LIVE WEBINAR

Plant Power:

Polyphenols for Inflammation and Enhanced Gut Health

Tuesday 30 July 2024 | 7PM AEST

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Meet your speakers

Dr Brad Leech
Nutritionist and Lead Clinical Educator

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Nutrition Specialist and Food Science Lead

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Nutritionist and Head of Co-Biome™ Healthcare

All participants have been muted

There is an optional 15 minutes for questions at the end

Add your questions in the chat to have them answered live

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Disclaimers

- The information provided in this webinar is for the use of qualified healthcare professionals.
- The information contained in this webinar is in no way to be taken as prescriptive or to replace a healthcare professional's duty of care and personalised care practices.
- The clinical opinions and patient case studies shared by presenters are solely those of the individual presenters and do not necessarily represent the view of Co-Biome.

Learning objectives

1. Understand how polyphenols can impact gastrointestinal health, the gut microbiome and common clinical conditions
2. Learn how gastrointestinal and gut microbiome testing can highlight intestinal inflammation and systemic inflammation and when to consider clinically
3. Understand the role of dietary and supplemental polyphenols in managing intestinal inflammation and systemic inflammation
4. Discover considerations and best practices for prescribing polyphenols
5. Review clinical scenarios where polyphenols can support patient outcomes

PART 1

Hannah Naismith

Polyphenols and their mechanisms of action

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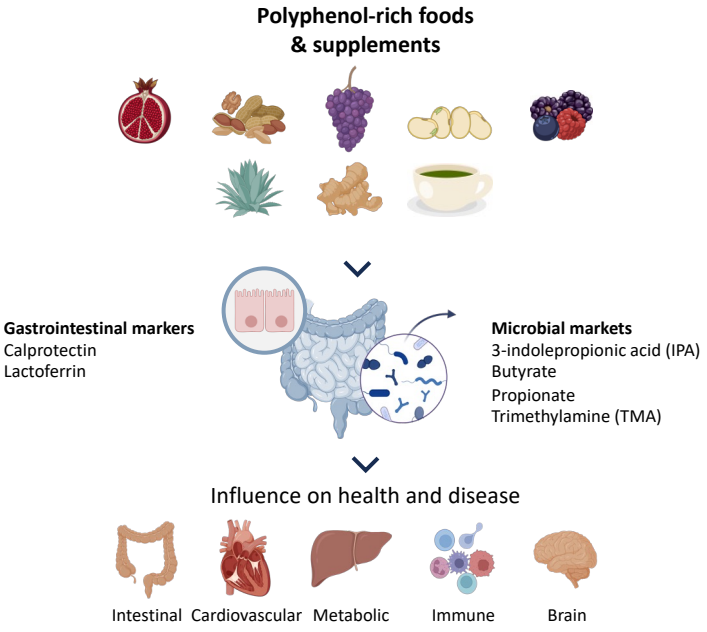

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What are polyphenols?

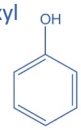
- Grouped based on their structural characteristics (flavonoids, stilbenes, phenolic acids, etc)

Found in fruits, vegetables, tea, coffee, chocolate, whole grains, nuts, seeds, spices, and more!

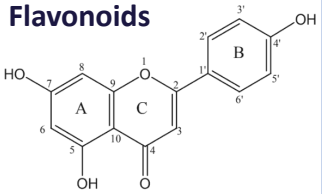
They can best be explained by their structure

"Polyphenols" are compounds containing more than one hydroxyl group (-OH) attached to one or more benzene rings[1].

"**Phenols**" contain an aromatic benzene ring bonded to a hydroxyl group.



Flavonoids



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1) Vermerris and Nicholson 2008

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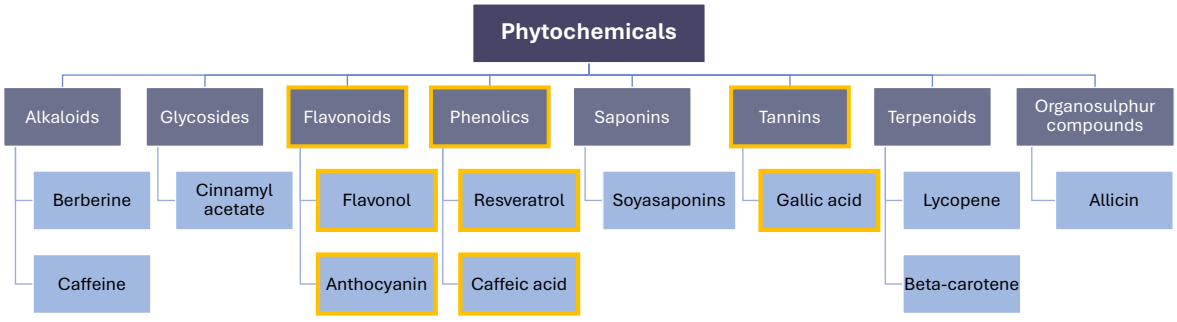
Polyphenols are plant phytochemicals BUT not all plant phytochemicals are polyphenols

Phytochemicals: bioactive compounds produced by plants

Note: this diagram does not list all potential phytochemicals!



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Doughari, 2012

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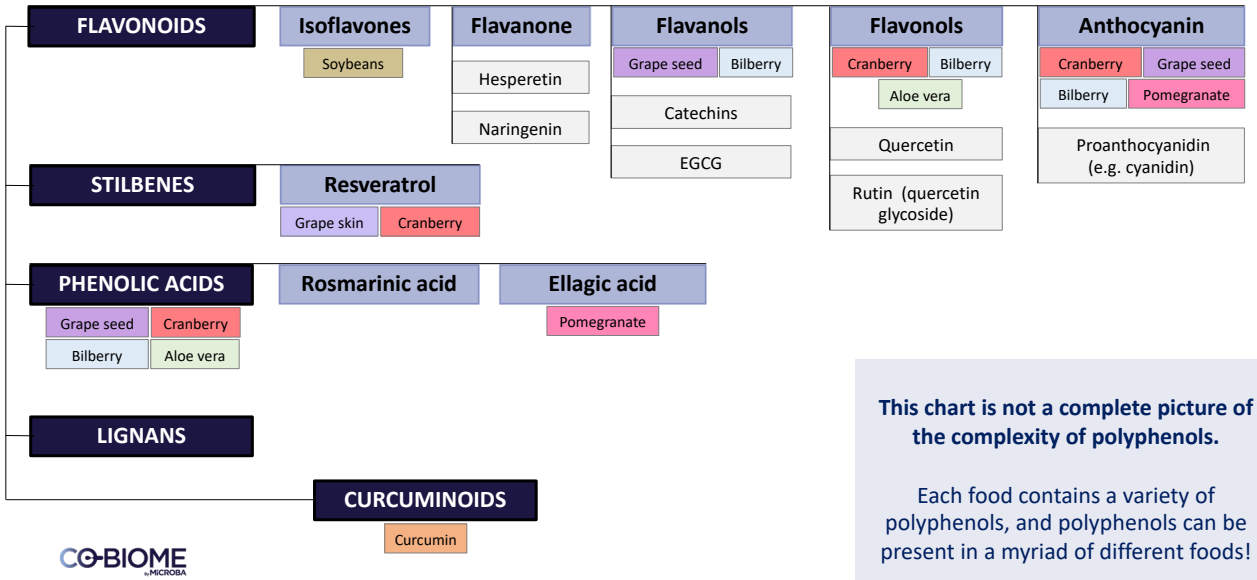
Types of polyphenols



This chart is not a complete picture of the complexity of polyphenols.

Each food contains a variety of polyphenols, and polyphenols can be present in a myriad of different foods!

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Richest sources of polyphenols

Flavonoids

- **Isoflavones**: soybeans
- **Flavones**: parsley and celery
- **Flavanones**:
  - Naringenin: grapefruit
  - Hesperetin: oranges
  - Eriodictyol: lemons
- **Flavanols**:
  - Primary polyphenol in apples
  - Catechins: primarily green tea and cocoa. Also, apricots and cherries.
- **Flavonols**: onions, curly kale, leeks, broccoli, and blueberries
- **Anthocyanin**: black elderberries, blackberries

Stilbenes

Resveratrol: small amount in grapes. Generally low quantities in foods.

Phenolic acids

Ellagic acid: Kakadu plum, walnuts, raspberries

Lignans

Flaxseeds

Gharras, 2009; Rothwell, 2013

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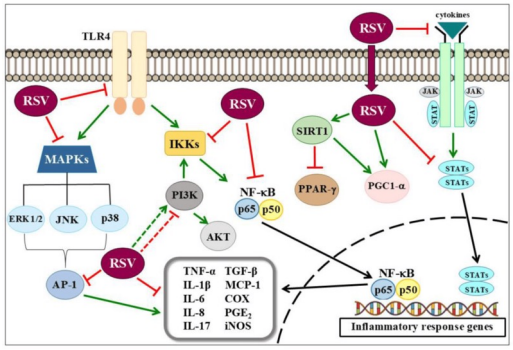
Mechanisms of action: anti-inflammatory

***Human** clinical evidence for polyphenol anti-inflammatory properties is limited – based on very small studies with very high heterogeneity among studies, and small effect sizes. Larger, well-designed studies are needed to confirm the results listed below.*

It is hypothesised many polyphenols suppress inflammation by blocking the Nf-kβ inflammatory pathway

Results from human RCTs on the action of polyphenols on serum inflammatory markers.

