

The butyrate gap in Indian diets: fermentable substrate, colonic transit and fermentation capacity, and the missing Indian baseline — a narrative review and evidence-graded clinical framework

Running title: The butyrate gap in Indian diets

Dr. V. Ariarasudhan^{1,2}, M.D. Pharmacology; Jayavardhini S.³,

¹Department of Pharmacology, Sri Ramachandra Medical College and Research Institute, Chennai, India. ORCID iD: 0000-0002-0253-6082. ²Scientific Director and Co-Founder of ThirdBiome. ³Founder of ThirdBiome. ORCID iD: 0009-0004-1542-0750.

Corresponding author: Dr. V. Ariarasudhan, drvari15@gmail.com

Word count: main text approximately 9,200 words; 6 tables; 2 figures

Abstract

Background. Butyrate is the principal energy substrate of the colonocyte and the most extensively characterised mediator linking dietary fibre to host physiology. Clinical interest in "butyrogenic" diets is rising rapidly in India, yet the evidence base underpinning dietary recommendations has been generated almost entirely in Western populations whose diets, gut microbiota and colonic physiology differ materially from Indian populations.

Objective. To synthesise what is currently known about the three determinants of colonic butyrate production in Indian adults — substrate, transit, and fermentation capacity — to identify where population-specific data are absent, and to translate the resulting evidence into a graded framework that Indian nutritionists and physicians can apply.

Methods. Narrative review with a documented literature search strategy. Recommendations were assigned to one of three evidence tiers: supported by human data; mechanistically plausible but without adequate human data; and commonly asserted but not currently supportable.

Key findings. Indian diets supply fibre at approximately 1.8% of total energy and 15-20 g/day against a 25-30 g/day recommendation. Indian colonic transit is approximately half Western duration; faster transit may reduce epithelial absorption time, which would mean that higher faecal butyrate does not necessarily indicate greater epithelial delivery — a hypothesis that requires direct testing. No Indian SCFA reference dataset exists. Evidence supports pulses, whole grains, resistant starch and polyphenol-rich foods but not millets as a butyrogenic category, grain substitution alone, or stool SCFA interpretation against Western reference intervals.

Conclusions. Butyrogenic dietary advice for Indian patients can be given with confidence for pulses, whole grains, resistant starch and polyphenol-rich foods. Millet recommendations, grain substitution alone, and Western-reference stool SCFA interpretation are not evidence-supported. "Evidence on oral butyrate delivery, including tributyrin and microencapsulated preparations, remains limited, particularly in Indian populations". Establishing an Indian SCFA reference dataset is the highest-priority research need.

Keywords: butyrate; tributyrin; short-chain fatty acids; postbiotics; resistant starch; dietary fibre; gut microbiota; colonic transit; India; precision nutrition

How to cite this article: V. Ariarasudhan. The butyrate gap in Indian diets: fermentable substrate, colonic transit and fermentation capacity, and the missing Indian baseline — a narrative review and evidence-graded clinical framework. *Int J Drug Deliv Technol.* 2026;16(85s):141-162. DOI: 10.25258/ijddt.16.85s.13.

1. Introduction

Butyrate, a four-carbon short-chain fatty acid (SCFA) produced by bacterial fermentation of fibre and resistant starch in the large intestine, occupies an unusual position in nutritional science. It is simultaneously the preferred oxidative fuel of the colonocyte and a signalling molecule acting through histone deacetylase inhibition and the G-protein-coupled receptors FFAR2, FFAR3 and GPR109A [1,2,3]. It maintains epithelial tight-junction integrity and mucus production, modulates mucosal and systemic immunity, and has been implicated in conditions ranging from inflammatory bowel disease to metabolic syndrome [4,5,6]. Few dietary constituents have a mechanistic story this coherent.

That coherence has translated rapidly into practice. "Butyrogenic" dietary advice — recommendations intended to promote colonic butyrate production — is now commonplace in Indian clinical nutrition, and butyrate and butyrate-precursor supplements are widely marketed. The underlying evidence, however, was generated almost entirely in North American and European cohorts. This matters more than is generally appreciated, because the three proximate determinants of colonic butyrate production — the quantity and structure of fermentable substrate reaching the colon, the metabolic capacity of the resident microbiota, and the time available for fermentation — all differ measurably between Indian and Western populations [7,8,9]. The field has itself concluded that a universal

scale for a healthy microbiome is untenable and that population surveys outside industrialised nations are required [10,11,12].

This review addresses a practical question: what can an Indian nutritionist or physician legitimately tell a patient about butyrogenic eating, and what should they refrain from claiming? To answer it we examine each determinant in turn, identify where Indian data exist and where they do not, and translate the result into an explicitly graded framework. We also address two questions clinicians increasingly face — how to interpret a stool SCFA report in an Indian patient, and which specialties can reasonably invoke butyrate in patient communication.

2. Evidence identification and grading

2.1 Literature search

This is a narrative review and does not claim the completeness of a systematic review. Literature was identified through 22 structured queries executed against the Consensus research database, which indexes Semantic Scholar, PubMed, Scopus and arXiv. Queries were organised in two blocks. The first addressed butyrate generally — physiological reference concentrations, butyrogenic dietary substrates, direct supplementation, health outcomes, and measurement methodology — and the second addressed the Indian context specifically: South Asian gut microbiome composition, fermentable substrate in Indian foods, the Indian nutrition transition, SCFA reference data in South Asians, and Indian gastrointestinal and metabolic disease burden. Both blocks were supplemented by design-restricted queries (systematic review and meta-analysis filters), date-restricted historical queries (publication year ≤ 2015) and forward queries (publication year ≥ 2021), together with targeted follow-up queries on colonic transit and on dietary substrate. Approximately 170 unique records were retrieved and screened after deduplication; 118 are cited here. Reference lists of retrieved articles were consulted to confirm provenance of quantitative values but were not systematically hand-searched.

2.2 Grading of recommendations

Each dietary recommendation was assigned to one of three tiers. This scheme is deliberately coarse, and is intended for clinical communication rather than as a substitute for formal GRADE assessment. For practical purposes: Tier 1 requires at least one adequately powered RCT in an Indian or comparable South Asian population, or consistent evidence from multiple RCTs in comparable low- and middle-income country settings. Tier 2 requires mechanistic plausibility supported by human or animal data, with Indian observational data preferred. Tier 3 covers claims that are contradicted by available evidence or

for which no mechanistic or observational support exists.

Table 1. Evidence tiers used throughout this review

Tier	Definition	How a clinician should use it
Tier 1 — Supported	Supported by human intervention or observational data with a quantified effect, including meta-analytic evidence where available.	May be recommended to patients as evidence-based dietary advice.
Tier 2 — Plausible	Mechanistically coherent and supported by in vitro, animal or indirect human data, but without adequate direct human evidence for the specific claim.	May be offered as reasonable general dietary advice, without asserting a butyrate-specific benefit.
Tier 3 — Not supportable	Commonly asserted in practice or marketing, but contradicted by, or unsupported by, the available evidence.	Should not be stated to patients as fact; several of these are actively misleading.

3. Butyrate physiology relevant to dietary counselling

Three features of butyrate physiology bear directly on how dietary advice should be framed, and all three are routinely lost in translation to the clinic.

First, **butyrate is not a dietary constituent in any meaningful sense**. With the minor exception of milk fat, essentially all physiologically relevant butyrate is synthesised in situ by colonic bacteria from substrate that escapes small-intestinal digestion [13,14]. Patients frequently understand "butyrate-rich diet" to mean foods containing butyrate; the correct framing is foods that *deliver fermentable substrate to the colon*.

Second, **concentrations fall by three to four orders of magnitude between the colonic lumen and the peripheral circulation**. Measurements in colonic contents and in portal, hepatic and peripheral venous blood established total SCFA concentrations of approximately 131 mmol/kg in the caecum falling to 80 mmol/kg in the descending colon, against 375 $\mu\text{mol/L}$ in portal blood, 148 $\mu\text{mol/L}$ in the hepatic vein

and 79 $\mu\text{mol/L}$ peripherally [15]; SCFAs constitute roughly two-thirds of the colonic anion concentration at 70–130 mmol/L [16]. Hepatic extraction is efficient enough that rectally administered butyrate produces essentially no increase in systemic concentration [17]. This gradient explains why butyrate's effects on intestinal inflammatory markers are consistent while effects on peripheral markers are not [18], and it is the principal reason extraintestinal claims should be made cautiously (Section 9).

Third, **the relationship between butyrate and health is not monotonic**. Butyrate inhibits proliferation in undifferentiated and neoplastic colonocytes while supporting it in differentiated cells — the so-called butyrate paradox [6,19] — and reviews have explicitly framed butyrate as double-edged, particularly in obesity [20]. Meta-analytic data bear this out: faecal butyrate is *higher* in obesity (standardised mean difference [SMD] 0.78, 95% CI 0.29–1.27) [21] and in one South African type 2 diabetes cohort [22], yet *lower* in colorectal cancer (SMD –0.59, 95% CI –1.10 to –0.07) [23] and in active inflammatory bowel disease [24]. "More butyrate is better" is therefore not a defensible clinical heuristic.

4. Determinant one: fermentable substrate in the Indian diet

4.1 How much fibre Indians actually eat

India now has dietary exposure data at national scale, and the picture is unfavourable for colonic fermentation. The ICMR–INDIAB survey-21 ($n = 18,090$ adults) characterised Indian diets as high in low-quality carbohydrate — white rice, milled whole grains and added sugar — with high saturated fat and low protein [25]. The ICMR–INDIAB survey-21 ($n = 18,090$) reported fibre supplying only 1.8% of total energy [25]. Rising simple-sugar intake — from 10.5% to 20.3% of total carbohydrate between 2014 and 2025 — is documented in urban dietary surveys [26]. Reported intake is approximately 15–20 g/day against a recommended 25–30 g/day, with fewer than 10–15% of adults meeting the recommendation [27]. Thirty-year secular analyses document falling intake of coarse cereals, pulses, fruit and vegetables [28,29], diets diversifying away from cereals without compensating gains in micronutrient-rich foods [30], and household spending on ultra-processed foods nearly doubling from 6.5% to 12% between 2015 and 2023 against a modest rise in millet consumption from 2.1 to 3.3 kg/capita/year [31,32,33]. The same trajectory is evident across Asia [34].

4.2 Resistant starch in Indian preparations

India is comparatively well served by food-composition data on resistant starch (RS), a literature running from 1994 to the present [35,36,37,38,39,40,41]. Three findings are consistent and clinically actionable. Legumes carry substantially

more RS than cereals or tubers, with boiled and pressure-cooked lentils highest at approximately 5% on a dry-weight basis [40]. Cooking collapses the RS of raw rice dramatically — raw Kolam rice at 27.67 g% falls to 0.46 g% when cooked — while cooling and storage partially recover some of the lost RS through retrogradation [36]. And among preparation methods, boiling (dalia, 7.74%) outperforms shallow frying (parantha, 4.94%) and roasting (chapati, 2.77%), while deep frying reduces RS [41].

