glucose levels and substrate oxidation in comparison to consuming dinner late (at 21:00) [48].[49]

According to the research, healthy people's postprandial glucose reaction to meals is substantially stronger at night than in the morning. Given that many lifestyle factors and changes have increased people's propensity to adopt a late-eating habit (later chronotype), it is critical to understand how diet can be controlled to achieve circadian synchronization to maximize glycaemic control. Along with meal timing, meal type appears to have an impact on blood glucose levels, suggesting strong evidence that glucose tolerance is worse at night [50].

Calories associated outlook on circadian cycle

As per the recent research, the number of calories consumed and the time of day can both impact have an impact on glycemic management. Despite no changes in daily total calorie intake, certain animal studies have demonstrated that skipping breakfast or eating less at the first meal of the day, combined with a high-calorie dinner, impairs the expression of peripheral clock genes, leading to increased daily glucose excursion management [51,52]. In a crossover trial, individuals with type

2 diabetes who were provided with a high-calorie breakfast and a low-calorie dinner (while the control group received a low-calorie breakfast and a high-calorie dinner) demonstrated reduced post-meal hyperglycemia and increased insulin and glucagon-like peptide-1 (GLP-1) levels over the course of the day. Jakubowicz et al.'s study findings indicated fluctuations in glycemic control among individuals with type 2 diabetes throughout the day. The daily pattern of post-meal glycemic fluctuations and insulin levels appeared to be influenced by the calorie intake at breakfast or dinner [45,52]. Among individuals with type 2 diabetes, consuming more calories later in the day is linked with higher overall daily food and energy consumption. Conversely, reducing overall energy intake is associated with consuming a greater amount of total carbohydrates in the morning [53].

Carbohydrates and circadian rhythmicity

Consuming high-quality carbohydrates and replacing low-quality carbohydrates with plant-based products are recommended strategies for preventing diabetes [54]. Postprandial glucose levels and insulin response are primarily determined by the amount, type, and rate of digestion of dietary carbohydrates[55,56]. As a result, regarding circadian rhythmicity and glycemic management, they all have a significant impact on our diet. The ability of foods high in carbohydrates to raise blood sugar levels is known as the GI. Low GI carbohydrates have been proven to be advantageous because they have less of an effect on blood glucose levels and prevent hypoglycemia [57,58]. Morgan et al. in a randomized crossover study involving healthy adults, researchers examined the glycemic effects of modifying the glycemic index (GI) and glycemic load (GL) (where GL equals GI multiplied by carbohydrate content) and altering the timing of meal consumption, focusing on distributing most energy intake either at breakfast or dinner. Initially, their findings revealed that consuming higher GL meals in the evening elicited a more pronounced response in glucose and insulin levels compared to consuming the same meal in the morning. In the subsequent phase of the study, high-GI foods consumed in the evening had an even greater impact on blood sugar and insulin levels. These results underscored the significance of both the quality and quantity of carbohydrates—namely, the GI and GL—as well as the timing of meal consumption, in influencing glycemic control and insulin secretion[59].

Circadian clock regulating cellular carbohydrates

Cells with cell walls are the building blocks of all plants. Our digestive system automatically breaks down these cell walls when we eat plants, allowing us to absorb nutrients from the entire cell. Plant cells that have been subjected to unnaturally high pressure and heat will have their cell walls damaged, leaving behind a highly condensed material without cell walls. These sugars are acellular. Our "ancestral foods"—like roots, tubers, seeds, leaves, and fruit—contain cellular carbs, which have far lower carbohydrate densities and assist in the moderate blood sugar response. According to some theories, processed meals and acellular carbohydrates like simple sugars cause the upper gastrointestinal tract to create an inflammatory microbiota. Small intestine bacterial overgrowth, or SIBO, is caused by this. This results in elevated insulin resistance and leptin levels. Therefore, maintaining a healthy metabolic profile should be possible with a diet that contains

more unprocessed whole fruit and starchy root vegetables because of the restoration of insulin sensitivity [59,60].

