DIETS AND HEALTH BENEFITS OF GUT MICROBIOTA-FERMENTED SHORT-CHAIN FATTY ACIDS: A PERSPECTIVE OF THE MALAYSIAN DIET CONTAINING PALM OIL

SIA-YEN, YAP¹*; PHOOI-TEE, VOON¹ and SELVADURAY, KANGA RANI¹

ABSTRACT

A healthy diet provides a favourable environment that allows the essential bacteria to grow and ferment beneficial metabolites, short-chain fatty acids (SCFA) through various metabolic pathways. SCFA, including linear- and branched-SCFA (BSCFA) are important in regulating energy haemostasis, inflammation, and appetite. A plant-based diet is associated with increased SCFA levels and SCFA-producing bacteria that regulate nutrient metabolism. Conversely, an animal-based diet is associated with lower SCFA levels and its producing bacteria. The Malaysian dietary guidelines are in line with other healthy eating recommendations that promote vegetables and fruit intake. Very few clinical studies are available to explore the association of gut microbiota and SCFA profiles following a Malaysian diet and the detailed amount of oil consumption was not reported. The available data demonstrated that acetate, propionate, and butyrate were the most abundant SCFA, while BSCFA, isobutyrate, was less abundant in Malaysian. Firmicutes and Bacteroidetes are the predominant phyla, while Faecalibacterium and Prevotella are the dominant SCFA-producing genera in Malaysian. Prevotella is associated with metabolic pathways for carbohydrates and fatty acids. However, more long-term cohort studies are needed to further elucidate the association between gut microbiota composition, SCFA profiles and the potential health effects of palm oil consumption in Malaysian diet.

Keywords: dietary pattern, gut microbiota, Malaysian diet, palm oil, short-chain fatty acids.

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INTRODUCTION

A healthy diet provides a friendly environment for diverse gut microbiota compositions to ferment essential metabolomes particularly SCFA to improve gut health (LeBlanc et al., 2017). In an increasingly fast-paced world, the traditional human healthy diet rich in whole grains, vegetables and fruits is quickly replaced with processed foods added with sugars, salt, food additives and preservatives which are low in nutritional value (Atzeni et al., 2022). The long-term consumption of these ultra-processed foods has been associated with diet-related chronic diseases such as obesity, type 2 diabetes (T2D), and cardiovascular disease (CVD) (Kopp, 2019).

More recently, studies reported that unhealthy dietary patterns promote gut dysbiosis (Liu et al., 2021; Zsálig et al., 2023), which is characterised by a lower proportion of commensal bacteria (Levy et al., 2017). The commensal bacteria have diverse gene families and are important in improving the efficiency of metabolic pathways for nutrient assimilation (Asnicar et al., 2021; Bolte et al., 2021; Tomova et al., 2019; Xiao et al., 2022). Gut dysbiosis has been linked to diseases such as diarrhoea, constipation, diverticulosis, irritable bowel syndrome (IBS), Crohn’s disease (Priya et al., 2022) and colorectal cancer (Sánchez-Alcoholado et al., 2020).

The composition of the gut microbiota is generally stable, as evident that it is resilient to short-term dietary modification (Schwedhelm et al.,

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A study has shown that an abrupt shift from a purely plant-based diet to a purely animal-based diet induced a rapid change in the gut microbiota profile but this change was promptly restored within 48 hr after discontinuing the animal-based diet (David et al., 2014). Similar temporal effects of diet on gut microbiota have also been reported with a low-carbohydrate or low-fat diet (Fragiadakis et al., 2020), suggesting that sustained dietary change should extend beyond 3 months (Pagliai et al., 2010; Wu et al., 2011). Long-term adherence to a diet enriched with fruits, vegetables, legumes, and grains as is the case with the Mediterranean and vegetarian diets, leads to a constant elevate in SCFA levels and cultivation of SCFA-producing bacteria such as Prevotella copri and Blastocystis spp. (Asnicar et al., 2021; Gibiino et al., 2021; Pagliai et al., 2020). Conversely, prolonged consumption of red meat and processed foods reduces the diversity of the gut microbiota and lowers SCFA levels (Agus et al., 2016) due to insufficient fibre to support the growth of gut microbiota (An et al., 2021).

Dietary pattern affects the proportion of macronutrient residues, including polysaccharides from carbohydrates, peptides from proteins, and fatty acids and glycerol from fats. These residues are fermented by bacteria into a wide range of SCFA (Figure 1). SCFA is a group of fatty acids consisting of six or fewer carbon atoms and exists as linear or branched chain molecules (Figure 1). They are typically obtained from various foods such as cheese, vinegar, yoghurt, palm kernel oil and coconut oil. Among these SCFA, acetate, propionate, and butyrate are the main linear chain SCFA, and they are mainly produced through anaerobic fermentation of dietary fibre (Wang et al., 2019) by saccharolytic bacteria, and through degradation of fatty acid residues by bacteria. Furthermore, a relatively small percentage of SCFA is also obtained from the fermentation of glycerol and ketone bodies such as beta-hydroxybutyrate and acetoacetate (Puchalska and Crawford, 2017). BSCFA, namely isobutyrate, iso-valerate, and 2-methylbutyrate are mainly produced through the degradation of branched amino acids such as leucine, isoleucine and valine by proteolytic bacteria (Xu et al., 2020a).

The Malaysian diet is unique as it offers a wide variety of foods while still ensuring a balanced nutrient intake. Palm oil is versatile and has been extensively used in Malaysia either as cooking oil or for food preparation. Palm oil has an almost equal proportion of saturated fatty acids (SFA) and unsaturated fatty acids (UFA), with palmitic acid comprising about 45%, oleic acid about 40% and linoleic acid about 10%. Palm oil can be fractionated into palm olein (liquid) and palm stearin (solid). The UFA content of palm olein increases by 5%-7% compared to palm oil. Palm

![Figure 1. The roles of gut microbiota in producing SCFA after fermenting different types of food. These SCFA are absorbed into the host and provide health benefits to the host.](image-url)
olein has a lower proportion of linoleic acid, which makes it very stable at high temperatures and ideal for deep frying. Additionally, solid palm stearin is often used as a hard fat and is blended with other soft oils such as sunflower or soybean oil to produce margarine, and shortening which are widely used in the confectionery and food industries (Dian et al., 2017).

The effects of SCFA on health are complex. Clinical randomised and cross-over trials have been conducted to investigate the effects of different individual dietary components on the profile of the gut microbiome and SCFA produced on potential health benefits, but an understanding of these effects is still lacking. Few studies have examined the effects of dietary patterns on the composition of the gut microbiota and the long-term effects of gut-fermented SCFA in healthy adults. There is limited information on the potential benefits of the effects of habitual consumption of palm oil-containing Malaysian food on the diversity of the gut microbiota and its effects on SCFA profiles. However, given the uniqueness of Malaysian cuisine and palm oil, the bacterial profile is expected to be more complex than in diets containing only SFA or UFA oils, although some core bacterial strains are previously identified in SFA and MUFA diets (Yap et al., 2022). This review explains the composition of the gut microbiota and SCFA content of people following specially designed diets that are high in certain dietary components and the long-term effects of different dietary patterns to adult health. Furthermore, this review also examines the potential effect of the Malaysian diet in this context.

**SCFA AND GUT HEALTH BENEFITS**

A balanced physiological level of SCFA is essential to promote gut health. The direct beneficial effects of SCFA have been demonstrated in the studies of oral administration in animals (den Besten et al., 2013; Vieira et al., 2012). In studies in which stable acetate-, propionate-, and butyrate- isotopes were infused into mice, different SCFA were reported to regulate different pathways (den Besten et al., 2013). Approximately two-thirds of the infused propionate was used for glucose production, while a higher proportion of acetate and butyrate was involved in lipid and cholesterol synthesis (den Besten et al., 2013). Acetate and butyrate are precursors in lipid metabolism and are especially important for the metabolism of fatty acids and cholesterol to yield palmitate and cholesterol. Vieira and co-workers reported that mice with ulcerative colitis in the caecal lymph nodes have reduced inflammation after oral ingestion of butyrate (Vieira et al., 2012).

