

Coffee and liver health: Exploring the protective benefits and mechanisms of coffee and its bioactive compounds in liver disorders

Naila Rasheed¹, Zafar Rasheed^{2*}

¹School of Nursing and Midwifery, Griffith University, Brisbane, Queensland, Australia, ²Department of Pathology, College of Medicine, Qassim University, Buraidah, Saudi Arabia

***Address for correspondence:**

Zafar Rasheed, PhD, PGDCA, TAE, Department of Pathology, College of Medicine, Qassim University, Qassim, Saudi Arabia. E-mail: zafarrasheed@qu.edu.sa

WEBSITE: ijhs.org.sa

ISSN: 1658-3639

PUBLISHER: Qassim University

Coffee, one of the most widely consumed beverages worldwide, has garnered significant attention for its health benefits. Beyond its stimulant effects, studies highlight its potential role in reducing the risk of liver diseases such as non-alcoholic fatty liver disease (NAFLD), cirrhosis, and hepatocellular carcinoma (HCC). This editorial explores the mechanisms underlying these protective effects, emphasizing the interplay between bioactive compounds in coffee and liver health. By integrating epidemiological, clinical, and biochemical insights, this article also explores how moderate coffee consumption can contribute to liver disease prevention and public health strategies.

Liver diseases constitute a significant global health burden, with millions affected annually by conditions ranging from fatty liver disease to advanced cirrhosis and liver cancer.^[1] NAFLD, driven largely by obesity and metabolic syndrome, is the leading cause of chronic liver disease worldwide. Furthermore, alcohol-related liver disease (ALD) and viral hepatitis remain prominent contributors to morbidity and mortality.^[2] Due to these challenges, consumption of coffee has emerged, to determine its potential on the onset of liver disorders. Coffee, a complex beverage containing over 1,000 bioactive compounds, is more than just a morning pick-me-up.^[3] Epidemiological studies over the past two decades consistently demonstrate an inverse association between coffee consumption and the risk of various liver conditions.^[4] Coffee contains a diverse array of compounds with antioxidant, anti-inflammatory, and metabolic properties. Key constituents include caffeine, chlorogenic acids, diterpenes, and melanoidins.^[3,5] Caffeine plays a central nervous system stimulant that modulates energy metabolism and exerts antioxidant effects.^[6] Whereas chlorogenic acids are a polyphenolic compound with potent antioxidant properties, contributing to the modulation of glucose metabolism and lipid profiles.^[7] Diterpenes such as cafestol and kahweol are compounds linked to anti-inflammatory and anticarcinogenic effects, though they may elevate cholesterol levels in unfiltered

coffee^[8] and melanoidins are other compounds present in coffee also reported to have antioxidant and antimicrobial activity.^[9] These bioactive compounds synergistically impact liver physiology, offering protective effects against oxidative stress, inflammation, and fibrosis.^[6-9] Regular coffee drinkers exhibit lower hepatic fat accumulation and improved liver enzyme profiles and reduce the chances of NAFLD onset.^[10] The possible mechanisms include improved lipid metabolism, reduced oxidative stress, and decreased pro-inflammatory cytokine levels.^[11] Caffeine and chlorogenic acids are believed to mediate these effects by modulating pathways such as AMP-activated protein kinase (AMPK), which regulates energy homeostasis.^[4,12,13] Whereas in cirrhosis, coffee appears to reduce both the incidence and risk for liver failure, cancer occurrence, and chronic hepatitis.^[13,14] An excellent review by Wadhawan and Anand pointed out that intake of more than 2 cups of coffee per day in individuals pre-existing liver disorders showed the reduction in incidence of fibrosis, cirrhosis, and liver cancer as well as decreased the mortality rate.^[4] Specifically, the antifibrotic effects of coffee may be linked to its ability to suppress transforming growth factor-beta, a key driver of hepatic fibrosis.^[15] HCC is another liver-associated disorder which is the most common form of primary liver cancer, with a strong association with cirrhosis and chronic Hepatitis B and C infections, ALD, and also metabolic dysfunction-associated steatotic liver diseases.^[16] Coffee has emerged as a protective factor, with studies indicating a dose-dependent reduction in HCC risk. A meta-analysis published by Kennedy *et al.* showed that individuals consuming one-five cups of coffee per day reduces the relative risk of HCC.^[17] Furthermore, antioxidant compounds in coffee, such as chlorogenic acids inhibit carcinogenesis by DNA damage.^[18] As we know, oxidative stress plays a pivotal role in liver injury and disease progression. Coffee's antioxidant capacity, attributed to chlorogenic acids and caffeine, reduces the formation of reactive oxygen species, thereby protecting hepatocytes from damage.^[19] On the other hand, chronic inflammation is

