DETERMINATION OF THE TARGET SIZE BY THE INDIRECT ACTION OF IRRADIATION

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1. Introduction

When we irradiate the dilute solution of solute (for example enzyme or virus), the number of the molecules of solute directly ionized or excited by radiation is very small compared with the number of solvent molecules ionized or excited. There is thus the possibility of an indirect effect on the molecule of solute, either due to transference of energy from excited or ionized solvent molecules, or due to chemical change occurring in the solvent and the products affecting the molecule of solute.

We can understand that most radiochemical reactions in dilute solution are indirect, chemical change in the molecule of solute occurring as the result of ionization and excitation in the solvent molecules. Of course, direct excitation or ionization of the molecule of solute, when it occurs, will lead to chemical change, but the number of direct solute ionizations and excitations in a dilute solution is very small compared with the number of ionizations and excitations of solvent molecules. As is well known in experiments of enzyme, when we use water molecule as solvent molecule, the probability that an ionized or excited water molecule causes change in a molecule of solute is nearly 1 and therefore direct action is negligible. This result strongly suggests that energy dissipated in the solvent is eventually handed on to the solute.

The irradiation of ordinary water not specially purified and de-aerated leads to decomposition with the production of H_2 and O_2 gases and the formation of some H_2O_2. That is, their reactions are:

$$H_2O^+ + e \rightarrow H^+ + OH$$

$$H_2O + e \rightarrow H + OH^- \text{ or } H^+ + e \rightarrow H,$$

and as the oxygen is dissolved,

$$H + O_2 \rightarrow HO_2 \text{ followed by } 2HO_2 \rightarrow H_2O_2 + O_2.$$

Furthermore, the removal of the hydrogen radicals by the oxygen reduces the rate of recombination of H and OH. With moderate doses of radiation not much oxygen is liberated as is expected in the formation of H_2O_2. But the concentration of H_2O_2 does not increase indefinitely, and with larger doses of radiation the reaction proceeds according to the equation $2H_2O=2H_2+O_2$, and the chemical reaction to the solute decreases relatively. The yield of H_2O_2 during the early stages of the reaction with *X*-rays is 0.8 molecules per ion-pair at acid *pH*. As stated in the above, the production of H_2O_2 in irradiated water requires the presence of dissolved oxygen. But the role of H_2O_2 in the irradiation of living cells has not yet been determined. And most of the molecules of solute (as enzyme or virus) which react have not been excited or ionized directly by the radiation, but their reaction follows radicals which are produced by excitation or ionization of the solvent molecules. That is, the excitation or ionization of a water molecule by an ionizing particle causes the production of an intermediary body of finite life, capable of causing reaction in many solutes. This intermediary is referred as activated water, and the nature of activated water has been discussed by many investigators to this day, and chemically, many of reactions are oxidation or reduction reactions, and some of reactions could be caused by H_2O_2. In the next section, assuming that the radical produced by the irradiation acts on the target (for example virus molecule or enzime), we shall determine the size of the target.

2. Calculating the target size in the indirect action.

As stated in the above, we can understand that most radiochemical reactions in dilute solution are indirect, chemical change in the target (for example virus molecule or enzyme) occurring as the result of ionization and excitation in the solvent molecule.

A reaction of an active radical and a target capable of reacting can result in one of the following alternatives:

a) The active radical eliminates after it gives chemical change in the target.

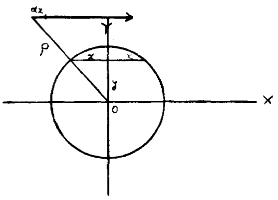
b) The active radical eliminates without chemical change in the target.

c) Change in neither radical nor target.

Therefore, it is infered from the above that not all relations between a target and an active radical which eliminate the latter lead to reaction in the target.

Let the target be the sphere of radius r. Then assuming that an ion-cluster produced at a distance ρ from the center of the target has a probability $e^{-\rho^2/r^2}$ of being an effective "hit", we shall derive the formula for calculating the size of the target.

As stated in the introduction, using the moderate dose, we can neglect ionization and excitation within the spherical target. Further, when we assume that an ionizing particle produces ion-clusters at a mean separation (L) of consecutive primary ionizations along its path, an ionizing particle which passes through a point at distance $y > r$ from the center (cp. Fig.) will produce a number dx/L of ion-clusters in any path length dx, and hence altogether will produce a mean number $\int_{-\infty}^{\infty} e^{-\rho^2/r^2} dx/L$ of effective hits in the target. That is;



$$(1)\qquad \frac{1}{L}\int_{y>r} e^{-\rho^2/r^2} dx = \frac{1}{L} e^{-y^2/r^2} \int_{-\infty}^{\infty} e^{-x^2/r^2} dx = \left(\frac{r\sqrt{\pi}}{L}\right) e^{-y^2/r^2} = z_1 .$$

Similarly, when an ionizing particle crosses the spherical target, and when we neglect the ionization within it, the mean number of effective hits at a distance $\rho > r (y \leqq r)$ is given by

$$(2)\qquad \frac{1}{L}\int_{\substack{\rho>r\\ y\leqq r}} e^{-\rho^2/r^2} dx = \frac{2}{L} e^{-y^2/r^2} \int_{\sqrt{r^2-y^2}}^{\infty} e^{-x^2/r^2} dx = z_2 .$$

Therefore, the mean number of effective hits at a distance $\rho > r$ from the center of the target is given by

$$(3)\qquad z = z_1 + z_2 = \delta_1\left(\frac{r\sqrt{\pi}}{L}\right) e^{-y^2/r^2} + \delta_2\left(\frac{2}{L}\right) e^{-y^2/r^2} \int_{\sqrt{r^2-y^2}}^{\infty} e^{-x^2/r^2} dx$$

where
$\delta_1 = 1$, $\delta_2 = 0$ if an ionizing particle passes through the domain $y > r$,
$\delta_1 = 0$, $\delta_2 = 1$ otherwise.

