



The Multifaceted Influence of Coffee Consumption on Gut Microbiota Composition, Gastrointestinal Function, and Overall Health Outcomes: A Comprehensive Review

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Abstract

Background: The gut microbiota plays a pivotal role in human health, influencing various physiological processes and disease outcomes. Recent studies have suggested that coffee consumption may significantly impact gut microbiota composition and function, potentially offering health benefits while also presenting certain risks.

Methods: A comprehensive literature review was conducted up to June 2023, utilizing databases such as PubMed and Web of Science. The search criteria included terms related to coffee, caffeine, microbiota, and gastrointestinal health. Both clinical studies involving human participants and preclinical investigations utilizing rodent models were included in the analysis.

Results: The findings indicate that moderate coffee consumption (3-4 cups daily) is associated with enhanced diversity and relative abundance of beneficial gut bacteria, including *Firmicutes* and *Actinobacteria* while reducing Bacteroidetes levels. Coffee intake also appears to exert antibacterial properties against harmful gut microbes, such as *Escherichia coli* and *Clostridium* species. Additionally, coffee enhances gastrointestinal motility and secretion, which may aid in digestive health. However, excessive consumption (beyond 5 cups daily) may contribute to adverse gastrointestinal effects and increase the risk of conditions like gastroesophageal reflux disease (GERD).

Conclusion: Coffee represents a double-edged sword regarding gut health; it possesses the potential to modulate gut microbiota positively and enhance gastrointestinal function while also carrying risks associated with high consumption. Further investigations are warranted to elucidate the mechanisms underlying these effects and to establish more definitive clinical guidelines.

Keywords: Gut microbiota, coffee consumption, gastrointestinal health, Firmicutes, dysbiosis.

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1. Introduction

Coffee is among the most widely consumed drinks worldwide, appreciated not only for its flavor and fragrance but also for its beneficial effects on several biological processes related to health and illness

[1,2]. Historically, coffee use was perceived to have mostly adverse health effects; nevertheless, emerging data indicates that coffee may provide significant health benefits in several domains. The physiological effects of coffee result from its intricate makeup, including over 1000 distinct bioactive components, including caffeine, kahweol, chlorogenic acid, cafestol, and several micronutrients such as magnesium, potassium, and vitamin E [3,4]. Recent research has identified coffee as an immunomodulator, antiobesity agent, antidiabetic, hepatoprotective substance, antioxidant, antigenotoxic agent, and inhibitor of cell proliferation [2,5,6]. Notwithstanding its health advantages, excessive coffee consumption has been linked to some cardiovascular and gastrointestinal deleterious effects and dysfunctions [7,8]. Therefore, it is recommended to drink a modest quantity of coffee (3–4 cups daily) and restrict caffeine consumption to 200 mg or fewer per day to harness health advantages while minimizing potential bad effects [9,10].

The use of coffee directly influences the gut microbiome. The microbiota is regarded as the second genome of the human body and influences several bodily processes and overall well-being [11,12]. The gut microbiota, comprising approximately 10 trillion microbial cells, represents the most substantial microbial reservoir in the body; however, the oral, respiratory, skin, and reproductive tract microbiotas also play significant physiological roles in various organs. The gut microbiota includes fungi, viruses, and bacteriophages, but is mostly composed of commensal and symbiotic bacteria. Firmicutes, Bacteroidetes, Proteobacteria, and Actinobacteria are the four predominant phyla of gut bacteria, with Firmicutes and Bacteroidetes comprising around 90% of the relative abundance of the gut microbiota. The microbiota is recognized for its impact on various physiological processes in the gut, including metabolism, digestion, absorption, motility, secretion, permeability, the enteric nervous system (ENS), gut-associated lymphatic tissue (GALT), immunity, infections, and inflammatory responses [13-16]. Furthermore, it has extensive impacts on systemic processes, including the cardiovascular, neurological, and musculoskeletal systems, as well as the development of the immune system [15-17]. Increasing data from human and animal research indicates that coffee influences gut microbiota and gastrointestinal processes, including motility, secretion, absorption, and immune response. Coffee may influence gastrointestinal functioning partially via its effects on bacteria. This article examines the unique effects of coffee on gut microbiota composition, diversity, and growth. We will examine the impact of coffee on certain gastrointestinal processes in both health and illness and explore the potential involvement of gut microbiota in these coffee-related functional alterations in the gastrointestinal tract. We conducted a literature review up to June 2023 using PubMed, Web of Science, and other sources, employing search criteria including coffee, caffeine, microbiota, gastrointestinal illness, motility, secretion, gut-brain axis, absorption, and drug interaction. Clinical research involving patients and preclinical investigations using rodent models were included.

