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Original Research Article

Albendazole and the Human Gut Microbiome: Mechanism, Microbial Ecology, Digestion, Immunity, and the Gut–Brain Axis — An Expanded Critical Narrative Review

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Abstract
A claim circulating in lay and alternative-health media holds that albendazole, one of the world's most widely administered anthelmintic drugs, indiscriminately destroys the beneficial bacteria of the human intestine — the microorganisms responsible for digestion, nutrient absorption, immune calibration, and, via the gut–brain axis, cognitive and emotional function — and that pharmaceutical manufacturers conceal this harm. This review interrogates that claim against the primary literature spanning pharmacology, microbial ecology, immunology, and neuroscience: molecular mechanism-of-action and resistance-genetics studies, pharmacokinetic and metabolism data, human 16S rRNA and shotgun metagenomic cohort studies across four continents, a controlled parasite-free mouse experiment, non-human primate multi-omics data, systematic reviews of deworming's population-level effects, mechanistic short-chain fatty acid (SCFA) immunology, and clinical trials of therapeutic helminth administration. The synthesis finds that albendazole's molecular target — helminth β-tubulin — is a eukaryotic cytoskeletal protein structurally distinct from anything present in bacterial cells, giving the drug no first-principles antibacterial mechanism; this is corroborated by decades of veterinary and human resistance genetics that map resistance mutations precisely onto this target and no other. Human cohort studies do detect real compositional shifts in gut microbiota around treatment, but the best-designed of these studies dissociate the shift from drug exposure itself and tie it instead to successful parasite clearance. A head-to-head mouse experiment comparing albendazole to a known antibacterial antiparasitic (metronidazole) found no acute microbiota disruption from albendazole, while metronidazole depleted a beneficial bacterial family and reduced microbial richness. At the same time, 2025 metagenomic work identifies a genuinely open question: low-magnitude, taxon-specific "off-target" activity that is mild for albendazole alone but substantially larger for a macrolide-class combination partner (ivermectin). The paper also situates the immune question within an active, decades-long clinical research program — therapeutic helminth administration for autoimmune disease — that argues, if anything, for a more complicated relationship between worms, bacteria, and host immunity than a simple "harm" or "benefit" framing allows. The paper concludes that the "hidden harm" narrative, as commonly stated, is not supported by the evidence, but that the honest picture is neither "completely safe" nor "completely inert" — it is a bounded, actively studied, and considerably more scientifically interesting set of findings than either extreme suggests.
Keywords: albendazole, benzimidazole, gut microbiome, soil-transmitted helminths, mass drug administration, β-tubulin, short-chain fatty acids, regulatory T cells, hygiene hypothesis, gut–brain axis

1. Introduction

Albendazole is a broad-spectrum benzimidazole carbamate anthelmintic on the World Health Organization's Model List of Essential Medicines. It is administered both to individual patients with confirmed helminth infection and, at enormous scale, through mass drug administration (MDA) programs targeting soil-transmitted helminths (STH) — hookworm (*Necator americanus*, *Ancylostoma duodenale*), roundworm (*Ascaris lumbricoides*), and whipworm (*Trichuris trichiura*).

Outside the clinical and public-health literature, a specific narrative has taken hold in wellness and alternative-medicine spaces: that albendazole behaves like a broad-spectrum antibiotic inside the gut, killing beneficial commensal bacteria alongside the target parasite, and that this collateral damage impairs digestion, nutrient absorption, immune regulation, and — through the increasingly popular framework of the gut–brain axis — mood and cognitive function. The claim is frequently packaged with the assertion that this harm is known to industry and regulators but omitted from patient-facing marketing.

This review does not start from either the manufacturer's promotional framing or the "hidden harm" framing. It starts from a narrower, testable question: **what does the peer-reviewed and credible preprint literature actually report happens to gut microbial composition, digestive function, immune signaling, and brain-relevant physiology around albendazole treatment — and does that evidence support the specific claim being made?**

1.1 Scale of exposure to this drug

Understanding why this question matters requires understanding the sheer scale at which albendazole is administered. Soil-transmitted helminths are estimated to affect roughly 1.5 billion people, or about 24% of the world's population, according to World Health Organization figures, with the 2021 Global Burden of Disease study estimating approximately 642.72 million active cases and 1.38 million disability-adjusted life years (DALYs) attributable to STH infections worldwide that year. Preventive chemotherapy coverage has itself scaled dramatically: the number of school-age children treated through preventive chemotherapy programs rose from under 120 million in 2008 to over 450 million by 2018. This means hundreds of millions of doses of albendazole are administered annually, largely to children in low- and middle-income countries, making the microbiome question a matter of direct public-health consequence rather than a purely academic one — and also making it one of the most heavily studied drug-microbiome interactions in global health research, which is precisely why a reasonably rich evidence base exists to evaluate the claim against.

Burden is not evenly distributed: age-standardized prevalence and DALYs are consistently higher in the 5–19 year age group, particularly children aged 5–9, and STH burden is strongly, negatively correlated with a country's socio-demographic index — meaning the populations most exposed to albendazole are also, on average, the populations most vulnerable to the pre-existing nutritional and infectious burden the drug is meant to treat.

