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Health Implications of Chlorogenic Acids

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Coffee is consumed as a functional beverage in worldwide due to its nutraceutical health benefits and positive physiological effects. It is an important source of several nutritious and therapeutic phytoconstituents including lipids, carbohydrates, minerals, vitamins, and nitrogenous compounds, along with bioactive compounds like cafestol and kahweol diterpenes, caffeine, and chlorogenic acid (CGA), which all possess great therapeutic potential. Chlorogenic acids (CGA), esters of trans-hydroxycinnamic acids and quinic acid were discovered in 1837. From the past few years, a number of epidemiological studies have been associated with moderate coffee consumption, independently of caffeine, with the reduction in the relative risk of development of chronic degenerative diseases and death. The beneficial effects of coffee can be attributed due to presence of many bioactive compounds. So, coffee is proved to be an primitive wonder drug that is endowed with a variety of phytobiomolecules of therapeutic potential (Han *et al*.,2017).

The CGA contribution to the preventive or healing effect of coffee are discussed below.

Antioxidant Activity: Coffee is the source of antioxidant compounds in the diet of many populations due to presence of high concentration of CGA and lactones in the brew it is associated with its high consumption (Torres & Farah, 2017). CGA are known to have similar antioxidant activity to ascorbic acid .They are able to chelate transition metals such as Fe^{2+} to scavenge free radicals and interrupt free radical chain reactions . In addition, they have been able to prevent low density lipoprotein (LDL) oxidation induced by different oxidizing agents (Kim *et al*.,2017).

Anti mutagenic and Anti carcinogenic Effects: This activity is partly related to CGA antioxidant activity because the overproduction of oxygen free radicals lead to oxidative damage of DNA which is primarily responsible for promoting various types of cancer as breast, bladder, colon, liver, pancreatic, prostate, and skin cancers (Toyokuni, 2016).

Anti-Inflammatory Effect and Wound Healing: Oxidative stress and chronic inflammation are closely related physio-pathological events. Experimental data show the simultaneous existence of low-grade chronic inflammation and oxidative stress in many chronic diseases like diabetic complications, cardiovascular and neurodegenerative diseases, alcoholic liver disease, and chronic kidney disease. Inflammation is a complex physiological reaction to tissue injury caused by exogenous or endogenous sources. Exaggerated or unregulated prolonged inflammatory process can induce tissue damage and is the cause for many chronic diseases. The reduction of inflammation resulting in enhanced wound healing has also been reported for CGA in different studies. In a study with diabetic rats, the oral administration of 5-CQA enhanced hydroxyproline and decreased malondialdehyde/nitric oxide levels in wound tissues, in addition to elevating reduced-glutathione (Cortan., 1994).

Hepatoprotective Effect: Hepatic injury may result from many different causes, including viral hepatitis, iron overload, obesity, and excessive alcohol consumption. The protective mechanisms are prevention of cell apoptosis and oxidative stress damage due to activation of natural antioxidant and anti-inflammatory systems. Such protective mechanisms have been linked mainly with CGA and caffeine among other coffee compounds. In general, experimental data suggest that the hepatoprotective activity of CGA is probably associated with an inflammatory response inhibition and anti-viral activity (Wang *et al*., 2009).

Anti-Diabetic Effect: Some studies suggest that coffee consumption prevents or delays the onset of type 2 diabetes. The beneficial effects have been attributed mainly to CGA and derivatives as well as trigonelline. They appear to target preferentially hepatic glucose metabolism by improving whole body insulin sensitivity. CGA lactones have also been able to increase hepatic and muscle glucose utilization among other mechanisms that result in lowering the blood glucose levels in rats (Shearer, 2003).

Cardioprotective and Antihypertensive Effects

Cardiovascular diseases are the leading cause of death in the world. Key mechanisms for cardiovascular protection are high antioxidant and anti-inflammatory properties which improve endothelial dysfunction and reduce insulin resistance. CGA exhibit both of these properties and a number of *in vitro* studies have demonstrated a positive role against endothelial dysfunction (Liang, 2016).

Antiobesity and Anti-Metabolic Syndrome Effects: Overweight and obesity are increasingly common conditions affecting a large population worldwide (Rayner & Lang,2009). Obesity being a serious medical condition is characterized by an excessive accumulation of adipose tissue that can cause complications such as metabolic syndrome, high blood pressure, atherosclerosis, heart disease, diabetes, high blood cholesterol, cancers and sleep disorders (Pi-Sunyer, 2009). CGA exert both antioxidant and anti-inflammatory properties, being promising candidates to help prevent and fight metabolic syndrome. The mechanism proposed was that 5-CQA scavenges reactive oxygen species (ROS) generated by consumption of high-fat diet, which suppresses the expression of inflammation, and consequently reduces fat accumulation, weight gain, and insulin resistance, while inhibition of PPARγ prevents and improves liver steatosis (Santana-Gálvez, 2017).

Neuroprotective Effects: lzheimer's disease is the most frequent cause of dementia, leading to a progressive cognitive decline. While there is currently no medication against Alzheimer's disease, several studies have observed an inverse association between regular coffee consumption and development of Alzheimer's disease. The mechanisms of coffee protective effect are believed to be related to the anti-inflammatory effects of caffeine and CGA on the A1 and A2 receptors as well as to the reduction of toxic β-amyloid peptide deposits in the brain, a pathological characteristic in patients with Alzheimer's disease. Other proposed mechanisms could be the inhibition of the enzyme's acetylcholinesterase and butyrylcholinesterase in the brain and prevention of oxidative stress-induced neurodegeneration due to its high antioxidative activity (Arendash and Cao, 2010).

Potential Prebiotic Effect: The consumption of prebiotic foods or compounds stimulate the growth of probiotic and other health promoting colonies in the intestine, with special emphasis given to *Bifidobacterium* and *Lactobacillus* spp. Some reported data suggest that the unabsorbed portion of CGA and caffeic acid in the human gastrointestinal tract serves as a substrate for beneficial intestinal bacteria and helps in stimulating their growth. While the bifidogenic effect of CGA seems to be a consensus, CGA effect on the multiplication of *Lactobacillus* spp. is found controversial, suggesting growth of selected strains (Rechner *et al*., 2001).

Conclusion

The contribution of CGA to the daily antioxidant intake for coffee drinkers is quite relevant. Several studies have demonstrated that CGA are partially bioavailable and potentially beneficial to human health. Consumption of CGA in suitable amount are beneficial for various metabolic disease.

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