2. Impact of Coffee on Microbiota Composition

The gut microbiota is in tight alignment with its surroundings. Alterations in nutrition, lifestyle, and health circumstances may lead to substantial modifications in microbiota structure and composition, culminating in dysbiosis. The complex significance of gut microbiota in several physiological systems means that dysbiosis has clinical consequences [18]. Numerous research including animals and human samples examined the alterations in gut microbiota resulting from coffee use. Table 1 delineates the particular alterations in gut microbiota resulting from coffee use or interventions using coffee constituents in both humans and animals. Most research examining human fecal samples indicated that coffee drinking increased the relative abundance of Firmicutes and Actinobacteria [19-24]. Conversely, Ref. [25] indicated a reduction in Firmicutes. Coffee use was shown to reduce the relative number of Bacteroidetes in the gut [21], while another research indicated that soluble coffee fiber enhanced the relative abundance of Bacteroides-Prevotella, a genus within the Bacteroidetes phylum, by 60% [26]. Human volunteer research shown that the intake of 3 cups of coffee daily for 3 weeks might induce substantial alterations in microbiota composition and enhance the prevalence of beneficial Actinobacteria and Bifidobacterium spp. inside the gastrointestinal tract [27].

Animal studies have the benefits of maintaining rigorous control and research groups, as well as examining the cellular and molecular processes behind the effects of coffee. Research using a mouse model shown that prolonged coffee intake resulted in an elevation of short-chain fatty acid (SCFA)

generating bacteria, including *Bifidobacterium longum* and *Faecalibacterium*, with a concomitant reduction in *Prevotella*, leading to an increase in SCFA levels [28]. Coffee consumption may influence alterations in microbiota via caffeine and/or other constituents or metabolites of coffee, such as micronutrients and phenolic chemicals. Caffeine intake partly mitigated amoxicillin-induced dysbiosis in the murine gut when compared to decaffeinated coffee, indicating a potential involvement of caffeine in this action [29]. Nonetheless, independent studies have shown no substantial difference in the impact of caffeinated vs decaffeinated coffee on gut microbiota, indicating that other constituents in coffee may possibly play a crucial role in influencing its effects on gut microbiota [30,31].

3. Coffee's Impact on the Diversity of Microbiota

Besides microbiota composition, the amount of microbial diversity is a crucial component influencing the overall influence of microbiota on its host. Generally, increased diversity correlates with favorable health outcomes, whereas decreased diversity correlates with detrimental health outcomes, including an elevated risk of colorectal cancer and inflammatory bowel disease (IBD) in the gastrointestinal tract [32- 34]. A comprehensive population-based metagenomics investigation revealed that the use of coffee, tea, and red wine, all rich in polyphenols, correlated with enhanced alpha diversity of the gut microbiota in stool samples [35]. A recent cross-sectional investigation indicated that the composition and organization of colonic mucosa-associated bacteria varied considerably according to daily caffeine and coffee use in adults. Dai et al. assessed the impact of low and high coffee consumption on the composition of colonic mucosa-associated microbiota utilizing human biopsies, revealing that increased coffee intake correlated with elevated alpha diversity and a greater relative abundance of *Alistipes* and *Faecalibacterium*, alongside a diminished relative abundance of *Erysipelatoclostridium* [36]. The impact of caffeine and coffee intake on health outcomes via modulation of gut microbiota diversity needs to be established.

