

Unit - V

Influence of temperature on rate of rxn

* The speed of many rxns is about two or three times with every 10 degree rise in temperature.

* Arrhenius equation explain the effect of temperature —

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

Integration of eqⁿ —

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

log form of equation

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

k = Specific rate constant.

R = Ideal gas constant

A = Frequency factor

T = Absolute temp.

E_a = Energy of activation

* Energy of activation is defined as minimum energy that a molecule possess to induce molecules collision to form product.

* Arrhenius factor (A) is defined as the frequency of collision b/w molecules.

* Collision theory states that collision must occur b/w molecules.

* The rxn b/w molecules does not take place unless they have certain energy.

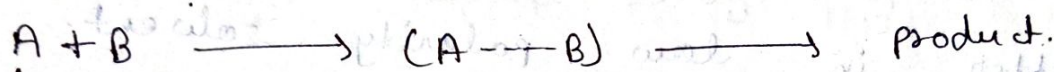
* At any given temperature a fix number of molecules have certain energy.

* As the temperature rises more molecules absorb energy and get activated.

* These activated molecules are responsible for ↑ ed rate of rxn.

Influence of solvent on rate of rxn

- * The effect of solvent is related to the relative solubility of the reactants and the product in the given solvent.



- * The quantitative relationship b/w rxn rate constant and the solubility is given by equation —

$$\log k = \log k_0 + \frac{V}{2.303R} \cdot \frac{1}{T} (\Delta\delta_A + \Delta\delta_B - \Delta\delta^*)$$

k = rxn rate constant

k_0 = Rate constant in infinitely dilute soln.

V = molar volume of reactants (A and B)

$\delta_A, \delta_B, \delta^*$ = solubility parameter of reactants A, B and complex.

* Polar solvent tend to accelerate rxn in which the product formed are more polar than the reactants.

* If the product formed are less polar than the reactant, then the rxn proceed better in low polarity solvent.

* Examples of non-aqueous solvent —

ethanol, glycerol, propylene glycol, vegetable oil etc.

Influence of ionic strength on rate of rxn

* The effect of ionic strength of a salt on rate of rxn may be expressed by following equation —

$$\log k = \log k_0 + 1.02 Z_A Z_B \sqrt{\mu}$$

Where $\rightarrow$ k = degradation rate constant for the rxn
 k_{∞} = Rxn rate constant at infinite dilution.

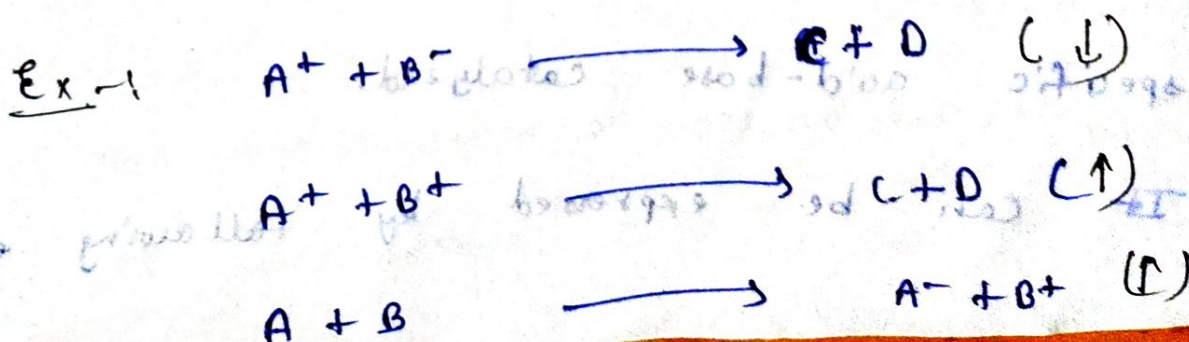
Z_A and Z_B = charges carried by the reactants A and B.

$\sqrt{\mu}$ = Ionic strength of the salt.

* A/c to above equatⁿ, Increase in ionic strength $\downarrow$ es the rate of rxn involving interaction b/w oppositely charged ions.

* It $\uparrow$ es the rate of rxn b/w similarly charged ions.

* Rxns which result in formatⁿ of oppositely charged ions (product) exhibit $\uparrow$ in rxn rate on $\uparrow$ ing ionic strength.



