

Diabetes mellitus and dietary starch in perspective of blood glycaemic control

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Abstract

Diabetes mellitus is a complex metabolic disorder which disrupts normal physiological functions of the body cells to take in and utilise glucose effectively. On the other hand, blood glycaemic control remains the primary therapeutic target for diabetic patients. Dietary starch is the main determinant of blood glucose. But dietary starch tolerance levels fluctuate between individuals, which might be due to difference in genetic variants of alpha-amylase enzyme. Additionally, genetic variability of cereal carbohydrates may also influence glucophenotype in terms of a specific glycaemic and biochemical derangement. Therefore, personalised carbohydrate/ starch based diets are needed to ensure optimum blood glycaemic control in diabetic subjects in prospective studies.

Keywords: Diabetes mellitus, Starch, Glycaemic control.

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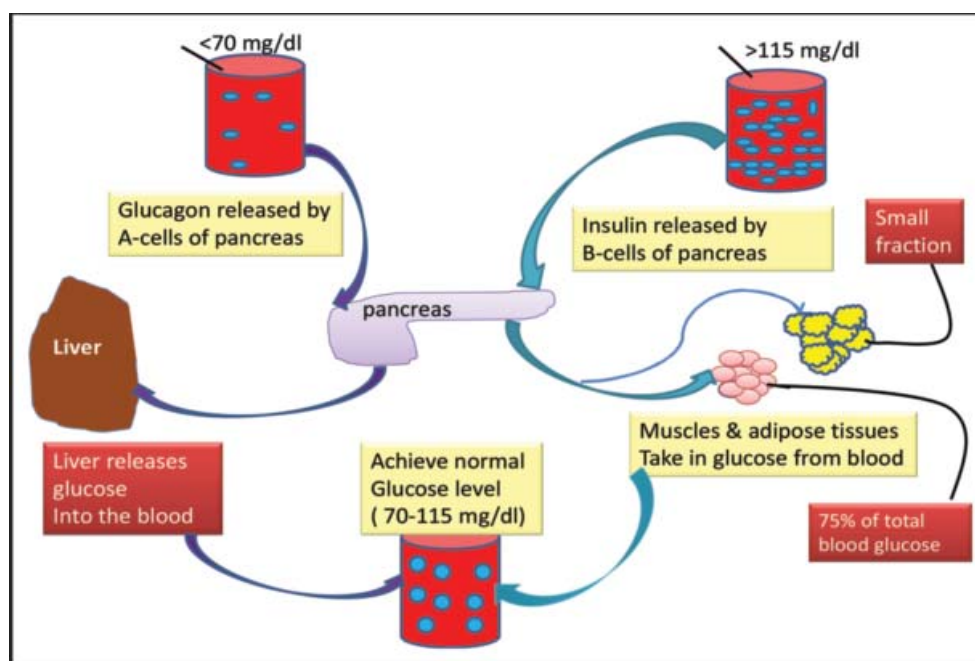
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Introduction

Diabetes mellitus (DM) is a multi-organs endocrine disorder of carbohydrate metabolism that lead to an excessive accumulation of glucose molecules in blood circulation.¹ Blood glucose level within normal range is an absolute requirement for human life.² Glucose transporter type 4 (GLUT4) channels in the plasma

membrane of insulin-sensitive target cells in various body tissues (e.g. skeletal muscles) are involved in the uptake of glucose from blood circulation. Skeletal muscles take in maximum of total blood glucose through GLUT4 channels, which are stimulated by insulin, a pancreatic hormone.³ Any alteration in insulin-stimulated glucose uptake can lead to the derangement of glucose disposal.⁴ As a consequence, GLUT4 get stuck inside the cells instead of their translocation to the surface of cell membrane.⁵ Chronically, high blood glucose leads to



