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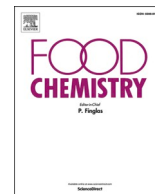
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Gut microbial modulation by culinary herbs and spices

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ABSTRACT

Culinary herbs and spices have previously been recognised for their potential impact on health through antioxidant and antimicrobial properties. They may also be promoters of positive microbial modulation by stimulating beneficial gut bacteria during fermentation, increasing the production of short chain fatty acids and thereby exhibiting a prebiotic effect. In the present paper, current literature around herb and spice consumption, gut microbiota modulation and prospective health benefits were reviewed. Herb and spice consumption can positively modulate gut microbes and possibly play an important role in inflammation related afflictions such as obesity. Current literature indicates that few human studies have been conducted to confirm the impact of herb and spice consumption on gut microbiota in connection with prospective health outcomes and inconsistencies in conclusions therefore remain.

1. Introduction

Herbs and spices have been used for culinary and medicinal purposes including digestive aids and various other improvements to health, for millennia. In recent times, they have gained attention in gut microbial studies for their high polyphenol content, antioxidant and anti-inflammatory properties. These aspects may result in potential health benefits such as a reduction in inflammation, reduced risk and or progression of non-communicable diseases such as obesity (Kim et al., 2017), cardiovascular disease (CVD) (Vamanu et al., 2019) and dementia (Hamaguchi et al., 2009). Advances in molecular and related methods have uncovered an abundance of diversity in the gut microbiome which has helped to identify potential biomarkers of gut health that may reveal connections between gut profiles and disease states (Zhernakova et al., 2016). Subsequently, studies have demonstrated the influence of culinary herbs and spices on the gut microbiome, intestinal barrier function and inflammation.

The main objective of this paper is to investigate current research on gut microbial modulation with culinary herbs and spices. A secondary objective is to highlight gut related health effects potentially associated with herb and spice consumption. A review of recent studies on gut microbial modulation with culinary herbs and spices will provide insight on potential health benefits associated with their intake and determine future research needs in this area.

2. Herb and spice consumption

Culinary herbs are associated with the fresh leaf and flowers (aerial parts) of a plant while the remainder i.e. root, seed, bark, stem, berries and bud, is categorised as a culinary spice and usually dried (Tapsell et al., 2006). Herbs and spices have been used for culinary purposes such as food preservation, taste enhancement, aromatics as well as medicinal purposes including digestive aids, nausea prevention and various other improvements to health in ancient and contemporary times. Assyrians documented the addition of liquorice root to a plant-based mixture used to cure a gastrointestinal illness with colic-like symptoms in first millennium BC (Böck, 2012). Texts containing recipes from Babylonia ca. 1700 BCE attest the use of garlic, coriander, cumin, juniper berries, and mint as culinary ingredients and condiments (Bottéro, 1987). Basil, mint, thyme and rosemary were consumed in ancient Greece and Rome (Tapsell et al., 2006). Ayurveda, an ancient system of traditional medicine originating in India and still practised today, advocates herb and spice use for two of its principles: the promotion of good health and prevention of disease or its risk. Among many herbs used in this regard, liquorice is used to combat gastrointestinal discomfort (Peterson, Vandana, et al., 2018), ginger is consumed to alleviate indigestion, and turmeric, known for its anti-inflammatory properties is advised for jaundice and gut disorders (Tapsell et al., 2006).

Many herbs and spices consumed in ancient times are still ingested today for culinary and medicinal purposes. Liquorice root is used as a

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natural sweetener and digestive aid (NCCIH, 2016). Basil, rosemary, thyme, mint and garlic are included in Mediterranean type diets. Dietary supplements of mint are ingested for improving symptoms of Irritable Bowel Syndrome (IBS) and garlic has been indicated to reduce blood cholesterol and high blood pressure (NCCIH, 2016). Although evidence may be inconclusive, Tapsell et al. (2006) suggested that these herbs may be responsible for health benefits conferred by the Mediterranean diet which may reduce risks associated with non-communicable diseases (NCDs) such as stroke, CVD, obesity and certain cancers (Martinez-Lacoba et al., 2018). As oxidative stress and inflammation are factors in many of these diseases, it is possible that herbs contribute to reduced oxidative stress and inflammation effects associated with the Mediterranean diet.

The reason that some herbs were consumed for certain illnesses in ancient times may not always rest on evidence-based evaluation of their benefits, but on other, sometimes metaphysical qualities of the herbs and perceived origin of illnesses. Ancient and traditional use of culinary herbs and spices can provide an indication for consumption, but are unable to serve as a guide or prescription for beneficial health without thorough scientific investigation. For example, Thumann et al. (2019) advised that a greater depth of investigation is required to understand the interactions of liquorice root constituents and gut microbes ahead of use for medicinal purposes. Evidence from laboratory experiments, i.e. characterising herb and spice substrates, *in vitro* testing of their efficacy in gut modulation and human studies to identify the health benefits which may stem from herb and spice modulation of the gut microbiome are needed to support any recommendation of culinary herb and spice consumption.