Later, researchers have also found that a high-fibre diet increases the levels of faecal acetate as well as butyrate and reduces pathogens or toxins such as bacterial lipopolysaccharides (LPS) (Biswas et al., 2022). At physiological concentrations, butyrate regulates the expression of tight junction proteins such as cladin-2 which consequently prevents LPS (Kelly et al., 2015). Otherwise, high levels of LPS in the blood will trigger the immune cells in the lamina propria of the gut, leading to an increase in pro-inflammatory cytokines and interferons which increases the risk of an inflammatory response (Rowart et al., 2018). Along with acetate, butyrate also stimulates mucus secretion to prevent pathogens or toxins from adhering to the colonic epithelium (Kelly et al., 2015; Pelaseyed et al., 2014) and to stop the growth and specification of cancer cells (Donohoe et al., 2011). Therefore, faecal butyrate concentration could be a useful preliminary biomarker for the diagnosis of colonic diseases such as diarrhoea, inflammatory bowel disease (IBD), IBS, and colon cancer.

SCFA can also suppress appetite by activating the G-protein coupled receptors (GPR) 41 and 43 on L-enteroendocrine cells in the gut and pancreas (Figure 2). The binding of propionate and butyrate is more selective for GPR41, while acetate and propionate have higher affinity for GPR 41 and 43 (Tazoe et al., 2009) (Figure 2). Consequently, these activated receptors induce the secretion of gut hormones such as glucagon-like peptide 1 (GLP-1) and peptide tyrosine tyrosine (PYY) (Larraufie et al., 2018) to suppress appetite, resulting in lower food intake (Byrne et al., 2015).

SCFA, especially butyrate and propionate, can also ameliorate the effects of a high-fat diet on insulin resistance and obesity. These SCFA activate the AMP-activated protein kinase (AMPK) by increasing the AMP/ATP ratio and consequently trigger the expression of Peroxisome proliferator-activated receptor-gamma coactivator-1 alpha (PGC-1a). This in turn increases adiponectin secretion and, enhances glucose uptake in skeletal muscle and liver, leading to increased energy utilisation and improved insulin sensitivity (Sanna et al., 2019) (Figure 3). Mice fed with a high-fat diet (45% calories from fat) supplemented with 5% sodium acetate lost 30% of their body weight compared to their non-supplemented counterparts (den Besten et al., 2015). Moreover, SCFA particularly via the free fatty acid receptor 2 (FFAR-2) dependent pathway has been associated with an increase in leptin secretion, stimulating fatty acid oxidation (Figure 3) to reduce appetite and food intake (Mitieau, 2013). This concomitantly suppresses the insulin signalling to inhibit fat storage in adipose tissue.
Note: PGC-1α - peroxisome proliferator activated receptor-gamma coactivator-1 alpha; PPAR - peroxisome proliferator-activated receptor; LXR - liver X receptor; FXR - Farnesoid X receptor.

**Figure 2.** The important of different G-proteins couple receptor on selection of different SCFA binding and affecting the food intake.

**Figure 3.** SCFA in regulating various metabolisms in the host.
The health benefits of BSCFA are still poorly understood. A six month study of severely obese individuals who had undergone bariatric surgery found decreased total linear SCFA and increased BSCFA due to higher protein and fibre intake, resulting in increased proteolytic fermentation by gut bacteria (Farup and Valeur, 2020). Another 12-month study of obese adults who had also undergone bariatric surgery found gut isobutyrate levels that are inversely correlated with changes in BMI and insulin resistance (Martínez-Sánchez et al., 2023). These results suggest that BSCFA also have the potential to promote weight loss and improve insulin sensitivity (Mohammadifard et al., 2022).

GUIDELINES OF DIFFERENT DIETARY PATTERNS

Dietary guidelines serve as a reference to form a dietary pattern which is tailored to the needs of different populations to meet nutritional requirements while preventing malnutrition and deficiencies. Adherence to these dietary guidelines yields a unique SCFA and gut microbiota profile of each population. The dietary guidelines of 96 countries have been comprehensively reviewed (Rong et al., 2021) and found that a healthy and balanced diet is commonly recommended, although there are minor differences due to the availability of local foods, cultural practices, and health status.

The dietary guidelines of most countries advise a high consumption of various vegetables and fruits of at least 300-500 g/day, maintaining a moderate protein intake, limiting fat intake to 25-30 g daily, reducing sugar consumption and sugary drinks, limiting salt intake to 6 g/day, and at least 1.5 to 2.0 L of water a day (Rong et al., 2021). There are some minor differences in the recommendations. For example, India discourages alcohol consumption, while Mediterranean countries typically recommend 2-3 glasses of alcohol intake in their diets (Table 1). Some Mediterranean countries such as Spain recommend consuming olive oil instead of other oils (Table 1), and Greece has no limit for olive oil intake. The United States, on the other hand, recommends consuming vegetable oils instead of solid fats, and China recommends consuming 25-30 g of oil daily (Wang et al., 2016). India recommends limiting the intake of ghee, butter and hydrogenated vegetable oils (Manual, 2011), while Japan advocated an adequate intake of vegetable oil and fish oil (Gabriel et al., 2018) (Table 1).

Some common guidelines for dietary patterns used in long-term cohort or epidemiological studies are summarised in Table 1. The USDA dietary guidelines recommend a well-balanced diet across all food groups, emphasising a high proportion of fruits, vegetables, legumes, nuts and whole grains. It also suggests limiting fats (less than 30% of total energy, of which less than 10% is saturated fat), industrially produced trans fats, added sugars and salt. In a similar vein, the Dutch diet encourages a high intake of vegetables, fruits, whole grains, legumes and nuts, and reasonable quantities of dairy products, fish, fats and oils, tea and coffee (Table 1). The diet also discourages the consumption of red meat, trans fats, sugar, sweetened beverages, processed foods and salt (Table 1).

The Mediterranean diet, originating in Mediterranean countries such as Greece and Italy, promotes a healthy diet by reducing red meat consumption and prioritising consumption of plant foods such as fruits, vegetables, grains and legumes (Table 1). Poultry, seafood and dairy products are recommended to be consumed in moderate amounts, with olive oil being the main source of fat (Widmer et al., 2015). Over the last two decades, vegan and vegetarian diets have increasingly gained popularity. These diets consist primarily of plant sources and exclude or limit animal products. Although vegetables are rich in fibre, they are relatively poor in protein content, leading vegetarians to rely on plant-based protein sources.

The Malaysian Ministry of Health revised the food pyramid (Ganapathy et al., 2019) to improve the healthy eating habits of the Malaysian population (Figure 4). In line with other healthy diet recommendations, the updated guidelines recommend more than 50% of vegetables and fruits. This should be supplemented by complex carbohydrates found in brown rice, whole grains products, unprocessed cereals, and oats. These natural foods are rich in vitamins and minerals which strengthen the immune system. The guide also emphasises a moderate intake of proteins from animals, seafood and plants such as nuts and legumes. The guide also recommends staying hydrated with plain water and reducing sugar, salt and oil intake (Figure 4).

Of note, there are also specific short-term dietary patterns such as Atkins and ketogenic diets, which are mainly adopted by individuals with certain health conditions such as obesity, pre-diabetes, epilepsy, and mild cognitive impairment (Haji-Ghazi Tehrani et al., 2022; Naggal et al., 2019). The Atkins diet encourages a higher protein intake from meat while reducing carbohydrate consumption. This approach has been heavily modified recently and is now known as the modified Atkins diet, serving as a transition towards the ketogenic diet (Kossoff et al., 2013). The modified Atkins diet has demonstrated promising results in weight loss (Bueno et al., 2013).
# Table 1. Different Dietary Patterns and Recommended Intake Portions

