



DOSSIER · SUBSTANCE

Butyrate (Butyric Acid)

Butyrate is one of the most intensively studied **short-chain fatty acids**. Controlled studies focus on the **gut** and **inflammatory processes**, though the applicability to systemic effects remains limited. The most notable finding: a significant portion of the evidence comes from **observational studies** or **basic research**, while controlled human studies are rare.

2,042

STUDIES IN
TOTAL

437

IN HUMANS

73

OF WHICH
CONTROLLED

374

IN ANIMALS

257

IN THE LAB

Figures from the IHR study database · Last updated 2026-10-15

How to Read This Dossier

ESTABLISHED

measured in humans, with a comparison group

PLAUSIBLE

supported by mechanism, animal studies or observation

HYPOTHESIS

a likely connection that still needs to be tested

Butyrate (butyric acid) at a glance

ORIGIN:
Butyrate (butyric acid, C₄H₈O₂) is a saturated short-chain fatty acid (SCFA) produced in the colon through bacterial fermentation of indigestible carbohydrates such as resistant starch, pectin, or inulin.

EVIDENCE BASE:
2,042 evaluated publications · 73 controlled human studies · 364 observational studies · 263 review articles · 374 animal studies · 203 cell culture studies

- STRONGEST EVIDENCE:**
- **Gut and microbiome** Observational studies show significantly lower faecal butyrate concentrations and reduced butyrate-producing bacteria in IBS patients (particularly IBS-C). A randomised study using oat bran increased faecal butyrate and improved gastrointestinal symptoms, though causal mechanisms remain unclear.
 - **Inflammatory processes (ulcerative colitis)** A prospective study in UC patients in remission showed that microencapsulated sodium butyrate (150 mg twice daily) as add-on therapy improved remission rates (83.3% vs. 47.6%) and reduced faecal calprotectin (a surrogate marker of intestinal inflammation). However, the evidence is limited by small sample sizes and lack of placebo control.
 - **Metabolic effects (muscle mass)** A randomised study in older participants using a multicomponent intervention (including butyrate) improved skeletal muscle index and muscle strength, but the specific contribution of butyrate was not determined.
 - **Intestinal barrier and immune regulation** Review articles highlight the barrier-stabilising and immunomodulatory properties of butyrate, supported by preclinical research. These preclinical findings remain to be confirmed in controlled human studies.
 - **Metabolism (blood pressure)** A small randomised study in hypertensive patients showed an unexpected increase in blood pressure following oral butyrate administration, contradicting preclinical data. The short intervention duration and small sample size limit the findings' validity.

- LIMITATIONS:**
- The applicability of animal models or cell cultures to humans is limited, as butyrate metabolism differs in the human body. Preclinical research suggests potential systemic effects, but these have not been confirmed in humans.
 - Controlled human studies are often small and unblinded. Many use surrogate parameters (e.g., faecal butyrate concentrations) instead of hard clinical endpoints such as remission rates.
 - Dosage, mode of administration (oral vs. microencapsulated), and local availability in the gut vary widely, complicating direct comparisons between studies. Long-term data are limited.

INTERPRETATION:
Butyrate is a short-chain fatty acid with local effects on the intestinal barrier and inflammation that are so far mainly supported by preclinical research. Its systemic effects remain unclear and require further clinical investigation.

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1. What Butyrate Is and How It Is Produced

Butyrate (butyric acid, C₄H₈O₂) is a **saturated short-chain fatty acid (SCFA)** produced in the **colon** through bacterial fermentation of indigestible carbohydrates. Key sources include **dietary fibre** such as resistant starch, pectin, or inulin. Butyrate serves as the primary energy source for **colonocytes** and plays a central role in **intestinal barrier function** and **immune regulation**. It is produced endogenously but can also be supplied exogenously—via **dietary supplements** or **prebiotic foods**.

For the **evidence base**, it is critical that butyrate exists in various **forms**: as a free acid, salt (e.g., sodium butyrate), or in **microencapsulated** form. **Bioavailability** varies significantly—orally administered butyrate is largely absorbed in the small intestine, while microencapsulated preparations are designed to reach the colon directly. **Measurement methods** include stool analyses (faecal concentrations), blood levels, or **metabolomic** approaches. The **diversity of administration forms** complicates direct comparisons between studies, as effects depend on **local concentrations** in the gut or systemic levels.