3. Gut microbiota composition, acquisition, development and function

Approaches to characterising and identifying gut microbiota can be culture dependent or culture independent. Culture-dependent approaches rely on traditional methods of plating bacteria. Culture-independent methods include fluorescent *in situ* hybridisation (FISH), a low throughput process where fluorescent DNA probes are used to illuminate select bacteria in the sample under investigation. Coupling FISH with flow cytometry is a widely used high throughput method for quantitative analysis of often non-culturable gut microbiota however autofluorescence from particles in samples may provide false counts of microbes (Shah et al., 2016; Szöllösi et al., 1995). Advances in other culture-independent approaches such as sequencing of 16S ribosomal RNA gene amplicons from polymerase chain reaction (PCR) and metagenomics sequencing (Jovel et al., 2016), are high throughput and have enabled increased knowledge of the human gastrointestinal (GI) microbiota over the past 15 years (Li et al., 2014). While DNA sequencing techniques help to understand abundance and diversity of gut microbial communities and are currently popular in the field of microbiome studies, investigation into microbial interactions between the immune system and the gut with immunoglobulin A sequencing (IgA-seq) may become more prominent due to the ability to target taxa associated with dysbiosis (Nakajima et al., 2018; Weis & Round, 2021). Although there is a better understanding of the composition of the gut microbiota, its complete functionality remains far from clear.

3.1. Composition

The gut microbiota is a diverse population of microorganisms within the GI tract which includes viruses, bacteria and eukaryotes. It is estimated to contain $\sim 3.8 \times 10^{13}$ microbial cells (Sender et al., 2016) with the majority of bacteria being found in the large intestine or colon. Bacteria which can be beneficial or pathogenic to the host, commensal or transient in the gut microbiota are categorised top-down into kingdoms, phyla, classes, orders, families, genera, species and strains. The Human Genome Project, which worked on the characterisation of the

gut microbiome in connection with disease, identified 2172 species from 12 phyla of which over 90 % were found in Firmicutes, Proteobacteria, Actinobacteria, and Bacteroidetes (Hugon et al., 2015). Although composition of gut microbiota may be more consistent in adults, it can vary in composition in response to influential factors such as diet, age, environment, health, disease and use of medication (Rodríguez et al., 2015).

3.2. Acquisition and development

Development of the gut microbiota progresses in stages from birth with each being marked by a different group of colonising microbes. These microbes may be influenced by genetics, and method of birth (Rodríguez et al., 2015). For example, *Lactobacillus* spp. are dominant colonisers in vaginal deliveries (Thursby & Juge, 2017). As development of gut microbiota progresses, it becomes impacted on by diet and may display a less diverse microbiota with dominance in *Bifidobacterium* spp. as seen in breast fed infants (Dogra et al., 2015). In contrast, a more diverse microbiota which excludes a dominance in *Bifidobacterium* spp. has been seen in formula fed infants (Yu et al., 2013). At 3 to 5 years of age, the microbiota is thought to be complete (Binns, 2013). Composition is relatively constant, yet exclusive to the host as it becomes similar to the microbiota of an adult. For the duration of life, microbial composition will continue to be affected by diet, environment, lifestyle, medicine and health status (Binns, 2013; Dogra et al., 2015; Thursby & Juge, 2017).

3.3. Function

To study the microbial community of the gut *in vitro* models, using human faeces in batch culture fermentations and more complex multiple stage gut models have explored functionality of the microbiome (Williams et al., 2015), to determine the likely impact of an additional dietary ingredient to the microbial community. This has enabled data to be gathered on the potential of different substrates to support members of the microbiota and metabolites within a controlled environment but does not reproduce physiological or anatomical interactions of the host. Animal studies can also provide a controlled model for investigating the function of host gut microbiota interactions in health and disease states (Zhang et al., 2017; Zhao et al., 2020), and can be promising when working with un-culturable bacteria. Human intervention studies involve more variation, in terms of dietary variations, exercise, age and genetics, but are the definitive way to determine the impact of an intervention on the faecal microbial community and on wellbeing. Indeed, host gut interactions affiliated with health or disease can be studied with the use of biomarkers in human intervention studies however, results are not always reproducible due to intrinsic microbial variation among subjects (Qin et al., 2022). Nevertheless, randomised controlled trials demonstrating health benefits in the host together with *in vitro* approaches are needed to confirm a potential prebiotic (Gibson et al., 2017). Observational studies have investigated the role of gut microbiota through comparisons in health and disease. Gut microbiota are thought to be crucial to host development and function as they play a significant role in vitamin synthesis (Rowland et al., 2018), harvesting energy during the metabolism of complex indigestible dietary components through anaerobic fermentation (Rowland et al., 2018), preservation of the gut barrier through epithelial regulation, pathogen deterrence (Assimakopoulos et al., 2018) and regulation of immune function, including inflammatory status (Larsen, 2017). These functions were discussed by Wang et al. (2017), however, understanding of the total functionality of gut microbiota remains incomplete.