Polyphenol	Pro-inflammatory	Anti-inflammatory
Curcumin[1,2]	↓ CRP, TNF-α, IL-6, IL-8, MCP-1	↑ IL-10
Ellagic acid[3-5]	↓ CRP, TNF-α, IL-6, MCP-1	
Pomegranate[6] (juice)	↓ CRP, IL-6, No diff: TNF-α	
Resveratrol[7]	↓ CRP, TNF-α, No diff: IL-6	
EGCG[8,9]	↓TNF-α, No diff: CRP, IL-6	
Quercetin	↓ CRP, No diff: TNF-α, IL-6	



Hypothesised action of resveratrol on various immune targets based on in-vitro and animal studies. *Figure from: De Sá Coutinho et al 2018, doi: 10.3390/ijms19061812*

[1]Naghsh et al 2023; [2]Ferguson et al 2021; [3]Ghadimi et al 2020; [4]Kazemi et al 2021; [5]Rafraf et al 2024; [6]Bahari et al 2023; [7]Molani-Gol and Rafraf 2024; [8]Haghighatdoost and Hariri 2019; [9]Souza et al 2024

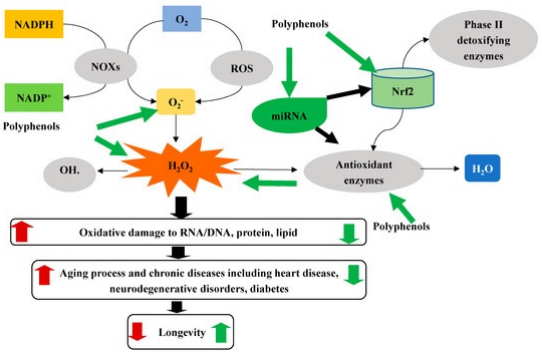
Mechanisms of action: antioxidant

***Human** clinical evidence for polyphenol antioxidant properties is limited – based on very small studies with very high heterogeneity among studies, and small effect sizes. Larger, well-designed studies are needed to confirm the results listed below.*

Results from human RCTs on the action of polyphenols on serum antioxidant markers.

Polyphenol	Antioxidant measure	Oxidative stress measure
Curcumin[1,2]	↑ TAC, SOD	↓ MDA
Ellagic acid[3-5]	↑ TAC; No diff: SOD	↓ MDA
Pomegranate[6] (juice)	↑ TAC; No diff: SOD	↓ MDA
Resveratrol[7]	↑ TAC; No diff: SOD	No diff: MDA
EGCG[8,9]	↑ TAC	Conflicting: MDA
Quercetin[10]	No diff: TAC	No diff: MDA

TAC = total antioxidant capacity
SOD = superoxide dismutase
MDA = malondialdehyde



Hypothesised polyphenol antioxidant mechanisms. *Figure from: Luo et al 2021, doi: 10.3390/antiox10020283*

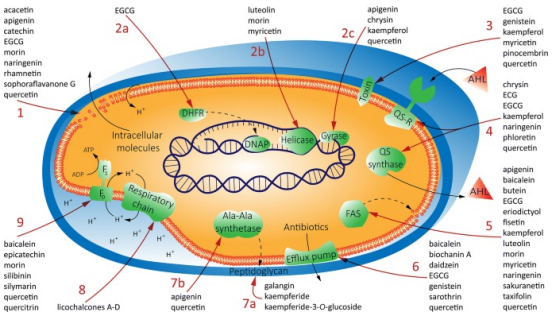
[1]Kavyani et al 2024; [2]Dehzad et al 2023; [3]Hosseini et al 2024; [4]Mirzaie et al 2022; [5]Kazemi et al 2021; [6]Bahari et al 2023; [7]Koushki et al 2020; [8]Asbaghi et al 2023; [9]Rasaei et al 2021; [10]Vasmehjani et al 2021

Mechanisms of action: antimicrobial

Human *clinical evidence for polyphenol antioxidant properties is limited – based on very small studies with very high heterogeneity among studies. Larger, well-designed studies are needed to confirm the results listed below.*

Examples of anti-microbial activity of polyphenols

Polyphenol	In-vitro	Human
Curcumin[1-4]	↓**Pathogens/pathobionts:** *Bacillus subtilis, Clostridioides difficile, Enterococcus faecalis, Escherichia coli, Helicobacter pylori, Klebsiella pneumoniae, Porphyromonas gingivalis, Proteus mirabilis, Pseudomonas aeruginosa, Salmonella typhi, Staphylococcus aureus, Streptococcus mutans* ↓***Commensal:*** *Bifidobacterium pseudocatenulatum, Lactobacillus acidophilus, Lactobacillus gasseri*	Inconclusive
Pomegranate[6-8] (juice)	↓**Pathogens/pathobionts:** *Clostridium perfringens, Clostridium ramosum, Staphylococcus aureus* ↓**Commensal:** *Bifidobacterium bifidum, Lactobacillus acidophilus, Lactobacillus pentosus, Lactobacillus rhamnosus*	↑*Faecalibacterium spp.*; Other taxa inconclusive/ conflicting
Resveratrol[9-11]	↓**Pathogens/pathobionts:** *Bacillus cereus, Escherichia coli, Enterobacter aerogenes, Fusobacterium nucleatum, Klebsiella pneumoniae, Pseudomonas aeruginosa, Providencia stuartii, Salmonella typhimurium, Staphylococcus aureus*	Inconclusive
EGCG[12-18]	↓**Pathogens/pathobionts:** *Clostridioides difficile, Clostridium paraputrificum, Clostridium perfringens, Escherichia coli, Pseudomonas aeruginosa, Vibrio cholerae*	↑*Bifidobacterium spp., Coprococcus spp.* ↓*Fusobacterium spp.*
Quercetin[19-22]	↓**Pathogens/pathobionts:** *Escherichia coli, Porphyromonas gingivalis, Proteus vulgaris, Pseudomonas aeruginosa, Salmonella enterica, Staphylococcus aureus, Streptococcus mutans, Streptococcus sanguis* **Commensal:** *Bacteroides galacturonicus, Lactobacillus acidophilus, Ruminococcus gauvreauii*	Inconclusive



Hypothesised mechanisms used by polyphenols to inhibit bacterial growth. *Figure from: Górniak et al 2019, doi: 10.1007/s11101-018-9591-z*

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[1]Mody et al 2020; [2]Zheng et al 2020; [3]Gunes et al 2016; [4]Jazayeri et al 2009; [5]Hussain et al 2022; [6]Bialonska et al 2009; [7]Sivamani et al 2024; [8]González-Sarrías et al. 2018; [9]Seukep et al 2016; [10]Promgool et al 2014; [11]He et al 2016; [12]Siriphap et al 2022; [13]Jeon et al 2014; [15]Ahn et al 1990; [16]Morishima et al 2023; [17]Yuan et al 2018; [18]Jin et al 2012; [19]Jaisinghani 2017; [20]Shu et al 2011; [21]Wang et al 2018; [22]Duda-Chodak 2012.

PART 2

Hannah Naismith

How gastrointestinal and gut microbiome testing can inform polyphenol prescription

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Gastrointestinal and gut microbiome testing for polyphenol prescription in **intestinal inflammation**

Diego, 32
Ulcerative colitis

Persistent diarrhoea
Abdominal pain
Weight loss

Candice, 23
Food allergy

Frequent loose stools
Abdominal cramps
Nausea

Peter, 56
Pathogenic infection

Watery diarrhoea
Abdominal pain
Loss of appetite

Evelyn, 47
Ischaemic colitis

Abdominal pain
Urgency to move bowels
Diarrhoea

Diagnostic gastrointestinal markers to consider: **Calprotectin** + **Lactoferrin**
Microbial markers to consider: **3-indolepropionic acid (IPA)**

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Gut microbiome testing for polyphenol prescription in **systemic inflammation**

Adam, 45
Cardiovascular disease

High cholesterol
Fatigue
Overweight

Cathy, 59
Metabolic syndrome

Weight gain
Fatigue
Poor appetite

Nadya, 36
Rheumatoid arthritis

Fatigue
Skin rashes
Digestive discomfort

Mia, 41
Depression

Negative thoughts
Trouble focusing
Mood swings

Microbial markers to consider: **Trimethylamine (TMA)** + **3-indolepropionic acid (IPA)**

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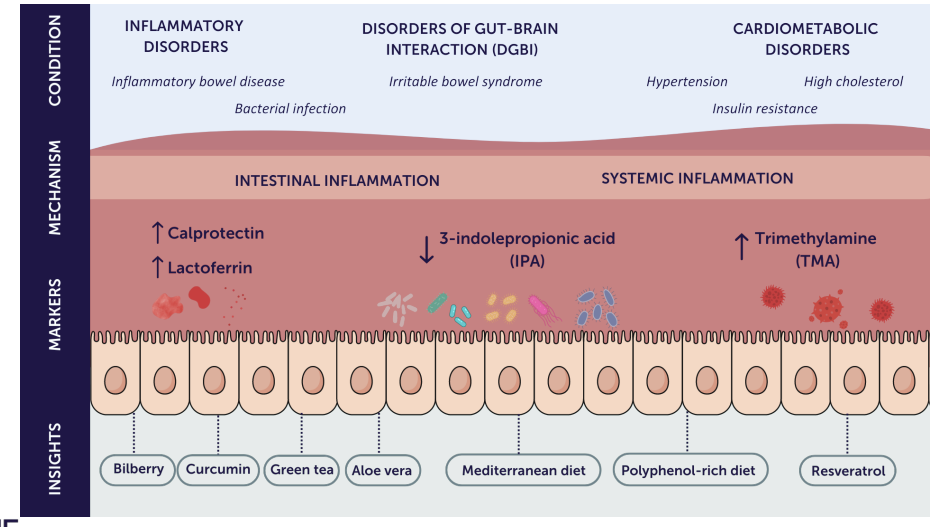
Specific polyphenols can impact systemic inflammation and/or intestinal inflammation through the management of specific gastrointestinal health and gut microbiome markers



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Gastrointestinal and gut microbiome markers that polyphenols have been shown to shift

		MetaXplore™	MetaXplore™ GI	MetaXplore™ GI Plus
Intestinal inflammation	Calprotectin	✗	✓	✓
	Lactoferrin	✗	✓	✓
	3-indolpropioic acid (IPA)	✓	✓	✓
Systemic inflammation	Trimethylamine (TMA)	✓	✓	✓

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Intestinal inflammation and the gut microbiome

Immune activation occurring within the gastrointestinal system

Microbial markers can assess the potential for the microbiome to prevent or exacerbate intestinal inflammation

Gastrointestinal health markers measure the level of active intestinal inflammation

Conditions associated with intestinal inflammation:

- Inflammatory bowel disease
  - Ulcerative colitis
  - Crohn's disease
- Pathogenic infection
- Ischaemic colitis
- Food allergy

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Clinical application of calprotectin

Clinical relevance

Calprotectin is a marker of **intestinal inflammation.**

High levels of calprotectin may be seen in patients with inflammatory bowel disease (IBD), bacterial diarrhoea, *Clostridium difficile* toxin infection and non-steroidal anti-inflammatory drug (NSAID) use.

