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STUDY OF HYDROLYSIS OF ACETYLSALICYLIC ACID

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Abstract

Acetylsalicylic acid is one of the most widely used therapeutic substances duet o its analgesic, antipyretic and anti-inflommatory properties. Acetylsalicylic acid decomposes rapidly in aqueous solutions. The acetylsalicylic acid hydrolysis reaction is a first order reaction, proven by the value of the reaction velocity constant relatively constant. In this experience it is observed that the acetylsalicylic acid hydrolysis reaction is faster at acid pH and at 60 ° C.

Key words: Acetylsalycilic acid, hydrolysis, pH

INTRODUCTION

Aspirin (acetylsalicylic acid, ASA) is one of the most widely used therapeutic substances duet o its analgesic, antipyretic and anti-inflommatory properties. Despite the proliferation in development of new non-steroidal antiinflammatory drugs (NSAIDs), ASA remains one of the most effective over-the counter drugs in the tratment of rheumatic diseases. Furthermore, duet o its anti-thrombotic prppertie, ASA is noe prescribed at low doses in the prevention and treatment of cardiovascular diseases, stokes and disorders associated with platelet aggregability.Acetylsalicylic acid decomposes rapidly in solutions of ammonium acetate or of the acetates, carbonates, citrates, phosphates or hydroxides of the alkali metals. Acetylsalicylic acid is stable in dry air, but gradually hydrolyses in contact with moisture to acetic and salicylic acids. In solution with alkalis, the hydrolysis proceeds rapidly and the clear solutions formed may consist entirely of acetate and salicylate. The principal cause of the hydrolysis of this family of the salicylic acid acyl esters (e.g. aspirin), in aqueous solution about pH 3, is the attack of these substances by water ions ($H3O^+$or HO^-)(Du, Hoag., 2000; Fersht, Kirby, 1967; Bender, 1960; Diaba et al, 2015)

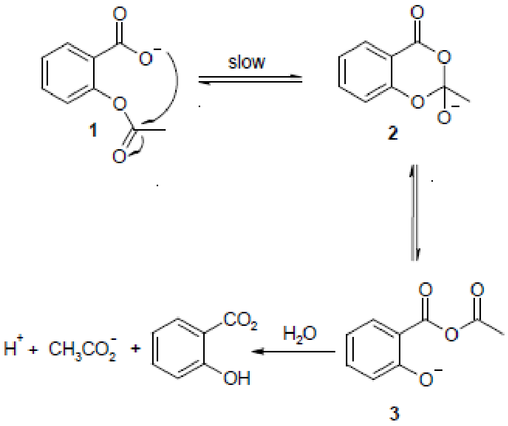

Figure 1. Mechanism of hydrolysis acetilsalicylic acid

Since Edwards has shown that the rate of hydrolysis of aspirin is independent of pH between pH 4 and 8, the reaction has been the subject of a number of studies, particularly by Garrett [1,3-5]. Edwards suggested that in this pH range, the hydrolysis reaction resulting from the attack by a water molecule on the anion of aspirin (Scheme 1), but several authors have pointed out that this mechanism is not consistent with Edwards' own demonstration, showing that the hydrolysis reaction is not catalyzed by acetate ion, a considerably more powerful nucleophile than water.

In this paper we present the results of the study of hydrolysis of acetylsalicylic acid at different values of the pH of the environment and temperature.

MATERIAL AND METHOD

Aspirin (acetylsalicylic acid), salicylic acid (2-hydroxybenzoic acid) were purchased from Merck. Other chemicals and reagents (NaH_2PO_4, Na_2HPO_4, Ethanol) were of analytical grade.

The spectrophotometric determinations of the salicylic acid content were performed with an ANALYTIC JENASPECORD Plus 210 spectrophotometer.

