



## Theoretical study on the structural and antioxidant properties of some recently synthesised 2,4,5-trimethoxy chalcones



Guirong Wang<sup>b</sup>, Yunsheng Xue<sup>a,b,\*</sup>, Lin An<sup>a,b</sup>, Youguang Zheng<sup>a,b</sup>, Yunyan Dou<sup>b</sup>, Ling Zhang<sup>a,b</sup>, Yi Liu<sup>a,b,\*</sup>

<sup>a</sup>Chemical and Biological Pharmaceutical Engineering Research Center, Xuzhou Medical College, No. 209, Tongshan Road, Xuzhou, Jiangsu 221004, China

<sup>b</sup>School of Pharmacy, Xuzhou Medical College, No. 209, Tongshan Road, Xuzhou, Jiangsu 221004, China

### ARTICLE INFO

#### Article history:

Received 26 April 2014

Received in revised form 27 July 2014

Accepted 26 August 2014

Available online 4 September 2014

#### Keywords:

Chalcones

Radical scavenging activity

DFT

HAT

SET-PT

SPLET

### ABSTRACT

The free radical scavenging activity of a series of 2,4,5-trimethoxy chalcones has been computationally explored using the density functional theory (DFT) method. Three potential working mechanisms, hydrogen atom transfer (HAT), stepwise electron transfer proton transfer (SET-PT) and sequential proton loss electron transfer (SPLET) have been investigated. The physicochemical parameters including O–H bond dissociation enthalpy (BDE), ionisation potential (IP), proton dissociation enthalpy (PDE), proton affinity (PA) and electron transfer enthalpy (ETE) have been calculated in gas phase and solvents. The order of antioxidant efficiencies predicted theoretically in this work is in good agreement with that reported by experimental results. The results obtained demonstrate that HAT would be the most favourable mechanism in the gas and benzene phases, whereas the SPLET mechanism is the thermodynamically preferred pathway in polar media. In addition, the importance of the A-ring on the radical scavenging capabilities of chalcones was also confirmed.

© 2014 Elsevier Ltd. All rights reserved.

## 1. Introduction

Cellular oxidative stress, produced by an increase in free radicals, plays a major role in the pathogenesis of ageing and other diseases, such as cancer, atherosclerosis, diabetes and Alzheimer's disease (Maritim, Sanders, & Watkins, 2003; Pieta, 2000). Therefore, the research and development of antioxidants have attracted a great deal of attention in recent years. Phenolic compounds, an important class of antioxidants, have been widely applied in the fields of commerce and biology to inhibit oxidation. Previous studies have suggested that the antioxidant capacity of phenolic compounds is mainly owing to their ability to scavenge radicals (Ndhkala, Moyo, & Van Staden, 2010). It is widely accepted that the radical scavenging abilities of these phenolic compounds depend greatly on the number and arrangement of phenolic hydroxyl groups. The nature of the scavenged radicals and solvents play an important role in the antioxidant mechanism (Alberto, Russo, Grand, & Galano, 2013; Iuga, Alvarez-Idaboy, & Russo, 2012; Leopoldini, Chiodo, Russo, & Toscano, 2011).

Chalcones (1,3-diaryl-2-propen-1-ones, Fig. 1) represent an important subgroup of the polyphenolic family. Structurally, chalcones are open-chain flavonoids bearing two aromatic rings linked by a three-carbon enone moiety. In addition, chalcones are biosynthetic precursors of flavonoids (Go, Wu, & Liu, 2005). In the last decade, chalcones have attracted great interest owing to their broad range of biological activities, such as antimalarial, anticancer, anti-inflammatory, antibacterial and antioxidant activities (Batovska & Todorova, 2010; Go et al., 2005).

To date, several reports have been published on the antioxidant activity of chalcones, especially on hydroxychalcones (Calliste et al., 2001; Chen, Song, Guo, & Wen, 2006; Kozłowski et al., 2007; Rezk, Haenen, van der Vijgh, & Bast, 2002; Todorova, Batovska, Stamboliyska, & Parushev, 2011). These experimental and theoretical studies have demonstrated that chalcones are efficient in the scavenging of various radicals. Moreover, some of them, such as 2,3,4,6-tetrahydroxychalcone and 2',4',3,4-tetrahydroxychalcone (butein), exhibit a more potent radical-scavenging activity than vitamin C and/or  $\alpha$ -tocopherol (Chen et al., 2006). Available literature also suggests that the radical-scavenging activities of chalcones are mainly affected by the aryl groups and their substitution patterns. Hydroxyl groups are one of the key moieties to enhance the antioxidant activity due to its easy conversion to phenoxy radicals through the hydrogen transfer mechanism (Rezk et al., 2002).

