ASSOCIATION OF DIETARY FATS WITH GUT MICROBIOTA PROFILE: HOW DOES PALM OIL FIT IN?

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ABSTRACT

Diet manipulation alters the gut microbiota composition. Gut dysbiosis is characterised by imbalanced bacteria composition that has been associated with high fat diet. Diets containing high animal fat induce pathogenic bacteria growth and similar bacterial profiles have been identified in obese adults and chronic disease patients. Conversely, diets containing high plant fat increase the abundance of beneficial bacteria. Habitual fat intakes modulate the bacterial species and their metabolites in different geographical locations and ethnicities. Dietary interventions using various degrees of fatty acid saturation reported reduced bacterial diversity in high saturated fatty acid (SFA) diet and increased in high monounsaturated fatty acid (MUFA) diet. However, high polyunsaturated fatty acid (PUFA) diet demonstrated a wide variation in bacterial diversity. These results suggested that the effects of dietary fats on gut microbiota composition are not fully established. Palm oil has almost balanced proportions of saturated and unsaturated fatty acids coupled with unique stereo-specificity fatty acids compositions and nutritional properties, making it the main vegetable oil in the Malaysian diet. However, its effect on the gut microbiota profile is still unknown. This review highlights the abundance of specific bacteria after consuming various dietary fats and proposes potential bacteria profile following the palm oil diet.

Keywords: dietary fats, dysbiosis, gut microbiota, palm oil.

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INTRODUCTION

The bacterial composition inhabiting the intestine is highly affected by the diet of the human host. The fractions of carbohydrate, fat, and protein in food residue affect the survival of different population of colonic bacteria. These bacteria degrade and ferment colonic food residue to synthesise a wide range of metabolites that affect the health of the host. The prevalence of a specific type of bacteria could serve as a potential dietary biomarker for diagnosing intestinal health and related systemic health of the host (Mokkala et al., 2019).

In healthy adults, the colonic bacterial composition is dominated by the phyla Firmicutes (60%-80%) and Bacteroidetes (20%-40%); while only a small amount of Actinobacteria, Proteobacteria, Verrucomicrobia and Fusobacteria are present among others (Clavel et al., 2014). The compositions are stable over time and any change in gut environment such as diet modification, and ingestion of probiotics or drugs will result in ‘gut dysbiosis’ (Leeming et al., 2019). Gut dysbiosis is characterised by the imbalance in the bacteria composition (Kriss et al., 2018), low bacteria diversity as indicated by lower total bacteria counts and Chao number which represents bacteria richness (Tsuji et al., 2018).
Diets alter gut microbiota composition as shown in urban and rural populations (Figure 1). Individuals living in urban cities with a diet that is high in animal fat and low in fibre have a significantly (p<0.05) lower abundance of butyrate-producing bacteria compared to individuals living in rural villages that have diet high in fibre and plant-based fats (De Filippo et al., 2010; Ou et al., 2013; Yatsunenko et al., 2012). Animal fat enriched diet induces gut perturbation by promoting opportunistic pathogenic bile-tolerant bacteria (Figure 1) such as Alistipes and Bilophila even in a short-term four days dietary intervention (David et al., 2014). This finding agrees with Muegge et al. (2011) who had concluded that animal-based fat diets have a very similar gut microbiota profile that is found in carnivorous mammals (Muegge et al., 2011).

Gut microbiota composition of high animal fat intake is correlated with the profile of individuals that are obese and/or have chronic diseases such as Type 2 diabetes, digestion disorder, cardiovascular disease and cancer (Illiano et al., 2020; Murphy et al., 2015; Requena et al., 2018). Hence, bacteria species that overgrows or depletes significantly are proposed as dietary biomarkers for early disease diagnosis.

Cohort studies have attempted to generalise the bacteria profile from constituents adopted different habitual diet. A distinguish variation in gut profile was identified in population depending on various geographical location and ethnicities (Gupta et al., 2017; Jain et al., 2018; Yasir et al., 2015) suggesting that individuals gut microbiota profiles are strongly associated with the host’s geographical location. Therefore, extrapolated data collected from different nations is simply too general to be used in the diagnosis of diseases. Researchers should instead use small-scale interpolated data to accurately identify dietary biomarkers and predict metabolic risk (He et al., 2018).

The effect of a high fat diet on the composition of gut microbiome is well known, but there exists little information on the type of geographically-based habitual fat intake on the profile of gut microbiota. Briefly, edible MUFA such as olive oil and PUFA such as fish oils are a staple in the diet of Mediterranean region (Pauwels, 2011). High PUFA soybean oil is extensively used by America, Argentina, Brazil, Russia and China (Jia et al., 2020), whereas sunflower oil is mainly used in European diet (Pilorgé, 2020). Palm oil which is balanced in saturated and unsaturated fats has become an increasingly important edible oil in the India, China, European Union, United Arab Emirates and Southeast Asian regions (Parveez et al., 2020).

To date, very few human clinical studies have focused on the effects of positional distribution of fatty acids varying in degree of saturation on the human gut microbiota profile. Therefore, this review highlights the association of dietary fat intakes with the composition of gut microbiota and their metabolites at different geographical locations. Moreover, we also propose a prospective palm oil nutritional research to identify specific genus or species and establish a baseline of gut microbiota profile in the Malaysian diet, which may be a potential dietary biomarker for predicting metabolic health.