4. Gut microbial modulation and health

Alteration or modulation of gut microbes through diet is a way to maintain and achieve homeostasis in the gut microbiota and improve

overall host health. Modulation of gut microbes can occur by enhancing a population of bacteria through habitual consumption of specific dietary components, i.e. prebiotics (Gibson et al., 2017). This may result in increased abundance and diversity of the gut bacterial population.

Poor nutrition, ageing, illness and ingestion of some medications including antibiotics are among the factors which can disrupt homeostasis in the gut, causing an unfavourable shift or dysbiosis amongst beneficial and pathogenic bacteria. Despite this, it is unknown whether similar changes in the composition of the gut microbial community is a causal or consequential circumstance in disease.

4.1. Prebiotics

Efforts to regain gut homeostasis can be made through consumption of substrates termed prebiotics, that are selectively utilised by beneficial bacteria to confer a health benefit on the host (Sanders et al., 2019). Confirmed prebiotics are mainly non-digestible dietary carbohydrates that surpass digestion in the upper gut and enter the large intestine or colon intact, such as galactans and fructans. Galactans are galacto-oligosaccharides (GOS) synthetically produced from lactose, while fructans are fructo-oligosaccharides (FOS) and inulin which are intrinsic to some plant-based foods such as garlic, onions, chicory root, banana, leek and Jerusalem artichokes.

4.2. Function

Upon reaching the colon, dietary prebiotics are selectively used by favourable bacteria such as bifidobacteria and lactobacilli for metabolism (Gibson et al., 2017). During this process, the substrate is fermented and becomes an energy source to enhance and modulate the microbiome (Sanders et al., 2019). Hence, dysbiosis resulting from distress such as poor nutrition, illness, antibiotic use, surgery, lifestyle and ageing, may be improved through consumption of prebiotics as foods or supplements (Gibson et al., 2017).

4.3. Short-chain fatty acids and health

Indigestible carbohydrate fermentation by anaerobic gut bacteria, thought to be positive for health (Rastall & Gibson, 2015), can form gases as well as organic acids as metabolic end products, known as short-chain fatty acids (SCFAs). SCFAs such as butyrate, propionate, and acetate positively influence genetic expression (Canfora et al., 2015), contribute towards a range of metabolic functions and potential health benefits such as reduced obesity markers and the progression of T2D as well as possibly functioning as anticarcinogens (Canfora et al., 2019).

Butyrate is the preferred source of energy for colonic epithelial cells and offers protection against colon cancer through its ability to instigate cell death or apoptosis in cancerous colonic cells (Zeng et al., 2019). Acetate and propionate may play roles in obesity and weight control through the stimulation of satiety hormones and regulation of appetite suppression (Canfora et al., 2019). Acetate and butyrate may inhibit lipolysis and improve insulin sensitivity in obese individuals (Vrieze et al., 2012).

4.3.1. Metabolite formation

Pathways of metabolite formation are not always straightforward. *Bifidobacterium* spp. do not produce butyrate, but certain metabolites formed following substrate fermentation e.g. acetate or lactate, may be utilised by other microorganisms which can yield butyrate (Lockyer & Stanner, 2019; Sanders et al., 2019). For example, Belenguer et al. (2006) showed that *Eubacterium hallii*, a lactate utiliser and butyrate producing strain of bacteria grows poorly on potato starch in monoculture, but when combined with *Bifidobacterium adolescentis* in coculture, it can utilise lactate produced by *B. adolescentis* for butyrate production. Another pathway suggests, butyrate production may also be driven by bacteria unable to degrade inulin type fructans, but are

capable of: consuming acetate, producing butyrate, and utilising partially degraded carbohydrate from bifidobacteria (Belenguer et al., 2006; Rivière et al., 2016). Microbial cross-feeding such as this, adds to the complexity of determining prospective health effects from metabolite formation and may support focussing on the end product instead of the initial substrate for speculating on beneficial health outcomes, particularly through the involvement of polyphenols (Dueñas et al., 2014).