central to liver disease pathogenesis. Bioactive compounds in coffee inhibit pro-inflammatory pathways, including nuclear factor-kappa B and cytokine production.^[20,21] These effects may help attenuate liver inflammation and fibrosis. Moreover, coffee consumption influences gut microbiota composition, promoting beneficial bacterial populations and reducing gut permeability. This, in turn, lowers the translocation of endotoxins to the liver, reducing inflammatory responses.^[22] Furthermore, coffee also improves insulin sensitivity, reduces hepatic lipid accumulation, and enhances lipid oxidation, mediated by pathways such as AMPK activation.^[23] The widespread consumption and affordability, coffee represents a promising adjunct in liver disease prevention strategies. Public health campaigns could leverage this evidence to promote moderate coffee consumption as part of a healthy lifestyle.^[24] However, it is crucial to address potential concerns, such as caffeine sensitivity, unfiltered coffee's impact on cholesterol, and the risks associated with excessive consumption. Now it is very important for us to know the correct usage of coffee consumption when taking as a health benefits. First is important to know the standardization of coffee consumption, variability in coffee preparation methods (e.g., filtered vs. unfiltered, roasting levels) complicates the assessment of its health effects, therefore standardizing measures of coffee intake and bioactive compound content in research is essential. Other than this, long-term clinical trials on usage of coffee as a health benefits should also be required. As observational studies provide compelling evidence, long-term randomized controlled trials are needed to establish causality. These trials should focus on diverse populations and explore dose-response relationships. Moreover, further studies are also required to elucidate the full and accurate molecular mechanisms underlying coffee's protective effects. Integrating omics technologies (e.g., genomics, transcriptomics, proteomics, metabolomics, epigenomics) could uncover novel pathways and biomarkers associated with coffee consumption and liver health. In short, the growing body of evidence underscores the health benefits of coffee in preventing liver disease. By controlling oxidative stress, inflammation, and metabolic dysfunction, coffee emerges as a simple yet effective tool in reducing the global burden of liver disease. As research advances, incorporating coffee into evidence-based dietary recommendations could offer a practical strategy for promoting liver health. Nonetheless, moderation and individualized approaches remain key, as the interplay between coffee, genetics, and overall health warrants careful consideration.

Competing Interests

The authors declare no competing interests.

