Hydrolysis of Acetyl Salicylic Acid Solution in Sorenson Phosphate Buffer at pH 8

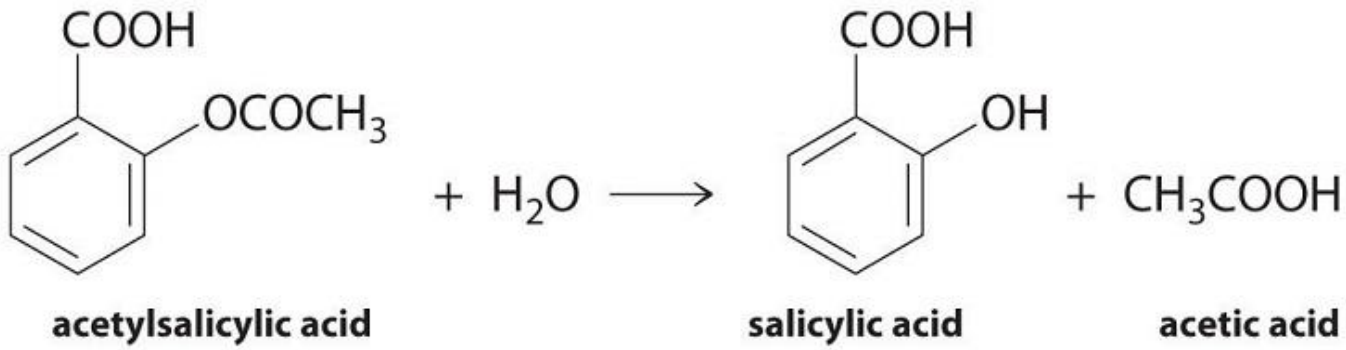
BIOPHARMACEUTICS

What is in?

- Why to study ?
- How to study ?

Introduction

- Aspirin is a weak acid .it is soluble at 20 C° in 300 parts of water .
- It is unstable in aqueous solutions degrading to salicylic acid and acetic acid



- Aspirin also degrades in solid dosage forms when exposed to moisture and therefore , should be stored in tightly closed containers and kept in a dry environment .

Aim of Experiment

- To study the effect of temperature on the hydrolysis of aspirin, and to calculate the shelf life of aspirin .

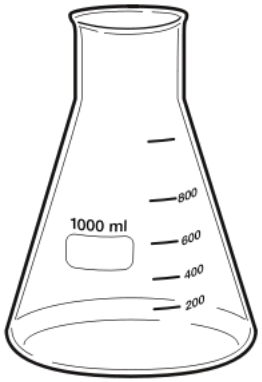
- **Shelf life** of any drug :it is the **time** required for the drug to **LOSE** 10% of its effectiveness


MAERSK
MAERSK
MAERSK
SPICA

How to work

ASA

250 ml



200 ml

Procedure :

- 1. Dissolve 0.695 g of aspirin in 250 ml of phosphate buffer (use a volumetric flask)

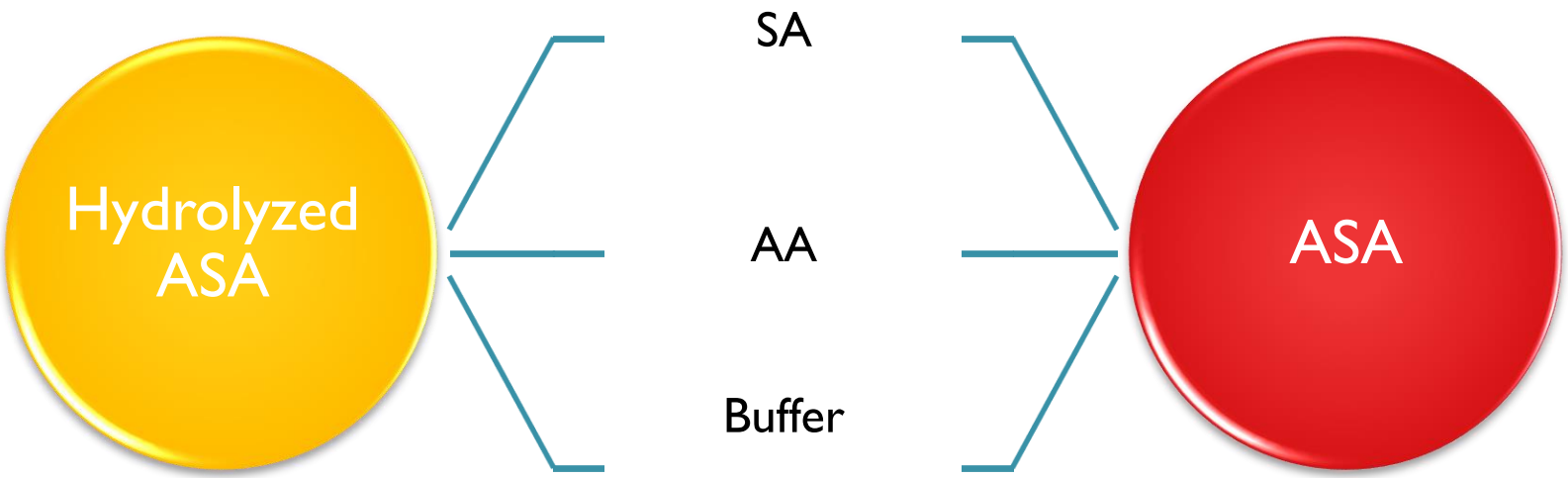
- 2. place 200 ml of this solution in an erlenmeyer flask , then keep the flask in a water bath for (30 min) at required temperature. the temperature that will be used are(40, 60, 80 ℃)