Specific and general acid-base catalysis

↓
Ionic form

↓
Uniformal

Catalyst →

A catalyst is defined as a substance which ↑ or decreases the rate of rxn without itself being changed chemically.

* A catalyst does not alter the equilibrium of reversible rxn.

* There are following types of catalysis —

1- Specific acid-base catalysis —

If drug salt is buffer, ~~the~~ decomposition may not take place by change in concentration of acid or base.

* The rxn may be catalysed by H^+ or OH^- .

* When the rate equation involving concentration of H^+ or OH^- , the rxn is said to be specific acid-base catalysed.

* It can be expressed by following equation —

$$\frac{dp}{dt} = (k_0 + k_1[H^+] + k_2[OH^-]) [S]$$

* Observed rate constant is given by —

$$k_{obs} = k_0 + k_1[H^+] + k_2[OH^-]$$

* At low pH, the H^+ ion concentration is greater than k_0 and $k_2[OH^-]$.

The observed rate constant becomes —

$$k_{obs} = k_1[H^+]$$

The reaction is acid catalysed.

* At higher pH, the OH^- concentration is greater than $k_0 + k_1[H^+]$.

The observed rate becomes —

$$k_{obs} = k_2[OH^-]$$

The reaction is base catalysed.

* At intermediate pH, the concentration of H^+ and OH^- are low.

The observed rate is —

$$k_{obs} = k_0$$

The rxn is said to be solvent catalysed.

2 - General acid - base catalysis -

A rxn in which undissociated acid or base produce catalytic effect on the rxn are

known as general acid - base catalyst.

Ex - 1 → Pharmaceutical formulation used buffers for maintaining the pH of the soln.

→ One or more components of the buffer catalyse the rate of rxn.

→ If the catalytic component is acidic, the rxn is said to be general acid catalysed.

→ If the catalytic component is basic, the rxn is said to be general base catalysed.

Influence of dielectric constant on rate of reaction

* The dielectric constant (ϵ_{∞}) of the solvent has effect on rate of rxn.

* It is given by equation

$$\ln k = \ln k_{\epsilon=\infty} - \frac{N z_A z_B e^2}{R T \epsilon^*} \cdot \frac{1}{\epsilon}$$

$$\int k = \int_{\epsilon=\infty} k - \frac{N z_A z_B e^2}{R T \epsilon^*} \cdot \frac{1}{\epsilon}$$

where $\rightarrow$

k = observed rxn rate in a solvent.

$k_{\epsilon=\infty}$ = rxn rate constant of a solvent of infinite dielectric constant.

N = Avogadro's number.

z_A and z_B = charges on ionic species.

e = Unit of electric charge.

ϵ^* = Distance b/w ionic species

ϵ = Dielectric constant of the solvent.

* Rxn involving ions of opposite charge are accelerated by ~~solvent~~ low dielectric constant.

* In rxns having similarly charged species the rate of rxn is $\uparrow$ ed by high dielectric constant solvent.

* Rxn b/w neutral molecules enhance / $\uparrow$ ed by high dielectric constant

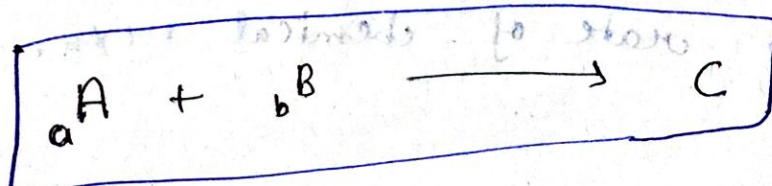


Rate of rxn

- * The rate is defined as the velocity with which a reactant or reactants undergo chemical change.
- * It can therefore be measured by measuring the change in the concentration of a reactant or product in a particular period of time.
- * It is given by $\pm \frac{dc}{dt}$

Rate constant :-

According to law of mass action, the rate of a chemical rxn is proportional to the product of molar concentration of reactants raised to a power equal to the number of molecules a and b of the substance A and B.



Rate of rxn is given by —

$$\text{Rate} = -\frac{1}{a} \frac{dA}{dt}$$

$$\text{Rate} = -\frac{1}{b} \frac{dB}{dt}$$

$$\text{Rate} = k[A]^a[B]^b$$

In this small k is rate constant.