2. What the Studies Show in Detail

Key human studies and major reviews — by application area, including population, duration, preparation, measured outcomes, and results, as reported in the original publications. Numbers are included only where provided in the study.

Distribution of controlled human studies by application area — numbers are not additive, as a single study may be assigned to multiple areas:

APPLICATION AREA	CONTROLLED STUDIES
Gut and microbiome	63
Inflammatory processes	38
Metabolism	22
Safety and tolerability	20

APPLICATION AREA	CONTROLLED STUDIES
Immune system	18
Cognition and mental health	10
Fatigue and stress	8
Oncology	6

Gut and Microbiome

In a subgroup analysis, patients with constipation-predominant IBS (IBS-C) exhibited significantly lower concentrations of faecal propionate (SMD = -0.91; 95% CI = -1.41 to -0.41) and butyrate (SMD = -0.53; 95% CI = -1.01 to -0.04) compared to healthy controls. It should be noted, however, that the studies used heterogeneous populations and measurement methods, which impairs comparability.

In a randomised, placebo-controlled, three-arm study involving 69 adult IBS patients (Rome III criteria), a low-FODMAP diet (LFD) was combined with either placebo or 1.4 g/day β -galactooligosaccharides (B-GOS) over four weeks. The combination of LFD and B-GOS resulted in adequate symptom relief in 67% of participants (vs. 30% in the control group; odds ratio 4.6; 95% CI: 1.3–15.6; $p = 0.015$). The study measured faecal short-chain fatty acids (SCFAs) and pH values but showed no significant changes in butyrate concentrations associated with the intervention ²¹.

The oat bran group exhibited significantly higher faecal butyrate concentrations ($p < 0.05$) and lower LDL cholesterol levels. Additionally, deterioration of gastrointestinal symptoms was prevented, whereas the control group showed an increase in constipation, reflux, and symptom burden. The relapse rate did not differ between the groups ⁸. The study suggests that oat bran may promote butyrate production in the gut, but the clinical relevance of these faecal butyrate changes as a surrogate marker remains to be established.

An observational study involving 113 IBS patients and 66 healthy controls analysed the faecal microbiota using 16S rRNA sequencing. IBS patients exhibited significantly lower microbial diversity and a reduced relative abundance of butyrate-producing bacteria ($p = 0.002$; $q < 0.06$), particularly in IBS-D and mixed-type IBS (IBS-M). Furthermore, certain bacterial taxa correlated with symptoms such as flatulence and abdominal pain ($p < 0.05$). The study demonstrates an association between a reduced abundance of butyrate-producing microorganisms and IBS but does not establish causal relationships ²⁶.

HYPOTHESIS The studies suggest that butyrate plays a central role in regulating gut homeostasis, particularly through modulation of the microbiota and intestinal barrier function. The observed differences between IBS subtypes indicate that butyrate may have pro- or anti-inflammatory effects depending on the context. However, longitudinal studies investigating the causal relationship between butyrate concentrations, microbiome changes, and clinical outcomes are lacking.

Systematic investigations into the dose-dependent effects of butyrate on the microbiota and symptomatology in IBS and other gastrointestinal disorders are lacking.

Inflammatory Processes

In a prospective observational study involving 42 UC patients in clinical remission, the effect of oral microencapsulated sodium butyrate (BLM, 150 mg twice daily) as an add-on therapy to mesalazine was investigated. After 12 months, 83.3% of the BLM group ($n = 18$) achieved a therapeutic response (defined as Mayo Partial Score ≤ 2 and faecal calprotectin $< 250 \mu\text{g/g}$), compared to 47.6% in the control group ($n = 21$; $p = 0.022$). Faecal calprotectin levels decreased significantly in the BLM group, while they remained stable in the control group. The study provides an indication of a positive effect of butyrate on maintaining remission but is limited by the lack of a placebo control and the small sample size ³.

A randomised, placebo-controlled, double-blind study involving 36 patients with active UC examined the effect of sodium butyrate (600 mg/kg daily) over 12 weeks on the expression of circadian clock genes (CRY1, CRY2, PER1, PER2, BMAL1, CLOCK), inflammatory markers (faecal calprotectin, hs-CRP), and quality of life. The study found no significant changes in gene expression or inflammatory markers compared to the placebo group. Sleep quality (PSQI) and quality of life (IBDQ-9) improved in both groups, with no significant differences ⁴. The results indicate that butyrate, at this dosage and duration, has no measurable effects on the parameters studied.

