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## EFFECTIVENESS OF COFFEE TO LOWER RISK OF HEPATIC PROBLEMS

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### ABSTRACT

*Coffee is one of world's most popular beverages, it has high level of antioxidants and beneficial and it also seems to be quite healthy. Studies show that coffee drinkers have a much lower risk of several serious diseases. Coffee can help people feel less tired and having increased energy level. This is because it contains a stimulant called "Caffeine"-the most commonly consumed psychoactive substance in the world. Coffee consumption benefits in hepatitis B and C, as well as in non-alcoholic fatty liver disease and alcoholic fatty liver disease. It is also associated with improvement in liver enzymes. Recently a lot of interest has been generated in the beneficial properties of coffee drinking. Coffee has long been recognised as having hepatoprotective properties; however the extent of any beneficial effect is still being elucidated. Coffee appears to reduce risk of hepatocellular carcinoma and have ability to reduce hepatitis C virus to replicate. This review aims to catalogue the evidence for coffee as universally beneficial across the spectrum of chronic liver diseases and also on other effects which improve health in general as well as to spotlight opportunities for future investigation into coffee and liver disease. This article reviews recent available literature and summarises the potential positive or preventive effects of coffee on liver malignancy as well as chronic liver diseases secondary to alcohol, viral hepatitis and fatty infiltration.*



**KEYWORDS :** *Coffee, chronic liver diseases, cirrhosis, hepatic-fibrosis, hepato-cellular cancer, non-alcoholic fatty liver diseases and alcohol related liver diseases.*

### INTRODUCTION:

Even if India is still a tea country, the growing trend shows how India might become one of the world's largest coffee producing countries. Even the last decade increasing coffee demand by 40 % is indicative of a growth in coffee culture. India's per capita coffee consumption stands at 0.03Kg in 2019. Coffee consumption is mainly concentrated in southern states as Tamil Nadu 60% Karnataka 25%.

Because of widespread skepticism regarding the safety of western medication, there is a great interest in studying alternative treatments that are considered natural and safe from toxicants many foods and diets are believed to promote health and longevity. Coffee is a beverage with distinct taste and aroma that is commonly consumed throughout the world and is being assessed for its potential health benefits. For instance a decreased risk of type 2 diabetes, heart disease and stroke has been described in regular coffee drinkers.

Chronic liver diseases (CLD) is a growing cause of morbidity and mortality worldwide, particularly in low to middle income countries with high disease burden and limited treatment

availability. Coffee consumption has been linked with lower rates of CLD, but little is known about the effect of different coffee types, which vary in chemical composition. This study aimed to investigate association of coffee consumption with chronic liver outcomes.

### **BENEFITS OF COFFEE IN LIVER DISEASES**

Chronic liver diseases (CLD) are a major health problem worldwide. Between 1990 and 2017, global death due to CLD increased from 1.9% to 2.4% of total. During this period, disability-adjusted life year's loss of CLD increased from 30.5 million to 41.4 million. The burden where treatment options are also limited. The commonest aetiologies of CLD are alcohol-related liver diseases (ALD), chronic hepatitis –B and C infection and non-alcoholic fatty liver diseases (NAFLD). These conditions involve destruction and regeneration of liver parenchyma leading to liver fibrosis and then cirrhosis. Cirrhosis can be fatal due to complication related to portal hypertension, liver failure on the development of hepatocellular carcinoma (HCC)<sup>1</sup>.

Coffee is the most widely used beverages in the world. It includes a wide array of components that can have potential implications for liver health. Epidemiological and experimental studies have demonstrated that positive effects of coffee on several liver diseases. Coffee consumption is associated with the prevention of hepatic steatosis and fibrosis, and a reduction in cirrhosis and the risk of hepatocellular carcinoma (HCC). There is a biological plausibility of a protective effect of coffee against CLD outcomes. Caffeine is a non-selective antagonist of A2aA receptor, activation of which stimulates collagen production by hepatic stellate cells, the primary mediators of fibrosis. Alternative active ingredients in coffee may include chlorogenic acid, kahweol and cafestol, which protect against liver fibrosis in animal studies.

Coffee can help people feel less tired and having increased energy level. This is because it contains a stimulant called "Caffeine"-the most commonly consumed psychoactive substance in the world. Caffeine is absorbed into blood stream after coffee consumption by humans as normal physiological mechanism; thereafter it improves various aspects of brain functions – including memory, mood vigilance, energy levels, reaction times and general mental functions<sup>2</sup>. According to a large review of 18 studies in a total of 457922 people, each daily cup of coffee was found associated with a 7 % reduced risk of type 2 diabetes<sup>3</sup>.