4. Impact of Coffee on Microbiota Proliferation

Numerous research has examined the impact of coffee on the development of gut bacteria. Jaquet et al. indicated that coffee facilitated the proliferation of certain bacterial species [27]. Nakayama et al. discovered that coffee may possess antibacterial properties against *Escherichia coli* [32]. Reports indicate that fecal bacteria were unaffected by coffee drinking [26]. Our previous investigation on mice showed that coffee extract markedly inhibited the proliferation of gut microbiota [31]. Intraluminal fecal matter was obtained from the distal ileum and colon of naïve rats. The fecal samples were diluted and cultivated on standard and coffee-infused LB agar plates. In LB agar containing 1.5% coffee, bacterial growth from the intraluminal colon content was significantly inhibited compared to standard LB agar (9.31×10^9 CFU/gram vs. 9.65×10^9 CFU/gram). The bacteriome growth was further inhibited to 5.02×10^5 CFU/gram with 3% coffee. An analogous inhibitory effect was seen in the ileal contents. Decaffeinated coffee extract had a comparable inhibitory impact on bacterial growth in vitro. We also assessed the in vivo impact of coffee on the overall bacterial community. Bacterial culture and quantitative RT-PCR analyses revealed that a 3-day oral gavage administration of coffee at a daily dosage of 250 mg substantially reduced the total bacterial count in the colon. Once again, decaffeinated coffee had an impact similar to that of ordinary coffee. Our findings indicate that both normal and decaffeinated coffee decreased Enterobacteria and γ -proteobacteria levels in rats administered coffee for three days, indicating that constituents or metabolites of coffee, excluding caffeine, are accountable for the noted antibacterial impact [31]. Mannooligosaccharides (MOS) derived from spent coffee grounds can exert a prebiotic effect on gut microbiota by promoting the proliferation of certain beneficial genera, including *Veillonella*, *Odoribacter*, *Butyricoccus*, *Coprococcus*, *Pseudoflavonifractor*, *Intestinimonas*, and *Barnesiella*. Conversely, furfural and polyphenols, generated from the spent coffee grounds matrix during hydrolysis, may inhibit the growth of other beneficial genera, such as *Ruminococcus*, *Faecalibacterium*, *Blautia*, *Dialister*, *Butyricimonas*, *Anaerostipes*, and *Collinsella* [37]. This indicates that various active constituents of coffee exert differing influences on microbial proliferation, and the coffee processing technique significantly impacts the health advantages or adverse consequences associated with coffee. In vitro, fecal M-batch culture investigations indicated that coffee promoted the proliferation of *Bifidobacterium*, *Lactobacilli*, and *F. Prausnitzii* in Lumen, while the XIVa group, *Coprococcus* genus, and *F. Prausnitzii* were

elevated in the mucosal environment, indicating that coffee has a specific influence on the microbial community, contingent upon microenvironmental parameters [38].

5. Impact of Coffee on Gastrointestinal Infections and Immune Function

The gut microbiota is essential for the competitive suppression of intestinal pathogens, maintaining intestinal homeostasis, and enhancing the immune system [39]. As previously stated, coffee has a non-specific antibacterial activity [31]. Furthermore, several research indicated that coffee may specifically reduce the prevalence of harmful microbes. For example, coffee drinking markedly reduced the *Escherichia coli* and *Clostridium* species population in both the murine small intestine and colon [32,40]. Numerous research has sought to identify the constituents in coffee that contribute to its antimicrobial properties. Coffee extracts possess elevated levels of chlorogenic acid, which have been associated with the antibacterial, antifungal, and antiviral effectiveness of coffee [41]. Phenolic acids and melanoidins, significant metabolites found in coffee, have shown antibacterial action against Gram-positive bacteria (*Listeria monocytogenes*, *Staphylococcus aureus*) and yeast (*Candida albicans*) [42].

