Coffee and Liver Disease

Manav Wadhawan [*], Anil C. Anand [†]

[*]Fortis Escorts Liver and Digestive Diseases Institute, Delhi, India and [†]Indraprastha Apollo Hospital, Delhi, India[1]

Coffee is the most popular beverage in the world. Consumption of coffee has been shown to benefit health in general, and liver health in particular. This article reviews the effects of coffee intake on development and progression of liver disease due to various causes. We also describe the putative mechanisms by which coffee exerts the protective effect. The clinical evidence of benefit of coffee consumption in Hepatitis B and C, as well as nonalcoholic fatty liver disease and alcoholic liver disease, has also been presented. Coffee consumption is associated with improvement in liver enzymes (ALT, AST, and GGTP), especially in individuals with risk for liver disease. Coffee intake more than 2 cups per day in patients with preexisting liver disease has been shown to be associated with lower incidence of fibrosis and cirrhosis, lower hepatocellular carcinoma rates, as well as decreased mortality. (J Clin Exp Hepatol 2016;6:40–46)

Coffee is the most commonly consumed beverage in the world. Recently, a lot of interest has been generated in the overall beneficial effects of coffee consumption in reducing total and cause-specific mortality.[1,2] Coffee is a very rich source of antioxidants and the protective effects of coffee have been proposed in a variety of conditions ranging from heart disease to stroke to type 2 diabetes, as well as Parkinson disease.[3–6] There is increasing evidence in favor of protective effects of coffee consumption in development and progression of liver disease. This article will analyze the effects of coffee on liver disease in detail and also briefly mention other effects on health.

PHARMACOLOGY OF COFFEE

Coffee fruits (cherries) are harvested and undergo pulp extraction to obtain green coffee seeds, which can then be either roasted or processed for decaffeination. It is only through roasting that the seeds gain the characteristic aroma and flavor of coffee. Another factor that can affect the chemical composition of coffee is the method of brewing, which can be percolation, boiling, French press or electric coffee maker, espresso machine, or Italian coffee maker.[7] Instant coffee production typically involves treating ground-roast coffee with hot water and use of high pressure to extract the water-soluble compounds. This soluble material is then cooled and sometimes centrifuged, again concentrated by heating, and dried through freeze-drying to reduce moisture to approximately 5%. The basic chemical composition of green coffee depends primarily on genetic aspects (species of plant), and on physiologic aspects, such as degree of maturation. Chemical composition on an average and proposed beneficial effects of coffee are shown in Tables 1 and 2, respectively. Most studies on pharmacology of coffee have focused on the effects of caffeine (1,3,7-trimethylxanthine), a purine alkaloid, which is just one of the myriads of chemicals that are contained in coffee. Diterpenes, cafestol, and kahweol have also been studied to a varying extent. Diterpenes have been blamed for coffee-induced rise in cholesterol levels in human studies.[8,9] There are at least 30 organic compounds that have been shown to impact the typical aroma of coffee. A detailed review of chemical constituents of coffee is outside the purview of this paper and has been discussed elsewhere.[10]

MECHANISM OF ACTION

The exact mechanism of beneficial effects of coffee is not clear. Coffee contains more than 1000 substances, including caffeine, diterphenoic alcohols, potassium, niacin, magnesium, and the antioxidants like chlorogenic acid (CGA), and tocopherols.[11] It should be noted that caffeine may not be the most important component, as other caffeinated drinks do not provide similar protection against liver disease. The polyphenols (CGA, etc.) may be responsible for the positive metabolic effects of coffee. There is experimental evidence that coffee with high CGA concentrations can modulate glucose intolerance and improve/decrease nonalcoholic fatty liver disease (NAFLD) development in obese rats.[12]

Keywords: coffee, hepatocellular carcinoma, fibrosis, cirrhosis, mortality, NAFLD

Received: 30.12.2015; *Accepted:* 19.02.2016; *Available online:* 27 February 2016

Address for correspondence: Manav Wadhawan, Senior Consultant, Fortis Escorts Liver and Digestive Diseases Institute, Delhi, India.

E-mail: manavwadhawan@gmail.com

Abbreviations: CGA: chlorogenic acid; MEC: multiethnic cohort; MRP: Maillard reaction products; NAFLD: nonalcoholic fatty liver disease

http://dx.doi.org/10.1016/j.jceh.2016.02.003

[1]President, Indian Society of Gastroenterology; *Quondam*: President's Honorary Surgeon; Chief Consultant (Gastroenterology), AFMS as Lieutenant General; Director General Medical Services (Navy) as Surgeon Vice Admiral; Professor and Head of Department (Gastroenterology and Hepatobiliary Unit, Army Hospital R and R, Delhi).