**THE LINK OF DIETARY FAT SOURCE WITH GUT MICROBIOTA COMPOSITION AND HEALTH**

The bioavailability of dietary fats influences the composition of gut microbiota. A plant-based Mediterranean, vegetarian and vegan diets contain a variety of grains, nuts, vegetables, and fruits that provide a variable range of plant fats, phytonutrients and polyphenols (Muralidharan et al., 2019). In contrast, modern diet has been associated with high intake of energy dense- and highly processed foods coupled with red meat consumption (Mozaffarian, 2016).

Effects of high plant-based or animal-based fats on gut microbiota compositions have been summarised into two general pathways (Valdes et al., 2018). High intake of plant-based diet

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**Figure 1. Gut dysbiosis and effects of dietary fat.**
stimulates butyrate-producing bacteria (De Filippo et al., 2010) which have been reported to reduce the risk of non-communicable chronic diseases such as hypertension (Silveira-Nunes et al., 2020) and cardiovascular diseases (Ganesan et al., 2018). Animal-based fat intake increases the abundance of pathogenic bile acid-tolerant bacteria (De Filippo et al., 2010) and leads to accumulation of toxins such as deconjugated bile acids and lipopolysaccharides (Requena et al., 2018) in the systemic circulation.

Animal fat promotes the growth of detrimental bile acids tolerant species such as Clostridium, Helicobacter, Catenibacterium, Fusobacterium, Enterobacterium, Bacteroides, Bilophila and Alistipes (Murphy et al., 2015; Shortt et al., 2018; Tomova et al., 2019; Yang et al., 2020b). These bacteria secrete toxic metabolites such as trimethylamine N-oxide (TMAO) which is derived from dietary choline or L-carnitine, a component of proteins. Bacteria ferment the trimethylamine (TMA) in these proteins to TMAO via flavin-containing monoxygenase 3 (FM03) enzyme and secrete it into the gut. High concentrations of TMAO in the circulating plasma activates the NF-kappa B pathway and increases the secretion of inflammatory cytokines such as IL-18 and IL-1β (Yang et al., 2019). These inflammatory markers are found to be elevated in the plasma of insulin-resistant obese adult subjects (Moreno-Indias et al., 2016). Similarly, elevated TMAO levels inhibit the synthesis of bile acid and trigger platelet hyperreactivity which increases the risk of thrombosis and cardiovascular diseases (CVD) (Yang et al., 2019).

A high fat diet alters the profile of gut microbiota and induces permeability of the intestinal barrier structure in the systematic circulation (Ghosh et al., 2020) and increases the expression of Paneth Cell-Antimicrobial Peptides which trigger intestinal inflammation followed by activation of circulating inflammatory cytokines (IFN-γ and TNF-α) (Guo et al., 2017). This finding sheds light on the importance of gut microbiota profile and metabolites in preventing intestinal tumorigenesis. Overgrowth of detrimental bile acids tolerant bacteria also produces deconjugated bile acid when accumulated and increases the rate of colonic cell proliferation and the risk of colon cancer (Fava et al., 2013; O’Keefe, 2016).

Plant-based fats are generally associated with short-chain fatty acid (SCFA) production. Among the SCFA, acetate and propionate are fatty acids which activate the G-protein coupled receptors 43 (GPR43) in the colon enterocytes and adipocyte. The GPR43 activates cellular signalling events and inhibits colonocytes proliferation (O’Keefe, 2016) as indicated by low Ki-67 proliferation and apoptotic indices. The ffar2 (gpr43) and ffar3 (gpr41), receptors of SCFA on glucagon-like peptide 1 (GLP-1) L cells, stimulate the GLP-1 secretion to regulate plasma glucose concentration and maintain glucose homeostasis (Tolhurst et al., 2012). Hence, SCFA that bind to these receptors may serve as therapeutic treatment for diabetes.

SCFA also demonstrate anti-inflammatory effect by suppressing the production of cytokines and inhibiting actions of the toll-like receptor (TLR) 4 (Mirmonsoef et al., 2012). Therefore, SCFA-producing bacteria such as Prevotella, Bifidobacterium spp. and Lactobacillus (Tomova et al., 2019) may have a protective effect against colon cancer as reported in the study on native Africans (Ou et al., 2013).

**DIVERSITY OF GUT MICROBIOTA IN DIFFERENT HABITUAL_diets**

High dietary fat intake is associated with a decrease in the Firmicutes and Proteobacteria phylum but with an increase in Bacteroidetes and Actinobacteria (Senghor et al., 2018), however contradictory results have also been documented. These contradictory results are likely due to the different ethnicity and lifestyle of populations from different geographical locations (Fontana et al., 2004; Gupta et al., 2017). Later, He et al. (2018) observed that variations in bacterial lineages occurred in different locations within the same ethnic group. Following this observation, they recommended establishing a localised baseline to identify gut microbial as dietary biomarkers (He et al., 2018).