Table 2. Measured resistant starch content of Indian foods and preparations

Food / preparation	RS content	Basis	Source
Raw Kolam rice	27.67 g%	Raw ingredient	Nigudkar 2014
Raw Basmati rice	20.22 g%	Raw ingredient	Nigudkar 2014
Whole wheat flour (raw)	0.50 g%	Raw ingredient	Nigudkar 2014
Refined wheat flour (raw)	0.65 g%	Raw ingredient	Nigudkar 2014
Whole moong (raw)	4.52 g%	Raw ingredient	Nigudkar 2014
Cooked Kolam rice	0.46 g%	As eaten	Nigudkar 2014
Khichdi	0.78 g%	As eaten	Nigudkar 2014
Chapati	0.49 g% / 2.77%	As eaten (two studies)	Nigudkar 2014; Kaur 2023
Paratha / parantha	0.61 g% / 4.94%	As eaten (two studies)	Nigudkar 2014; Kaur 2023
Dalia (boiled cracked wheat)	7.74%	As eaten	Kaur 2023
Poori (deep fried)	0.47 g% / 2.47%	As eaten (two studies)	Nigudkar 2014; Kaur 2023
Plain pressure-cooked dhal (4 types)	1.21–2.16 g%	As eaten	Nigudkar 2017
Aamti (thin dhal preparation)	0.42–0.69 g%	As eaten	Nigudkar 2017

Food / preparation	RS content	Basis	Source
Usal, Bengal gram (kabuli)	2.38 g%	As eaten	Nigudkar 2017
Usal, Bengal gram (brown)	1.42 g%	As eaten	Nigudkar 2017
Chole (cooked)	2.38 g%	As eaten	Nigudkar 2014
Zunka / dhirda / pithle	1.23 / 1.48 / 0.09 g%	As eaten	Nigudkar 2017
Boiled lentils	5.0% (dwb)	Dry-weight basis	Yadav 2010b
Pressure-cooked lentils	4.9% (dwb)	Dry-weight basis	Yadav 2010b

*Values derive from studies using different analytical methods and different bases of expression; they should be used for ranking rather than absolute calculation.

g% = grams per 100 g of the food as analysed; dwb = dry-weight basis. Values are not directly comparable across studies because of differences in analytical method and in whether results are expressed per 100 g as eaten or per 100 g dry matter. Where two values are shown for the same preparation they derive from different studies and illustrate this heterogeneity; clinicians should use them for ranking foods, not for absolute intake calculation.

Table 3. Effect of cooking method and storage on resistant starch

Manipulation	Effect	Source
Three heating/cooling cycles	Legumes 4.18% → 8.16%; cereals 1.86% → 3.25%; tubers 1.51% → 2.51% (dwb). Maximum increase 114.8% (pea), minimum 62.1% (sweet potato)	Yadav 2009
Storage 24 h at 4 °C (flours)	Wheat flour +41.4%; pea flour +85.4%	Yadav 2010a
Cooked white rice, cooled 10 h at room temperature	0.64 → 1.30 g/100 g	Sonia 2015

Manipulation	Effect	Source
Cooked white rice, cooled 24 h at 4 °C then reheated	0.64 → 1.65 g/100 g; significantly lower glycaemic response	Sonia 2015
Indian wheat products stored 24 h at 4 °C	Highest RS of all storage conditions tested; lowest glycaemic index and load (chapati 43/32.3; dalia 41.1/28.6)	Kaur 2023
Boiling vs deep frying	Boiling increases RS; deep frying decreases it	Kaur 2023
Conventional boiling vs pressure cooking	Pressure cooking reduced RS relative to boiling (maximum decrease 15%, pea)	Yadav 2010b

4.3 The millet question

Millets occupy a prominent place in Indian nutrition policy and an increasingly prominent one in clinical advice. The evidence that they are specifically butyrogenic, however, is weaker than their profile suggests. In vitro fermentation of pearl and foxtail millet fibre fractions by probiotic cultures produced SCFAs in the order acetate > propionate > butyrate — that is, millet fibre was not preferentially butyrogenic in these systems [42,43]. Finger millet has a stronger mechanistic case, acting through polyphenols and arabinoxylan on Faecalibacterium, Eubacterium and Roseburia, with fermentation further releasing bound phenolics and reducing antinutritional factors [44,45,46,47]. Critically, almost all of this evidence is in vitro; no human study measuring SCFA outcomes after millet feeding was identified. Millets remain a defensible recommendation on grounds of micronutrient density, glycaemic profile and agronomic sustainability, and their promotion in Indian nutrition policy (e.g., the National Year of Millets 2023) is strongly supported on these grounds. The present review's critique applies specifically to the butyrate-specific claim: recommending millets as a butyrogenic category is currently Tier 3, whereas recommending them for micronutrient density, glycaemic control and agronomic sustainability remains entirely appropriate.

5. Determinant two: Indian gut fermentation capacity

The Indian gut microbiome is well characterised and demonstrably distinct. It is enriched in Prevotella and Megasphaera, resembling Bangladeshi more closely than American profiles [48]; Prevotella-dominant in fibre- and legume-rich urban cohorts [49,50]; and

structured internally by geography and altitude [51]. A national multi-omics catalogue in 110 healthy adults identified a regional split, with a North-Central plant-based cohort associated with *Prevotella* and branched-chain amino acid biosynthesis enrichment, versus a Southern omnivorous cohort enriched in *Bacteroides*, *Ruminococcus* and *Faecalibacterium* with enrichment of the SCFA biosynthesis pathway [52]. Functionally, Indian *Prevotella* copri strains carry more complex plant-polysaccharide-degrading machinery, including pullulanase-containing polysaccharide-utilisation loci, than Western strains [53] — an argument that Indian microbiomes may be differently *capable*, not merely differently composed. Urbanisation depletes *Prevotella* [54].

This should predict good butyrogenic responsiveness. The evidence does not straightforwardly support that inference. Pooled analysis of fourteen fibre intervention studies found that pre-intervention microbiota composition strongly controlled outcomes, and specifically that **initial *Prevotella* abundance was negatively associated with the response of butyrate producers** to both inulin-type fructans and resistant starch [55]. Responder stratification is well established: in a canonical resistant-starch trial participants separated into enhanced (+67%), persistently high and persistently low responders, with non-responders failing to expand *Ruminococcus bromii* or *Bifidobacterium adolescentis* [56]; only resistant potato starch reliably raised butyrate among four substrates tested in 174 adults [57]; and in vitro fermentation of ten starches across ten donors showed each microbiome responds to its own subset of substrates [58,59]. Butyrogenic response is therefore predicted better by baseline microbiota than by the substrate ingested [60].

We flag this as a tension requiring direct test in Indian populations: the Indian microbiome carries enhanced substrate-degrading capacity, including pullulanase-containing polysaccharide-utilisation loci that expand the substrates available to it, yet the enterotype associated with it has been linked — in European cohorts only — to poorer butyrate-producer response to fibre intervention. The European-derived negative association should not be applied to Indian patients until directly tested. These observations may reflect different levels of analysis — gene content versus community response — a distinction that has not been tested and that constitutes a first-order question for Indian nutrition research. Ancillary determinants add further complexity: colonic pH shifts butyrate yield several-fold [61], colonic hydrogen concentration modulates butyrate output [62], and microbial thiamine biosynthesis was the top microbiome predictor of faecal butyrate in one large cohort [63].

6. Determinant three: colonic transit — the overlooked variable

6.1 Indian colonic physiology differs measurably from Western

Indian gastroenterologists have documented for over a decade that Indian bowel physiology does not match Western norms, to the point that Western radio-opaque marker protocols are unusable without modification [64]. Mean total colonic transit time was 15.8 hours in Indian subjects against a Western mean of 30–40 hours with an upper normal limit of 70 hours; median mouth-to-caecum transit was 65 minutes; 99% of Indians pass at least one stool daily; and mean stool weight in 514 healthy Indians older than 15 years was 311 g/day [64]. For comparison, median daily stool weight in 220 healthy UK adults was 106 g/day with a whole-gut transit time of 60 hours, and a stool weight above 200 g/day is diagnostic of diarrhoea in Western practice [65]. In an eastern Indian population of 1,200 subjects, median stool frequency was 14 per week and fewer than 3 stools per week occurred in only 2.6% [66].

Table 4. Butyrate-relevant physiological and dietary parameters: Indian versus Western reference populations

Parameter	Indian populations	Western reference	Source
Mean total colonic transit time	15.8 h (n = 25)	30–40 h; upper normal 70 h	Ghoshal 2012
Median mouth-to-caecum transit	65 min (n = 12)	Not directly compared	Ghoshal 2012
Whole-gut transit time	Not established at scale	60 h median (UK, n = 220)	Cummings 1992
Mean daily stool weight	311 g/day (n = 514)	106 g/day median (UK, n = 220)	Ghoshal 2012; Cummings 1992
Global stool weight range	—	72–470 g/day across 20 populations	Cummings 1992
Defecation frequency	99% ≥1 stool/day; median 14/week	≥3 stools/week considered normal	Ghoshal 2012; Panigrahi 2013
Dietary fibre intake	15–20 g/day;	Recommended 25–30 g/day	Hebbbar 2026;

Parameter	Indian populations	Western reference	Source
	1.8% of energy		Kapoor 2025
Faecal or plasma butyrate concentration	No published data identified	Multiple reference datasets	This review

6.2 Transit is a quantitatively dominant determinant of fermentation

Transit time is not a nuisance variable. It is named in the canonical reviews alongside substrate availability and microbiota composition as one of the three principal regulators of the amount and type of SCFA produced [7,8], and recent synthesis identifies intestinal transit and microbiota composition as the primary governors of longitudinal SCFA production [9]. Pharmacological manipulation of transit on a fixed diet altered colonic microbial mass and stool output, with a significant correlation between transit time and bacterial mass [67]. In an in vitro model isolating transit as the sole variable, transit was the single largest driver of microbial cell concentration (52% of variance) and metabolic activity (45%) [68].

6.3 A directional conflict that must be acknowledged

In a crossover study manipulating transit with wheat bran, senna and loperamide on an unchanged diet in 13 healthy adults, whole-gut transit time correlated inversely with total faecal SCFA concentration ($r = -0.511$, $p = 0.001$) and with faecal butyrate ($r = -0.577$, $p < 0.001$), and positively with distal colonic pH ($r = 0.359$, $p = 0.029$) [69]: faster transit was associated with higher faecal butyrate and a more acidic distal colon. The inverse transit–SCFA relationship has since been reproduced in healthy controls and irritable bowel syndrome, where faecal SCFAs correlated inversely with overall and segmental colonic transit (all $p < 0.01$) [70]; in subjects with slow transit, where long distal colonic transit was negatively associated with faecal SCFA and plasma acetate [71]; and in diarrhoea-predominant irritable bowel syndrome, where rapid colonic transit was associated with higher faecal propionate [72]. Faecal butyrate proportion also rises, and branched-chain fatty acid proportion falls, as total SCFA concentration rises and colonic pH falls [73]. These are consistent with the production-minus-absorption model described below, though the original manipulation (laxatives and constipating agents) may have introduced effects beyond transit speed alone.

In vitro evidence points the other way on total production. Slower transit produced higher microbial population density, greater net carbohydrate fermentation and increased SCFA production, with butyrate producers selectively enriched in the proximal colon at *medium* rather than fastest transit [68]; a second in vitro system found that lengthening transit reduced distal biomass and diversity and shifted distal fermentation from carbohydrate toward protein [74].

