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BETTER YOU, BETTER TOMORROW

THE POWER OF YOUR GUT

WHITEPAPER

GUT MICROBES

Microbes such as bacteria are common inhabitants of the human body. They are found externally and internally, both on the inside and outside of our bodies. Interestingly, the total number of these microbial inhabitants, matches closely that of our own cells (about 3×10^{13} – an extremely large number!)[1]. The largest and the most diverse group of bacteria live in the gut, where a recent research study managed to identify over 1,950 different species[1, 2, 3]. Everyone has a unique composition of gut bacteria[4]. This microbial mix varies from person to person but depends strongly on age, diet, genetic makeup and medications[5].

Gut bacteria are responsible for some crucial functions beneficial to human function. For instance, they digest dietary fibre, produce nutrients, produce vitamins, protect us from harmful bacteria and help to support a healthy immune system[2, 6, 7, 8]. There is a growing body of research indicating that gut microbial imbalances (also known as dysbiosis) can be harmful and, as currently suspected, lead to the development of various illnesses, such as inflammatory digestive disorders such as IBS and Crohn's disease, mental health such as stress and anxiety as well as other conditions such as obesity and type 2 diabetes[9, 10, 11, 12, 13, 14, 15, 16, 17, 18].

MICROBIAL PRODUCTS

Microbes within the gut assist the body with the digestion and production of many substances which are beneficial to health. Short-Chain Fatty Acids or SCFAs are the most abundant products of gut bacteria and therefore can be used to quantify as an important biomarker of gut performance and health.

Microbes produce SCFAs from nondigestible dietary fibre – i.e. complex carbohydrates which are present in various plant foods[19]. These fibre rich foods include wholegrain products, fruits, vegetables, legumes, nuts and seeds. Research has indicated that the consumption of fibre has a positive effect on our gut microbes and results in an increase in the level of SCFAs. Modern Western-style diets often rely on the consumption of high amounts of refined processed food, animal protein, starch, fat and sugar, yet with limited amounts of fibre. As a result, Western-style diets provide a limited supply of fibrous food sources for the bacteria to feed from, which in turn can have an adverse effect on gut microbial diversity, and overall health[2]. Studies have begun to link the dietary habits of Western populations to the rising incidence of health conditions, including inflammatory digestive disorder, type 2 diabetes and poor mental health.

Without the help of gut microbes, our digestive system would not be capable of breaking down fibrous food sources. A healthy gut microbiome is instrumental in these digestive processes. It is important to note that our microbiota produces many other molecules other than SCFAs, for example, bile acids, amino acid derivatives that may have essential regulatory functions in our bodies[2].

MEASURING SCFAS

Advancements in technology now mean that SCFAs can be extracted from a fecal sample, detected and measured to determine their concentration. In the laboratory, the SCFAs are extracted from a fecal sample and then analysed using GCMS (Gas chromatography–mass spectrometry), which allows for the exact concentrations of each SCFA to be accurately measured. The fecal concentration of SCFAs can serve as an indicator of the overall level of these compounds produced by bacterial fermentation.

The quantity of SCFAs produced depends on microbial content of the GI tract. In other words, the presence of different species and the number of individual microbes present, as well as diet composition and quantities[25, 26, 27, 28, 29]. Therefore, SCFAs act as a gut health indicator as well as a measure of the combined performance of an individual's diet and presence of good gut bacteria.