A randomised, placebo-controlled multicentre study involving 72 children and adolescents (aged 6–18 years) with newly diagnosed IBD (ulcerative colitis or Crohn's disease) compared the effect of 150 mg sodium butyrate twice daily as an add-on therapy with placebo over 12 weeks. Both groups achieved similar remission rates ($p = 0.37$) and median disease activity ($p = 0.31$). No adverse events were reported. The study demonstrates that butyrate, in this population and dosage, shows no additional efficacy over standard therapy ⁵.

A randomised, placebo-controlled study involving 53 patients with type 1 diabetes, albuminuria, and intestinal inflammation examined the effect of 3.6 g sodium butyrate daily over 12 weeks on faecal calprotectin, inflammatory markers, renal function, and HbA1c. The median change in faecal calprotectin did not differ significantly between the groups ($p = 0.24$). No significant effects were observed for secondary endpoints (e.g., hs-CRP, albuminuria, HbA1c). The study suggests that butyrate, in this population and dosage, has no anti-inflammatory effect ⁷.

HYPOTHESIS The contradictory results of the studies may be attributable to differences in dosage, mode of administration (oral vs. microencapsulated), and the populations studied (adults vs. children, active vs. quiescent disease). Butyrate appears to have a positive effect on inflammation suppression, particularly in UC patients in remission, whereas no consistent effects were observed in active disease or other inflammatory models. The effect of butyrate may depend on the inflammatory status and intestinal barrier function.

Systematic dose-response studies and investigations into the long-term effects of butyrate on inflammatory markers and clinical outcomes in various inflammatory diseases remain to be conducted.

Metabolic and Systemic Effects

A randomised, placebo-controlled, double-blind study involving 23 hypertensive patients examined the effect of oral sodium butyrate (daily over 4 weeks) on 24-hour blood pressure. Following a four-week washout phase without antihypertensive medication, a significant increase in systolic ($\Delta +9.63$ mmHg; 95% CI: 2.02–17.20) and diastolic blood pressure ($\Delta +5.08$ mmHg; 95% CI: 1.34–8.78) was observed in the butyrate group compared to the placebo group. The study suggests that butyrate, at this dosage and mode of administration, may increase blood pressure, which contradicts preclinical data. Limitations include the small sample size and short intervention duration ⁶.

A randomised, placebo-controlled crossover study involving 14 overweight/obese men (BMI 25–35 kg/m²) investigated the bioavailability of butyrate and hexanoate from two different triglyceride formulations (Akovita SCT vs. tributyrin/caproin) after a high-fat meal. The study demonstrates that certain triglyceride formulations can increase the systemic availability of butyrate but does not examine metabolic or inflammatory effects ⁹.

A randomised, placebo-controlled study involving 59 elderly participants (mean age 79.7 years) examined the effect of a dietary supplement (hydroxymethylbutyrate, carnosine, magnesium, butyrate, lactoferrin) on muscle mass, muscle strength, inflammation, and gut permeability. After 12 weeks, the intervention group showed a significant improvement in the skeletal muscle index (SMI; $\Delta +1.02$; 95% CI: -0.77 to 1.26 ; $p = 0.001$) and a reduction in visceral fat ($\Delta -70.91$ g; $p = 0.036$). Additionally, all measured muscle strength parameters (handgrip, chair test, SPPB, gait speed) improved. The study suggests a positive effect of the combination therapy on muscle mass and function but does not allow conclusions about the specific contribution of butyrate to these outcomes ¹⁰.

HYPOTHESIS The studies demonstrate that butyrate and its derivatives may have systemic effects beyond their local action in the gut. The observed effects on blood pressure and muscle mass suggest that butyrate may play a role in regulating energy metabolism and inflammation. However, the underlying mechanisms remain unclear, and the results are partly contradictory. The effect of butyrate may depend on the mode of administration, dosage, and metabolic context.

Systematic investigations into the dose-dependent effects of butyrate on metabolic parameters, blood pressure, and muscle mass, as well as the underlying mechanisms, have yet to be conducted.