4.4. Mechanisms leading to health benefits

Sanders et al. (2019) discussed several pathways in which a prebiotic may lead to health benefits. These include: production of organic acids during fermentation which lower pH of the intestine, create an unfavourable environment for pathogens, promote satiety through hormonal regulation and improve gut-barrier function by maintaining integrity of the colonic epithelium; increased absorption of calcium which also results from a decrease in luminal pH and helps bone integrity; modulation of the immune system by decreasing T-cell responses which may result in a reduced allergic response; enhancement of bowel function through both microbial growth allowing for faecal bulking and stool softening owed to the prebiotic or carbohydrate ability to attract water to the bowel. Benefits of prebiotic use can extend beyond the gut, but efficacy and prospective benefits are dependent on the gut composition of the host.

5. Phytochemicals, polyphenols, bioavailability and bioactive constituents

Prebiotics were defined by Gibson et al. (2017) as “a substrate that is selectively utilized by host microorganisms conferring a health benefit” (p. 493). It was noted that this broad definition could possibly include polyphenols, once health benefits in the host were shown. At present, substrates e.g. herbs and spices, which demonstrate gut microbial modulation due to their polyphenol content, could exhibit a prebiotic effect.

5.1. Phytochemicals and polyphenols

Polyphenols or phenolic compounds are a group of phytochemicals classed as secondary metabolites found in a variety of plant-derived foods including herbs and spices (Fig. 1). In their fresh and more so in dried forms, some herbs and spices are known to contain more polyphenols than other polyphenolic rich foods (Opara & Chohan, 2014). Dietary polyphenols may contribute to maintenance of gut homeostasis by stimulating the growth of beneficial bacteria such as bifidobacteria and lactobacilli, i.e. acting selectively as prebiotics (Dueñas et al., 2014). They are also known to exhibit antioxidant and antipathogen properties (Duda-Chodak et al., 2015), and are thought to play a role in insulin sensitivity, cell signalling and the synthesis of inflammatory mediators (Fraga et al., 2019). Dietary polyphenols can be categorised into two main groups, flavonoids and non-flavonoids according to their structure. Flavonoids share a basic carbon skeleton structure and include flavan-3-ols, flavonols, isoflavones, flavones, anthocyanins, and flavanones. Non-flavonoids include stilbenes and lignans and phenolic acids grouped as hydroxycinnamic and hydroxybenzoic acids (Fraga et al., 2019). Tannins and coumarins are also classed as dietary polyphenols. Other notable phytochemicals include terpenoids, nitrogen and sulphur-containing compounds.

5.2. Bioavailability and bioactive constituents

Polyphenols are often present in food as glycosides or combinations with sugars and can be transformed into organic compounds by lipids, sugars or organic acids (Rowland et al., 2018). It is estimated that only 5–10 % of dietary polyphenols are absorbed in the small intestine.

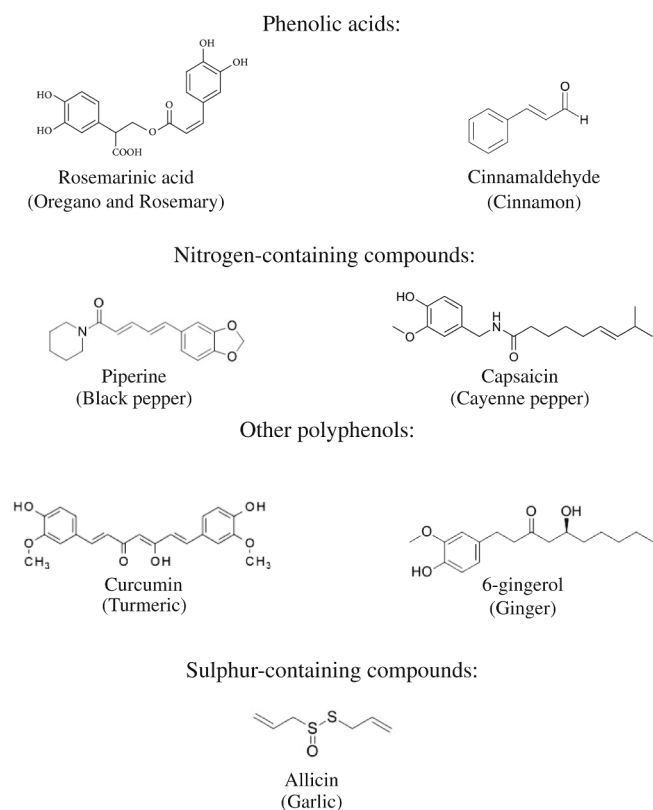


Fig. 1. Common culinary herbs and spices and their major bioactive constituents.

However, the remaining 90–95 % of dietary polyphenols are able to reach the colon for metabolism by gut microbiota (Dueñas et al., 2014), where transformation into various metabolites may affect bioavailability of the polyphenol, depending on host resident microbiota (Duda-Chodak et al., 2015). As benefits associated with dietary polyphenol consumption are believed to arise from bioactive components and their resulting metabolites (Dueñas et al., 2014), it may be more appropriate to look at biotransformation of the herb or spice by the host gut microbiota and bioavailability, or how accessible active compounds in herbs and spices are for absorption, when considering potential health benefits (Duda-Chodak et al., 2015).

