

4) Ampoules should be stored in a cool, dry place and should be used within 24 hours as they are added with water.

6.2.2. Physical and Chemical Factors Influencing The Chemical Degradation of Pharmaceutical Product

The different physical and chemical factors which affect the chemical degradation of pharmaceutical products are:

- 1) Temperature,
- 2) Solvent,
- 3) Ionic strength,
- 4) Dielectric constant, and
- 5) Specific and general acid-base catalysis.

6.2.2.1. Temperature

Generally the speed of many reactions can be increased two to three times with each increase of 10°C in temperature.

The effect of temperature on reaction rate is given by the **Arrhenius equation** which in the exponential form is:

$$k = Ae^{-E_a/RT}$$

Where,

k = Specific reaction rate constant.

A = Arrhenius factor.

E_a = Energy of activation.

R = Gas constant (1.987 calories/deg mole).

T = Absolute temperature.

The **Arrhenius factor** (A) is a measure of the frequency of collisions between the reacting molecules. The **energy of activation** (E_a) is the energy required for effective collisions to cause a reaction between the molecules.

On expressing the Arrhenius equation to logarithmic form:

$$\ln k = -\frac{E_a}{RT} + \ln A$$

On converting the above equation to common logarithmic form:

$$\log k = \frac{-E_a}{2.303 RT} + \log A$$

Where, $\log A = \text{Constant}$.

The values of constants A and E_a can be established by determining the value of k at various temperatures. Plot of $\log k$ versus $1/T$ gives a straight line with slope equal to $-E_a/2.303R$ and intercept at y-axis equals to $\log A$ (figure 6.2). This graph can also be used to determine the value of k at any other temperature. For example, k_{25° , i.e., the rate constant at room temperature can be obtained by extrapolation of Arrhenius plot.

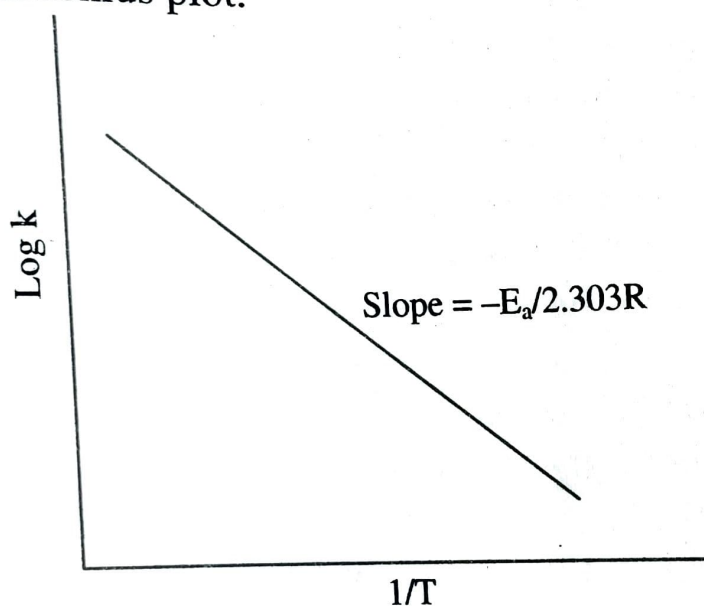


Figure 6.2: Arrhenius Plot

E_a can also be determined by plotting $\log t_{1/2}$ against $1/T$ which yields a straight line with slope equal to $E_a/2.303 R$.

E_a can also be obtained by determining k_1 at T_1 and k_2 at T_2 and using the following equation:

$$\log \frac{k_2}{k_1} = \frac{E_a}{2.303 R} \cdot \frac{(T_2 - T_1)}{T_2 \cdot T_1}$$

The Arrhenius equation is useful when the energy of activation is in the range of 10-30kcal/mole. If E_a is only 2-3kcal/mole (as in case of photolytic reactions), little advantage is gained from the equation. Similarly if the energy of activation is more (as in case of pyrolysis), the degradation rate is so fast that it becomes difficult to make use of this relationship.