Preparation of solutions

a. *Preparation of acetyl salicylic acid solution*: exactly 0,200 g of acetylsalicylic acid are weighed and dissolved in 10 ml ethyl alcohol in a volumetric flask. 5 ml of this solution are diluted with 25 ml buffer in a flask. The concentration of this solution is 3.036 mg acetylsalicylic acid / ml solution = 0.022 moles / ml.
b. *Preparation of salicylic acid standard solutions*: weigh exactly 0.0525 g of salicylic acid and dissolve with ethanol in a 10 ml flask.

This is the stock solution. By successive dilutions standard solutions are prepared – 5,25; 2,62; 0,786; 0,0786; 0,0393; 0,00395; 0,00177 mg/ml .

Procedure

a. For the determination of the calibration curve of the salicylic acid content, the absorbance at the 300 nm wavelength is measured for each calibration solution (salicylic acid).
b. Acetylsalicylic acid solutions prepared in different pH buffers are introduced into the thermostated water bath at different temperatures and stored for 200 minutes. At some time, 4 ml of solution is extracted, placed in the spectrophotometer cuvette and the absorbance measured at 300 nm.

RESULTS AND DISCUSSION

In Table 1 are the results obtained in measuring the absorbance of standard solutions of salicylic acid. The calibration curve is shown in Fig.1.

Table 1

The variation in the absorbance of salicylic acid solutions with the concentration

Absorbance	0,0323	0,0856	0,2125	0,2778	0,8033	1,9473	3,3758
Concentration (mg/ml)	0,00177	0,00395	0,0393	0,0786	0,786	2,62	5,25

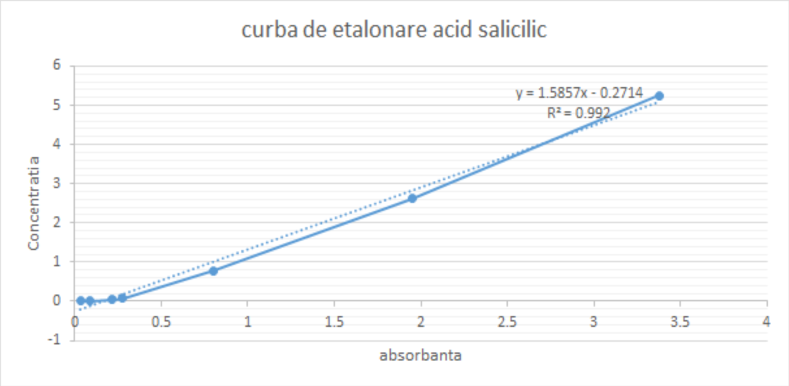

Fig. 1. The calibration curve of the salicylic acid content

A curve which shows the linear dependence of the absorbance with the concentration is obtained, obtaining a straight line with the correlation coefficient $R^2 = 0.992$. The equation of the straight line is:

C = 1,5857 x A – 0,2714where: C - concentration
A - absorbance

The hydrolysis reaction study was performed at 40 ° C and 60 ° C in neutral pH 7 and in mildly acid pH 5. The results are shown in Tables 2 and 3.

Table 2

Time variation of concentration at 40 ° C

	40°C pH5			40°C pH7		
time	absorbance	conc ac. Salicilci (mg/ml)	Aspirineconc (mg/ml)	absorbance	Salicilic ac. conc (mg/ml)	Aspirineconc (mg/ml)
0	0.6484	0.5801	2.2793	0.6484	0.5801	2,2793
50	2.91290	2.0081	0,4167	2.73630	1.8968	0,5619
100	2.97220	2.0455	0,3679	2.79750	1.9354	0,5115
150	3.01050	2.0697	0.3364	2.80870	1.9424	0.5024
200	3.03270	2.0837	0.3181	2.91140	2.0072	0.4179

