CHEMICAL KINETICS AND STABILITY

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CHEMICAL KINETICS AND STABILITY

All the drug changed with time in concentration and other physical properties.

- Physical factors such as temperature, light and humidity influence chemical stability of drugs.
- The stability of drug product with time is important in determination of shelf life and expired date.
- For example, **thiamine hydrochloride** is **most stable at a pH of 2 to 3** and is **unstable** above pH 6, so in preparation, the pharmacist should select the buffered vehicle that prevents the degradation.

RATES, ORDER, AND MOLECULARITY OF REACTIONS

- Molecularity is the number of molecules, atoms, or ions reacting in an elementary process. molecularity classify the reaction into :

- Unimolecular

- bimolecular

- Termolecular.

- molecularity cannot gives complete detail about order of reaction specially those of several steps while kinetic study gives details.

- **Example:**

- $Br_2 \longrightarrow 2Br$ ....unimolecular

- $H_2 + I_2 \longrightarrow 2HI$ ....bimolecular

- $2NO + O_2 \longrightarrow 2NO_2$ ....Termolecular

SPECIFIC RATE CONSTANT

- The rate limiting step is the lowest step in the reaction.

- The half-life is the time required for one-half of the material to disappear; the time at which C has decreased to ½ C.

- The shelf-life is the time required for 10% of the material to disappear; it is the time at which C has decreased to 90% of its original concentration (i.e., 0.9C).

KINETIC STUDY

- Zero-Order Reactions: Garrett found that the loss in color of a multisulfa product followed a zero-order rate.
- The rate expression for the change of concentration, C, with time is therefore

(dc/dt = k0)

<u>It means that the rate of reaction not depend on concentration of reactant, it is constant with time.</u>

KINETIC STUDY

- First-Order Reactions: Harried showed that the decomposition rate of hydrogen peroxide catalyzed by 0.02 M KI was proportional to the concentration of hydrogen peroxide remaining in the reaction mixture at any time.
- The data for the reaction 2H202 = 2H2O + O2 Although two molecules of hydrogen peroxide appear in the equation, the reaction was found to be first order.
- The rate equation is written $(-\, dc/dt = k\, C)$
- where C is the concentration of hydrogen peroxide remaining undecomposed at time t and k is the first order rate constant.

KINETIC STUDY

Second-Order Reactions

• The rates of bimolecular reactions, which occur when two molecules come together, are frequently

described by the second-order equation.

• A + B Products When the speed of the reaction depends on the concentrations of A and B with each term raised to the first power, the rate of decomposition of A is equal to the rate of decomposition of B, and both are proportional to the product of the concentrations of the reactants:

$$-\ d[A]/dt = -\ d[B]/dt = K\ [A][B]$$

DETERMINATION OF ORDER

- The order of a reaction can be determined by several methods.

1. Substitution Method.
2. Graphic Method.
3. Half-Life Method

FACTORS EFFECTS ON STABILITY

A number of factors other than concentration may affect the reaction velocity like:

- Temperature
- Solvents
- Catalysts
- Light

TEMPERATURE EFFECT

- Collision Theory Reaction rates are expected to be proportional to the number of collisions per unit time.

- Because the number of collisions increases as the temperature increases, the reaction rate is expected to increase with increasing temperature.

OTHER FACTORS

- <u>Effect of the Solvent</u>

In summary, it can be said that the polarity of solvents affect the rate of reactions depending on the polarity of reactant.

- <u>Effect of the ionic strength</u>

- ionic compound

- neutral molecule.

- <u>Effect of the Dielectric Constant</u>

For a reaction between ions of opposite sign, an increase in dielectric constant of the solvent results in a decrease in the rate constant.