Abbreviations: A=alpha and B=Beta.^{3,4}

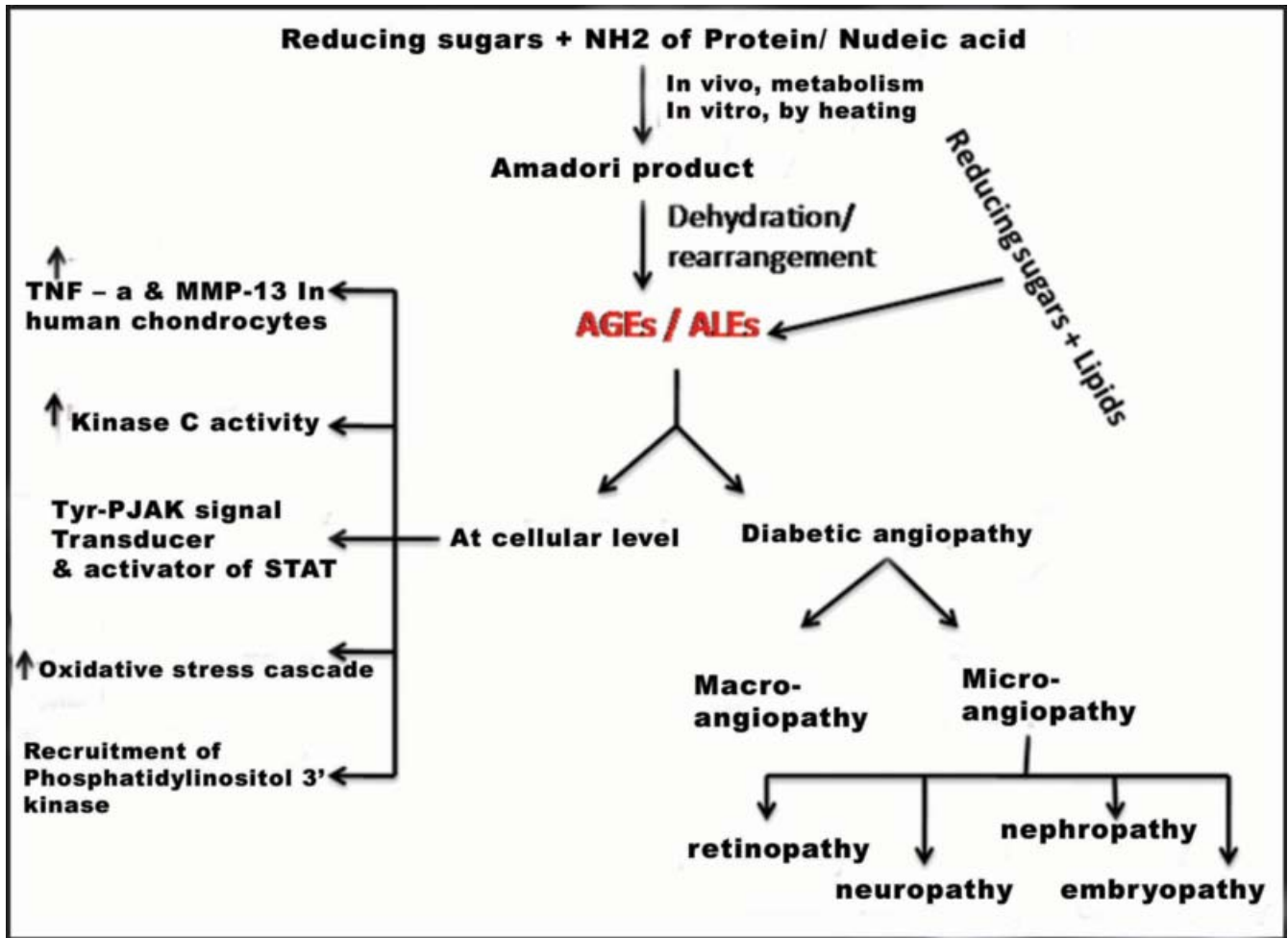
Figure-1: An overview of key tissues/organs in the glucose homeostasis.

overt hyperglycaemia, which is a clinical hallmark of DM development⁶ (Figure-1).