\* Corresponding authors at: Chemical and Biological Pharmaceutical Engineering Research Center, Xuzhou Medical College, No. 209, Tongshan Road, Xuzhou, Jiangsu 221004, China. Tel.: +86 516 83262137 (Y. Xue), +86 516 83262136 (Y. Liu).

E-mail addresses: [xueyunsheng@xzmcc.edu.cn](mailto:xueyunsheng@xzmcc.edu.cn) (Y. Xue), [njliuyi2003@gmail.com](mailto:njliuyi2003@gmail.com) (Y. Liu).

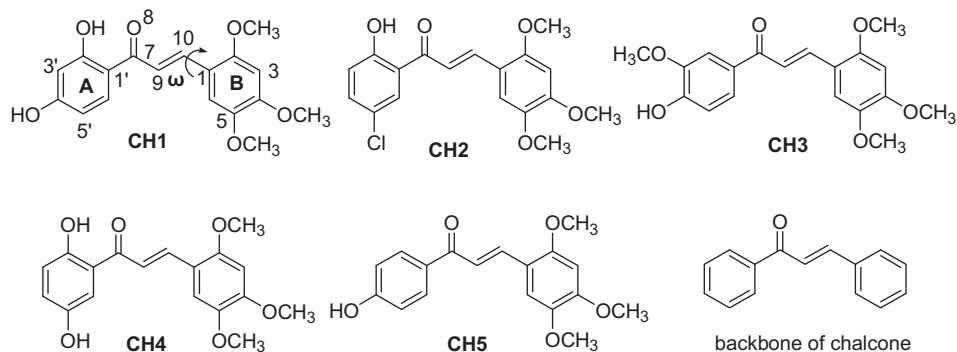


Fig. 1. The backbone structure of chalcone and molecular structures and atomic numbering of the studied 2,4,5-trimethoxy chalcones CH1–CH5.

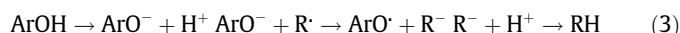
Very recently, a series of 26 derivatives of 2,4,5-trimethoxy chalcones and analogues were synthesised by Shenvi et al. (2013), and the antioxidant activities were evaluated by means of DPPH, NO and PhNHNH<sub>2</sub> assays. The former two methods are based on radical scavenging, while the latter is based on lipid peroxidation. Among the synthesised chalcones, five of them bear OH group(s). Their experimental results displayed that 2,4,5-trimethoxy-2',5'-dihydroxychalcone ( $IC_{50} = 2.653 \mu\text{g/ml}$ ) showed superior DPPH radical scavenging activity over other tested chalcones and the reference antioxidant ascorbic acid ( $IC_{50} = 3.039 \mu\text{g/ml}$ ) in DPPH assay.

In recent years, a lot of computational studies have been devoted to the elucidation of the antioxidant activity of phenolic compounds (Amic et al., 2014; Francisco-Marquez & Galano, 2012; Kozłowski et al., 2007; Leopoldini, Russo, & Toscano, 2011; Mazzone, Malaj, Russo, & Toscano, 2013; Nenadis & Tsimidou, 2012; Sadasivama & Kumaresan, 2011; Trouillas, Marsal, Siri, Lazzaroni, & Duroux, 2006; Wright, Johnson, & DiLabio, 2001). Antioxidant activity of the considered molecules can be evaluated thermodynamically through several physicochemical parameters such as bond dissociation enthalpy (BDE), proton dissociation enthalpy (PDE), proton affinity (PA), ionisation potential (IP) and electron transfer enthalpy (ETE). Moreover, density functional theory (DFT) has been found to give accurate evaluations about these parameters.