Referral to a medical specialist is recommended, if calprotectin levels are high.

Clinical considerations – elevated calprotectin levels

- **Curcumin** to reduce intestinal inflammation in patients with ulcerative colitis
- **Green tea** to reduce intestinal inflammation
- **Aloe vera** to reduce intestinal inflammation
- Omega-3 fatty acid to reduce intestinal inflammation in patients with ulcerative colitis
- Inulin to reduce faecal calprotectin

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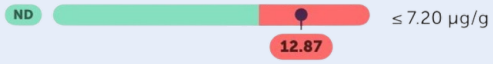
Clinical application of lactoferrin



Clinical relevance

Lactoferrin is a marker of **intestinal inflammation.**

High levels of lactoferrin may be seen in patients with inflammatory bowel disease (IBD), *Clostridium difficile* toxin infection and bacterial infection.

Referral to a medical specialist is recommended, if lactoferrin levels are high.

Clinical considerations – elevated lactoferrin levels

- **Curcumin** to reduce intestinal inflammation in patients with ulcerative colitis
- **Green tea** to reduce intestinal inflammation
- **Aloe vera** to reduce intestinal inflammation
- Omega-3 fatty acid to reduce intestinal inflammation in patients with ulcerative colitis

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Polyphenols as an adjunct treatment in the management of intestinal inflammation

Bilberry	Curcumin	EGCG	Aloe vera
Biedermann, 2013: 160g/day bilberry preparation corresponding to 95g dry weight (600g fresh fruit, equivalent to 840mg/day anthocyanins) for 6 weeks.	**Banerjee, 2021**: 50mg bio-enhanced curcumin twice daily for 6 weeks. **Lang, 2015:** 1.5g twice daily of capsules containing 95% pure curcumin for 1 month. **Hanai, 2006**: 1g curcumin twice daily for 6 months.	**Zeng, 2022:** 1g/day green tea extract for 28 days. **Dryden, 2013:** 400mg or 800mg Polyphenon E per day in split doses of 200mg for 56 days. *Consideration: Polyphenon E has highest incidence of adverse effects.*	**Langmead, 2004:** 100 mL aloe vera gel, twice per day for 4 weeks.

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Systemic inflammation and the gut microbiome

Systemic inflammation can be detected via elevated markers of immune activation within the blood

The microbial markers can assess the potential for the microbiome to prevent or exacerbate systemic inflammation

Conditions associated with systemic inflammation:

- Autoimmune disease
- Cardiovascular disease
- Metabolic disease
- Mental health disorders

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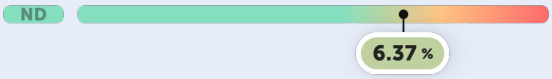
Clinical Application of TMA



Clinical Relevance

Trimethylamine (TMA) is an inflammatory compound produced by some gut bacteria when they break down choline and carnitine.

High levels of TMA may be associated with **systemic inflammation**.

Clinical Considerations - High TMA Production

- Limit carnitine intake (e.g. kangaroo and beef)[1]
- Resveratrol supplement[2]
- Choosing lipid-soluble supplements[3]
- Increasing cruciferous vegetable intake[4]

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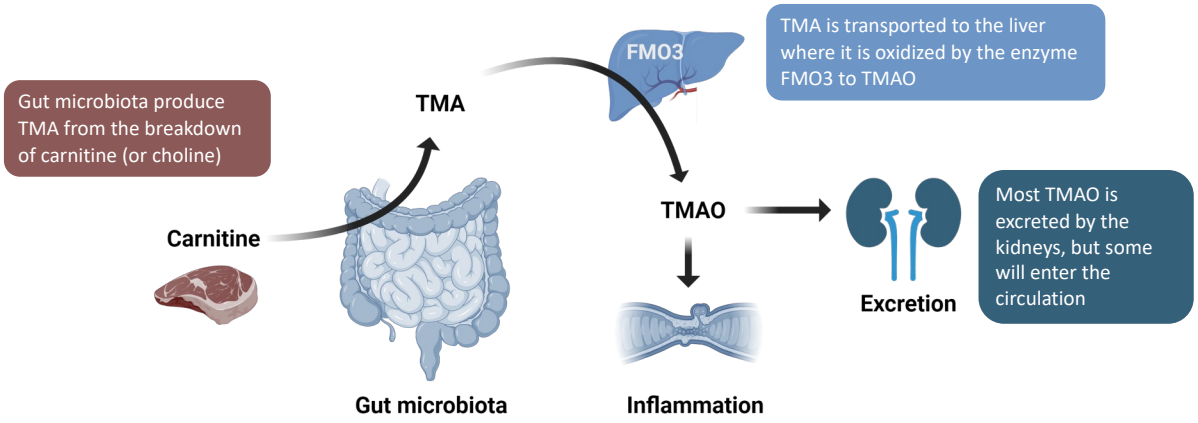
[1]Wang, 2019; Krishnan, 2022; [2]Annunziata, 2019; [3]Wilcox, 2021; Cho, 2020; Taesuwan, 2021; [4]Cashman, 1999

Trimethylamine → Trimethylamine N-oxide



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Resveratrol supplementation to reduce plasma TMAO [B]

One study in healthy subjects[1] and one study in overweight/obese subjects[2]

- **Intervention:** 300mg resveratrol capsules, twice daily for 4 weeks
- **Finding:** significantly reduced plasma TMAO levels

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[1]Annunziata, 2019a; [2]Annunziata, 2019b

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Clinical application of IPA

Clinical Relevance

3-indolepropionic acid (IPA) is a beneficial substance produced by some gut bacteria when they break down the amino acid tryptophan.

Low levels of IPA may be associated with **intestinal and systemic inflammation** and **impaired intestinal barrier integrity**.

Clinical Considerations – Low IPA Production

- Polyphenol-rich diet[1]
- Mediterranean diet[2]
- Foods rich in ellagic acid (e.g., Kakadu plum, walnuts, raspberries and pecans)[3]

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[1]Peron, 2022 ; [2]Zhu, 2020; Lécuyer, 2020; [3]Yang, 2020

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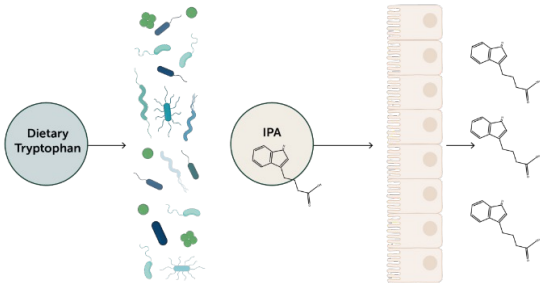
IPA as a marker for inflammation

3-indolpropioic acid (IPA) is a beneficial substance produced by some gut bacteria when they breakdown the amino acid tryptophan.

- Higher levels of plasma IPA are associated with lower systemic inflammation as shown by a decreased hsCRP
- Decreased plasma IPA levels are associated with an increased body mass index.
- Studies in human cell lines and animals suggest IPA reduces intestinal inflammation by inhibiting immune receptor TLR4 activation, and by promoting anti-inflammatory T regulatory cell development.



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Polyphenol-rich diet to increase plasma IPA [C]

8-week intervention with diet consisting of 3 serves per day of polyphenol-rich foods (average of 724 mg/day polyphenols) significantly increased plasma IPA levels[1]

- 10g dark chocolate
- 2g cocoa powder
- 150g apple
- 100g apple purée
- 120g berry purée
- 120g blueberry
- 200ml green tea
- 200ml blood orange juice
- 125ml pomegranate juice

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[1]Peron, 2022

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PART 3

Hannah Naismith

Polyphenols in the diet vs supplements

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Mediterranean diet (MedDiet) is rich in polyphenols

The MedDiet one of the more defined diets that is rich in polyphenols.

Classified by a high intake of fruit, vegetables, legumes, nuts, seeds, omega-3 fish, olive oil, and reduced animal products and processed foods.

High MedDiet adherence is associated with higher intakes of polyphenols such as flavonoids and lignans[1].

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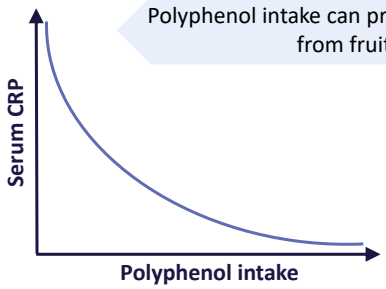
[1]Pounis, 2015

Polyphenol-rich diets may reduce systemic inflammation

Several studies with large sample sizes have found negative correlations between total daily polyphenol intake and serum CRP levels [1,2,3,4]

An inverse correlation has been shown to remain even when controlling for fruit and vegetable intake[4]

Polyphenol intake can predict serum CRP independent from fruits and vegetable consumption



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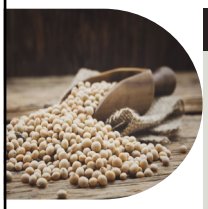
[1]Dryer-Beers, 2024; [2]Pounis, 2016; [3]Harms, 2019; [4]Chun, 2008

Menopausal symptoms reduce with isoflavones from both diet and supplements



Dietary soy intake

Prospective cohort studies have shown:

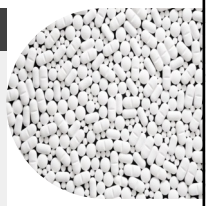
- Frequent consumption of soy products (includes soybeans, tempeh and tofu) but not soy milk was associated with lower likelihood of reporting hot flashes and/or night sweats[1]
- Hot flashes were significantly inversely associated with consumption of soy products in terms of both total amount of soy and isoflavone intake[2]

Isoflavone supplementation

Meta-analyses have shown:

Reduced frequency and severity of hot flashes compared to placebo. Reduced scores of menopausal symptom questionnaires[3,4]

Supplements providing >18.8mg genistein (a type of isoflavone) for at least 12 weeks were more than twice as effective at reducing hot flash frequency than lower genistein supplements



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[1]Dunnerman, 2019; [2]Nagata, 2001; [3]Oh, 2024; [4]Taku, 2012

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Green tea beverage compared to supplements

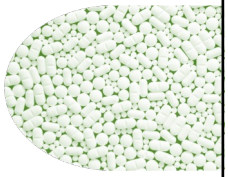
The effect of a green tea intervention may depend on the form of green tea administered

Lipid profile

Total cholesterol and LDL-C reduced in interventions using green tea beverage and those using green tea extracts[1]

Glycemic control

Green tea only lowered fasting blood glucose concentrations in subjects prescribed green tea extract, not green tea beverage[2]



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[1]Xu, 2020a; [2]Xu, 2020b

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Pomegranate juice compared to supplements

Fresh juice has a greater effect than extracts at reducing systemic inflammation and blood pressure. The opposite is true for improving lipid profile.

