ANTI-INFLAMMATORIES

Do anti-inflammatory foods and lifestyle habits actually lower hs-CRP and gut-driven systemic inflammation?

Separating reproducible dietary, microbial, and circadian inputs from single-strain supplement marketing in the control of chronic low-grade inflammation.

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A proprietary bacterial strain printed on a daily sachet does not resolve gut barrier permeability, mood disturbance, or systemic vascular inflammation when sleep regularity and fermentable substrate are absent.

Chronic low-grade inflammation—termed inflammaging when observed across middle and late adulthood—is characterised by a persistent, two- to four-fold elevation in circulating pro-inflammatory cytokines, acute-phase proteins, and immune cell activation in the absence of overt infection. Unlike acute inflammation, which resolves via active lipid mediator class-switching once a pathogen or tissue injury is cleared, sterile systemic inflammation persists when metabolic, microbial, and circadian inputs continuously trigger innate immune sensors. Consumer wellness markets frequently reduce anti-inflammatory intervention to isolated botanical capsules or single-strain synbiotic powders marketed for gut-brain axis repair. In human clinical trials, however, single-strain sachets rarely alter systemic inflammatory biomarkers unless paired with structural changes in substrate availability and autonomic timing. The reproducible levers in adults aged 40 to 65 remain dietary patterns high in marine polyunsaturated fatty acids and polyphenols, diverse fermentable fibres, live fermented foods if tolerated, skeletal muscle contraction, and circadian alignment of sleep and feeding windows.

What it is

Chronic low-grade inflammation is driven at the molecular level by the continuous activation of pattern recognition receptors—most notably Toll-like receptors such as TLR4—and intracellular multiprotein complexes called inflammasomes, particularly the NLRP3 inflammasome. When activated in human tissues by damage-associated molecular patterns (DAMPs like oxidised LDL, excess free fatty acids, or extracellular ATP) or pathogen-associated molecular patterns (PAMPs like bacterial lipopolysaccharide, or LPS, translocating across a compromised intestinal barrier), these sensors trigger the transcription factor nuclear factor kappa B (NF-kB). NF-kB translocates to the nucleus and drives the transcription of pro-inflammatory cytokines, including tumour necrosis factor-alpha (TNF-alpha), interleukin-1 beta (IL-1beta), and interleukin-6 (IL-6). IL-6 subsequently stimulates hepatocytes to synthesise acute-phase reactants such as C-reactive protein (CRP) and fibrinogen. In preventive medicine, an anti-inflammatory lifestyle is a structured set of nutritional, microbial, physical, and circadian inputs designed to downregulate this sterile innate immune activation and promote the active resolution of inflammation. It is mechanistically distinct from pharmacological immunosuppression (such as corticosteroids or biologics) and from acute analgesic therapy (such as non-steroidal anti-inflammatory drugs, or NSAIDs, which inhibit cyclooxygenase enzymes). Anti-inflammatory foods and lifestyle practices act upstream of the NF-kB and NLRP3 cascades. Rather than blocking a single downstream enzyme like COX-2, they reduce the antigenic and metabolic load entering the portal and systemic circulation, strengthen tight junction proteins (claudins, occludin, and zonula occludens-1) in the intestinal epithelium, supply polyunsaturated lipid precursors for specialised pro-resolving mediators (SPMs), and restore vagal cholinergic

tone.