In light of these facts, and as a part of our ongoing work concerning the antioxidant activity of chalcones and other phenolics antioxidants (Xue, Zheng, An, Dou, & Liu, 2014; Xue et al., 2012, 2013a, 2013b), herein we wish to utilise the DFT method to investigate the radical scavenging properties of five recently synthesised 2,4,5-trimethoxy hydroxychalcones, CH1–CH5 (Fig. 1 Shenvi et al., 2013). The aim of this study is to elucidate and compare their potentials as antiradical agents, in order to provide new clues for antioxidant development. The aforementioned thermodynamic descriptors including BDE, IP, PDE, PA, and ETE were calculated to examine the action mechanisms involved in the process of free radical scavenging for the title compounds. In addition, the influence of the polarity of solvent on the activity was also discussed.

## 2. Materials and methods

As reported in literatures, the phenolic antioxidants play a protective role in the oxidative process by three possible mechanisms (Leopoldini et al., 2011; Nenadis & Tsimidou, 2012; Wright et al., 2001), namely, hydrogen atom transfer (HAT, Eq. (1)), single electron transfer followed by proton transfer (SET-PT, Eq. (2)) and sequential proton loss electron transfer (SPLET, Eq. (3)).



In the first mechanism (HAT), antioxidant (ArOH) reacts with the free radical ( $R^{\cdot}$ ), by transferring a hydrogen atom to  $R^{\cdot}$  through homolytic rupture of the O–H bond. The reactivity of an ArOH can be estimated by the O–H BDE, where the lower the BDE value, the higher the expected activity. The SET-PT mechanism involves two steps: electron abstraction from ArOH, followed by proton transfer from the radical cation,  $\text{ArOH}^{+\cdot}$ . In this case, the IP and PDE are the most significant energetic factor for the scavenging activity evaluation. Molecules with low IP and PDE values are expected to have high activity. The SPLET mechanism is governed by proton affinity (PA), as well as the electron transfer enthalpy (ETE) of the phenoxide anion,  $\text{ArO}^{-}$ . Thus, in the present study BDE, IP, PDE, PA and ETE values were used as the main molecular descriptors to elucidate the radical scavenging activity of the investigated compounds.

The BDE values were calculated according to the formula

$$\text{BDE} = H_r + H_h - H_p$$

where  $H_r$ ,  $H_h$  and  $H_p$  are the enthalpies of the phenoxyl radical, hydrogen atom and the parent molecule at 298.15 K, respectively. Double bond dissociation enthalpy ( $\text{BDE}_D$ ) corresponds to a second H abstraction from the  $\text{ArO}^{\cdot}$  radical.  $\text{BDE}_D$  are calculated by the following formula:

$$\text{BDE}_D = H_{rs} + H_h - H_r$$

where  $H_{rs}$  is the enthalpy of the phenoxyl radical generated from the second hydrogen atom transfer. The IP and PDE values were obtained via the equations of

$$\text{IP} = H_{cr} + H_e - H_p \quad \text{and} \quad \text{PDE} = H_r + H_H^{+\cdot} - H_{cr}$$

where  $H_{cr}$ ,  $H_e$  and  $H_H^{+\cdot}$  are the enthalpies of the cation radical, electron and proton, respectively. The PA and ETE values were calculated from the following equations

$$\text{PA} = H_{an} + H_H^{+\cdot} - H_p \quad \text{and} \quad \text{ETE} = H_r + H_e - H_{an}$$

where  $H_{an}$  is the enthalpy of anion. The molecular enthalpy ( $H$ ) at 298.15 K is consisted of B3LYP/6-311++G(2d,2p) calculated single point energy (SPE) values and B3LYP/6-31G(d) thermal contributions to enthalpy (TCE, in which the vibrational contributions include zero-point vibrational energy). As in our previous studies (Xue et al., 2012, 2013a, 2013b) gas-phase corrections were employed to calculate the molecular enthalpy in the aqueous phase. In order to calculate the aforementioned parameters, the enthalpies of H-atom, proton, and electron in the gas phase and solvents are needed. The gas phase enthalpy of a hydrogen atom predicted using the B3LYP/6-311++G(2d,2p) method is  $-0.499897$  hartree (Nenadis

Download English Version:

<https://daneshyari.com/en/article/7593981>

Download Persian Version:

<https://daneshyari.com/article/7593981>

[Daneshyari.com](https://daneshyari.com)