Circadian clock managing cell Fats

Epidemiological research indicates that prioritizing carbohydrate consumption over fats in the morning may help prevent the onset of diabetes [60,61]. In a few experimental studies, the impact of varying the number of fats and carbs in daytime and evening meals on postprandial glycemic response has been investigated. A randomized crossover trial in healthy males investigated whether consuming a high-carbohydrate or high-fat diet at various times throughout the day would lead to differing plasma glucose responses. The study found that compared to a high-fat diet, a high-carbohydrate diet resulted in a greater increase in plasma glucose levels. Plasma glucose concentration also showed a diurnal pattern, with high-fat meal consumption being the cause of the circadian pattern. A recent randomized crossover trial was conducted in overweight individuals with elevated fasting lipid levels to contrast two meals with equal caloric content but differing in total sugar and saturated fat. Although the results of this study did not significantly alter the expression of circadian genes, changing a meal by cutting back on sugar and saturated fat was linked to an enhanced glycemic response. Although the impact of fat type on metabolism is recognized, there is a lack of substantial data regarding how post-meal blood sugar and lipid levels are influenced by the saturation level and chain length of fatty acids. This emphasizes even more the importance of examining the chronobiology of dietary fat consumption on glucose homeostasis [62,63].

Circadian clock managing cell Proteins

High protein breakfast helps to regulate postprandial glucose levels throughout the day, However, if lunch is skipped, the high protein breakfast does not have the same effect on reducing post-dinner blood sugar levels. These results imply that increasing the protein content of a meal can lower postprandial glucose levels at night [64]. Delaying food intake until noon, referred to as an "extended postabsorptive state," can adversely affect the expression of clock genes and disturb the regulation of body weight, post-meal and overall blood sugar levels, skeletal muscle protein synthesis, and appetite. It may also result in reduced energy expenditure. Various studies have shown that skipping the first meal of the day, akin to having a delayed breakfast until noon, disrupts and diminishes the rhythmic patterns of clock gene expression in both animal models and humans. Fasting in the morning seems to be less advantageous for weight management compared to fasting in the evening [65]. The consumption of carbohydrates and soluble fiber in between meals significantly influences the impact of the subsequent dinner on blood sugar levels. Incorporating snacks into one's diet helps maintain stable blood glucose levels and reduces the likelihood of experiencing both high and low blood sugar episodes [66].

People with late chronotypes or late-night diners may benefit from this because it lowers their risk of hyperglycemia because they are more likely to experience glycemic excursions [67]. The timing of eating appears to have an impact on the ability of dietary protein to reduce blood sugar levels.

There are not many studies that support this, and more research is needed to determine how protein in meals affects blood sugar and insulin levels throughout the day [68].

Viability of the protein blends on glycemic responses

Mixing carbohydrate with protein does not enhance the glucose response in individuals with type 2 diabetes, as no notable variations in glucose responses were noted following the consumption of the beverages [69].

Postprandial hyperglycemia, which is the primary predictor of glycated hemoglobin levels, may be an independent risk factor for both microvascular and macrovascular consequences of T2DM. A sustained reduction in postprandial plasma glucose level can enhance glycemic management and prevent major, life-threatening consequences [70]. Dietary factors, particularly the type, and quantity of meals, cause the postprandial glycemic response. Since slowly digested carbs can delay the blood's absorption of glucose and decrease postprandial hyperglycemia, they are frequently the primary source of carbohydrates in diabetic-friendly enteral formulations and beverages [71,72]. In a recent randomized, controlled, crossover study conducted among the Asian population, researchers examined the post-meal glycemic, insulin, and active glucagon-like peptide-1 (GLP-1) responses following the consumption of a whey protein-based multi-ingredient nutritional drink (WD) compared to a typical breakfast consisting of boiled white rice with chicken (BC) in individuals with type 2 diabetes mellitus (T2DM). The study found that WD resulted in superior post-meal glycemic control and higher levels of active GLP-1 without causing significant increases in insulin levels compared to the standard breakfast in patients with T2DM. This suggests that a nutritional formula containing a blend of slowly digested carbohydrates and whey protein may offer beneficial glycemic management when used as a meal replacement instead of a regular breakfast [73]. A study was undertaken in China to explore the connection between the diversity and amount of protein intake from various dietary sources and the risk of developing diabetes. The research, which utilized data from the China Health and Nutrition Survey, revealed a negative correlation between consuming a diverse range of proteins in appropriate quantities from various food sources and the likelihood of developing diabetes. These results underscore the importance of incorporating proteins from a variety of food sources in the primary prevention of diabetes [74].