5.2.1. Possible mechanism of action

A possible mechanism of action for gut microbial modulation by herbs and spices may be in biotransformation of intrinsic compounds in polyphenols as well as their metabolic pathway. Flavonoids are known to have an impact on gut microbial modulation and may undergo transformation from their unabsorbable parent form to an absorbable metabolite by hydrolysis, ring cleavage or reduction reaction (Stevens & Maier, 2016). Li et al. (2023) showed that (-)-epicatechin, also present in tea is transformed into numerous derivatives in the body over a 36-hour period. The specific metabolite formed, quantity of polyphenol consumed and actions by gut microbiota may play a role in determining a health outcome. For example, it has been shown that high consumption compared to low consumption of cocoa derived flavanols, significantly stimulated growth of *Bifidobacterium* spp. and *Lactobacillus* spp. in a randomised controlled trial (Tzounis et al., 2010). Tannins can also impact gut microbiota as they can convert ellagitannins found in triphala herbal formulations into urolithin metabolites, which may be responsible for some health benefits received from dietary consumption of nuts and berries (Olennikov et al., 2015). Both of these pathways, have potential for improving health as they may lead to homeostasis in gut bacteria (Tomás-Barberán et al., 2017), prevention of inflammation,

oxidative damage (Olennikov et al., 2015) and antimicrobial behaviour against pathogens (Puljula et al., 2020).

As herbs and spices generally have low bioavailability, this may affect the extent of health benefits of that substrate. This is thought to be one reason for inconsistent results in some herb and spice interventions and also why results seen in *in vitro* experiments are not always replicable to *in vivo* studies (Lee, 2013). In addition to this, polyphenol content is not consistent and may vary according to use of the bioactive compound versus its natural form, harvesting methods, storage time, processing and cooking method (Opara & Chohan, 2014). Despite the low bioavailability of herb and spice compounds and variance of polyphenol contents, some studies have demonstrated that herbs and spices may beneficially alter gut microbial populations (Tables 1–3).

6. Studies demonstrating influence of culinary herbs and spices on gut microbial modulation

Studies summarised in Tables 1–3 demonstrate the influence of culinary herbs and spices on gut microbial modulation. Although outcome measures of these studies vary, comparison is based on demonstrations of gut microbiota stimulation with the use of culinary herbs or spices in human, animal and *in vitro* studies, as information is limited on culinary spice and effects on the microbiome.

Lu et al. (2017) showed that six of seven aqueous culinary spice extracts of oregano, ginger, rosemary, cinnamon, black pepper and cayenne pepper were able to promote the growth of *Bifidobacterium* spp. *in vitro*, whereas turmeric was not. The same study demonstrated stimulation of *Lactobacillus* spp. and inhibition of certain *Clostridium* spp. by all seven spices. However, Peterson, Vaughn, et al. (2018) recorded an increase in most *Clostridium* spp. after turmeric and curcumin intervention in a human study.

This could be due to differences in study methods, interactions between herbs as well as between fibre and polyphenols. *In vitro* experimentation provides a more controlled test environment, however interactions of herbs together may also be responsible for the effects seen. In addition to this, *in vitro* work by Lu et al. (2017) reported pure cultures which showed the impact of herbs on individual bacterial species rather than as a group. Peterson, Vaughn, et al. (2018) examined the effects of herbal intervention in humans, which is a less controlled environment where interactions between bioactive components of herbs and gut microbiota were not restricted. Polyphenol and fibre interactions are not completely understood, but it is thought that fermentation of fibre, e.g. from turmeric root, may influence microorganisms which breakdown polyphenols into their useable forms (Edwards et al., 2017). This may also be why Peterson, Vaughn, et al. (2018) saw different host microbial activity with curcumin, which presumably had no interaction with fermentable fibre, than with turmeric intervention.

Lu et al. (2019) also demonstrated positive changes in the abundance of beneficial bacteria following *in vivo* intervention with a 5 g mixed spice capsule on healthy humans. Results from Lu et al. (2019) were consistent with habitual consumption of polyphenol-rich foods by humans i.e. an increase in *Bifidobacterium* and *Lactobacillus* spp. and a decrease in *Clostridium* spp. (Bamberger et al., 2018; Shinohara et al., 2010).

