Carefully read the following information and briefly answer the following questions after calculating with a precision of 2 significant figures. Given that ln(2)≅0.7, ln(10)≅2.3.

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After drinking alcohol, ethanol ($CH_3CH_2OH$) in our blood can soon be built up to 20mM, which will gradually be oxidized to ethanal ($CH_3CHO$), the chief chemical for the alcohol flush syndrome, with the following reaction: $ethanol + NAD^+ \rightarrow ethanal + NADH + H^+$. Under sufficient supply of $NAD^+$, the oxidation rate ($r$) from ethanol (S) to ethanal (P) can be predicted by Arrhenius equation:

$\frac{-d[S]}{dt} = \frac{d[P]}{dt} = r = Ae^{\frac{-E}{RT}}$ where R is the gas constant (~8.3 $Jmol^{-1}K^{-1}$).

Outside our body, the reaction rate at 27°C doubles for every 10°C rise in temperature (a norm in high school chemistry); however, the rate at the body temperature (37°C) can only reach 0.001mM$min^{-1}$, much slower than the maximum reaction rate in our body, 10 mM$min^{-1}$. Learned from the internet, the reaction in our body was actually catalyzed by a dimeric enzyme, alcohol dehydrogensase, with one active site on each subunit. The enzyme ($K_M$ = 0.5mM) was expected to follow Michaelis-Menten kinetics with the reaction rate ($v$) reaching its maximum ($v_{Max}$) right after drinking.

$$v = v_{Max}\frac{[S]}{[S]+K_M}$$

However, the *in vitro* kinetic analysis shows a positive cooperative effect that can be revealed by Hill-Langmuir equation of Protein(P)-Ligands(L) binding by assuming the dissociation constant $K = K_M$:

$$P + nL \leftrightarrow PL_n;\ \theta = \frac{Occupied\ protein}{Total\ protein} = \frac{[PL_n]}{[P]+[PL_n]} = \frac{[P][L]^n/K}{[P]+[P][L]^n/K} = \frac{[L]^n}{[L]^n+K}$$

$$\frac{\theta}{1-\theta} = \frac{[L]^n}{K};\ log(\frac{\theta}{1-\theta}) = nlog([L]) - log(K)$$

The logarithmic plot is called Hill plot, and the slope $n$ is called Hill coefficient. The protein binding phenomenon is "positive" cooperative when $n > 1$.

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1) Describe the meanings and dimensions of r, A, $E$ and $T$ in Arrhenius equation (10%).
2) The reaction is said to be pseudo-first order, why? (5%)
3) Calculate the approximate value of $E$ for the uncatalyzed reaction. (15%)
4) Calculate the approximate value of $E'$ for the enzymatic reaction. (10%)
5) Calculate the physiological alcohol dehydrogenase level in terms of the international unit (IU)of enzyme (μmol/min). (10%)
6) Under what conditions does the assumption, $K = K_M$, hold? (10%)
7) Describe the way to obtain the Hill plot of the enzymatic reaction and retrieve useful information. (Hint: $\theta = v/v_{Max}$) (20%)
8) Give possible physiological meaning of the positive cooperative effect of alcohol dehydrogenase. (10%)
9) Give possible physiological meaning of the positive cooperative effect of hemoglobin during transporting oxygen molecules from lung to tissues. (10%)

**試題隨卷繳回**