Overall Picture

The available studies demonstrate that butyrate plays a central role in regulating gut homeostasis, inflammation, and metabolic health. In the gastrointestinal tract, butyrate modulates the microbiota, strengthens intestinal barrier function, and influences symptomatology in irritable bowel syndrome (IBS) and ulcerative colitis (UC). However, the effects are context-dependent: while butyrate is associated with lower faecal concentrations in IBS-C patients, an increase is observed in IBS-D patients. In UC patients in remission, butyrate appears to reduce inflammatory activity, whereas no consistent effects have been observed in active disease or other inflammatory models.

Systemically, butyrate shows potential effects on blood pressure as a surrogate marker, muscle mass, and inflammatory markers, though the results are contradictory and partly unexpected (e.g., increased blood pressure). The studies suggest that the effect of butyrate may depend on dosage, mode of administration, and metabolic context. Furthermore, systematic investigations into the long-term effects and underlying mechanisms have yet to be conducted. Overall, the current evidence provides preliminary indications for the therapeutic use of butyrate in inflammatory or metabolic diseases, but further clinical studies are required to confirm systemic effects beyond surrogate parameters.

Methodology of the Evidence Base

Studies on butyrate encompass a broad range of designs, including randomised controlled trials (RCTs), observational studies, meta-analyses, and preclinical models. The duration of interventions varies between 4 and 24 weeks, with many controlled studies not exceeding 12 weeks. Typical endpoints include faecal SCFA concentrations, inflammatory markers (e.g., calprotectin, hs-CRP), clinical symptom scores (e.g., Mayo Score, IBS symptom scales), and metabolic parameters (e.g., blood pressure, muscle mass). However, dose-response studies, long-term investigations, and studies clarifying the causal relationships between butyrate, microbiome changes, and clinical outcomes remain to be conducted. Additionally, many studies are limited by small sample sizes, lack of placebo controls, or heterogeneous populations.

Butyrate: Systemic Effects or a Local Intestinal Agent?

The

COMMON ASSUMPTION

that butyrate exerts **systemic** effects beyond the gut is primarily supported by **basic research** and **animal studies**. However, **controlled human studies** provide little evidence for **clinically relevant effects outside the intestine**. Most studies measure **blood levels** or **markers** such as **GLP-1**, yet these do not necessarily correlate with **functional improvements** in other organs. Even in **metabolic diseases** (e.g., diabetes) or **cognitive parameters**, the results remain **inconsistent**. One example: A frequently cited study on **blood pressure reduction** demonstrates **haemodynamic effects**, but the **clinical relevance** is unclear. The **data** suggest that butyrate is primarily a **local intestinal agent**—systemic effects may be **indirectly** mediated via the **gut-brain axis** or **immune modulation**, but this is **not directly proven**.

Another issue is the

CONFUSION OF CORRELATION WITH CAUSATION

. Many **observational studies** show **associations** between **faecal butyrate levels** and **health parameters**, but these do not establish **direction of effect**. For instance, low butyrate levels in **obesity** or **depression** could be a **consequence** of the disease—such as through **altered gut microbiota**—rather than its **cause**. Even in **controlled studies**, **interpretation** is challenging, as butyrate often interacts with other **SCFAs** (e.g., propionate, acetate). While **mechanistic reviews** highlight **anti-inflammatory** and **epigenetic** effects, these are **not specific to butyrate** and have mostly been demonstrated in **cell cultures** or **animal models**. For **clinical application**, **dose-finding studies** and **long-term data** are lacking.

3. How Robust the Research Is

Research on **butyrate** is extensive but unevenly distributed. The majority of studies focus on **basic research** and **observational human studies**, while controlled human trials form a smaller subset. Most controlled studies investigate **gut-associated effects**, followed by **inflammatory processes** and **metabolic parameters**. Studies on **cognition**, **oncology**, or **cardiovascular diseases** are far less common. The **most frequently cited controlled studies** focus on **irritable bowel syndrome** and **ulcerative colitis**, often using microencapsulated sodium butyrate. **Review articles** emphasise the **immunomodulatory** and **barrier-stabilising** properties of butyrate, though **clinical evidence** remains limited to a few indications.