ACCELERATED STABILITY TESTING

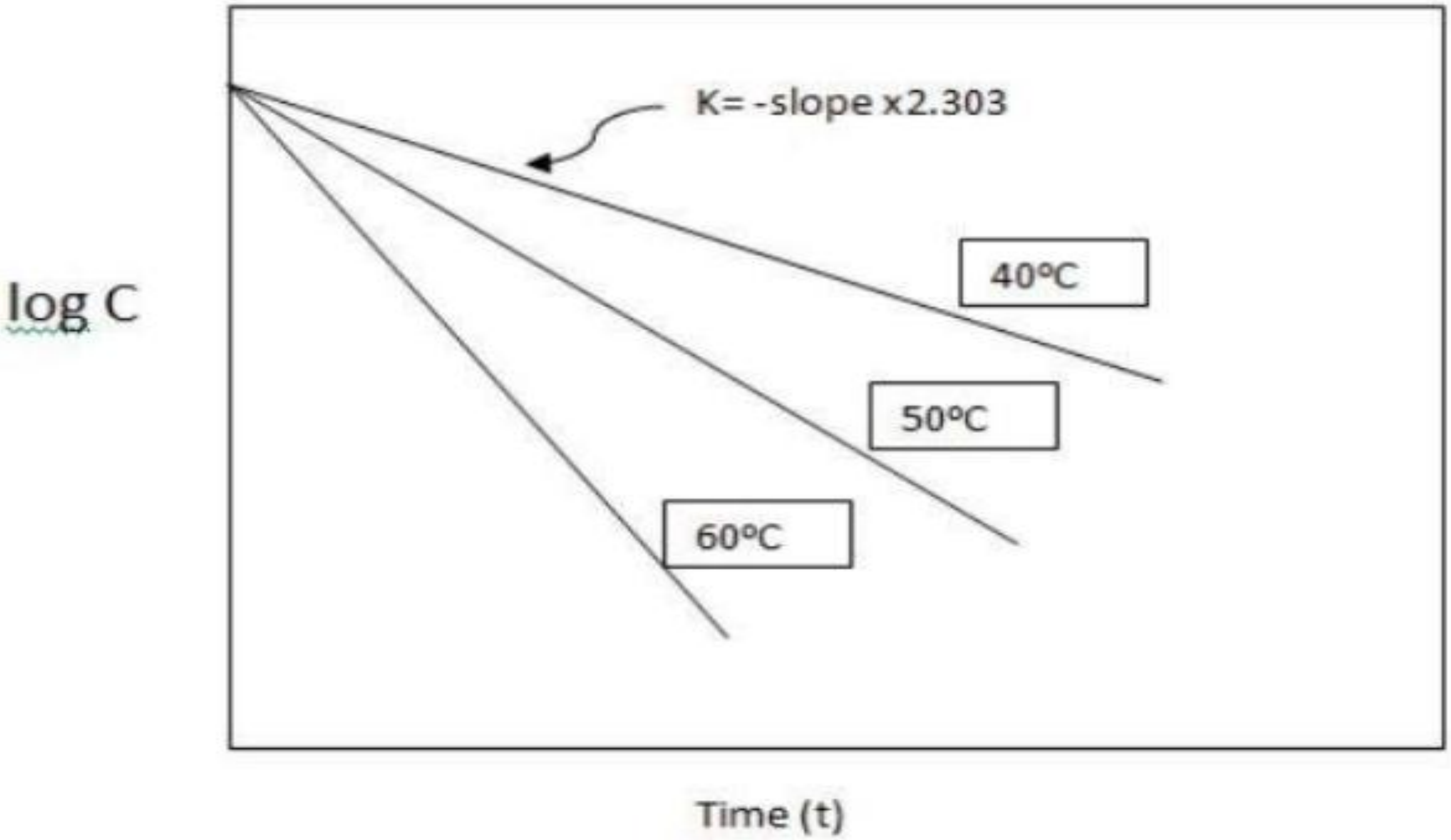
- A design to increase the rate of chemical degradation and physical change of a drug by using exaggerated storage conditions as part of the formal stability testing program.

