



Comparative study of the antioxidative activities of caffeoylquinic and caffeic acids



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ABSTRACT

A detailed conformational analysis was performed to determine the most stable conformers of chlorogenic, cryptochlorogenic, and neochlorogenic acids. The simulated and experimental NMR spectra of caffeoylquinic acids are in excellent agreement. The bond dissociation enthalpies, proton affinities, electron transfer enthalpies, ionisation potentials, and proton dissociation enthalpies for these compounds and caffeic acid in benzene, methanol, and water were used for thermodynamic consideration of the major antioxidative mechanisms: HAT (Hydrogen Atom Transfer), SPLET (Sequential Proton-Loss Electron-Transfer), and SET-PT (Single Electron Transfer – Proton Transfer). All compounds are characterised with very similar values of each enthalpy, suggesting that they will exhibit comparable antioxidative activities. This assumption is in perfect accord with the experimental findings. It was suggested that HAT may be the predominant mechanism in nonpolar solvents, while HAT and SPLET are competitive pathways in polar media. All calculations were performed using the B3LYP-D2/6-311++G(d,p) and M06-2X/6-311++G(d,p) levels of theory and CPCM solvation model.

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1. Introduction

Caffeoylquinic acids are esters of caffeic acid (CA) with quinic acid. According to the difference in binding site, there are three isomers of these phenolic acids (Fig. 1): chlorogenic acid (5-O-caffeoylquinic acid, **5CQA**), cryptochlorogenic acid (4-O-caffeoylquinic acid, **4CQA**), and neochlorogenic acid (3-O-caffeoylquinic acid, **3CQA**).

5CQA is a constituent of various plants, where it acts as an antioxidant, and thus protects against lipid peroxidation (Kasai, Fukada, Yamaizumi, Sugie, & Mori, 2000; Ohnishi et al., 1994). This compound is especially abundant in coffee, but it is also the major soluble polyphenol found in potato, tomato and eggplant, and it also accumulates to considerable levels in apples, pears, plums, and blueberries (Wang, Wang, & Yang, 2007). Green coffee extract is used for production of encapsulated food supplements, some beverages, and conventional coffee products (Farah, Monteiro, Donangelo, & Lafay, 2008). **3CQA** was found in the fresh and dried

plum at significant concentration (Fang, Yu, & Prior, 2002), whereas the concentrations of **4CQA** and **5CQA** were smaller (Fang et al., 2002; Nakatani et al., 2000).

The studies on caffeoylquinic acids are mainly focused on experimental examinations of **5CQA** (Clifford, Wu, Kirkpatrick, & Kuhnert, 2007; Nakatani et al., 2000). This compound proved to exhibit anticarcinogenic, antimutagenic (Friedman, 1997), and glucose lowering effects (Thompson, Yoon, Jenkins, Wolever, & Jenkins, 1983), antioxidative activity for human low-density lipoprotein (Rice-Evans, Miller, & Paganga, 1996), as well as anti-obesity properties and ability to improve lipid metabolism (Cho et al., 2010). In addition, **5CQA** acts as a scavenger of reactive oxygen and nitrogen species (Kono et al., 1997). Surprisingly, theoretical investigations of caffeoylquinic acids have been initiated only recently, where **5CQA** was included in a set of twenty natural polyphenols whose structure-thermodynamics-antioxidant relationships were examined by means of the DPPH[•] scavenging assay, B3LYP/6-311++G(d,p) calculations, and quantitative structure-activity relationship modelling (Chen, Xiao, Zheng, & Liang, 2015). It is reasonable to expect that other two isomers, **3CQA** and **4CQA**, will also exhibit various biological effects, including

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