- Withdraw (5 ml) sample at the end of 30 mins , then continue withdrawing (5 ml) sample at 15 min interval for 90 min.

What to do with the sample ???

What is the sample ?

- Sample contains Aspirin


Hydrolyzed ASA
SA
AA
Buffer
ASA

Notes:

- absorbance increases with time
- Concentration of S.A at zero time is **ZERO** since ASA is not hydrolyzed yet , however , the initial concentration of ASA is 2.78 mg/ml ??

ASA initial conc. Is 2.78 mg/ml?

- We dissolved 0.695 **g** of Aspirin in 250 ml

Therefore :

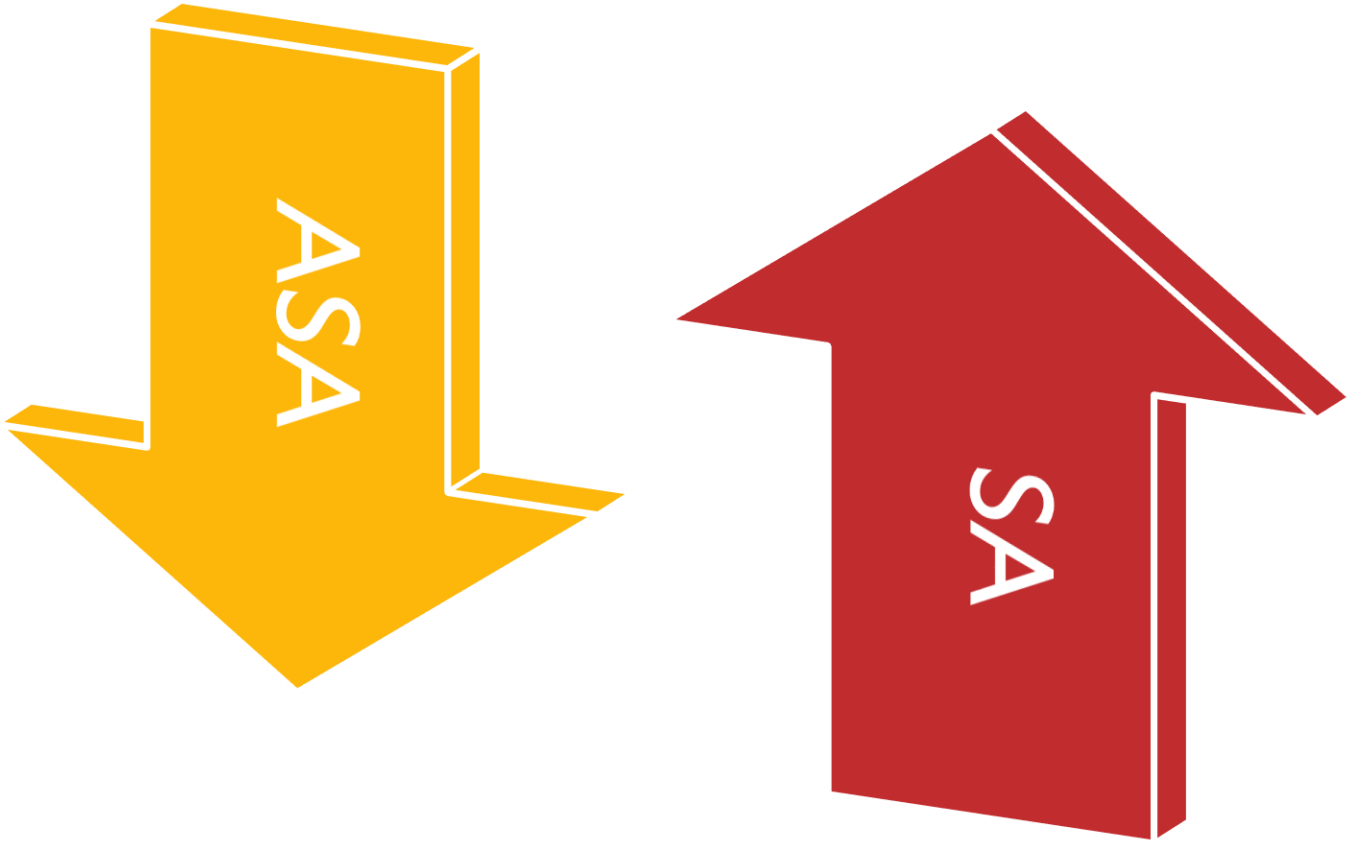
$\frac{0.695\ gram}{250\ ml}$ = 0.00278 gram per ml