<table>
<thead>
<tr>
<th>Dietary patterns</th>
<th>Proximate ratio of macronutrients, % kcal</th>
<th>Food recommendation</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>USDA diet</strong></td>
<td>• Carbohydrates, ~55%-60%</td>
<td>• Consume large portion of grains (preferable whole grains), vegetable (variety of vegetables, including legumes, starchy)</td>
<td>DeSalvo et al. (2016); Fernandez et al. (2021)</td>
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<td></td>
<td>• Proteins, ~15%</td>
<td>• Variety fruits, preferable whole fruits (2-4 servings)</td>
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<td></td>
<td>• Fats, 21%-30%</td>
<td>• Variety proteins from lean meat, poultry, fish, eggs, seafood, dry beans, soy products, lentils, peas and nuts (2-3 servings)</td>
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<td>• Moderate dairy, including milk, cheese, yogurt, fortified soy beverages (2-3 servings)</td>
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<td>• Sufficient Vitamin D and calcium supplements</td>
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<td>• Sufficient intake of vegetable oils</td>
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<td>• Limit trans and saturated fats, red meat, butter, salt, sugars, refined grains and alcoholic beverages</td>
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<td></td>
<td></td>
<td>• Consume large portion of grains (preferable whole grains), vegetable (variety of vegetables, including legumes, starchy)</td>
<td>DeSalvo et al. (2016); Fernandez et al. (2021)</td>
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<tr>
<td><strong>Dutch diet</strong></td>
<td>• Carbohydrates, 40%-70%</td>
<td>• Eat plenty of vegetables, fruits, wholegrain, nuts, and legumes</td>
<td>Looman et al. (2017)</td>
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<td></td>
<td>• Proteins, 10%-25%</td>
<td>• Moderate dairy, fish, fats and oils, tea and coffee</td>
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<tr>
<td></td>
<td>• Fats, 20%-40%</td>
<td>• Limit consumption of red meat, processed meat, sweetened beverages, alcohol, salt</td>
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<tr>
<td><strong>Japanese diet</strong></td>
<td>• Carbohydrates, 50%-70%</td>
<td>• 5-7 servings of grain dishes</td>
<td>Gabriel et al. (2018)</td>
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<td></td>
<td>• Proteins, 20%-30%</td>
<td>• 5-6 servings of vegetables</td>
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<td></td>
<td>• Fats, 15%-25%</td>
<td>• 3-5 servings of fish and meat dishes</td>
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<td>• 2 servings of milk or milk products</td>
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<td>• 2 servings of fruits</td>
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<td>• Moderate intake of snacks, confection and alcohol</td>
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<td>• Drink plenty of water or teas</td>
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<tr>
<td><strong>Indian diet</strong></td>
<td>• Carbohydrates, 30%-60%</td>
<td>• Eat plenty of cereals, millets, and pulses</td>
<td>Manual (2011)</td>
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<td></td>
<td>• Proteins, 10%-15%</td>
<td>• Milk as protein source</td>
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<td></td>
<td>• Fats, 20%-30%</td>
<td>• Moderate intake of eggs, fish, and animal proteins</td>
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<td>• Reduce intake of butter, ghee, and hydrogenated fats and red meat</td>
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<td>• Eat nuts</td>
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<td>• Eat plenty of vegetables and fruits</td>
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<td>• Diversity food choice</td>
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<td></td>
<td></td>
<td>• Avoid alcohol and smoking</td>
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<td><strong>China diet</strong></td>
<td>• Carbohydrates, 55%-65%</td>
<td>• 5-6 servings of cereals, tubers, legumes</td>
<td>Wang et al. (2016)</td>
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<td></td>
<td>• Proteins, 20%-30%</td>
<td>• 4-5 servings of vegetables (priorities dark-coloured vegetables)</td>
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<td>• Fats, 15%-20%</td>
<td>• 3-4 servings of fruits</td>
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<td>• 2-3 servings of lean meat, eggs and fish</td>
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<td>• 2-3 servings of soybeans or soy products, nuts and dairy products</td>
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<td>• Moderate intake of oil</td>
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<td>• Limit salt, sugar, and alcohol intake</td>
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<td>• Drink plenty of water</td>
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<td>Dietary patterns</td>
<td>Proximate ratio of macronutrients, % kcal</td>
<td>Food recommendation</td>
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<td>Spain diet</td>
<td>Carbohydrates, 50%-60%</td>
<td>Moderate intake of meat and meat products, fish and eggs</td>
<td>Aranota et al. (2001)</td>
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<td></td>
<td>Proteins, 25%-35%</td>
<td>2-4 servings of milk and dairy products</td>
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<td>Fats, 20%-30%</td>
<td>2 or more servings of legumes and nuts</td>
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<td>4-6 servings of cereals and potatoes</td>
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<td>2 or more servings of vegetables (250-300 g daily)</td>
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<td>3 servings of fruits</td>
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<td>Moderate lean meats and plant oils intake; recommended use olive oil</td>
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<td>Limit animal fats and trans-fat intake</td>
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<td>Reduce sugary foods and drinks</td>
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<td>Drink plenty of water, moderate intake of tea</td>
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<td>Reduce alcohol intake</td>
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<td>Mediterranean diet</td>
<td>Carbohydrates, ~55%-60%</td>
<td>Drink plenty water</td>
<td>Serra-Majem et al. (2020)</td>
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<td></td>
<td>Proteins, ~15%</td>
<td>2 portions of vegetables with a variety of colours/textures</td>
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<td>Fats, 21%-30%</td>
<td>Olive oil as the main choice of fat source</td>
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<td>1-2 portion(s) whole grain bread/ pasta/ rice/ couscous/ cereals/ potatoes</td>
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<td>1-2 portion(s) nuts/ seeds</td>
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<td>Herbs/ spices/ garlic/ onions</td>
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<td>Legumes</td>
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<td>2 portions of dairy</td>
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<td>Variety of flavours</td>
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<td>1/3 portion of egg/ fish/ seafood/ white meat</td>
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<td>Less read meat and processed meat and sweet</td>
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<td>Vegen diet (without all flesh foods)</td>
<td>Carbohydrates, ~60%</td>
<td>Legumes, soya foods and meat analogues, nuts and seeds, grains, potatoes, tomatoes, avocados, fruits and vegetables</td>
<td>Orlich et al. (2014)</td>
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<td>Vegetarian diets (without all flesh foods, but also include egg (ovo) and/or dairy (lacto) products)</td>
<td>Proteins, ~10%-15%</td>
<td>Some amounts of eggs and dairy products for those following the ovo-lacto diet</td>
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<td>Fats, ≤20%</td>
<td>Low intake of eggs and dairy products</td>
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<td>Drink plenty of water</td>
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<td>Dietary patterns</td>
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<td>Food recommendation</td>
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<td>Atkins diet</td>
<td>Carbohydrates, ≤40%</td>
<td>• Large portion of protein sources such as fish, seafood and beef, poultry, pork and soy products&lt;br&gt;• Vegetables – green leafy vegetables (2 cups per day); broccoli, cauliflower, spinach, asparagus (1 cup per day)&lt;br&gt;• Fruits – blueberries, pears, raspberries, avocados&lt;br&gt;• Oils – vegetable and seed oils&lt;br&gt;• Unlimited eggs&lt;br&gt;• cheese and milk (4 ounces per day)&lt;br&gt;• Legumes, nuts and whole grain foods&lt;br&gt;• Carbohydrate (25 to 50 g/d)&lt;br&gt;• 8-ounce glasses of water (at least 6 cups)</td>
<td>Atkins (2002)</td>
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<td>Proteins, ~30%</td>
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<td>Fats, 30%-55%</td>
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<td>Ketogenic diet</td>
<td>Carbohydrates, ~5%-10%</td>
<td>• Natural fats – olive oil, coconut oil, avocado&lt;br&gt;• Moderate amounts of meats, fish, poultry&lt;br&gt;• Dairy (cheese, heavy cream, butter, ghee)&lt;br&gt;• Eggs&lt;br&gt;• Vegetables (green leafy vegetables, avoid starchy root vegetables)&lt;br&gt;• Small amounts of berries, dark chocolate (&gt;90% cocoa)&lt;br&gt;• Avoid soda drinks, milk, yogurt, candy, pastries, all starch foods including grains, limit intake of beans and lentils</td>
<td>Carroll and Koenigsberger (1998)</td>
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<td>Proteins, ~10%-20%</td>
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<td>Fats, 50%-70%</td>
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DIETS AND HEALTH BENEFITS OF GUT MICROBIOTA-FERMENTED SHORT-CHAIN FATTY ACIDS: A PERSPECTIVE OF THE MALAYSIAN DIET CONTAINING PALM OIL

The ketogenic diet is characterised by consuming exceptionally high-fat content, moderate protein intake and very little carbohydrates (Table 1). Foods commonly found in the ketogenic diet include olive oil, coconut oil, avocado, moderate amounts of meat, poultry, seafood, eggs, nuts and green leafy vegetables, berries and dark chocolate (Table 1). This diet induces a state of ketosis, where the body utilises fat instead of glucose for energy, resulting in elevated levels of ketone-bodies. This metabolic shift has been associated with a reduction in pro-inflammatory Th17 cells in the gut and visceral adipose tissue (Ang et al., 2020), which may reduce the risk of inflammation and obesity (Mohammadifard et al., 2022). Notably, a meta-analysis on individuals following a ketogenic diet has shown that BSCFA levels are increased due to the degradation of branched amino acids from protein sources (Ferraris et al., 2021), but total SCFA levels decrease due to limited fibre intake (Rew, 2022). These dietary changes are reflected in the gut microbiota composition, which is characterised by a lower abundance of butyrate-producing bacteria (Louis and Flint, 2017).