Why it is used

Human genetic Mendelian randomisation studies establish that elevated IL-6 receptor signalling is causally linked to coronary heart disease, whereas CRP itself serves as a stable downstream clinical readout of this upstream IL-1beta and IL-6 cascade. In the arterial wall, cytokines and oxidised lipoproteins promote endothelial expression of adhesion molecules (VCAM-1, ICAM-1), recruiting monocytes into the intima where they differentiate into foam cells and destabilise atherosclerotic plaques. In metabolic tissues, TNF-alpha and IL-6 activate c-Jun N-terminal kinase (JNK) and IkappaB kinase beta (IKK-beta) in human adipocytes and myocytes, phosphorylating insulin receptor substrate-1 (IRS-1) at serine residues and impairing GLUT4 translocation. This impairs peripheral glucose uptake, driving hyperinsulinaemia and hepatic de novo lipogenesis. In the central nervous system, circulating cytokines and translocated microbial metabolites signal across the blood-brain barrier to prime microglia, shifting tryptophan metabolism away from serotonin synthesis and toward the neurotoxic kynurenine pathway. While consumer marketing frequently attributes cognitive and affective shifts to vague notions of intestinal permeability treatable with a single probiotic sachet, clinical physiology demonstrates that barrier dysfunction and neuroinflammation are consequences of low fermentable substrate, excess dietary emulsifiers and refined sugars, visceral adiposity, and circadian disruption. Clinical trial data also explain why an inflammatory biomarker can move while hard clinical outcomes do not—or vice versa. In large cardiovascular randomised controlled trials (RCTs), pharmacological agents that fail to inhibit the specific IL-1beta to IL-6 pathway (such as low-dose methotrexate in the CIRT trial, n=4,786) neither lowered IL-6/CRP nor reduced cardiovascular events, whereas targeting IL-1beta directly (canakinumab in the CANTOS trial, n=10,061) reduced major adverse cardiovascular events by 15% independently of lipid lowering. Similarly, taking an isolated antioxidant or single-strain probiotic rarely alters arterial stiffness, insulin sensitivity, or visceral fat mass even if it transiently shifts a stool assay. Conversely, a Mediterranean dietary pattern and regular aerobic exercise reduce cardiovascular mortality and incident type 2 diabetes across meta-analyses of RCTs even when short-term reductions in resting hs-CRP are modest (0.3 to 0.7 mg/L), because they simultaneously improve endothelial nitric oxide bioavailability, lower apolipoprotein B (ApoB) particle retention, and reduce visceral adipose tissue.

How it helps

Five primary mechanisms link dietary, microbial, exercise, and circadian inputs to the downregulation of systemic inflammation in human tissues and controlled clinical trials: 1. Microbiome Fermentation, Short-Chain Fatty Acids, and Fermented Foods: When adults consume diverse plant polysaccharides (soluble and insoluble fibres, resistant starches, inulin, beta-glucans, and arabinoxylans), colonic anaerobes (such as Faecalibacterium prausnitzii and Roseburia species) ferment these substrates into short-chain fatty acids (SCFAs): acetate, propionate, and butyrate. Butyrate serves as the primary beta-oxidation fuel source for human colonocytes, maintaining luminal hypoxia that favours obligate anaerobes over facultative pathogenic Enterobacteriaceae. In human colonic mucosa, butyrate inhibits histone deacetylases (HDACs) and signals through G-protein-coupled receptors (GPR41, GPR43, and GPR109A) to promote the differentiation of regulatory T cells (Tregs) that secrete anti-inflammatory interleukin-10 (IL-10). In a 10-week randomised clinical trial (Wastyk et al., 2021, n=36 healthy adults), assigning participants to a diet high in live fermented foods (yoghurt, kefir, fermented cottage cheese, kimchi, vegetable brine drinks, and kombucha) increased overall gut microbiota diversity and decreased 19 inflammatory proteins—including IL-6, IL-10, and IL-12b—alongside reduced activation of effector memory CD4+ T cells, monocytes, and B cells. The parallel high-fibre arm in that 10-week trial showed mixed inflammatory responses depending on starting point microbial diversity, indicating that depleted microbiomes require live fermented inputs and gradual titration to process high fibre loads