The type of food, meal preparation, drinks, and other socio-cultural rituals co-influence the gut microbiota profile of people in different regions (Senghor et al., 2018). The typical gut microbiota profile in urban European and American population, and rural African population have been extensively reviewed (Almeida et al., 2019; Snijder et al., 2017). Therefore, this review focuses on the gut microbiota profile of Asians in geographically different locations (Table 1).

**Comparison of Gut Microbiota Profile within Same Country but on Different Diets**

Gut microbiota profile differs across geographical locations in urban and rural populations in Asian countries (Table 1). Generally, individuals from rural areas have diverse bacteria species as a result of variety of unprocessed plant-based diet intake; whereas the gut microbiome of urban population is dominated by Bacteroides, Faecalibacterium and Ruminococcus as a consequence of high modern processed food intake (Table 1).

Dietary patterns segregate the gut microbiota profile from different parts in the countries, particularly in Indian and Chinese populations (Table 1). Similar observation was also reported in South Korea, where Jeju Islanders who typically consume more animal lipid have high abundance of Butyricimonas than people who lived in Seoul city (Nam et al., 2011).
| Country            | Region                        | Study population; Sample size | Diets/ lifestyle                                                                 | Sequencing method                  | Gut microbiota compositions                                                                 | Reference                          |
|--------------------|-------------------------------|-------------------------------|--------------------------------------------------------------------------------|------------------------------------|---------------------------------------------------------------------------------------------|------------------------------------|
| Saudi Arabia       | • Urban • adults; n=18        | • limited food variety, low fruits and vegetables intake compared to French | • 16S rRNA Illumina MiSeq (V3-V4) | • Arabic: ↑ Proteobacteria, Blautia viitenerae, ↓ Verrucomicrobia, Bifidobacterium breve compared to French | Yasir et al. (2015)                 |
|                    | Jeddah (Urban) • healthy males; n=18 | • limited food variety, fruit, vegetables, fast food and snacks | • 16S rRNA Illumina MiSeq (V3-V4) | • ↑ Bacteroides                                                                          | Angelakis et al. (2016)            |
|                    | Bedouins (rural) • healthy males; n=10 | • vegetables, chicken, dairy products, fermented food and rice | • 16S rRNA Illumina MiSeq (V3-V4) | • ↑ Verrucomicrobia ↑ Spirochaetae Treponema berlinense, T. succinifaciens due to fermented food intake |                                |
| Arabian Peninsula  | • healthy native Arab Kuwaitis • n=10 | • meats, dairy products, grains, legumes, nuts, vegetables (leafy greens, herbs), fruits and nuts | • 16S rRNA Illumina MiSeq (V3-V4) | • ↑ Bacteroides dorei/ vulgatus                                                            | Plummer et al. (2020)              |
| India              | • North (Bhopal, Ludhiana, Lucknow, New Delhi) • n=247 | Details dietary records were not provided | • 16S rRNA Ion Torrent (V3-V4) | • Eastern and Western: ↑ Bacteroides ↑ Northern and Southern: ↑ Spirochaetes ↑ Facalibacterium and Prevotella genus across the geographic landscape | Shetty (2018)                     |
|                    | East (Guwahati, Kolkata, Patna) • n=250 | • fruits, vegetables, wheat, millet, sorghum, dairy products, sprouts, leafy vegetables, rice, pulses, low meat and fish intake | • 16S rRNA Illumina MiSeq (V3-V4) | • ↑ Prevotella, Sutterella and Succinibrio phylum Proteobacteria | Tandon et al. (2018)               |
|                    | West (Ahmedabad, Ajmer, Mumbai, Nagpur) • n=263 | • vegetarian, eggetarian, non-vegetarian | • 16S rRNA Illumina MiSeq (V3-V4) | • Urban: ↑ Lactobacillus Rural: ↑ Parabacteroides, Blautia, Brevundimonas, Pelomonas and Meganonas Leh: ↑ Prevotella copri, uncharacterised species of Facalibacterium and Lachnospiraceae High ghee intake: ↑ Collinsella High sunflower oil: ↑ Roseburia and Sporobacter | Das et al. (2018)                  |
|                    | South (Chennai, Cochin, Mangalore) • n=226 | • lack of dairy intake, high consumption of sunflower oil | • 16S rRNA pyro-sequencing (V1-V5) | • Central region: ↑ Prevotella Southern region: ↑ Bacteroides, Ruminococcus and Facalibacterium | Dhabakan et al. (2019)             |
|                    | Leh, Ladakh district, high altitude • n=35 | • plant-based diet omnivorous diet | • 16S rRNA sequencing, whole genome shotgun | • Central region: ↑ Prevotella Southern region: ↑ Bacteroides, Ruminococcus and Facalibacterium |                               |
| Country | Region | Study population; Sample size | Diets/ lifestyle | Sequencing method | Gut microbiota compositions | Reference |
|---------|--------|------------------------------|------------------|------------------|----------------------------|-----------|
| Ladakh  | (cold desert) | healthy adults; n=31 | noodles, whole wheat bread, yak butter, barley, alcoholic beverage | whole genome sequencing Illumina HiSeq-2500 | Ladakh: ↑ Prevotella | Kaur et al. (2020) |
| Jaisalmer | (hot and semi-arid) | young healthy adults; n=31 | whole wheat bread, spicy curries, lentils, grains and butter milk | 16S rRNA SOLID sequencing | Overall: ↑ Bifidobacterium, Meganonas, Phascolarctobacterium, Lactobacillus or Akkermansia | Tyakht et al. (2013) |
| Khargone | (subtropical to tropical climate) | healthy adults; n=96 | lentils, grains, rice, whole wheat bread, vegetables, spices, tea and milk | Overall: ↑ Bifidobacterium, Faecalibacterium | ↑ Bifidobacterium | Zhang et al. (2015) |
| Russia  | Saint Petersburg, Saratov, Rostov-on-Don and Novosibirsk (urban) | urban: high processed food intake; rural: high unprocessed natural food intake | | Overall: ↑ Bifidobacterium, Faecalibacterium, Coprococcus and Faecalibacterium | ↑ Roseburia, Faecalibacterium, Faecalibacterium and Ruminococcus genera | Tyva: ↑ Bifidobacterium |