MACRONUTRIENTS AND PATHWAYS FOR FERMENTING SCFA

Recent studies have shown that diets rich in certain dietary components significantly affect gut microbiota compositions. These bacteria exhibit different abilities to ferment SCFA based on different rate-limiting catalytic enzyme pathways (Xu et al., 2020b). Short-term dietary intervention studies, ranging from a single day to several months (David et al., 2014; Pagliai et al., 2020), have shown that altering macronutrient proportions can influence gut microbiota composition and SCFA profiles.

Effects of Macronutrients on SCFA-Producing Bacteria in Short-term Interventions

Carbohydrates. A diet rich in unprocessed, high-fibres foods is a good food source for the gut microbiota especially for the phyla Actinobacteria and Firmicutes, which play an important role in SCFA metabolism (Bolte et al., 2021). Resistant starch (RS) is a type of carbohydrate naturally found in grains, legumes, seeds, raw bananas and potatoes, and precooked rice (Ashwar et al., 2015). It serves as an excellent precursor for gut-fermented SCFA (Abreu et al., 2021). A study of 20 healthy volunteers who consumed 48 g of raw potato starch, containing 50% RS for one week showed a significant increase in the relative abundance of SCFA producing bacteria, particularly Ruminococcus bromii, Bifidobacterium adolescentis, and Eubacterium rectal (Venkataraman et al., 2016). These bacteria are responsible for RS degradation and butyrate production (Ze et al., 2012). Of particular interest, *R. bromii* has a distinct organisation of some amylolytic enzymes that form complexes through cohesion and dockerin.
interaction, enhancing their ability to degrade starch (Xu et al., 2015). Furthermore, Clostridiales and Dorea are also involved in the assimilation of starch, as shown in a study with mice that were fed isotopically labelled RS (Herrmann et al., 2018).

Other indigestible starch components such as soluble dietary fibre also increase SCFA levels. Consumption of 5-12 g of inulin or oligosaccharides, which consist of highly branched molecules, was found to result in significant fermentation by Faecalibacterium prausnitzii and Bifidobacterium (Holscher et al., 2015; Vandeputte et al., 2017). This finding is in accordance with a meta-analysis conducted by So et al., (2018), who found higher faecal butyrate with a high abundance of Bifidobacterium spp. and Lactobacillus spp. in individuals following a high-fibre diet.

Foods rich in whole grains and high in insoluble fibre such as cellulose are also excellent sources of nutrition for the gut microbiota but to a lesser extent. A diet rich in cellulose materials promotes the growth of acetate and propionate producers, especially Xylanibacter and Prevotella (Iljazovic et al., 2021; Ueki et al., 2006). High proportions of Prevotella and Xylanibacter are often linked to vegetarian and high-fibre diets, suggesting their role in the hydrolysis of cellulose and xylan from dietary fibre (De Filippo et al., 2010; Sánchez-Tapia et al., 2019).

**Proteins.** The effect of proteins on gut microbiota compositions has not yet been fully researched. Depending on the type of diet, approximately 6-18 g of proteins is further degraded in the colon to peptides or amino acids daily by the host or bacterial-derived proteases and peptidases (Neis et al., 2015). These degradation products can be further utilised by proteolytic bacteria and lead to the production of SCFA and BSCFA. Excessive protein consumption has been associated with an increased abundance of peptide and amino acid-fermenting bacteria that degrade branched-chain amino acids, such as Bacteroides and Clostridium, leading to increased levels of BSCFA, namely isovaleric acid and isobutyric acid, and smaller amounts of 2-methylbutyric acid (Aguirre et al., 2016). These bacteria are also known to possess strong peptidase activity (Olphant and Allen-Vercoe, 2019). A study of 17 obese men who underwent a high-protein but low-carbohydrate diet for 4 weeks showed that a high-protein diet increased BSCFA concentrations in the presence of toxic compounds such as phenylacetic acid and N-nitroso compounds while lowering butyrate levels and decreasing Roseburia and E. rectale (Russell et al., 2011).

Some SCFA-producing bacteria such as Prevotella bryantii (Trautmann, et al., 2020) and Lactobacillus casei (Chen et al., 2019) can efficiently degrade peptides especially peptides that consist of more than three amino acids in their chain such as casein into nitrogen for growth (Kim et al., 2017; McIntosh et al., 2009). These bacteria possess dipeptidyl peptidase activity that is involved in protein digestion and the host metabolism such as regulating the secretion of glucagon-like peptide 1 (GLP-1) and gastric inhibitory polypeptide (GIP) involved in glucose haemostasis (Olivares et al., 2018). Studies have also shown that different protein sources in the diet have an impact on gut bacterial species and BSCFA (Table 2). Consumption of chicken meat promotes the growth of Faecalibacterium, Prevotella 9, Dialister and Megamonas, but consumption of pork leads to the growth of Bacteroides, Faecalibacterium, Roseburia, Dialister and Ruminococcus 2. This results in different levels of SCFA and BSCFA in the gut (Shi et al., 2021). Similarly, animal-derived protein sources such as fish promote the growth of Lactobacillus and Oscillibacter (Ján et al., 2014), while consumption of dried skimmed milk and milk casein increased Lactobacilli and Bifidobacterium (Zhang et al., 2020) but lower Staphylococci, Clostridia and Streptococci counts (Zhao et al., 2018) in porcine and rat. Conversely, less digestible plant proteins such as peanuts and soybeans (Day et al., 2022), consist of indigestible cell wall components that demonstrated a higher fermentability. This leads to an increased content of acetic and lactic acid and an increased abundance of Bifidobacterium. Different proteins possess different amino acids that make up the protein structure and yield different gut microbiota compositions. For example, vegetarians showed significantly higher plasma concentrations of methionine, tryptophan, alanine, glutamate, glycine, and tyrosine but lower lysine compared to meat- and fish-eaters (Schmidt et al., 2016). Gut microbiota synthesises butyrate from lysine and glutamate, while propionate is mainly synthesised from alanine, methionine and threonine and acetate from glycine, alanine and lysine (Figure 3).

**Dietary fats.** The effects of fats on gut microbiota composition and SCFA production generally depend on the degree of fat saturation and the amount of dietary fat consumed. Extensive clinical studies in human and animals have consistently demonstrated that diets high in SFA promote the growth of Firmicutes, Enterobacteriacea and Proteobacteria, while concurrently reducing the abundance of Bacteroidetes and Lactobacillus (Heinritz et al., 2016; Ley et al., 2006; Wu et al., 2011; Zhang et al., 2012). High SFA content is often used as a comparator when studying the effects of dietary fats on gut microbiota. However, it is important to note that an increase in fat intake may inadvertently lead to lower energy intake from other macronutrients such as complex carbohydrates, and this reduces the abundance of saccharolytic
TABLE 2. EFFECTS OF DIET COMPONENTS ON GUT MICROBIOTA PRODUCING SCFA

