COMMENTS

Comment on "Effects of Metal Ions Distinguishing between One-Step Hydrogen- and Electron-Transfer Mechanisms for the Radical-Scavenging Reaction of (+)-Catechin"[5]

Hong-Yu Zhang*,[†] and Lan-Fen Wang[‡]

Laboratory for Computational Biology, School of Life Sciences, Shandong University of Technology, Zibo 255049, P. R. China, and Department of Chemistry, Shandong Teachers' University, Jinan 250014, P. R. China

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As known to all, two mechanisms are involved in the radical-scavenging process of phenolic antioxidants (ArOH). Taking alkoxyl radical ($RO^\bullet$) as an example, the first mechanism is a one-step H-atom-abstraction reaction (eq 1), while the second is an electron-transfer reaction followed by a proton-transfer process (eq 2).

$$RO^\bullet + ArOH \rightarrow ROH + ArO^\bullet \qquad (1)$$

$$RO^\bullet + ArOH \rightarrow RO^- + ArOH^{\bullet+} \rightarrow ROH + ArO^\bullet \qquad (2)$$

Apparently, both pathways give the same net products. However, to select or rationally design more effective ArOH, we have to distinguish which pathway is preferred in a certain chemical/biological system, because the physicochemical parameters characterizing the two mechanisms are different. The first pathway is governed by O−H bond dissociation enthalpy (BDE) to a large extent, whereas the second is mainly determined by ionization potential (IP).[1] The lower the parameters are, the faster the radical-scavenging reaction is.

Up to now, most of the studies focus on the first mechanism;[2−4] hence it is very interesting to note that Nakanishi and co-workers proposed that the second mechanism was favored in the radical-scavenging process of (+)-catechin in acetonitrile (MeCN) or propionitrile (EtCN).[5] However, we have to indicate that the radical-scavenging mechanism is solvent-dependent. For instance, in hydrogen-accepting solvents, an intermolecular hydrogen bond (IHB) can form between the phenolic hydroxyl and the solvent molecule. The IHB will hamper the H-atom-abstracting process and dramatically slow the one-step radical-scavenging reaction.[6,7] Moreover, it has been revealed that the ArOH containing a catechol group, such as 3,5-di-*tert*-butylcatechol (DTBC), quercetin, and epicatechin, are more sensitive to the solvent effects than the monophenolic counterparts, e.g., α-tocopherol (α-TOH) and 3,5-di-*tert*-butyl-4-methylphenol (BHT).[8,9] As MeCN and EtCN are strong hydrogen-accepting solvents and (+)-catechin contains a catechol moiety, it is reasonable to consider that the preferred mechanism observed for (+)-catechin in Nakanishi et al's experiment substantially arises from the solvent effect, and one cannot deduce that in non-hydrogen-bonding solvents, such as chloroform and hexane, (+)-catechin also prefers the second pathway to scavenge radicals.

TABLE 1: Relative O−H BDE (kcal/mol), IP (kcal/mol), and Logarithm of Rate Constants of ArOH

substituted phenols	O−H BDE[a]	IP	log $k_{DOPPH^\bullet}$[c]	log $k_{ROO^\bullet}$[d]
4-CF_3	3.3	9.54[b]	−1.36	
4-CN	2.3	10.82[b]		2.63
H	0	0[b]	−0.66	3.63
4-Cl	−1.5	−0.74[b]	0.04	3.50
4-Me	−2.5	−8.20[b]		4.13
4-OH	−5.8	−14.58[b]		4.83
4-OMe	−6.1	−19.18[b]	2.38	4.84
catechol	−10.0	−9.37[b]	3.26	5.74
1,8-DIOL	−15.7	−25.58	5.49	6.63
4-MeO-1,8-DIOL	−20.1	−34.08	6.30	6.78

[a] Data from ref 10. [b] Data from ref 11. [c] Logarithm of rate constants for ArOH to scavenge 2,2-bis(4-*tert*-octylphenyl)-1-picrylhydrazyl radical ($DOPPH^\bullet$).[10] [d] Logarithm of rate constants for ArOH to scavenge peroxyl radical ($ROO^\bullet$).[10]

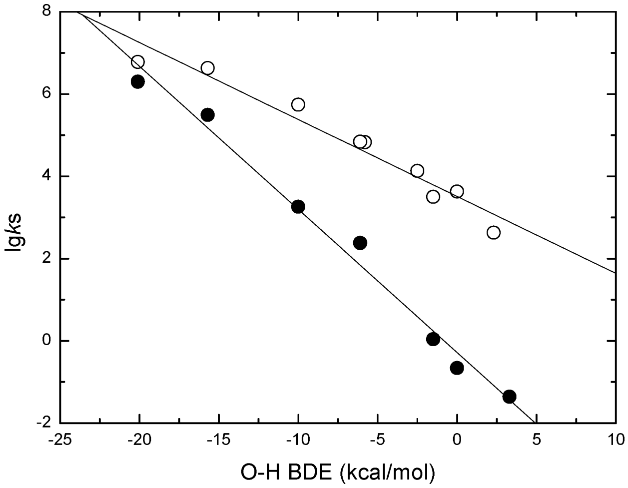

Figure 1. Correlations between O−H BDE and logarithm of rate constants (log k_s) for ArOH to scavenge $DOPPH^\bullet$ (●, $r = -0.99309$) and $ROO^\bullet$ (○, $r = -0.97466$).

