

A KINETIC STUDY OF AQUO-ETHANOL REACTION MEDIA ON THE PHARMACEUTICAL EFFICIENCY OF SOLVOLYSIS PRODUCTS OF NICOTINATES.

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ABSTRACT

For studying the solvent effect of aquo-ethanol solvent systems on the insecticidal efficiency of the Solvolysis Products of nicotine ester the kinetics of alkali catalysed hydrolysis of methyl nicotine was studied in aquo-EtOH media having varying concentration of ethanol from 20 to 80% (v/v) at five different temperatures ranging from 20 to 40°C. From enhancement and depletion found in E_C and E_D values respectively is due to Solvation and desolvation of unital and transition State to different extent. With decreasing number of water molecules from 1.341 to 0.329 with increasing temperature from 20 to 40°C, it is concluded that the mechanism of the reaction is changed from unimolecular to bimolecular with addition of ethanol in the reaction media. Simultaneously increase in all the three thermodynamic activation parameters i.e. ΔH^ , ΔS^* and ΔG^* , it may be inferred that the solvent ethanol acts enthalpy stimulator and entropy controlled. From the evaluated numerical value of Iso-Kinetic temperature of the reaction, i.e. 321.10, it is concluded that due to strong solvent solute interaction in aquo-ethanol media it may be used for manufacturing insecticide of desired strength.*

KEYWORDS - Pharmaceutical Efficiency, Nicotines, Insecticide, Solvolysis Iso-Kinetic Temperature, entropy controlled,

INTRODUCTION : The studies in the kinetics of alkali catalysed hydrolysis of methyl nicotinate in aquoethanol media were proposed as the study of solvent effect of primary alcohol on medicinal properties of nicotinate ester has not been paid adequate attention by the kineticists so far. It has been planned to perform the reaction in aquo-ethanol media having varying concentration of ethanol at 5 different temperatures i.e. at 20, 25, 30 and 40°C.

EXPERIMENTAL : Export quality of Methyl nicotinate of Fluka AG grade packed in Switzerland and extra pure ethanol were used. The kinetics of the reaction were studied as usual 1-4 by keeping the strength of alkali 0.1 M and that of the ester 0.05 M in the reaction mixture. The reaction was found to obey the second order kinetic equation and the evaluated values of specific rate constants have been recorded in Table-I, From the recorded values of $\log k$ and $10^3/T$, in Table - II, $\log k$ values were plotted against $10^3/T$, The values of iso-composition activation energy (E_C) and iso-dielectric activation energy (E_D) have been mentioned in Table - III and IV respectively. The $\log k$ values were plotted against $\log [H_2O]$ from their values recorded in Table - V, the evaluated values of the slopes of these plots have been noted in Table - VI. The consolidated values of the thermodynamic activation parameters, i.e. ΔH^* , ΔG^* and ΔS^* were calculated by using Wynne-Jones and Eyring⁵ relation are enlisted in Table - VII.

Effect of Solvent on the Specific Rate Constant values of the Reaction :

From the survey of the data recorded in Table - I, it is obvious that the rate of the reaction decreases regularly with gradual addition of ethanol in the reaction media at all the temperatures at which the kinetics of the reaction has been studied. In order to study the variation in rate constant values with increasing concentration of ethanol in the reaction media, the $\log k$ values have been plotted against mol % of ethanol content in the reaction media. the rate of reaction go on decreasing having different slopes due to two intersecting straight lines in the plots at about 21.25 mol % of ethanol in the reaction media. the degree of depletion in the rate become shallow (slow). Such decrease in the rate with increasing proportion of the organic co-solvent like ethanol is not new, but a number of researchers like Laidler-Landskroener⁶ and recently Rakesh & Singh et al⁷ have also reported such observation about the depletion in rate with increasing concentration of the organic co-solvent in the reaction media. Howerer, the possible rate

depleting factors in the rate may be listed as follows:

- (i) decrease in the bulk dielectric constant of the reaction media
- (ii) decreasing the polarity of the reaction media on adding less polar ethanol.

The above noted two rate depleting factors are quite in operation and this is in support of the earlier reports of Singh & Lal et.⁸, and recent report of Pathak & Singh et al⁹ that the rate ought to decrease with decreasing dielectric constant value of the reaction media with addition of ethanol to it.

Solvent Effect on the Iso-composition Activation Energy of the Reaction:

From the slopes of the Arrhenius plots of log k values against $10^3/T$ (from their values enlisted in Table - II) ,the iso-composition activation energy (E_C) of the reaction were evaluated and mentioned in Table -III.From the values recorded in Table-III, it is obvious that E_C or E_{exp} values go :

Table – I

Specific rate constant values of Alkali catalysed hydrolysis of Methyl in water- Nicotinate EtOH media
 $K \times 10^2$ in $(dm)^3 mol^{-1} min^{-1}$

Temp in °C	% of EtOH(v/v)						
	20%	30%	40%	50%	60%	70%	80%
20°C	55.26	45.38	37.69	29.73	23.98	18.54	12.69
25°C	119.89	94.10	81.06	67.07	56.05	45.23	33.71
30°C	224.08	196.92	173.98	150.87	130.86	110.20	87.08
35°C	436.42	391.02	351.36	320.04	288.81	255.68	213.75
40°C	838.30	785.60	733.16	685.80	643.72	595.94	526.26

Table – II

Variation of log k values of the reaction with $10^3/T$ in water-EtOH media.