Circadian clock governed by dietary fibers

Dietary fiber plays a crucial role in chrono nutrition for individuals with diabetes, because it impacts the timing and quality of nutrient absorption and can help prevent postprandial blood glucose spikes. The substantial amount of fiber in this diet holds importance in nutrition as it assists in reducing blood glucose levels. Those with diabetes can achieve better management of their blood sugar levels and enhance overall glycemic control by incorporating a diet abundant in dietary fiber [75]. Contemporary guidelines for managing type II diabetes and obesity advocate for boosting dietary fiber consumption. According to the American Diabetes Association, adults with diabetes should aim to consume at least women are advised to consume 25 grams of dietary fiber daily, while men are recommended to aim for 38 grams per day. The ability of dietary fiber to

modulate the blood glucose profile is an essential factor in chrono nutrition for individuals with diabetes [76]. Dietary fiber acts as a bulking agent, slowing down the digestion and absorption of carbohydrates, resulting in a slower release of glucose into the bloodstream. This slower release helps prevent sharp increases in blood glucose levels after meals, which can be particularly beneficial for individuals with diabetes. Moreover, dietary fiber also promotes a feeling of fullness or satiety, which can aid in weight management and prevent overeating.[77]

Dietary fiber has several well-established evidence-based advantages. Fiber serves as a prebiotic along with improved phytochemicals, flavonoids, and antioxidants [78]. Consuming foods high in dietary fiber, such as fruits, can help regulate blood glucose levels and prevent spikes and drops in sugar levels after meals [79]. Consuming breakfast rich in fibers like beta-glucans and whole grain cereals may lead to a reduction in post-meal glucose responses in a manner that depends on the dosage, as it slows stomach emptying, decreases intestinal glucose absorption, and enhances feelings of fullness. To evaluate the metabolic effects of inulin-type fructan intake, two systematic reviews and meta-analyses of 33 randomized controlled trials (RCTs) involving healthy individuals, overweight/obese individuals, prediabetics, those with type 2 diabetes mellitus (T2DM), and people with hyperlipidemia were conducted. The findings indicate that individuals with diabetes exhibit lower levels of blood glucose, total cholesterol, and triglycerides [79]. Both diabetics and non-diabetic experience improved insulin sensitivity with increased soluble fiber intake [78]. Research results have also indicated that consuming nutrients such as fiber before meals, known as "preloads," slows down the rate at which glucose is absorbed after eating and reduces both insulin release and glucose fluctuations [80].

Additionally, it appears that the greatest foods for increasing satiety and reducing calorie intake are those that include slower-releasing carbs, low GI/GL, and high quantities of fiber and protein, such as whole-grain cereals, beans, lentils and pasta. Therefore, the order of meals and foods may be important for decreasing postprandial hyperglycemia and IR and may be emphasized in dietary guidelines [81,82].

Offering of Prebiotics and probiotics supplementation on glycemic control

A recent minireview suggests that probiotics, along with the incorporation of prebiotics and/or plant-derived products, exhibit a greater capacity to regulate post-meal blood sugar levels. These components contain probiotic strains with enhanced proteolytic and exopolysaccharide-forming abilities. These strains inhibit digestive enzymes such as alpha-amylase, which breaks down polysaccharides into glucose and maltose oligosaccharides, as well as glucosidases, enzymes found in the small intestine's brush border epithelium. Glucosidases break down oligosaccharides, releasing bound glucose, thereby elevating blood sugar levels [8] [83]. According to one study's findings, eating meals containing beta-glucan, which is fermented in the colon, lowers postprandial glucose levels because the gut's absorption of carbohydrates is delayed and somewhat reduced rather than because of the effects of colonic fermentation. Moreover, there is a proposition that carbohydrate fermentation might regulate the rise in blood sugar after a meal by diminishing competition from non-esterified fatty acids (NEFA) for glucose clearance and, to a certain extent, by impacting intestinal movement [84].