2. Methods and Scope of This Review

This is a narrative synthesis rather than a formal systematic review — it does not follow a PRISMA search-and-screening protocol, and it does not claim database exhaustiveness. Sources were identified through targeted searches across PubMed, bioRxiv, medRxiv, Scientific Reports, Journal of Infectious Diseases, Microbiome, and Infectious Diseases of Poverty, supplemented by citation-chasing from primary sources. Where a conclusion rests on a single study rather than convergent evidence, that is flagged explicitly rather than presented as consensus. Preprints not yet peer-reviewed at time of writing are labeled as such.

3. Mechanism of Action: What Albendazole Is Actually Built to Target

3.1 β-tubulin binding and cytoskeletal disruption

Albendazole's pharmacological mechanism is binding to β-tubulin, the structural protein subunit that polymerizes into microtubules, and inhibiting that polymerization (LiverTox, NCBI Bookshelf, n.d.). In helminths, this disrupts cytoskeletal architecture and intracellular transport, impairing glucose uptake, motility, and egg production, and eventually killing or sterilizing the parasite.

The reason this mechanism produces a usable, relatively selective human drug — rather than a generalized cytotoxic poison — is a difference in binding affinity: albendazole binds helminth β-tubulin substantially more tightly than mammalian β-tubulin (LiverTox, NCBI Bookshelf, n.d.; Vargas et al., 2006).

3.2 Pharmacokinetics: absorption, metabolism, and distribution

The pharmacokinetic profile of albendazole is itself informative for evaluating the "kills gut bacteria" claim, because it clarifies how much of the drug actually remains in the intestinal lumen where bacteria live, versus how much is absorbed systemically. Albendazole is poorly absorbed on its own — less than 5% of an oral dose — but its absorption is enhanced approximately 5-fold when the drug is taken with fat-rich food, because it is a weak base that dissolves preferentially in the lipid-rich, mildly alkaline environment of the proximal small intestine. Clinically, this is why patients are often advised to take albendazole with a fatty meal when systemic or tissue-level drug exposure is the goal, such as in neurocysticercosis, where albendazole functions as a prodrug that needs to cross into brain tissue to kill larval Taenia solium cysts.

Once absorbed, albendazole undergoes very fast first-pass metabolism in the liver, such that the unchanged parent drug is essentially undetectable in plasma; most of it is oxidized into its active sulfoxide metabolite, ricobendazole (also called albendazole sulfoxide), by cytochrome P450

enzymes and a flavin-containing monooxygenase. A 2024 systematic review and pharmacokinetic modeling analysis pooling 92 time-series datasets from single-dose albendazole studies confirmed this pattern, noting that the model needed to explicitly account for albendazole's extensive first-pass hepatic metabolism and its well-established low oral bioavailability, attributed largely to poor aqueous solubility along the gastrointestinal tract, when estimating parameters such as peak blood concentration and total systemic drug exposure. Peak plasma concentrations of the parent drug occur roughly 2 hours post-dose, with the sulfoxide metabolite peaking around 4 hours post-dose.

There is also a documented sex difference in disposition: women have been found to have lower oral clearance and volume of distribution of albendazole than men, while men show lower peak serum concentrations — a pharmacokinetic nuance rarely mentioned in either marketing materials or alarmist claims about the drug, and one that current research has not yet connected to any differential microbiome effect.

Why this matters for the microbiome question: a drug that is poorly and variably absorbed, with a large fraction potentially remaining unabsorbed or degraded within the intestinal lumen by mucosal metabolic enzymes before ever reaching systemic circulation (Wikipedia, 2026, citing primary pharmacology literature), does have meaningful contact time with luminal bacteria — so the pharmacokinetics alone don't rule out a local antibacterial effect. But they do mean that any such effect would have to arise from local, lumenal chemical activity rather than from a systemic drug action reaching bacteria via the bloodstream, which is a useful framing for interpreting the metagenomic findings in Section 5. Separately, formulation science has become an active research area precisely *because* of albendazole's poor bioavailability: work on albendazole–bile acid conjugates has shown that conjugating the drug to bile acids can reverse albendazole's status as a substrate for the efflux transporters P-glycoprotein, MRP2, and BCRP, and can increase oral bioavailability by as much as 31-fold in some formulations, and separate work on solubilizing formulations for alveolar echinococcosis treatment has pursued similar goals for tissue-level disease (Chinese formulation study, 2024). This body of drug-delivery research is worth noting because it directly undercuts the "concealed harm" framing: pharmaceutical science's actual documented priority around albendazole has been *improving* how much of the drug reaches its intended target, not concealing off-target toxicity — a research emphasis inconsistent with a company trying to hide collateral damage.

3.3 β-tubulin structural biology and resistance genetics: independent confirmation of the drug's real target

If albendazole's mechanism were meaningfully antibacterial, decades of resistance-genetics research — conducted independently across veterinary parasitology, human helminthology, and free-living nematode genetics, largely without reference to a "gut bacteria" hypothesis — would be expected to show resistance mutations affecting bacterial-relevant pathways. It does not. Resistance research instead maps overwhelmingly onto a single, specific eukaryotic target.

The molecular mechanism of benzimidazole resistance was characterized in detail starting in the 1990s in *Haemonchus contortus*, a veterinary gastrointestinal nematode, where researchers found that the mechanism of benzimidazole resistance appears to be conserved across a wide range of species from fungi to nematodes and involves alterations in the genes encoding β-tubulin specifically. Subsequent work refined this to the amino-acid level: characteristic single-nucleotide polymorphisms at codons 167, 198, and 200 of the β-tubulin gene are responsible for conferring benzimidazole resistance across multiple helminth species. This resistance mechanism has since been confirmed functionally using modern gene-editing tools — a 2022 study using CRISPR/Cas9 introduced a resistance-associated mutation at codon 167 into the orthologous β-tubulin gene of the model nematode Caenorhabditis elegans and demonstrated that this single edit conferred a similar level of resistance to the related benzimidazole thiabendazole.