SCFAS IN THE BODY

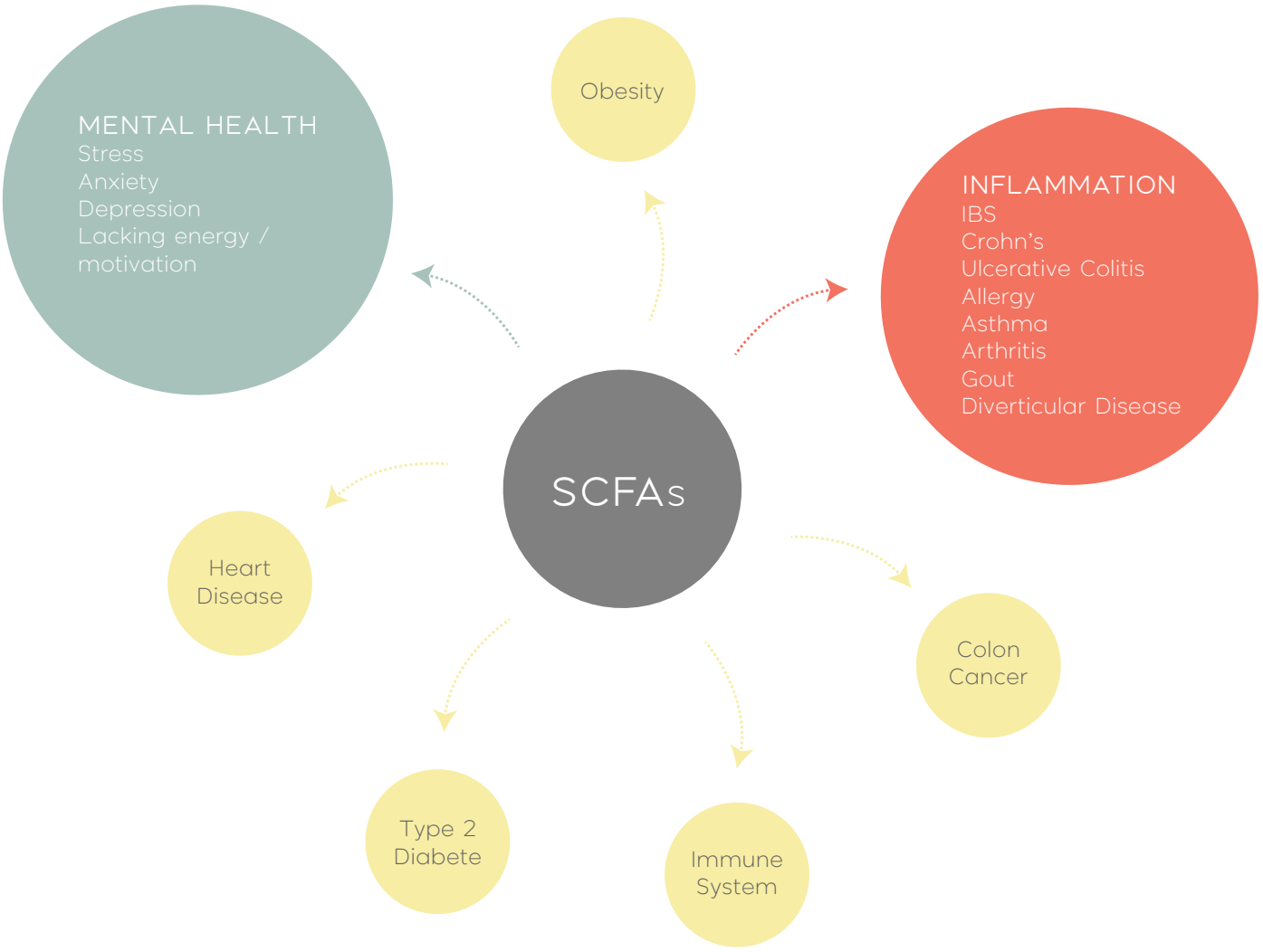
Once fibrous food sources have passed through the small intestine undigested, they reach the cecum (a small pouch at the beginning of the large intestine) and the large intestine where they are the subject for bacterial degradation by these microbes with principal products being: SCFAs, heat and gases[20, 21].

In a typical adult, the gut bacteria synthesise the most abundant SCFAs: acetate, butyrate and propionate in an approximate ratio of 3:1:1, accordingly. Acetate is usually present at higher concentrations (about three times more) than the two other compounds; butyrate and propionate. Interestingly, the concentration of SCFAs is not the same along the entire length of the GI tract. The levels are highest in the cecum with a gradual decline towards the descending colon[22]. This reduction is explained by the absorption of the newly generated SCFAs as a food source for the body as the gut content moves gradually along the GI tract to be excreted.

SCFAS AND HEALTH

Approximately 95% of SCFAs (acetate, propionate and butyrate) are absorbed by the colon and the remaining 5% are excreted in feces[23, 24]. From here the SCFAs enter blood circulation, and are distributed to a variety of different body tissues/organs and induce various beneficial effects:

- SCFAs are an important source of energy for the gut and liver cells strengthening our digestive system and providing protection against obesity and type 2 diabetes[30].
- In the liver, acetate is involved in the synthesis of cholesterol and fatty acids while propionate can be converted into glucose[31].
- In the gut, SCFAs stimulate the production of hormones, which, in turn, can affect the brain and its functions[33, 34, 43].
- Have anti-inflammatory effects and regulate our immune system to protect against inflammatory bowel disease, cancer and asthma[35, 56, 57, 59, 60, 64, 65, 135].
- Accumulating evidence now suggests that the unbalanced gut's microbiota or dysbiosis is the characteristic of many frequent conditions, which are outlined below.



INFLAMMATION AND RELATED CONDITIONS

Inflammation is a normal response of our body to injuries and infections. It is usually a natural defensive reaction of an organism, yet sometimes inflammation can turn into a persistent process. In this case it is known as a chronic inflammation. Chronic inflammation can be triggered by certain events (obesity, dysbiosis, diet) and is believed to be a major contributor to some conditions, including cancer, asthma, allergies and rheumatoid arthritis[115].

INFLAMMATION BOWL DISEASE (IBD)

Inflammation bowl disease (IBD) involves the inflammation of the gut and includes two conditions: ulcerative colitis and Crohn's disease. IBD is characterised by a SCFA profile different from those of healthy individuals - the concentrations of butyrate and propionate is found to be decreased in IBD patients[54]. Most research studies are finding a positive role of SCFA or a high-fibre diet in the treatment of IBD[55, 56, 57].