Components of coffee, including polyphenols, may influence both innate and adaptive immune responses in the gastrointestinal tract [43,44]. Caffeine inhibits the secretion of proinflammatory cytokines, thereby reducing the activity of many immune cells, including natural killer (NK) cells, macrophages, and the proliferation of T and B cells [44]. Kahweol, a bioactive component in coffee, facilitates anti-inflammatory effects by regulating the expressions of macrophage cyclooxygenase-2, nitric oxide synthase, and NF- κ B. Caffeic acid supplementation in a murine model of colitis mitigated colonic inflammation by suppressing proinflammatory cytokines and elevating IL-10 levels, while concurrently reducing the relative abundance of *Bacteroides* and *Turicibacter* and augmenting the relative abundance of *Alistipes* and *Dubosiella* in the gut [46]. Conversely, Ref. [47] indicated a favorable connection between coffee intake and upper gastrointestinal tract symptoms in individuals with active *Helicobacter pylori* infection.

Inflammatory bowel disease (IBD), including Crohn's disease and ulcerative colitis, is a chronic condition marked by recurrent intestinal inflammation. Inflammatory bowel disease (IBD) often has a multifaceted etiology, with dysbiosis of gut microbiota involved in its pathogenesis. Numerous studies indicated that in individuals with Crohn's disease and ulcerative colitis, coffee intake exacerbated symptoms and correlated with the recurrence of inflammatory bowel disease (IBD) [48,49]. Conversely, others indicated that IBD was not linked to coffee. Indeed, coffee drinking has been found to have a preventive effect against ulcerative colitis [50,51]. Additional research is required to determine if the effect of coffee on IBD is direct or mediated by its influence on microbial dysbiosis.

Irritable bowel syndrome (IBS) is a prevalent gastrointestinal condition in the Western world that significantly impacts the quality of life, healthcare expenditures, mental health, and the social conduct of those afflicted. Modified gut-brain interactions are a primary feature of IBS, with gut dysbiosis suggested as a potential cause of the condition [53,54]. Acute bacterial gastroenteritis may induce persistent, low-grade inflammation of the intestinal wall, which might sufficiently modify gut neuromuscular and epithelial cell functions, hence precipitating IBS [55,56]. Caffeine and other bioactive components in coffee may influence many pathways involved in the pathophysiology of IBS. Various research assessed the impact of habitual coffee intake on the likelihood of acquiring IBS symptoms, yielding incongruous findings. A recent meta-analysis of existing datasets on IBS patients indicated that coffee consumers had a lower probability of getting IBS compared to control subjects [57]. Conversely, an extensive study of IBS patients indicated that heightened gastrointestinal symptoms, such as diarrhea, correlate with coffee use [58]. Additional controlled and targeted studies are required to rigorously assess whether caffeine or other bioactive constituents of coffee directly contribute to the onset and aggravation of IBS.

6. Impact of Coffee on Gastrointestinal Motility and Secretion

Gastrointestinal motility and secretion are essential for digestive health, facilitating mechanical and chemical digestion while propelling food and other intraluminal substances at a suitable rate through the alimentary canal. Irregular motility and secretion may result in several illnesses, including

gastroesophageal reflux disease (GERD), peptic ulcer, gastric dyspepsia, constipation, and functional blockages such as postoperative ileus.

Coffee is recognized for its ability to enhance gastric and pancreatic secretion in individuals without abnormalities [59,60]. Feldman et al. found that decaffeinated coffee elicited stomach acid secretion, achieving 70% of the maximum acid production response to pentagastrin. They also discovered that it elevated serum gastrin levels. Decaffeinated coffee was shown to be more effective than the previously prevalent protein test meal (Bacto-peptone) in promoting acid secretion and gastrin release [59]. Acquaviva et al. discovered that a coffee solution equivalent to 2 cups of handmade coffee dramatically elevated blood gastrin levels by 2.3-fold, whereas decaffeinated coffee had a comparable impact with a 1.7-fold rise in gastrin levels in the blood [61]. Subsequent research indicates that caffeine and other constituents of coffee may directly influence G-cells to promote gastrin production and augment gastric secretion [62,63]. Coffey et al. validated the impact of coffee on gastrin release, finding that both caffeinated and decaffeinated coffee enhanced gastric secretion as well as exocrine pancreatic trypsin secretion [60].