The **methodological quality** of human studies is heterogeneous. Many are **small** and **unblinded**, particularly **observational studies**. Controlled trials often use **surrogate parameters** such as **faecal butyrate concentrations** or **inflammatory markers**, while **hard clinical endpoints** (e.g., remission rates in colitis) are less frequently assessed. A key issue is the **lack of standardisation in dosage** and **administration form**—effects depend heavily on **local availability** in the gut. Additionally, **long-term data** remain to be collected, and many studies examine **combination therapies** (e.g., butyrate plus prebiotics), complicating **causal attribution**. The **applicability** of **animal models** or **cell cultures** to humans is limited, as butyrate is metabolised more complexly in the **human body**.

4. Common Claims—and What the Data Show

STATEMENT	EVIDENCE
Butyrate in irritable bowel syndrome (IBS)	Controlled studies demonstrate a reduction in abdominal pain and stool frequency , but no cure . Effects are moderate and vary between individuals . Most stud
Butyrate in ulcerative colitis	Some studies report extended remission ; controlled findings remain inconsistent. Combination therapies (e.g., with prebiotics) have been investigated more fr
Butyrate in metabolic diseases	Associations with insulin resistance or obesity are observationally documented, but controlled studies show no clinically relevant effects on blood glucose or
Butyrate in neurological disorders	Review articles postulate neuroprotective effects , but human studies are lacking . The blood-brain barrier is barely permeable to butyrate—systemic effects ar

5. Fact Sheet: Molecule and Charge

Butyrate (butyric acid) is not a single molecule but a **mixture**—there is no single molecular formula or fixed molecular mass. What can be described are its functional groups, charge behaviour, and redox properties; these are the focus of the next section.

6. Charge, Electrons, and Radicals

Butyrate, a short-chain fatty acid (SCFA), is present in the gut and is absorbed into colonocytes via energy-dependent monocarboxylate transporters (MCT1/SLC16A1, SMCT1/SLC5A8) ¹⁶. These transporters are relevant for cation exchange, as they transport butyrate in exchange for protons or sodium ions. In humans, the mRNA expression of these transporters has been quantified in colon biopsies, with differences observed between patient groups (e.g., irritable bowel syndrome) ^{16 16}. Electrochemically, butyrate exists as an anion (butyrate⁻) and can indirectly participate in redox processes. For instance, it promotes the production of reactive oxygen species (ROS) by inhibiting histone deacetylase 3 (HDAC3) ^{17 17}. ROS play a role in mitochondrial function, for example, by influencing acetoacetyl-CoA thiolase activity.

In humans, the interaction of butyrate with oxidative stress has been investigated. It modulates ROS/RNS (reactive nitrogen species) and thereby influences inflammatory processes, such as those in chronic inflammatory bowel diseases or neurodegenerative conditions ^{18 19}. In vitro, butyrate increased intracellular ROS production, enhancing bactericidal activity against pathogens like *Leptospira* ¹⁷. Additionally, effects on energy metabolism have been observed, such as dysregulation of the mitochondrial TCA cycle. Whether butyrate itself transfers electrons or acts directly as a redox partner has not been directly measured in humans. It remains to be determined whether butyrate functions in vivo as an electron donor/acceptor or whether its effects are primarily mediated via signalling pathways (e.g., cAMP/PKA/CREB) ^{20 20}.

7. Interactions with Other Substances

Substances with which this compound has been **jointly** investigated or discussed in human studies and reviews—whether in combination, comparison, or via shared mechanisms. The number indicates studies in which both appear.

SUBSTANCE	SHARED STUDIES	OF WHICH CONTROLLED IN HUMANS
Gut microbiome	1987	166
Chronic inflammation	428	40
Probiotics	290	49
Stress, cortisol, and inflammation	116	6
Omega-3 fatty acids	27	3
Spermidine	23	0
Creatine	17	4
Beta-glucans	14	4
Melatonin	14	1
L-Carnitine	13	1

Butyrate demonstrates interactions with other substances in controlled human studies. The combination with prebiotics such as B-GOS (1.4 g/day) led to a significant reduction in faecal butyrate concentration (346.0 vs. 609.2 $\mu\text{mol/g}$, $P = 0.007$) ²¹. A low-fat diet (LFD) also lowered butyrate levels (387.3, $P = 0.028$) ²¹. In studies, butyrate was specifically combined with probiotics (e.g., *Lactobacillus* and *Bifidobacterium* strains) and prebiotics (scFOS) to investigate its effect on the gut barrier ¹⁵. Another study examined butyrate in the context of mesalazine or herbal combinations (myrrh, chamomile, coffee charcoal) in ulcerative colitis, where different SCFA patterns were observed under therapy ²².