During hyperglycaemia, non-enzymatic protein glycation occurs in the form of advanced glycated end-products (AGEs) in various body tissues,

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AGEs: Advanced glycosylated end-products, ALEs: Advanced lipoglycosylated end-products, TNF- α : Tumour necrosisfactor alpha, MMP: Matrix metalloproteinase, Tyr-P JAK: Tyrosine phosphate Janus kinase, STAT: Signal transducer and activator of transcription.^{12,13,75}

Figure-2: AGEs synthesis and their biological effects

spontaneously.⁷ This glycation process is accompanied by Maillard reactions that entail Amadori adduct formation through Schiff base intermediate when amino groups of proteins react with carbonyl moieties of glucose molecules.⁸ Successively, Amadori adducts undergo further rearrangements to form AGEs.⁹ There are receptors for AGEs (RAGEs) found on various cells, especially those affected in diabetic condition.¹⁰ An interaction of AGEs with RAGEs induces intracellular reactive oxygen species (ROS) production. These ROS would in turn activate transcriptional nuclear factor NF- κ B that triggers transcription of several genes of intracellular signalling pathways implicating in the pathogenesis of metabolic diseases including diabetes-related complications.^{8,11} The pivotal roles of AGEs and RAGEs

in the glycation processes highlight them to be attractive candidates for therapeutic intervention to restrict diabetes damage and its long-term adverse health consequences^{12,13,76} (Figure-2).

Factors contributing to the diabetes development

Incidence of diabetes, especially type 2 diabetes mellitus (T2DM), is continuously increasing due to changes in lifestyles, physical inactivity, unhealthy diets and obesity.¹⁴ Unhealthy diets along with high carbohydrate consumption are associated with increased risk of T2DM.¹⁵ Dietary carbohydrates are transformed directly into blood glucose at different metabolic rates. Therefore, carbohydrate type is more important than the total amount of carbohydrate for T2DM management. In order

to control blood glucose within permissible limits, diabetic patients avoid sugars and opt for starchy foods.¹⁶ Furthermore, meals rich in carbohydrate may reveal adverse immunometabolic responses associated with obesity.¹⁷ Obesity is a major cause which significantly contributes and predisposes to insulin resistance (IR) in T2DM. Obesity and T2DM are twin-disorders and most of the obese are prone to getting T2DM and its related complications.¹² In addition, obesity is also regarded as a latent phase for cardiovascular disorders, hypertension (HTN) and pulmonary complications.^{1,18} Obesity causes an alteration in lipid metabolism in adipose tissues of obese subjects which leads to IR in skeletal muscles and perturbation in insulin signalling pathways due to increased free fatty acid (FFA) levels.¹⁹

Prevalence of diabetes

In 2017, more than 450 million diabetes cases were recorded and this number is expected to increase up to 690 million by 2045.²⁰ Globally, diabetes prevalence varies from region to region. A relative cross-country comparison data for 2011 indicated that Pakistan was facing a high-prevalence of diabetes (9.1%) with 7 million affected people in 2010 which was expected to

be 11% by 2030, with 14 million diabetics. Furthermore, by including pre-diabetes, the prevalence becomes more than 22%. This alarming increase of diabetes ranked Pakistan at seventh, which could be converted to 4th position by 2030.²¹

Dietary options to regulate blood glucose

DM is a disorder of defective glucose metabolism.⁴ In the digestive tract, carbohydrates are degraded into glucose with its successive increase in blood circulation.²² The quality and quantity of carbohydrate-based foods are assessed by their glycaemic indices (GIs) or glycaemic loads (GLs).²³ These GIs/GLs provide dietary options to control blood glucose within the desired limits.²⁴