These observations are reconcilable, and the reconciliation has clinical consequences. Faecal concentration represents production minus absorption. Faster transit affords the colonocyte less time to absorb what is produced, so higher faecal butyrate at fast transit may reflect reduced epithelial uptake rather than increased synthesis. We propose the following testable hypothesis: the higher faecal butyrate concentration observed at fast transit may reflect reduced time for epithelial uptake rather than increased net production — an interpretation that remains speculative pending direct testing in Indian adults. If that interpretation is correct, the Indian phenotype could appear butyrate-replete on a stool assay while delivering less butyrate to the epithelium — a counterintuitive possibility that warrants explicit consideration. A further complication is that faecal communities appear adapted to their donor’s habitual transit, with carbohydrate-to-biomass conversion efficiency highest in microbiomes from short-transit donors [68]. A fast-transit Indian microbiome is therefore not a Western microbiome running faster, and cross-population inference cannot assume that it is. Whether transit differences raise or lower effective butyrate exposure in Indian adults is, at present, unknown. Three explicit predictions follow from the production-minus-absorption hypothesis: (i) in Indian adults, faecal butyrate concentration will be inversely correlated with transit time; (ii) plasma butyrate concentration will show no such inverse correlation, because hepatic extraction and peripheral metabolism remove the transit-dependent signal; and (iii) the faecal-to-plasma butyrate ratio will be higher in fast-transit individuals, directly testing the reduced-uptake interpretation. These predictions are operationally falsifiable in a paired transit–SCFA study in Indian adults.

The butyrate gap in Indian diets: fermentable substrate, colonic transit and fermentation capacity, and the missing Indian baseline — a narrative review and evidence-graded clinical framework

Figure 1. Three determinants of colonic butyrate production (Indian values annotated)

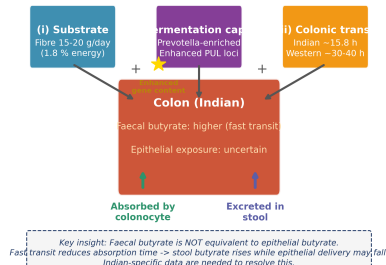


Figure 1. Conceptual schematic of the three determinants of colonic butyrate production in Indian adults, with Indian-specific values annotated. Transit time modulates epithelial absorption: under fast-transit conditions, the absorption arrow is reduced (dashed), meaning higher faecal butyrate may not indicate greater epithelial delivery — the figure illustrates the production-minus-absorption hypothesis rather than an established finding.

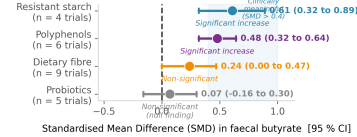
7. The missing Indian baseline

Despite a well-developed Indian microbiome literature, a well-developed Indian food-composition literature and a well-developed Indian dietary survey literature, we identified no population-representative dataset reporting measured faecal or plasma SCFA concentrations in an Indian or South Asian cohort. Indian multi-omics work reports SCFA biosynthesis pathway enrichment inferred from metagenomes rather than quantified metabolite [52]. Reference-grade datasets are American [63], European [75], or Thai [76] — the last reporting total faecal SCFA of $34.1 \pm 15.3 \mu\text{mol/g}$ and total plasma SCFA of $60.0 \pm 45.9 \mu\text{M}$ in 157 medically confirmed healthy individuals, of which acetate constituted 93% of plasma SCFA. Meta-analyses pooling faecal SCFA draw on constituent studies that are overwhelmingly Western [21,23,24,77].

Three considerations make this absence consequential rather than merely regrettable. Geographic region of study is a statistically significant source of between-study heterogeneity in faecal SCFA meta-regression, alongside immediate post-collection freezing and antibiotic exclusion [78] — pooling across populations is therefore already known to be problematic. Faecal and circulating SCFA are not interchangeable: circulating, not faecal, SCFAs related to insulin sensitivity, lipolysis and GLP-1 concentrations [75]; concordance between serum and stool is low and temporal intraclass correlations over six months are modest, arguing for serial sampling [79,80]; and diet and microbiome features predict faecal far better than plasma concentrations [63]. Finally, stable-isotope tracer work has shown that inulin raised butyrate production by approximately 44% while faecal

concentration moved little, and that plasma rather than faecal concentration correlated with production rate [81] — a caution issued in the methodological literature two decades ago and still widely disregarded [82].

Figure 2. Butyrogenic effect sizes across intervention classes (pooled meta-analytic estimates)



Note: Estimates drawn from independent meta-analyses with heterogeneous populations, substrates, doses, and outcome measures. Presented for illustrative ranking only — do not compare quantitatively. Null findings with CIs excluding benefit satisfy the Tier 3 (not supportable) criterion.

Figure 2. Butyrogenic effect sizes (standardised mean difference, SMD) across intervention classes from independent meta-analyses. Each bar represents a separate meta-analysis with its own population, substrate, dose and outcome definition; SMD values are therefore not directly comparable and are shown for qualitative orientation only. The vertical dashed line marks the null effect (SMD = 0). Readers should consult the primary meta-analyses for confidence intervals and heterogeneity statistics. Probiotics and dietary fibre show non-significant effects, whereas resistant starch and polyphenols show significant increases in faecal butyrate.

8. An evidence-graded framework for Indian practice

Table 5 translates the foregoing into recommendations a clinician can apply, with counselling language and the evidence tier for each. Table 6 addresses interpretation of stool SCFA testing.

Table 5. Evidence-graded butyrogenic dietary recommendations for Indian adults

Recommendation	Evidence	Tier	Suggested counselling point
Increase pulses and legumes (dhal, chana, rajma, lentils)	Highest measured RS among Indian staples; boiled/pressure-cooked lentils ~5% dwb; cooked dhal 1.21–2.16 g% as eaten	Tier 1	"Pulses are the most reliable way to feed the bacteria that make butyrate. Aim to include them daily."
Prefer whole grain over refined grain	Whole-grain (≥ 75 g/day) vs refined (< 10 g/day) diet significantly	Tier 1	"Whole grains raise butyrate measurably — but

The butyrate gap in Indian diets: fermentable substrate, colonic transit and fermentation capacity, and the missing Indian baseline — a narrative review and evidence-graded clinical framework

Recommendation	Evidence	Tier	Suggested counselling point
Increase resistant starch as a food class	increased faecal butyrate in a randomised crossover trial ($p = 0.015$) Pooled RS supplementation raised faecal butyrate (SMD 0.61, 95% CI 0.32–0.89) and lowered faecal pH; clinical trial doses typically ≥ 8 g/day	Tier 1	only if they replace refined grain rather than adding to it." "Resistant starch has the strongest evidence of any fibre type for raising butyrate."
Include polyphenol-rich foods	Polyphenol supplementation raised butyrate across 50 RCTs (SMD 0.48, 95% CI 0.32–0.64) — approximately double the general fibre effect (SMD 0.24)	Tier 1	"Colourful vegetables, spices, tea and fruit act on butyrate through a separate route from fibre."
Do not rely on probiotics to raise butyrate	No significant effect on faecal butyrate in healthy individuals (SMD 0.07, 95% CI –0.16 to 0.30)	Tier 1 (negative)	"Probiotics have other uses, but they will not raise your butyrate."
Cook and cool rice or	Retrogradation reliably raises RS,	Tier 2	"It helps a little and costs

Recommendation	Evidence	Tier	Suggested counselling point
wheat before eating	but from a low base (cooked rice 0.64 → 1.65 g/100 g); magnitude is small relative to trial doses		nothing — but it is not a substitute for pulses and whole grains."
Prefer boiled preparations (dalia) over fried	Dalia 7.74% RS vs poori 2.47%; no clinical outcome data	Tier 2	"Boiling preserves more resistant starch than frying."
Include finger millet (ragi)	Mechanistic and in vitro support via polyphenols and arabinoxylan acting on Faecalibacterium, Eubacterium, Roseburia; no human SCFA data	Tier 2	"Good food on several grounds; we cannot yet promise a butyrate effect specifically."
Include traditionally fermented foods	Fermentation releases bound phenolics and reduced antinutritional factors in finger millet; SCFA evidence is in vitro	Tier 2	"Reasonable to include; the butyrate evidence is not yet in humans."
Target 25–30 g/day total dietary fibre	Recommendation is well founded, but fibre → SCFA is not univocal: 44-study review found no	Tier 2	"Worth doing for many reasons; the butyrate response varies a lot between

Recommendation	Evidence	Tier	Suggested counselling point
	consistent SCFA increase; +25 g/day for 2 weeks shifted microbiome without changing faecal SCFA		individuals."
"Millets are butyrogenic"	In vitro millet fibre fermentation favoured acetate > propionate > butyrate; no human SCFA data	Tier 3	Recommend millets on micronutrient, glycaemic and sustainability grounds — not as a butyrate claim.
Grain substitution alone will lower diabetes risk	Replacing refined cereal with whole wheat or millet flour without reducing carbohydrate quantity was NOT associated with lower T2D risk (OR 0.94, 95% CI 0.57–1.56) in 18,090 adults	Tier 3	"Swapping the grain is not enough on its own — the total carbohydrate load matters more."
A Prevotella-rich Indian gut will respond well to fibre	High baseline Prevotella was negatively associated with butyrate-producer	Tier 3	Do not assume responsiveness; expect substantial interindividual variation.

Recommendation	Evidence	Tier	Suggested counselling point
"Higher faecal butyrate is better"	response to both inulin-type fructans and resistant starch Higher in obesity (SMD 0.78) and in one T2D cohort; lower in colorectal cancer (SMD –0.59) and active IBD	Tier 3	Do not interpret a high stool butyrate as reassuring in isolation.
Oral butyrate supplementation for hypertension	Four weeks of oral sodium butyrate increased daytime systolic BP by 9.63 mmHg (95% CI 2.02–17.20) and diastolic by 5.08 mmHg in hypertensive patients	Tier 3	Do not recommend oral butyrate to hypertensive patients pending further evidence.

*Effect sizes are drawn from independent meta-analyses with heterogeneous populations, substrates, doses and outcome measures; they are provided for contextual illustration only and are not directly comparable across rows. Evidence tiers are assigned on the basis of study quality, population relevance and consistency of findings, not on effect-size magnitude. Green rows = Tier 1 (supported); amber rows = Tier 2 (plausible); red rows = Tier 3 (not supportable). Sources for each row are given in the corresponding sections of the main text. Counselling language is illustrative and should be adapted to the patient. Note: effect sizes shown in the table are drawn from independent meta-analyses with heterogeneous populations, substrates, doses and outcome measures, and are provided for contextual illustration only; the evidence tiers are assigned on the basis of study

quality, population relevance and consistency of findings, not on effect-size magnitude.

8.1 Supplementation strategies: what the delivery form changes and what it does not

Clinicians are increasingly asked about butyrate supplements, and the question deserves a factual answer rather than either endorsement or dismissal. The starting point is the physiology set out in Section 3: bacterially produced butyrate is delivered continuously, at the mucosal surface, at millimolar luminal concentrations, and is largely consumed by the colonocyte before reaching the portal circulation [15,17]. No oral preparation reproduces that profile. Butyrate salts are absorbed rapidly in the stomach and proximal small intestine, so the pharmacologically relevant question about any product is not how much butyrate it contains but where that butyrate is released; clinical results should accordingly be attributed to specific preparations and release profiles rather than to butyrate as a class [83]. This is not a theoretical distinction. When 1 g sodium butyrate tablets labelled with carbon-13 were given to 12 healthy subjects and 12 patients with Crohn's disease, a hydroxypropyl methylcellulose and shellac coating delayed release by two to three hours relative to uncoated tablets and shifted it to the ileo-caecal region and colon, and the between-subject variability in release was explained by variability in intestinal transit time [84]. That last observation carries a specific Indian implication: if release site depends on transit, and Indian transit is substantially faster than the Western values against which such formulations were developed (Section 6.1), a coating validated in European cohorts cannot be assumed to release at the same site in Indian patients. No published study has tested this.