effectively. 2. Marine Omega-3 Fatty Acids and Specialised Pro-Resolving Mediators (SPMs): Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) from cold-water fatty fish (salmon, sardines, mackerel, anchovies) incorporate into human cell membrane phospholipids, partially displacing arachidonic acid (AA). This reduces the substrate available for COX and lipoxygenase (LOX) enzymes to produce pro-inflammatory 2-series prostaglandins and 4-series leukotrienes. Confirmed in human blood and tissue lipidomics, EPA and DHA also serve as direct precursors for SPMs—resolvins (E- and D-series), protectins, and maresins. SPMs bind specific receptors (ChemR23 and GPR32) on human neutrophils and macrophages to halt polymorphonuclear leukocyte infiltration and stimulate efferocytosis (the clearance of apoptotic cells and cellular debris), actively terminating the inflammatory response without immunosuppression. Meta-analyses of RCTs show marine omega-3 intake lowers hs-CRP by roughly 0.2 to 0.4 mg/L and fasting triglycerides by 15% to 30% in hypertriglyceridaemic adults. 3. Dietary Polyphenols and Extra-Virgin Olive Oil (EVOO): Phenolic compounds—including oleocanthal and hydroxytyrosol in EVOO, anthocyanins in dark berries, flavanols in cocoa and green tea, and curcuminoids in turmeric—exert dual effects in human cells and feeding studies. They activate nuclear factor erythroid 2-related factor 2 (Nrf2), which binds the antioxidant response element (ARE) to upregulate endogenous phase II detoxifying enzymes (heme oxygenase-1 and glutathione peroxidase), and they inhibit IKK phosphorylation to prevent NF-kB translocation. Because over 90% of dietary polyphenols are not absorbed in the small intestine, they reach the colon where microbial biotransformation converts them into bioactive phenolic metabolites (such as urolithins from ellagitannins) that suppress local mucosal inflammation. In the PREDIMED randomised trial (n=7,447 older adults at high cardiovascular risk followed for a median of 4.8 years), a Mediterranean diet supplemented with EVOO or mixed nuts reduced major cardiovascular events by roughly 30% compared to a control diet, with biomarker sub-studies confirming reductions in hs-CRP, IL-6, and soluble endothelial adhesion molecules. 4. Skeletal Muscle Contraction and Myokine Signalling: Acute exercise causes a transient spike in muscle-derived IL-6 independently of TNF-alpha activation. In human physiology, contraction-induced IL-6 acts as an anti-inflammatory myokine: it stimulates circulating IL-1 receptor antagonist (IL-1ra) and IL-10 and inhibits endotoxaemia-induced TNF-alpha production. Across meta-analyses of RCTs lasting 12 weeks or longer, regular aerobic and resistance training lowers resting hs-CRP by 0.3 to 0.6 mg/L, mediated in part by reducing visceral adipose tissue depots where infiltrating M1 macrophages generate up to 30% of basal circulating IL-6. 5. Circadian Alignment, Sleep Regularity, and Timed Feeding: Peripheral immune cells and intestinal epithelial cells express autonomous molecular clock genes (CLOCK, BMAL1, PER, CRY) that regulate cytokine secretion and tight junction integrity over a 24-hour cycle. In controlled human inpatient circadian misalignment crossover trials (Scheer, Wright, Morris, and colleagues), shifting sleep and feeding times out of phase with the central suprachiasmatic nucleus increases 24-hour hs-CRP by 10% to 15% and elevates IL-6 and TNF-alpha. Eating during the biological night when endogenous melatonin is elevated impairs beta-cell insulin secretion, prolongs post-prandial lipaemia, and disrupts gut mucosal repair cycles. Consolidating food intake to daytime hours and finishing the final meal 3 to 4 hours before sleep onset reduces nocturnal heart rate, increases heart rate variability (HRV), and lowers morning fasting glucose and inflammatory markers.

Who should try it

Adults aged 40 to 65 with persistently elevated hs-CRP between 1.0 and 3.0 mg/L across two consecutive tests (after ruling out acute infection or trauma) derive the highest clinical yield from structured anti-inflammatory nutrition and circadian alignment. Additional target profiles include: - Individuals with immunometabolic strain, characterised by elevated ApoB, fasting insulin above 8 uIU/mL, a triglyceride-to-HDL ratio above 2.0 (in mg/dL units), visceral adiposity (waist-to-height ratio >0.5 or elevated visceral fat area on DXA), or metabolic dysfunction-associated steatotic liver disease (MASLD). - Adults experiencing functional gastrointestinal symptoms (bloating, irregular motility) or post-prandial fatigue who use commercial single-strain probiotic sachets without addressing total plant diversity, meal timing, or ultra-processed food intake. - Shift workers or