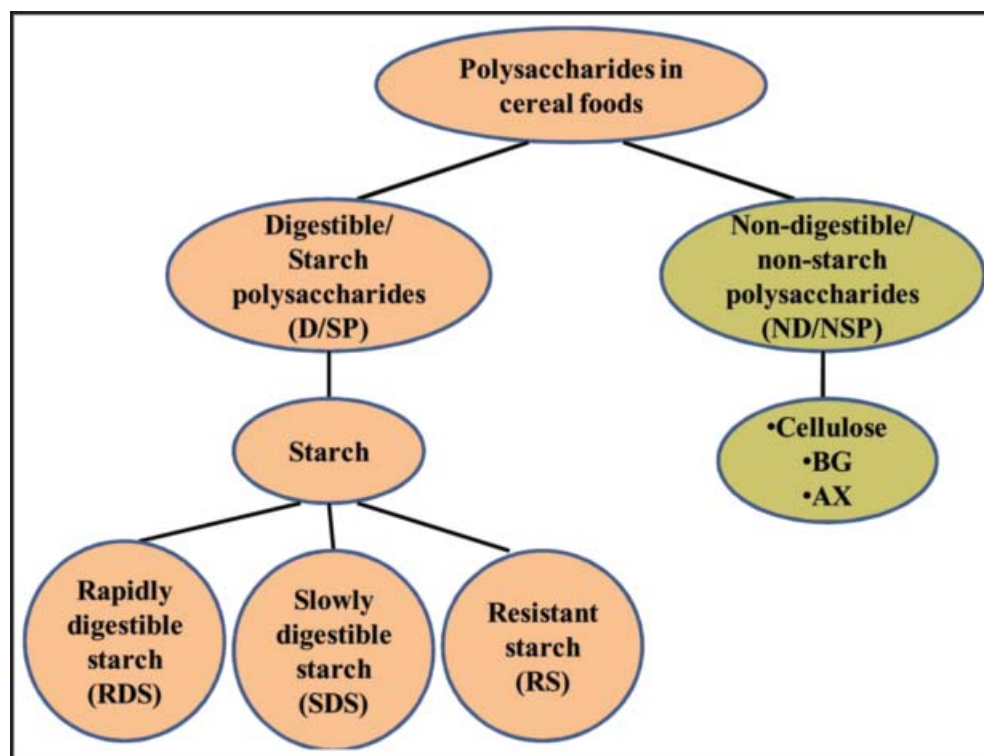
Carbohydrates/polysaccharides in cereal crop grains

Among three energy-yielding food components (i.e. carbohydrate, lipid and protein), carbohydrate is the only macronutrient that acts as a primary and instant source of energy for cells. Most of the carbohydrates/polysaccharides, especially starch, are synthesised and stored in grains of cereal crops, such as wheat, rice, maize etc.²⁵ The polysaccharides present in cereal grains are categorised into two groups: non-digestible

polysaccharides (NDPS) i.e. arabinoxylan (AX) and beta glucan (BG), and digestible polysaccharides (DPS) such as starch.²⁶ A cereal grain has three: germ, endosperm and coat bran. Starch is mainly stored in the endosperm of cereal grains and regarded as a major human food constituent worldwide²⁷ (Figure-3).

Nutritional aspect of starch

Starch is composed of two types of polymers: amylose and amylopectin. An alteration in amylose and amylopectin ratio changes the quality of starch. An increased amount of amylose content may be a factor to reduce starch digestion in gastrointestinal tract. In addition, NDPS, such as AX and BG, present in endosperm and outer layer



D: Digestible, SP: Starch polysaccharides, RDS: Rapidly digestible starch, SDS: Slowly digestible starch, RS: Resistant starch, BG: Beta glucan, AX: Arabinoxylan.^{27,28}

Figure-3: Classification of polysaccharides on the basis of their nutritional aspect.

Table-1: Glycemic index and load values of crops, fruits, roots, vegetables/nuts.