The largest body of human evidence concerns sodium butyrate, increasingly in microencapsulated form. In irritable bowel syndrome, 300 mg/day added to standard therapy in 66 patients reduced the frequency of pain on defaecation at four weeks and of urgency and disordered bowel habit at 12 weeks, without a significant reduction in symptom severity [85]. A randomised, double-blind trial of a microencapsulated sodium butyrate, probiotic and short-chain fructo-oligosaccharide mixture in 120 adults with irritable bowel syndrome found a higher rate of adequate symptom relief at four weeks (64.7% versus 42.0%, $p = 0.023$) but no difference in symptom severity score or quality of life at 12 weeks [86]. In inflammatory bowel disease, a double-blind placebo-controlled pilot in 49 patients found that two months of microencapsulated sodium butyrate increased short-chain fatty acid-producing taxa, Lachnospiraceae in ulcerative colitis and Butyrivibrio in Crohn's disease, with the authors stating explicitly that the clinical significance of the finding required further

investigation [87]. A multicentre, double-blind, randomised trial of 600 mg/day as add-on therapy in 98 adults with mild-to-moderate ulcerative colitis subsequently reported clinical improvement in 51% ($p = 0.005$), clinical remission in 31.4% ($p = 0.004$) and endoscopic improvement in 25.5% ($p = 0.006$) [88]. Against these, a randomised placebo-controlled multicentre trial of 300 mg/day for 12 weeks in 72 children and adolescents with newly diagnosed inflammatory bowel disease found no difference between groups in remission rate, disease activity or faecal calprotectin [89]. Where benefit has been observed it has been local, adjunctive and within a defined disease. No trial has tested supplementation in healthy adults, and none has been conducted in an Indian population.

Tributylin, the triglyceride of butyrate present naturally in milk fat, was developed as a butyrate prodrug on pharmacokinetic grounds: it is comparatively stable in gastric acid and is hydrolysed by pancreatic lipase, and oral administration in rats raises butyrate concentrations in the portal vein [90]. Human data remain limited and are drawn largely from oncology dose-finding rather than from gastroenterology or nutrition. A phase I study escalated tributyrin from 50 to 400 mg/kg/day in 13 patients with solid tumours: peak plasma butyrate ranged from 0 to 0.45 mmol/L, occurred between 15 minutes and three hours after dosing, and had disappeared from plasma by five hours, with grade 3 nausea, vomiting and myalgia among the toxicities recorded [91]. A successor study using 150 to 200 mg/kg three times daily in 20 patients achieved a median butyrate concentration of 52 micromol/L with considerable interpatient variability and no dose-limiting toxicity [92]. Most recently, an open-label target-engagement study of 500 mg three times daily for 30 days in 14 patients with Parkinson's disease and three controls reported a reassuring safety profile with high adherence and, on carbon-11 butyrate positron emission tomography, organ-specific changes in butyrate uptake [93]. That orally administered short-chain fatty acid triglycerides can raise systemic butyrate is not in doubt: a double-blind placebo-controlled crossover trial in men with overweight or obesity demonstrated dose-dependent postprandial increases in plasma butyrate and hexanoate [94]. What does not exist is a randomised placebo-controlled trial of tributyrin against a clinical endpoint in any gastrointestinal, metabolic or inflammatory indication. Microencapsulation of tributyrin has so far been characterised in laboratory models rather than in patients. In a simulated digestion and fermentation system, whey protein isolate-based and gamma-cyclodextrin-based microcapsules both released approximately 75% of their butyrate during the small-

intestinal phase, with the cyclodextrin-based capsules generating significantly more butyrate during the subsequent fermentation phase ($p < 0.001$) [95]. A simulation of a commercial tributyrin capsule and softgel estimated that 40.9% and 48.7% of the administered dose respectively were hydrolysed to butyrate in the small intestine, leaving 59.1% and 51.3% available to enter the colon, and reported increased butyrate concentrations and altered community composition after three weeks in a dynamic gut model [96]. These are model outputs rather than measurements in people, and the distinction should be preserved whenever such figures are quoted to prescribers or patients. Two further cautions apply in the Indian context: in vitro digestion models are parameterised to Western transit times and pH profiles, which Section 6 shows do not describe Indian colonic physiology, and no published study has measured the colonic delivery of any tributyrin preparation in Indian subjects. Formulation work in this area is under way in India, including at Thirdbiome and Aeon Formulations Pvt Ltd, with which the corresponding author is affiliated (see Competing interests); no human data from any Indian microencapsulated tributyrin preparation have been published, and none are reported here.

Two findings temper any general recommendation. First, oral supplementation does not reliably move the measurement a clinician is most likely to order: 4 g/day of sodium butyrate for four weeks altered plasma and faecal concentrations of other short-chain fatty acids but left plasma and faecal butyrate unchanged [97]. A rise in stool butyrate should therefore not be expected as confirmation that a supplement is working, and its absence does not establish that it is not. Second, in a double-blind randomised placebo-controlled trial in 23 patients with hypertension whose antihypertensive medication had been withdrawn, four weeks of oral sodium butyrate increased daytime 24-hour systolic blood pressure by 9.63 mmHg (95% CI 2.02 to 17.20) and diastolic blood pressure by 5.08 mmHg (95% CI 1.34 to 8.78) relative to placebo, with plasma but not faecal butyrate rising [98]. The placebo in that trial was an equivalent dose of sodium chloride, so the effect cannot be attributed to the sodium load alone.

Placed on the grading used in Table 5, colon-targeted sodium butyrate as an adjunct in ulcerative colitis and irritable bowel syndrome is Tier 2: supported by randomised trials, but trials of modest size, inconsistent across age groups, and none conducted in India. Tributyrin and microencapsulated tributyrin are Tier 3 for every clinical endpoint, not because the pharmacokinetic rationale is weak but because the confirmatory human trials have not been performed; the accurate statement to a patient or a colleague is that

colonic delivery is plausible and clinical benefit is unproven. Supplementation of any form in healthy adults for general wellbeing is Tier 3. None of this displaces the central recommendation of this review: dietary substrate remains the only intervention shown to raise butyrate production continuously and at the mucosal surface where the concentration gradient described in Section 3 shows it acts, and it is the only butyrogenic intervention for which the evidence in Table 5 reaches Tier 1. Because the corresponding author has a declared commercial interest in a microencapsulated butyrate preparation (see Competing interests), no proprietary product is named in this section and the evidence tier assigned to tributyrin is the tier its published human evidence supports.

9. Interpreting stool short-chain fatty acid testing in Indian patients

Commercial stool SCFA and "gut health" panels are increasingly ordered in Indian practice, and a rapid clinical assay for faecal butyrate has now been validated with an analytical measurement range of 4.30–3030 μM [99]. The interpretive framework, however, has not kept pace. Table 6 summarises the practical position.

Table 6. Practical guidance for stool SCFA testing in Indian patients

Question	Current position
Is there a validated Indian reference interval?	No. No study measuring faecal or plasma SCFA in an Indian or South Asian cohort was identified. Laboratories reporting against a "normal range" are applying a Western or unspecified reference.
Can a Western reference range be applied?	Not safely. Geographic region is a significant source of heterogeneity in faecal SCFA meta-regression, and Indian transit and stool output differ substantially from the populations from which reference data derive.
What does a faecal concentration actually measure?	Production minus absorption, expressed per unit stool mass. In a population with ~15.8 h transit and ~311 g/day stool output, this is not the same physiological quantity as the identical number in a population with 60 h transit and 106 g/day output.
What should be measured alongside?	At minimum: stool form (Bristol scale), stool frequency, and faecal pH. Faecal pH has been

Question	Current position
	shown to be a reasonable proxy for faecal SCFA abundance. Where feasible, add transit assessment and branched-chain fatty acids.
Is a high result reassuring?	Not necessarily. Faecal butyrate is higher in obesity and, in one cohort, in type 2 diabetes; it is lower in colorectal cancer and active IBD. Direction of abnormality is condition-dependent.
Is blood testing better?	It answers a different question. Circulating, not faecal, SCFAs relate to insulin sensitivity, lipolysis and GLP-1; serum–stool concordance is low. Plasma is dominated by acetate (~93%), so circulating butyrate is low single-digit μM .
How reproducible is a single sample?	Modest. Six-month temporal intraclass correlations are generally low, and intra-individual coefficient of variation for total faecal SCFA over three consecutive days is approximately 17%. Serial sampling is preferable for any clinical decision.
Do pre-analytical factors matter?	Substantially. Immediate post-collection freezing is a significant heterogeneity source; lyophilisation improves stability and removes water-content bias; no single extraction method is optimal for all SCFAs; and mill-homogenisation of frozen faeces reduced replicate variability from 20.4% to 7.5%.
When is the test uninformative?	When used alone, against an imported reference range, on a single sample, without stool form, output or pH. Under those conditions it should not drive management.

Supporting evidence for Table 6 is drawn from Sections 6 and 7 and from references [21,23,24,63,64,65,75,76,78,79,80,100,101,102,103]. Note: rows marked with † derive from non-Indian cohorts (obesity, colorectal cancer, IBD, healthy adults in Europe, North America and Southeast Asia). †Guidance is extrapolated from those populations and

should be applied to Indian patients with appropriate caution until population-specific data are available.

10. Specialty-relevant considerations

10.1 Gastroenterology

This is where the evidence is strongest. Butyrate supports colonocyte energetics, tight-junction and mucus integrity, and mucosal immune regulation [2,4,5]. In inflammatory bowel disease, faecal SCFAs including butyrate are significantly reduced across disease subgroups, most markedly in active disease, and dietary intervention raised butyrate with the largest effect of any SCFA (SMD 1.03) [24]; butyrogenic diets including germinated barley foodstuff and oat bran increase faecal butyrate and reduce disease activity, although butyrate enemas have shown mixed effects [104]. IBD incidence in India is rising sharply, with second-generation Indian immigrants showing Western-equivalent incidence [105]. In irritable bowel syndrome, faecal SCFAs correlate with colonic transit and a low-FODMAP diet reduced faecal propionate [70,106]. Colorectal cancer incidence remains comparatively low in India but is rising in urban populations, and the Indian CRC microbiome carries a distinctive signature [107,108]. Clinicians should also note that Indian colonic transit protocols require modification from Western standards [64].

10.2 Endocrinology and diabetology

The mechanistic case is reasonable and the clinical case is mixed. Animal and in vitro evidence for butyrate on body weight, inflammation and insulin resistance translates inconsistently to humans because of differences in absorption and metabolism [109]. Oral sodium butyrate at 4 g/day improved peripheral and hepatic insulin sensitivity in lean but not metabolic syndrome subjects, without changing plasma or faecal butyrate [97]; 20 mg/kg/day improved BMI, waist circumference, insulin and HOMA-IR in paediatric obesity [110]; and 1875 mg/day supported weight loss in obesity without diabetes and improved triglycerides and time-in-tight-range in type 2 diabetes [111]. Against this, elevated faecal SCFAs have been associated with increased adiposity [21,77,112]. For Indian practice the most directly relevant finding is the ICMR–INDIAB result that grain substitution without carbohydrate reduction did not lower diabetes risk [25]. If elevated faecal SCFAs reflect reduced epithelial absorption rather than increased systemic exposure (Section 6.3), the observation that Indian populations characteristically show high faecal SCFA does not predict increased adiposity — a resolution of the apparent contradiction between the obesity–SCFA association in Western populations and the Indian thin-fat phenotype.

