Practice 34.1.

Stability Test of Aspirin

A. Materials

Aspirin		9 g
Sodium citrate		27 g
Distilled water	q.s	500 ml

a) Prepare the solution given above and measure its pH. Take 50 ml of this solution and place each 50 ml in 4 bottles or flasks.

b) Label the bottles containing the prepared solution, place the bottles in the room temperature, 37˚C, 45˚C and 60˚C water baths or heat cabinets. Start the timer. Record by measuring the room temperature.

c) Immediately determine the quantitative amount of aspirin in the solution that you will store at room temperature, accept this amount as 100%.

d) At 30th, 60th, 90th, 120th and 180th minutes, take samples from the solutions kept at four different temperatures and titrate with 0.1 N NaOH solution, and thereafter determine the quantitative amount of aspirin.

B. Methods

Add 2-3 drops of phenolphthalein indicator to 10 ml of aspirin solution and titrate with 0.1N NaOH. Color change should remain constant for 1 minute.

$$\text{Active substance concentration non-degraded} = \frac{(2A-B)}{A} \times 100$$

A = 0.1 N NaOH amount (ml) spent while aspirin is 100% in the medium, prior to the onset of hydrolysis. (The amount spent when aspirin is fully hydrolyzed is 2A ml 0.1 N NaOH.)

B = The amount of 0.1N NaOH neutralizing the hydrolysed and non-hydrolyzed aspirin in the sample after a certain time.

After a certain time, the amount of aspirin remaining in the medium without hydrolysis corresponds to (2A - B) ml 0.1 N NaOH. For each temperature, show the results by making a table as below.

C. Evaluation of results

Table 34.1.

Time (min, t) (**x**)	0.1 N NaOH (B ml)	Active substance % concentration (C) non-degraded	ln C (**y**)

Use the values in Table 34.1 and graph by plotting the time (t) values as the independent variable (x) and the ln concentration values as the dependent variable (y). Calculate the values of m (slope), n (intersection) and r^2 (coefficient of determination). As four different temperatures are used, four different lines are obtained.

1. The equation of these reaction lines that fits to 1st degree kinetics;
   ln C = ln Co - kt
   k = Reaction rate constant ($time^{-1}$)
   Co = Initial active substance concentration

According to this equation, calculate the reaction rate constant (k) at that temperature from the slope of the line obtained for each temperature (T) and prepare Table 34.2.

Table 34.2.

Temperature (˚C)	Temperature (°K)	1 / T **x**	slope (k) $time^{-1}$	(ln k) **y**

Use the values in Table 34.2 and graph by plotting the time 1/T values as the independent variable (x) and the ln k values as the dependent variable (y). Calculate the values of m (slope), n (intersection) and r^2 (coefficient of determination).

The relationship between the reaction rate and temperature is defined by the Arrhenius equation;

ln k = ln S - (Ea / R) x (1 / T)

S = Frequency factor (frequency of collisions of molecules)

Ea = Activation energy ($kcal.mol^{-1}$)

R = Gas constant (1.987 $cal.mol^{-1}.degree^{-1}$)

T = Temperature (Kelvin)

Calculate the activation energy (Ea) from the slope of the line you calculated according to Table 34.2, and the frequency factor that gives the frequency of collision of the molecules from the intersection value.

Interpretation of results;

Since reactions with an activation energy of less than 10 kcal.mol^{-1} will occur easily, the solution will degrade more quickly at room temperature. Since reactions with an activation energy of higher than 30 kcal.mol^{-1} will ocur harder the solution is stable at room temperature. Based on this information, please comment on the stability of your solution.

Questions:

1. Calculate the molarity and normality of the aspirin solution you have prepared and indicate its importance for the experiment. Explain the difference of NaOH consumption when there is complete hydrolysis and no hydrolysis.

2. Write the equation of the hydrolysis reaction of aspirin in clear formulas. Explain the difference of NaOH consumption when there is complete hydrolysis and no hydrolysis.

3. Describe the relationship between aspirin hydrolysis and pH of the medium.

4. In the room temperature, calculate the elapsed time for 10% degradation of the active substance in the solution, according to the k value you find. According to this comment on the stability of the solution.

5. Interpret in which dosage forms and which cases accelerated stability tests are made,