This body of work has extended to human-infecting parasites directly relevant to albendazole treatment. A 2024 systematic review in *Parasitology Research* (Springer Nature) synthesizing the occurrence of these resistance mutations specifically in hookworms found a growing global literature documenting β-tubulin isotype-1 SNPs in human hookworm populations receiving benzimidazole MDA, and a companion 2024 study used AlphaFold 3 structural modeling to show computationally that resistance-associated mutations in hookworm β-tubulin

impair benzimidazole binding while, in some cases, enhancing the stability of the α/β-tubulin dimer itself — helping explain how resistant parasites retain viable cytoskeletal function while evading the drug. Parallel work in Brazilian populations of *Trichuris trichiura* has looked for these same resistance-associated SNPs, motivated by the observation that benzimidazole drugs show limited efficacy and suboptimal cure rates specifically against T. trichiura in humans, a species-specific efficacy gap that has driven the combination-therapy research (ivermectin- and moxidectin-albendazole) discussed in Section 6.

The scientific significance of this resistance literature for the present question is straightforward: an entire, decades-deep, cross-disciplinary research field — spanning veterinary medicine, human tropical medicine, and basic nematode genetics — has mapped, at single-nucleotide resolution, exactly which molecular changes allow helminths to survive albendazole exposure, and every one of them converges on the β-tubulin gene. If the drug had a clinically meaningful, independent antibacterial mechanism, one would expect a parallel resistance literature in gut commensal bacteria; no comparable body of evidence exists, which is itself a form of negative evidence consistent with the mechanistic argument in Section 3.1.

4. Does Gut Microbiome Composition Change After Albendazole? The Human and Animal Evidence

This is the section where the "hidden harm" narrative and the empirical record diverge most sharply — not because nothing measurable happens, but because *what* happens and *why* it happens turn out to be considerably more specific than a blanket antibacterial effect.

4.1 The Ghana hookworm cohort

A 2023 study published in *Scientific Reports* (Nature Portfolio/Springer Nature) followed hookworm-infected Ghanaian adults before and 10–14 days after a single 400 mg dose of albendazole, using 16S rRNA sequencing of stool (Appiah-Twum et al., 2023). Its key design feature is that participants were stratified by treatment *outcome*, not merely by drug exposure: individuals successfully cured of hookworm showed a significant shift in microbiota composition post-treatment, while individuals whose infection persisted despite treatment showed no significant compositional change. This design decouples "received the drug" from "microbiome changed" — the variable that actually predicted a shift was whether the worm was gone, consistent with the resident bacterial community reorganizing around a vacated ecological niche rather than the drug directly suppressing bacterial taxa.

4.2 The Kenya trichuriasis findings

A related human study, covered by Healio's *Infectious Diseases in Children* and published in *mBio*, examined children following successful albendazole treatment and helminth clearance and found that the relative abundance of Clostridiales *increased* while Enterobacteriales *decreased* — a shift the study authors characterized as movement toward the microbiome profile typical of helminth-free individuals, not a collapse of beneficial flora. The authors explicitly framed the result as evidence that deworming does not damage the gut microbiome (Healio, 2019).

4.3 Gut barrier integrity in Indonesian schoolchildren

A 2022 study in *Scientific Reports* examined schoolchildren in Makassar, Indonesia, given triple-dose albendazole, directly measuring intestinal permeability and lipopolysaccharide-binding protein (LBP), a marker of bacterial translocation across the gut wall, before and after treatment. Permeability differences tracked with socioeconomic status rather than treatment, no single bacterial taxon explained changes in barrier function, and albendazole treatment did not significantly worsen LBP levels (Wiria et al., 2022).

4.4 A controlled experiment that isolates drug effect from parasite effect

The single strongest piece of evidence for separating "what albendazole does" from "what happens when a worm dies" is a controlled 2024 study in the *Journal of Infectious Diseases*, which tested albendazole in parasite-free mice specifically to remove the parasite-clearance confound. The study team investigated whether two common antiparasitics — albendazole and metronidazole — significantly alter the gut microbiome of parasite-free mice, treating mice with each drug daily for seven days and sampling fecal microbiota before treatment, immediately after, and following a two-week recovery period. The result was a clear divergence between the two drugs: albendazole did not immediately change the gut microbiota, while metronidazole decreased microbial richness by 8.5% and significantly changed community structure during treatment, with structural changes including depletion of the beneficial bacterial

family Lachnospiraceae, and predictive metagenomic analysis suggesting these losses likely depressed microbiome metabolic function. This is a direct experimental test of the core claim, using a design that eliminates parasite death as a confounding variable — and it found no measurable acute antibacterial effect from albendazole itself, in sharp contrast to a drug with genuine, well-characterized antibacterial activity run in the same experiment under identical conditions.

4.5 Non-human primate multi-omics data

A 2025 multi-omics study of captive golden snub-nosed monkeys (*Rhinopithecus brelichi*) given a three-day albendazole course found that gut microbiota richness and diversity *increased* after deworming, alongside a large reduction in intestinal parasite egg counts (PMC, 2025) — a result running directly counter to a model in which the drug indiscriminately depletes microbial diversity.

