Citations

(1) American Diabetes Association. "What Can I Eat?" *Diabetes.org*. American Diabetes Association, 2015. Web. 18 June 2015.

(2) "Diabetes Mellitus." Wikipedia. Wikimedia Foundation, n.d. Web. 19 June 2015.

(3) "Human Body Digestive System Organs, How It Works, and More." WebMD. WebMD, n.d. Web. 19 June 2015.

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Diabetes User's Manual

IGEM AT THE UNIVERSITY OF VIRGINIA

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The Human Body and Diabetes

What is Diabetes?

Diabetes is a metabolic disease in which blood glucose levels remain high over a prolonged period of time. This disease is caused by the decreased production of insulin by the pancreas, or the cells of the body not responding properly to the insulin produced. Insulin functions to regulate the metabolism of carbohydrates and fats by promoting the absorption of blood glucose from skeletal muscles and fatty tissue. When blood sugar levels fall below a certain point, the body begins to break down glycogen stored in the liver and muscles into free glucose, which can then be used as an energy source. The danger of diabetes is that the body can no longer produce insulin and control blood sugar levels. Prolonged hyperglycemia resulting from insufficient insulin production or cell recognition can affect many organ systems. The major complications resulting from diabetes are heart and kidney disease. To reduce the risk of such complications, blood sugar control is key. For this reason, our team has focused our research on regulating the absorption of free glucose in the gut via the insertion of a bacterial chassis.

Diabetes and the Human Digestive System

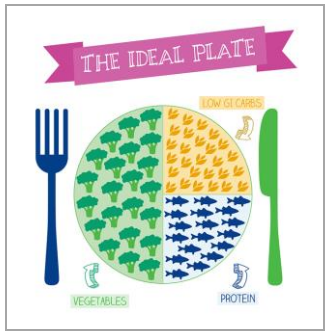
The digestive system is composed of a series of organs working together to convert food into basic nutrients that feed the body. In order for a bacterial chassis to be able to compete for glucose, it is crucial that a time-delay capsule system is implemented to allow for the bacteria to reach the correct area of the intestine. When food reaches the stomach, it is churned and bathed in gastric juices, changing its consistency to a pasty substance known as chyme.

The Diabetes Diet

Guidelines

Diabetes patients generally want to avoid carbohydrates with a high glycemic index. Choose artificial sweeteners over sugar for less calories and carbohydrates. In order to decrease heart disease risk, one should minimize the amount of saturated and trans fat they eat. Alcohol should be limited to 1-2 drinks per day. Fiber is very beneficial to digestive health and should be consumed daily. [1]

Making Smart Food Choices



When eating starchy foods, always choose a whole grain alternative. It is important to intake high-protein foods, especially low-fat ones. Try vitamin and mineral filled non-starchy vegetables. Low fat dairy products offer calcium and protein, and fruits are a smart way to satisfy a diabetic's sweet tooth. [1]

Diabetes Superfoods

The following foods are excellent choices for any diabetes patient. They all have a low glycemic index and provide key nutrients including calcium, potassium, fiber, magnesium, and vitamins A, C, and E. The superfoods: beans, dark green leafy vegetables, citrus fruit, sweet potatoes, berries, tomatoes, fish high in omega-3 fatty acids, whole grains, nuts, and fat-free milk and yogurt. [1]

Exercise

Along with changing diet paradigm, exercise is a self-empowering way to combat diabetes mellitus. Both aerobic and resistance exercise have been documented as efficient techniques to reduce diabetic complications in normal and diabetic populations. Exercise, in general, helps to increase the body's sensitivity to insulin as well as decrease blood glucose. Most dieticians and endocrinologists recommend a consistent routine of exercise to decrease diabetic complications.

Exercise helps to increase insulin sensitivity as well as decrease blood glucose.

Physiological Effects of Exercise and Insulin Sensitivity

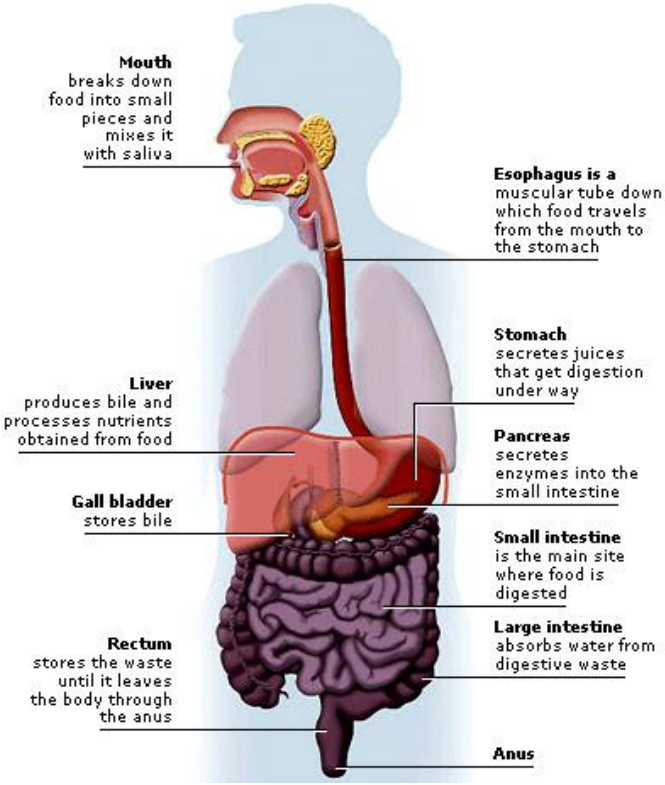
After exercise, blood glucose uptake is increased due to GLUT-4 transporters bonding with the plasma membrane and T-tubules of the muscle. Two hours after exercise, blood glucose decreases significantly due, in part, to increased muscle GLUT-4 transporters and depletion of muscle glycogen storage.