A vast majority of the data supporting the concept that coffee prevents unhealthy outcomes in patients with chronic disease comes from retrospective population based studies. Coffee consumption is inversely related with a variety of chronic liver disease and there is a dose – response relationship. One important trial indicated that consumption of a single cup of coffee offered an odds ratio of 0.47, and four cups of coffee a day offered an odd ratio of 0.16 for risk of cirrhosis in patient of chronic liver disease<sup>4</sup>. In a recent analysis of the national institute of health study data published by Freedman et al, the investigators described a dose dependent inverse association between coffee consumption and total mortality<sup>5</sup>. Several studies consistently show that coffee drinkers with chronic liver diseases have reduced risk of cirrhosis and lower incidence of hepatocellular carcinoma regardless of primary etiologic. With the increasing prevalence of non-alcoholic fatty liver disease (NAFLD) worldwide, there is renewed interest in the effect of coffee intake on NAFLD severity and positive clinical outcomes. This review gives an overview of growing epidemiological and clinical evidence which indicate the coffee consumption reduces severity of NAFLD. These studies vary in methodologies and potential confounding factors have not always been completely excluded. However, it appears that coffee and particular components other than coffee reduce NAFLD prevalence and inflammation of non-alcoholic steatohepatitis.

Several possible mechanisms underlying coffee's hepatoprotective effects in NAFLD include anti-oxidative, anti-inflammatory and anti-fibrotic effects, while a chemopreventive effect against hepato-carcinogenesis seems likely. The so far limited data supporting such effects will be discussed and the need for further study is highlighted<sup>6</sup>. In many studies it has been noted that coffee consumption has been associated with decreased levels of aspartate- aminotransferase (AST), alanine-aminotransferase (ALT), gamma-glutamyltransferase (GGT) and alkaline phosphatase (ALP). These

studies began an investigation into elucidating a more direct relationship between coffee and possible hepato-protective properties. One such study performed in 1993, tested Italian population of 2240 with findings indicating not only a decrease in GGT but also ALT and ALP in users of three or more cups of coffee daily, when compared with the group that taking less than this amount of coffee<sup>7</sup>. Later 2000 Japanese study on 1353 people demonstrated lower GGT levels in coffee drinkers. A follow up study by the same group noted lower AST and ALT in Japanese men aged between 35-65 years, noting a decrease in their liver enzymes over 4 years period with increased coffee consumption<sup>8</sup>. Transaminase was significantly lower in groups reporting increased coffee usage. Of note, men reporting on going alcohol use with concurrent coffee consumption exhibited a relatively reduced risk of AST compared to non- coffee drinking alcohol users. Furthermore, A 2010 study in Japan evaluated levels of AST, ALT and GGT amongst various subgroups of men and women with high BMI, low BMI and high and low alcohol consumption. Transaminases were noted to be lower amongst men and women with higher coffee consumption, the relationship appearing to be stronger in those with higher alcohol consumption and lower BMI<sup>9</sup>.

Experimental studies show that coffee consumption reduces fat accumulation and collagen deposition in the liver and promotes anti-oxidant property through an increase in glutathione level as well as modulation protein expression of several pro-inflammatory (IL-1, TNF- $\alpha$ ) and pro-fibrotic mediators. Several studies indicate that among other compounds, cafestol and kahweol may operate by modulating multiple enzymes involved in detoxification process of carcinogens causing HCC.

Beyond the taste and stimulating effects, coffee has been associated with improved outcomes with chronic liver disease – hepatocellular cancer (HCC), cirrhosis, colorectal cancer, oesophageal cancer, breast cancer, prostate cancer, pancreatic cancer, ovarian cancer, kidney cancer, hepatitis B virus, hepatitis C virus and non- alcoholic fatty liver disease. A recent 2015 meta- analysis of 16 case-control and cohort studies of Western population demonstrated significantly reduced incidence of cirrhosis amongst coffee drinkers when compared to those who didn't drink the beverage<sup>10</sup>. As coffee continues to grow in popularity, with daily consumption of coffee-based beverages increasing from 19% to 41% in the 25-39 years old age group from 2008, the documented benefits of increased coffee intake have also grown. Furthermore coffee is generally considered to have a wide safety profile, with the American food and drug administration noting caffeine as a substance generally recognized as safe, not known to be a health hazard<sup>11</sup>. Over 30 million Americans have chronic liver disease and about 3100 deaths have been attributed to it yearly. Studies evaluating coffee's potential hepato-protective effect on liver disease are important as they may represent a simple lifestyle modification that patients can incorporate to enhance their own health.