IRRITABLE BOWEL SYNDROME (IBS)

In terms of symptoms, IBS is similar to IBD. However, the inflammation experienced is often less prominent in cases of IBS. Patients with this condition can be distinguished by the presence of microbiota with higher number of proinflammatory bacterial species and lower than average numbers of beneficial butyrate-producing microbes[122, 123, 124].

ASTHMA AND ALLERGIES

A high-fibre diet suppresses allergic airway diseases by enhancing the functions of immune cells (regulatory T cells)[64]. There are recent studies pointing out the importance of SCFAs as potential therapeutic agents in allergic inflammatory airway diseases[64, 65, 135].

RHEUMATOID ARTHRITIS (RA)

Together with genetics, the involvement of the microbiota in the development of RA has been studied. Several scientific reports indicate a particular marker of RA-related microbiota, which is the dominance of Prevotella species[128]. Some periodontal bacteria inhabiting our mouth are also suspected to be the cause of this condition[130, 131].

GOUT

The increased level of uric acid is a predisposition to this disease. Recent research indicates that the ability of the microbiota to produce uric acid is increased in patients with gout. This correlates with the diminished numbers of butyrate-producing bacteria in the gut[165].

DIVERTICULAR DISEASE AND DIVERTICULITIS

Differences in the gut microbiome have been identified in individuals with and without the diverticular disease. The main characteristic of the microbiota with diverticular disease is the reduction in the number of bacteria with known anti-inflammatory effects, a trait linked with a number of other gastrointestinal conditions[123].

MENTAL HEALTH AND THE GUT-BRAIN AXIS

A vast number of studies indicate that the intake of beneficial bacteria (probiotics), the ingredients for their growth (prebiotics), or adherence to a fibre-rich diet, positively influence the production of SCFAs and therefore benefit psychophysiological health[32].

Studies suggest that SCFAs influence the level of several gut hormones - GLP1, PPY, leptin, ghrelin and insulin[33, 34]. These compounds impact the brain in humans and are implicated in the control of cognitive processes (learning, memory and problem solving), mood, and have a role in neuropsychiatric disorders (Alzheimer's disease, depression, bipolar disorder and schizophrenia)[35, 36, 37, 38, 39, 40, 41, 42].

There are some convincing results pointing out to the role of SCFAs in neuropsychiatric disorders (Parkinson's, Alzheimer's, autistic spectrum disorder and depression) in animal models and further work is now being undertaken to understand the effects in humans[32].

OTHER CONDITIONS

OBESITY AND WEIGHT CONTROL

It has been shown that SCFAs can play a role in the regulation of appetite, fat storage, energy production and weight loss consequently. In the gut, propionate regulates the release of two hormones (GLP1 and PYY) involved in the suppression of food intake[43]. Acetate acts directly in the area of the brain called the hypothalamus which is responsible for the maintenance of energy balance and feeding regulation[44]. In addition, SCFAs can regulate the balance of fatty synthesis and degradation – which can result in a reduction of fatty acids concentrations in the blood, leading to better weight control[19].

TYPE 2 DIABETES (T2D)

It has been demonstrated that T2D in humans is linked to reduced amounts of bacterial species involved in the production of butyrate[47, 48]. Also, there is evidence that SCFAs can lower glucose levels in the blood by both increasing the concentration of circulating insulin and improving the sensitivity of cells to this compound[49, 50, 51].

COLON CANCER

Chronic inflammation over time represents a risk factor for colon cancer[58]. Animal and human studies showed that higher fecal levels of SCFAs often correlates with lower instances of colon cancer[59, 60]. The profile of SCFAs in colon cancer patients is different from that of healthy individuals. Humans with colon cancer were distinguished by reduced number of butyrate-producing bacteria and therefore lower amounts of butyrate present[61, 62, 63].

CARDIOVASCULAR DISEASE (CVD)

Studies of the gut microbiota have identified some traits in patients with CVD. Their microbiota is distinguished by the decreased production of anti-inflammatory butyrate and the increased levels of trimethylamine-N-oxide (TMAO)[140, 141, 142, 143].

IMMUNE SYSTEM

The microbiota is in constant interaction with our immune system. Microbes play a fundamental role in the training and shaping of the host immune system. Modern life in high-income countries eliminates the diversity of the microbiota in the gut by the overuse of antibiotics, a naturally poor urban microbial biodiversity and a western diet pattern. This phenomenon, the lack of microbial diversity, is thought to be responsible for unbalanced immune system and a dramatic increase in autoimmune and inflammatory disorders[157, 161, 167].

CONCLUSIONS

- The idea that a diet which is high in fibre content is beneficial to human health is becoming increasingly accepted.
- Our guts are often referred to as our “second brain” and play a vital role in our health.
- Short-Chain Fatty Acid analysis of fecal samples can be used as an important biomarker to measure the combined performance of an individual’s diet and gut microbiome.
- There is increasing evidence that SCFAs can reduce the risks or alleviate the symptoms of different health conditions which are currently on the rise such as IBS, mental health, type 2 diabetes.

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