| Babu district, He Zhou (Southern China) | young healthy adults; n=134 (Han, n=47; Zhuang, n=28; Yao, n=59) | frequencies of 21 types regular food intakes | 16S rRNA Illumina MiSeq (V3-V4) | Overall: ↑ Bacteroides and Prevotella | Hans: ↑ Meganonas significantly (p <0.05) due to high intake of beans | Liao et al. (2018) |
| Beijing (Northern) | healthy adults; n=131 | details dietary records was not provided | 16S rRNA Illumina MiSeq (V3-V4) | Overall: ↑ Bacteroides and Prevotella | ↑ Bacteroides, Bacteroides, Blautia, Clostridium, Coprococcus, Escherichia/Shigella, Faecalibacterium, Gemmiger, Paraseuterella, Roseburia and Ruminococcuscore | Zhang et al. (2019) |
| Jinan (Eastern) | details dietary records was not provided except fruits, yogurt and drink intakes | | | Overall: ↑ Faecalibacterium | Faecalibacterium, Faecalibacterium, Gemmiger, Paraseuterella, Roseburia and Ruminococcuscore | Ling et al. (2013) |
| Zigong (Southwest) | details dietary records were not provided | | | Overall: ↑ Faecalibacterium | Faecalibacterium | Zhang et al. (2019) |
| Zhejiang (Eastern China) | healthy; n=10 | | | Overall: ↑ Faecalibacterium | Faecalibacterium | Ling et al. (2013) |
| Shanghai, Jiangyin (Eastern China) | healthy, native; n=29 | high fat diet (>40% of dietary calories were from fat); low fat diet (<40%); fats were mainly from cooking oil, data of oil types were not provided | 16S rRNA Illumina MiSeq (V3-V4) | Faecal samples: ↑ Prevotella and Akkermansia | Colon mucosa tissue, ↑ uncultured genus of S24-7 from HDF compared to LFD | Qian et al. (2018) |
| Country        | Region                     | Study population; Sample size | Diets/ lifestyle                                                                                                                                                                                                 | Sequencing method | Gut microbiota compositions                                                                                                                                                                                                 | Reference                     |
|---------------|----------------------------|-------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------|
| South Korea   | Seoul (inland)             | healthy, elderly n=9          | • 24 hr diet recall • subjects from Jeju Island consumed significantly (p<0.05) more animal lipid than those from Seoul                                                                                       | 16S rRNA Ion Torrent (V1-V2) | • ↑ Catenibacterium                                                                                                                                                                                                                    | Shin et al. (2016)            |
|               | Jeju Island                | healthy, elderly n=10         |                                                                                                                                                                                                               |                   | • ↑ Butyricimonas                                                                                                                                                                                                                       |                                |
| Korea         | NA                         | healthy n=20                  | • details dietary records were not provided                                                                                                                                                                   | 16S rRNA pyro-sequencing (V1-V3) | • Overall: • ↑ Faecalibacterium, Prevotella and Bacteroides • Core gut microbiota: Bacteroides, Parabacteroides, Prevotella, Clostridium, Eubacterium, Facalibacterium, Lachnospira, Oscillibacter, Roseburia, Ruminococcos, Subdoligranum, uncultivated human intestinal clones and Fusobacterium | Nam et al. (2011)            |
| Japan         | Sendai city                | healthy adults n=32           | • traditional Japanese diet: soya products, fishes, vegetables, fruit, green tea, seaweed, mushrooms, rice, condiments, soup stock ‘Dash’, fermented seasoning (soya sauce, miso, vinegar, mirin and sake) • modern Japanese diet contains deep fried dishes, grilled fishes added salts, soya sauce, butter, cheeses, sugars | 16S rRNA Illumina MiSeq (V3-V4) | • Traditional Japanese diet: • ↑ Sutterella, ↓ unclassified Lachnospiraceae, Parabacteroides, unclassified Rikenellaceae                                                                                                         | Kushida et al. (2019)         |
|               | Azabu University (Eastern Japan) | healthy adults n=106            | • details dietary records were not provided                                                                                                                                                                   | 16S rRNA Ion Torrent, pyro-sequencing, Illumina MiSeq (V1-V2) | • ↑ Bifidobacterium • ↓ Methanobrevibacter smithii                                                                                                                             | Nishijima et al. (2016)       |
| Thailand      | NA                         | healthy adults non-vegetarian | • santi-Asoke vegetarian diets: vegetables, fruits • ovo-lacto, ovo lacto vegetarian diets: include eggs, milk, and yoghurt • non-vegetarian diet: pork, fish and chicken, eggs, yoghurt, milk, fruits | 16S rRNA pyro-sequencing (V6-V8) | • Overall: • ↑ Facalibacterium prausnitzii and Gemmiger formicilis • Vegetarian diets: • ↑ Clostridium nexile, Eubacterium eligens, and Prevotella copri • Non-vegetarian diets: • ↑ Collinsella aerofaciens, Ruminococcus torques, various species of Bacteroides, Parabacteroides, Escherichia, Clostridium and Eubacterium | Ruengsomwong et al. (2016)   |
| Indonesia     | Bali                       | healthy adults n=41           | • white rice, bread, fried tofu, chicken, palm oil, tempeh, egg, pork, fish, soto, milk and papaya                                                                                                                                                               | 16S rRNA Illumina MiSeq (V4) | • Overall: • ↑ Prevotella-rich (type-P) and Bacteroides-rich (type-B)                                                                                                         | Febinia et al. (2020)         |