Cereal crop	Glycemic index (GI)	Glycemic load (GL)	Reference
Indian rice	WR:(GI=79.2), HFWR:(GI=61.3)	-	66
Bangladeshi rice varieties	BR-14: (GI=54.5) BR-29: (GI=50.3) BR-44: : (GI=43.1)	BR-14: (GL=25) BR-29: (GL=22) BR-44: (GL=20)	67
Irani rice brands	SP:(GI= 52.2) K:(GI=67.6) B: (GI=61.2)	SP:(GL= 21.8) K:(GL=27.4) B:(GL=31.7)	68
Sri Lankan rice varieties	Bg360 Samba: (GI= 66) B At405:(GI= 73) PbNBg 352:(GI= 40)	-	69
Thailand rice varieties	Jasmine rice:(GI=90.7) Basmati rice:(GI=66.2) PK+4#1_E06 (GI=54.6) PK+4#00B09 (GI=66.1) PK+4#117A08 (GI=63.8) PK+4#20A09:(GI= 48.1)	-	70
Wheat bread	WWB: (GI=75) WW: (GI= 74) UWB:(GI= 70) WR: (GI=62) C: (GI=52)	-	32
Indian wheat	WWF: (GI=44.6) MgF: (GI=28.4)	-	71
Belgian wheat	WWB (GI= 93)	-	72
Malawi Maize	PPWMF:(GI=94.06) PPFMG:(GI=65.49)	-	73
Nigerian maize	-	MMSP:(GL=16)	23
Glycaemic indices of selected Philippine foods:			
Bakery/Rice products	Biscuits (GI=88-94) Biscuits with oat fibers (GI=52) Sugar coated donut (GI=70) Noodles (GI=49)	-	74
Starchy roots, vegetables & beans/nuts	Potato (GI=43) Carrot (GI=35) Squash (GI=44) String beans (GI=23) Lima beans (GI=16) Cashew nuts (GI=36)	-	74
Fruits	Banana (GI=62) Grapes (GI=46) Pear (GI=29) Watermelon (GI=48) Mango (GI=46) Red Apple (GI=42) Guava (GI=19)	-	74

WR: White rice, HFWR: High fibers white rice, BR: Bangladeshi rice, SP: Sorna pearl, K: Kazemi, B: Basmati, PbN: Parboiled-Nadu, PK: Pinkaset, WWB: White wheat bread, WW: Whole wheat, UWB: Unleavened wheat bread, WR: Wheat roti, C: Chapatti, WWF: Whole wheat flour, MgF: Multigrain flour, PPWMF: Porridges prepared from whole maize flour, PPFMG: Porridges prepared from fermented maize grits, MMSP: Maize meal stiff porridge.

of the grains may interact with starch, reducing its degradation and absorption in the gut.^{28,29} Thus, in nutritional perspective, starch may be glycaemic and non-glycaemic in terms of its conversion into blood glucose.³⁰

The former contributes to blood glucose, while the latter (mostly called dietary fibres) are not broken down by digestive enzymes. Carbohydrate-based foods may be sugary and starchy due to their fast and slow conversion

into blood glucose, respectively.³¹

GI is a measure of the rise in blood glucose after eating a specific food. This physiological parameter is used to classify the starch originated from various crops as low (<55), medium (55-69) and high (≥ 70) GI starch types.³² High GI starch causes sharp rise of blood glucose than medium and low indexed starch type. GI helps to improve glycaemic control in diabetic and pre-diabetic individuals.^{33,34} On the basis of gastrointestinal digestion and absorption, various starch types have different degrees of appetite-suppressing effect. High GI starch is less satiating because of rapid gut-emptying rate compared with the low or moderate GI starch.³⁴ Several studies reported that whole grain/fibre containing flour causes more satiety than refined white flour. However, available data is not sufficient to prove long-term satiety-enhancing effect of a specific type of starch product.^{35,36} Therefore, researchers are paying attention to evaluating various staple crops on the basis of GI values. Some studies worked out the GI values of rice, wheat and maize products (Table-1).

Factors affecting the starch quality and composition

Ecological stresses: Quality of starch is also affected by seasonal and climatic conditions. Environmental stresses, such as soil, water, nutrients and atmospheric conditions, affect starch composition in grain endosperm. Fluctuations in amylose content are reported under tropical and subtropical/temperate conditions.^{37,38}

Genetic variations

Genetic variability of starch in endosperm of crop grain is determined by several enzymes i.e. ADP-glucose pyrophosphorylases, synthases, branching, debranching enzymes and their isoforms involved in a committed pathway. These variations include inconsistent amylose/amylopectin ratio, differences in the size and shape of starch granules, crystallinity, lipid and protein contents surrounding the starch granules.³⁹ High ratio of amylose creates compactness/rigidity by reducing starch enzymatic disintegration.^{27,40}