Since 1 gm = 1000 mg

So :

0.00278 * 1000 = 2.78 mg / ml

Concept



Sorenson phosphate buffer (pH 8)

Consist of two solutions

A-1/15 M Monopotasium phosphate KH_2PO_4

B- 1/15 M Disodium phosphate $Na_2HPO_4.2H_2O$

- The rate of ASA hydrolysis follows First Order reaction

How to calculate ?

- Use the calibration curve equation
- Y= C + b*X

We are seeking ASA not SA

Since each MOLE of aspirin give 1 mole of salicylic acid and 1 mole of acetic acid

$$\text{Mole} = \frac{Wt}{M\,Wt}$$

MWT OF ASP.=180
MWT OF S.A = 138

Therefore

$$\frac{wt\ of\ SA}{M\ wt} = \frac{Wt\ of\ ASA}{M\ wt}$$

Conc. S.A in mg/ml from calib. curve equation

So : 0.35 (from the example) * 180 =X * 138

X= 0.456 ≈ 0.46 → Conc. Of ASP. Degrade

- Calculate remaining ASA from

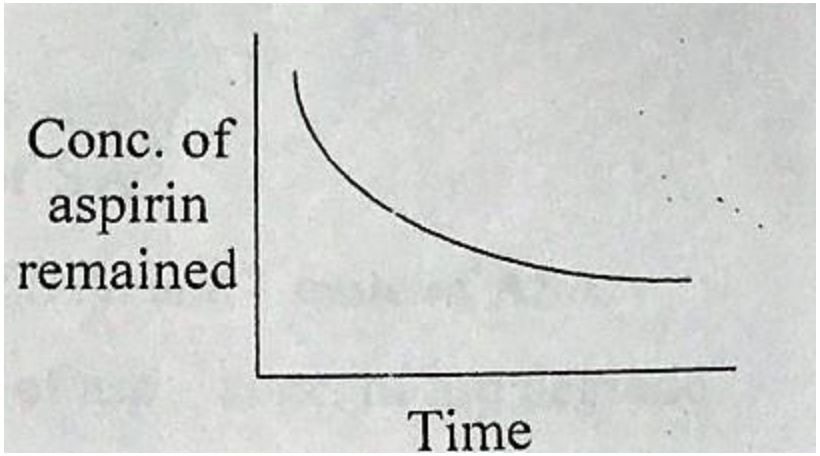
Initial conc. Of ASA – conc. Of ASA degraded

2.78 – 0.46 = 2.38

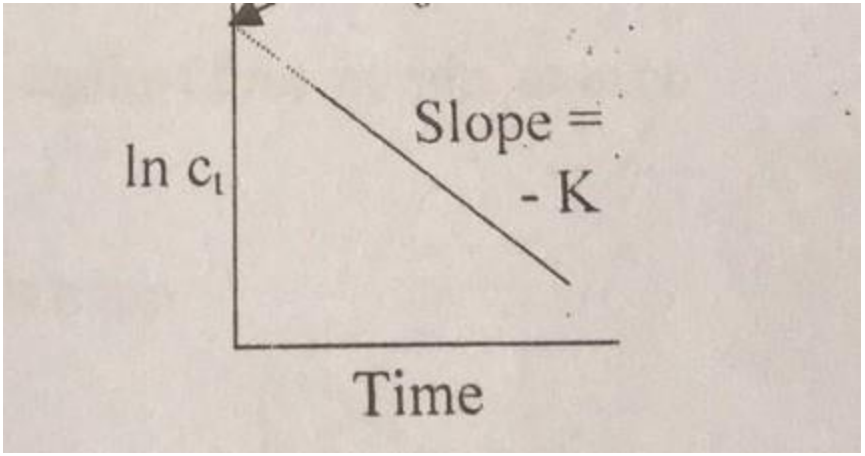
Time	Absorbance	Conc. of S. A	Conc. of aspirin hydrolyzed	Conc. Of aspirin remined (ct)	Log ct
0	0	0	0	2.78	
30		Y= c + bx	X *180/138	2.78 - Ct	
45					
60					
75					
90					