Exercise and Metabolism

Exercise affects the body metabolism and the biochemical pathways of respiration. Most glucose and fructose lie in the blood or are sent to the muscle or liver (where they form glycogen). The muscle uses glucose in cellular respiration and, when the body undergoes physical stress, the demand for glucose increases. The muscle utilizes those simple sugars to power its mechanical movement as well as the contraction and relaxation of myosin and actin fibrils in myocytes.

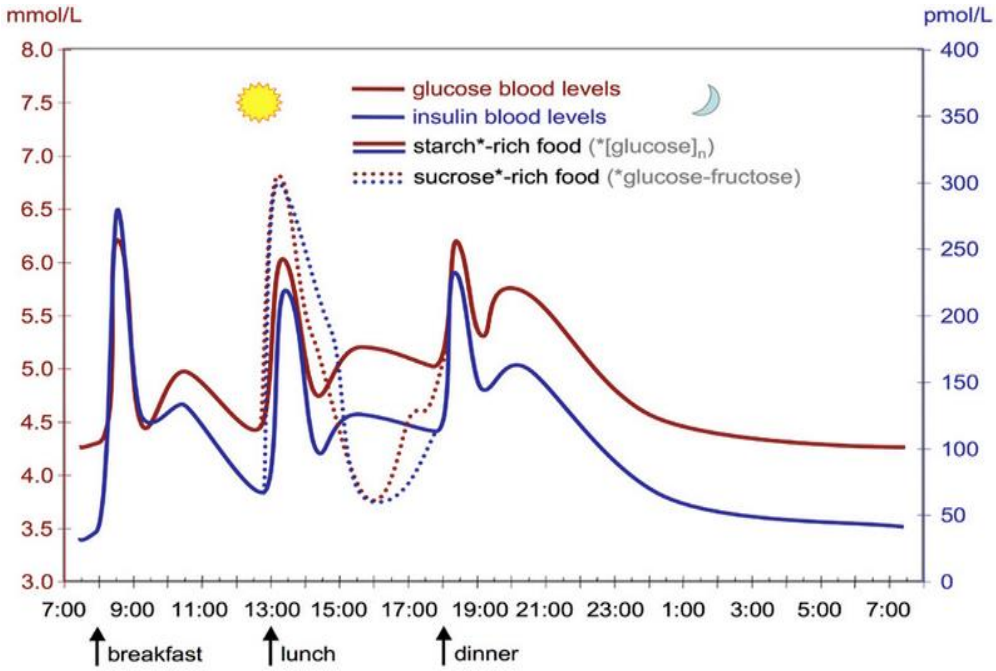
The partially digested food is then transported to small intestine which is composed of three segments: duodenum, jejunum, and ileum. The duodenum is largely responsible for this continued breakdown of chyme, whereas the jejunum and ileum are function mainly in nutrient absorption. The pancreas and liver function to aid the small intestine in nutrient absorption by releasing digestive enzymes and bile, respectively, into the lumen of the duodenum. It is in the ileum and jejunum that the modified bacteria must be activated.

The Human Digestive System



A diagram of the human digestive system.

Complex Sugars vs. Simple Sugars



Jakob Suckale, Michele Solimena - Solimena Lab and Review Suckale Solimena 2008 Frontiers in Bioscience PMID 18508724, preprint PDF from Nature Precedings, original data: Daly et al. 1998 PMID 9625092

Starch-rich Food Causes Smaller Post Prandial Glucose Spikes

Research has shown that starch-rich (complex sugar) food leads to smaller post-prandial glucose spikes compared to sucrose-rich (simple sugar) food. It is due to the fact that human body does not readily absorb complex sugars or polysaccharides.

Our Solution

Delaying Glucose and Reducing Fructose Absorption by Polymerization

Taken before meals, our synthetically modified *E. coli* strain Nissile 1917 localizes to small intestine where the most abundant simple sugars in human body, glucose and fructose, are absorbed. Nissle 1917 uptakes and polymerize glucose into glycogen. At the same time, the Nissle 1917 also polymerizes fructose into levan. Levan cannot be absorbed by human and will eventually cause the bacterial cells to lyse to release the glycogen. Thus the absorption of simple sugars is both reduced and delayed.