Consequences of GI foods on glycemic regulation

The glycemic index categorizes carbohydrate-containing foods according to how they affect blood glucose and insulin levels after a meal. The GI is a measure of how quickly carbohydrates in a food increase blood glucose level. This concept is closely related to chrono nutrition, which focuses on the timing of meals and how they affect metabolism and overall health [85]. GI plays a crucial role in chrono nutrition by providing insights into how different foods impact our blood sugar levels and thus our energy levels throughout the day. By understanding the GI of foods, individuals can make informed choices about what to eat and when to eat it in order to maintain stable blood sugar levels and optimize their energy levels. Research has shown that consuming foods with a low GI can help regulate blood sugar levels, prevent spikes and crashes in energy, and promote satiety and weight management. Chrono nutrition involves more than just the timing of meals; it also considers the quality and composition of those meals. For example, if someone follows a chrono nutrition approach, they may choose to consume foods with a low GI during the first half of the day to provide sustained energy and prevent mid-morning crashes. Furthermore, the GI can be used to determine the appropriate timing of meals in chrono nutrition.
Research indicates that adhering to low-glycemic index (GI) diets can enhance glycemic management, lower lipid levels in the blood, raise HDL-cholesterol levels, and mitigate the risk of developing diabetes and cardiovascular issues [86]. Chrono-nutrition refers to the interplay between the circadian system and nutrition, and it has been suggested that the timing of eating can have significant implications for personalized nutrition and chronic disease prevention [1]. The timing of food intake can entrain the peripheral circadian clock and influence energy partitioning and fat deposition[87]. The circadian rhythm also regulates the intake, distribution, processing, and elimination of nutrients, indicating a bidirectional relationship between circadian rhythms and nutrition [88]. Therefore, the GI, which affects postprandial blood glucose and insulin responses, can be considered as one of the factors to be considered in chrono-nutrition strategies for managing chronic diseases [89].

A diet with a low glycemic index (LGI) notably enhances glycemic regulation in individuals with diabetes [90]. It is also recommended to use nutrient-dense, low GI, and high-dietary fiber foods for the elderly with T2D [91]. Managing blood sugar levels is the central concern of nutrition and dietary strategies for individuals with diabetes, which includes modifying carbohydrate intake throughout the day according to the glycemic index (GI) [91]. Adopting a diet with a low glycemic index (GI) or glycemic load (GL) is a successful approach to managing blood glucose levels (decreasing post-meal glycemia) and insulin levels (insulin levels) throughout the day, but it does not influence feelings of fullness[92].

Food	GI Value	Mechanism of Action	Ref
Oats	≈ 58	Soluble fibre is abundant, delaying carbohydrate digestion and absorption, resulting in a slow release of glucose into the bloodstream.	[57]
Legumes	≈ 21 - 33	With a high content of fiber and protein, these foods contribute to a delayed release of glucose into the bloodstream, resulting in improved regulation of blood sugar levels. Examples include lentils and chickpeas	[93]
Sweet Potatoes	≈ 44	Rich in complex carbohydrates and dietary fiber, which stabilize blood sugar levels and provide sustained energy.	[94]
Barley	≈ 25-35	High in beta-glucans, a type of soluble fiber, which creates a gel-like substance in the digestive tract, slowing down carbohydrate absorption and reducing post-meal blood sugar spikes.	[95]
Quinoa	≈ 53	High in fiber and nutrients, leading to a steady release of glucose and better blood sugar control.	[96]
Nuts	≈ 15	Low in digestible carbohydrates and high in healthy fats, protein, and fiber, which slow carbohydrate absorption and promote satiety. (e.g., Almonds, Walnuts)	[97]
Non-Starchy	≈ 15	Very low in carbohydrates and high in fiber, resulting in minimal impact on blood sugar levels. Vegetables (e.g., Broccoli, Spinach)	[98]
Bulgur Wheat	≈ 48	These meals are high in dietary fibre, which slows carbohydrate digestion and absorption, resulting in a consistent release of glucose into the bloodstream.	[57]
Spaghetti	≈ 44	Cooking pasta (Al Dente) results in a firm texture, slowing carbohydrate digestion and absorption, and reducing the glycemic response.	[99]
Steel-Cut Oatmeal	≈ 42	Less processed than rolled oats and higher in fiber, leading to slower carbohydrate digestion and better blood sugar control.	[57]
Buckwheat	≈ 54	Rich in fiber and nutrients, leading to a steady release of glucose and better blood sugar control.	[100]
Bran Cereals	≈ 45	High in dietary fiber, which slows carbohydrate digestion and absorption, leading to better blood sugar control.	[101]
Yogurt	≈ 30	The probiotics in yogurt may have a positive impact on gut health and blood sugar regulation. Note to identify if with live cultures or just plain yogurt, since GI differs.	[102]

Table 1: List of low GI food sources that make relevance for managing diabetes with mechanisms of action, and relevant scientific reference.