individuals with irregular sleep-wake schedules and late-night eating habits. Trade-offs, Side Effects, and Contraindications: - Fermented foods and histamines: Live fermented foods (kimchi, sauerkraut, aged cheeses, kefir, kombucha) contain biogenic amines, including histamine and tyramine. In individuals with reduced diamine oxidase (DAO) enzyme activity, mast cell activation phenotypes, or severe gastroesophageal reflux, high fermented-food intake triggers headaches, flushing, tachycardia, urticaria, or gastrointestinal distress. - Rapid fibre escalation and FODMAPs: Abruptly increasing fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs—found in legumes, onions, garlic, cruciferous vegetables, and inulin) in an unconditioned microbiome causes rapid hydrogen and methane gas production, luminal distension, osmotic diarrhoea, or constipation. In patients with active inflammatory bowel disease (Crohn's disease or ulcerative colitis with intestinal stricturing) or severe irritable bowel syndrome (IBS), insoluble fibres and high-FODMAP substrates are contraindicated or require slow clinical titration until mucosal healing occurs. - Concentrated botanicals and marine oils: While culinary herbs and whole fatty fish have broad safety margins, concentrated botanical extracts (such as curcumin formulated with piperine, or concentrated green tea extract/EGCG) carry documented risks of idiosyncratic drug-induced liver injury (DILI) in human case series and inhibit hepatic cytochrome P450 enzymes (CYP3A4) and P-glycoprotein, altering the clearance of statins, anticoagulants, and antiplatelet drugs. Concentrated omega-3 supplements prolong bleeding time slightly and, in cardiovascular RCTs, show a dose-dependent increase in the relative risk of atrial fibrillation in predisposed individuals. - Cost and opportunity cost: Spending monthly budgets on unvalidated proprietary probiotic sachets, intravenous antioxidant drips, or commercial IgG food-sensitivity blood panels (which measure normal physiological food exposure rather than pathological inflammation) diverts resources from whole-food substrate, resistance training, and sleep regularity.

Measurements that show improvement

Serial blood biomarkers, body composition scans, and autonomic wearables measured at 8- to 16-week intervals quantify the resolution of chronic low-grade inflammation: 1. High-Sensitivity C-Reactive Protein (hs-CRP): The primary clinical standard for systemic vascular and metabolic inflammation. Measure twice, two weeks apart, while free of viral infections, dental procedures, or intense unaccustomed eccentric exercise in the prior 48 hours. Direction of improvement: a reduction toward <1.0 mg/L (and <0.5 to 0.7 mg/L for optimal vascular risk). Values >10 mg/L indicate an acute infection, trauma, or systemic rheumatological flare rather than chronic low-grade inflammation. 2. Glycoprotein Acetyls (GlycA): Measured via nuclear magnetic resonance (NMR) spectroscopy, GlycA reflects the integrated concentration and glycosylation state of multiple acute-phase proteins (alpha-1-acid glycoprotein, haptoglobin, alpha-1-antitrypsin, and transferrin). In large human cohort studies, GlycA demonstrates lower week-to-week intra-individual variability than hs-CRP and independently predicts cardiovascular events and incident type 2 diabetes. Direction of improvement: a downward trend into the lowest quartile of the reference range (<350 to 400 umol/L, depending on the assay). 3. Fasting Insulin, HbA1c, and ApoB: Because adipose tissue macrophage infiltration and hyperinsulinaemia are bidirectionally linked, resolving immunometabolic stress lowers fasting insulin (target <6 to 8 uIU/mL), stabilises HbA1c (<5.3% to 5.4%), lowers the fasting triglyceride-to-HDL ratio (<1.5 in mg/dL units), and reduces ApoB particle concentration. 4. Complete Blood Count (CBC) Derived Ratios—Neutrophil-to-Lymphocyte Ratio (NLR): Calculated by dividing the absolute neutrophil count by the absolute lymphocyte count on a standard CBC with differential. NLR reflects the balance between innate immune activation (neutrophils) and adaptive immune regulation (lymphocytes). Direction of improvement: reduction toward 1.0 to 2.0; chronically elevated values (>2.5 to 3.0 in the absence of acute illness) associate with higher all-cause mortality in epidemiological cohorts. 5. Hepatic and Iron Acute-Phase Markers (GGT, ALT, and Ferritin): Gamma-glutamyl transferase (GGT) rises with oxidative stress and intracellular glutathione depletion; alanine aminotransferase (ALT) rises with hepatic steatosis. Serum ferritin is both an iron storage protein and an acute-phase reactant that rises during systemic inflammation even when iron stores are normal. Direction of improvement: reduction of ALT (<25 U/L in men,