Table 1 A Representative Composition per 100 ml of Coffee Brew from Medium-Roasted Coffee. Composition of Coffee Varies According to Blend, Roasting Degree, Grid, and Method of Preparation.

Constituent	Amount
Caffeine	50–380 mg
Melanoidins	500–1500 mg
Soluble fiber	200–800 mg
Protein	100 mg
Niacin	10 mg
Lipids	0.8 mg
Trigonelline	40–50 mg
Chlorogenic acids	35–500 mg
Minerals	250–700 mg

Modified from Farah et al.[7]

Coffee is a rich source of dietary antioxidants. The antioxidant capacities of both hydrophilic components (like caffeine and CGA) and hydrophobic components (like cafestol, kahweol, and trigenolline) have been extensively investigated using both chemical assays and biological systems, including cell culture and animal and human studies.[13] Maillard reaction products (MRP) that provide the aroma, flavor, and color of different brewed coffees are generated during the roasting process and significantly contribute to its antioxidant activity.[14,15]

There are various studies linking the lower circulating levels of inflammatory biomarkers in coffee drinkers. A recently published study used luminex-based bead assays to measure 77 immune and inflammatory markers in more than 1700 adults. This trial reported significantly lower levels of IFN-γ, CX3CL1/fractalkine, CCL4/MIP-1b, FGF-2, and sTNFRII in coffee drinkers than noncoffee drinkers.[16] Another European nested case–control study has suggested an inverse association of coffee intake with HCC risk that was partly accounted for by biomarkers (IL-6, etc.) of inflammation and hepatocellular injury.[17] The role of biomarkers in protection provided by coffee against various diseases requires further investigation.

Recently, autophagy has gained a lot of attention as a global health-promoting and antiaging property. Autophagy is a lysosomal degradation pathway responsible for the selective renewal of cytoplasmic organelles. Autophagy preferentially targets damaged proteins and organelles (such as dysfunctional mitochondria), thus contributing to getting rid of aged structures in the cytoplasm. Hence, autophagy is responsible for renewal of nonnuclear portions of the cell. There is some evidence to suggest that coffee may be acting partially by inducing autophagy in vivo.[18]

Effect of coffee on evolution of liver disease has also been attributed to its antifibrotic effects. In a rat model, coffee has been shown to attenuate thioacetamide-induced liver inflammation and fibrosis.[19] Animal studies have shown that coffee decreases expression of transforming growth factor-β and connective tissue growth factor, thus contributing to reduced fibrosis.[20] Furthermore, in rat models of alcohol-induced liver injury, caffeine has been shown to be protective against alcohol-induced liver fibrosis by dampening the cAMP/PKA/CREB pathway in rat hepatic stellate cells.[21]

Table 2 Proposed Mechanisms of Main Beneficial Effects of Coffee on the Liver.

Effect on liver	Site of action	Chemical involved	Mechanisms
Antifibrotic	Hepatic Stellate Cell (HSC)	Caffeine	Inhibit focal adhesion kinase (FAK) and actin synthesis
			Increase HSC apoptosis and intracellular F-actin and cAMP expression
			Inhibit procollagen type 1C and alpha-SMA expression
	Hepatocyte	Caffeine	Decrease transforming growth factor beta (TGF-B)
			Stimulate ARE-regulated signaling
Cancer prevention	Hepatocyte	Cafestol and Kehweol	Inhibit phase I activating enzyme expression and activity
			Induce phase II detoxifying enzymes (i.e. glutathione S-transferase)
			Stimulate antioxidant responsive element (ARE)-regulated signaling
			Induction of gamma-glutamyl cysteine synthetase (GCS)
Antioxidant effect	Hepatocytes	Hydrophilic (caffeine and polyphenols, such as chlorogenic acids); hydrophobic (cafestol, kahweol, and trigenolline), including MRP	Preventing inflammatory reaction downregulation of immune and inflammatory markers, such as interferon-gamma (IFN-γ), chemokine coded by CX3CL1 or fractalkine, chemokine ligand4 or CCL4 also called macrophage inhibitory protein (MIP-1b), fibroblast growth factor-2 (FGF-2), and tumor necrosis factor receptors (sTNFRII)

Modified from Saab et al.[77]