Amylase gene variants and glycaemic control

Individuals show different response in terms of digesting dietary starch, although they consume the same quality of food. This might be due to differential expression of genes involved in amylase synthesis.⁴¹ Briefly, within a population, starch digestion rate varies due to variable level of amylase enzyme.⁴² Ecological adaptation also causes alteration in composition/nature of cereal starch.³⁷ Therefore, at individualised level, identification of

compatible starch diet is expected to prevent the overwhelming effects of high postprandial blood glycaemia and its associated metabolic consequences.⁴³⁻⁴⁵ When the diabetes is full blown, there are limited chances to reverse the disease phenotype. The disease's clinical features appear after several years of latent asymptomatic phase.⁴⁶ This pre-symptomatic period prior to the disease onset provides a number of opportunities for disease prevention, if individuals diagnosed/screened accurately for amylase genes copy number variations.⁴⁷ High amylase gene copies are related to increased production of salivary and pancreatic amylases with increased glycaemic response to refined starch enriched diets and vice versa.⁴⁸

Evidences for turning high GI foods into low glycaemic diets

Several studies tailored refined high GI starch into low GI diet/s by adding NDPS/fibres from other sources. Dietary fibres, lipids and proteins' interaction with starch greatly reduce degradation.⁴⁹ For example, pea fibre-enriched breads can reduce postprandial blood glucose level and enhance satiety.⁵⁰ It was manifested that whole yellow pea flour attenuates the postprandial blood glucose level effectively than the whole wheat flour biscotti.⁵¹ Furthermore, rye flour which was enriched with indigestible carbohydrates improved glycaemic profile.⁵² Thus, it can act as an appetite regulator by delaying the gastric emptying span. Studies have demonstrated that addition of spices to the diet significantly reduce the circulating glucose with concomitant increase of antioxidant status.⁵³ Different spices like cloves, turmeric and cinnamon have insulin-potentiating activity.^{54,56} It is emphasised that cinnamon must be added to the diet of diabetics.⁵⁷ Another study also reported the hypoglycaemic effect and delayed gastric-emptying rate of cinnamon when ingested with steamed rice.⁵⁸ So in order to keep the glycaemic and energy balance, the selection of diet is very important.⁵⁹

Low glycaemic diets and body weight

Frequent intake of high GI diets stimulates excessive insulin secretion, which leads to enhanced lipogenesis with the successive accumulation of fats in adipose tissue.^{60,61} This fat overloading causes leptin-resistant adiposity in susceptible individuals.^{61,62} In addition, high GI foods are responsible for the inordinate production of ghrelin hormone, which is fast-acting and promotes appetite.⁶³ Consequently, food intake exceeds energy expenditure by body cells.⁶⁴ However, consumption of restricted low GI diet can improve the glycaemic profile and may also become useful for body weight control.⁶⁵

Conclusion and future prospect

Dietary starch restriction is regarded as the primary

approach in diabetes management for keeping blood glucose in optimum range. Starch in cereals crops is important because it constitutes the largest portion of the diet and is the major blood glucose generating component in humans. Due to the influence of various factors, such as differences in crop varieties, degree of processing, amylose content, fluctuations in seasonal and climatic conditions, crops behave differently to be converted into blood glucose. The proper amounts and types of carbohydrates owning low GI and GL indices hold a lot of potential for futuristic research activity in this area to manage diabetes.

To our knowledge, no comprehensive research has been conducted yet that indicate an interactive influence of genetic variability of cereal carbohydrates and genetic variants of human amylase on starch conversion rate from the gastrointestinal tract into the blood circulation. Pertinent to this, more large-scale prospective cohort studies are needed to develop personalised starch-based diets to control hyperglycaemia in the perspective of diabetes, especially at pre-symptomatic stage and during obesity. Such personalised carbohydrate-based diets relating to a particular human group would be more effective rather generalising starch for the entire obese and diabetic population at large.

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