<table>
<thead>
<tr>
<th>Diets</th>
<th>SCFA</th>
<th>Gut microbiota</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resistant starch</td>
<td>Butyrate, acetate</td>
<td>Ruminococcus bromii, Bifidobacterium adolescentis, Eubacterium rectal</td>
<td>Venkataraman et al. (2016)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bifidobacterium</td>
<td>Afia et al. (2018)</td>
</tr>
<tr>
<td>Oligosaccharides</td>
<td>Butyrate</td>
<td>Bifidobacterium spp., Lactobacillus spp.</td>
<td>So et al. (2018)</td>
</tr>
<tr>
<td>Insoluble fibres</td>
<td>Acetate, propionate</td>
<td>Xylanibacter, Prevotella, Faecalibacterium</td>
<td>Iljazovic et al. (2021);</td>
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<td></td>
<td></td>
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<td>Lieki et al. (2006);</td>
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<td>Holscher et al. (2015);</td>
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<td>Vandeputte et al. (2017)</td>
</tr>
<tr>
<td>Proteins</td>
<td>SCFA and BSCFA</td>
<td>Bacteroides, Clostridium, Faecalibacterium, Roseburia, Dialister, and Ruminococcus 2</td>
<td>Agrume et al. (2016);</td>
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<tr>
<td></td>
<td></td>
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<td>Smith and Macfarlane (1998)</td>
</tr>
<tr>
<td>High SFA</td>
<td>SCFA</td>
<td>Firmicutes, Enterobacteriaceae, Proteobacteria, Lactobacillus,</td>
<td>Heinritz et al. (2016); Wu et al. (2011);</td>
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<td></td>
<td></td>
<td>Prevotella, and Alistipes</td>
<td>Zhang et al. (2012); Zhao et al. (2018)</td>
</tr>
<tr>
<td>High MUFA</td>
<td>Propionate</td>
<td>Oscillator, Faecalibacterium prausnitzii, and Roseburia</td>
<td>Haro et al. (2016); Muralidharan et al. (2019)</td>
</tr>
<tr>
<td>High PUFA (EPA, DHA)</td>
<td>Butyrate</td>
<td>Coprococcus, Roseburia, and Blautia</td>
<td>Ochoa-Repáraz and Kasper (2016)</td>
</tr>
</tbody>
</table>

Note: SCFA - short chain fatty acids; SFA - saturated fatty acids; MUFA - monounsaturated fatty acids; PUFA - polyunsaturated fatty acids; EPA - eicosapentanoic acid; DHA - docosahexaenoic acid.

bacteria such as Bifidobacterium, F. prausnitzii, and Ruminococcus (Fava et al., 2013; Shen et al., 2012).

In a study comparing the effects of diets high in SFA, MUFA, carbohydrate, or sugar on the gut microbiota of 88 subjects at risk of metabolic syndrome over a 24 weeks period, it was found that a diet high in SFA yielded greater SCFA abundance compared to other diet groups (Fava et al., 2013). Conversely, a diet rich in MUFA, akin to the Mediterranean diet, increases the abundance of SCFA-producing bacteria (Haro et al., 2016; Muralidharan et al., 2019). It is noteworthy that the Mediterranean diet is also high in vegetables and fruits and the effect of MUFA could be confounded by these dietary fibres. PUFA-rich diets, particularly those rich in omega-3 fatty acids, have been shown to elevate the abundance of butyrate-producing colonic bacteria, namely Coprococcus, Roseburia, and Blautia (Ochoa-Repáraz and Kasper, 2016) (Table 2).

Some researchers suggest that various dietary fats indirectly influence the gut microbiota composition by influencing bile acid secretion from the colon (Just et al., 2018). It is known that a high-fat diet increases bile acid secretion, resulting in these bile acids being converted into secondary forms to prevent reabsorption in the colon (Park et al., 2022). These secondary bile acids may subsequently reshape the composition of the gut microbiota by enhancing the abundance of bile-tolerant bacteria (Yokota et al., 2012).

Pathways involved in SCFA production. The pathways of SCFA production have been summarised in detail by Xu and colleagues (Xu et al., 2020b). Four general pathways for SCFA production have been identified. First, SCFA is produced from carbohydrates, which involves the degradation of dietary fibre to monomers (pentoses) and various sugars and oligosaccharides. These substrates are degraded by glycolysis, yielding pyruvate molecules (Figure 5). In addition, SCFA can be synthesised from acetate and ethanol by extending the carbon chain. Acetate, derived from beta-oxidation of dietary fats and deamination of amino acids from proteins, reacts with coenzyme A (CoA) to form acetyl-CoA (Figure 5). Pyruvate and acetyl-CoA serve as the main precursors in the citric acid cycle and contribute to the production of SCFA. Third, amino acids such as valine, leucine and iso-leucine undergo decarboxylation and reduction to synthesise BSCFA. Lastly, unique substrates such as carbon dioxide molecules are involved in the synthesise of acetate via the Wood–Ljungdahl pathway, while lactate contributes to the synthesise of propionate (Figure 5).
Recent studies have identified 74 key SCFA-producing bacterial species in different research groups (Xu et al., 2020b). Approximately 80% of these SCFA-producing bacteria are members of Firmicutes phylum, mainly from the Clostridiaceae and Lachnospiraceae families. Of these, many species are recognised as butyrate producers, including Clostridium, Eubacterium, F. prausnitzii, Subdoligranulum variabile, Anaerostipes, Coprococcus, and Roseburia. Some of these bacteria such as Clostridium sp., Coprococcus and Roseburia, A. muciniphila, Ruminococcus spp. produce acetate and propionate in addition to butyrate (Flint et al., 2015; Reichardt et al., 2014).

Certain bacterial strains such as Prevotella copri and P. stercora are major producers of longer-chain SCFA valerate (C5) (Almeida et al., 2019), whereas Veillonellaceae, such as Megasphaera elsdenii and Megasphaera sp. Roseburia, Megasphaera and Clostridium have demonstrated an excellent ability to produce multiple types of SCFA (Reichardt et al., 2014). These results suggest that certain gut bacterial species can efficiently utilise different food residues, possibly highlighting the role of a few “core” gut bacteria in regulating SCFA production pathways.

Roseburia and Faecalibacterium (Table 2) are most abundant in those following high-protein and high-fat diets. These bacteria are postulated to have diverse genes which are involved in several important functional metabolic pathways or that their genes interact with other dietary components. Although short-term replacement of dietary components may affect overall gut health, the gut microbiota is resilient and tends to regenerate back to its original composition when the original diet is resumed. Therefore, holistic nutritional epidemiological studies, can shed light on the true effects of the whole diet and provide a better understanding of the complex relationship between the diet, gut microbiota composition, and the functional pathways for the production of metabolites.
EFFECTS OF LONG-TERM DIETARY PATTERNS ON GUT MICROBIOTA COMPOSITIONS AND SCFA PROFILES ON HEALTH OUTCOMES

Long-term dietary patterns have been explored in detail in several large human cohort studies. Their profound effects on gut microbiota composition, SCFA profiles, associated metabolic pathways and resulting health outcomes are summarised in Table 3.

In general, a plant-based diet, such as vegan or vegetarian, is associated with higher total SCFA content and promotes greater numbers of SCFA-producing bacteria such as Roseburia, Ruminococcus, Lachnospira, Dorea, Lactobacillus, Bifidobacterium and Prevotella (Table 3). Conversely, high consumption of animal foods has been associated with a reduction in gut bacterial diversity, higher levels of valeric acid, capric acid and BSCFA, and dominance of Firmicutes, Streptococcus and Ruminococcus, possibly stimulating endotoxin synthesis pathways.

The Mediterranean diet promotes a healthy diet high in fibre (Table 3). High adherence to this diet results in increased total SCFA, particularly acetate (Mitsou et al., 2017) and growth of butyrate-producing taxa such as Roseburia faecis, R. bromii, and Oscillospira plautii, with a strong association observed for Bifidobacterium animalis. In addition, consumption of animal proteins inhibits the growth of Bacteroidetes, while consumption of PUFA, particularly from fish and vegetal proteins, tends to cultivate Prevotella copri, Dorea and Lactobacillus (Table 3).

Both the Mediterranean and vegetarian diets, which are both rich in plant-based foods, exhibit slight differences in intake of animal protein and olive oil, resulting in slight variations in the composition of gut microbiota at the genus level, while alpha diversity, richness and evenness remain similar (Table 3). When comparing the effects of gut microbiota composition of a vegetarian and vegan diet to an omnivorous diet (Table 3), Shannon index, which indicates bacterial richness, are found to be significantly different between those who follow vegetarian and omnivorous diets (Ghosh et al., 2020; Trefflich et al., 2021). It is noteworthy that faecal SCFA levels, especially acetate, propionate and butyrate, are higher in plant-eaters, suggesting a correlation between gut microbiota composition, gut fermented SCFA, and dietary fibre content.