Measure	Pomegranate form	Impact
Systemic inflammation	Fresh juice	May reduce serum IL-6 at ≤ 200mL/day and serum CRP at > 200mL/day
	Extract	May reduce serum CRP *No effect on IL-6*
Lipid profile	Fresh juice	May increase serum HDL-C *No effect on TC, LDL-C or TG*
	Extract	May reduce serum TG at any dose. May reduce serum LDL-C at < 1000mg/d. May reduce serum TC and increase HDL-C at ≥ 1000mg/d
Blood pressure	Fresh juice	May reduce systolic blood pressure at any dose, but especially at ≤ 200mL/day *May reduce diastolic blood pressure but more research needed to confirm dose*
	Extract	May reduce systolic blood pressure at ≥ 1000mg/day *No effect on diastolic blood pressure*

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Bahari, 2023a; Bahari, 2023b; Bahari, 2024

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Polyphenol	Health effect	Dosage	Duration	Reference
Resveratrol **Max dose:** **150 - 450mg/day** *EFSA, 2016; Edwards, 2011*	May reduce CRP and TNF-a	Not dose-dependent	Not duration-dependent	Molani-Gol and Rafraf 2024
	May reduce blood pressure	300mg/day; 600-1000 mg/day	At least 3 months; 2-3 months	Batista-Jorge, 2024
	May reduce LDL-C	≥ 500mg/day	≥ 12 weeks	Cao, 2022
	May reduce total cholesterol	Not dose-dependent	Not duration-dependent	Cao, 2022
	May reduce plasma TMA/TMAO	2 x 300mg	28 days to 8 weeks	Annunziata, 2019a; Annunziata, 2019b
Ellagic acid **Max dose:** **2 x 500mg/day** (limited number of studies. 2 x 500mg/day has been used safely for 12 weeks with no adverse effects) *Hidalgo-Lozada, 2022*	May reduce LDL-C	≥ 180mg/day	Not duration-dependent	Wang, 2024
	May reduce total triglycerides	≥ 180mg/day	≥ 8 weeks	Wang, 2024
	May reduce fasting blood glucose	≥ 180mg/day	≥ 8 weeks	Wang, 2024
	May reduce insulin	Not dose-dependent	≥ 8 weeks	Wang, 2024
	May reduce HOMA-IR	Not dose-dependent	Not duration-dependent	Wang, 2024
	May reduce CRP	180mg/day; 200mg/day; 2 x 450mg/day	60 days; 8 weeks; 8 weeks	Ghadimi, 2020; Kazemi, 2021; Rafraf, 2024
	May reduce TNF-a	180mg/day; 200mg/day	60 days; 8 weeks	Ghadimi, 2020; Kazemi, 2021

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Polyphenol	Health effect	Dosage	Duration	Reference
Curcumin **No established safe dose** (based on 2023 TGA report on potential hepatic effects) *TGA, 2023*	Reduces CRP	≤ 700mg/day; Not dose-dependent (most studies ~500mg)	> 7 weeks; Greatest effect seen at ~13 weeks	Naghsh, 2023; Ferguson, 2021
	Reduces IL-6	Not dose-dependent	Not duration-dependent	Naghsh, 2023; Ferguson, 2021
	May reduce intestinal inflammation	2 x 50mg/day (bio-enhanced); 2 x 1.5g/day; 1g/day	6 weeks; 1 month; 6 months	Banerjee, 2021; Lang, 2015; Hanai, 2006
	May reduce self-reported gastrointestinal complaints	500mg/day	4 weeks	Lopresti, 2021
Aloe vera **No established safe dose.** Avoid if hydroxyanthracene derivatives are present (whole leaf extract or aloe latex) as evidence of genotoxicity. *EFSA, 2018*	May reduce IBS symptoms (primarily in IBS-D patients)	500mg/day (freeze-dried gel)	4 weeks	Hong, 2018; Ahluwalia, 2021
	May reduce intestinal inflammation	2 x 100mL/day (aloe gel)	4 weeks	Langmead, 2004

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Polyphenol	Health effect	Dosage	Duration	Reference
EGCG **Max dose: 300mg/day** (risk of hepatic and gastrointestinal adverse effects if exceeded) *Hu, 2018; Dekant, 2017*	May reduce TC and LDL-C	~200mg/day EGCG	3 months	Bogdanski, 2012; Maron, 2003; Nantz, 2009
	May reduce fasting blood glucose	May require > 300mg/day	> 12 weeks	Xu, 2020b; Zamani, 2023
	May reduce intestinal inflammation	May require > 300mg/day. Need more studies to confirm if necessary.	28 weeks; 56 weeks	Zeng, 2022; Dryden, 2013
Isoflavones **Max dose:** No adverse effects at 300mg/day for 2 years or 120mg/day for 3 years *Alekel, 2010; Messina, 2022*	Isoflavone supplementation may improve symptoms of menopause (frequency of hot flashes)	30 to 80mg/day Supplements providing >18.8mg genistein for at least 12 weeks were more than twice as effective	6 weeks to 12 months	Oh, 2024; Taku, 2012
	Isoflavone supplementation may improve symptoms of menopause (severity of hot flashes)	30 to 135mg/day	12 weeks to 12 months	Oh, 2024; Taku, 2012
	Dietary soy intake may improve symptoms of menopause	115.9g/day soy intake; 86g cooked soybeans	N/A; 12 weeks	Nagata, 2001; Barnard, 2021; Dunnerman, 2019

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Clinical considerations for polyphenol prescription

Intake	○ What is the patient's current intake of polyphenols through diet and supplements?
Absorption & bioavailability	○ Which individual patient factors could influence absorption and bioavailability?
Gut microbiome	○ Does your patient's unique microbiome aid polyphenol efficacy?
Nutrient & drug interaction	○ Is your patient's diet, supplements or medication interfering with polyphenol absorption and vice versa?
Safety	○ Is your patient at risk of an adverse event from polyphenol supplement intake?

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An estimated 90-95% of dietary polyphenols reach the lower gut

Only 5-10% of polyphenols are absorbed, leaving a high proportion of polyphenols available for interaction with gut microbiota[1]

Most well-absorbed: gallic acid and isoflavones, followed by catechins, flavanones, and quercetin glucosides[2]

Least well-absorbed: proanthocyanidins, galloylated tea catechins, and anthocyanins[2]

Limited bioavailability of native polyphenols may correlate with greater prebiotic effects

Acylated anthocyanins (present in purple sweet potato or purple carrot) are more stable, less absorbable, and may have a higher prebiotic effect compared to nonacylated anthocyanin (present in berries)[3]

In 2017, the International Scientific Association for Probiotics and Prebiotics (ISAPP) decided that polyphenols should be considered prebiotics[4]

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[1]Clifford, 2004; [2]Manarch, 2005; [3]Jokioja, 2021; [4]Gibson, 2017

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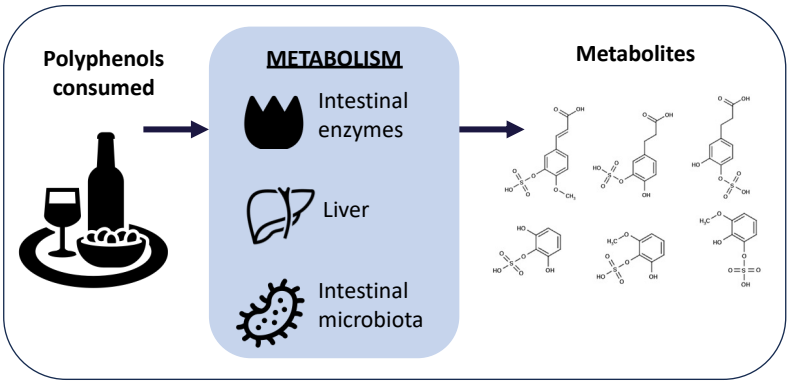
Bioavailability of polyphenols is complex

Bioavailability of polyphenols is low. Unabsorbed polyphenols are metabolised in different ways, including via intestinal microbiota.



Metabolism is just one factor affecting bioavailability

Other factors include the food matrix, interaction with other nutrients and drugs, their chemical structure, excretion, and individual variability (genetics, age, etc)

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Bertelli, 2021

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Polyphenol efficacy (sometimes) depends on the gut microbiome

The breakdown of different polyphenols depends on **specific bacterial strains**. Although polyphenols provide direct health benefits, the complete advantages may be diminished without bacterial conversion to beneficial metabolites.

Note: This is emerging research and not all bacterial strains capable of breaking down polyphenols have been identified!

