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Kinetic Study of Degradation of Tiaprofenic Acid by HPLC

RYMGUELMAMI CHAYEH*, M. BEN SALAH† and CHEMLI RACHID†
Institute of Higher Learning of the Studies in Biology and Geology of Sokra Tunis:
1, Rue Mohamed Bayrem V El Menzah V -Carnoy, Tunis 1004, Tunisia
E-mail: rymguelmami@yahoo.fr

The kinetic study of the decomposition of tiaprofenic acid in three different mediums: acid (2 N, HCl), basic (2 N, NaOH) and oxygenated H_2O_2 30 % by HPLC was carried out. To know the kinetics parameters of each degradation reaction and to calculate its speed, its partial order as well as the order of the reaction, the kinetics apparent constant and the time of half-reaction for each medium of degradation were calculated.

Key Words: Tiaprofenic acid, HPLC, Degradation, Kinetic.

INTRODUCTION

The stability of any molecule requires studying its kinetics initially, in fact the kinetics of degradation according to standards' established by the International Conference of Harmonization (ICH)[1,2] allows studying the reactivity of the active ingredient with respect to various mediums of stress. The study of this reactivity belongs to the study of stability of the molecule. The object of this paper is to study the decomposition of tiaprofenic acid under various conditions of stress and to know the kinetic parameters of each reaction of degradation by liquid chromatography high performance[3-6].

Tiaprofenic acid, (R,S)-2-(5-benzoyl-2-thienyl) propionic acid (Fig. 1) belongs to the family of antiinflammatory drugs not steroidien propionic derivatives[7]. This molecule has an action primarily antiinflammatory[8,9] antalgic and antipyretic and also antiagregant plate. Its principal mechanism of action is the inhibition of the cyclooxygenase and prostaglandins[10,11] which make it possible to have the feeling of pain during the ignition.

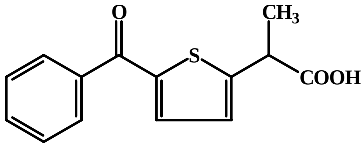

Fig. 1. Chemical structure of tiaprofenic acid

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†Département de Pharmacognosie, Faculté de Pharmacie de Monastir, Tunisia.

EXPERIMENTAL

Module HPLC is composed of a pump and of a UV-Visible detector Shimadzu, of an injector RH EODYNE 7125, a loop of injection of 20 µL, of a column C_{18} (SUPELCOSIL TM LC-18-DB) and of a pH meter SCHOTT CG 825. Tiaprofenic acid is gotten from AVENTIS TUNISIE. Octyl sulphates sodium from (LNCM). The acid, hydrogen peroxide, sulphate sodium and the sodium chloride are procured from PROLABO, France.

Chromatographic conditions: The mobile phase used is made up of 1 % of acetic acid-acetonitrile (60:40, v/v) with 0.05 mol/L of octyl sulphate of sodium (OSS) at pH = 4.5. The wavelength detection is fixed at 254 nm.

Degradation of tiaprofenic acid: 100 mg of the product is dissolves in 20 mL of ethanol and mixed with the solutions of HCl 2 N, NaOH 2 N and H_2O_2 30 % (v/v) until 100 mL, respectively then heat under backward flow during 12 h on takes 0.5 mL which have neutralizes with 0.5 mL, respectively NaOH 2 N, HCl 2 N to stop the reaction then one dilutes until 5 mL with the mobile phase. Then these solutions will be injected.

RESULTS AND DISCUSSION

Table-1 indicates the quantity of tiaprofenic acid for the three mediums to t = 0 s.

TABLE-1
QUANTITY OF THE ACTIVE INGREDIENT FOR EACH MEDIUM WITH t = 0 s

Medium of degradation	Quantity µmol L^{-1}	Quantity mg for 100 mL
HCl (2 N)	39.0165194	100.99
NaOH (2 N)	38.7975413	101.72
H_2O_2 (30 % v/v)	39.0779869	101.72

Kinetics of dégradation: The evolution of the concentration of tiaprofenic acid after the acid, basic hydrolysis and oxygenation by H_2O_2 according to time shows a linear line for the three mediums (Fig. 2-4).

Kinetics parameters: The initial tiaprofenic acid concentration is much weaker than that of the acid, the base and the hydrogen peroxide. Thus, one can estimate that the concentration of these solutions are practically constant during the reaction and that of Tiaprofenic acid passes from an initial value:

$[Ket]_0$ to a zero value to the time which tends towards the infinite one: $t = t_\infty$ thus the equation speed is written: $V_{Tia} = -d\,[Tia]/dt = k_{Tia}[Tia]^\alpha\,[HCl]^\beta = k'_{Tia}\,[Tia]^\alpha$ avec $k'_{Tia} = k_{Tia}\,[HCl]^\beta$ in acidic medium.

$V_{Tia} = -d[Tia]/dt = k_{Tia}\,[Tia]^\alpha\,[NaOH]^\beta = k'_{Tia}[Tia]^\alpha$ avec $k'_{Tia} = k_{Tia}[NaOH]^\beta$ in basic medium.

$V_{Tia} = -d[Tia]/dt = k_{Tia}[Tia]^\alpha\,[H_2O_2]^\beta = k'_{Tia}[Tia]^\alpha$ avec $k'_{Tia} = k_{Tia}\,[H_2O_2]^\beta$ in oxygenate medium.

