

## Probing the antioxidant potential of phloretin and phlorizin through a computational investigation

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**Abstract:** Dihydrochalcones (DHCs) are a class of polyphenols that attract considerable attention for being used in the human diet as functional foods due to their pharmacological activity, including antioxidant, antibacterial, anti-inflammatory, antitumor, and antiviral properties [1]. In terms of antioxidant activity, it is well known that the potential of a given substance can be probed through its capability to scavenge free radicals by (mainly) the mechanisms of hydrogen-atom transfer (HAT) and single electron transfer (SET) [2,3]. In HAT, where an H-atom is transferred to a free radical, there is a strong dependence on the O-H bond dissociation enthalpy (BDE), since there will be higher antioxidant activity when there is a weaker O-H bond. The BDE (i.e., energy to break the O-H bond) is computed as the difference in the heat of formation between the neutral molecule (ArOH) and corresponding radical (ArO<sup>\*</sup>). On the other hand, in SET, a single electron is transferred from the molecule (ArOH) to the free radical. Clearly, the smaller the ionization potential (IP) for ArOH, the lower the energetic cost to abstract an electron.

Very recently, our group performed a computational study on two flavonols that were isolated from Loranthaceae family plant extracts: *kaempferol 3-O- $\alpha$ -L-arabinofuranosyl-(1 $\rightarrow$ 3)- $\alpha$ -L-rhamnoside* and *quercetin 3-O- $\alpha$ -L-arabinofuranosyl-(1 $\rightarrow$ 3)- $\alpha$ -L-rhamnoside* [4], which are glycosylated versions of kaempferol and quercetin, respectively. One of the goals of the previous study was to probe how much the presence of the sugar group would affect the values of BDEs and IPs. In the present work, we extend this idea to examining phloretin and its glycoside phlorizin (see Figure 1 for chemical structures).

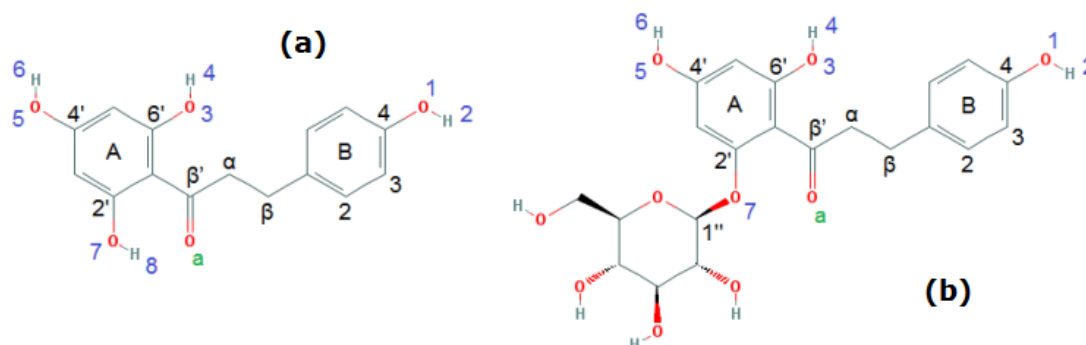
In this work, the structures and energetics of phloretin and phlorizin were examined with density functional theory, using the B3LYP [5,6], M06-2X [7], and LC- $\omega$ PBE [8] functionals with both the 6-311G(d,p) and 6-311+G(d,p) basis sets [9]. Properties connected to antioxidant activity, i.e, bond dissociation enthalpies (BDEs) for OH groups and ionization potentials (IPs), were computed in a variety of environments including the gas-phase, *n*-hexane, ethanol, methanol, and water. All the computations were performed using the Gaussian 09 software suite [10].



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**Figure 1.** Representation of chemical structures, along with atom numbering for (a) phloretin and (b) phlorizin.

The smallest BDEs among the four OH groups for phloretin (three for phlorizin) were determined (using B3LYP/6-311+G(d,p) in water, for instance) to be 79.36 kcal/mol for phloretin and 79.98 kcal/mol for phlorizin while the IPs (at the same level of theory) were obtained as 139.48 and 138.98 kcal/mol, respectively. By comparing with known antioxidants, these values for the BDEs indicate both phloretin and phlorizin show promise for antioxidant activity. In addition, the presence of the sugar moiety has a moderate (0-6 kcal/mol depending on functional) effect on the BDEs for all OH groups. Interestingly, the BDEs suggest that (depending on the functional chosen) the sugar moiety can lead to an increase, decrease, or no change in the antioxidant activity. Therefore, further experimental tests are encouraged to understand the substituent effect on the BDEs for phloretin and to help determine the most appropriate functional to probe BDEs for DHCs. Additional results will be presented and discussed during the Conference.

**Key-words:** Antioxidant activity, dihydrochalcones, bond dissociation energy, ionization potential, density functional theory

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## References:

- [1] I. Fernandez-Pastor *et al.*, J. Nat. Prod. 79, 1737 (2016).
- [2] J. S. Wright *et al.*, J. Am. Chem. Soc. 123, 1173 (2001)
- [3] M. Leopoldini *et al.*, J. Phys. Chem. A 108, 4916 (2004).
- [4] G. L. C. de Souza *et al.*, J. Mol. Model. 22, 100 (2016).
- [5] A. D. Becke, J. Chem. Phys. 98, 5648 (1993).
- [6] C. Lee, W. Yang, and R. G. Parr, Phys. Rev. B 37, 785 (1988).
- [7] Y. Zhao and D. G. Truhlar, Theor. Chem. Account. 120, 215 (2006).
- [8] O. A. Vydrov and G. E. Scuseria, J. Chem. Phys. 125, 234109 (2006).
- [9] M. J. Frisch, J. A. Pople and J. S. Binkley, J. Chem. Phys. 80, 3265 (1984).
- [10] M. J. Frisch *et al.*, Gaussian Inc., Wallingford CT, G09, Revision D.01 (2009).