Polyphenol	Major end-products produced	Human gut bacteria (identified to date) capable of polyphenol conversion
Isoflavones (Daidzein)	**Equol:** may have anti-cancer properties (in-vitro, animal), may reduce menopausal symptoms (human)	**Conversion of daidzein to equol:** *Adlercreutzia equolifaciens, CAG-1427 sp000435475, Enteroscipio sp000270285, Hugonella massiliensis [RUG013 sp00148644], Senegalimassilia faecalis [Senegalimassilia MIC8876], Slackia equolifaciens*, Slackia_A isoflavoniconvertens [Slackia_A MIC8451]*
		Conversion of daidzein to daidzein-intermediates: *Bifidobacterium adolescentis, Bifidobacterium animalis, Bifidobacterium longum, Bittarella massiliensis, Collinsela aerofaciens, Collinsella massiliensis, Collinsella stercoris, Eggerthella lenta, Enterococcus lactis, Escherichia coli, Gordonibacter urolithinfaciens, Slackia exigua*
Ellagic acid	**Urolithin-A**: may improve mitochondrial function and may be anti-inflammatory (in-vitro, animal) **Urolithin-B**: may be associated with disease and dysbiosis (observational human)	**Conversion of ellagic acid to Uro-intermediates:** *Ellagibacter isourolithinifaciens [Eggerthellaceae* MIC8667*], Gordonibacter pamelaeae, Gordonibacter urolithinfaciens*
		Conversion of ellagic acid to Uro-A: *Bifidobacterium pseudocatenulatum INIA P815, Enterococcus_B faecium FUA027, Lactococcus garvieae FUA009, Streptococcus thermophilus FUA329*
		Conversion of Uro-intermediates to Uro-A and Uro-B: *Enterocloster [Clostridioides] bolteae, Enterocloster [Clostridioides] asparagiformis, Enterocloster [Clostridioides] citroniae*
Quercetin	**DOPAC** (3,4-Dihydroxyphenylacetic acid): may have antioxidant properties (in-vitro, animal)	*Bacteroides eggerthii, Eubacterium_I ramulus, Flavonifractor plautii, Lachnospira eligens_B*
Resveratrol	**Dihydroresveratrol:** may have weak anti-cancer properties (in vitro, animal)	*Adlercreutzia equolifaciens, Adlercreutzia rubneri [Adlercreutzia MIC8014], Bacteroides uniformis, Eggerthella lenta, Slackia equolifaciens**
	Lunularin: may have anti-cancer properties (in-vitro, animal)	No species identified yet

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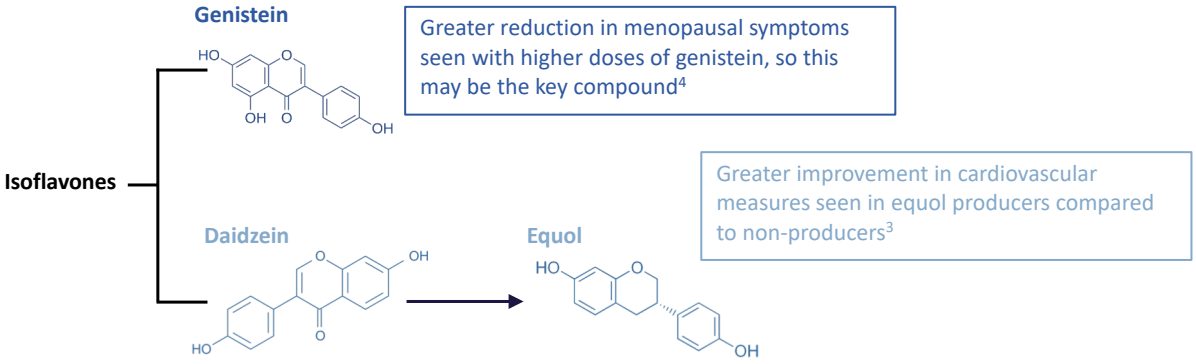
Benefits of isoflavones may be dependent on the specific type

Studies indicate that equol producers may not have greater reductions in menopausal symptoms compared to non-producers[1,2], but equol producers may benefit more from the cardiovascular effect of isoflavones[3]



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[1]Khaodhiar, 2008; [2]Crawford, 2013; [3]Hazim, 2016; [4]Taku, 2012

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Polyphenols interact with nutrients

The intake of polyphenols can affect how our bodies absorb certain nutrients and vice versa

Iron	Folic acid	High-fat foods
A systematic review and meta-analysis[1] found that **polyphenol supplementation** had an inhibitory effect on serum iron concentration and transferrin saturation. Polyphenols have iron-chelating effects, where they form complexes with the iron, inhibiting its absorption. A separate study found 300 mg of **EGCG** significantly reduced iron absorption[2]	300 mg of **green tea extract** has been shown to potentially reduce absorption of folic acid supplementation[3]	Compared to a standard breakfast, a high-fat breakfast delays the absorption and reduces the exposure to **resveratrol**[4] On the other hand, dietary fat has been shown to increase **quercetin** bioavailability[5]

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[1]Xu, 2021; [2]Ullman, 2005; [3]Alemdaroglu, 2008; [4]Porte, 2010; [5]Guo, 2013

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Polyphenols interact with drugs

The intake of polyphenols can affect how our bodies absorb certain drugs

High inter-individual variability
This may be due to differences in expression or activity levels of drug-metabolising enzymes or genetic polymorphisms in genes encoding these enzymes.

Modulating cytochrome P450 (CYP) enzymes

CYP enzymes are responsible for the metabolism of most drugs.

Resveratrol has been shown to inhibit CYP2C9. This enzyme contributes to the metabolism of warfarin. Inadequate metabolism leads to increased plasma levels of the drug, enhancing its anticoagulant effect.

CYP3A4: metabolises vast majority of drugs, including immunosuppressive drugs for transplant patients, HIV protease inhibitors, statin drugs, and chemotherapeutics.

CYP2D6: metabolises many antidepressants, antipsychotics, and beta-blockers. Responsible for converting tamoxifen to the potent anti-estrogen, endoxifen.

CYP2C9: metabolises NSAIDs, COX-2 inhibitors, oral anticoagulants and oral hypoglycemics.

Altering influx (e.g. OATPs) or efflux (e.g. P-glycoprotein and BCRP) transporters

Expressed in protective barriers (e.g. intestine, kidneys and liver). Efflux transporters mediate drug excretion from cells whereas influx transporters mediate drug uptake into cells.

Ellagic acid inhibited P-glycoprotein (removes drug from enterocytes back into gut lumen) activity, increasing bioavailability of diltiazem.

Green tea inhibited OATP1A2 (removes drug from gut lumen into enterocytes) activity, decreasing bioavailability of rosuvastatin.

Quercetin inhibited OATP1B1 (removes drug from bloodstream into liver cells) activity, increasing exposure to pravastatin.

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Drug-polyphenol interactions

This is not an exhaustive list of potential drug-polyphenol interactions

**Preclinical evidence in animals: clinical experiments are needed to assess these drugs when concomitantly administered with this polyphenol*

Polyphenol	Drug	Exposure	Proposed mechanism	Reference
Curcumin	Sulfasalazine	Increased	Inhibited BCRP	Kusuhara, 2012
	Talinolol	Decreased	Induced P-gp	Juan, 2013
	Caffeine, theophylline, clozapine, and acetaminophen (not yet assessed)	Increased	Inhibited CYP1A2	Chen, 2010
	Caffeine, nicotoine and cotinine (not yet assessed)	Decreased	Induced CYP2A6	Chen, 2010
Resveratrol	Warfarin	Increased	Inhibited BCRP* and CYP2C9	Huang, 2020
	Losartan	Increased	Inhibited CYP2C9	Chow, 2010
	Buspirone	Increased	Inhibited CYP3A4	Chow, 2010
	Dextromethorphan	Increased	Inhibited CYP2D6	Chow, 2010
	Caffeine	Decreased	Induced CYP1A2	Chow, 2010
Isoflavones	Theophylline	Increased	Inhibited CYP1A2	Soyata, 2021
	Midazolam	Decreased	Induced CYP3A4	Soyata, 2021
	Celecoxib*	Increased	Inhibited CYP2C9	Soyata, 2021
	Paclitaxel*	Increased	Inhibited CYP3A4 and P-gp	Soyata, 2021
	Repaglinide* and omeprazole*	Increased	Inhibited P-gp	Soyata, 2021
	Imatinib* and carbamazepine*	Decreased	Induced CYP3A4	Soyata, 2021

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Drug-polyphenol interactions (cont.)

This is not an exhaustive list of potential drug-polyphenol interactions

**Preclinical evidence in animals: clinical experiments are needed to assess these drugs when concomitantly administered with this polyphenol*

Polyphenol	Drug	Exposure	Proposed mechanism	Reference
Ellagic acid	Metoprolol*	Increased	Inhibited CYP2D6	Athukuri, 2016
	Diltiazem*	Increased	Inhibited CYP3 and P-gp	Athukuri, 2017
Green tea	Simvastatin and tacrolimus	Increased	Inhibited CYP3A4 and P-gp	Werba, 2018
	Sildenafil	Increased	Inhibited CYP3A4	Werba, 2018
	Buspirone	Increased	Inhibited CYP3A4	Albassam, 2017
	Rosuvastatin and nadolol	Decreased	Inhibited OATP1A2 or OATP2B1	Werba, 2018
	Digoxin	Decreased	Induced P-gp	Kim, 2018
Quercetin	Cyclosporine	Increased	Inhibited CYP3A4	Choi, 2004
	Pravastatin	Increased	Inhibited OATP1B1	Wu, 2012
	Fexofenadine	Increased	Inhibited P-gp	Kim, 2009
	Talinolol	Decreased	Induced P-gp	Wang, 2013
	Midazolam	Decreased	Induced CYP3A	Duan, 2012
	Paracetamol*	Increased	Inhibited P-gp	Pingli, 2015

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Polyphenol safety considerations

Polyphenol	Max dose	Adverse events	References
Resveratrol	150 - 450mg/day	Generally well-tolerated but GI symptoms, especially diarrhoea, are common (mild up to 1.5g/day, most common when of at least 2.5g/day). EFSA Panel suggests 150mg/day. resVida® is a trans-resveratrol supplement with GRAS status at 450mg/day. Caution when taking with warfarin as may increase anticoagulant effects.	*EFSA, 2016; Edwards, 2011*
Ellagic acid	2 x 500mg/day	Limited number of studies. 2 x 500mg/day has been used safely for 12 weeks with no adverse effects	*Hidalgo-Lozada, 2022*
Curcumin	No established safe dose	2023 TGA report on potential hepatic effects determined there is no established safe dose. There are new TGA label requirements for curcumin products. Liver injury is idiosyncratic; therefore, dose cannot predict it.	*TGA, 2023*
Aloe vera	No established safe dose.	Avoid if hydroxyanthracene derivatives are present (whole leaf extract or aloe latex) as evidence of genotoxicity.	*Younes, 2018*
EGCG	300mg/day	Mild-moderate GI symptoms observed in 400 to 4000mg/day. Liver injury can occur when consumed in supplement form but does not appear to occur from green tea beverage consumption. Highest incidence from Polyphenon E supplement.	*Hu, 2018; Dekant, 2017*
Isoflavones	No adverse effects at 300mg/day for 2 years or 120mg/day for 3 years	In 2015, the European Food Safety Authority declared soy isoflavones do not adversely affect the breast, thyroid, or uterus of postmenopausal women and is in support of their safety. However, more research is required on utero isoflavone exposure and the effects of isoflavone on thyroid in cases of iodine deficiency.	*Alekel, 2010; Messina, 2022*

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And don't forget about other drug interactions!