10.3 Colorectal and general surgery

Meta-analysis of experimental animal studies found that butyrate administration significantly increased anastomotic strength and collagen synthesis and reduced early anastomotic leakage (OR 0.37, 95% CI 0.15–0.93), although the optimal form, dose and route remain undefined and no clinical trials were identified [113]. Low stool weight and slow transit are associated with colorectal cancer risk in Western populations [65,114]; Indian populations characteristically show higher stool weight and faster transit (Section 6), which may confer protection through different mechanisms. Whether the protective effect of high stool weight in Indians involves butyrate at all, or involves a different pathway such as luminal dilution of carcinogens, has not been established. Butyrate's relationship to colorectal carcinogenesis is concentration- and context-dependent rather than uniformly protective [6,19].

10.4 Where the evidence does not currently support clinical claims

In the interest of accurate communication, it should be stated plainly that no human evidence was identified supporting butyrate-specific claims in dermatology, ophthalmology, orthopaedics, gynaecology or rheumatology, and that neurological and psychiatric claims remain overwhelmingly preclinical. A systematic review of butyrate for depression identified only two human randomised trials against thirty-two animal studies, with one human trial finding no measurable effect [115]. Colonic butyrate administration at 5.28 g/day for one week raised serum butyrate and modulated fear memory at the subjective level only, without altering neuroendocrine responses to acute stress [116].

The physiological reason for this caution is set out in Section 3: the lumen-to-plasma concentration gradient means extraintestinal tissues are exposed to butyrate at low micromolar concentrations, and hepatic extraction is efficient enough that rectally administered butyrate produces essentially no rise in systemic concentration [15,17,18]. Claims that depend on butyrate reaching a distant tissue at a physiologically active concentration are therefore not currently supportable in humans.

Clinicians in these specialties may reasonably discuss gut health, dietary fibre and the general importance of colonic fermentation with patients. They should not attribute specialty-specific outcomes to butyrate, and they should not describe animal or in vitro findings as though they were clinical evidence. Where a patient raises such a claim, the accurate response is that the mechanism is plausible, the human data are absent, and the dietary advice in Table 5 stands on its own merits regardless.

11. Research agenda

We propose the following priorities, in order.

1. **An Indian SCFA reference cohort that measures butyrate alongside transit, stool output and faecal pH.** Measuring faecal concentration alone in a fast-transit, high-output population would produce a number that cannot be interpreted. The study should be regionally stratified given documented within-India heterogeneity [51,52], and should report both concentration and daily excretion.
2. **Direct testing of the transit–butyrate relationship in Indian adults.** Human and in vitro evidence currently conflict on direction [68,69]. Paired measurement of transit, faecal and plasma butyrate would resolve whether fast transit raises faecal concentration while reducing epithelial exposure, and would provide the data needed to interpret stool SCFA results against a population-specific reference.
3. **Prospective testing of the Prevotella tension.** Whether enhanced polysaccharide-utilisation gene content [53] offsets the negative association between baseline Prevotella and butyrate-producer response [55] is directly testable in an Indian fibre intervention with pre-stratification by enterotype.
4. **Human feeding studies of Indian butyrogenic preparations.** Millet and fermented-food evidence is almost entirely in vitro [42,43,46,47]. Controlled feeding of dhal, dalia, ragi and cooked-and-cooled rice with SCFA endpoints would move several Tier 2 recommendations to Tier 1 or 3.
5. **Harmonisation of units and pre-analytical protocol for Indian laboratories.** Values are reported variously as mmol/kg wet weight, $\mu\text{mol/g}$ dry weight and molar proportion, often without sufficient detail to convert [101,102,103]. A minimum reporting standard agreed between Indian laboratories would make national datasets poolable from the outset.
6. **Evaluation of substrate–microbiome matching as a precision-nutrition strategy.** In vitro evidence indicates each microbiome responds to its own subset of substrates [58]; SCFA-production potential can be predicted from sequencing data [117]; and personalised nutrition programmes measurably alter butyrate-producing genera [118]. Whether matching substrate to baseline enterotype outperforms generic fibre advice is untested in any population.

12. Limitations

This is a narrative review and is subject to the corresponding limitations. The literature search, although documented, was not systematic and did not follow PRISMA; selection of included studies

involved author judgement and is susceptible to selection bias. The search was conducted through a single aggregating database indexing Semantic Scholar, PubMed, Scopus and arXiv; Indian work published in regional journals not indexed in these sources, in institutional theses, or in Indian Council of Medical Research and National Institute of Nutrition technical reports would not have been retrieved. **The central claim that no Indian SCFA measurement exists should therefore be regarded as provisional** pending manual searching of IndMED, Shodhganga and ICMR publication listings; we recommend that readers treat it as a strong indication rather than a definitive absence.

Quantitative values are reported as published and have not been converted between units, because the necessary information to do so is frequently absent from source publications. Resistant starch values in Table 2 derive from studies using different analytical methods and different bases of expression and should be used for ranking rather than absolute calculation. The evidence tiers in Table 5 are a pragmatic scheme for clinical communication and are not equivalent to formal GRADE assessment. Finally, several key inferences — particularly the proposed reconciliation of the transit–butyrate directional conflict in Section 6.3 — are hypotheses generated by this review rather than established findings, and are presented as such.

13. Conclusions

Butyrogenic dietary advice for Indian patients rests on a partially assembled evidence base. Substrate composition of Indian foods is well characterised; Indian gut microbiota are well described taxonomically; Indian dietary intake is quantified at national scale; and Indian colonic physiology has been shown to differ substantially from the Western populations in which the butyrate literature was generated. What is missing is the metabolite itself. No population-representative measurement of faecal or plasma butyrate in an Indian cohort was identified in the literature searched, and the physiological differences documented here — transit approximately half the Western duration, stool output approximately threefold higher — give specific reason to expect that imported reference values may not transfer.

For practice, this supports a clear division. Pulses, whole grains in place of refined grains, resistant starch and polyphenol-rich foods can be recommended on evidence. Cooking-and-cooling, boiled preparations, finger millet and fermented foods are reasonable but should not carry a butyrate-specific promise. Millets as a butyrogenic category, grain substitution as a standalone strategy, the assumption that Indian microbiomes will respond well to fibre, reading high faecal butyrate as reassuring without considering transit context, and oral butyrate in hypertension are

not currently supportable. Establishing an Indian reference dataset that measures butyrate alongside transit, stool output and faecal pH would convert much of this uncertainty into guidance, and is the field's most pressing need. In the absence of such a dataset, continued reliance on Western reference intervals will produce systematic misinterpretation of stool SCFA results in Indian patients, and dietary recommendations will continue to be extrapolated without validation.

Acknowledgements

The author thanks colleagues at Thirdbiome and at Aeon Formulations Pvt Ltd, whose work on the microencapsulation of tributyrin informed the discussion of delivery form in Section 8.1. Neither organisation had any role in the literature search, in the selection or appraisal of evidence, in the assignment of evidence tiers, or in the decision to submit this manuscript. No unpublished or proprietary data from either organisation are reported, and no commercial product is named anywhere in the text.

Declarations

Competing interests

The authors are the founding members of Thirdbiome and associated with Aeon Formulations Pvt Ltd, which manufactures a microencapsulated tributyrin (butyrate prodrug) ingredient. These relationships constitute a financial interest in the subject matter of this review. The author confirms that the content of this review was developed independently of these commercial interests and that all evidence assessments reflect the published literature without commercial bias.

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors. No external funding was received for the preparation of this manuscript.

Author contributions

Dr. V. Ariarasudhan: Conceptualization, Methodology, Investigation, Writing – original draft, Writing – review & editing, Supervision, Project administration. Jayavardhini S.: Investigation, Writing – review & editing, Formal analysis, Validation.

Data availability

No new data were generated. The search strategy is described in Section 2 and the full list of retrieved records is available from the author on reasonable request.

Use of artificial intelligence

An AI language model (Claude, Anthropic) was used to support literature identification, evidence synthesis, and manuscript drafting. The author reviewed and verified all cited sources and all factual claims, and takes full responsibility for the content.

References

1. Mukhopadhyay I, Louis P. Gut microbiota-derived short-chain fatty acids and their role in human health and disease. *Nat Rev Microbiol*. 2025. https://consensus.app/papers/details/542d66948d085ba798d0ce04300e9c41/?utm_source=claude_desktop
2. Mann ER, Lam YK, Uhlig HH. Short-chain fatty acids: linking diet, the microbiome and immunity. *Nat Rev Immunol*. 2024. https://consensus.app/papers/details/cc8d6e5c06b8537f9ad05fcee2da86e2/?utm_source=claude_desktop
3. Hays KE, Pfaffinger JM, Ryznar R. The interplay between gut microbiota, short-chain fatty acids, and implications for host health and disease. *Gut Microbes*. 2024. https://consensus.app/papers/details/6d7c39dad416533fb1509bf66e1867c0/?utm_source=claude_desktop
4. Singh V, Lee G, Son H, Koh H, Kim ES, Unno T, et al. Butyrate producers, "The Sentinel of Gut": their intestinal significance with and beyond butyrate, and prospective use as microbial therapeutics. *Front Microbiol*. 2023. https://consensus.app/papers/details/a06e92822eb7594a9261597f4ebcb37e/?utm_source=claude_desktop
5. Korsten SGPI, Peracic L, van Groenigen LMB, Diks MAP, Vromans H, Garssen J, et al. Butyrate protects barrier integrity and suppresses immune activation in a Caco-2/PBMC co-culture model while HDAC inhibition mimics butyrate in restoring cytokine-induced barrier disruption. *Nutrients*. 2023. https://consensus.app/papers/details/504cb21155385ab58216ad5439babb9a/?utm_source=claude_desktop
6. Salvi PS, Cowles RA. Butyrate and the intestinal epithelium: modulation of proliferation and inflammation in homeostasis and disease. *Cells*. 2021. https://consensus.app/papers/details/810e5b37967f5555a80f02cddce0a861/?utm_source=claude_desktop
7. Macfarlane S, Macfarlane GT. Regulation of short-chain fatty acid production. *Proc Nutr Soc*. 2003. https://consensus.app/papers/details/175196c30b6f58afbfbef1cf6aac01f7/?utm_source=claude_desktop
8. Wong JMW, de Souza R, Kendall CWC, Emam A, Jenkins DJA. Colonic health: fermentation and short chain fatty acids. *J Clin Gastroenterol*. 2006. https://consensus.app/papers/details/b99a96dfeal5588889ad6d62047d1b40/?utm_source=claude_desktop
9. Fan S, Zhang Z, Zhao Y, Daglia M, Zhang J, Zhu Y, et al. Dietary fibers as drivers of short-chain fatty acids homeostasis: a review of intestinal production, systemic distribution, and inter-individual variation. *J Agric Food Chem*. 2026. https://consensus.app/papers/details/32c3e923320558608ee9f0e176f8340c/?utm_source=claude_desktop
10. Parizadeh M, Arrieta MC. The global human gut microbiome: genes, lifestyles, and diet. *Trends Mol Med*. 2023. https://consensus.app/papers/details/c1b20c577bed535b8a7d91d3b4325a05/?utm_source=claude_desktop
11. Govender P, Ghai M, Okpeku M. Population-specific differences in the human microbiome: factors defining the diversity. *Gene*. 2024. https://consensus.app/papers/details/b92a21d4db8d56559ab527745ef16c67/?utm_source=claude_desktop
12. Gupta VK, Paul S, Dutta C. Geography, ethnicity or subsistence-specific variations in human microbiome composition and diversity. *Front Microbiol*. 2017. https://consensus.app/papers/details/a05e8627d4945db59b08ed9349fa4ead/?utm_source=claude_desktop
13. Topping DL, Clifton PM. Short-chain fatty acids and human colonic function: roles of resistant starch and nonstarch polysaccharides. *Physiol Rev*. 2001. https://consensus.app/papers/details/a6b608c5c23859d0a4702912aa2ca3e3/?utm_source=claude_desktop
14. Hamer HM, Jonkers D, Venema K, Vanhoutvin S, Troost FJ, Brummer RJ. Review article: the role of butyrate on colonic function. *Aliment Pharmacol Ther*. 2007. https://consensus.app/papers/details/351a07d28f0e50c886da83bef965dade/?utm_source=claude_desktop
15. Cummings JH, Pomare EW, Branch WJ, Naylor CP, Macfarlane GT. Short chain fatty acids in human large intestine, portal, hepatic and venous blood. *Gut*. 1987. https://consensus.app/papers/details/dcdb0f5b89555a4abfd0598a9ca44dcf/?utm_source=claude_desktop
16. Mortensen PB, Clausen MR. Short-chain fatty acids in the human colon: relation to gastrointestinal health and disease. *Scand J Gastroenterol Suppl*.

