LETTERS TO THE EDITOR

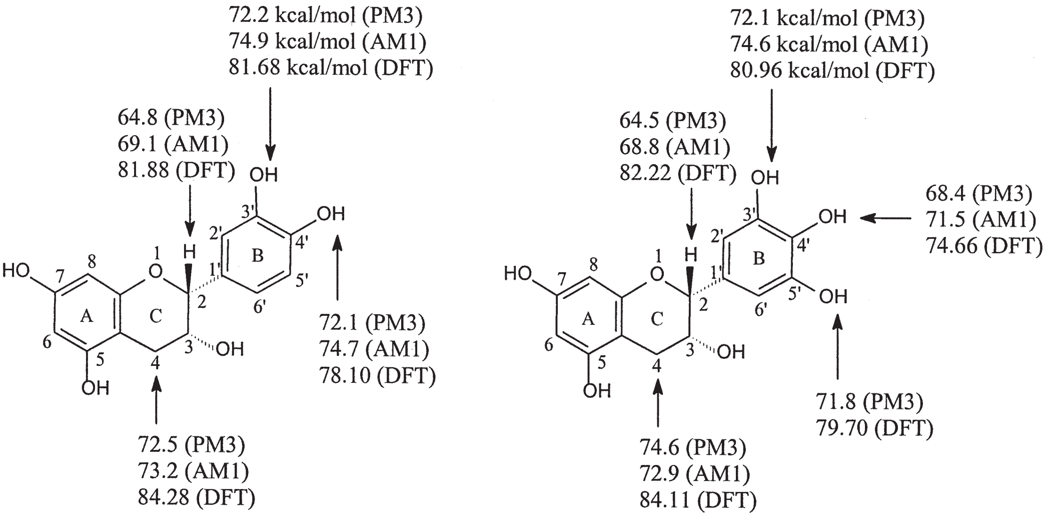
Are Allylic Hydrogens in Catechins More Abstractable Than Catecholic Hydrogens?

Sir:

Catechins, the main components of green tea polyphenols, including (−)-epicatechin (EC), (−)-epigallocatechin (EGC), (−)-epicatechin gallate, and (−)-epigallocatechin gallate, are excellent antioxidants (1,2). The free radical scavenging activity of catechins arises from their abstractable phenolic hydrogens, specifically, the catecholic hydrogens in ring B (Fig. 1) (1,2). In fact, the O–H bond dissociation enthalpies (BDE) of hydroxyls in ring B are comparable to that of α-tocopherol, a good radical scavenger (3). Kondo and coworkers (4–6) have proposed that the allylic hydrogens of catechins are more abstractable than the catecholic hydrogens, because the C–H BDE calculated by using the parametric method 3 (PM3) or Austin model 1 (AM1) for allylic hydrogens were much lower than O–H BDE of the catecholic hydrogens (Fig. 1). If this is true, the structure–activity relationships for catechins will have to be reevaluated, as the allylic hydrogens were taken out of consideration in recent studies. However, taking into account that the typical C–H BDE of toluene is ~89 kcal/mol (7) and that the substituents have little effect on the C–H BDE (8), the unexpectedly low C–H BDE in catechins may result from the inaccuracy of the quantum chemical method used in the calculations.

Semiempirical quantum chemical methods, such as PM3 (9), AM1 (10), and modified neglect of diatomic overlap (MNDO) (11), employ experimental data as a part of the parameters in the calculation process. Hence, these methods are time saving and rather accurate in many cases, especially for optimizing geometries. MNDO is a preliminary semiempirical method; however, it is invalid in calculating hydrogen bond energy. AM1 was modified on the basis of MNDO, with the advantage of accurately estimating hydrogen bond energy. PM3 is the newest semiempirical method and is especially good at calculating molecules containing sulfur and nitrogen atoms.

Although the semiempirical methods are capable of calculating relative O–H BDE (12-15), there is no evidence that these methods are appropriate to calculate the absolute O–H or C–H BDE. In this letter, BDE in catechins were recalculated by a combined quantum chemical method, and the results are compared with those of Kondo and coworkers. The calculation procedures are as follows. The most stable geometries of molecules were constructed according to the



(−)-Epicatechin (−)-Epigallocatechin

FIG. 1. Bond dissociation enthalpies for catechins calculated by semiempirical quantum chemical methods [parametric method 3 (PM3) and Austin model 1 (AM1)] and combined density functional theory (DFT).

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previous methods (16,17). The geometry optimization and the determination of vibration frequencies were performed using the semiempirical AM1 method (10) and then single-point electronic energies were obtained by density functional theory using the B3LYP functions (18–20) on the 6-31G(p′) level. The calculation was achieved by the Gaussian-94 program. By using the electronic energies and the scaled zero-point energies (the scaled factor is 0.947), the C–H and O–H BDE were obtained. The accuracy of this method is well established for calculations on C–H and O–H BDE (7,21,22).

As shown in Figure 1, the recalculated O–H BDE of EC are slightly higher than those of EGC, which is consistent with the fact that EGC scavenges peroxyl radicals more quickly than EC (4,6). Furthermore, the C–H BDE in catechins are higher than the O–H BDE, indicating that allylic hydrogens are not more abstractable than catecholic hydrogens and that the hydrogen abstraction at position 4′ will most likely occur more quickly than the reactions at other positions. However, the C–H BDE for position 2 of catechins are comparable to the O–H BDE for position 3′, implying that the 2-H can compete with 3′-OH to scavenge peroxyl radicals. Hence, the radical-scavenging mechanisms for catechins proposed by Kondo *et al.* (4–6) are still reasonable, and the interesting part of their theory is that allylic hydrogens also participate in the radical-scavenging processes for catechins.

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