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Best practice in polyphenol prescription

- What are their current dietary habits? How can they add more polyphenol-rich foods?
- What polyphenols and at what dosage/duration will help their specific health concerns?
- If the polyphenol should be consumed with food, what type of nutrients should/should not be present in the food to maximise benefits?
- Are their current dietary polyphenol habits affecting the absorption of other nutrients, or vice versa (e.g. multiple cups of tea per day + iron deficiency)?
- Will a prescribed polyphenol enhance or inhibit their exposure to relevant drugs?
- How is their gut microbiome affecting the metabolism of polyphenols?
- Will any existing health conditions affect polyphenol metabolism (e.g. liver disease)?
- Do they have increased risk factors that may lead to side effects from polyphenols?

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PART 4

Dr Brad Leech

Clinical application and case studies

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Clinical application of polyphenols

Comprehensive Patient Assessments

- Evaluate patients' dietary habits, health conditions, and medication use.
- Use this information to determine the need for polyphenol intervention and tailor recommendations.

Utilise Gut Microbiome Testing

- Incorporate gut microbiome testing to assess patients' microbiome profiles.
- Use test results to personalise polyphenol prescriptions, enhancing efficacy and minimising adverse effects.

Educate Patients on Polyphenol-Rich Foods

- Encourage patients to include a variety of polyphenol-rich foods in their diets, such as fruits, vegetables, nuts, seeds, tea, and coffee.
- Provide practical dietary advice and recipes to help patients integrate these foods into their daily meals.

Prescribe Targeted Polyphenol Supplements

- Identify specific health conditions that may benefit from polyphenol supplementation, such as IBS, cardiovascular disease, and metabolic disorders.
- Recommend appropriate polyphenol supplements based on individual patient needs and microbiome profiles.

Monitor and Manage Drug Interactions

- Be aware of potential interactions between polyphenols and common medications.
- Educate patients on these interactions and adjust medication dosages as necessary to ensure safety and efficacy.

Incorporate Polyphenols in Chronic Disease Management

- Use polyphenols as part of a comprehensive treatment plan for managing chronic diseases.
- Monitor patient outcomes and adjust polyphenol prescriptions based on clinical response.

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Clinical recommendations for polyphenols

Eat a Variety of Colourful Vegetables Daily: Aim to consume at least 5 different coloured vegetables every day (e.g., red peppers, green spinach, yellow squash, orange carrots, and purple eggplant) to ensure a diverse intake of polyphenols.

Switch to Extra Virgin Olive Oil: Replace your regular cooking oils with extra virgin olive oil for all cooking and salad dressings.

Add Cacao to Your Diet: Incorporate 1 tablespoon of raw cacao powder into your diet 3 times a week (e.g., in smoothies, hot chocolate, or chia pudding).

Incorporate Berries into Your Breakfast: Add 1/2 cup of mixed berries (blueberries, raspberries, blackberries, strawberries) to your breakfast at least 5 times a week.

Add Nuts and Seeds to meals: Add a handful (about 30g) of polyphenol-rich nuts (such as hazelnuts, pecans, or almonds) and seeds (such as flaxseeds) to one meal daily.

Include Flaxseed in Meals: Add 2 tablespoons of ground flaxseed to your daily diet, such as in oats, smoothies, or yogurt.

Use Herbs and Spices in Cooking: Include 1 teaspoon of polyphenol-rich herbs and spices (such as cloves, rosemary, thyme, ginger, and turmeric) in your meals at least 4 times a week.

Drink Green Tea: Replace one of your daily beverages with a cup of green tea at least 5 times a week.

Follow a Mediterranean Diet: Adopt a Mediterranean-style diet, focusing on polyphenol-rich foods like fruits, vegetables, nuts, seeds, whole grains, and olive oil, for at least 30 days.

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Available databases to assess polyphenol intake

USDA flavonoid database 3.3 (last updated in 2018):
https://doi.org/10.15482/USDA.ADC/1178142

- Composition of 506 foods
- 26 predominant dietary flavonoids
- Separate databases for isoflavone and proanthocyanidin contents

eBASIS (Bioactive Substances in Food Information Systems, last updated in 2017):
https://doi.org/10.3390/nu9040320

- Composition of 267 foods
- 794 bioactive compounds (not exclusive to polyphenols) and includes health effects from intervention studies
- 1,147 peer-reviewed publications

Phenol-Explorer 3.0 (last updated in 2013):
https://doi.org/10.1093/database/bat070

- Composition of >100 foods
- 161 polyphenols or groups of polyphenols
- 129 peer-reviewed publications

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Patient case study

CVD prevention

Age – 45 years

BMI – 26 kg/m^2 (overweight)

Diagnosis – Diverticulosis, high cholesterol

Gastrointestinal – Regular bowel motions, mild stomach pain after gluten

Family history - Father heart attack age 44, brother heart attack 43, uncle heart attack 45, diabetes with mum, uncle had bowel cancer

Systemic - Fatigue

Medication – Atorvastatin 20mg for 22 years

Dietary – Paleo diet for 5 plus years

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MEDAS score

Questions	Criteria for 1 point	Score
1. Do you use olive oil as main culinary fat?	Yes	1
2. How much olive oil do you consume in a given day (including oil used for frying, salads, out-of-house meals, etc.)?	≥4 tbsp	0
3. How many vegetable servings do you consume per day? (1 serving : 200 g [consider side dishes as half a serving])	≥2 (≥1 portion raw or as a salad)	0
4. How many fruit units (including natural fruit juices) do you consume per day?	≥3	0
5. How many servings of red meat, hamburger, or meat products (ham, sausage, etc.) do you consume per day? (1 serving: 100–150 g)	<1	0
6. How many servings of butter, margarine, or cream do you consume per day? (1 serving: 12 g)	<1	0
7. How many sweet or carbonated beverages do you drink per day?	<1	0
8. How much wine do you drink per week?	≥7 glasses	0
9. How many servings of legumes do you consume per week? (1 serving : 150 g)	≥3	0
10. How many servings of fish or shellfish do you consume per week? (1 serving 100–150 g of fish or 4–5 units or 200 g of shellfish)	≥3	1
11. How many times per week do you consume commercial sweets or pastries (not homemade), such as cakes, cookies, biscuits, or custard?	<3	1
12. How many servings of nuts (including peanuts) do you consume per week? (1 serving 30 g)	≥3	0
13. Do you preferentially consume chicken, turkey, or rabbit meat instead of veal, pork, hamburger, or sausage?	Yes	1
14. How many times per week do you consume vegetables, pasta, rice, or other dishes seasoned with sofrito (sauce made with tomato and onion, leek, or garlic and simmered with olive oil)?	≥2	0

doi:10.1371/journal.pone.0043134.t001

High Adherence (9-14 points)
Moderate Adherence (6-8 points)
Low Adherence (0-5 points) ✓

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CVD pathology

	Calcium score:
Left main coronary artery:	0
Left anterior descending artery:	19.8
Circumflex artery:	35.4
Right coronary artery:	79.5
Other:	-
TOTAL:	**134.6**

CONCLUSION:
1. The total coronary artery calcium score is 134.6.
2. The 10-year risk of major adverse cardiovascular events is moderate.

Explanatory notes:

CT Calcium score:	10-year risk of major adverse cardiovascular events:	Interpretation:
0	<1%	Very low risk.
1-100	<10%	Low risk.
101-400	10-20%	Moderate risk.
>400	>20%	High risk.

Lipid Profile

Cholesterol	6.0 H	(	<5.6)	mmol/L
Triglyceride	0.8	(	<2.1)	mmol/L
HDL	1.11	(	>0.89)	mmol/L
LDL	4.6 H	(	<4.1)	mmol/L
Tot Chol/HDL	5.4 H	(	<4.6)	
Non HDLC	4.89 H	(	<3.81)	mmol/L

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Microbiome results: microbial and GI markers

Inflammation
Markers indicating intestinal and systemic inflammation

High Levels
Increased potential for CVD

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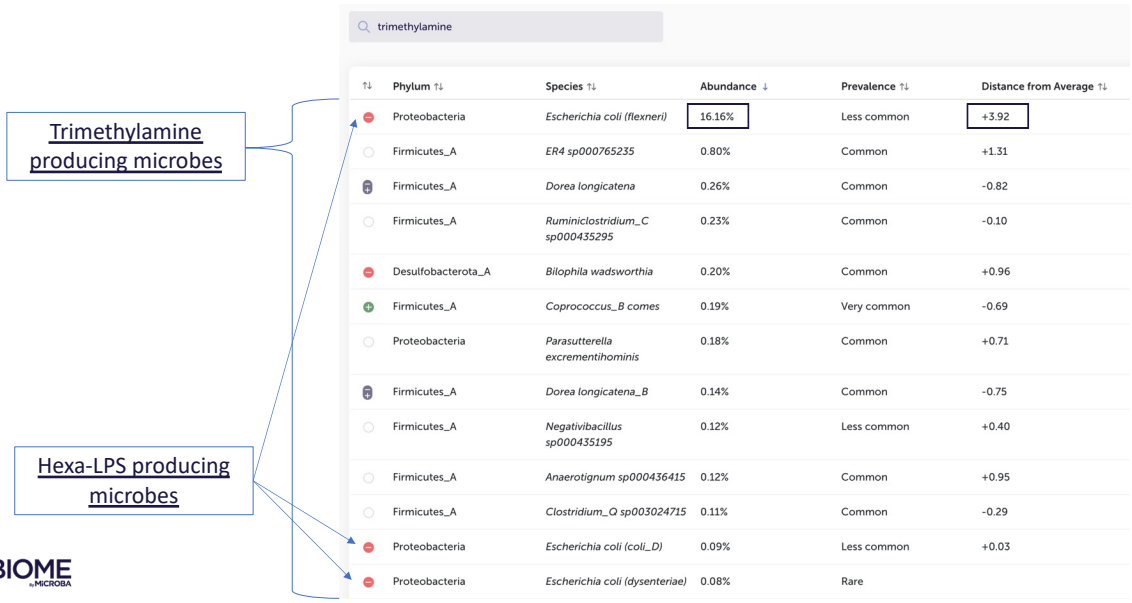
Microbiome results: species