References

- Devarbhavi H, Asrani SK, Arab JP, Nartey YA, Pose E, Kamath PS. Global burden of liver disease: 2023 update. *J Hepatol* 2023;79: 516-37.
- Pouwels S, Sakran N, Graham Y, Leal A, Pintar T, Yang W, Kassir R, *et al.* Non-alcoholic fatty liver disease (NAFLD): A review of pathophysiology, clinical management and effects of weight loss. *BMC Endocr Disord* 2022;22:63.
- Makiso MU, Tola YB, Ogah O, Endale FL. Bioactive compounds in coffee and their role in lowering the risk of major public health consequences: A review. *Food Sci Nutr* 2023;12:734-64.
- Wadhawan M, Anand AC. Coffee and liver disease. *J Clin Exp Hepatol* 2016;6:40-6.
- Barrea L, Pugliese G, Frias-Toral E, El Ghoch M, Castellucci B, Chapela SP, *et al.* Coffee consumption, health benefits and side effects: A narrative review and update for dietitians and nutritionists. *Crit Rev Food Sci Nutr* 2023;63:1238-61.
- Ósz BE, Jitcă G, Ștefănescu RE, Pușcaș A, Tero-Vescan A, Vari CE. Caffeine and its antioxidant properties-it is all about dose and source. *Int J Mol Sci* 2022;23:13074.
- Nguyen V, Taine EG, Meng D, Cui T, Tan W. Chlorogenic acid: A systematic review on the biological functions, mechanistic actions, and therapeutic potentials. *Nutrients* 2024;16:924.
- Ren Y, Wang C, Xu J, Wang S. Cafestol and kahweol: A review on their bioactivities and pharmacological properties. *Int J Mol Sci* 2019;20:4238.
- Iriondo-DeHond A, Rodríguez Casas A, Del Castillo MD. Interest of coffee melanoidins as sustainable healthier food ingredients. *Front Nutr* 2021;8:730343.
- Wijarnpreecha K, Thongprayoon C, Ungprasert P. Coffee consumption and risk of nonalcoholic fatty liver disease: A systematic review and meta-analysis. *Eur J Gastroenterol Hepatol* 2017;29:e8-12.
- Amer MG, Mazen NF, Mohamed AM. Caffeine intake decreases oxidative stress and inflammatory biomarkers in experimental liver diseases induced by thioacetamide: Biochemical and histological study. *Int J Immunopathol Pharmacol* 2017;30:13-24.
- Vasileva LV, Savova MS, Amirova KM, Balcheva-Sivenova Z, Ferrante C, Orlando G, *et al.* Caffeic and chlorogenic acids synergistically activate browning program in human adipocytes: Implications of AMPK-and PPAR-mediated pathways. *Int J Mol Sci* 2020;21:9740.
- Shan L, Wang F, Zhai D, Meng X, Liu J, Lv X. Caffeine in liver diseases: Pharmacology and toxicology. *Front Pharmacol* 2022;13:1030173.
- Dranoff JA. Coffee consumption and prevention of cirrhosis: In support of the caffeine hypothesis. *Gene Expr* 2018;18:1-3.
- Arauz J, Moreno MG, Cortés-Reynosa P, Salazar EP, Muriel P. Coffee attenuates fibrosis by decreasing the expression of TGF- β and CTGF in a murine model of liver damage. *J Appl Toxicol* 2013;33: 970-9.
- GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: A systematic analysis for the global burden of disease study 2019. *Lancet* 2020;396:1204-22. Erratum in: *Lancet* 2020;396:1562.
- Kennedy OJ, Roderick P, Buchanan R, Fallowfield JA, Hayes PC, Parkes J. Coffee, including caffeinated and decaffeinated coffee, and the risk of hepatocellular carcinoma: A systematic review and dose-response meta-analysis. *BMJ Open* 2017;7:e013739.
- Burgos-Morón E, Calderón-Montaño JM, Orta ML, Pastor N, Pérez-Guerrero C, Austin C, Mateos S, *et al.* The coffee constituent chlorogenic acid induces cellular DNA damage and formation of topoisomerase I- and II-DNA complexes in cells. *J Agric Food Chem* 2012;60:7384-91.
- Rebollo-Hernanz M, Aguilera Y, Martín-Cabrejas MA, Gonzalez de Mejia E. Activating effects of the bioactive compounds from coffee by-products on FGF21 signaling modulate hepatic mitochondrial bioenergetics and energy metabolism *in vitro*. *Front Nutr*

- 2022;9:866233.
20. Kim SR, Jung YR, Kim DH, An HJ, Kim MK, Kim ND, *et al.* Caffeic acid regulates LPS-induced NF- κ B activation through NIK/IKK and c-Src/ERK signaling pathways in endothelial cells. *Arch Pharm Res* 2014;37:539-47.
 21. Frost-Meyer NJ, John V. Logomarsino, Impact of coffee components on inflammatory markers: A review. *J Funct Foods* 2012;4:819-30.
 22. González S, Salazar N, Ruiz-Saavedra S, Gómez-Martín M, De Los Reyes-Gavilán CG, Gueimonde M. Long-term coffee consumption is associated with fecal microbial composition in humans. *Nutrients* 2020;12:1287.
 23. Ontawong A, Boonphang O, Pasachan T, Duangjai A, Pongchaidecha A, Phatsara M, *et al.* Hepatoprotective effect of coffee pulp aqueous extract combined with simvastatin against hepatic steatosis in high-fat diet-induced obese rats. *J Functional Foods* 2019;54:568-77.
 24. Samoggia A, Riedel B. Consumers' perceptions of coffee health benefits and motives for coffee consumption and purchasing. *Nutrients* 2019;1:653.