Note: n - number of subjects; FFQ - food frequency questionnaire; V - variable region; HFD - high fat diet; LDF - low fat diet; NA - not available; SCFA - short-chain fatty acids; 16S rRNA - 16S ribosomal RNA.
China and India have varying geographical locations and thus, create diverse dietary habits in their people and compositions of gut microbiota. In China, the predominated core genus was *Phascolarctobacterium* from the phylum of *Firmicutes* (Zhang et al., 2015), which is also in high abundance in Russian population (Tyakht et al., 2013). Other core genera in Chinese population include *Roseburia, Bacteroides, Faecalibacterium* and other bacteria from SCFA-producing lineages (Table 1).

Contrary in India, *Prevotella copri* and *Faecalibacterium prausnitzi* (Pulipati et al., 2020) from the butyrate producing bacteria lineages (Kaur et al., 2020), are the most predominant core bacterial genera as identified in the ‘Landscape of Gut Microbiome-Pan India Exploration’ (LogMPIE) study results suggesting that the majority of Indian populations are still adhering to the whole grains, legumes and plant-based diet (Kaur et al., 2020). However, this result was not in agreement with the smaller cohort study conducted in unique geographical locations (Das et al., 2018).

Das et al. (2018) reported that gut microbiota compositions of non-vegetarian adults in high altitude areas of Leh was predominated by *Prevotella* compared with vegetarian or ovo-vegetarian diet from sea level Ballabhgarh urban region (Das et al., 2018). These results suggest that *Prevotella* has distinct oligo types that mediate the carbohydrate-enzyme activities in different diets (Das et al., 2018; Kaur et al., 2020).

The diversity of gut microbiota in Leh and Ballabhgarh populations was significantly associated with the types of dietary fat consumption, especially from cooking oils, butter and milk (Table 1). Individuals from Leh has high sunflower oil intake but low in dairy intake. Hence, *Roseburia* (Devillard et al., 2007) and *Sporobacter* (Pu et al., 2016) which are able to degrade PUFA oil, especially linoleic acids, were identified as the predominated gut bacteria in Leh individuals; but genera such as *Pseudomonas* and *Bifidobacterium* which have been associated with dairy products were rare. Furthermore, *Collinsella* was identified as the most abundant genus in Ballabhgarh subjects who have high ghee consumption (Das et al., 2018).

**Comparison of Gut Microbiota Profile between Countries but on Similar Diets**

Although *Prevotella* has been related with high plant-based diet intake, but the core genera of individuals from different countries following the same diet are different (Table 1). For instance, vegetarian groups from Thailand were high in abundance of *Clostridium nexile, Eubacterium eligens* and *Prevotella copri* which was different from residence in Leh, India that made up of *Prevotella, Coprococcus, Clostridium, Ruminococcus, Howardella, Erysipelotrichaceae* and *Peptococcus* (Table 1). Similarly, *Spirochaetae* was enriched in Arabs who consumed fermented foods made from pearl millet flour with starter culture (Angelakis et al., 2016) but absent in Japanese who were also on high fermented food intake from soya (Kushida et al., 2019).

*Megamonas* was the predominant bacteria in Hans population who have high bean intake (Liao et al., 2018) which is rich with unsaturated fats. *Megamonas* was also of the core species in Russian (Tyakht et al., 2013) and in Ballabhgarh, Indian populations (Das et al., 2018). Linear discriminant analysis (LDA) effect size (Lefse) analysis could be used to cluster and identify the potential biomarkers from profile of these gut bacteria of distinct populations (Jain et al., 2018).

These studies provided a good foundation of gut microbiota profile to establish localised baseline from complex dietary patterns in Asia and to predict metabolic disorder in niche community. In Southeast Asia, studies regarding the microbial diversity of healthy adults related to the gut health is limited, but effect of dietary pattern on gut microbiota profile in Bali (Febinia et al., 2020) and a comparison on effects of vegetarian diet on gut microbiota on healthy adults in Thailand (Ruengsomwong et al., 2016) are among the few reported works of healthy adults on habitual diet. More comprehensive studies should be conducted to establish the baseline of gut microbiota profile in this region.