Trimethylamine producing microbes

Hexa-LPS producing microbes

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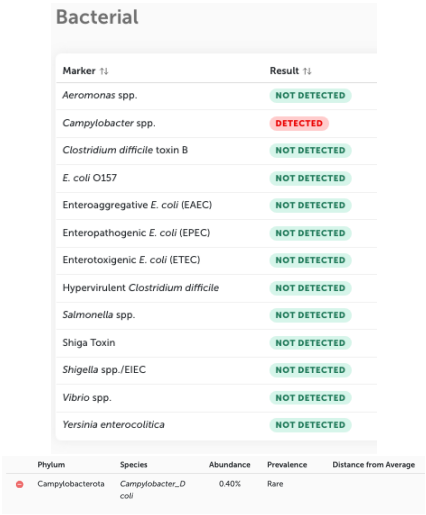
Target pathogen panel



Bacterial

Marker	Result
Aeromonas spp.	NOT DETECTED
Campylobacter spp.	DETECTED
Clostridium difficile toxin B	NOT DETECTED
E. coli O157	NOT DETECTED
Enteroaggregative *E. coli* (EAEC)	NOT DETECTED
Enteropathogenic *E. coli* (EPEC)	NOT DETECTED
Enterotoxigenic *E. coli* (ETEC)	NOT DETECTED
Hypervirulent *Clostridium difficile*	NOT DETECTED
Salmonella spp.	NOT DETECTED
Shiga Toxin	NOT DETECTED
Shigella spp./EIEC	NOT DETECTED
Vibrio spp.	NOT DETECTED
Yersinia enterocolitica	NOT DETECTED

Phylum	Species	Abundance	Prevalence	Distance from Average
Campylobacterota	*Campylobacter_D coli*	0.40%	Rare	

Campylobacter spp.
Campylobacter jejuni and *coli* are foodbourne pathogens that can cause gastroenteritis. Most cases are self-limiting. Medical treatment is likely only required for immunocompromised patients and those with severe or persistent symptoms; however, consideration of the patient's clinical presentation is recommended. If faecal occult blood is also positive or haemorrhagic colitis is suspected, urgent further investigation and specialist consultation is recommended

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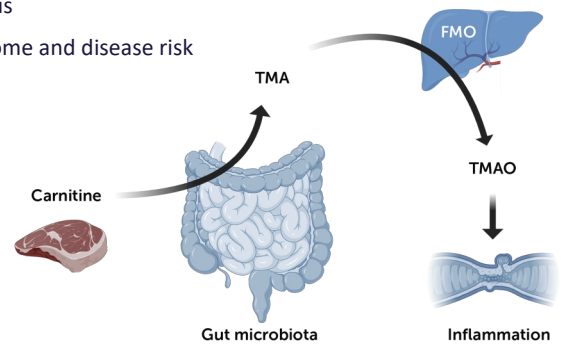
Clinical interpretation and objectives

Clinical interpretation

- High TMA/TMAO is a risk factor for CVD
- Pathobionts are contributing to functional dysbiosis
- Dietary intake is not suitable for patient's microbiome and disease risk

Objectives

1. Reduce impact of TMAO on systemic health
2. Reduce pathobiont (*E.coli*)
3. Provide fuel source for microbiome



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Patient management plan for gut health

Supplement	Dosage	Duration	Related condition
Resveratrol	Take 200mg with dinner	8 months	TMAO, E.coli
GOS	Take 5g with breakfast	8 months	Pathobionts
Fish oil	Take 1500mg with breakfast and dinner	8 months	Inflammation, heart health
HMO	Take 600mg after breakfast and dinner	8 months	Dysbiosis, leaky gut

Dietary/ Lifestyle	Related condition
Consume a Mediterranean style diet	Pathobionts
Aim to consume 38g of dietary fibre every day	Pathobionts
Consume 1/3 cup of mixed organic berries 5x weekly	Cardiovascular health
Limit red meat and carnitine intake	High TMA
Consume 1 cup of cooked cruciferous veggies each day	High TMAO

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Change in species after 8 months

Baseline

Phylum	Species	Abundance	Prevalence	Distance from Average
Proteobacteria	*Escherichia coli (flexneri)*	16.16%	Less common	+3.92
Firmicutes_A	*Blautia_A obeum*	5.60%	Common	+2.70
Firmicutes_A	*Fusicatenibacter saccharivorans*	3.66%	Very common	+0.30
Firmicutes_A	*Agathobacter rectale*	3.27%	Common	+0.58
Firmicutes_A	*Ruminococcus_E bromii_B*	3.21%	Common	+0.32
Bacteroidota	*Bacteroides_B vulgatus*	2.62%	Common	+0.56
Bacteroidota	*Alistipes putredinis*	2.56%	Common	+0.85
Firmicutes_A	*Ruminococcus_D bicirculans*	1.78%	Common	+0.62
Firmicutes_A	*Faecalibacterium prausnitzii_C*	1.63%	Common	+0.80
Firmicutes_A	*Agathobacter faecis*	1.58%	Common	+0.45
Proteobacteria	*CAG-495 sp000436375*	1.46%	Less common	+1.05
Firmicutes_A	*Gemmiger formicilis*	1.41%	Common	+0.49
Bacteroidota	*Parabacteroides distasonis*	1.33%	Very common	+2.31
Firmicutes_A	*CAG-217 sp000436335*	1.32%	Common	+0.37
Firmicutes_A	*CAG-83 sp000435975*	1.28%	Less common	+1.55
Bacteroidota	*Bacteroides uniformis*	1.07%	Very common	+0.11
Firmicutes_A	*Eubacterium_E hallii*	1.05%	Common	+0.64
Firmicutes_A	*Blautia_A massiliensis*	1.02%	Common	+0.63
Bacteroidota	*Alistipes shahii*	0.88%	Common	+1.47
Firmicutes_A	*Anaerostipes hadrus*	0.81%	Very common	-0.15

After 8 months

Phylum	Species	Abundance	Prevalence	Distance from Average
Firmicutes_A	*Ruminococcus_D bicirculans*	7.92%	Common	+1.69
Firmicutes_A	*Ruminococcus_E bromii_B*	6.54%	Common	+0.87
Firmicutes_A	*Agathobacter faecis*	6.09%	Common	+1.49
Firmicutes_A	*Blautia_A obeum*	4.96%	Common	+2.57
Proteobacteria	*Escherichia coli (flexneri)*	4.41%	Less common	+3.03
Actinobacteriota	*Bifidobacterium adolescentis*	3.11%	Common	+0.72
Bacteroidota	*Bacteroides_A sp000432735*	3.04%	Rare	
Firmicutes_A	*Blautia_A wexlerae*	2.93%	Very common	+0.44
Bacteroidota	*Bacteroides_B vulgatus*	2.88%	Common	+0.63
Bacteroidota	*Bacteroides uniformis*	2.72%	Very common	+1.03
Firmicutes_A	*Agathobacter rectale*	2.65%	Common	+0.41
Firmicutes_A	*Ruminococcus_C callidus*	1.77%	Less common	+0.76
Firmicutes_A	*Fusicatenibacter saccharivorans*	1.71%	Very common	-0.44
Bacteroidota	*Alistipes putredinis*	1.61%	Common	+0.38
Firmicutes_A	*Gemmiger formicilis*	1.56%	Common	+0.57
Firmicutes_A	*Blautia_A massiliensis*	1.25%	Common	+0.81
Firmicutes_A	*Faecalibacterium prausnitzii_G*	1.08%	Very common	+0.28
Actinobacteriota	*Bifidobacterium pseudocatenulatum*	0.99%	Less common	+0.59
Firmicutes_A	*Eubacterium_E hallii*	0.94%	Common	+0.50
Firmicutes_A	*Faecalibacterium prausnitzii_O*	0.94%	Very common	+0.55

Escherichia coli (flexneri) ↓ 72%

Commensals ↑

Pathobionts ↓

Change in specie profile

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Diversity and richness

Baseline

After 8 months

Small change in richness, HUGE change in species

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Hexa-LPS & *E.coli* after 8 months

Baseline

	Phylum	Species	Abundance	Prevalence	Distance from Average
⊖	Proteobacteria	*Escherichia coli (flexneri)*	16.16%	Less common	+3.92
⊖	Proteobacteria	*Escherichia coli*	0.10%	Less common	+0.49
⊖	Proteobacteria	*Escherichia coli (coli_D)*	0.09%	Less common	+0.03
⊖	Proteobacteria	*Escherichia coli (dysenteriae)*	0.08%	Rare	

After 8 months

	Phylum	Species	Abundance	Prevalence	Distance from Average
⊖	Proteobacteria	*Escherichia coli (flexneri)*	4.41%	Less common	+3.03

↓72%

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Removal of pathogen, without high dose of antimicrobial herbs

Baseline

Bacterial

Marker	Result
Aeromonas spp.	NOT DETECTED
Campylobacter spp.	DETECTED
Clostridium difficile toxin B	NOT DETECTED
E. coli O157	NOT DETECTED
Enteroaggregative *E. coli* (EAEC)	NOT DETECTED
Enteropathogenic *E. coli* (EPEC)	NOT DETECTED
Enterotoxigenic *E. coli* (ETEC)	NOT DETECTED
Hypervirulent *Clostridium difficile*	NOT DETECTED
Salmonella spp.	NOT DETECTED
Shiga Toxin	NOT DETECTED
Shigella spp./EIEC	NOT DETECTED
Vibrio spp.	NOT DETECTED
Yersinia enterocolitica	NOT DETECTED