Comparative studies between the Mediterranean diet and different dietary habits among the British, French, Dutch, Italians, and Poles revealed some interesting patterns. Strong adherence to the Mediterranean diet for an extended period enhances the abundance of SCFA-producing bacteria. These bacteria have anti-inflammatory properties as evidenced by the negative correlation with pro-inflammatory markers such as the highly-sensitive C-reactive protein (hsCRP) and IL-17, and this ultimately lowers the risk of frailty in the elderly (Ghosh et al., 2020). Conversely, low adherence to the Mediterranean diet is associated with an abundance of taxa such as Collinsella aerofaciens, Coprococcus comes, Clostridium ramosum, and Veillonella dispar, which are associated with a higher risk of T2D, colorectal cancer, and IBD (Table 3).

Vegetarian diets typically result in higher proportions of butyrate and valerate, but lower concentrations of branched-chain amino acids. However, in a small cohort study in southern India, contradictory results have reported omnivorous diets increase the abundance of Clostridium cluster XIVA and upregulation of the butyryl-CoA: CoA transferase gene, leading to increased butyrate production compared to vegetarian diets (Table 3). In a larger cohort of healthy adults following vegan or omnivorous diets, no significant difference was found between SCFA and BSCFA levels (Table 3).

Specific core taxa are identified in shaping the effects of a long-term dietary pattern. Omnivorous diets are dominated by three specific core taxa, namely Lachnospira, the NK4A136 group of the Lachnospiraceae and Ruminiclostridium. Conversely, the vegetarian diet resulted in an abundance of seven core taxa, mainly SCFA-producing bacteria together with three rare genera. The rare taxa are Tyzzerella, Succinivibrio and Shuttleworthia, which are positively correlated with SCFA and BSCFA levels (Table 3).

A well-studied Dutch cohort study provided insight into certain bacterial taxa with significant health implications. Of these bacterial taxa, Christensenellaceae stands out as being inversely proportional to the size of very-low-density lipoprotein (VLDL) particles, small high-diversity-lipoprotein (HDL) particles and triglycerides in medium HDL. These results suggest a possible role in lipid metabolism, cardiovascular risk reduction and body weight regulation (Goodrich et al., 2014). Clostridiales 1 and the genus Clostridium sensu stricto are associated with very large and large HDL particles, suggesting an association with lower BMI and lower blood triglyceride levels, which reduces the risk of stroke and CVD. Ruminococcaceae is associated with acetate production, while Lachnospiraceae and Blautia are involved in upregulating 7α-dehydroxylation genes to accelerate metabolism from primary to secondary bile acids (Ridlon et al., 2013; Vital et al., 2019) and producing butyrate from lactate (Duncan et al., 2004). Overall, these long-term cohort studies have shown that diet undoubtedly affects the gut microbiota composition at the lower phylogenetic level and the metabolome produced by these bacteria. Adherence to certain dietary patterns is important to maintain a stable “core” community of gut microbiota to perform certain core functional metabolic pathways.
### TABLE 3. EFFECTS OF DIFFERENT DIETS PATTERN ON SCFA PRODUCING GUT MICROBIOTA (continued)

<table>
<thead>
<tr>
<th>Diet</th>
<th>Study design, duration, participants</th>
<th>Main food sources/ food components</th>
<th>Outcomes</th>
<th>References</th>
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<tbody>
<tr>
<td>Mediterranean diet</td>
<td>Cross-sectional, Healthy 251 F and 109 M, 45.0 ± 10.5 yo; BMI: 25-30 kg/m². Adherence of med diet was accessed using MedDietScore. Low MedDietScore indicates high intake of fast food, high fats, sugar and processed food.</td>
<td>Macronutrients intake: Carbohydrate 54%-55%; Proteins 21%-22%; Fats 23%-24%; Fibre 24%-36%</td>
<td>• A strict Mediterranean diet is associated with increased abundance of butyrate-producing bacteria such as Roseburia faecis, R. bromii and Oscillospira plautii</td>
<td>Rosés et al. (2021)</td>
</tr>
<tr>
<td>Mediterranean diet</td>
<td>116 subjects: 61 M, 55 F; mean age 42 yo; BMI 25-30 kg/m². Adherence of med diet was accessed using MedDietScore. Low MedDietScore indicates high intake of fast food, high fats, sugar and processed food.</td>
<td>Non-refined cereals, potatoes, legumes, fruits, vegetables, olive oil, fish, moderate meat, meat products, poultry, dairy; low alcohol</td>
<td>• 68% subjects showed moderate to high adherence to the Mediterranean diet</td>
<td>Mitsou et al. (2017)</td>
</tr>
<tr>
<td>Mediterranean diet</td>
<td>27 healthy adults (11M, 16 F; 39.5 ± 7.3 yo; lived in Valencia-Spain): PREDIMED score</td>
<td>Non-refined cereals, potatoes, legumes, fruits, vegetables, olive oil, fish, moderate meat, meat products, poultry, dairy; low alcohol</td>
<td>• High protein intake lowers the abundance of Bacteroidetes, whereas animal proteins, saturated fats and sugars reduced bacteria diversity</td>
<td>García-Mantrana et al. (2018)</td>
</tr>
<tr>
<td>Mediterranean, vegan dan vegetarian diets</td>
<td>Cohort study: 153 healthy Italian; 51 omnivores (23M, 28F; BMI 22.1 ± 2.0 kg/m²); 51 vegan (23M, 28F; BMI 21.3 ± 2.2 kg / m²); 51 vegetarian (18M, 33F; BMI 21.9 ± 2.5 kg/m²), with 88% of them are medium or highly adhered to the Mediterranean diet.</td>
<td>High intake of cereals, fruits, vegetables and legumes</td>
<td>• Alpha diversity did not significantly vary across these three diets</td>
<td>Filippis et al. (2016)</td>
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- *Mediterranean diet* refers to a diet pattern that involves a high intake of cereals, fruits, vegetables, olive oil, fish, moderate meat, and a low intake of fast food, high fats, sugar, and processed foods.
- *Mediterranean, vegan dan vegetarian diets* refer to a diet pattern that involves a high intake of cereals, fruits, vegetables, and legumes, with varying levels of animal proteins, saturated fats, and sugars.
- *Outcomes* include changes in the abundance of certain gut bacteria and SCFA levels, as well as relationships with various dietary factors.
- *References* provide the sources for the studies mentioned.

