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DFT and TD-DFT studies on a schiff base containing phenylalanine derived from curcumin

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Abstract. The structure of a schiff base containing phenylalanine derived from cuicumin has been studied by computational simulations using density functional theory (DFT) and time-dependent density functional theory (TD-DFT) at B3LYP/6-311G** level. According to the theoretical calculations of three tautomers, enolic tautomer (A), eneamine tautomer (B) and ketonic tautomer (C), of the schiff base molecular, the geometry, relative stability, charge density population and UV-Vis characteristics of every tautomer are investigated. The calculation results demonstrate that the eneamine tautomer (B) is the most stable one and the stability of tautomers decreases in the sequence: $B>A>C$. The λ_{max} of each tautomer mainly originates from the $\pi-\pi^*$ electronic transition, involving the intramolecular charge transfer. The intramolecular proton transfer caused by electron transitions can result in the interconversion of A and B with a low energy barrier. Water can make the UV-Vis spectra of A and B exhibit remarkable red shift, increasing oscillator strength and absorption intensity. On the contrary, water can make C demonstrate a spectrum without shift, decreasing oscillator strength and absorption intensity.

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Key words: curcumin derivative, schiff base, phenylalanine, density functional theory (DFT)

1 Introduction

Curcumin, a natural yellow pigment in Curcuma longa *L.*, is attractive for its biological activity including anti-inflammatory, antioxidant and antitumor properties. Curcumin can change the redox property of cell and thus adjust the anti-inflammatory activity [1] and inhibit or

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promote apoptosis [2], and inhibit capillary hyperplasia [3]. In addition, Curcumin has been found to be effective in treating the squamous cell carcinoma of head and neck, melanoma, sarcoma, leukemia, lymphoma, and the cancers of colon, breast, nervous system, lung, pancreas and ovarian [4–11]. For its low molecular weight, hypotoxicity, and definite biological activity, curcumin is considered as one potential ideal anti-cancer drug in chemotherapy. Unfortunately, its poor water solubility and inadequate absorption in vivo result in low bioavailability and greatly limit its clinical application. The structural modification of curcumin molecular, in order to increase its anti-tumor activity and water solubility while retaining its hypotoxicity, is hot in this field [12]. Amino acid schiff bases and their derivatives have attracted great attention because of their good biological activity and bio-solubility [13]. Seven 5-fluorouracial derivatives containing schiff bases with certain anti-tumor activity had been synthesized by Shi *et al.* [14].

As amino acid schiff bases have good biocompatibility with the carboxyl groups which can form salts to improve their water solubility, we design a schiff base containing phenylalanine derived from curcumin (Fig. 1). In vivo, this compound can hydrolyze and decompose into curcumin and phenylalanine. Then it may play the pharmacological role of curcumin. Furthermore, the designed compound contains a carboxyl group and then can be transformed into a water-soluble salt with good water solubility and bioavailability.

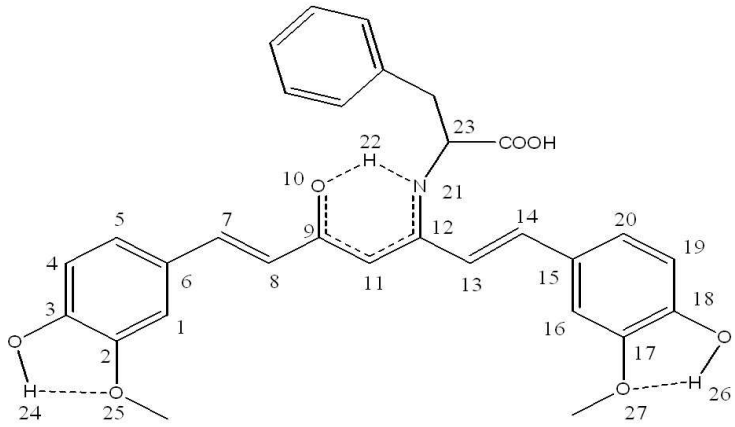

Figure 1: Schematic diagram and atomic numbers of the designed schiff base containing phenylalanine derived from curcumin.

Curcumin molecular possesses two isomers. One is di-ketonic while another is keto-enolic [15]. The disigned schiff base may also possesses isomers. In this work, we carry out theoretical studies on the geometry, relative stability, charge density population and UV-Vis characteristics of the designed schiff base to provide valuable reference for the synthesis. As widely used in the theoretical studies on molecular electronic structure and spectral properties, density functional theory (DFT) and time-dependent density functional theory (TD-DFT) [16] are used in the simulations in this work to do high-level computational analysis of the designed compound.