Order of reaction →

The order of rxn is

the sum of the power of the concentration involved in the rate equation.

* The order of above rxn is $(a+b)$.

* ✓ The order of rxn refers to the way in which the concentration of reactant or reactants influence the rate of chemical rxn.

1- Zero order rxn - Plot shows (axis) 0

If the rate of a rxn is independent of the concentration of reacting species, the rxn is said to be zero order rxn.

The rate of zero order rxn is given by —



$$-\frac{dA}{dt} = k$$

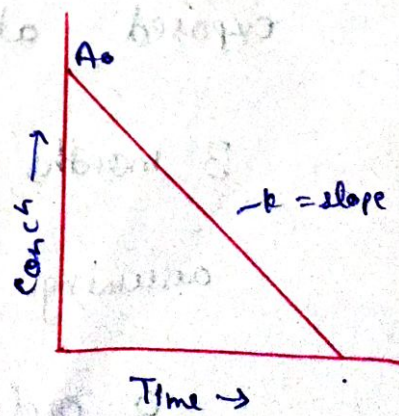
* dA is the change in concentration with respect to change in time.

* $(-)$ indicates the concentration after time interval (t) .

$$\int_0^t dA = -k \int_0^t dt$$

$$A_t - A_0 = -kt$$

$$A_t = A_0 - kt$$



0 (zero) order half life

Half life ($t_{1/2}$) of a chemical rxn is the time required for the initial concentration of the reactant to get reduced to half.

$$A_t = \frac{1}{2} A_0$$

Substituting —

$$A_t = A_0 - kt$$

$$\frac{1}{2} A_0 = A_0 - kt_{1/2}$$

$$kt_{1/2} = \frac{A_0}{2}$$

$$t_{1/2} = \frac{1}{2} \frac{A_0}{k}$$

Q.11

The colour intensity of a drug preparation

exposed at 45°C fell from 1.920 — 1.400 in

3 months. estimate the react rate.

assuming that the colour fading follows

0 order rxn.

Ans $\rightarrow$

$$1.900 = 1.920 - k \times 90$$

$$90k = 0.020$$

$$k = 0.0002$$

2- First order rxn $\rightarrow$

When the rate of rxn is directly proportional to the first power of the concentration of a single reactant, the rxn is said to be first order rxn.



The rate of rxn is first order.

$$\frac{-dc}{dt} = kc$$

$$\frac{dc}{c} = -kdt$$

Integratⁿ of equatⁿ

$$\int_0^t \frac{dc}{C} = -k \int_0^t dt$$

$$\ln C - \ln C_0 = -kt$$

$$\boxed{\ln C = \ln C_0 - kt}$$

log form —

$$\log C = \log C_0 - kt / 2.303$$

$$\boxed{k = \frac{2.303}{t} \log \frac{C_0}{C}}$$

Exponential form —

$$\boxed{C = C_0 e^{-kt}}$$

First order half life

Definitly same as 0 order —

$$t_{1/2} = \frac{C_0}{k}$$

$$t = \frac{2.303}{k} \log \frac{C_0}{C}$$

$$t = \frac{2.303}{k} \log \frac{C_0}{\frac{1}{2}C_0}$$

$$t_{1/2} = \frac{0.693}{k}$$

Q-1 $\rightarrow$ A solⁿ of drug contain 680 units/ml when prepared. It was analysed after a period of 60 days and was found to contain 400 units/ml. Assuming that the composition is first order, at what time will the drug have decomposed to $\frac{1}{2}$ of its original concentration.

Ans $\rightarrow$

$$60 = \frac{2.303}{k} \log \frac{680}{400}$$

$$k = 4.66 \times 10^{-2} \text{ day}^{-1}$$

$$t_{1/2} = \frac{0.693}{k} = 14.8 \text{ days}$$

Ans: 14.8 days

3- Second order rxn -

A reaction is said

to be second order, when the overall order is two.

* The rate of second order rxn may be proportional to the product of two concentrations.

* Example are -



→ This is second order in the reactant NO_2 and zero order in the reactant CO .

→ The observed rate is independent of concentration of CO .

→ The rate of rxn is proportional to concentration squared.