**SIGNIFICANCE OF SFA, MUFA AND PUFA ON COMPOSITIONS OF GUT MICROBIOTA COMPOSITION**

Dietary fat is composed of 90% triglycerides (TG) that are made up of three fatty acid chains linked to a glycerol backbone. A substantial amount of the fatty acid is released by cleavage of the TG by the lingual lipase in the mouth and gastric lipases in the stomach (Mu and Hoy, 2004). The remaining TG are almost completely hydrolysed in the proximal small intestine by the sn-1, 3 stereospecific pancreatic lipase and yield two free fatty acids (FFA) and a 2-monoacylglycerol (2-MG) (Rogalska et al., 1990). The ionised FFA and 2-MG mix with the bile acid to form mixed micelles with phospholipids and up to 95% of these fatty acids are absorbed by the epithelial cells in the small intestine. These fatty acids are then randomly re-esterified and re-synthesised through a predominant 2-MG pathway to form new TG in the distal small intestine. These plasma TG are then packed with cholesterol, phospholipids, apoproteins to form chylomicrons and absorbed into the lymphatic and blood circulation systems. The remaining fatty acids reach the colon, where they are metabolised by the community of gut microbiota (Bauer et al., 2005).
Dietary Fats Saturation

Dietary fats have fatty acids that vary in chain length, saturation, and positional distribution of fatty acids. Fatty acids are classified into SFA, MUFA, or PUFA based on their degree of saturation. Population or intervention studies of the effects of SFA, MUFA and PUFA rich diets on gut microbiota composition have either been reviewed systematically and extensively (Mokkala et al., 2019; Yang et al., 2020b).

SFA Rich Diet

Generally, a high SFA intake (18E% of SFA, >35E% of total fat) is inversely correlated with bacteria diversity and richness indices (Fava et al., 2013), and higher Firmicutes to Bacteroidetes (F/B) ratio (David et al., 2014). High F/B ratio has been associated with obese individuals (Kasai et al., 2015). A study involving monozygotic twins shows that habitual SFA intake resulted in similar Bacteroides spp. profiles (Simões et al., 2013) but a higher number of Faecalibacterium prausnitzii was demonstrated to reduce intestinal inflammation by inducing goblet cell proliferation and mucus production (Fava et al., 2013) to maintain the epithelial integrity (Wrzosek et al., 2013). Although SFA is frequently correlated with increased incidences of CVD and colon cancer, meta-analysis and systematic reviews do not support this claim (Dehghan et al., 2017; Kang et al., 2020; Kim and Park, 2018).

MUFA Rich Diet

A 24 weeks MUFA rich diet did not result in any significant changes in body mass index (BMI), waist circumference, body fat percentage, blood pressure or insulin resistant in 88 adults with metabolic syndrome (Fava et al., 2013). High MUFA consumption also did not significantly affect bacteria richness as measured by Shannon, Chao1 and abundance based coverage (ACE) indices, the phylum distribution or F/B ratio (Pu et al., 2016).

After a year of adhering to a MUFA-rich Mediterranean diet, 20 obese patients with coronary heart disease showed no significant difference in plasma glucose, and insulin and lipoprotein profile but enhanced significant growth in colonic Roseburia, Oscillospira, Faecalibacterium prausnitzii and Parabacteroides distasonis compared to the baseline using 16S rRNA pyrosequencing (454 Roche) (Haro et al., 2016). However, another study reported that a MUFA-rich Mediterranean diet reduced the number of colonic Prevotella in obese healthy adults but increased it in adults with metabolic syndrome (Pu et al., 2016). Individuals who had highly adhered to the Mediterranean diet demonstrated lower Escherichia coli counts and increased commercial Bifidobacteria to E. coli ratio, which is an established healthy gut indicator (Mitsou et al., 2017). The enrichment of these SCFA-producing and beneficial bacteria could also be related to the Mediterranean diet which consists of a high concentration of polyphenols and other phytochemicals found in vegetables and fruits (Muralidharan et al., 2019).

PUFA Rich Diet

PUFA-based diets showed inconsistent results on gut microbiota compositions. Randomised controlled trials have demonstrated that high n-3 long-chain PUFA diets did not significantly alter bacterial diversity, richness, or phylum distribution compared to the control diet. The study duration varied from 30 days for adults with metabolic syndrome (Pu et al., 2016), to 42 days for healthy overweight individuals (Rajkumar et al., 2014), and to six months for patients with Type 2 diabetes (Ballegó et al., 2016). A high dose of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) supplements failed to demonstrate any significant impact on the composition of gut bacteria (Watson et al., 2017), although these fatty acids have been associated with lower plasma inflammatory markers such as C-creative protein (CRP) (Yang et al., 2020a).