Table 1 represents select low GI foods, their GI values, mechanisms of action, and references. These foods encompass a variety of categories, including grains, legumes, vegetables, and dairy products. Notably, the low GI values of these foods are attributed to their high fiber content, complex carbohydrates, and protein, which collectively slow down carbohydrate digestion and absorption. For example, oats and barley contain beta-glucans, a soluble fiber that forms a gel-like substance, leading to a gradual release of glucose into the bloodstream. Legumes, rich in both fiber and protein, contribute to improved blood sugar control by ensuring a slower release of glucose.
Furthermore, foods like sweet potatoes, quinoa, and non-starchy vegetables, with their unique nutritional profiles, support stable and sustained energy release. The al dente preparation of spaghetti minimizes the glycemic response, offering an effective option for pasta lovers with diabetes. Steel-cut oatmeal and buckwheat, thanks to their higher fiber content and minimally processed nature, provide steady glucose release.
Nuts and yogurt are highlighted for their low GI values and added benefits. Nuts, due to their low carbohydrate content and high healthy fats and protein, contribute to both glycemic control and satiety. Yogurt, especially when containing live cultures, exhibits a low GI and supports gut health, which can positively influence blood sugar regulation.
Diabetes Specific Nutrition Formulation of Nucgnex Life sciences NUC-RDM, with a low GI of 44 potentially a Low GI category (Figure 1) for the study was carried out in the Madras Diabetes Research Foundation, Chennai, India registered in the Clinical Trial Registry of India as CTRI/2023/04/051530. Nuc-RDM contains 25g of available carbohydrate: 69g of Nuc-RDM mixed with water (235ml) and 27.5 g of reference glucose dissolved in 125 ml of water.

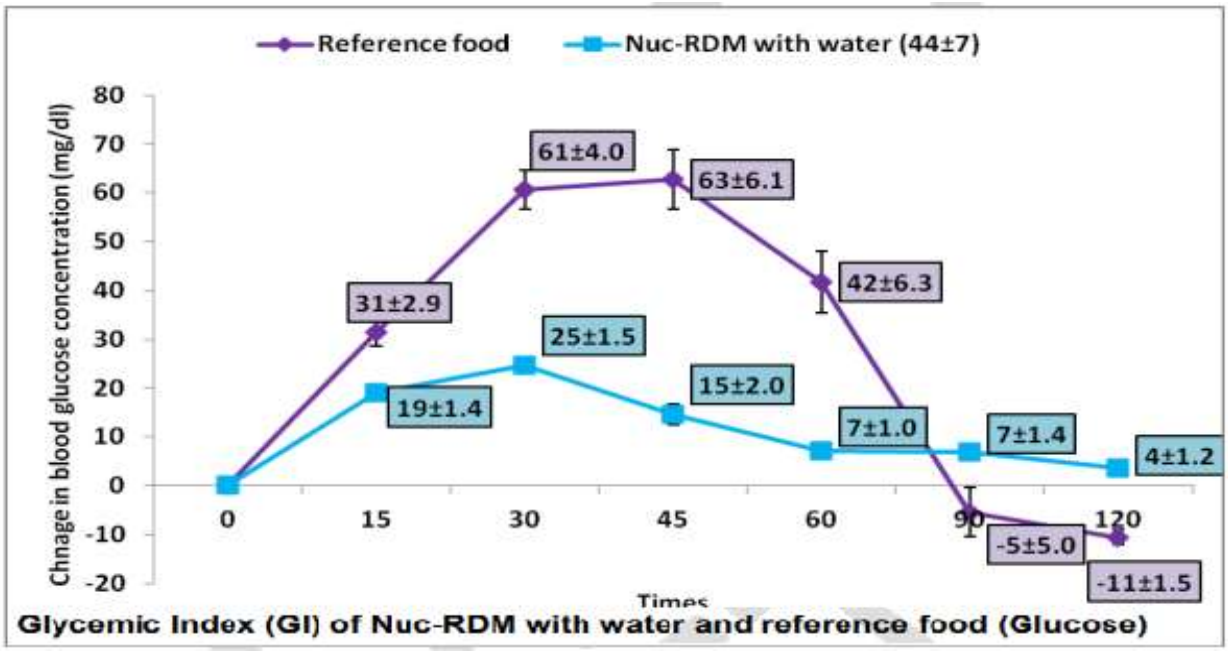

Figure 1: Chart illustrating fluctuations in blood glucose levels between control foods (glucose) and experimental foods over a span of 2 hours.