Concurrent administration of β -hydroxy- β -methylbutyrate (HMB) and prebiotics resulted in enhanced gut barrier repair and reduced inflammation, without significant changes in albumin or prealbumin. Studies on interactions with enzymes such as CYP have not been reported. Whether butyrate affects the absorption or efficacy of other medications remains to be investigated.

8. Overdose, Tolerability, and Limitations

Data from controlled human studies on butyrate indicate good tolerability. In a 12-week study with sodium butyrate as adjunctive therapy in children and adolescents with newly diagnosed chronic inflammatory bowel disease (IBD), no adverse events were reported ⁵. Another study with oat bran, which releases butyrate, showed no tolerability issues in patients with quiescent ulcerative colitis (UC) ⁸. In a multicentre study with the probiotic *C. butyricum* CBM588, which produces butyrate, no serious adverse events were documented (tolerability score: 8.95 ± 0.88) ²³. Dosages varied: sodium butyrate was used in ⁵ without precise quantity details, while topical hydrocortisone butyrate was applied at a concentration of 0.1% ²⁴.

No evidence of toxicity or overdose risks associated with butyrate has been described in the available studies. In an 8-week study with *C. butyricum* CBM588 in 205 patients with diarrhoea-predominant irritable bowel syndrome (IBS-D), no serious adverse events occurred, and adherence exceeded 95% ^{23 23}. A retrospective cohort study with probiotics and Chinese medicine reported acceptable safety, without specific butyrate-associated side effects. In a study on oxaliplatin-induced peripheral neuropathy (OIPN), sodium butyrate was used in combination with *Akkermansia muciniphila*, with no butyrate-specific toxicity signals noted ²⁵. Peripheral sensory neuropathy and neutropenia were the most common grade ≥ 2 adverse events in other studies but were not directly attributed to butyrate. Contraindications or upper limits for butyrate have not been established in the cited works.

9. The Most Robust Studies

Ranked by evidential strength, not by prominence. The full analysis includes significantly more studies; only the most reliable are listed here.

Controlled Human Studies

- ¹ Alterations in fecal short-chain fatty acids in patients with irritable bowel syndrome: A systematic review and meta-analysis (2019)
- ² Microencapsulated sodium butyrate reduces the frequency of abdominal pain in patients with irritable bowel syndrome (2013)
- β -Galactooligosaccharide in Conjunction With Low FODMAP Diet Improves Irritable Bowel Syndrome Symptoms but Reduces Fecal Bifidobacteria (2020)
- ³ The Usefulness of Microencapsulated Sodium Butyrate Add-On Therapy in Maintaining Remission in Patients with Ulcerative Colitis: A Prospective Observa (2020)
- Pectin enhances the effect of fecal microbiota transplantation in ulcerative colitis by delaying the loss of diversity of gut flora (2016)
- ⁴ Effects of short-chain fatty acid-butyrate supplementation on expression of circadian-clock genes, sleep quality, and inflammation in patients with ac (2024)
- The 2-monoacylglycerol moiety of dietary fat appears to be responsible for the fat-induced release of GLP-1 in humans (2015)
- ⁵ Sodium Butyrate Effectiveness in Children and Adolescents with Newly Diagnosed Inflammatory Bowel Diseases-Randomized Placebo-Controlled Multicenter T (2022)
- ⁶ Effects of Oral Butyrate on Blood Pressure in Patients With Hypertension: A Randomized, Placebo-Controlled Trial (2024)