Table 3

Time variation of concentration at 60°C

	60°C pH5			60°C pH7		
time	absorbance	Ac. Salicilic conc. (mg/ml)	Aspirineconc (mg/ml)	absorbance	Ac. Salicilicconc (mg/ml)	Aspirine conc. (mg/ml)
0	0.6484	0.5801	2,2793	0.6484	0.5801	2,2793
50	2.93410	2.0215	0,3992	2.81320	1.9453	0,4986
100	2.9903	2.0569	0,3531	2.8626	1.9764	0,4581
150	3.0355	2.0855	0,3158	2.9014	2.0009	0,4261
200	3.0611	2.1016	0,2947	2.9118	2.0074	0,4176

There is a decrease in the concentration of acetylsalicylic acid and the increase in salicylic acid over time, especially during the first 50 minutes. Figures 2 and 3 show the variation of salicylic acid concentration over time at 40 ° C and 60 ° C.

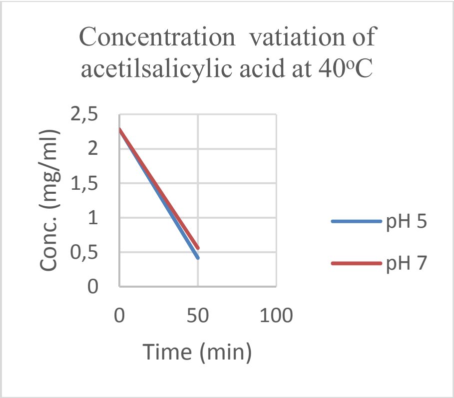

Fig. 2. Variation of acetilsalicylic concentration at 40°C

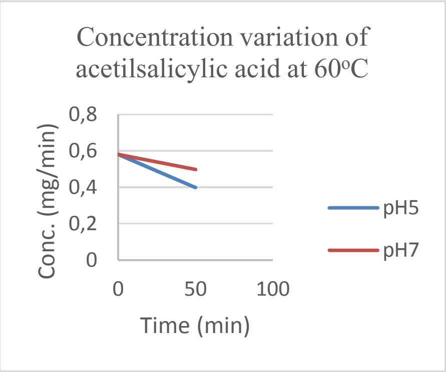

Fig. 3. Variation of acetilsalicylic concentration at 60°C

The reaction rate is defined as the variation in the amount of substance in the unit of time, usually reported at the volume of the system. If the volume is constant, the amount of substance (number of moles) per volume is the molar concentration (ci), the reaction rate in relation to the substance can be written:

Factors influencing the reaction rate are very numerous: substance concentrations, temperature, pressure, solvent, presence of catalytic, inhibitory substances, etc. The speed law for a chemical reaction highlights the influence of the concentration on the reaction rate. The velocity constant k is independent of the concentrations, it does not depend on time for simple reactions but depends on all other factors that influence the reaction rate, eg temperature, catalysts, etc. For a 1st order reaction, the speed constant is calculated with:

$\lg\frac{c}{c_i} = k\,t$ where: c - concentration at t time

c_i - initial concentration
k - velocity constant
t - time

The results obtained for the studied reaction are presented in table no 4:

Table 4

The results obtained: k, pH, T

Condition	pH5, temp 40°C	pH 7, temp 40°C	pH 5, temp 60°C	pH 7, temp 60°C
k	0,0136	0,132	0,0131	0,0132

From the analysis of the data obtained, it is observed that in all experiments comparable values of the velocity constant are obtained, which proves that the acetylsalicylic acid hydrolysis reaction is a first order reaction

CONCLUSIONS

The acetylsalicylic acid hydrolysis reaction is a first order reaction, proven by the value of the reaction velocity constant relatively constant (k=0.0132) at various temperatures or pH values.

From the analysis of the obtained experimental results it is observed that the acetylsalicylic acid hydrolysis reaction is faster at acid pH and at 60 ° C, the concentration of acetylsalicylic acid reaching 0.2947 mg / ml. The hydrolysis reaction at pH 7 is slightly influenced by temperature, the acetylsalicylic acid concentration reaching 0.4176 mg / ml (60 ° C) or 0.4179 mg / ml (40 ° C).

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