Food Chemistry 243 (2018) 74–81

Contents lists available at ScienceDirect

Food Chemistry

journal homepage: www.elsevier.com/locate/foodchem

Interactions of cinnamaldehyde and its metabolite cinnamic acid with human serum albumin and interference of other food additives

Qiaomei Sun[a], Hongqin Yang[a], Peixiao Tang[a,*], Jiuyang Liu[b], Wan Wang[a], Hui Li[a,*]

[a] School of Chemical Engineering, Sichuan Uiversity, Chengdu 610065, China
[b] School of Life Sciences, University of Science and Technology of China, Hefei 230026, Anhui, China

ARTICLE INFO

Chemical compounds studied in this article:
Cinnamaldehyde (PubChem CID: 5430)
Cinnamic acid (PubChem CID: 444539)
tert-Butylhydroquinone (PubChem CID: 16043)
Propyl gallate (PubChem CID: 4947)
Acid red 14 (PubChem CID: 6321394)
Carthamin yellow (PubChem CID: 45358114)

Keywords:
Interaction
Cinnamaldehyde
Cinnamic acid
Human serum albumin
Saturation transfer difference nuclear magnetic resonance
Interference

ABSTRACT

Considering the adverse effect of food additives on humans, thorough research of their physiological effects at the molecular level is important. The interactions of cinnamaldehyde (CNMA), a food perfume, and its major metabolite cinnamic acid (CA) with human serum albumin (HSA) were examined by multiple-spectroscopies. NMR analysis revealed CNMA and CA both bound to HSA, and STD-NMR experiments established CNMA and CA primarily interacted with site I and site II of HSA, respectively. The ligands caused strong quenching of HSA fluorescence through a static quenching mechanism, with hydrophobic and electrostatic interaction between CNMA/CA and HSA, respectively. UV–vis absorption and CD results showed ligands induced secondary structure changes of HSA. Binding configurations were proved by docking method. Furthermore, binding constants of CNMA/CA–HSA systems were influenced by the addition of four other food additives. These studies have increased our knowledge regarding the safety and biological action of CNMA and CA.

1. Introduction

Cinnamaldehyde (CNMA, Fig. 1A) is the major component in cassia and cinnamon bark oils. CNMA, which is a generally approved ingredient of perfumes and essences, imparts a cinnamon flavor to foods and is also used as a natural food preservative to protect aquatic and meat products from fungi. The major metabolite of CNMA is cinnamic acid (CA, Fig. 1A), oxidized by β-oxidation analogous to that of fatty acids (Peters & Caldwell, 1994). CA is mainly used as an antioxidant and preservative in food (Li et al., 2014; Zanetti et al., 2015). However, some researches have indicated that large doses of CNMA by gavage in mice and rats produced nearly 100% mortality, and CNMA causes skin and mucosa toxicity in humans (Cocchiara, Letizia, Lalko, Lapczynski, & Api, 2005; Hébert, Yuan, & Dieter, 1994). Thus, detailed studies of CNMA/CA interaction with physiologically important proteins contribute to elucidate safe utilization of food additives.

Recently, many researchers have paid attention to the interactions between food additives and biomacromolecules. Ferraro and partners have studied the interactions of rosmarinic acid and bovine milk whey protein (Ferraro, Madureira, Sarmento, Gomes, & Pintado, 2015). Shahabadi and colleagues researched the interaction of food colorant quinoline yellow with bovine serum albumin (Shahabadi, Maghsudi, & Rouhani, 2012). Food dye amaranth and allura red AC interacting with human serum albumin (HSA) has been characterized by Zhang and Wu (Wu, Jin, Wang, Wang, & Li, 2015; Zhang & Ma, 2013). The binding process of CA and its hydroxyl derivatives with HSA and CA with bovine serum albumin has been studied by multispectral methods (Bian, Zhang, Yu, Chen, & Liang, 2007; Min et al., 2004). Investigating the binding characteristics of food additives and these metabolites to HSA is helpful to shed light on the physiological effect and possible relevant health risks of food additives at the molecular level.

Nuclear magnetic resonance (NMR) has attracted attentions of researchers to further ascertain interaction mechanism in recent years (Bewley & Shahzadulhussan, 2013; Cox et al., 2015; Wang, Zhang, Xu, & Du, 2011). Wang and partners used proton spin–lattice relaxation rate, molecular rotational correlation time, affinity index, and transferred nuclear overhauser enhancement to investigate the binding affinity and conformation of chlorogenic acid with HSA and bovine serum albumin. Their study provided a better understanding of chlorogenic acid binding and contributed to modification design for therapeutic purposes.