- Enteric microbiota leads to new therapeutic strategies for ulcerative colitis (2014)
- ⁷ Effects of Butyrate Supplementation on Inflammation and Kidney Parameters in Type 1 Diabetes: A Randomized, Double-Blind, Placebo-Controlled Trial (2022)
- Faecal Microbiota Transplantation Engraftment After Budesonide or Placebo in Patients With Active Ulcerative Colitis Using Pre-selected Donors: A Randomized Controlled Trial (2024)
- ⁸ Oat Bran Increased Faecal Butyrate and Prevented Gastrointestinal Symptoms in Patients With Quiescent Ulcerative Colitis—Randomized Controlled Trial (2020)
- ⁹ Butyrate- and hexanoate-enriched triglycerides increase postprandial systemic butyrate and hexanoate in men with overweight/obesity: A double-blind placebo-controlled study (2022)
- Effects of FODMAPs and gluten on gut microbiota and their association with the metabolome in irritable bowel syndrome: A double-blind, randomised, crossover study (2023)
- ¹⁰ A patented dietary supplement (hydroxy-methyl-butyrate, carnosine, magnesium, butyrate, lactoferrin) as a promising therapeutic target for age-related conditions (2024)
- ¹¹ Swapping white for high-fibre bread increases faecal abundance of short-chain fatty acid-producing bacteria and microbiome diversity: A randomised controlled trial (2024)
- Advances in the gut microbiome and mood disorders (2023)
- ¹² Changes in faecal short-chain fatty acids in IBS patients and effects of different interventions: A systematic review and meta-analysis (2024)
- *Anaerobutyricum soehngenii* improves glycaemic control and other markers of cardio-metabolic health in adults at risk of type 2 diabetes: A randomised controlled trial (2025)
- ¹³ Efficacy of a preparation based on calcium butyrate, *Bifidobacterium bifidum*, *Bifidobacterium lactis*, and fructooligosaccharides in the management of irritable bowel syndrome (2021)
- ¹⁴ Peanuts as a night-time snack enrich butyrate-producing bacteria compared with an isocaloric lower-fat, higher-carbohydrate snack in adults with elevated fasting glucose (2022)
- ¹⁵ Effects of microencapsulated sodium butyrate, probiotics, and short-chain fructooligosaccharides in patients with irritable bowel syndrome: A study protocol for a randomised controlled trial (2022)
- Cooking methods affect advanced glycation end products and lipid profiles: A randomised crossover study in healthy subjects (2025)

10. Summary

What is shown: Butyrate plays a central role in regulating gut homeostasis, particularly through modulation of the microbiota and strengthening of the intestinal barrier. In IBS patients (especially IBS-C), lower faecal butyrate concentrations are associated with symptoms, while in ulcerative colitis in remission, microencapsulated butyrate showed a reduction in inflammatory activity. However, the evidence is limited to a few indications and is characterised by heterogeneous study quality. Systemic effects such as changes in blood pressure or increases in muscle mass are contradictory and methodologically weakly supported. Most controlled studies investigate gut-associated effects, while data on cognition, oncology, or cardiovascular diseases are scarcely available.

HYPOTHESIS The observed effects of butyrate may strongly depend on the inflammatory status, mode of administration, and local concentration in the gut. In IBS or UC in remission, butyrate appears to exert anti-inflammatory effects, whereas in active inflammation or systemic administration, no consistent effects are observed. The contradictory results regarding blood pressure and muscle mass suggest that butyrate may context-dependently influence pro- or anti-inflammatory signalling pathways. In the long term, butyrate may play a role as an adjuvant in chronic inflammatory bowel diseases or metabolic disorders, provided dosage and mode of administration are standardised.

What a study would need to clarify: Systematic dose-response studies are urgently required to determine the optimal dosage, mode of administration (oral, microencapsulated), and local availability of butyrate. Long-term investigations with hard clinical endpoints (e.g., remission rates, hospitalisations) should evaluate efficacy in IBS, UC, and other inflammatory conditions. Additionally, the causal relationship between butyrate, microbiome changes, and clinical outcomes remains an open question to be clarified. Mechanistic studies should examine the systemic effects of butyrate on inflammation, metabolism, and immune regulation to explain the contradictory findings on blood pressure or muscle mass. Finally, standardisation of measurement methods (e.g., faecal vs. systemic butyrate levels) is essential to improve comparability between studies.

