Genotoxic effects of the hydroxycinnamic acid derivatives – caffeic, chlorogenic and cichoric acids

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Abstract: In this paper genotoxic effects of caffeic, chlorogenic and cichoric acids were investigated in three bacterial assay systems: (i) the Ames test with *Salmonella typhmiurium* TA98, TA100 and TA102; (ii) the SOS chromotest with *Escherichia coli* PQ37; and (iii) differential repair test using *Escherichia coli* strains with different capacities for DNA repair. Using the Ames assay, we demonstrated genotoxic activity of cichoric acid on the tester strains TA98 and TA100. Both caffeic acid and chlorogenic acid slightly induced mutations in TA102 strain. Tested phenolic acids did not induce SOS error-prone DNA repair in *Escherichia coli*. The differential sensitivity assay revealed that *Escherichia coli* WP2*uvr*A strain is most sensitive to cichoric acid. Postreplication repair mechanism dependent on *rec*A gene participates in the restoration of DNA damage caused by both caffeic and chlorogenic acids. Our studies indicate that caffeic, chlorogenic and cichoric acids have genotoxic potential and *uvr*A and *rec*A genes play a certain role in the repair of DNA damage induced by these compounds.

Key words: caffeic acid, chlorogenic acid, cichoric acid, genotoxicity, DNA repair.

Introduction

Derivatives of hydroxycinnamic acid (caffeic acid) and their esters (chlorogenic and neochlorogenic acids, ferulic, cichoric and other acids) have been commonly found in plant-derived food. In the last years, researchers and food manufacturers are increasingly interested in these compounds, which may be exploited for the development of functional foods or in the chemoprevention. The main reason for this interest is the recognition of the antioxidant properties of polyphenols, their great abundance in our diet, and their probable role in the prevention of various diseases associated with oxidative stress, such as cancer, cardiovascular or neurodegenerative diseases (Manach et al., 2004). Fortification of foods with materials rich in phenolic compounds has been shown to impart antimutagenic, antiinflammatory and antioxidant properties, which may be exploited for the development of health foods or cosmetics (Friedman, 1997).

Some phenolic acids were reported to be antimutagenic/anticarcinogenic. Caffeic acid, ferulic acid, *p*-coumaric acid and gentisic acid reduce mutagenicity of acridin orange and ofloxacin in *Salmonella typhimurim* (Belicová et al., 2001) and in *Euglena gracilis* (Križková et al., 2000). Caffeic and chlorogenic acids possess inhibitory effect on the mutagenicity of Trp-P-1 and Glu-P-2 (Yamada & Tomita, 1996). The same phenolic acids may inhibit the formation of mutagenic and carcinogenic N-nitroso-compounds because they are inhibitors of the N-nitrosation reaction *in vitro* (Kono et al., 1995). Chlorogenic acid acts as an inhibitor of 8-hydroxydeoxyguanosine formation *in vitro* and in a rat carcinogenesis model (Kasai et al., 2000). Tanaka et al. (1993) described the inhibition of 4-nitroquinoline-1-oxide-induced rat tongue carcinogenesis by the caffeic, ellagic, chlorogenic and ferulic acids.

However, not all polyphenols as well as not all actions of individual polyphenols are necessarily beneficial. Some of them have mutagenic and/or pro-oxidant effect, and they may interfere with essential biochemical pathways (Ferguson, 2001). A number of polyphenols, including quercetin, can bind to DNA (Alvi et al., 1986) and this direct interaction may be an important mechanism of bacterial mutagenicity.

Progress in genetic toxicology has led to the development of several bacterial short-term tests for detecting genotoxic and anti-genotoxic agents. The Ames test (Maron & Ames, 1983) is a well-known bacterial mutagenicity test. In this test reverse $His^- \rightarrow His^+$ mutations are visualised by plating *Salmonella typhimurium* bacteria on a histidine-poor growth medium. The SOS

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