<19 U/L in women), GGT (<20 U/L), and normalisation of elevated ferritin alongside stable transferrin saturation. 6. Autonomic and Biometric Markers (Resting Heart Rate, HRV, and Visceral Adipose Tissue): Vagal nerve activity regulates the cholinergic anti-inflammatory pathway, wherein acetylcholine released by the vagus nerve binds alpha-7 nicotinic acetylcholine receptors on macrophages to suppress TNF-alpha release. Tracking overnight heart rate variability (RMSSD via validated wearables) and resting heart rate (RHR) provides a daily readout of autonomic balance, particularly in response to eliminating late-night meals and alcohol. Dual-energy X-ray absorptiometry (DXA) quantifies visceral adipose tissue (VAT) mass and cross-sectional area. Direction of improvement: higher overnight HRV, lower RHR, and a reduction in VAT mass toward <500 grams (or <100 cm^2 cross-sectional area). Within physician-led platforms such as LetsGo, these markers are evaluated longitudinally alongside body composition and sleep data to verify whether a nutritional or circadian intervention is altering systemic physiology.

Products and services

These LetsGo products and services sit next to this subject. They are not a prescription. A link is not evidence that the product causes the change discussed above. - [LetsGo supplement shelf](/supplements) — Bottles LetsGo stocks for members. Read the label before the first order. A link is not a dose. - [LetsGo programmes](/programs) — Coached programmes. Not a clinic menu and not a promise of a result.

Practical takeaways

- Consume 30 or more distinct plant foods per week (vegetables, legumes, whole grains, nuts, seeds, herbs, and spices) for 12 weeks, ramping fibre gradually over the first 4 weeks to prevent bloating while driving colonic short-chain fatty acid production.
- Eat 1 to 2 servings daily of unsweetened live fermented foods (yoghurt, kefir, kimchi, sauerkraut) for 10 to 12 weeks to lower circulating IL-6 and inflammatory proteins; stop or reduce intake if histamine-related flushing, headache, or reflux occurs.
- Replace saturated culinary fats with polyphenol-rich extra-virgin olive oil daily and consume cold-water fatty fish (salmon, sardines, mackerel, anchovies) 2 to 3 times per week to target a 15% to 30% reduction in fasting triglycerides and a 0.2 to 0.4 mg/L reduction in hs-CRP.
- Finish the final caloric meal and any alcohol at least 3 to 4 hours before sleep onset every night for 4 weeks, verifying autonomic recovery via a measurable drop in overnight resting heart rate and an increase in overnight HRV (RMSSD).
- Re-test hs-CRP, GlycA, fasting insulin, ALT, and CBC-derived neutrophil-to-lymphocyte ratio (NLR) at 12 weeks under standardised conditions (no acute infection for 14 days and no heavy eccentric exercise for 48 hours), targeting hs-CRP <1.0 mg/L, fasting insulin <8 uIU/mL, and NLR between 1.0 and 2.0.

Safety note

Do not discontinue prescribed anti-inflammatory, immunosuppressive, or cardiovascular medications without consulting your prescribing physician. Individuals with active inflammatory bowel disease, intestinal strictures, severe irritable bowel syndrome, or histamine intolerance should individualise fibre and fermented food intake with clinical guidance. Concentrated botanical extracts (such as curcumin with piperine or green tea extract) and high-intake marine oils interact with anticoagulants, antiplatelet agents, and cytochrome P450-metabolised medications, and carry documented risks of hepatotoxicity or atrial fibrillation.

Disclaimer

This educational article is for informational purposes only and does not constitute medical advice, diagnosis, or a prescription. Biomarker interpretation and nutritional or lifestyle changes should be reviewed with a qualified healthcare

professional familiar with your personal medical history.

Controlling chronic low-grade inflammation does not rely on proprietary probiotic sachets or isolated botanical capsules. In human clinical studies, the most reliable reductions in hs-CRP, pro-inflammatory cytokines, and immunometabolic risk come from upstream physiological inputs: diverse fermentable plant fibres, live fermented foods where tolerated, marine omega-3 fatty acids and polyphenol-rich olive oil, regular skeletal muscle contraction, and strict alignment of feeding and sleeping windows with the circadian clock. Tracking objective markers—such as hs-CRP, GlycA, fasting insulin, visceral fat mass, and overnight heart rate variability—over 12-week intervals allows adults and their physicians to confirm that these habits are measurably resolving systemic inflammatory load.