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Multifaceted Roles of Resistant Starch (RS) on Human Health

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Starch is a polysaccharide, which is made up of glucose monomers. Heteropolymeric nature of starch arises due its amylose and amylopectin constituents. Amylose is a linear polymer- composed of α 1-4 linkages of glucose molecules. In contrast, amylopectin has both linear and branched structures, where the linear chains are linked by α 1-4 linkages and branched chains are crosslinked by α 1-6 linkages [1,2]. Depending on the enzyme hydrolysis, starch can be classified as digestible starch and Resistant Starch (RS). Digestible starch, based on the rate at which the starch digests, can be further classified into Slowly Digestible Starch (SDS) and Rapidly Digestible Starch (RDS). RS is a fraction of starch that escapes the digestion in the small intestine and reaches the large intestine for fermentation [3]. The Glycemic Index (GI), which measures the concentration of glucose in the blood after the consumption of a meal, of digestible (SDS and RDS), and RS shows that RS has a lower GI (≤ 55) compared to digestible starch [3,4]. Due to the lower GI of RS, it is worth to look into the detailed investigations of RS and its health benefits from a nutritional point of view.

RS can be classified into 5 major classes. RSI is a physically inaccessible form of starch found in whole grains. RSII is mainly due to the B crystallinity of starch granules. The B form of starch is a densely packed compact structure, which reduces the accessibility to the starch hydrolyzing enzymes. RSIII is a retrograded form of starch; repeated cooking-cooling cycles can gelatinize and recrystallize the starch. Repeated re-crystallization of starch forms a retrograded structure, which does not fit into the active site of starch hydrolyzing enzyme- making the starch resistant. RSIV is a chemically modified starch, where new linkages other than α 1-4 and α 1-6 are formed. The starch can be chemically modified during processing conditions. RSV is formed due to the amylose-lipid complex. Helical structure of amylose can form a "cage" like structure around the lipids making enzymes resistant for digestion. Therefore, since these starches do not get digested in the small intestine, due to the inaccessibility of starch hydrolyzing enzymes, they reach the large intestine for fermentation. Fermentation products of RS benefits human health in multiple ways [2,3].

Human gastrointestinal tract, is a host for many microflora. This host-guest relationship has pronounced effects on human health [5]. Especially, the gut health is dictated by the microbiota housed in the gastrointestinal tract. The biological function of the microflora is in turn determined by the dietary intake. RS, mainly RSIII, plays a vital role in the functioning of microflora. Gut microflora binds to RSIII, which escapes the digestion in the upper gastrointestinal tract and small intestine, and ferments in the large intestine to form various fermentation products: methane, hydrogen, carbon dioxide, branched and unbranched Short Chain Fatty Acids (SCFAs), and organic acids [5,6]. During the fermentation process, a large amount of Adenosine Triphosphate (ATP) is produced, which acts as an energy source for the colonocytes. In addition, the SCFAs can prevent colorectal cancer. The acidic intracellular environment in the gut can contribute towards micronutrient uptake [7,8]. Not only the fermentation products, but also the lower GI of RS can prevent type 2 diabetes [4]. Therefore, the multifaceted roles of RS: prevention of colonic cancer, prevention of type 2 diabetes, micronutrient uptake, and contribution towards Parkinson's disease will be discussed briefly in the following section.

Prevention of colon cancer

Uncontrolled growth of colonocytes, which is also known as colorectal cancer, is influenced by the colon health. Colorectal cancer can be caused by the alteration and/or dysregulation of cells life cycle in terms of cell proliferation, differentiation, and cell death (apoptosis).

The alteration in any of these processes is stemmed from an enzyme called Histone Deacetylase (HDAC); HDAC causes transcriptional regression, which in turn leads to malfunctioning of cells. However, inhibition of HDAC can facilitate the well-being of colonocyte. Sodium butyrate was the first HDAC inhibitor that was discovered in the early 1970s [9]. Nevertheless, one of the fermented products of gut microflora is butyrate, which can act as an inhibitor for HDAC. In addition, butyrate is also known to have anti-tumerogenic property. Both, the inhibition of HDAC and the anti-tumerogenic properties of butyrate facilitates and enhances the health of colonic cells [10-12]. Therefore, RSIII fermentation is one of the major biological processes, which has substantial contributions towards the gut health.

Prevention of type 2 diabetes

Diabetes is a non-communicable disease, which was the cause for 1.6 million deaths around the world in 2015 [13]. One of the main factors that causes type 2 diabetes is the food pattern. Increased intake of starchy foods can accelerate the glucose levels in blood leading to type 2 diabetes. Therefore, an alternative will be to consume foods with high RS content. The lower GI of RS prevents the rise of glucose in blood, thus benefiting postprandial glucose metabolism [3]. A change in diet pattern from "starchy" food to "RS rich" food can prevent type 2 diabetes and reduce the mortality rates due to diabetes.

Micronutrient uptake

Micronutrients, although required in trace amounts, contribute vastly towards growth and development in human [14]. Micronutrient deficiency affects both developed and developing countries. RS plays an important role in the micronutrient uptake mainly through two mechanisms. Firstly, the fermentation products of RS results in SCFA, which reduces the pH in the gut. Reduced pH can enhance the uptake of micronutrient in the gut. Secondly, the SCFAs are protonated and upon reaching the intracellular environment in the gut they get deprotonated. Once the H^+ ions are formed due to deprotonation, they can be exchanged with Ca^{2+} through Calcium Binding Protein (CaBP) to facilitate Ca^{2+} absorption [14]. Therefore, RS fermentation contributes towards micronutrient uptake, which can combat micronutrient deficiency.

Prevention of Parkinson's disease

According to Parkinson's disease Foundation (PDF), approximately 10 million people are prone to Parkinson's disease around the world. Parkinson's disease, is a neurodegenerative disorder, where the brain cells die rapidly [15]. Accumulation of α-synuclein and colonic inflammation are two main indicators of Parkinson's disease. Colonic inflammation arises due to the lack of production of SCFA; inadequate substrate for colonic microflora results in insufficient production of SCFAs, which can result in colonic inflammation [16]. Therefore, consumption of RS rich diets can prevent colonic inflammation, which in turn can mitigate the disease conditions in Parkinson's disorder.

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