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Synergic application of spectroscopic and theoretical methods to the chlorogenic acid structure elucidation

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ABSTRACT

Although chlorogenic acid (5-*O*-caffeoylquinic acid, **5CQA**) is a dietary polyphenol known for its pharmacological and nutritional properties, its structural features have not been completely elucidated. This is the first study whose aim is to contribute to clarification of the **5CQA** structure by comparing the experimental and simulated IR, Raman, ¹H NMR, ¹³C NMR, and UV spectra. For this purpose, a comprehensive conformational analysis of **5CQA** was performed to reveal its most stable conformations in the gas-state and solution (DMSO and methanol). The lowest-energy conformers were used to predict the spectra at two levels of theory: B3LYP-D3/and M06-2X/6-311+G(d,p) in combination with the CPCM solvation model. Both methods provide very good agreement between all experimental and simulated spectra, thus indicating correct arrangement of the atoms in the **5CQA** molecule. The quinic moiety is characterized with directed hydrogen bonds, where the carboxylic hydrogen is not oriented towards the carbonyl oxygen of the carboxylic group, but towards the oxygen of the proximate hydroxyl group. In the gas-state the lowest-energy conformers are characterized with the O4H4...O9' hydrogen bond, whereas in the solvated state the structures with the O4H4...O10' hydrogen bond prevail. Knowing the fine structural details, i.e. the proper conformation of **5CQA**, provides a solid base for all further investigations related to this compound.

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1. Introduction

It has been widely accepted that dietary antioxidants play a protective role against the development and progression of the pathological conditions related to oxidative stress. Epidemiological studies showed that consumption of fruits and vegetables is helpful in preventing some chronic diseases [1,2]. Fruits and vegetables are rich in natural polyphenols, whose antioxidative properties proved to contribute to the protective role of these foods [3]. An important class of polyphenols is phenolic acids. The interest in these compounds originates from their numerous biological roles [4]. One of the phenolic acids that is wide spread in human diet is chlorogenic acid (Fig. 1).

Chlorogenic acid (5-*O*-caffeoylquinic acid, **5CQA**) is an ester of the caffeic and quinic acids. It can be isolated from natural plants such as coffee, pears, plums, potatoes, tomatoes, carrots and oilseeds. Like other dietary polyphenols, chlorogenic acid shows pharmacological and nutritional properties, such as antitumor, antidiabetic, and

antihypertensive activities [5–7]. It has been recognized that **5CQA** can limit low-density lipoprotein oxidation, so it exhibits various antiatherosclerotic activities [8]. Furthermore, **5CQA** possesses anti-inflammatory, hypolipidemic, and antioxidative properties [9–12]. Theoretical investigations regarding antioxidative activity of **5CQA** have been initiated only recently [13,14]. Due to its high availability in the foods, the antioxidative potential of **5CQA** is very accessible. By scavenging alkylperoxyl radicals **5CQA** removes very toxic reactive species and prevents the damage they cause on DNA.

Chlorogenic acid exists in the form of white powder. Taking into account that the X-ray powder diffraction analysis for **5CQA** has not been carried out yet, the exact structure of solid **5CQA** is not known. There are few experimental studies devoted to the Raman and NMR spectra of **5CQA** [15–18]. In addition, UV–vis absorption spectroscopy has been used to investigate complex formation of some metal ions with **5CQA** [19,20]. The effects of solvent polarity on the UV–vis spectra of **5CQA** have been recently investigated [21]. It was shown in a recent work [18] that, in comparison to **5CQA**, (1S,3R,4S,5R)5-*O*-caffeoylquinic acid features an inverted configuration at the C4 atom. On the basis of the NMR study the preferential conformations of both isomers were

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