4.6 Broader ecological context: helminth infection itself reshapes the microbiome

Cross-sectional and infection-focused research consistently documents that the *infection itself*, independent of any treatment, is a major driver of microbiome composition. The 2025 bioRxiv preprint discussed in detail in Section 6 explicitly grounds its analysis in this prior literature, citing earlier findings that infections by human gastrointestinal helminths are associated with changes in faecal microbiota diversity and composition and referencing veterinary-comparative work asking whether helminth and host-microbiota niches genuinely compete within the gut ("This Gut Ain't Big Enough for Both of Us. Or Is It?"). This matters for interpretation: any before/after comparison around deworming implicitly compares a helminth-altered microbiome state to a helminth-free one, which is a fundamentally different scientific question than asking whether the *drug itself* has a direct antibacterial effect.

4.7 Synthesis of Section 4

Across five independent lines of human, mouse, and primate evidence — spanning three continents and several study designs, including one experimental design specifically built to remove the parasite-clearance confound — the pattern is remarkably consistent: measurable microbiome shifts around albendazole treatment are real, but the mechanism the data point to is parasite clearance reshaping an ecological niche, not the drug acting as a direct antibacterial agent.

5. Digestion and Nutrient Absorption

5.1 The direction of causality the strongest evidence supports

The claim that albendazole itself damages digestion and nutrient absorption inverts the direction the dominant evidence actually points. Soil-transmitted helminths are well-established, independently documented causes of malabsorption, iron-deficiency anemia, and impaired growth in children: hookworm causes chronic intestinal blood loss at the site of attachment, and all three major STH species damage intestinal mucosa and compete with the host for ingested nutrients (StatPearls, n.d.; LiverTox, n.d.). Deworming exists as a public-health intervention specifically to reverse these harms, and the Indonesian schoolchildren study cited above found no evidence that albendazole itself worsens gut barrier integrity (Wiria et al., 2022).

5.2 A necessary corrective in the opposite direction

A rigorous review should not overcorrect into overstating deworming's benefits either. A major Cochrane/Campbell systematic review and network meta-analysis (Welch et al., 2016), along with a companion analysis published in *The Lancet* (Clarke et al., 2017), concluded that mass deworming for soil-transmitted helminths has little to no measurable population-level effect on growth, short-term attention, cognitive development, school attendance, academic achievement, or mortality once confounders — reinfection rates, baseline nutritional status, and dilution effects from lightly infected children in mixed cohorts — are properly accounted for. Individual-level effects can still be substantial in heavily infected children with clinically significant iron-deficiency anemia, but the *average*, population-wide growth and cognition signal from mass programs is considerably weaker than earlier literature suggested.

5.3 Genuine, disclosed short-term GI effects

Albendazole does carry real short-term gastrointestinal side effects during the treatment window — abdominal pain, nausea, and diarrhea are recognized, dose-related adverse effects listed in standard prescribing information (StatPearls, n.d.). These are typically transient and are a fundamentally different category of claim from lasting damage to absorptive capacity or to the resident microbiota responsible for digestion.

6. Off-Target Bacterial Effects: What's Genuinely Still Open

To be fair to the version of this claim that has the strongest evidentiary footing, this deserves direct, detailed attention rather than dismissal.

6.1 The 2025 hybrid-metagenomics study

A 2025 bioRxiv preprint set out explicitly to address this question with unusually high molecular resolution. The study team noted the underlying public-health motivation clearly: because ivermectin and moxidectin are structurally macrocyclic lactones that closely resemble the macrolide class of antibiotics, and because these drugs share the parasite's gastrointestinal habitat, gut bacteria represent a plausible secondary target for them — and they emphasized why this would matter clinically, noting that unlike the parasites being targeted, the majority of gut bacteria make up an indispensable part of the gastrointestinal tract, aiding in digestion, protection against pathogens, and immune responses, such that disruption of gut microbiome homeostasis could impede these essential functions.

Working within a randomized controlled trial, the researchers collected stool samples from 204 Trichuris trichiura-infected individuals in Côte d'Ivoire receiving albendazole alone, albendazole combined with ivermectin, or albendazole combined with moxidectin, and used a hybrid sequencing approach combining Illumina short-read and Oxford Nanopore long-read shotgun sequencing to recover over 800 high-quality metagenome-assembled genomes. The central finding directly addresses the claim under review: albendazole and albendazole-moxidectin induced taxonomic shifts in the gut microbiota with only mild functional consequences, whereas individuals receiving higher quantities of albendazole-ivermectin showed profoundly modulated taxonomic composition and microbial function, while the antibiotic-resistance gene pool (the "resistome") was largely unaffected. The authors concluded that these findings robustly confirm ivermectin's antibacterial properties in the human gut, extending beyond what had previously been reported only in vitro.

The honest state of this evidence as of mid-2026: albendazole alone appears to have mild-to-negligible direct antibacterial effects on the gut microbiome, while a chemically distinct combination-partner drug — ivermectin — shows clearer, structurally plausible antibacterial activity. A blanket "albendazole kills gut bacteria" claim erases this distinction and, if anything, misattributes to albendazole an effect the data more strongly implicate a different drug in producing.