In 1980, Thomas et al. discovered that coffee markedly reduced lower esophageal sphincter pressure in both healthy individuals and patients with reflux esophagitis [64]. Decaffeinated coffee had effects comparable to those of regular coffee [65,66]. In vitro investigations showed that coffee induced stomach muscular spasms, subsequently followed by relaxation [67,68]. Nonetheless, in vivo human investigations indicated that coffee does not substantially affect stomach emptiness [69]. Numerous research has investigated the potential associations between coffee intake and the risks of gastroesophageal reflux disease, dyspepsia, and peptic ulcer, considering the effects of coffee on lower esophageal sphincter pressure and stomach secretion [49,66]. Recent findings indicate that little coffee intake (fewer than 4 cups daily) seems to not affect the incidence of GERD [70]. Nonetheless, elevated coffee intake (exceeding 4 cups daily) may heighten the risk of GERD [70]. Conflicting evidence exists about the associations between coffee intake and the risks of functional dyspepsia and peptic ulcer diseases [49].

The impact of coffee on colonic motility is well established [71,72]. Research involving 99 healthy individuals indicated that 29% had a strong need to defecate after the consumption of a cup of coffee, suggesting colonic stimulation by coffee [71]. Separate research demonstrated that distal colonic motility significantly enhanced within minutes after coffee consumption [71]. Decaffeinated coffee had a comparable impact. The findings indicate that coffee may aid in the prevention of constipation. Population-based research indicates that coffee intake is negatively correlated with the occurrence of constipation [31]. Given that gut microbiota may significantly influence gut motility via microbial metabolites such as short-chain fatty acids (SCFAs) and tryptophan metabolites, it is plausible that coffee-induced changes in gut microbiota might explain its impact on motility [73]. It is indisputable that coffee may directly influence the neuromuscular system, hence affecting gastrointestinal motility. In the in vitro examination of isolated rat colonic smooth muscle strips, we observed that both regular and decaffeinated coffee induced muscular contractions in a dose-dependent manner (0.1 to 10 mg/mL). The coffee-induced contractions were unaffected by the neural activity inhibitor tetrodotoxin or the nicotinic receptor antagonist hexamethonium but were entirely inhibited by the muscarinic receptor antagonist atropine. The observations indicate that coffee induces muscular contractions via directly interacting with muscarinic receptors in stomach smooth muscle cells or by inhibiting acetylcholinesterase, an enzyme responsible for the degradation of acetylcholine, independent of caffeine [31]. In the in vivo investigation, we observed that coffee intake over three days resulted in a modest enhancement of ileal smooth muscle contractility and a reduction in Enterobacteria copy numbers. The causal relationship between changed gut microbiota and heightened ileal motility in coffee-treated mice remains uncertain [31].

Recent research indicates that coffee considerably influences small intestine motility. Postoperative ileus (POI) is a dysmotility disorder characterized by substantial inflammatory alterations occurring after a laparotomy procedure. Motility impairment and delayed transit mostly manifest in the small intestine in post-operative ileus (POI). Numerous studies have shown the advantages of coffee drinking in POI [74]. Various studies indicate that coffee is an economical means to enhance postoperative recovery of

gastrointestinal function and motility after colorectal and gynecological surgeries [74,75]. Our recent investigation in a preclinical model shown that coffee does not influence the inflammatory response in POI in mice, but it dramatically enhances intestinal transit and stimulates ileal smooth muscle contractions in a muscarinic receptor-dependent way [76]. These effects may enhance the advantages of coffee in POI.

7. Summary

Increasing data indicates that coffee use modifies the makeup and development of gut bacteria. Moderate coffee use (<4 cups daily) correlates with enhanced microbiota diversity, elevated relative abundance of advantageous bacterial phyla such as *Firmicutes* and *Actinobacteria*, and reduced levels of *Bacteroidetes*. Coffee may possess antibacterial properties in the gastrointestinal tract, with phenolic acids and chlorogenic acid potentially contributing to this effect. Caffeine has anti-inflammatory qualities, and other components in coffee, such as phenolic acid, may influence immunological responses.