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Discussion

Breakfast skipping is associated with poor glycemic control among patients with T2D mellitus, and is linked to higher glycated hemoglobin (HbA1c) levels, which is an indicator of poor glycemic control. However, there are also studies that have reported no significant association between breakfast skipping and glycated hemoglobin level among patients with diabetes. In addition to breakfast skipping, late-night eating has been associated with poor glycemic control in patients with T2D. Late dinner intake is correlated with higher BMI and higher HbA1c levels. Overall, the association between breakfast skipping, glycemic control, and diabetes is complex and can be influenced by various factors such as meal timing, individual characteristics, and lifestyle. Therefore, further investigation of the effects of meal timing, amount, chronotype, and GI on diabetes management [103,104].

However, more large-scale observational and interventional studies are needed to further advance our understanding of the impact of chrono-nutrition on diabetes management [13]. These studies should include detailed dietary assessments and examine the long-term effects of

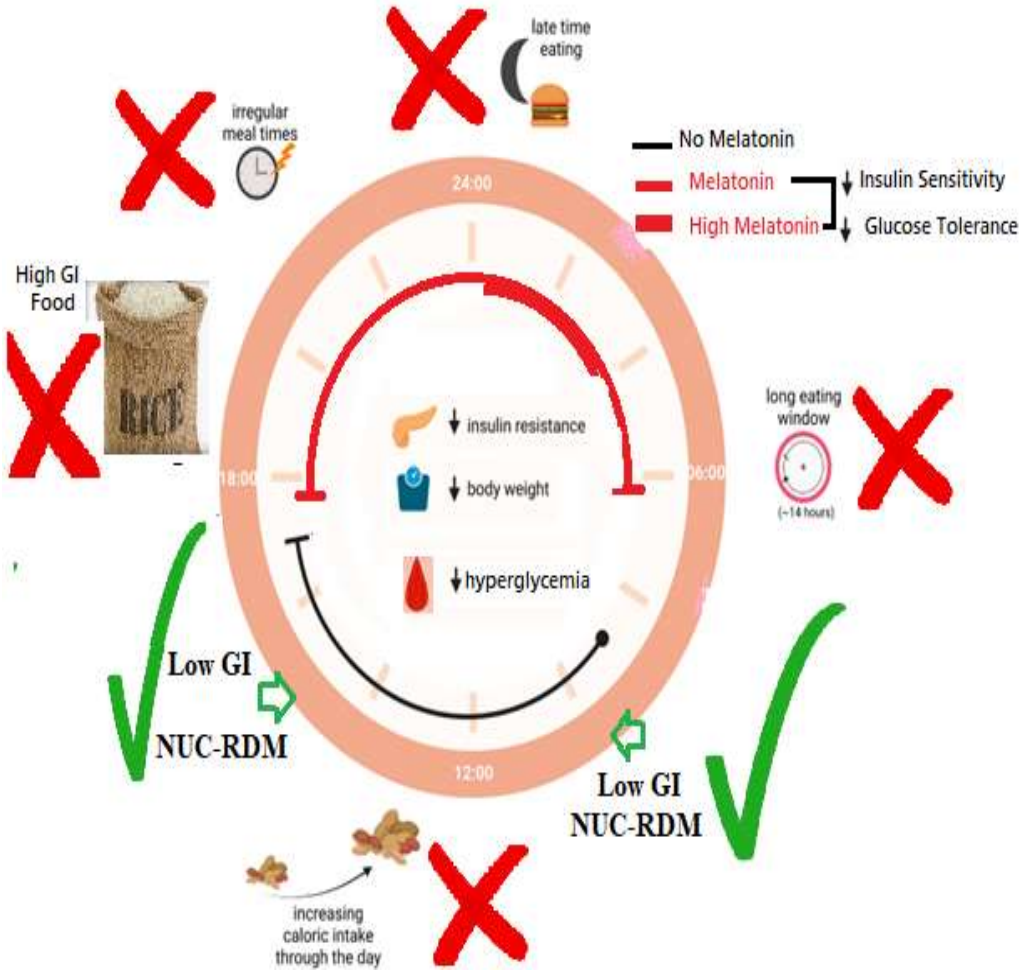

Figure 2: Intake of Low GI NUC-RDM linked with 24 hours as chrononutrition for diabetic care.

chrono-nutrition on blood sugar control, insulin sensitivity, weight management, and overall metabolic outcomes in individuals with diabetes. Additionally, there is a need for research to explore the specific mechanisms through which chrono-nutrition affects diabetes management. Diabetic individuals who adhered to an early meal schedule and consumed meals with a low glycemic index experienced superior management of their blood sugar levels compared to those who consumed low glycemic index meals but followed a later eating schedule [105].