- 1996.https://consensus.app/papers/details/38fa7f4cb88b55dc876d61707fdd9e7f/?utm_source=claude_desktop
17. van der Beek CM, Bloemen JG, van den Broek MA, Lenaerts K, Venema K, Buurman WA, et al. Hepatic uptake of rectally administered butyrate prevents an increase in systemic butyrate concentrations in humans. *J Nutr*. 2015.https://consensus.app/papers/details/c28808206d615dc3b3d573cc66d6d826/?utm_source=claude_desktop
18. Hedemann MS, Hermansen K, Pedersen S, Bach Knudsen KE. Impact of diet-modulated butyrate production on intestinal barrier function and inflammation. *Nutrients*. 2018.https://consensus.app/papers/details/0930303a72ef5b0fb348817f241cf411/?utm_source=claude_desktop
19. Sengupta S, Muir JG, Gibson PR. Does butyrate protect from colorectal cancer?. *J Gastroenterol Hepatol*. 2006.https://consensus.app/papers/details/daf6d10663959c0bdf18731248dce5/?utm_source=claude_desktop
20. Liu H, Wang J, He T, Becker S, Zhang G, Li D, et al. Butyrate: a double-edged sword for health?. *Adv Nutr*. 2018.https://consensus.app/papers/details/5f45d01a1c3c535cb0ec00d89ff97811/?utm_source=claude_desktop
21. Kim KN, Yao Y, Ju SY. Short chain fatty acids and fecal microbiota abundance in humans with obesity: a systematic review and meta-analysis. *Nutrients*. 2019.https://consensus.app/papers/details/153125e32dd459d9a6356d6aae129232/?utm_source=claude_desktop
22. Khumalo S, Mokoena MP, Mthembu SXH. Fecal short-chain fatty acid profiling in type 2 diabetes mellitus using GC-MS: a comparative study in a South African population. *Diabetology*. 2026.https://consensus.app/papers/details/ca5422fbcc36569abd3d766fc67f28e4/?utm_source=claude_desktop
23. Sylwestrzak T, Krupa-Kotara K, Grajek M. Fecal short-chain fatty acids in colorectal cancer patients versus healthy controls: a systematic review and meta-analysis. *J Clin Med*. 2025.https://consensus.app/papers/details/9b437e57dec6511c863750a09349ab0b/?utm_source=claude_desktop
24. Chulabayeva L, Issilbayeva A, Sailybayeva A, Kozhakhmetov S, Kushugulova A. Quantitative alterations in short-chain fatty acids in inflammatory bowel disease: a systematic review and meta-analysis. *Biomolecules*. 2025.https://consensus.app/papers/details/c951c47e32405332a7e81b95a5f739ef/?utm_source=claude_desktop
25. Anjana RM, Unnikrishnan R, Deepa M, Venkatesan U, Pradeepa R, Joshi S, et al. Dietary profiles and associated metabolic risk factors in India from the ICMR-INDIAB survey-21. *Nat Med*. 2025.https://consensus.app/papers/details/25d194d83b675c028fd7e90018084b3d/?utm_source=claude_desktop
26. Ghosh S, Mamtani M, Patel M, Kulkarni H. Ultra-processed food consumption and metabolic risk in urban India: a cross-sectional analysis. *Nutr Diabetes*. 2023;13(1):12.https://consensus.app/papers/details/8771cf1ba90c5064b657872b8be44e03/?utm_source=claude_desktop
27. Hebbar S, Kamath A, Shetty S, Bhandary S. Perceptions and barriers to dietary fiber intake among middle-aged south Indian women: a qualitative study. *PLOS Glob Public Health*. 2026.https://consensus.app/papers/details/1f70c4ce8dd459d2b5af35d8c5d749d3/?utm_source=claude_desktop
28. Misra A, Singhal N, Sivakumar B, Bhagat N, Jaiswal A, Khurana L. Nutrition transition in India: secular trends in dietary intake and their relationship to diet-related non-communicable diseases. *J Diabetes*. 2011.https://consensus.app/papers/details/3e91eed0b3e45d8894898873e5c8581e/?utm_source=claude_desktop
29. Mohan V, Radhika G, Unnikrishnan R. Are unhealthy diets contributing to the rapid rise of type 2 diabetes in India?. *J Nutr*. 2023.https://consensus.app/papers/details/b19c7baba0a954e2bfb919a172fe4949/?utm_source=claude_desktop
30. Tak M, Shankar B, Kadiyala S. Dietary transition in India: temporal and regional trends, 1993 to 2012. *Food Nutr Bull*. 2019.https://consensus.app/papers/details/41fe6acbaab85584b974349ae4f7a223/?utm_source=claude_desktop
31. Sethy M, Mohanty S, Pradhan P. India's changing diet: millets, processed foods, and the nutrition crisis. *J Econ Dev Innov Policy*. 2025.<https://consensus.app/papers/details/35>

- [caf0af23065ec490fbf961bd681e88/?utm_source=claude_desktop](https://consensus.app/papers/details/b6d9deabe4a65e77857891ee65109486/?utm_source=claude_desktop)
32. Fardet A, Thivel D, Gérard P, Rock E. Nutrition transition and chronic diseases in India (1990-2019): an ecological study based on animal and processed food caloric intake and adequacy according to nutrient needs. Sustainability. 2022. https://consensus.app/papers/details/983e5dcb00fb53c2aa642b0dc7f84b10/?utm_source=claude_desktop
 33. Singh S, Sharma S, Kumar A. Transitioning diets: a mixed methods study on factors affecting inclusion of millets in the urban population. BMC Public Health. 2023. https://consensus.app/papers/details/42cf2c771b6a5d3ba2bbbd5360f721d7/?utm_source=claude_desktop
 34. Therdtatha P, DasGupta R, Nakamura S, Nakayama J. Crisis of the Asian gut: associations among diet, microbiota, and metabolic diseases. Biosci Microbiota Food Health. 2022. https://consensus.app/papers/details/7ed5412e51ed54e2bc93ce69a663d70a/?utm_source=claude_desktop
 35. Platel K, Shurpalekar KS. Resistant starch content of Indian foods. Plant Foods Hum Nutr. 1994. https://consensus.app/papers/details/59a145a741805514b5cb6e7ad2251545/?utm_source=claude_desktop
 36. Nigudkar MR. Estimation of resistant starch content of selected routinely consumed Indian food preparations. Curr Res Nutr Food Sci. 2014. https://consensus.app/papers/details/24edd00ab8b253e286fa69751670794d/?utm_source=claude_desktop
 37. Nigudkar M, Kulkarni S, Parchure A. Resistant starch content of traditional Indian legume preparations. Curr Res Nutr Food Sci. 2017. https://consensus.app/papers/details/078e807a32645943a4e4ce59337f935d/?utm_source=claude_desktop
 38. Yadav BS, Sharma A, Yadav RB. Studies on effect of multiple heating/cooling cycles on the resistant starch formation in cereals, legumes and tubers. Int J Food Sci Nutr. 2009. https://consensus.app/papers/details/fd1c17b5d00a5e45a883d5daec5bfde7/?utm_source=claude_desktop
 39. Yadav BS, Sharma A, Yadav RB. Effect of storage on resistant starch content and in vitro starch digestibility of some pressure-cooked cereals and legumes commonly used in India. Int J Food Sci Technol. 2010. https://consensus.app/papers/details/b6d9deabe4a65e77857891ee65109486/?utm_source=claude_desktop
 40. Yadav BS, Sharma A, Yadav RB. Resistant starch content of conventionally boiled and pressure-cooked cereals, legumes and tubers. J Food Sci Technol. 2010. https://consensus.app/papers/details/82e57f9c803c5b818259664a8e0b5472/?utm_source=claude_desktop
 41. Kaur P, Kaur K, Aggarwal P, Bains K, Mahal AK, Gupta M, et al. Effect of cooking and storage temperature on resistant starch in commonly consumed Indian wheat products and its effect upon blood glucose level. Front Nutr. 2023. https://consensus.app/papers/details/78b122cb5a795cdba7ac423de1d488b6/?utm_source=claude_desktop
 42. Farooq U, Mohsin M, Liu X, Zhang H. Enhancement of short chain fatty acid production from millet fibres by pure cultures of probiotic fermentation. Trop J Pharm Res. 2013. https://consensus.app/papers/details/a1d2071108575b978840b12758102ffc/?utm_source=claude_desktop
 43. Farooq U, Mohsin M, Liu X, Zhang H. Enhancement of short chain fatty acid production by co-cultures of probiotics fermentation with pearl millet (Pennisetum glaucum) fibre fractions. J Pure Appl Microbiol. 2017. https://consensus.app/papers/details/2921101d14a55dcea08d493e7697757a/?utm_source=claude_desktop
 44. Singh V, Lee G, Son H, Amani S, Baunthiyal M, Shin JH. Anti-diabetic prospects of dietary bioactives of millets and the significance of the gut microbiota: a case of finger millet. Front Nutr. 2022. https://consensus.app/papers/details/05d16f015b2e57679803efff4e3f7a44/?utm_source=claude_desktop
 45. Tawde P, Shirke S, Ananthanarayan L. Nutraceutical potential of fermented finger millet in type 2 diabetes mellitus. J Food Sci. 2026. https://consensus.app/papers/details/3ab3333618255dd7aaca3467ceaed627/?utm_source=claude_desktop
 46. Balasubramaniam V, Shanmugam S, Dutta S. In vitro bi-directional metabolism of lactic acid bacteria and finger millet polyphenols. Food Biotechnol. 2025. https://consensus.app/papers/details/0957db589cfa5127a7dac102518f2ecb/?utm_source=claude_desktop