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<thead>
<tr>
<th>Diet</th>
<th>Study design, duration, participants</th>
<th>Main food sources/ food components</th>
<th>Outcomes</th>
<th>Reference</th>
</tr>
</thead>
</table>
| Mediterranean diet           | Mediterranean diet = 141 M, 182 F, from UK, France, Netherlands, Italy, and Poland; Control diet = 145 M, 144 F, 1 year | Mediterranean (NU_AGE) diet (tailored for elderly): Whole grains, fruits, vegetables, and legumes, dairy and cheese, seafood, meat and poultry, nuts, potatoes, rice, eggs, and olive oil | - Data from these countries showed no significance, but high adherence to Mediterranean diet increased microbiota biodiversity
- The control group had higher fat intake than Mediterranean Diet intervention group
- Among the 44 Predictive OTUs positively associated with a high MedDiet score were *E. prausnitzii*, *Roseburia hominis*, *Eubacterium*, *Bacteroides thetaiotaomicron*, *P. copri* and *Anaerostipes hadrus*. These bacteria are associated with SCFA or BSCFA production and possess anti-inflammatory properties, showing negative correlation with proinflammatory markers hsCRP and IL-17
- Predictive OTUs inversely associated with MedDiet score primarily belonged to taxa of *Collinsella aerofaciens*, *Ruminococcus torques*, *Coprococcus comes*, *Dorea formicigenerans*, *Clostridium ramosum*, *Veillonella dispar*, *Flavonifractor plautii* and *Actinomyces lingnae*. Increase abundance of these taxa has been associated with higher risk of T2D, colorectal cancer, IBD
- The commercial gut microbiota is positively correlated with dietary fibre, vitamins C and D, plant proteins, and carbohydrates, resulting elevated SCFA levels and decreased secondary bile acids | Ghosh et al. (2020) |
| Vegetarian diet (VD) vs. omnivorous (O) | 32 lacto-vegetarian and 24 omnivorous women from South India | VD, Dietary intakes:
Simple Carbohydrate: 29.5 (g/d)
Complex Carbohydrate: 225 (g/d)
Proteins: 30 (g/d)
Fats: 21.5 (g/d)
Fibre: 2.3 (g/d)
O, Dietary intakes:
Simple Carbohydrate: 25.5 (g/d)
Complex Carbohydrate: 216 (g/d)
Proteins: 32 (g/d)
Fats: 20.5 (g/d)
Fibre: 2.95 (g/d) | - In the omnivorous group, the faecal microbiota composition exhibited an increase in *Clostridium* cluster XIVa, specifically *Roseburia–E. rectale*
- *Clostridium* cluster XIVa and *Roseburia–E. rectale* are positively associated with faecal butyrate, with a weaker correlation observed for *Clostridium leptum* and *E. prausnitzii*
- Omnivores have displayed a higher proportion of *Clostridium* cluster XIVa and butyryl-CoA-CoA-transferase gene compared to vegetarians | Kabeerdoss et al. (2012) |
<table>
<thead>
<tr>
<th>Diet</th>
<th>Study design, duration, participants</th>
<th>Main food sources/ food components</th>
<th>Outcomes</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vegetarian diet (VD) vs. omnivorous (O)</td>
<td>healthy vegans (n = 57) and omnivore (n = 33) subjects. Cross-sectional study. 3 days dietary record</td>
<td>VD: Dietary intakes (g/d): Carbohydrate: 250 Proteins: 69 Fats: 70 Fibre: 33 O: Dietary intakes (g/d): Carbohydrate: 232 Proteins: 81 Fats: 83 Fibre: 18</td>
<td>• Long-term adherence to a vegan diet has greater effects (43.3%) on faecal metabolomes than the faecal bacterial genera • Vegans diet resulted in higher proportion of poly-saccharide fermentation products such as MCFA, SCFA (especially butyric and valeric acids) and their derivatives in faeces, and lower proportion of branched chain amino acid compared to omnivores • Of 58 genera detected in both vegetarian and omnivorous diets, ten genera are identified as the core microbiome. Three of them (Lachnospira, Lachnospiraceae NK4A136 group, and Ruminiclostridium) were found to be more abundant in the omnivores, whereas seven genera (Anaerostipes, Blautia, Alistipes, Dorea, Fusicatenibacter, Bifidobacterium, and Ruminococcaceae_uncultured) were less abundant in the vegans compared to omnivores</td>
<td>Prochazkova et al. (2022)</td>
</tr>
<tr>
<td>Vegetarian diet (VD) vs. omnivorous (O)</td>
<td>Healthy vegans (n = 36); omnivores (n = 36) Cross-sectional study</td>
<td>VD: Vegetables, legumes, mushroom, confectionery, fruits, cereal, wholegrains, nuts, vegetable oils, soy milk, soy-products, vegetarian spread O: meat, fish, poultry, processed meat, dairy products, animal fats, alcohol, vegetables, grains, fruits, confectionery, butter.</td>
<td>• Random forest regression analysis indicated no significant SCFA and BCFA concentration differences between vegans and omnivores, implying bacterial adaptability to diverse nutrient availability in these diets • At the species level, omnivores exhibited significantly higher Shannon diversity (p = 0.04) than vegans • In vegans, a cluster of F. prausnitzii, Prevotella copri, Dialister spp., and Eubacterium spp. affect SCFA and BCFA concentrations • For omnivores, Bacteroides spp., Clostridium spp., Ruminococcus spp, and Prevotella spp affect SCFA and BCFA concentrations.</td>
<td>Trefflich et al. (2021)</td>
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### Table 3. Effects of Different Diets Pattern on SCFA Producing Gut Microbiota (continued)

<table>
<thead>
<tr>
<th>Diet</th>
<th>Study design, duration, participants</th>
<th>Main food sources/ food components</th>
<th>Outcomes</th>
<th>Reference</th>
</tr>
</thead>
</table>
| Dutch diet    | 1425 subjects from four cohorts: Crohn’s disease, ulcerative colitis, irritable bowel syndrome and the general population | Dairy, cheese, meat (sausage, meatball), breads, potatoes, cereals, boiled vegetables, salad, fruits, butter, egg, legume, alcohol. Dietary intakes (g/d): Carbohydrate: 208.24-228.37 Proteins: 67.09-74.79 Plant protein: 27.34-30.85 Animal protein: 38.65-44.05 Fats: 71.77-80.66 Alcohol: 4.13-8.53 | • Regular intake of processed and animal-derived foods correlated with higher abundance of *Firmicutes*, *Ruminococcus* and *Blautia*; along with pathways related to endotoxin production  
• Conversely, plant-based foods and fish were positively associated with SCFA-producing bacterial and pathways related with nutrient metabolism | Bolte et al. (2021) |
| Dutch diet    | 2309 individuals from Rotterdam Study and the LifeLines-DEEP cohort                                             | Grains, dairy, fruits, vegetables, legumes, potatoes, poultry, meat, processed meat, eggs, tea, coffee, soda, alcohol                                           | • The *Christensenellaceae* family, being highly heritable, has an inverse correlation with various VLDL particle sizes, small HDL particles and triglycerides in medium HDL  
• *Clostridiaceae 1* and genus *Clostridium sensu stricto* are associated with very large and large HDL particles, and potentially decrease risk of stroke and CVD  
• *Clostridiaceae 1* is inversely related to BMI and blood TG levels  
• *Ruminococcus gnavus* is associated with serum triglycerides levels  
• *Lachnospiraceae* and *Blautia* are associated with small HDL particle  
• *Ruminococcaceae UCG-005* was associated with acetate  
• *Ruminococcaceae, Lachnospiraceae* and *Blautia* convert primary bile acids into secondary bile acids and production SCFAs | Vojinovic et al. (2019) |

Note: RCT - Randomised cross over trial; T2D - Type 2 Diabetes; %en - percent energy; hsCRP - high-sensitivity C reactive protein; IL-17 - interkeulin 17; BMI - body mass index; MCFA - medium chain fatty acid; VLDL - very low density lipoprotein; HDL - high density lipoprotein; TG - triglycerides; yo - years old.
PROSPECTIVE OF MALAYSIAN DIET CONTAINING PALM OIL

The Malaysian diet is unique in that it offers a wide variety of food choices. However, findings from the National Health and Morbidity Survey NHMS 2019 Technical Report (Ganapathy et al., 2019) revealed a concerning high consumption of energy-dense foods and sugary beverages. Approximately, 94.9% of Malaysians have neglected to consume the recommended amounts of fruits and vegetables coupled with inadequate dietary fibre intake. Therefore, the Malaysian public is encouraged to reduce the consumption of refined sugar and sugary drinks and increase consumption of fruits, vegetables and unprocessed foods. When high adherence to this dietary guideline is achieved, a healthy gut environment with a stable gut microbiota community follows.

Around 25 years ago, a study examining the fat intake of Malaysians found that the nation diet contained 40-66 g of fat daily which is equivalent to 22%-26% of total calorie intake (Ng, 1997). Two decades later, Malaysians are found to typically consume 58 g of fat, accounting for 29.2% of total calorie intake. This approaches the upper bound of the recommended limit (Lee and Muda, 2019). Malaysians are also found to have a marginal increase in protein consumption and decreased carbohydrate intake, albeit dipping slightly below the recommended range (Lee and Muda, 2019).

Malaysian Diet and SCFA-Producing Bacteria

A comprehensive understanding of the composition of gut microbiota and its SCFA profiles in the context of long-term Malaysian dietary patterns remains limited. Some noteworthy works have been conducted to investigate either the SCFA or the gut microbiota profiles alone for specific aspects. These include studies conducted in pre-adolescents (Chong et al., 2015) and young adults following Helicobacter pylori eradication (Yap et al., 2016), probiotic intake in adolescents (Joseph et al., 2019) and the effects of fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAP) (Khoo et al., 2023) in both healthy adults and patients with IBD (Huda-Faujan et al., 2010), and the effect of ethnicity on gut microbiota composition and SCFA profile (Dwiyanto et al., 2021) (Table 4). Of these, only two studies (Dwiyanto et al., 2021 and Khoo et al., 2023) provide detailed dietary records and explore the correlation of SCFA to gut microbiota.

Very few studies have been conducted to investigate the composition of the gut microbiota and the corresponding SCFA concentrations in people following a typical Malaysian diet. Analysis of some available data in Table 4 suggests that the SCFA profiles of healthy adults (control) contain mainly acetate, propionate and butyrate, and relatively low levels of BSCFA such as isobutyrate (Table 4). The higher concentration of butyric acid compared to propionic acid suggests a higher consumption of starchy staple foods, particularly rice, by the Malaysian population (Huda-Faujan et al., 2010) or subtle differences in the diets of different ethnic groups (Shafiee et al., 2022).

