

Mechanistic Aspects of DNA – and Cancer – Protective Effects of Coffee

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SUMMARY

A number of epidemiological studies indicate that consumption of coffee is inversely related to the incidence of specific forms of cancer in the liver and in the gastrointestinal tract. In order to provide mechanistic explanations for this phenomenon, we evaluated the literature concerning the prevention of DNA damage (which plays a key role in the formation of malignant cells) and cancers by adduct forming genotoxic carcinogens in the human diet and reactive oxygen species (ROS). Furthermore, we conducted animal experiments and human intervention trials to substantiate putative protective effects. We failed to find protective effects towards induction of DNA damage by heterocyclic aromatic amines (which are pyrolysis products of amino acids) in animal and human studies but a strong reduction of formation of aflatoxin B₁ induced preneoplastic lesions was seen with caffeinated and decaffeinated metal filtered coffee preparations in rats. Furthermore, a pronounced reduction of BPDE (the reactive metabolite of benzo[a]pyrene) induced DNA-damage in human lymphocytes was found in a human intervention study. These effects are probably due to induction of glutathione-S-transferases – in particular the GSTP isoform is induced. Results of animal and human experiments indicate that coffee consumption causes a pronounced induction of these detoxifying enzymes. Another important mechanism of protection elicited by coffee is the inactivation of ROS, which was observed in a number of earlier *in vitro* studies. We could demonstrate in a human intervention trial (i.e. in single cell gel electrophoresis assays) that consumption of coffee results in a significant reduction of endogenous formation of oxidised bases and reduces the sensitivity of lymphocytes towards ROS (hydrogen peroxide) induced DNA-damage. It can be tentatively assumed that the reduced incidence of liver cirrhosis and hepatocellular carcinomas in coffee drinkers may be causally related to the antioxidant properties effects of coffee, since it is assumed that ROS mediated damage plays a key role in the aetiology of these diseases.