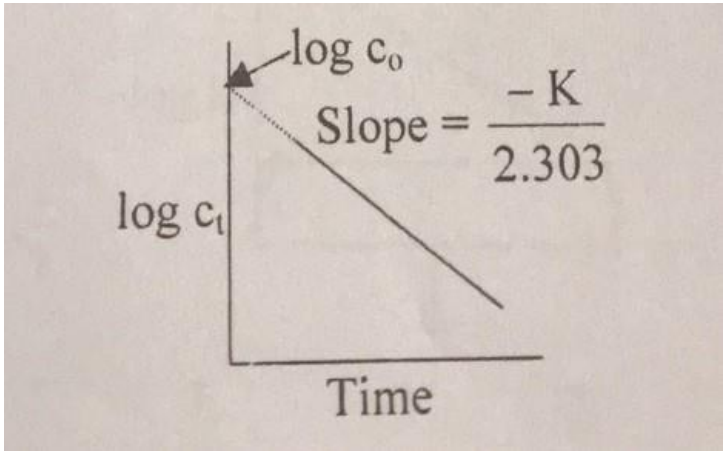
First order Kinetics

- $\frac{dc}{dt} \propto C$
- $-\frac{dc}{dt} \propto C$ (since conc. Of aspirin decrease with time as hydrolyzed)
- $-\frac{dc}{dt} = KC$



- $\int_{c0}^{ct} \frac{dc}{c} = -k \int_{0}^{t} dt$
- $-(\ln Ct - \ln Co) = kt(t-0)$
- $\ln Ct - \ln Co = -kt$
- $\ln Ct = \ln Co - kt$
- Since $\ln = \log \times 2.303$
- $\log Ct * 2.303 = \log Co * 2.303 - kt$
- $\log Ct = \log Co - kt/2.303$





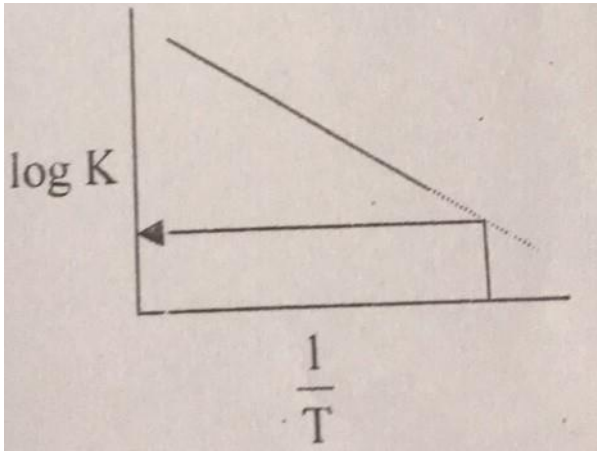
What to do with data ?

1. take the Log, or Ln for each calculated conc.

2. Plot the log/ ln of conc. against time in min for each temp.
   - You will have 3 plots

3. calculate K for each temp.

4. take log K and plot $1/T$
   - (draw Arrhenius plot) to find K at 25 °C



- Arrhenius equation :
- Log K= log A - $(Ea)/(2.303\ R)$ *1/T
- Where A= frequency factor ,Ea = energy of activation ,T= absolute temp.(temp. +273)
- R= gas constant .
- **t10%= 0.105/ $K_{25℃}$**

Repot to have done according to this results

1- calculate K for each temp.

2- calculate Aspirin shelf life

The results for ASA hydrolysis in pH 8 was as the follow

Time in min	Absorbance at 40 C	Absorbance at 60 C	Absorbance at 80 C
0	0	0	0
30	0.095	0.125	0.33
45	0.118	0.2	0.5
60	0.15	0.27	0.64
75	0.2	0.31	0.76
90	0.23	0.4	0.76

Knowing that the calibration curve was $y = x + 0.0897$

Note: the calibration curve was in mg/ml


thank
you!