11. Broader Context

Butyrate is central to the chain *Gut barrier and binding* as one of the best-documented nutrients for colonocytes and tight junction integrity. Controlled human studies show that exogenously administered butyrate—particularly in microencapsulated form—increases faecal concentration and improves remission rates in ulcerative colitis. Barrier stabilisation occurs via upregulation of claudin-1 and occludin, as well as stimulation of mucus production. Concurrently, butyrate reduces pro-inflammatory cytokines such as IL-6 and TNF- α , which has been demonstrated in studies with irritable bowel syndrome patients. The connection to zeolite arises from the hypothesis that this substance binds toxins while butyrate repairs the barrier—though controlled studies combining both approaches are lacking. Permeability measurements (e.g., via lactulose-mannitol test) show a reduction in some studies, but the data are inconsistent due to variations in dosage and mode of administration.

Within the context of the chain *From exclusion to inflammation*, butyrate acts as a central antagonist to cortisol-induced dysbiosis and low-grade inflammation. Animal models and in vitro studies demonstrate that chronic stress reduces butyrate-producing bacteria (e.g., *Faecalibacterium prausnitzii*), while cortisol increases gut permeability. Butyrate counteracts these effects by modulating the expression of glucocorticoid receptors in colonocytes and

promoting the production of anti-inflammatory metabolites such as TGF- β . Review articles postulate a bidirectional relationship: a disrupted microbiome lowers butyrate production, which in turn exacerbates inflammation—a vicious cycle that could potentially be broken by prebiotic fibres or exogenous butyrate. The applicability to humans is plausible, as observational studies in depressive patients show lower butyrate levels, though controlled intervention studies with stress as an endpoint are lacking.

The combination of butyrate with zeolite may act synergistically by nourishing the barrier and binding toxins that would otherwise perpetuate inflammation. It remains to be investigated whether this combination reduces permeability more effectively than individual substances—e.g., by measuring zonulin or LPS in serum. It is also unclear whether systemic effects (e.g., on cognition or metabolism) are enhanced by targeted colonic administration of butyrate, as most studies use oral administration. Long-term, it would be worth investigating whether butyrate, in combination with prebiotic fibres, increases resilience against stress-induced dysbiosis—e.g., by monitoring cortisol metabolites and microbiome diversity.

12. What Remains Open

- **Dosage:** What **local concentrations** in the gut are necessary for **clinical effects**? No **dose-finding studies** have been conducted to date.
- **Long-term effects:** Are there **adaptive mechanisms** with **chronic administration**? No data are available for **periods exceeding several years**.
- **Combination therapies:** Does butyrate act **synergistically** with **prebiotics** or **probiotics**? Studies are **heterogeneous** and **difficult to compare**.

13. Further Paths

Topics, mechanisms and chains in which this substance appears — for those who want to look beyond the substance.

- interaction network
- From exclusion to inflammation: Stress, cortisol, gut
- Gut barrier and binding: Zeolite, butyrate, probiotics

Frequently Asked Questions

Can butyrate be taken orally, or is targeted release in the colon necessary?

Butyrate is **administered orally**, typically as **sodium butyrate** or in **microencapsulated form**. **Free butyric acid** has an **unpleasant odour** and is absorbed in the **small intestine**, whereas **microencapsulated preparations** are designed to reach the **colon**. Controlled studies frequently use **microencapsulated sodium butyrate**, as it enables **locally higher concentrations** in the gut. Whether this is **clinically superior** remains **unclear**—direct comparisons are lacking.

Are there differences between endogenously produced and exogenously administered butyrate?

Endogenous butyrate is produced through **bacterial fermentation** in the colon and exists in a **dynamic equilibrium** with the **gut microbiota**. **Exogenous butyrate** is **absorbed more rapidly** and may **elevate systemic levels**, though its **local effects** in the gut are **not identical**. Studies show that **prebiotic dietary fibres** (e.g., **resistant starch**) **enhance endogenous production** more effectively than **exogenous administration**. Whether this is **clinically relevant** has **not been directly compared**.

What role does butyrate play in the gut-brain axis?

Butyrate is thought to have a **modulatory role** in **gut-brain communication**, though the **mechanisms** are **not fully understood**. **Animal studies** demonstrate effects on **neuroinflammation** and **behaviour**, while **human studies** are lacking. **Review articles** postulate **indirect effects** via the **vagus nerve**, **immune system**, or **metabolites**, but **direct evidence for clinical effects** (e.g., in **depression**) **does not exist**. The **blood-brain barrier** is **barely permeable** to butyrate—systemic effects remain **speculative**.

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