Recently, Barclay and co-workers provided a series of rate constants (k_s) for monophenols and catechols to scavenge 2,2-bis(4-*tert*-octylphenyl)-1-picrylhydrazyl radical ($DOPPH^\bullet$) and peroxyl radical ($ROO^\bullet$) in hexane.[10] The good linearity between log k_s and O−H BDE suggested that the first pathway was favored in the system.[10] However, it is still interesting to investigate whether there exists linear correlation between log k_s and IP for the ArOH. Most of IPs have been calculated by means of density functional theory (DFT) method B3LYP/6-31G(d,p),[11,12] and the IPs for 1,8-naphthalenediol (1,8-DIOL) and 4-methoxy-1,8-naphthalenediol (4-MeO-1,8-DIOL) were calculated using the same method (Table 1).[13] It is interesting to note that for the two kinds of radicals, the correlations between log k_s and O−H BDE are better than those between log k_s and IP (Figures 1 and 2),[14] suggesting the first mechanism

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* Corresponding author. Phone: (86) 533-2780271. Fax: (86) 533-2780271. E-mail: zhanghy@sdut.edu.cn.

[†] Shandong University of Technolog.

[‡] Shandong Teachers' University.

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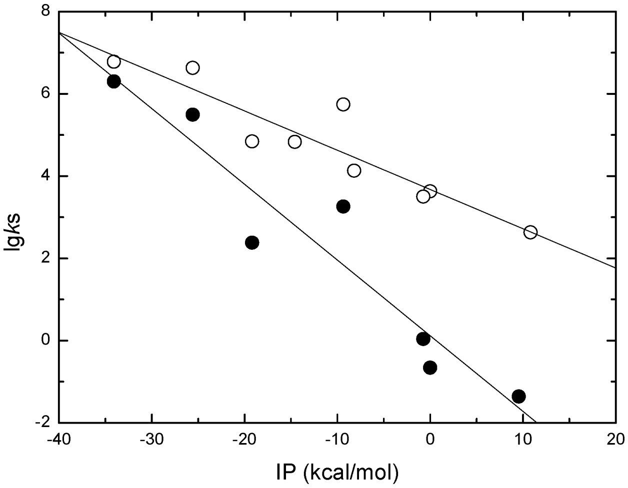

Figure 2. Correlations between IP and logarithm of rate constants (log k_s) for ArOH to scavenge DOPPH$^\bullet$ (●, $r = -0.95484$) and ROO$^\bullet$ (○, $r = -0.92615$).

was indeed more important than the second one in non-hydrogen-bonding solvents, despite the diversity of the antioxidant structure.[15]

In summary, the solvent effect must be taken into consideration for interpreting the radical-scavenging mechanisms of ArOH. Although (+)-catechin proceeds via the second mechanism to scavenge galvinoxyl or cumylperoxyl radical in hydrogen-accepting solvents, the first mechanism may be preferred in non-hydrogen-bonding solvents.

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References and Notes

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(12) It should be pointed out that IP is sensitively dependent on solvent polarity. Polar solvents are favorable to stabilize the charged molecule, so the IP of ArOH decreases dramatically in strong polar solvents compared with that in gas phase. As Foti et al's radical-scavenging experiments were performed in nonpolar solvents,[10] the IPs for all of the phenols were calculated in gas phase.

(13) The total electronic energy (TE) and zero-point vibrational energy (ZPVE) of 1,8-DIOL were calculated to be −536.3495228 and +0.156415 hartree, respectively, and those of its cation radical were −536.0963218 and +0.157041 hartree, respectively. The TE and ZPVE of 4-MeO-1,8-DIOL were calculated to be −650.8725711 and +0.189047 hartree, respectively, and those of its cation radical were −650.6332517 and +0.190021 hartree, respectively. The ZPVEs were scaled by a factor of 0.9805. The IP of 4-MeO-1,8-DIOL is higher than that of α-TOH (−36.1 kcal/mol),[1] indicating the former ArOH is more stable than the latter to air oxidation.

(14) The good correlation coefficient between log k_s and IP partially results from the intercorrelation between O−H BDE and IP ($r = 0.93665$).

(15) During the review of this comment, an important paper appeared and drew a similar conclusion that in ethyl acetate a H-atom-transfer rather than a proton-coupled electron-transfer predominates in radical-scavenging process of various ArOH: Hussain, H. H.; Babic, G.; Durst, T.; Wright, J. S.; Flueraru, M.; Chichirau, A.; Chepelev, L. L. *J. Org. Chem.* **2003**, *68*, 7023−7032.