*6.2 A narrower, older finding: anti-*Wolbachia *activity*

Separately, patent and screening literature has identified a specific, mechanistically distinct off-target effect worth noting for completeness. Structural analysis of compounds active against *Wolbachia* — an intracellular bacterial endosymbiont living inside certain filarial parasites — found that a benzthiazole compound sharing structural similarity to albendazole showed anti-Wolbachia activity, and that additional structurally related benzthiazole and benzimidazole compounds implied that albendazole-like molecules share a common anti-Wolbachia activity. This is scientifically interesting and is being explored as a possible additional antifilarial mechanism, since eliminating a parasite's bacterial endosymbiont can itself be antiparasitic — but it describes activity against an obligate intracellular bacterium living *inside* a parasite's tissues, a different biological compartment entirely from the free-living, luminal gut commensal bacteria the "hidden harm" claim is actually about. Citing this finding as evidence that albendazole kills beneficial intestinal flora would be a category error.

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7. Immunity: Mechanism, Nuance, and the Helminth-Therapy Research Program

This is the most genuinely complex and actively researched dimension of the topic, and it resists resolution into either a simple "protects immunity" or "damages immunity" narrative. To evaluate it properly requires understanding the actual molecular mechanism by which gut bacteria and their metabolites shape immune function — and then situating albendazole's effect (removing a parasite that influences that mechanism) within it.

7.1 The SCFA–Treg mechanism in molecular detail

Chronic helminth infection reprograms host immunity substantially, skewing the immune system toward a T-helper-2 (Th2) and regulatory phenotype, partly via changes the worm induces in gut microbial composition and in the short-chain fatty acids (SCFAs) that gut bacteria produce (Berbudi et al., 2026). SCFAs — principally acetate, propionate, and butyrate, generated by bacterial fermentation of dietary fibers in the colon — are among the best-

characterized molecular links between the gut microbiome and systemic immune regulation.

The mechanism is now understood at considerable molecular resolution. A landmark pair of *Nature* studies established that the colonic microbial fermentation product butyrate significantly accelerates the differentiation of colonic regulatory T (Treg) cells and ameliorates colitis in mouse models, an effect linked to increased histone H3 acetylation at the promoter of the Foxp3 gene — Foxp3 being the master transcription factor that defines regulatory T cell identity and suppressive function. Follow-up mechanistic work has clarified that this occurs largely through butyrate's inhibition of histone deacetylase (HDAC) activity, which suppresses pro-inflammatory Th17 cell production while promoting Treg differentiation and Foxp3 expression, and that SCFAs act through multiple parallel receptor pathways: acetate acts as a ligand for the GPR43 receptor and inhibits HDAC activity upon binding, which stabilizes Foxp3 expression and enhances Treg suppressive function, while butyrate can also initiate Treg differentiation via the high-affinity SCFA transporter Slc5a8 in dendritic cells, or through activation of the cell-surface receptor GPR109a on colonic macrophages and dendritic cells.

Notably, this system is dose-dependent and can flip direction: one study found that while lower butyrate concentrations facilitated Treg differentiation under steady-state conditions, higher concentrations instead induced expression of the transcription factor T-bet across T cell subsets, producing pro-inflammatory interferon-gamma-secreting cells instead — a finding that complicates any simple "more SCFA equals more anti-inflammatory protection" model, and underscores that SCFA immunology is a genuinely active, unsettled field rather than a fully mapped system.

7.2 Why this matters for the helminth-albendazole question specifically

Here the research becomes genuinely counterintuitive: evidence indicates that helminth-associated SCFA shifts can *suppress* the type of immune response the host needs to expel the parasite in the first place — meaning the worm may be partially engineering the microbiome and its metabolite output to protect itself from clearance (Fan & Pedersen, 2021). A related line of work published in *Microbiome* (Springer Nature) showed in mouse models that helminth-evoked changes to the microbiome and SCFA production help suppress experimentally induced colitis (White et al., 2021). Because albendazole's entire clinical purpose is to remove the helminth, this raises a legitimate, published theoretical concern: successful treatment could, in specific individuals or contexts, remove a source of anti-inflammatory signaling.

7.3 The helminth-therapy clinical research program: direct evidence this mechanism is clinically real

This theoretical concern is not merely speculative — it has motivated an entire, decades-long clinical research program built on the premise that helminth-driven immunomodulation is powerful enough to be therapeutically useful, which is worth reviewing in detail because it provides the strongest available human evidence that removing a helminth (as albendazole does) genuinely changes immune tone, even though it says nothing about bacterial killing specifically.

The foundational epidemiological observation dates back decades: researchers first suggested in 1966 that high levels of sanitation were associated with increased risk of developing certain inflammatory and autoimmune diseases, a finding confirmed by subsequent epidemiological surveys — the origin of the broader "hygiene hypothesis." This was extended specifically to helminths through observational work: an observational study of patients with relapsing-remitting multiple sclerosis found dramatic clinical, immunological, and neuroimaging improvements specifically in patients who had been naturally infected with human helminth parasites in the field.

This observation was then tested prospectively using *Trichuris suis* ova (TSO), eggs of the pig whipworm, which is the species most closely related to the human-infecting Trichuris trichiura, and which typically produces only a self-limiting, non-pathogenic colonization when ingested by humans. In inflammatory bowel disease, an initial trial studied four patients with active Crohn's disease and three with ulcerative colitis, giving a single oral dose of 2,500 live Trichuris suis eggs, and found the treatment safe with a striking suppressive effect on the autoimmune response, grounded in the hypothesis that IBD probably results from a failure to properly downregulate a chronic Th1 intestinal inflammatory process, and that helminth-induced Th2 immune responses can diminish that Th1 responsiveness.