Photolytic D. →

Decomposition of drug substance by light is called as photodegradation. Light energy catalyzes or initiates some rxn.

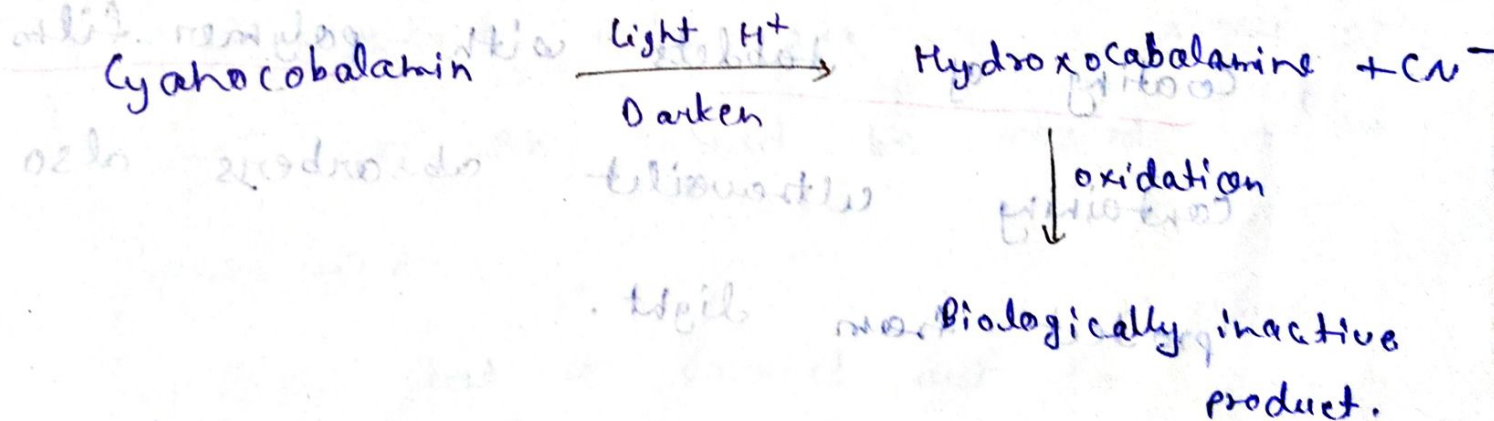
Photolytic degradation

* Many pharmaceutical compounds including ascorbic acid, cyanocobalamine, riboflavin, folic acid, hydrocortisone, prednisone etc. undergo degradation

when it exposure to light.

* Exposure to light may produce oxidation and reduction, ring arrangement, malification and polymerization.

Ex-1:



* Photochemical rxn may be accompanied by thermal rxn.

* The thermal rxn once induced by light may continue after the light source has been

withdrawn.

* prevention -

It can be reduced by

using amber coloured glass container.

- By using black thermo setting plastic it

can also be reduced.

- By storing product in dark place or

by packing in cartons also act as

barrier to light.

- Coating of tablets with polymer films

containing ultraviolet absorbers also

protect from light.

- Ordinary containers can be wrapped with black paper also provide protection against light.

Accelerated stability testing in expiration dating

1- Accelerated stability testing -

Stability is defined as the time during which the drug product retains the same properties existing at the time of manufacture.

* Accelerated stability test is designed to test stability and predict shelf life of formulations under normal or recommended storage conditions.

* The study is carried out under accelerated conditions of temp., moisture and light.

* The products which are to be stored at 25°C and 45% Rh should be stored at 40°C and 60% Rh.

* Similarly test is carried out for product to be stored cool and cold temperature.

Common high stress conditions are —

(i) Temperature → ↑ in temperature increase degradation.

(ii) Humidity → High humidity results in hydrolysis.

(iii) Light → Artificial light can be used to accelerate the effect of sun light.

2- Self life

It is defined as the time required for the conc. of the reactant to reduce 90% of its original/initial conc.