The effect of PUFA diet demonstrated contradictory results on the compositions of gut microbiota. High habitual intake of PUFA resulted in an increase in bacteria diversity in overweight middle-aged adults (Menni et al., 2017) and this diet also promoted the abundance of Actinobacteria but lowered Firmicutes in the gut of postpartum women (Mandal et al., 2016). Diets enriched with n-3 long-chain PUFA was positively associated with the Lactobacillus group, whereas n-6 long-chain PUFA was negatively correlated with the abundance of Bifidobacteria in 11 healthy and 29 overweight or obese monozygotic twin (Simões et al., 2013). Reyes et al. (2016) reported that high habitual intake of unsaturated fatty acid and fibre diet increased the content of Bifidobacterium longum in young adults, with the increase being higher in lean participants than in overweight or obese participants (Reyes et al., 2016). In men, the abundance of the genus Blautia in serum was negatively associated with n-3 and n-6 PUFA content (Org et al., 2017). The abundance of Blautia was increased in participants with higher BMI (Liu et al., 2019; Org et al., 2017), or higher levels of low-density lipoprotein (LDL) and waist circumference in Chinese adults (Zeng et al., 2014), but inversely associated with visceral fat accumulation in Japanese adults (Ozato et al., 2019).

The discrepancy in PUFA diet studies is probably related to the study duration, variation in
the amount and sources of fats, and the pre-existing health condition of the subjects. This is proven in a study on premature infants that were fed with a mixture of fish oil and safflower oil via enterostomies for nine weeks, and the outcomes were compared to that of infants who had received standard treatment (Young et al., 2017). The fish oil-enriched diet yielded varying gut microbial communities at different points in time between the study groups (Young et al., 2017). Different functional pathways were inferred using microbial gene function analysis, and it revealed that the changes in the diversity of microbiota are associated with pathways related to lipid metabolism, followed by pathways related to butyrate and also specific amino acids metabolism between the intervention groups (Young et al., 2017).

These studies showed inconsistent effects of fatty acid saturation on the diversity of gut microbiota and this could be due to the effect of stereo-specificity of fatty acid chains on TG, the sequencing and bioinformatic analysis methods.

**EFFECTS OF STEREOSPECIFICITY ON TG OF PALM OIL AND GUT MICROBIOTA**

Recently, palm oil has been identified as one of the most affordable EAT-Lancet diets along with transformation toward sustainable global food system (Hirvonen et al., 2019). Palm oil is a unique oil, in which it has almost equal percentages of saturated and unsaturated fatty acids compositions (Koushki et al., 2015) on the TG backbone. Similar to other vegetable oils, the sn-2 position in the TG of palm oil is mainly occupied by unsaturated fatty acids (May and Nesaretnam, 2014; Ong and Goh, 2002). However, in certain animal fats, particularly in lard, the sn-2 position is occupied by SFA (Table 2).

Increasing evidence demonstrates that the stereospecificity of fatty acids in TG molecules affects its absorbability (Ramíreza et al., 2001). Differing from other vegetable oils, the sn-1,3 position of palm oil is predominated by long-chain SFA, C18:0 and C16:0. This is evidenced by a study in which high fat palm oil diet was fed to mice and it was found that a high palm oil diet (45% E fat) resulted in overflow of palm oil into the distal intestine, probably due to lack of absorbitivity of long-chain fatty acids which then trigger dysbiosis (Wit et al., 2012) rather than the type of diet itself. Therefore, clinical human study using palm oil at recommended dietary intake level should be conducted to avoid pre-mature claim.

The longer fatty acid chains at sn-1,3 position have a low tendency of fat deposition in the adipose tissue compared to high PUFA oils in animal studies (Gouk et al., 2013; 2014). It is hypothesised that at certain threshold concentration, long-chain SFA at the sn-1,3 position are poorly absorbed in the small intestine due to these fatty acids having a higher melting point than the core human body temperature and therefore are more prone to form insoluble calcium soap in the high pH small intestinal environment. However, the effect of fatty acid positional distribution on palm oil intake from the habitual diet composition of gut microbiota in humans is unknown.

**FUTURE PROSPECTIVES**

Dietary fats alter certain species of gut microbiota and their metabolites following regular diet intake. If dietary fat could alter the gut microbiota compositions alone, the bacteria profile in Malaysians may have similar relative abundance to SFA and MUFA diets, but a lower similarity to PUFA diet. The simplified bacteria profile may consist of high abundance of Bacteroides spp. (phylum of Bacteroidetes) as identified in high SFA; Roseburia, Oscillospira, Faecalibacterium prausnitzii (phylum of Firmicutes), and Parabacteroides distasonis (phylum of Bacteroidetes) from MUFA diet; and Actinobacteria, and Lactobacillus (Firmicutes) as identified in high PUFA diet. However, more complex bacteria composition is anticipated as Malaysia is a multiracial country comprising of different ethnicities and cultures, each having their unique heritage food, which is also influenced by culinary attributes within Malaysia and neighbouring countries. Diversity in food, ethnicities and culture may give rise to a unique gut microbiota profile in Malaysians. Moreover, palm oil remains the most widely consumed oil in Malaysia (Kushairi et al., 2019), although other imported vegetable oils are available in the Malaysian market. Therefore, the effects of fatty acids saturation and stereo-specificity of various cooking oils on Malaysian population’s gut microbiota profiles might be of interest to explore.