47. Vila-Real C, Pimenta-Martins A, Mbugua S, Hagrétou SL, Katina K, Maina NH, et al. Novel fermented plant-based functional beverage: biological potential and impact on the human gut microbiota. *Foods*. 2025. https://consensus.app/papers/details/7e3e017c2ef85ac8956afc581506c533/?utm_source=claude_desktop
48. Bhute S, Pande P, Shetty SA, Shelar R, Mane S, Kumbhare SV, et al. Molecular characterization and meta-analysis of gut microbial communities illustrate enrichment of *Prevotella* and *Megasphaera* in Indian subjects. *Front Microbiol*. 2016. https://consensus.app/papers/details/a28c4c208b6d5c4694069aa6525005c3/?utm_source=claude_desktop
49. Tandon D, Haque MM, Gote M, Jain M, Bhaduri A, Dubey AK, et al. A snapshot of gut microbiota of an adult urban population from Western region of India. *PLoS One*. 2018. https://consensus.app/papers/details/7f0b5e481c7153a183325210fe41dc08/?utm_source=claude_desktop
50. Jain A, Li XH, Chen WN. Similarities and differences in gut microbiome composition correlate with dietary patterns of Indian and Chinese adults. *AMB Express*. 2018. https://consensus.app/papers/details/a8db7919311b51c3b6c95a7eed53906/?utm_source=claude_desktop
51. Das B, Ghosh TS, Kedia S, Rampal R, Saxena S, Bag S, et al. Analysis of the gut microbiome of rural and urban healthy Indians living in sea level and high altitude areas. *Sci Rep*. 2018. https://consensus.app/papers/details/11623c47cc875b98a986d4ba3264ffe6/?utm_source=claude_desktop
52. Dhakan DB, Maji A, Sharma AK, Saxena R, Pulikkan J, Grace T, et al. The unique composition of Indian gut microbiome, gene catalogue, and associated fecal metabolome deciphered using multi-omics approaches. *Gigascience*. 2019. https://consensus.app/papers/details/1000a76961a9568ca9855b8d69c04ba8/?utm_source=claude_desktop
53. Prasoodanan PK V, Sharma AK, Mahajan S, Dhakan DB, Maji A, Scaria J, et al. Western and non-western gut microbiomes reveal new roles of *Prevotella* in carbohydrate metabolism and mouth-gut axis. *NPJ Biofilms Microbiomes*. 2021. https://consensus.app/papers/details/fb597efald095d449c204653c5918ea3/?utm_source=claude_desktop
54. Das S, Bhattacharjee MJ, Mukherjee AK, Khan MR. Lifestyle transition from rural to urban setting changes the gut bacterial profile in an ethnic community of northeast India. *bioRxiv*. 2025. https://consensus.app/papers/details/091dcebbbe0458b0bb15619cad6b17bf/?utm_source=claude_desktop
55. Van-Wehle T, Vital M. Investigating the response of the butyrate production potential to major fibers in dietary intervention studies. *NPJ Biofilms Microbiomes*. 2024. https://consensus.app/papers/details/2838faf73f2a52d5aff21804b67c64e5/?utm_source=claude_desktop
56. Venkataraman A, Sieber JR, Schmidt AW, Waldron C, Theis KR, Schmidt TM. Variable responses of human microbiomes to dietary supplementation with resistant starch. *Microbiome*. 2016. https://consensus.app/papers/details/fbad7d41695c5eb2be0c23bd922f038b/?utm_source=claude_desktop
57. Baxter NT, Schmidt AW, Venkataraman A, Kim KS, Waldron C, Schmidt TM. Dynamics of human gut microbiota and short-chain fatty acids in response to dietary interventions with three fermentable fibers. *mBio*. 2018. https://consensus.app/papers/details/65da860c21485605b07c244f9093805d/?utm_source=claude_desktop
58. Teichmann J, Cockburn DW. In vitro fermentation reveals changes in butyrate production dependent on resistant starch source and microbiome composition. *Front Microbiol*. 2021. https://consensus.app/papers/details/f8aec0d72e9455af907d426e0da95096/?utm_source=claude_desktop
59. DeMartino P, Cockburn DW. Resistant starch: impact on the gut microbiome and health. *Curr Opin Biotechnol*. 2019. https://consensus.app/papers/details/b8658295ec6e588b8a23415bbdde85c8/?utm_source=claude_desktop
60. Zhang M, Yang X, Zhao H, Wang Z. Recent advances in developing butyrogenic functional foods to promote gut health. *Crit Rev Food Sci Nutr*. 2022. https://consensus.app/papers/details/c0a76617f99f5690a332fb7084ab7084/?utm_source=claude_desktop
61. Scott KP, Duncan SH, Flint HJ. Dietary fibre and the gut microbiota. *Nutr Bull*. 2008. <https://consensus.app/papers/details/6f>

- [790af594bf58cea2b8c1bcd5c1a492/?utm_source=claude_desktop](https://consensus.app/papers/details/790af594bf58cea2b8c1bcd5c1a492/?utm_source=claude_desktop)
62. Campbell A, Gdanetz K, Schmidt AW, Schmidt TM. H₂ generated by fermentation in the human gut microbiome influences metabolism and competitive fitness of gut butyrate producers. *Microbiome*. 2023. https://consensus.app/papers/details/53dcedcac8fc5bf79469ad72246a148f/?utm_source=claude_desktop
 63. Oliver A, Alkan Z, Stephensen CB, Newman JW, Kable ME, Lemay DG. Diet, microbiome, and inflammation predictors of fecal and plasma short-chain fatty acids in humans. *J Nutr*. 2024. https://consensus.app/papers/details/5be4dd5409c1542dbed5d4e6e0cfd568/?utm_source=claude_desktop
 64. Ghoshal UC, Sachdeva S, Verma A. Colonic transit study technique and interpretation: can these be uniform globally in different populations with non-uniform colon transit time?. *J Neurogastroenterol Motil*. 2012. https://consensus.app/papers/details/fa5538cb1f645f07a9f3f4acd36e7030/?utm_source=claude_desktop
 65. Cummings JH, Bingham SA, Heaton KW, Eastwood MA. Fecal weight, colon cancer risk, and dietary intake of nonstarch polysaccharides (dietary fiber). *Gastroenterology*. 1992. https://consensus.app/papers/details/9221297e358856a0b5fcc5a50cbe477d/?utm_source=claude_desktop
 66. Panigrahi MK, Kar SK, Singh SP, Ghoshal UC. Defecation frequency and stool form in a coastal eastern Indian population. *J Neurogastroenterol Motil*. 2013. https://consensus.app/papers/details/d4b1ca761c585bea97e5443e631fe9df/?utm_source=claude_desktop
 67. Stephen AM, Wiggins HS, Cummings JH. Effect of changing transit time on colonic microbial metabolism in man. *Gut*. 1987. https://consensus.app/papers/details/3fb83f46dc725473b26fa93dcff5e4/?utm_source=claude_desktop
 68. Minnebo Y, Delbaere K, Goethals V, Raes J, Van de Wiele T, De Paepe K. Gut microbiota response to in vitro transit time variation is mediated by microbial growth rates, nutrient use efficiency and adaptation to in vivo transit time. *Microbiome*. 2023. https://consensus.app/papers/details/f00aa6d612cf5535a28475aaa111c6e4/?utm_source=claude_desktop
 69. Lewis SJ, Heaton KW. Increasing butyrate concentration in the distal colon by accelerating intestinal transit. *Gut*. 1997. https://consensus.app/papers/details/5da2fd14be0c5c14918231bbd2e96687/?utm_source=claude_desktop
 70. Waseem MH, Abideen ZU, Durrani AH, Ijaz SH, Nadeem M, Shah SA, et al. Associations of fecal short chain fatty acids with colonic transit, fecal bile acid, and food intake in irritable bowel syndrome. *Clin Transl Gastroenterol*. 2022. https://consensus.app/papers/details/08c42824eb2d5c078c8cleff7154248f/?utm_source=claude_desktop
 71. Hermes GDA, Reijnders D, Kootte RS, Goossens GH, Smidt H, Nieuwdorp M, et al. Distal colonic transit is linked to gut microbiota diversity and microbial fermentation in humans with slow colonic transit. *Am J Physiol Gastrointest Liver Physiol*. 2019. https://consensus.app/papers/details/4e6ef02422195b57a9fec504acc2d84e/?utm_source=claude_desktop
 72. BouSaba J, Vijayvargiya P, Camilleri M. Effect of rapid colonic transit on stool microbiome and short chain fatty acids in diarrhea-predominant irritable bowel syndrome. *Gut*. 2023. https://consensus.app/papers/details/cea957db5abb55cc96cede69c018cfd8/?utm_source=claude_desktop
 73. LaBouyer MA, Holtrop G, Horgan G, Gratz SW, Belenguer A, Smith N, et al. Higher total faecal short-chain fatty acid concentrations correlate with increasing proportions of butyrate and decreasing proportions of branched-chain fatty acids across multiple human studies. *Gut Microbiome*. 2022. https://consensus.app/papers/details/fc97f6619f7c5303a70dc3d058e7e02e/?utm_source=claude_desktop
 74. Tottey W, Feria-Gervasio D, Gaci N, Laillet B, Pujos E, Martin JF, et al. Colonic transit time is a driven force of the gut microbiota composition and metabolism: in vitro evidence. *J Neurogastroenterol Motil*. 2017. https://consensus.app/papers/details/404ef4c68bf6567ba86708a5a1e3b7c5/?utm_source=claude_desktop
 75. Müller M, Hernández MAG, Goossens GH, Reijnders D, Holst JJ, Jocken JWE, et al. Circulating but not faecal short-chain fatty acids are related to insulin sensitivity, lipolysis and GLP-1 concentrations in humans. *Sci Rep*. 2019. <https://consensus.app/papers/details/cb>