Coffee and decaffeinated coffee promote the release of gastrin and increase gastric and pancreatic secretions. They are also seen to reduce the lower esophageal pressure. Excessive coffee drinking (>5 cups daily) may increase the risk of gastroesophageal reflux disease. Coffee has been shown to enhance ileal and colonic motility independently of caffeine. The stimulating effect is partially due to coffee's influence on muscarinic receptors in gastrointestinal smooth muscle cells. Coffee may influence the gut- brain axis, affecting visceral pain perception and central nervous system activities. Evidence suggests that these effects may be linked to the changed gut microbiome.

Coffee consumption is seen to influence lipid absorption, maybe via altering the gut flora. Coffee drinking may elevate HDL-cholesterol and vitamin D levels while diminishing zinc, calcium, and vitamin B levels. The use of coffee may influence medication interactions and metabolism. Coffee enhances aspirin absorption by altering the α - and β -diversities of the gut microbiota. Research indicates that coffee drinking significantly influences the makeup and diversity of the oral microbiome. Moderate coffee intake correlates with increased diversity within the oral microbial population. Excessive coffee consumption has been linked to the advancement of periodontal diseases. Collectively, recent research has shown several contradictory findings about the effects of coffee on the gastrointestinal system. Additional investigation on the impact of coffee on gut flora and bowel functions is necessary.

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التأثير متعدد الأوجه لاستهلاك القهوة على تكبير ميكروبيوتا الأمعاء، ووظيفة الجهاز الهضمي، والنتائج الصحية العامة: مراجعة شاملة الملخص

الخلفية: بنوعه نَسْتَدًا الأعماء دَسًا جَسًا ف صحح الإسنا، حبّ نُوَس عبي اعياخ افسنخج ابحرفج زأنج الألباض. نَسش اندساساخ احنجج إبي أ اسرلاك الفجّ قد وُس نَسنو مَس عبي ذُنْ طُفج نَسْتَدًا الأعماء، إ فُس فأنذ صحح جرج، نُن قد حُو أَعًا تعط ابحاعش.

الطرق: ذُ إحصاء شباحح شايح بلأدناح حري 2023 تاسرخذا قأعد نأاح بو PubMed. Web of Science شيد عائش احنح صطباح ذرعيق تالفج، أنافِ، أنَسْتَدًا، صحح انداص اع. ذعدُ ارحيلاخ اندساساخ اسسشع انر شيد ناسمِ ائس ارحفجاق اقر اسسشع تاسرخذا أرح افاض.

النتائج: نَسش ارنالح إبي أ الاسرلاك اعزده يفج (4-3 أمب أ) سُذك تصأج ارعُ أفسج اسنح بيثرشيا الفج ف الأعماء، نا ف ربل Firmicutes Actinobacteria، ع ذقبو سبرأح. Bacteroidetes ذُ أ ذاه الفج أَسط خصائص عأج بيثرشيا اعاسج ف الأعماء، بو Escherichia coli أع Clostridium. تالإظافح إبي ربل، ذعضص الفج حشم إفاص انداص اع، إ قد ساعد ف صحح انداص اع. ع ربل، قد ودي الاسرلاك الفج (أمش) 5 أمب أ إبي ذائشاح سيح عبي انداص اع. صأج خطش الإصالح تحالاح بو شيص اسذع الشيء (GERD).

الاستنتاج: ذنو الفج سلاخا را حدُ فإ رُعي تصح الأعماء؛ ف ذبل افسج عبي ذعدو نَسْتَدًا الأعماء نَسو إاُ ذعضص طُفج انداص اع، نأ نَحو أَعًا جاعش شذتطح تالاسرلاك الفج. إك حاخ إبي صبذُ إ اندساساخ برطح اناح نأ ساء ز اراثشاح لإعداد إسشادح سسشع أمش نحدُ.

الكلمات المفتاحية: نَسْتَدًا الأعماء، اسرلاك الفج، صحح انداص اع، Firmicutes، اخلاه اراض انَسْت.