Therefore, the probability that there exists at least one hit is $(1 - e^{-z})$. For a dose of radiation corresponding to the production of n ion-clusters per unit volume the number of ionizing particles passing through the band between y and $y + dy$ from the center of the target is $nL2\pi y dy$, and the mean number of hits per target for this dose is

$$(4)\qquad p=nL\int_{\rho>r}(1-e^{-z})2\pi y dy=nL\int_{y>r}(1-e^{-z_1})2\pi y dy+nL \times\int_{\substack{\rho>r\\ y\leqq r}}(1-e^{z_2})2\pi y dy\,,$$

Putting $y=rw$, $2r=L\xi$, the first term of the right hand side in the equation (4) becomes:

$$p_1=nL\int_{y>r}(1-e^{-z_1})2\pi y dy=\frac{n\pi}{2}\xi^2L^3\int_1^\infty\left\{1-\exp\left[-\frac{\sqrt{\pi}}{2}\xi e^{-w^2}\right]\right\}wdw\,,$$

furthermore, putting $\frac{\sqrt{\pi}}{2}\xi e^{-w^2}=u$,

$$=\frac{n\pi}{4}\xi^2L^3\int_0^{\frac{\sqrt{\pi}}{2}\xi e^{-1}}(1-e^{-u})\frac{du}{u}$$

$$=\frac{n\pi}{4}\xi^2L^3\left\{\log\left(\frac{\sqrt{\pi}}{2}\xi\right)+E_i\left(\frac{\sqrt{\pi}}{2}\xi e^{-1}\right)+\int_0^1\frac{1-e^{-u}}{u}du-\int_1^\infty\frac{e^{-u}}{u}du-1\right\}$$

$$(5)\qquad =\frac{n\pi}{4}\xi^2L^3\left\{\log\left(\frac{\sqrt{\pi}}{2}\xi\right)+E_i\left(\frac{\sqrt{\pi}}{2}\xi e^{-1}\right)-0{:}4228\right\}$$

where $E_i\left(\frac{\sqrt{\pi}}{2}\xi e^{-1}\right)=\int_{\frac{\sqrt{\pi}}{2}\xi e^{-1}}^\infty\frac{e^{-u}}{u}du$ is the exponential integral. Similarly, the second term is;

$$(6)\qquad p_2=nL\int_{\substack{\rho>r\\ y\leqq r}}(1-e^{-z_2})2\pi y dy$$

$$=\frac{n\pi}{2}\xi^2L^3\int_0^1\left\{1-\exp\left[-\xi e^{-w^2}\int_{\sqrt{1-w^2}}^\infty e^{-x^2}dx\right]\right\}wdw$$

Therefore, for a dose of radiation corresponding to the production of n ion-clusters per unit volume, we have as the mean number of effective hits on the target

$$(7)\qquad p=\frac{n\pi}{4}\xi^2L^3\left\{\log\left(\frac{\sqrt{\pi}}{2}\xi\right)+E_i\left(\frac{\sqrt{\pi}}{2}\xi e^{-1}\right)-0.4228\right\}+\frac{n\pi}{2}\xi^2L^3\int_0^1\left\{1-\exp\left[-\xi e^{-w^2}\int_{\sqrt{1-w^2}}^\infty e^{-x^2}dx\right]\right\}wdw$$

Using the above equation (7), we can determine the target size $2r$ from experimental value p.

3. Conclusion

Although the experiments in the indirect action suggest very strongly that H_2O_2 may be the product involved in the oxygen effect, they do not establish this point unequivocally. The possibility exists that other products of the radio-decomposition of water is concerned. For example, the observations of Krenz and Dewhurst on the effect of dissolved oxygen on the oxidation of ferrous sulphate in aqueous solution by gamma rays can apparently best be explained by a mechanism involving the HO_2 radical. But the experimental results with alpha particles in the presence and absence of oxygen appear to make it unlikely that HO_2 is the intermediate involved. H_2O_2 is formed directly in large amounts by alpha particles because of the very close proximity of the OH radicals produced in the particle track. What kind of radical act on the molecule of solute in the indirect action? This question on radio-chemical grounds will be investigated successively by many radio-biochemists in future.

Assuming that in the indirect action some radical produced by ionizing radiation acts on the solute molecule depending on the distance ρ from the center of the molecule of solute as stated in section 2, we derived the formula for calculating the size of the molecule of solute. In contract to the above theory, Lea (1946) thought that an effective hit is supposed to be scored when in its passage though the target, which is a sphere of radius r, one or more ion-clusters (i.e. primary ionizations) are produced within the target, and he derived the mathematical relation between the target size and inactivation dose in direct action, but even in the experiments of direct action we can not deny that there is the possibility of an indirect effect on the target, either due to transference of energy from ionized molecules and atoms or the products affecting the target. Judging from the fact that the accuracy of estimation of the target size by Lea's method is not so good, we can conceive that there is the above possibility. Therefore, we can suggest that the present concept of mechanisms in direct action may need modification in the light of more recent development. But our result (7) must be solved by the future experiments in indirect action whether it is correct or not.

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