High throughput sequencing and analytical technologies coupled with extensive bioinformatics database using analytical software (Onywera and Meiring, 2020; Zhao et al., 2018) had accelerated the process of identifying colonic bacteria and predicting the functional profiles of metabolites in establishing the baseline of gut bacteria profile of Malaysian. The hope is that changes of the identified species or metabolite from the baseline could be used as a non-invasive biomarker for clinical diagnosis of diet-related cardio-metabolic or non-communicable diseases in the early stage.

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### TABLE 2. STEREOSPECIFIC POSITIONING OF FATTY ACID (MOL %) IN TRIACYL-SN-GLYCEROLS OF PLANT-BASED OIL AND ANIMAL-BASED FAT

| Oil/Fat       | Position | 14:0 | 16:0 | 16:1 | 18:0 | 18:1 | 18:2 | 18:3 | 20-24 |
|---------------|----------|------|------|------|------|------|------|------|-------|
| Peanut        | TG       | 9    | 3    | 58   | 23   | 7    |      |      |       |
|               | 1        | 14   | 5    | 59   | 19   | 4    |      |      |       |
|               | 2        | 2    | trace| 59   | 39   | 1    |      |      |       |
|               | 3        | 11   | 5    | 57   | 10   | 15   |      |      |       |
| Soybean       | TG       | 3    | 2    | 26   | 17   | 10   | 43   |      |       |
|               | 1        | 4    | 2    | 23   | 11   | 53   |      |      |       |
|               | 2        | 1    |      | 37   | 36   | 6    | 6    |      |       |
|               | 3        | 4    |      | 3    | 17   | 4    | 20   | 70   |       |
| Linseed       | TG       | 9    | 4    | 24   | 54   | 8    |      |      |       |
|               | 1        | 14   | 6    | 23   | 48   | 9    |      |      |       |
|               | 2        | 1    | trace| 22   | 70   | 7    |      |      |       |
|               | 3        | 13   | 6    | 28   | 45   | 9    |      |      |       |
| Corn          | TG       | 11   | 2    | 29   | 57   | 1    |      |      |       |
|               | 1        | 1    | 3    | 28   | 50   | 1    |      |      |       |
|               | 2        | 18   | trace| 27   | 70   | 1    |      |      |       |
|               | 3        | 2    | 3    | 31   | 52   | 1    |      |      |       |
| Olive         | TG       | 10   | 2    | 76   | 10   | 1    |      |      |       |
|               | 1        | 13   | 3    | 72   | 10   | 1    |      |      |       |
|               | 2        | 1    |      | 83   | 14   | 1    |      |      |       |
|               | 3        | 17   | 4    | 74   | 5    |      |      |      |       |
| Palm          | TG       | 48   | 4    | 36   | 10   |      |      |      |       |
|               | 1        | 60   | 3    | 27   | 9    |      |      |      |       |
|               | 2        | 13   | trace| 68   | 18   |      |      |      |       |
|               | 3        | 72   | 8    | 14   | 3    |      |      |      |       |
| Cacao butter  | TG       | 24   | 35   | 36   | 3    | trace| 1    |      |       |
|               | 1        | 34   | 50   | 12   | 1    | 1    |      |      |       |
|               | 2        | 2    | 2    | 87   | 9    |      |      |      |       |
|               | 3        | 37   | 53   | 9    | trace| 2    |      |      |       |
| Beef          | TG       | 5    | 27   | 6    | 17   | 33   | 5    | 1    |       |
|               | 1        | 4    | 41   | 6    | 177  | 20   | 4    | 1    |       |
|               | 2        | 9    | 17   | 6    | 9    | 41   | 5    | 1    |       |
|               | 3        | 1    | 22   | 6    | 24   | 37   | 5    | 1    |       |
| Lard          | TG       | 2    | 27   | 3    | 13   | 45   | 9    |      |       |
|               | 1        | 1    | 10   | 2    | 30   | 51   | 6    |      |       |
|               | 2        | 4    | 72   | 5    | 2    | 13   | 3    |      |       |
|               | 3        |      | trace| 2    | 7    | 70   | 18   |      |       |
| Chicken       | TG       | 1    | 30   | 6    | 6    | 45   | 11   | 1    |       |
|               | 1        | 1    | 47   | 7    | 8    | 31   | 5    | 1    |       |
|               | 2        |      | trace| 13   | 5    | 6    | 55   | 19   | 1     |
|               | 3        |      | 31   | 7    | 3    | 49   | 8    | 1    |       |
| Mutton#       | TG       | 3    | 22   | 2    | 35   | 36   | 2    |      |       |
|               | 1        | 1    | 35   | 2    | 47   | 4    | -    |      |       |
|               | 2        | 4    | 14   | 2    | 15   | 52   | 5    |      |       |
|               | 3        | 3    | 16   | 1    | 42   | 26   | 2    |      |       |

Note: Trace = <0.5%, TG = intact triacylglycerols, #Results are listed for cis-18:1 isomers only; trans-18:1 was present in positions sn-1, sn-2 and sn-3 as 5%, 2% and 6%, respectively.

Source: Brockerhoff and Yurkowski (1991); Brockerhoff et al. (1966); Christie and Moore (1971).
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