The same logic was extended to multiple sclerosis across a series of phase 1 and phase 1b trials. In the first (HINT 1), five subjects with newly diagnosed, treatment-naive relapsing-

remitting MS were given 2,500 TSO orally every two weeks for three months in a baseline-versus-treatment controlled design. A larger follow-up (HINT 2) studied sixteen disease-modifying-treatment-naive relapsing-remitting MS subjects through five months of screening, ten months of TSO treatment, and four months of post-treatment surveillance using serial brain MRI, and found no serious symptoms or adverse events during treatment. A companion mechanistic study tracking immune cells in these same trial participants found that MS patients treated with TSO showed a continuous increase in serum IgG and IgE antibodies specific to T. suis antigens persisting up to 12 months after treatment, confirming the immunological engagement was real and sustained, not merely transient. A dedicated placebo-controlled trial (TRIOMS) was subsequently designed explicitly to test whether TSO could reduce new MRI lesion activity in RRMS, built on the hypothesis that helminth-induced immunomodulation would shift the Th1/Th17 proinflammatory response toward the more anti-inflammatory Th2 phenotype.

It is important, for scientific honesty, not to overstate the clinical payoff of this research program: despite safety and tolerability being consistently demonstrated, clinical phase 1 and 2 studies of TSO treatment in MS patients have been safe and well tolerated but have reported only modest clinical efficacy, and a broader review noted that exploratory phase 1a clinical trials of helminth therapy in MS have been inconclusive overall, likely due to small sample sizes and other study design limitations. Similarly, a Cochrane review of helminth therapy for allergic rhinitis found insufficient evidence of benefit, and a companion TSO trial in allergic rhinitis did not demonstrate a change in symptom scores, illustrating that helminth-driven immunomodulation, while mechanistically real, does not translate into a reliable clinical treatment across every immune-mediated condition it has been tested in.

Mechanistically, this immunosuppressive effect has been traced down to the level of specific innate immune cells: in vitro work found that soluble products of Trichuris suis directly suppress TLR4-induced inflammatory responses in human macrophages, offering a plausible cellular mechanism — separate from, but likely interacting with, the SCFA-microbiome pathway — for how a resident helminth dampens host inflammation.

7.4 Synthesis of Section 7

Taken together, the SCFA-immunology mechanistic literature and the therapeutic helminth-administration clinical trial literature converge on the same conclusion from two independent directions: helminths measurably and mechanistically alter host immune tone, partly via the gut microbiome and its SCFA output, and this effect is robust enough that researchers have spent over two decades trying to harness it therapeutically — with real but modest and inconsistent clinical success. This is strong evidence that *removing* a helminth (which is what albendazole does) has genuine immunological consequences worth taking seriously. But — and this is the critical distinction for the claim under review — none of this literature describes albendazole killing beneficial gut bacteria. It describes the helminth itself as the primary driver of the immune-microbiome axis, with the drug's role being simply to eliminate the organism responsible for that modulation. Working in the opposite direction, chronic helminth infection is also associated with impaired responses to unrelated pathogens and to vaccines in some populations, and with worse outcomes in co-infections such as tuberculosis (Berbudi et al., 2026) — findings that argue in favor of treatment, not against it, and that the helminth-therapy field's own modest results (rather than dramatic ones) suggest the immune trade-offs of clearing a helminth are real but bounded, not catastrophic.

8. The Gut–Brain Axis ("Mind")

There is, as of this writing, no published study directly linking albendazole treatment to cognition, mood, or mental function via the gut microbiome. What does exist is a well-established, broader body of gut–brain-axis research: SCFAs produced by gut bacteria are known to influence blood–brain barrier integrity, neurotransmitter availability, and vagal nerve signaling, and this axis is actively studied in relation to neurological and neurodegenerative conditions such as amyotrophic lateral sclerosis (Moțățăianu et al., 2023). This is legitimate, active neuroscience — but it describes the gut–brain axis in general terms, not any documented, drug-specific effect of albendazole. Extending these general SCFA-and-brain findings into a specific claim about albendazole and cognition would extrapolate well beyond anything any cited study has actually tested; no controlled human or animal study has measured cognitive, mood, or

behavioral outcomes following albendazole treatment via a microbiome-mediated pathway.

It is worth noting that the helminth-therapy trials described in Section 7.3 do intersect the nervous system directly — multiple sclerosis is a central nervous system disease — but their outcome measures (MRI lesion activity, relapse rate) reflect autoimmune neuroinflammation, not cognition or mood in the sense the "hidden harm" claim usually invokes, and none of those trials involved albendazole; they involved live helminth administration, the therapeutic opposite of deworming.

Separately, albendazole does have one well-documented, direct neurological consideration — but it is mechanistically unrelated to the gut microbiome. In treatment of neurocysticercosis, killing the parasite can provoke local inflammation around the dying cyst, producing headaches or seizures (StatPearls, n.d.). This is a real, clinically important, and well-disclosed phenomenon, but it involves inflammation around a dying brain-resident parasite, not gut bacteria or digestion, and should not be conflated with the "mind" claim under review here.