Phylum	Species	Abundance	Prevalence	Distance from Average
Campylobacterota	*Campylobacter_D coli*	0.40%	Rare	

After 8 months

Bacterial

Marker	Result
Aeromonas spp.	NOT DETECTED
Campylobacter spp.	NOT DETECTED
Clostridium difficile toxin B	NOT DETECTED
E. coli O157	NOT DETECTED
Enteroaggregative *E. coli* (EAEC)	NOT DETECTED
Enteropathogenic *E. coli* (EPEC)	NOT DETECTED
Enterotoxigenic *E. coli* (ETEC)	NOT DETECTED
Hypervirulent *Clostridium difficile*	NOT DETECTED
Salmonella spp.	NOT DETECTED
Shiga Toxin	NOT DETECTED
Shigella spp./EIEC	NOT DETECTED
Vibrio spp.	NOT DETECTED
Yersinia enterocolitica	NOT DETECTED

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Immune response/ inflammation

Baseline

Phylum	Species	Abundance	Prevalence	Distance from Average
Proteobacteria	*Escherichia coli (flexneri)*	16.16%	Less common	+3.92
Proteobacteria	*Escherichia coli*	0.10%	Less common	+0.49
Proteobacteria	*Escherichia coli (coli_D)*	0.09%	Less common	+0.03
Proteobacteria	*Escherichia coli (dysenteriae)*	0.08%	Rare	
Campylobacterota	*Campylobacter_D coli*	0.40%	Rare	

Campylobacter spp. DETECTED

Secretory IgA — ND — 10000.00 — 500.00 µg/g - 2,000.00 µg/g

After 8 months

Phylum	Species	Abundance	Prevalence	Distance from Average
Proteobacteria	*Escherichia coli (flexneri)*	4.41%	Less common	+3.03

Secretory IgA — ND — 3,833.26 — 500.00 µg/g - 2,000.00 µg/g

Reduction in pathobionts and pathogens has reduced SIgA

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Increase in *Bifidobacterium*

Baseline

Phylum	Species	Abundance	Prevalence	Distance from Average
Actinobacteriota	*Bifidobacterium pseudocatenulatum*	0.12%	Less common	-0.78
Actinobacteriota	*Bifidobacterium animalis*	0.08%	Less common	-0.57

After 8 months

Phylum	Species	Abundance	Prevalence	Distance from Average
Actinobacteriota	*Bifidobacterium adolescentis*	3.11%	Common	+0.72
Actinobacteriota	*Bifidobacterium pseudocatenulatum*	0.99%	Less common	+0.59
Actinobacteriota	*Bifidobacterium MIC6680*	0.53%	Rare	
Actinobacteriota	*Bifidobacterium longum*	0.09%	Common	-1.10
Actinobacteriota	*Bifidobacterium MIC7686*	0.06%	Rare	

HMO/GOS supplementation increased the number of *Bifidobacterium* species and their abundance

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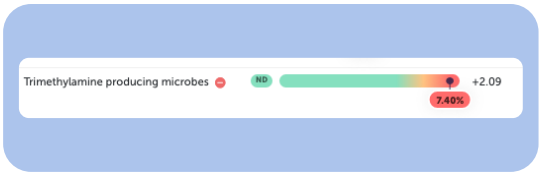
TMA risk factor for CVD

60%



Phylum	Species	Abundance	Prevalence	Distance from Average
Proteobacteria	*Escherichia coli (flexneri)*	16.16%	Less common	+3.92
Proteobacteria	*Escherichia coli*	0.10%	Less common	+0.49
Proteobacteria	*Escherichia coli (coli_D)*	0.09%	Less common	+0.03
Proteobacteria	*Escherichia coli (dysenteriae)*	0.08%	Rare	

Phylum	Species	Abundance	Prevalence	Distance from Average
Proteobacteria	*Escherichia coli (flexneri)*	4.41%	Less common	+3.03

The gut may drive cardiovascular disease without the client presenting with digestive symptoms.

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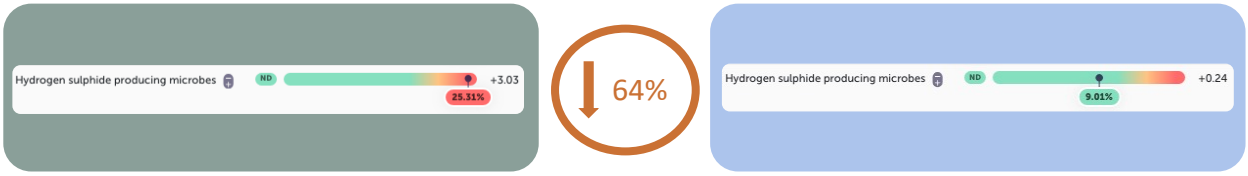
H2S back in normal range



Increasing dietary prebiotics (FOS/GOS) reduced H2S back to healthy range

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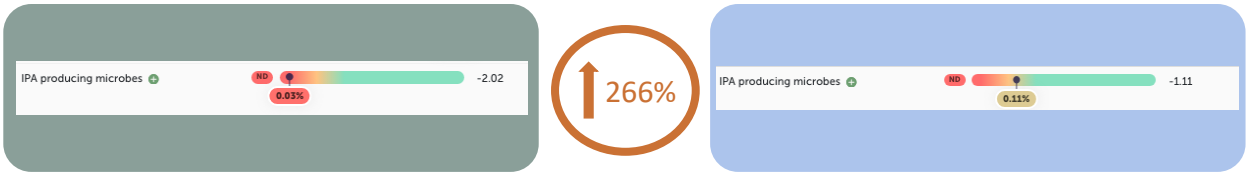
IPA increased



Species	Abundance	Prevalence	Distance from Average
UBA9502 MIC7149	0.03%	Less common	-0.77

Species ↑↓	Abundance ↓	Prevalence ↑↓	Distance from Average ↑↓
CAG-83 sp000435555	0.08%	Common	-1.59
CAG-83 MIC7830	0.03%	Common	-0.77

Increasing dietary ellagic acid increased IPA producing species

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Metabolites and GI function

Baseline

After 8 months

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Patient management plan for gut health

Supplement	Dosage	Duration	Related condition
Resveratrol	Take **300mg** with **lunch** and dinner	3 months	TMAO
GOS	Take 5g with breakfast **and dinner**	3 months	Pathobionts
Fish oil	Take 1500mg with breakfast and dinner	3 months	Inflammation, heart health
HMO	Take 600mg after breakfast, **lunch** dinner	3 months	Dysbiosis, leaky gut

Dietary/ Lifestyle	Related condition
Consume a Mediterranean style diet	Pathobionts
Aim to consume 38g of dietary fibre every day	Pathobionts
Consume 1/3 cup of mixed organic berries 5x weekly	Cardiovascular health
Limit red meat and carnitine intake	High TMA
Consume 1 cup of cooked cruciferous veggies each day	High TMAO
Consume 1 can of legumes each day	**Pathobionts**

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Key Takeaways

1. Polyphenols have antioxidant, anti-inflammatory, and gut microbiome-modulating effects.
2. Gastrointestinal and gut microbiome testing can highlight when to consider dietary and supplement polyphenols for the management of intestinal inflammation and/or systemic inflammation in conditions like IBS, cardiovascular diseases, and inflammatory disorders.
3. SPECIFIC polyphenol diet and supplement recommendations can impact intestinal inflammation through the management of calprotectin, lactoferrin and 3-indolepropionic acid.
4. SPECIFIC polyphenol diet and supplement recommendations can impact systemic inflammation through the management of trimethylamine and 3-indolepropionic acid.
5. When prescribing polyphenol supplements consider dietary intake, nutrient and drug interactions and safety.
6. Incorporating a variety of polyphenol-rich foods as part of a Mediterranean-style diet can provide comprehensive health benefits.
7. Retesting our client's microbiome provides evidence for further management modification.

Live Q&A

Hayley Parcell

Hannah Naismith

Dr Brad Leech

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Resources to support polyphenol prescription

Our range of Clinical Guides and Patient Handouts are available at Co-Education.
You can access these and more via your Practitioner Portal

PATIENT HANDOUTS

CLINICAL GUIDES

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Testing systemic inflammation and intestinal inflammation using the MetaXplore™ range

MetaXplore™ — $369
MetaXplore™ provides a metagenomic driven gut microbiome profile, together with the latest research insights for healthcare professionals.
Technology: metagenomics

MetaXplore™ GI — $489
MetaXplore™ GI provides the same comprehensive microbiome profile as MetaXplore™ as well as reporting on seven gastrointestinal health markers and science backed clinical insights to assist clinical decision-making and intervention.
Technology: metagenomics + diagnostic GI health markers + faecal pH

MetaXplore™ GI Plus — $529
MetaXplore™ GI Plus is Co-Biome's most comprehensive functional gut microbiome profile. It provides all the features found in MetaXplore™ and MetaXplore™ GI, plus targeted pathogen panels.
Technology: metagenomics + diagnostic GI health markers + faecal pH + RT-PCR

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Thank you for attending

Visit the Co-Education Hub All Resources page for additional resources and to watch the webinar replay. You can access this via your Practitioner Portal.

Register as a Co-Biome Clinician today for microbiome educational resources at your fingertips!

Additional resources:

- Polyphenol Guide *(coming soon)*
- Prebiotic Guide
- Low FOMAP Prebiotic Guide
- Dietary Impacts on the Gut Microbiome Guide
- Pathogen and Pathobiont Management Guide
- Interpretation Guide
- MetaXplore Range Report Interpretation Checklist
- Patient Referral Letter Template
- Testing Your Microbiome Patient Brochure
- Patient Handouts – Mediterranean diet *(new)*; Polyphenols *(coming soon);* Ellagic acid; Arabinoxylan; Beta-glucan; Inulin; FOS; GOS; Pectin; Resistant starch

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