Considering that CNMA can transform into CA in the body, the

* Corresponding authors at: College of Chemical Engineering, Sichuan University, Chengdu, Sichuan, China.
E-mail addresses: tangpeixiao@126.com (P. Tang), lihuilab@sina.com (H. Li).

http://dx.doi.org/10.1016/j.foodchem.2017.09.109
Received 9 June 2017; Received in revised form 8 August 2017; Accepted 20 September 2017
Available online 21 September 2017

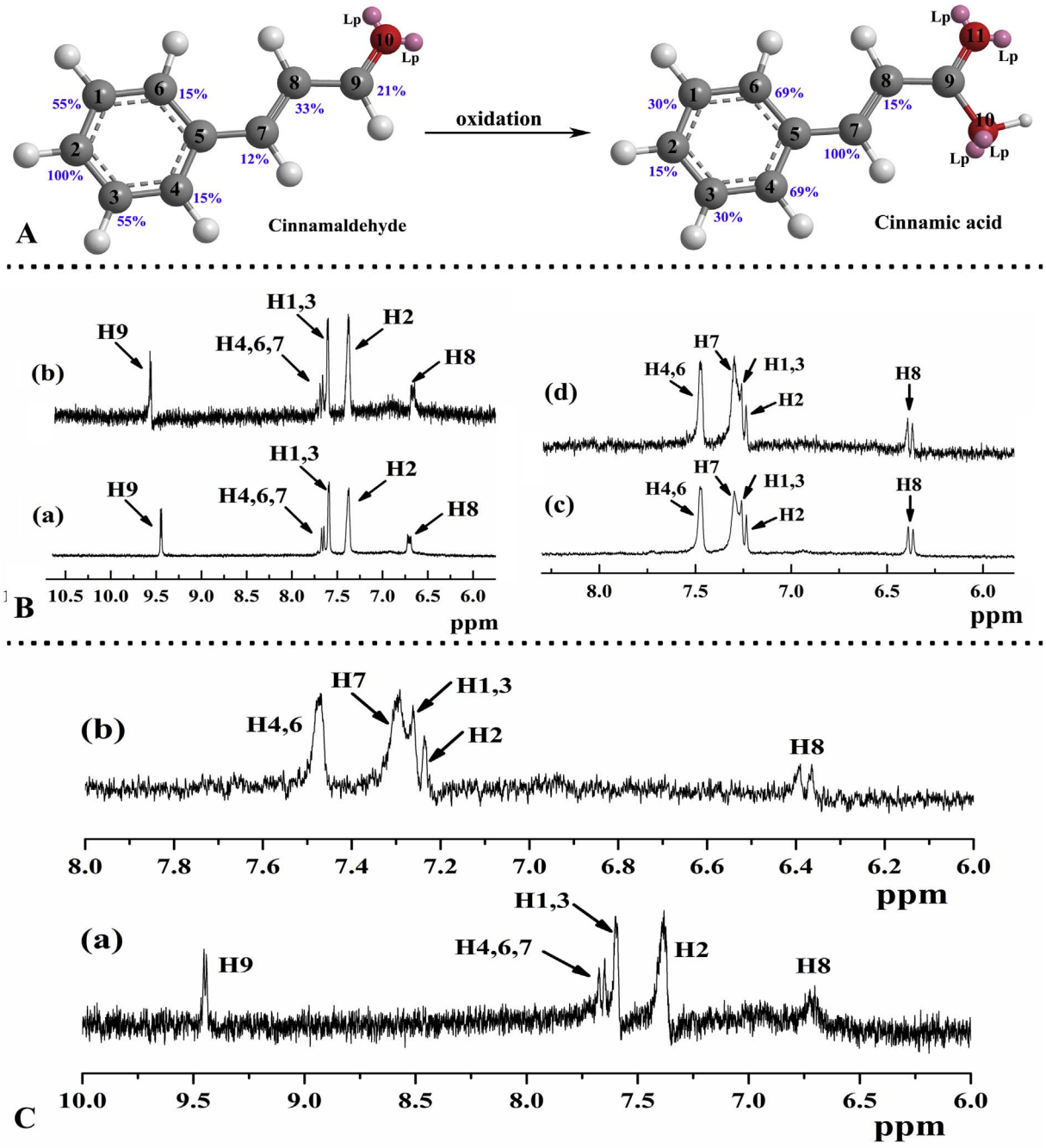

Fig. 1. (A) shows the molecular formula of cinnamaldehyde and cinnamic acid with STD (%). (B) shows the ^{1}H NMR spectrum and ^{1}H STD-NMR spectrum of CNMA (a, b) and CA (c, d) recorded with a Watergate scheme for solvent suppression. (C) shows the WaterLOGSY NMR spectrum of CNMA (a) and CA (b) with HSA. [CNMA] = 400 μM, [CA] = 400 μM, [HSA] = 10 μM, pH = 7.4, T = 298 K.

exploration of interaction mechanisms between CNMA/CA and HSA is the main purpose of this work. Combined with the results of previous reports (Bian et al., 2007; Min et al., 2004), information about the binding mechanisms and interaction between HSA and food additives will be more detailed. STD-NMR and WaterLOGSY-NMR technology were applied to obtain more accurate information about the interactions and the binding sites at the molecular level.

In the present study, STD-NMR and WaterLOGSY were used to determine interaction, and STD competition experiments were used to judge the possible binding sites on HSA binding pocket. Interaction mechanism and binding forces were explored by fluorescence. Then, UV–vis absorption and CD were employed to examine HSA conformation. Molecular docking methods were utilized to validate the binding site and process. The present study can not only explore interactions at the molecular level, but also provide information on the rational use of CNMA and CA. More importantly, it helps in the understanding of the physiological effects of CNMA and its derivative CA with four kinds of additives.

2. Materials and methods

2.1. Materials

Fatty acid-free HSA was purchased from Sigma-Aldrich (Milwaukee, USA) and used without further purification. The stock solution of HSA (2.0×10^{-5} M) was prepared by dissolving solid HSA in 0.01 M PBS at