9. Weighing the Evidence

Well-supported by the literature:

- Albendazole's primary mechanism is selective binding to parasite β-tubulin, a target structure that decades of independent resistance-genetics research — spanning veterinary nematodes, human hookworm and whipworm populations, and free-living C. elegans — confirms is the drug's real site of action, with no comparable resistance literature implicating bacterial targets.
- The drug's poor, food-dependent oral bioavailability and rapid first-pass hepatic metabolism are well-characterized pharmacokinetic facts, disclosed in standard references, not hidden ones.
- Gut microbiome composition shifts measurably around successful albendazole treatment in multiple independent human cohorts across different countries.
- That shift tracks with successful parasite clearance rather than drug exposure per se; a controlled parasite-free mouse study found no immediate microbiome disruption from albendazole at all, in direct contrast to a known antibacterial comparator drug tested under identical conditions.
- Untreated helminth infection itself causes malabsorption, anemia, and, in heavily infected individuals, growth impairment; deworming exists specifically to reverse these effects, although rigorous population-level meta-analyses find the average growth/cognition benefit of mass deworming programs is smaller than earlier literature assumed.
- Helminths measurably modulate host immunity via SCFA-dependent Treg induction and other mechanisms — a finding robust enough to have supported two decades of clinical helminth-therapy research, with real but modest results.

Genuinely unresolved, active research areas — not settled in either direction:

- Whether albendazole has meaningful, taxon-specific "off-target" antibacterial activity independent of parasite clearance: 2025 metagenomic evidence suggests this effect is mild for albendazole alone, but the question remains actively studied, and is considerably larger for a structurally distinct combination-partner drug (ivermectin).
- Whether losing helminth-associated, SCFA-linked anti-inflammatory signaling after successful treatment carries meaningful downsides for specific individuals — a legitimate, actively funded line of inquiry within hygiene-hypothesis and helminth-therapy research.
- Any specific cognitive or mood effect of albendazole via the gut–brain axis: no direct study exists on this question; it remains extrapolation rather than established science.

Not supported by the literature as reviewed here:

- A general claim that albendazole "kills the beneficial microorganisms of the intestine" in the manner a broad-spectrum antibiotic depletes commensal flora. The mechanism does not support it, the resistance genetics confirm the drug's real target is eukaryotic and parasite-specific, and the studies that specifically tested for direct bacterial killing — including the one experimental design that isolated the drug from parasite death entirely — found no such effect.

10. Limitations of This Review

This is a narrative synthesis, not a formal systematic review or meta-analysis; it does not follow a PRISMA search-and-screening protocol and draws on a bounded rather than exhaustive set of studies. Several of the human microbiome studies discussed involve modest sample sizes

and single-population cohorts (Ghana, Kenya, Indonesia, Côte d'Ivoire), which limits generalizability to other populations, infection intensities, and co-endemic disease contexts. The 2025 hybrid-metagenomics off-target study is a preprint and had not completed formal peer review at the time of writing. The helminth-therapy trials reviewed in Section 7 involve live *Trichuris suis* administration, not albendazole, and are cited only to establish that helminth-driven immunomodulation is a real, clinically studied phenomenon — not as direct evidence about albendazole itself. Where a conclusion rests on a single study rather than convergent evidence, that has been flagged explicitly in the text rather than presented as settled consensus.

11. Conclusion

The evidence does not support the claim that albendazole broadly kills the beneficial bacteria of the human intestine in a manner comparable to a broad-spectrum antibiotic, nor does it support framing this as a truth concealed by manufacturers — the drug's actual, disclosed risk profile (bone marrow suppression, hepatotoxicity, teratogenicity, transient GI upset, variable and food-dependent absorption) is published in standard prescribing information and pharmacokinetic literature, and differs substantially from the "gut flora destruction" claim in question. At the same time, the honest picture is not a simple exoneration either: helminth infection and its removal genuinely reshape the gut ecosystem and its downstream immune signaling — via a well-characterized SCFA–Treg mechanism robust enough to have anchored two decades of therapeutic helminth research — in ways still being actively characterized, and a narrow, mechanistically distinct off-target antibacterial question remains open for combination-therapy partner drugs like ivermectin. The most accurate summary is also the least dramatic one: albendazole clears a parasite that itself was reshaping the gut environment and modulating host immunity, and the changes visible in the data track that clearance rather than a hidden antibacterial action of the drug itself.

References

Appiah-Twum, F., Akorli, J., Okyere, L., Sagoe, K., Osabutey, D., Cappello, M., & Wilson, M. D. (2023). The effect of single dose albendazole (400 mg) treatment on the human gut microbiome of hookworm-infected Ghanaian individuals. *Scientific Reports, 13*, 11302. https://doi.org/10.1038/s41598-023-38376-3

Arpaia, N., et al. (2013). Metabolites produced by commensal bacteria promote peripheral regulatory T-cell generation. *Nature, 504*, 451–455.

Berbudi, A., et al. (2026). Helminth infection, gut microbiome alterations, and their impact on pulmonary tuberculosis susceptibility. *Journal of Tropical Medicine*. https://doi.org/10.1155/jotm/3767562

Clarke, N. E., Clements, A. C. A., Doi, S. A., Wang, D., Campbell, S. J., Gray, D., & Nery, S. V. (2017). Differential effect of mass deworming and targeted deworming for soil-transmitted helminth control in children: A systematic review and meta-analysis. *The Lancet, 389*(10066), 287–297.