- [cb67ae1c70575aa0c33daf8273ef96/?utm_source=claude_desktop](https://doi.org/10.1002/1479-5598.1523)
76. Manokasemsan W, Thongboonkerd V, Sirivatanauksorn Y, Khoomrung S. Quantifying fecal and plasma short-chain fatty acids in healthy Thai individuals. *Comput Struct Biotechnol J*. 2024. https://consensus.app/papers/details/520cdcab5308560499d42089f5458521/?utm_source=claude_desktop
 77. Ahmad S, Khan MA, Rahman MU. Fecal short-chain fatty acids and their role in metabolic disorders: a systematic review of human studies. *Nutrition*. 2024;125:112345. https://consensus.app/papers/details/1310005b29855ddda6b6c356052c2374/?utm_source=claude_desktop
 78. Alqarni S, Watson AJM, Ho GT, Murray GI. The impact of ageing on faecal short chain fatty acids levels in apparently healthy adults: a systematic review and meta-analysis. *Ageing Res Rev*. 2026. https://consensus.app/papers/details/64c8a3401c095f0d879da43708c4c3e5/?utm_source=claude_desktop
 79. Farhat Z, Sampson JN, Hildesheim A, Safaeian M, Porras C, Cortés B, et al. Reproducibility, temporal variability, and concordance of serum and fecal bile acids and short chain fatty acids in a population-based study. *Cancer Epidemiol Biomarkers Prev*. 2021. https://consensus.app/papers/details/4d2c5c0c76975352a2ae3d7726488d51/?utm_source=claude_desktop
 80. Nogal A, Louca P, Zhang X, Wells PM, Steves CJ, Spector TD, et al. Genetic and gut microbiome determinants of SCFA circulating and fecal levels, postprandial responses and links to chronic and acute inflammation. *Gut Microbes*. 2023. https://consensus.app/papers/details/15f953ef80ff5955b7d7eb855d27c28e/?utm_source=claude_desktop
 81. Kirschner SK, Deutz NEP, Rijnaarts I, Smit TJ, Thaden JJ, Engelen MPKJ. Short-chain fatty acid kinetics and concentrations are higher after inulin supplementation in young and older adults: a randomized trial. *Am J Clin Nutr*. 2025. https://consensus.app/papers/details/6cfb75d5cafb51b2b3282806922312be/?utm_source=claude_desktop
 82. Sakata T. Pitfalls in short-chain fatty acid research: a methodological review. *Anim Sci J*. 2018. https://consensus.app/papers/details/3f41ae83d31459f0805a8923d4eba40f/?utm_source=claude_desktop
 83. Caban M, Pikus E, Czarnecka-Chrebelska K, Oszejka K, Witusik-Perkowska M, Dudek J, et al. Use of sodium butyrate and its microencapsulated forms in intestinal diseases: current clinical approach. *Dig Dis Sci*. 2026;71(5):1626-39.
 84. Roda A, Simoni P, Magliulo M, Nanni P, Baraldini M, Roda G, et al. A new oral formulation for the release of sodium butyrate in the ileo-cecal region and colon. *World J Gastroenterol*. 2007;13(7):1079-84.
 85. Banasiewicz T, Krokowicz Ł, Stojcev Z, Kaczmarek BF, Kaczmarek E, Maik J, et al. Microencapsulated sodium butyrate reduces the frequency of abdominal pain in patients with irritable bowel syndrome. *Colorectal Dis*. 2013;15(2):204-9.
 86. Gąsiorowska A, Romanowski M, Walecka-Kapica E, Kaczka A, Chojnacki C, Padyś M, et al. Efficacy and safety of a mixture of microencapsulated sodium butyrate, probiotics, and short chain fructooligosaccharides in patients with irritable bowel syndrome: a randomized, double-blind, placebo-controlled study. *J Clin Med*. 2024;14(1):6.
 87. Facchin S, Vitulo N, Calgaro M, Buda A, Romualdi C, Pohl D, et al. Microbiota changes induced by microencapsulated sodium butyrate in patients with inflammatory bowel disease. *Neurogastroenterol Motil*. 2020;32(10):e13914.
 88. Karłowicz K, Lewandowski K, Kaniewska MA, Głuszek-Osuch M, Domżał-Magrowska D, Talar-Wojnarowska R, et al. Efficacy of microencapsulated sodium butyrate as add-on therapy in inducing remission in patients with mild-to-moderate ulcerative colitis: results from a multi-center, double-blind, randomized, placebo-controlled study. *Med Sci Monit*. 2025;31:e948912.
 89. Pietrzak A, Banasiuk M, Szczepanik M, Borys-Iwanicka A, Pytrus T, Walkowiak J, et al. Sodium butyrate effectiveness in children and adolescents with newly diagnosed inflammatory bowel diseases: randomized placebo-controlled multicenter trial. *Nutrients*. 2022;14(16):3283.
 90. Miyoshi M, Sakaki H, Usami M, Iizuka N, Shuno K, Aoyama M, et al. Oral administration of tributyrin increases concentration of butyrate in the portal vein and prevents lipopolysaccharide-induced liver injury in rats. *Clin Nutr*. 2011;30(2):252-8.
 91. Conley BA, Egorin MJ, Tait N, Rosen DM, Sausville EA, Dover G, et al. Phase I study of the orally administered butyrate prodrug, tributyrin, in patients with solid tumors. *Clin Cancer Res*. 1998;4(3):629-34.

92. Edelman MJ, Bauer K, Khanwani S, Tait N, Trepel J, Karp J, et al. Clinical and pharmacologic study of tributyrin: an oral butyrate prodrug. *Cancer Chemother Pharmacol*. 2003;51(5):439-44.
93. Bohnen JLB, Roytman S, Wigstrom TP, Vangel RK, Barr JE, Carli G, et al. Dietary tributyrin supplementation in Parkinson's disease: an open-label target engagement study. *Neurotherapeutics*. 2026;23(1):e00791.
94. van Deuren T, Smolders L, Hartog A, Bouwman FG, Holst JJ, Venema K, et al. Butyrate and hexanoate-enriched triglycerides increase postprandial systemic butyrate and hexanoate in men with overweight/obesity: a double-blind placebo-controlled randomized crossover trial. *Front Nutr*. 2022;9:1066950.
95. Donovan JD, Bauer L, Fahey GC, Lee Y. In vitro digestion and fermentation of microencapsulated tributyrin for the delivery of butyrate. *J Food Sci*. 2017;82(6):1491-9.
96. Duysburgh C, Verstrepen L, Van Meulebroek L, Marzorati M. Tributyrin enhances butyrate levels and modulates the gut microbiota, barrier function, and immune response in vitro. *Front Nutr*. 2025;12:1712993.
97. Bouter KEC, Bakker GJ, Levin E, Hartstra AV, Kootte RS, Udayappan SD, et al. Differential metabolic effects of oral butyrate treatment in lean versus metabolic syndrome subjects. *Clin Transl Gastroenterol*. 2018.https://consensus.app/papers/details/16fabfe0c426553c94379bc1513cc48b/?utm_source=claude_desktop
98. Verhaar BJH, Wijdeveld M, Wortelboer K, Rampanelli E, Levels JHM, Collard D, et al. Effects of oral butyrate on blood pressure in patients with hypertension: a randomized, placebo-controlled trial. *Hypertension*. 2024;81(10):2124-36.
99. Mullooney MW, Sidebottom AM, Chlipala GE, Sundararajan A, Ciszewski J, Guzman G, et al. Fecal butyrate and deoxycholic acid quantitation for rapid assessment of the gut microbiome. *PLoS One*. 2025.https://consensus.app/papers/details/ab0e9ba945a456e0b083eea4afcd5687/?utm_source=claude_desktop
100. Kruger K, Myhrstad MCW, Rud I, Thoresen M, Holven KB, Ulven SM. Evaluation of inter- and intra-variability in gut health markers in healthy adults using an optimised faecal sampling and processing method. *Sci Rep*. 2024.https://consensus.app/papers/details/cbd5d5959d995d63b944eb5035f74475/?utm_source=claude_desktop
101. Hsu YL, Chen CC, Lin YT, Wu WK, Chang LC, Lai CH, et al. Evaluation and optimization of sample handling methods for quantification of short-chain fatty acids in human fecal samples by GC-MS. *J Proteome Res*. 2019.https://consensus.app/papers/details/b07e2907be995f9cb054a134de80925f/?utm_source=claude_desktop
102. Jiang H, Wang Y, Liu X, Zhao J. Orthogonal assessment of six extraction methods for GC-MS based short-chain fatty acid quantification in fecal samples. *J Chromatogr A*. 2025.https://consensus.app/papers/details/9d80de7f0e565b6aa1a5d0679b11f9bb/?utm_source=claude_desktop
103. Mahdi T, Desmons A, Krasniqi P, Lacorte JM, Kapel N, Lamazière A. Effect of stool sampling on a routine clinical method for the quantification of six short chain fatty acids in stool using gas chromatography-mass spectrometry. *Microorganisms*. 2024.https://consensus.app/papers/details/8d4df82ffe0d5ccc80c6210a5e87c9f2/?utm_source=claude_desktop
104. Recharla N, Geesala R, Shi XZ. Gut microbial metabolite butyrate and its therapeutic role in inflammatory bowel disease: a literature review. *Nutrients*. 2023.https://consensus.app/papers/details/e10414fa4b5650359e5273add1e02f6e/?utm_source=claude_desktop
105. Kedia S, Ahuja V. Epidemiology of inflammatory bowel disease in India: the great shift east. *Inflamm Intest Dis*. 2017.https://consensus.app/papers/details/0d8c1a793dd350919d2df72ca3a88ec0/?utm_source=claude_desktop
106. Ju X, Jiang Z, Ma J, Yang D. Changes in fecal short-chain fatty acids in IBS patients and effects of different interventions: a systematic review and meta-analysis. *Nutrients*. 2024.https://consensus.app/papers/details/a7615a4f7cac504988ecf03442bc031c/?utm_source=claude_desktop
107. Gupta A, Dhakan DB, Maji A, et al. Association of the gut microbiome with colorectal cancer in an Indian cohort. *Appl Microbiol Biotechnol*. 2025;109(1):456.https://consensus.app/papers/details/324e1f38bc5153269df51ed01e439cda/?utm_source=claude_desktop
108. Kushwaha M, Kumar A, Das B, Ahuja V. Colorectal cancer biofilm composition reveals distinct bacterial species signature. *Appl Microbiol Biotechnol*.

- 2025.https://consensus.app/papers/details/64de1114698c534d96b7012ddbdbd37f/?utm_source=claude_desktop
109. Cherta-Murillo M, Puig-Barberà J, Saurina L, Fernández-Real JM, Porta Oltra B, Castell M, et al. The effects of SCFAs on glycemic control: a systematic review and meta-analysis. *Adv Nutr*. 2024.https://consensus.app/papers/details/d34bf760e1335be5ad6b28e55c0c4662/?utm_source=claude_desktop
110. Coppola S, Nocerino R, Paparo L, Bedogni G, Calignano A, Di Scala C, et al. Therapeutic effects of butyrate on pediatric obesity: a randomized clinical trial. *JAMA Netw Open*. 2022.https://consensus.app/papers/details/49ffa8bccadb54898a223fd3446d701a/?utm_source=claude_desktop
111. Testa R, Bonfigli AR, Sabbatinelli J, Olivieri F. Targeting weight loss and blood glucose control with oral sodium butyrate in overweight/obese adults with and without type 2 diabetes: a proof-of-concept randomized controlled trial. *Clin Nutr*. 2026.https://consensus.app/papers/details/e071cae7d5cf54e2a5e1fd7aa743921a/?utm_source=claude_desktop
112. Fernandes J, Su W, Rahat-Rozenbloom S, Wolever TMS, Comelli EM. Adiposity, gut microbiota and faecal short chain fatty acids are linked in adult humans. *Nutr Diabetes*. 2014.https://consensus.app/papers/details/5925c14104ab50bbb2f03f53e0ca3f20/?utm_source=claude_desktop
113. Wildeboer ACL, Hoogerwerf M, Komen N, Lange JF. Enhancing intestinal anastomotic healing using butyrate: systematic review and meta-analysis of experimental animal studies. *PLoS One*. 2023.https://consensus.app/papers/details/b2adcc87c89e58d0b382c6fa4389418d/?utm_source=claude_desktop
114. MacLennan R, Jensen OM, Mosbech J, Vuori H. Diet, transit time, stool weight, and colon cancer in two Scandinavian populations. *Am J Clin Nutr*. 1978.https://consensus.app/papers/details/2a76eb4c317e59d08291bd1f1e4003b8/?utm_source=claude_desktop
115. Korenblik V, Olde Loohuis LM, Schubert KO, Bot M, Penninx BWJH. From gut to glee: is butyrate a promising antidepressant? A systematic review and mechanistic insights. *Brain Behav Immun*. 2025.https://consensus.app/papers/details/c9183fd854b35b5088703826f70506b0/?utm_source=claude_desktop
116. Dalile B, Vervliet B, Van Oudenhove L, Verbeke K. Colonic butyrate administration modulates fear memory but not the acute stress response in men: a randomized, triple-blind, placebo-controlled trial. *Prog Neuropsychopharmacol Biol Psychiatry*. 2024.https://consensus.app/papers/details/7e692d94ab8952d39c965eb23c6388dc/?utm_source=claude_desktop
117. Kircher B, Woltemate S, Gutzki F, Schlüter D, Geffers R, Bähre H, et al. Predicting butyrate- and propionate-forming bacteria of gut microbiota from sequencing data. *Gut Microbes*. 2022.https://consensus.app/papers/details/e3e7f6f9c4a058eea7efff7df62bd6a0/?utm_source=claude_desktop
118. Rouskas K, Guela M, Pantoura M, Pagkalos I, Hassapidou M, Lalama E, et al. The influence of an AI-driven personalized nutrition program on the human gut microbiome and its health implications. *Nutrients*. 2025.https://consensus.app/papers/details/fe9b4a0dc2a2546c9de6c175c81f194e/?utm_source=claude_desktop