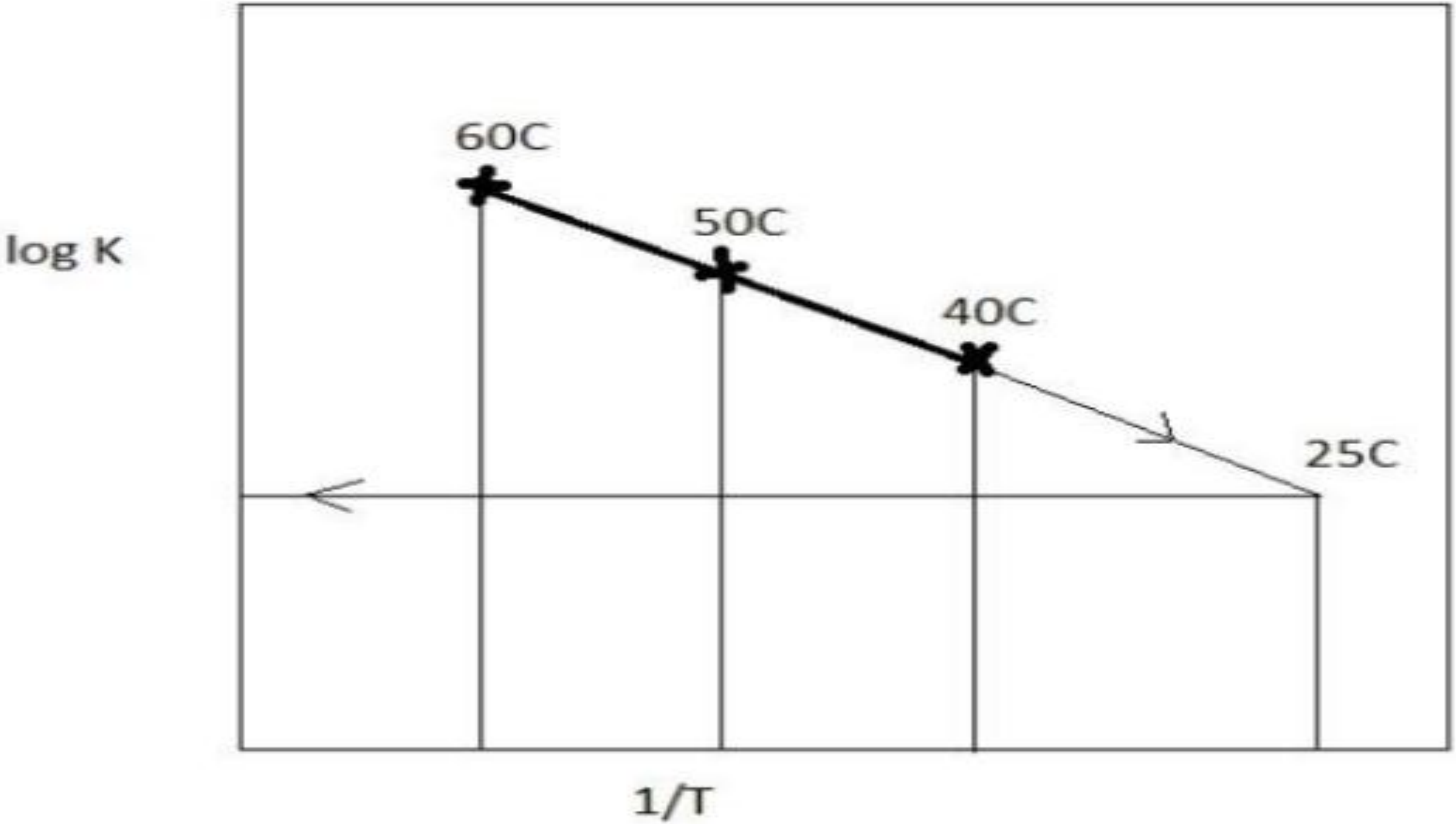
- The drug stored at 40°C, 50°C and 60°C then the <u>logarithm of rate constants (k) at various temperatures are plotted against reciprocal of absolute temperature and the resulting line extrapolated to the room temperature to get K25°C.</u>

SHELF LIFE DETERMINATION

- The shelf life t90% can be calculated from previous process by plotting the following equation:

t90% = 0.105/ K25°C


K= -slope x2.303
40ºC
50ºC
60ºC
log C
Time (t)



log K
60C
50C
40C
25C
1/T


Thank You!