Easton, A., et al., as reported in Healio Infectious Diseases in Children. (2019, May 8). *Deworming programs do not have harmful effects on gut microbiome*. https://www.healio.com/news/pediatrics/20190507/deworming-programs-do-not-have-harmful-effects-on-gut-microbiome

Fan, Y., & Pedersen, O. (2021). Control of lymphocyte functions by gut microbiota-derived short-chain fatty acids. *Cellular & Molecular Immunology, 18*, 1161–1171. https://doi.org/10.1038/s41423-020-00625-0

Fleming, J., Hernandez, G., Hartman, L., Maksimovic, J., Nace, S., Lawler, B., et al. (2019). Safety and efficacy of helminth treatment in relapsing-remitting multiple sclerosis: Results of the HINT 2 clinical trial. *Multiple Sclerosis Journal, 25*, 81–91. https://doi.org/10.1177/1352458517736377

Furtado, L. F. V., Dos Santos, T. R., de Oliveira, V. N. G. M., & Rabelo, É. M. L. (2020). Genotypic profile of benzimidazole resistance associated with SNP F167Y in the beta-tubulin gene of Necator americanus helminths obtained from Brazilian populations. *Infection, Genetics and Evolution, 86*, 104594. https://doi.org/10.1016/j.meegid.2020.104594

Global burden of soil-transmitted helminth infections, 1990–2021. (2024). *Infectious Diseases of Poverty, 13*. https://doi.org/10.1186/s40249-024-01238-9

Hybrid-metagenomics reveal off-target effects of albendazole, ivermectin-albendazole and moxidectin-albendazole on the human gut bacteria [Preprint]. (2025). *bioRxiv*. https://doi.org/10.1101/2025.06.27.660518

LiverTox: Clinical and Research Information on Drug-Induced Liver Injury. (n.d.). *Albendazole*. National Institute of Diabetes and Digestive and Kidney Diseases, NCBI Bookshelf. https://www.ncbi.nlm.nih.gov/books/NBK548360/

Moțățăianu, A., Șerban, G., & Andone, S. (2023). The role of short-chain fatty acids in microbiota–gut–brain cross-talk with a focus on amyotrophic lateral sclerosis: A systematic review. *International Journal of Molecular Sciences, 24*(20), 15094. https://doi.org/10.3390/ijms242015094

Differential effects of two common antiparasitics on microbiota resilience. (2024). *Journal of Infectious Diseases, 229*(3), 908–917. https://doi.org/10.1093/infdis/jiad547

Multi-omics insights into the response of the gut microbiota and metabolites to albendazole deworming in captive *Rhinopithecus brelichi*. (2025). *PMC*. https://pmc.ncbi.nlm.nih.gov/articles/PMC12058082/

Furuhashi, M., et al. (2024). Benzimidazole resistance-associated mutations improve the in silico dimerization of hookworm tubulin: An additional resistance mechanism. *Veterinary World, 17*(12). https://veterinaryworld.org/Vol.17/December-2024/5.php

Prichard, R. (2024). Benzimidazole Resistance-Associated Mutations in the β-tubulin Gene of Hookworms: A Systematic Review. *Parasitology Research*. https://link.springer.com/article/10.1007/s00436-024-08432-6

Sato, Y., et al. (2024). Studies on absorption mechanism and pharmacokinetic properties of albendazole-bile acid conjugate: In vivo and in vitro. *[Journal not specified in source]*. https://pubmed.ncbi.nlm.nih.gov/39243427/

StatPearls. (n.d.). *Albendazole*. NCBI Bookshelf. https://www.ncbi.nlm.nih.gov/books/NBK553082/

Systematic review: Factors associated with variation in single-dose albendazole pharmacokinetics: A systematic review and modelling analysis. (2022). *medRxiv*. https://www.medrxiv.org/content/10.1101/2022.05.18.22275185

Trichuris suis ova in relapsing-remitting multiple sclerosis and clinically isolated syndrome (TRIOMS): Study protocol for a randomized controlled trial. (2013). *Trials*. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3680966/

Vargas, V. M., et al. (2006). Non-disjunction events induced by albendazole in human cells. *Mutation Research/Genetic Toxicology and Environmental Mutagenesis*. https://www.sciencedirect.com/science/article/abs/pii/S1383571806003214

Welch, V. A., Ghogomu, E., Hossain, A., Awasthi, S., Bhutta, Z., Cumberbatch, C., Fletcher, R., McGowan, J., Krishnaratne, S., Kristjansson, E., Sohani, S., Suresh, S., Tugwell, P., & Wells, G. (2016). Deworming and adjuvant interventions for improving the developmental health and well-being of children in low- and middle-income countries: A systematic review and network meta-analysis. *Campbell Systematic Reviews, 12*, 1–383. https://doi.org/10.4073/csr.2016.7

White, E. C., et al. (2021). Cooperation between host immunity and the gut bacteria is essential for helminth-evoked suppression of colitis. *Microbiome, 9*, 187. https://doi.org/10.1186/s40168-021-01146-2

Wiria, A. E., et al. (2022). Intestinal permeability before and after albendazole treatment in low and high socioeconomic status schoolchildren in Makassar, Indonesia. *Scientific Reports, 12*, 3540. https://doi.org/10.1038/s41598-022-07086-7

Worm-specific immune response in multiple sclerosis patients receiving controlled Trichuris suis ova immunotherapy. (2021). *Life, 11*(2), 101. https://doi.org/10.3390/life11020101