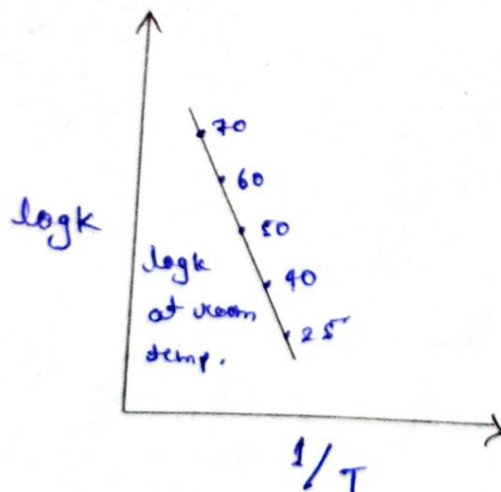
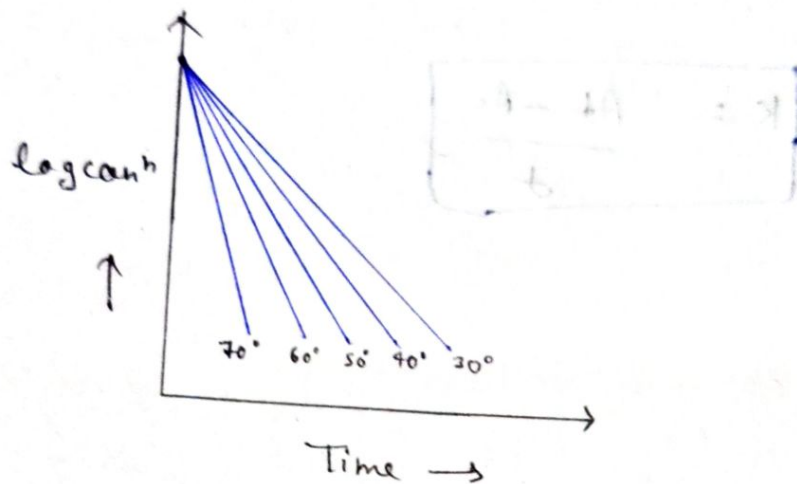
* The various steps for self life are as follows —

→ Each portion is stored at different temp. such as 40°C, 50°C, 60°C, 70°C.

→ Samples from each portion are withdrawn at various interval of time.

→ The order of reaction is determined by plotting $\log a/(a-x)$ versus time graph.

→ The slope of line gives the rate constant 'k' for degradation at each temperature.



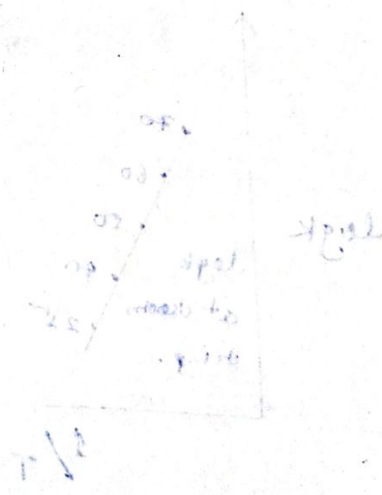
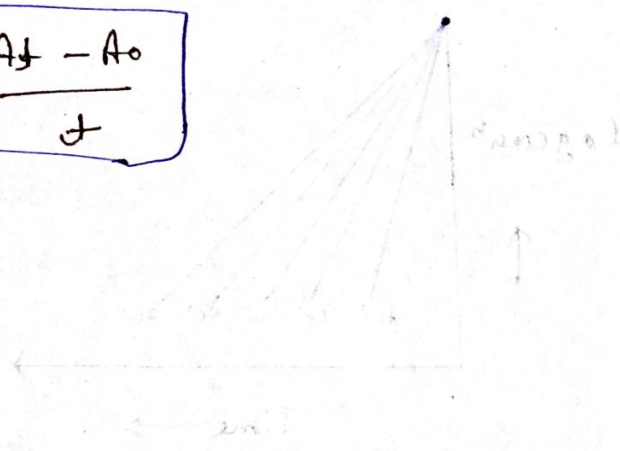
→ From Arrhenius equations, the rate constant 'k' for degradation at room temp (25°C) is determined.

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

* The value of 'k' at 25°C is substituted in appropriate rate equation and estimate for self life of the product is obtained.

$$k = \frac{2.303}{t} \log \left(\frac{C_0}{C} \right)^{1/n}$$

$$k = \frac{A_t - A_0}{t}$$



From the above graph, the value of k can be determined at 25°C.