6.1. Inflammation

Prebiotic effects exhibited by these herbs may stimulate other polyphenol associated benefits such as decreased inflammation and reduced risk of certain cancers (Fraga et al., 2019) among others in humans. Moreover quercetin, a flavonol from apple intake, also found in oregano, has been noted to extend preventative effects of cardiovascular disease in individuals at risk of the disease in a randomised controlled clinical trial (Bondonno et al., 2018). Rosmarinic acid in oregano oil in a randomised controlled trial (Zou et al., 2016) and shogaol and 6-

Table 1
Human studies investigating gut microbial modulation with herbs, spices, or polyphenols as intervention.

| Study reference | Objective | Major bioactive ingredients | Participant No. | Subject | Intervention | Control/ placebo | Dose per day | Study design | Duration | Methods of analysis | Microbial outcome |
|--|--|---|-----------------|------------------------------------|--|--|--------------------|-------------------------------------|----------|---|---|
| NCT03066791 Peterson et al., 2018 ⁽³⁸⁾ | To investigate the effects of turmeric and curcumin supplements on human gut microbiota | Curcumin (curcumin C3 complex) from turmeric root (curcuma longa) black pepper extract (piperine alkaloid, BioPerine) | 32 | Healthy subjects - omnivorous diet | Turmeric tablet: 1000 mg turmeric root (<i>Curcuma longa</i>), 1.25 mg black pepper derived piperine alkaloid extract (BioPerine); Curcumin tablet: 1000 mg curcumin (Curcumin C3 Complex), 1.25 mg black pepper (BioPerine) | Placebo tablet: microcrystalline cellulose, dicalcium phosphate, PVPK30, sodium starch glycolate, magnesium stearate, OpaDry orange coating, created to resemble the size, shape and colour of the intervention tablets. | 6 tablets/ 6000 mg | Randomised placebo-controlled pilot | 8 weeks | 16S rDNA sequencing | Change in observed bacterial species: Placebo: decrease 15 %; Turmeric group: increase 7 %; Curcumin group: increase 69 %; Increased bacterial species with intervention: most <i>Clostridium</i> spp., <i>Bacteroides</i> spp., <i>Citrobacter</i> spp., <i>Cronobacter</i> spp., <i>Enterobacter</i> spp., <i>Enterococcus</i> spp., <i>Klebsiella</i> spp., <i>Parabacteroides</i> spp., <i>Pseudomonas</i> spp.; Reduced bacterial species with intervention: some <i>Blautia</i> spp., most <i>Ruminococcus</i> spp. |
| NCT030676803 Lu et al., 2019 ⁽⁴⁰⁾ | To investigate the effect of 5 combined spices (cinnamon, black pepper, ginger, oregano, and cayenne pepper) at culinary doses on the production of short-chain fatty acids (SCFAs) and gut microbiota | Not provided in study | 31 | Healthy subjects - beige diet | 5 g capsule of mixed spice: 1.5 g (30 %) oregano, 1.5 g (30 %) ginger, 1.0 g (20 %) cinnamon, 0.85 g (17 %) black pepper, 0.15 g (3 %) cayenne pepper | 5 g capsule of maltodextrin | 1 capsule | Randomised placebo-controlled pilot | 2 weeks | Gas chromatography, high-performance liquid chromatography (HPLC), 16S rRNA sequencing, | Significant reduction in Firmicutes with intervention (p = 0.033); Increase in Bacteroidetes with placebo (p = 0.097); Change in faecal short chain fatty acids (SCFA): Greater increase in all measured faecal SCFA with intervention than placebo |

Note. The literature search was performed by using electronic databases Web of Science and PubMed through ProQuest Summon. Key words and search terms used to identify relevant articles included (microbiota) AND (culinary herbs) AND (modulation). Google Scholar was used to source articles. Key article reference lists were manually searched for. Article eligibility included peer reviewed articles on the combined topic of *in vitro* or *in vivo* gut microbe modulation with influence of culinary herbs and spices. Both human and animal studies were included for a wider perspective on the topic.

Table 2
Characterisation of animal studies investigating gut microbial modulation with herbs, spices or polyphenols as intervention.

| Study reference | Objective | Major bioactive ingredients | Participant No. | Subject | Intervention | Control/ placebo | Dose per day | Study design | Duration | Methods of analysis | Microbial outcome |
|-----------------------------------|--|--|---------------------|--|--|--|--|---|----------|--|---|
| Wang et al., 2020 ⁽⁴⁶⁾ | To investigate alterations in gut microbiota and metabolic processes resulting from ginger supplementation in normal chow (NCD) and high-fat diet (HFD) fed mice | Fresh ginger rhizomes (<i>Zingiber officinalis</i> Roscoe) and high-Roscoe) | 48 (4 groups of 12) | C57BL/6J male mice at 5 and 8 weeks of age | Orally fed mice: fresh ginger rhizomes (<i>Zingiber officinalis</i> Roscoe); Faecal microbiota recipients: microbiota from HFD and HFD-G donors | Orally fed mice: saline solution; Faecal microbiota recipients: not applicable | Orally fed mice: 500 mg/kg body weight | mouse model; faecal microbiota transplant (FMT) | 16 weeks | 16s rRNA gene sequencing, gas chromatography, FMT, | Oral high-fat diet with ginger supplementation (HFD-G); Increase in <i>Bifidobacterium</i> genus, <i>Alloprevotella</i> , <i>Allobaculum</i> , faecal SCFA concentrations; HFD-G gut microbiota recipients: Similar anti-obesity and gut modulatory effects visible after FMT as seen in orally fed HFD-G mice. |