In fact, as little as one cup of coffee consumed daily resulted in 15 % reduction in risk of death from liver disease; four cup of coffee daily was associated with 71% reduction, suggesting a dose dependent response. This study appear to reaffirm finding of an earlier 2005 study noting that consumers of coffee and tea exhibited significantly decreased risk of chronic liver diseases<sup>12</sup>. A 2003 Norwegian study had similar findings, noting progressively improved mortality with increasing coffee consumption, though the effect appears to negligible beyond drinking four cups of coffee daily<sup>13</sup>.

Hepatic fibrosis and cirrhosis are the major cause of mortality and morbidity in patients with chronic liver disease (CLD) and are global health burden. Persistent liver injury caused by CLD can induce scar formation and healing, which consequently lead to fibrosis and cirrhosis<sup>14</sup>. The five year cumulative incidence of de-compensation in cirrhotic patients is approximately 20 %. Those patients with decompensated cirrhosis only have a 5 year survival rate of 14-35%. Worst still, the risk for hepatocellular carcinoma greatly increases after the development of cirrhosis<sup>15</sup>. Controlling CLD is the most important approach to prevent hepatic fibrosis. However, dietary factors may also have protective effects on liver diseases. Moreover coffee is able to prevent hepatocellular carcinoma development that is mainly caused by hepatic fibrosis and cirrhosis. Recently, some studies have evaluated the association of coffee consumption with fibrosis and cirrhosis.

Given the above information the association between coffee and relative reduction of liver enzymes appears clear, however, the benefits of coffee extend further. In a 2015 population based

prospective cohort study demonstrated coffee intake with reduced mortality from chronic liver disease. Hepatic fibrosis and cirrhosis caused by CLD are global health problems. Therefore, it is important to develop some simple approaches to prevent fibrosis and cirrhosis in patients with high risk. Through subgroup meta-analysis, we identified significant hepatoprotective effects of coffee consumption on hepatic fibrosis and cirrhosis in patients with alcoholic liver disease and chronic HCV Infection, which mainly contribute to CLD in western countries. The consumption of coffee seems to be an attractive lifestyle for CLD patients, as coffee intake is popular in those areas<sup>16</sup>.

### MECHANISM OF BENEFICIAL EFFECT OF COFFEE

The exact mechanism of beneficial effect of coffee is not clear. Coffee contain more than 1000 substances, including caffeine, dietrophenoic alcohols, potassium, niacin, magnesium, and antioxidant like chlorogenic acid (CLD) and tocopherols. It should be noted that caffeine may not be the most important component, as the caffeinated drink do not provide similar protection against the 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 concentration can modulate glucose intolerance and improve/decrease non-alcoholic fatty liver disease development in rats<sup>17</sup>.

Effect of coffee on evolution of liver disease has also been attributed to its anti-fibrotic effects. In a rat model, coffee has been shown to attenuate thioacetamide induced liver inflammation and fibrosis. Animal studies have shown that coffee decreases expression of transforming growth factor-b and connective tissue growth factor, thus contributing to the reduced fibrosis<sup>18</sup>.

### LIMITATIONS

As the present study is based on the evidence of observational studies, it is difficult to determine whether it is occasional for the inverse associations of coffee consumption. This could have rendered a spurious protective effect of coffee on hepatic fibrosis and cirrhosis. However, all the included CLD patients as to controls to eliminate such possibility. There are some limitations in present study. First, most of the studies were in western countries. Thus generalization of the current findings to other populations should be made with caution. Second, there are variance in consumption duration among the included studies, which might have a potential source of heterogeneity. Therefore, the conclusion of current study that coffee consumption can reduce the risk for hepatic problem might be underestimated because some differences among the study groups.

### CONCLUSION

In conclusion, the present meta-analysis suggests that coffee consumption can prevent the development of hepatic fibrosis and cirrhosis and overall performance of liver. It has ability to lower the concentration of certain liver enzymes which are associated with patients at higher risk of liver injury. However, further prospective studies are needed to control the bias and confounding factors. Thus, we propose that coffee should be prescribed as consumption of two to three cups daily for patients with chronic liver diseases. Finally, it is noteworthy that coffee, once considered a negative contributor to health, may actually be one of mankind's good 'bad habits'. Emerging data showing that coffee is inversely associated with all-cause mortality are highly worthy of our attention, including well-constructed pre-clinical trials investigating the mechanism by which coffee drinking may be such a good habit.

Increasing evidences accumulation on beneficial effects of coffee in the liver; thus although it is premature to prescribe coffee as a medication, it should be recommended as an adjuvant for liver disease treatment. . These studies collectively suggest a simple lifestyle modification patients may be able to incorporate their own health. Authors have keen interest to aware and encourage the Indian population for drinking coffee for protecting them from numerous liver diseases by entrusting the scientific findings about this topic.

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