Significance of introducing LGI foods into the meals manages diabetes. LGI foods provides a spectrum of vital nutrients and satiety in addition to improving glycemic management. Because LGI foods include fiber, complex carbs, and protein, which delay breakdown of carbohydrates, the release of glucose into the bloodstream, LGI foods have low GI values. This helps to prevent blood sugar rises that occur after meals. The NUC-RDM study highlights LGI foods potential as useful diabetic treatment strategies. Moreover, diabetic-specific formula like NUC-RDM aid in efficient management of T2D.

This will help in develop more targeted interventions and personalized recommendations for individuals with diabetes.

Conclusions

The complex issue of postprandial hyperglycemia is influenced by a variety of factors. For the prevention of T2DM, their treatment is essential. The key to glucose metabolism is diet, and IR can be treated by losing weight. From the articles that were published, it can be concluded that consuming meals at night as opposed to during the day results in a greater glycemic excursion and decreased insulin sensitivity. Research studies have focused on how the timing of meals and the types of nutrients consumed carbohydrates, fats, and proteins—affect glucose metabolism. The timing of consuming foods high in fat and protein during a meal high in carbohydrates is also included in the application of these observations. A more recent discovery suggests that a combination of slow-releasing carbohydrates and a mixture of proteins may offer advantageous control over blood sugar levels when utilized as a substitute for a regular breakfast.

Food alone does not determine glycemic response; the new area of chrono nutrition suggests that the sequence and timing of food delivery between meals may also have a substantial influence on postprandial glycemia, contributing to the rising prevalence of T2D. A growing body of study evidence in humans suggests that eating early in the day and mixing a large breakfast and lunch, with a modest dinner are favorable for diabetic health by metabolic homeostasis. Low-GI diets have a role to play in diabetes prevention and control, particularly in groups with high levels of insulin resistance and glucose intolerance.

Low GI foods, including oats, legumes, sweet potatoes, barley, quinoa, nuts, non-starchy vegetables, bulgur wheat, spaghetti, steel-cut oatmeal, buckwheat, bran cereals, and yogurt, offer a vital means of stabilizing blood glucose levels in diabetic individuals. Their low GI values, combined with mechanisms such as fiber, complex carbohydrates, and protein, enable a gradual release of glucose, reducing post-meal blood sugar spikes. These foods, rich in essential nutrients, underscore their significance in diabetes management, making them essential components of a balanced diet for glycemic control.

Collectively, these findings are easily transferable to populations that depend on a high-carb diet and have a high prevalence of T2D (pre-diabetes) as public health advocacy. According to previous studies, food components may impact circadian clocks depending on when they are consumed. Although much more research is required, the following are some important findings from the available scientific evidence regarding the reduction of postprandial hyperglycemia and insulin resistance (IR): (a) eating the majority of the day's carbohydrates at lunch, (b) adding high biological value proteins, and "healthy" fats (such olive oil, seeds, nuts, and almonds) to the diet, and (c) decreasing the total intake of carbohydrates to 40–50% of daily energy consumption. (d) following a meal plan that includes eating vegetables first, followed by proteins and fats, then carbohydrates, especially those that are not processed, and (e) selecting foods that do not cause raise glucose excursions and peaks f) refraining from eating late at night; and h) eating at consistent/regular intervals; i) incorporating meal plan with slow releasing carbohydrate and high biological value protein to improve glycemic and insulinemic responses in people with T2DM (Figure 2).

Chrono-nutrition shows potential in the dietary control of diabetes. Chrono-nutrition, which takes into account both the quantity and timing of food consumption, can play an important role in improving glycemic control, insulin sensitivity, and weight management in people with diabetes. Furthermore, chrono-nutrition could have a broader impact on the prevention and treatment of metabolic illnesses like obesity and metabolic syndromes. To summarize, chrono-nutrition is a rapidly growing field of study that focusses on the timing and distribution of food intake, as well as the impact on health. It recognizes that meal timing, frequency, and regularity are critical factors in maintaining a healthy biological clock and sleep-wake cycle. By aligning our eating patterns with our body's natural rhythms, chrono-nutrition can optimize metabolic function and promote overall well-being. NUC-RDM being LGI formula, makes it ideal for T2D management.