Note. The literature search was performed by using electronic databases Web of Science and PubMed through ProQuest Summon. Key words and search terms used to identify relevant articles included (microbiota) AND (culinary herbs) AND (modulation). Google Scholar was used to source articles. Key article reference lists were manually searched for. Article eligibility included peer reviewed articles on the combined topic of *in vitro* or *in vivo* gut microbe modulation with influence of culinary herbs and spices. Both human and animal studies were included for a wider perspective on the topic.

gingerol in ginger extract in an animal study (Kim et al., 2017) have been shown to decrease inflammatory responses associated with impairment of the gut-barrier function, as seen in Inflammatory Bowel Disease.

Turmeric and curcumin tablets were better able to modulate gut microbes of healthy humans in comparison to placebo by Peterson, Vaughn, et al. (2018). The authors suggested alterations in bacteria as seen with intervention (Table 1), were thought to be due to a prebiotic effect of the turmeric and a similar effect of curcumin. SCFAs were not measured here, however Peterson et al. (2019) recorded an increase in butyrate producing microbes with turmeric in *in vitro* experimentation. Butyrate has anti-inflammatory properties in humans and may protect against colon cancer (Zhang et al., 2017), as it helps to reduce systemic inflammation through upkeep of the gut-barrier function. This may explain the benefits of curcumin as seen with cell line experimentation in Wang et al. (2017), and why curcumin may decrease risk of developing metabolic diseases associated with chronic inflammation.

6.2. Obesity

While a higher Firmicutes to Bacteroidetes ratio has been associated with obesity, Lu et al. (2019) saw a decrease in Firmicutes and increase in Bacteroidetes following spice intervention in humans, which was also seen by Bamberger et al. (2018). SCFA production seen following stimulation of beneficial bacteria, was thought to possibly support development of obesity due to the host's ability to harvest extra energy during this process (Canfora et al., 2015), however Wang et al. (2020) showed that ginger root consumption could increase *Bifidobacterium* spp., enhance faecal SCFA production as well as invoke anti-obesity effects in obese mice. Consistent with this, acetic acid, a product of *Bifidobacterium* spp. known to function as an appetite suppressant (Ejtahed et al., 2019), was found to be most abundant in the faeces of mice following ginger supplementation.

6.3. Culinary herb and spice possible provision of health through gut microbial modulation

Consumption of certain culinary herbs and spices may help to increase beneficial bacteria available for fermentation and metabolite production. Dietary carbohydrate components in the root structure of some herbs and spices such as turmeric and ginger (McCance, 2015) may account for their contributions toward health. These components may be a selective energy source for certain beneficial gut microbiota and aid in increasing numbers. As detailed above, SCFAs, which are important for the human body are produced through fermentation of carbohydrates.

6.4. Inconsistencies and limitations

Lu et al. (2019) and Peterson, Vaughn, et al. (2018), were pilot trials, and although positive results were reported, there were also inconsistencies in results. As such, results among subjects were reported as being highly variable in human studies. This may be due to differences between participant gut microbiota which may affect absorption of bioactive compounds, (Rowland et al., 2018; Sanders et al., 2019), differences in diet between study groups (e.g. omnivorous and beige diet), small sample size or duration and study design, but it supports the need for additional work of a larger magnitude to be completed. All studies, apart from the animal study by Wang et al. (2020), added black pepper or piperine extract, to the intervention which is known to increase bioavailability of polyphenols, hence it may be difficult to decipher effects of the individual polyphenols. Although herbal supplements are easier to standardise, inconsistencies in, and absence of, results in studies using extracts of polyphenols has been recognised (Ejtahed et al., 2019; Peterson, Vaughn, et al., 2018). Following this, it is thought that consumption of whole foods may be more effective. Lu et al. (2019) and

Table 3
Characterisation of *in vitro* studies investigating gut microbial modulation with herbs, spices or polyphenols as intervention.

