

Comment on: Is there an Equilibrium between Ascorbic and Dehydroascorbic Acids? [1]

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The formation of ascorbic acid radicals (AH^\cdot) through a reaction between ascorbic acid (AH_2 , or ascorbate, AH^-) and dehydroascorbic acid (A), as shown,



is treated controversially in the literature. Evidence from electron spin resonance (ESR) [2] that this reaction takes place was questioned on basis of thermodynamics and ESR [1, 3]. Elsewhere [4], thermodynamic arguments were used to support the existence of equilibrium (1). This confusing situation must be, and can be, resolved.

The pertinent equations which govern the thermodynamics of (1) are

$$K = \frac{[\text{AH}^\cdot]_e^2}{[\text{AH}^-]_e[\text{A}]_e[\text{H}^+]_e}$$

$$\text{or } K_{\text{const.}} [\text{H}^+] = \frac{[\text{AH}^\cdot]_e^2}{[\text{AH}^-]_e[\text{A}]_e} \quad (2)$$

where K is the equilibrium constant and $[\text{X}]_e$ are the equilibrium concentrations, which are assumed to equal activities. Again for constant $[\text{H}^+]$ one may write,

$$E = E^\circ - \frac{RT}{F} \ln \frac{[\text{AH}^\cdot]^2}{[\text{AH}^-][\text{A}]} \quad (3)$$

here E and E° are the electromotive force (emf) and the standard emf of (1), respectively, R is the ideal gas constant, F is the Faraday constant, and T is the temperature in $^\circ\text{K}$. Also,

$$E = 0 \text{ at equilibrium, therefore, } E^\circ = \frac{RT}{F} \ln K \quad (4)$$

Now, E° can be calculated from available standard electrode potential estimates:

$E^\circ = -0.52 \text{ V}$ at $\text{pH} = 7$ in aqueous solution (ref. [4] and citations therein). This value is to be preferred to -0.58 V of ref. [1], as the latter number includes measurements in nonaqueous media with unspecified pH. The present argument is in no way affected by this substitution. This E° is based on total ascorbic acid concentration, however, at a pH of 7 the $[\text{AH}^-]$ is nearly equal to the total ascorbic acid, so that the equations can be used as written above.

At standard conditions the \ln term in (3) equals zero so that $E = E^\circ = -0.52 \text{ V}$. A negative E precludes spontaneous *net* reaction, in case (1), from left to right. Restated, this merely means that more reactions will proceed from right to left than from left to right in (1) at *standard conditions*. The conclusion [1, 3] that no radical forming reaction will take place is, therefore, erroneous and represents the kernel of the confusion.

Standard conditions require that $[\text{AH}^\cdot] = 1 \text{ mol/l}$, a highly unlikely proposition in aqueous medium. If one substitutes biologically more realistic values (as an example: $[\text{AH}^-] = 10^{-3}$, $[\text{A}] = 10^{-4}$, $[\text{AH}^\cdot] = 10^{-8} \text{ mol/l}$ which is detectable by ESR!) into equation (3), together with $E^\circ = -0.52 \text{ V}$, one obtains

$$E = +0.01$$

indicating spontaneous *net* reaction from left to right. With the concentrations of ref. [1], namely 0.3 and 0.03 mol/l for ascorbic and dehydroascorbic acids, one receives $E = +0.31 \text{ V}$. It follows that if there are only AH^- and A, initially, the reaction will only proceed toward the radical until enough have formed to enable collisions between them.

If one uses equation (3) to predict reaction spontaneity, one must also accept equation (4) which has been pointed out [4] to yield a $K_{(1)} = 1.5 \times 10^{-9}$, thereby also indicating that radicals are created. Incidentally, this K agrees reasonably well with the one of ref. [2] (5×10^{-9} at $\text{pH} = 6.4$), though they are based on data from different methods. Substituting the above K and the substrate concentrations of ref. [1] into equation (2), an $[\text{AH}^\cdot]$ of about 10^{-7} mol/l obtains which can easily be detected by ESR instruments. This is demonstrated by ref. [2]. As ref. [1] neither lists ESR spectrometer settings, nor any external standard results, one is unable to ascertain why radicals were not seen in that work when air was excluded.

That ascorbic acid solutions at physiological pH

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readily yield the corresponding radical when contacted by air (O_2) has been reemphasized recently [5]. However, the mechanism for this reaction must be

considered equivocal as at least two possibilities exist: a one electron oxidation to the radical or a two electron oxidation to A with radical production via (1).

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