Firmicutes and Bacteroidetes are the main phyla among healthy Malaysians, and Actinobacteria and Proteobacteria were also found in lower abundance. In addition, SCFA-producing genera such as Faecalibacterium and Prevotella have also been identified. Indigenous children were found to have a higher abundance of Aeromonadales and Ruminococcaceae (Table 4), which is probably related to the degradation of high-fibre foods such as ulam, a popular food in the indigenous diet (Shafiee et al., 2022). A multi-ethnic study by Dwiyanto et al. (2021) demonstrates that the influence of ethnicity on the composition of gut microbiota is related to different lifestyles and dietary patterns of different ethnic groups (Table 4). Conversely, Khine et al. (2019) found that dietary habits affect gut microbiota composition even among individuals from the same ethnic group living in different geographical areas, including Chinese from Guangzhou city (China), Penang city (west coast of Malaysia) and Kelantan city (Malaysia). However, these studies lack detailed information on dietary intake, especially on the type and quantity of edible oils.

The inclusion of palm oil in a balanced Malaysian diet has promising health benefits and should be further explored. Palm oil is known for its unique fatty acid profile and antioxidant properties and has long been used as an important ingredient in Malaysian cuisine. High adherence to the balanced Malaysian diet, which is typically prepared with palm oil, has the potential to create a favourable environment for gut microbiota (Yap et al., 2022) and improve SCFA production in promoting gut health in Malaysians.

CONCLUSIONS AND FUTURE PERSPECTIVES

A healthy Malaysian diet should consist of a large proportion of complex carbohydrates from fruits and vegetables which are mainly indigestible fibre, approximately 25% of proteins and 25% of fats, and the remainder being carbohydrates from fruits and vegetables, and also staple foods such as rice. This composition is broadly in line with the recommended ratios of macronutrients found in other notable dietary patterns. Strict adherence to the recommended intake promotes a healthy intestinal environment for gut bacteria.
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<th>Diet</th>
<th>Results / outcomes</th>
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| Malays (n = 24), Chinese (n = 17) and the Orang Asli (indigenous) (n = 20), 7-12 yo 5 weeks on normal Malaysia diet | Not provided                                                         | • The prominent phyla of gut microbiota were *Firmicutes* and *Bacteroidetes*, while *Facabacterium* and *Prevotella* are the dominant genera  
• Analysis of 16S rRNA sequencing revealed elevated abundance of *Aeromonadales* and an unclassified genus related to *Ruminococcaceae* in Orang Asli children compared to Malays and Chinese | Chong *et al.* (2015) |
| Young healthy volunteers, with Helicobacter pylori positive, 18-30 yo, n=17 | Not provided                                                         | • Alpha indexes indicated no significant diversity shifts between baseline and post-eradication; likewise, beta diversity indexes showed no substantial alternations in bacterial community composition across these time point  
• At baseline, the most abundant phyla were *Bacteroidetes*, *Firmicutes*, *Actinobacteria*, and *Proteobacteria*  
• No SCFA was tested | Yap *et al.* (2016) |
| Healthy and overweight (BMI ≥ 23 kg/m$^2$) adults. 4 weeks MCP supplement, n=12 placebo, n=14 | No dietary record                                                   | • No notable differences were observed in fasting blood glucose, body weight, waist circumference, and SCFA content between the treatment and the control group  
• The content of acetate was 242.0±107.7 mmol/g; propionate, 36.8±16.4 mmol/g; and isobutyrate, 204.4±116.3 mmol/g at the baseline. Results after MCP supplement are not of interest of this article  
• Gut microbiota composition was not measured | Mahadzir *et al.* (2017) |
| School children, 7-10 yo, normal weight, n=19 (BMI 16.07 kg/m$^2$); overweight, n=21 (BMI 23.82 kg/m$^2$); Probiotic drink was provided to the treatment group. | No dietary record                                                   | • At the baseline, acetic concentration was 20.5 mmol/g, butyric, 23.07 mmol/g and propionate, 58.51 mmol/g, respectively  
• Overweight children showed higher total faecal SCFAs concentration, particularly butyrate and propionate than normal weight children  
• Only investigated the abundance of *Lactobacillus* spp and *Bifidobacterium* spp. None of these bacteria were detected in the control group | Joseph *et al.* (2019) |
| Compared SCFA content in normal healthy adults (M = 18, F = 32) to IBD patients (M = 6, F = 2) | Normal Malaysian diet, details were not provided                     | • The concentration of SCFA µmol/g wet faeces (mean ± SEM) in healthy adults are listed below:  
• Acetate = 209.7 ± 14.0  
• Butyrate = 176.0 ± 16.0  
• Propionate = 93.3 ± 5.3  
• Formic acid = 21.5 ± 9.7  
• Isobutyrate = 179.3 ± 13.2  
• Gut microbiota composition was not measured | Huda-Faujan *et al.* (2010) |
| Investigated impact of FODMAP and ethnicity on gut microbiota variation in IBS patients (n = 34, 14M, 19F, 8 Chinese, 20 Malay, 6 Indians; BMI of 23.9 kg/m$^2$) and healthy controls (n = 15, 6 M, 9 F, 2 Chinese, 11 Malay, 2 Indian, BMI of 20.6 kg/m$^2$) | 3 days self-dietary record. Diet record for control group was not highlighted | • Healthy adults have higher proportions of fermenter bacteria, such as *Succinivibrio dextrinosolvens* and *Intestinibaculum porci* along with SCFA producer *F. prausnitzii* when compared to IBS patients | Khoo *et al.* (2023) |
### TABLE 4. STUDIES ON SCFA CONTENTS AND GUT MICROBIOTA COMPOSITIONS IN MALAYSIANS (continued)

<table>
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<th>Results / outcomes</th>
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<td>Gut microbiota composition of different ethics in Segamat area n = 214 (46 Malay, 65 Chinese, 49 Indian, and 54 Jakun), 10 to 83 yo</td>
<td>Main food items are ulam, pork, beef, chicken, fish, fermented food fruits, coffee, tea, probiotics, raw food</td>
<td>• When all variables were adjusted, ethnicity (Malay, Chinese, Indian, and indigenous people) emerged as the most influential factor shaping the gut microbiota compositions in Malaysian (PERMANOVA, p = 0.002).&lt;br&gt;• Three distinct enterotypes were identified: <em>Prevotella</em>-dominant, <em>Bacteroides</em>-dominant and <em>Bifidobacterium</em>-dominant. Jakun volunteers exhibited a higher prevalence of <em>Prevotella</em>-dominant enterotype, Chinese had more <em>Bacteroides</em>-dominant enterotype; while Malays and Indians showed similar distribution between the first two enterotypes.&lt;br&gt;• Among volunteers, Malay displayed an increased abundance of <em>Clostridiales</em>, while Jakun and Indian participants exhibited unique taxa associations attributed to variations in health-related factors.&lt;br&gt;• Functional pathway analysis of the gut microbiota revealed ethnic disparities. Jakun participants displayed elevated pathways connected to pyruvate fermentation, NAD biosynthesis, protocatechuate degradation, methylglyoxal degradation, and maltose degradation. Indians had elevated in L-arginine and fatty acid biosynthesis pathways compared to Chinese and Malays and they are associated respectively to demographic and health-related factors.</td>
<td>Dwiyanto <em>et al.</em> (2021)</td>
</tr>
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Note: FODMAP - fermentable oligosaccharides, disaccharides, monosaccharides, and polyols; BMI - body mass index; IBD - inflammatory bowel disease; MCP - microbial cell preparation; yo - years old.
Although the health benefits of SCFA are well known, there is limited data on the SCFA profile of healthy Malaysians who regularly consume palm oil. Therefore, more clinical data is needed to establish a link between the SCFA profile and other potential health benefits of regular palm oil consumption. This data would not only guide researchers in designing human clinical trials but also allow comparisons with other dietary oils in a balanced diet. These results can also provide valuable insights for policy makers to facilitate the effective implementation of health-conscious dietary recommendations, hopefully reducing the burden of medical costs.

Awareness of healthy diets can be achieved through collaboration between the government and private sectors to create a stable market for healthy foods while providing nutrition education programmes to enhance the public’s understanding of good eating habits.

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