| Study reference | Objective | Major bioactive ingredients | Intervention | Control | Duration | Methods of analysis | Microbial outcome |
|---------------------------------------|---|--|---|-----------------------------|------------------|---|---|
| Lu et al., 2017 ⁽³⁷⁾ | To examine the prebiotic effect, chemical constituents, antioxidant activity and <i>in vitro</i> microbial modulatory effect of 7 spice extracts on <i>Bifidobacterium</i> spp. and <i>Lactobacillus</i> spp. | Curcumin, demethoxycurcumin, bisdemethoxycurcumin, luteolin-3-glucuronide, lithospermic acid, rosmarinic acid, p-coumaric acid, vanillin, 6-gingerol, cinnamaldehyde, cinnamic acid, apigenin, luteolin, ferulic acid, dihydrocapsaicin, capsaicin, piperine | Aqueous extracts of black pepper, cayenne pepper, cinnamon, ginger, Mediterranean oregano, rosemary and turmeric at 9.0, 4.50, 2.25, 1.13, 0.56, 0.14 and 0.07 mg/mL concentrations | <i>Bricella</i> agar plates | 48 h at 37 °C | culture | Increase in selected <i>Bifidobacterium</i> spp. with: all tested spices apart from turmeric; Increase in selected <i>Lactobacillus</i> spp. with: all tested spices apart from turmeric; High, modest, minimal/ no decrease in selected bacteria species/ tested spice: High- <i>Ruminococcus</i> spp. - all tested spices; Modest- <i>Fusobacterium</i> spp.: cinnamon, oregano, rosemary; Modest - C. difficile; cinnamon, rosemary, turmeric; Minimal/ none: <i>Bacteroides</i> , <i>Finnegoldia</i> , <i>E. coli</i> , <i>Salmonella</i> , <i>Staphylococcus</i> : all tested spices |
| Peterson et al., 2019 ⁽⁴⁷⁾ | To investigate the modulatory effect of turmeric, ginger, long pepper, and black pepper. | | 1 %: turmeric (n = 4), ginger (n = 4), long pepper (n = 5) or black pepper (n = 4) in chemically defined medium | 1 % glucose (n = 6) | 72–96 h at 37 °C | Anaerobic faecal cultivation - Hungate tubes, 16s rRNA sequencing | Turmeric enhanced butyrate producing microbes. |

Note. The literature search was performed by using electronic databases Web of Science and PubMed through ProQuest Summon. Key words and search terms used to identify relevant articles included (microbiota) AND (culinary herbs) AND (modulation). Google Scholar was used to source articles. Key article reference lists were manually searched for. Article eligibility included peer reviewed articles on the combined topic of *in vitro* or *in vivo* gut microbe modulation with influence of culinary herbs and spices. Both human and animal studies were included for a wider perspective on the topic.

Wang et al. (2020) of the *in vivo* studies as well as the *in vitro* study by Peterson et al. (2019) obtained positive results using whole herbs and spices rather than extract, which may be encouraging for food-based dietary guidelines. Also, while the benefits of culinary herbs and spices on health have been explored, there have been few studies investigating their role in the gut microbiome. It should also be considered that knowledge of the interactions of herbs and spices on the gut microbiota is incomplete and needs further research.

7. Conclusion

The studies featured in this paper show evidence of gut microbial modulation with whole culinary herbs and spices as well as extracts. Literature revealed that culinary herbs and spices have been recognised for their ability to exert a potential prebiotic effect, polyphenol content and health benefits they may bestow in connection to these. It has been noted that bioactive constituents of herbs and spices outlined in these studies may play important roles in afflictions and diseases associated with chronic inflammation such as gut-barrier function impairment and obesity. Studies have demonstrated that some bioactive constituents of polyphenols have been able to extend benefits regardless of low bioavailability and modulate gut microbes as well. Inconsistencies in results after herb and spice intervention together with incomplete knowledge of their impact on gut microbiota serve as a basis for additional research. More investigation on herb and spice impact on gut microbes, may help to confirm potential health benefits following ingestion and warrant their inclusion in dietary guidelines for promotion of gut and overall host health, particularly *in vivo*. Analyses of culinary herbs and spices beyond those discussed here would contribute to current knowledge of effects of herb and spice consumption on the gut microbiota and their potential health benefits.

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Authorship

VR and GEW provided research and editorial support. GRG provided structural-planning, research and editorial support. SMD wrote, revised and edited the manuscript. All authors reviewed and revised multiple versions of the manuscript and approved the final version for print.

CRedit authorship contribution statement

Sasha M. Dahl: Investigation, Conceptualization, Visualization, Writing – original draft, Writing – review & editing. **Vivien Rolfe:** Resources, Writing – review & editing. **Gemma E. Walton:** Writing – review & editing. **Glenn R. Gibson:** Supervision, Writing – review & editing.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: VR works for Pukka Herbs Ltd who manufacture herbal teas and supplements. SMD is in receipt of a PhD studentship funded by PUKKA Herbs Ltd who manufacture herbal teas and supplements. GEW has no financial interests or personal relationships which may be considered as potential competing interests. GRG has no financial interests or personal relationships which may be considered as potential competing interests.

Data availability

No data was used for the research described in the article.

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