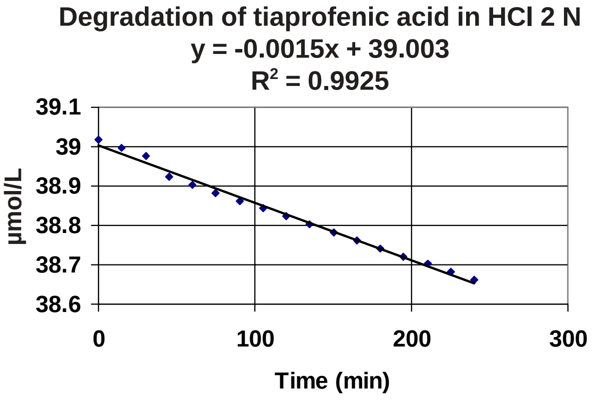

Fig. 2. Evolution in acidic medium

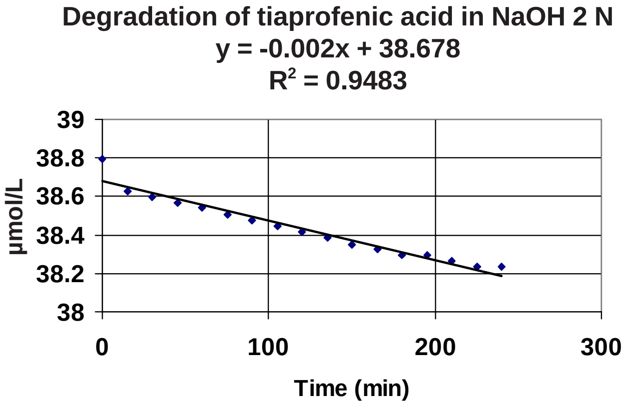

Fig. 3. Evolution in basic medium

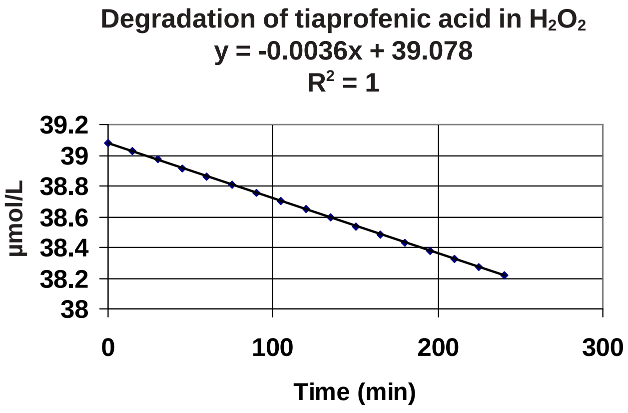

Fig. 4. Evolution in oxygenate medium

Determination of the value of the partial order: In the case of the transfer of variable about $\alpha + \beta$ to α. The order required is then a partial order. To determine this value one limits oneself initially to the whole orders 0, 1, 2 and 3. Values of $k'_{Ket\ (i)}$ for i various taking away carried out each 15 min.

$$\text{For order 0 : } k'_{Tia\ (i)} = [Tia]_0 - [Tia]/t$$

$$\text{For order 1 : } k'_{Tia\ (i)} = \ln[Tia]_0 - \ln[Tia]/t$$

$$\text{For order 2 : } k'_{Tia\ (i)} = 1/[Tia] - 1/[Tia]_0/t$$

$$\text{For order 3 : } k'_{Tia\ (i)} = 1/[Tia]^2 - 1/[Tia]_0^2/2t$$

The best value of the order is that which gives the smallest relative variation, the suggested order will be that or the values of $k'_{Tia\ (i)}$ according to time which give a line. In order to confirm the partial order by the graphic method, one plots the curve representing the variations of [Tia] according to time. If it is a segment of line the order is well that suggested.

Determination the apparent constant of kinetics: The calculation of the apparent constant kinetics k' is carried out starting from the linear transform of the curve [Ket] = f(t). These amounts determining the slope of this line which is equal to $-k_{Ket}$. Thus, it may finds according to the equation of the curve which is: $[Tia] = -k'_{Tia} + [Tia]_0$.

The law speed in the case of order 0 is written: $V_{Tia} = -d[Tia]/dt = k'_{Tia}$

Determination of the time of the half reaction: Knowing that with $t_{1/2}$ one in $[Tia] = [Tia]_0/2$ one with according to the equation [Tia] = f(t): $t_{1/2} = [Tia]_0/2k'_{Tia}$. In the three mediums the suggested order is 0 (Figs. 2-4). The determination of the constant kinetics is deduced from the equations:

[Tia] = f(t) and $t_{1/2}$ (Table-2)

TABLE-2
KINETICS PARAMETERS OF DECOMPOSITION OF KETOPROFEN IN THE THREE MEDIUMS

Degradation medium	2 N HCl	2 N NaOH	H_2O_2 30 % (v/v)
Partial order	0	0	0
Equation [Tia] = f(t) $[Tia] = -k'_{Tia}\, t + [Tia]_0$	[Tia] = -0.0015t + 39.003	[Tia] = -0.002t + 38.678	[Tia] = -0.0036t + 39.078
R^2	0.9925	0.9483	1
Apparent kinetics constant (s^{-1}): k'_{Tia}	90×10^{-3}	120×10^{-3}	216×10^{-3}
Speed of the reaction (mol m^{-3} s^{-1}): $V_{Tia} = d[Tia]/dt = k'_{Tia}$	90×10^{-3}	120×10^{-3}	216×10^{-3}
time of the half-reaction (s): $t_{1/2} = [Tia]_0/2k'_{Tia}$	780.06×10^3	580.17×10^3	651.3×10^3

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