Thermodynamic Analysis of Hepatitis C Virus Vitality in Syringes

TO THE EDITOR—We read with interest the article by Paintsil et al [1], and we found that the experimental technique reported could be directly applied to the study of an important topic, hepatitis C virus (HCV) vitality. In this letter, we show our own analysis of the results in the article, and suggest a means of applying the technique to examine HCV infectivity (ie, vitality). One of the main results reported by Paintsil et al [1] is temperature-dependent HCV vitality. Assuming the HCV decay (losing infectivity) as a chemical reaction, we can analyze it in terms of chemical kinetics, which will allow us to characterize it quantitatively. This approach has been found to be useful in understanding molecular phenomena [2, 3]. Among the 2 different examinations that the authors performed, we found that the one conducted with the low-void volume syringes to be suitable for quantitative analysis because it showed a monotonic decrease in HCV infectivity [1]. First, the half-life ($t_{1/2}$) of HCV vitality was obtained from the article’s Figure 3A. The half-life we used corresponds to the time point for 50% HCV-positive syringes. From the half-life values, we can obtain the rate constant ($k$) of HCV decay using Equation-(1), assuming it follows first-order kinetics:

$$k = \frac{\ln 2}{t_{1/2}}. \quad (1)$$

This assumption is in agreement with the result reported in Figure 2 of the article, in that HCV decay is described as an exponential function. $k$ can be related to standard molar Gibbs free energy ($\Delta G_a^o$) of activation at temperature $T$ using Equation-(2).

$$\Delta G_a^o = -RT \ln \frac{k}{k_B T} \quad (2)$$

where $R$ is the gas constant ($= 8.314 \text{ J} / (\text{K mol})$), $h$ is Planck’s constant ($= 6.63 \times 10^{-34} \text{ J} \cdot \text{s}$), and $k_B$ is the Boltzmann constant ($= 1.38 \times 10^{-23} \text{ J} / \text{K}$). The resulting values of $\Delta G_a^o$ are shown in Figure 1 and suggest that HCV decay needs more activation free energy at a higher temperature.

$\Delta G_a^o$ is composed of 2 energy terms: standard molar enthalpy ($\Delta H_a^o$) and entropy ($\Delta S_a^o$) of activation. Each of these energy terms provides molecular information on the decay of HCV. The values of $\Delta H_a^o$ and $\Delta S_a^o$ can be obtained from a regression analysis of the $\Delta G_a^o$ values in accordance with Equation-(3).

$$\Delta G_a^o = \Delta H_a^o - T \Delta S_a^o \quad (3)$$

According to our analysis, the values of $\Delta H_a^o$ and $\Delta S_a^o$ are $25.6 \pm 3.0 \text{ kJ/mol}$ and $-254.3 \pm 10.0 \text{ J/(mol K)}$. The positive value of $\Delta H_a^o$ suggests that HCV decay requires an input of energy. The molecular events requiring the energy input might be unfolding of HCV envelope proteins, as suggested by Chapel et al [4], who found that misfolded envelope proteins reduce the infectivity of HCV. Another possible mechanism would be disruption of the viral membrane structure, leading to the loss of the viral infectivity. The negative value of $\Delta S_a^o$ indicates an increase of order of the system. One explanation could be ordering of solvent water molecules at the hydrophobic surface of the envelope proteins or aliphatic phospholipid chains that are exposed on denaturation. In Figure 3 of the article, Paintsil et al [1] measured HCV decay with a relatively big temporal gap between measurements. It would provide more accurate information on the kinetics of HCV decay if the measurement were performed more frequently, as Paintsil and colleagues did in...
One useful feature of the protocol reported in the article is the ease of manipulation of physical and chemical conditions. A useful feature of the technique is that it can be used to identify chemicals that enhance the decay of HCV by modulating the thermal stability of viral proteins or perturbing the integrity of the viral membrane. This approach was taken in our observation that magnesium ion is an effective inhibitor of the binding of *Escherichia coli* to heparin [5]. One can readily take this approach by monitoring HCV decay, as in Figure 2 of the article, with potential activators of the process. In this way, one may identify molecules that can accelerate the process, which may have therapeutic potential. Furthermore, with use of the analysis introduced above, one can characterize activators in terms of thermodynamics, which may provide valuable information in drug design [6]. In the editorial commentary that accompanies the article, Rich and Taylor [7, p. 981] state that the article may mark “the beginning of a new era in understanding HCV prevention.” We hope that our analysis and suggestion, introduced in this letter, will add to the value following adoption by the HCV research community.

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**References**