Temp in °C	$10^3/T$	2+log k values at different % of EtOH (V/V)						
		20%	30%	40%	50%	60%	70%	80%
20 °C	3.413	1.7424	1.6569	1.5762	1.4732	1.3798	1.2681	1.1035
25 °C	3.356	2.0788	1.9736	1.9088	1.8265	1.7486	1.6554	1.5278
30 °C	3.300	2.3504	2.2943	2.2405	2.1786	2.1186	2.0422	1.9399
35 °C	3.247	2.6399	2.5922	2.5458	2.5052	2.4606	2.4077	2.3299
40 °C	3.195	2.9234	2.8952	2.8652	2.8362	2.8087	2.7752	2.7212

increasing with increasing concentration of ethanol reaction media. This trend is probably due to solvation changes taking place either at initial state level or at the reansition statte level or at the level of bothe the state as reported earlier by several researchers in this field.Considering the extent of solvation to be a dominant factor, the following three factore seem to be responsible for increase in E_C values with gradual addition of ethanol in the reaction media -

- (1) The initial state is more solvated than the transition state,
- (2) The initial state is less desolvated than the transition state, and
- (3) The transition state is desolvated and the initial state is solvated.

The transition state being large anion(ester + OH) available less for solvation by solvent molecule than the initial state, so the first factor seems to be operative in this case and it also gets support when the values entropy of activation(ΔS^*) go on increasing with increasing concentration of ethanol (Table-VII). Similar interpretation for enhancement in the values of activation energy of the reaction with gradual addition of the organic content in the reaction media have also been reported recently by Haider Singh et al.¹⁰

Table – III

Evaluated values of Iso-composition Activation Energy (E_C or E_{exp}) of the reaction in water-EtOH media.

% of EtOH(v/v)	20%	30%	40%	50%	60%	70%	80%
E_C value in kJ/mol	106.51	109.76	116.65	121.59	129.07	133.71	144.41

Table – IV

Evaluated values of Iso-Dielectric Activation Energy (E_D) of the reaction at different desired 'D' values of the water-EtOH media.

D values	D = 35	D = 40	D = 45	D = 50	D = 55	D = 60	D = 65
E_D values in kJ/mol	137.77	135.26	128.95	124.53	119.74	114.19	108.97

Table - V

Variation of log k values of the reaction with log [H₂O] values of water-EtOH system (media) at different temperatures.

% of EtOh	% of H ₂ O	log [H ₂ O]	2 + log k values				
			20°C	25°C	30°C	35°C	40°C
20%	80%	1.6478	1.7424	2.0788	2.3504	2.6399	2.9234
30%	70%	1.5898	1.6569	1.9736	2.2943	2.5922	2.8952
40%	60%	1.5229	1.5762	1.9088	2.2405	2.5458	2.8652
50%	50%	1.4437	1.4732	1.8265	2.1786	2.5052	2.8362
60%	40%	1.3468	1.3798	1.7486	2.1168	2.4606	2.8087
70%	30%	1.2218	1.2681	1.6554	2.0422	2.4077	2.7752
80%	20%	1.0458	1.1035	1.5278	1.9399	2.3299	2.7212

Effect of Solvent on the Iso-dielectric Activation Energy (E_D) of the reaction :

On perusal of the data of Table - IV, it is observed that the iso-dielectric activation energy (E_D) values of the reaction go on decreasing from 137.77 kJ/mol to 108.97 kJ/mol with increase in D values from $D = 35$ to $D = 65$ respectively. Such depletion in E_D values with increase in D values of the reaction media are in accordance with the increase in E_C values with increasing concentration of the organic content (EtOH) in the reaction media. Since D values of the reaction media decreases with addition of organic solvent in it, so it can also be concluded that E_D values of this reaction also increases like E_C values with decrease in D values of the reaction media. However, these findings and interpretations regarding change (decrease) in E_D values with increase in D values of the reaction media are in support of the past views of Elsemongy¹¹ and Wolford¹² and have been found in support of the earlier report of Singh & Navendu et al.¹³ and also of the recent report of Singh & Singh et al¹⁴.

Effect of number of water molecules of the reaction media in the Mechanism of the Reaction:

For establishing the mechanistic pathways of the reaction, Robertson¹⁵ gave an idea of solvation number 'n' which is the number or the number of water molecules involved in the formation of the activated complex and for its evaluation he proposed the equation:

$$\log k = \log k' + n \log [\text{H}_2\text{O}]$$

Robertson et al¹⁶ have established the principle that the values of solvation number (n) for the reaction following unimolecular mechanistic pathway is fairly high but for the reaction following bimolecular path, it will be low. The number of water molecules 'n' involved in the formation of the activated complex of the reaction were determined by plotting $\log k$ values against $\log [\text{H}_2\text{O}]$ value for alkali catalysed hydrolysis of methyl nicotinate in aquo-ethanol media. The value of $\log k$ and $\log [\text{H}_2\text{O}]$ have been tabulated in Table – V. The numerical values of the slopes of plots have been recorded in Table - VI. It is clear that at each temperature of the reaction, the plots of $\log k$ versus $\log [\text{H}_2\text{O}]$, two intersecting straight lines having, different values of slopes are obtained at $\log [\text{H}_2\text{O}]$ value at about 1.475 which corresponds to 53.70% of

water in aquo-ethanol media. From the values recorded in Table - VI, it is clear that below log [H₂O] value 1.475, which corresponds to 53.70% of water in the reaction media, the number of water molecules associated with the activated complex decreases from 0.930 to 0.329 with rise in temperature of the reaction from 20 to 40°C. Similarly, in case of above, 53.70% of water concentration in the reaction media, the values of slopes decreases from 1.341 to 0.329 with increase in temperature from 20 to 40°C of the reaction. Overall, it may be inferred that number of water molecules associated with the activated complex in its formation decreases from 1.341 to 0.329. In the light of guidelines of Robertson et al.¹⁶ from the decreasing number of water molecules from 1.341 to 0.329 involved in the formation of the activated complex, it may be inferred that the mechanistic pathway followed by the reaction is changed from unimolecular to bimolecular in presence of ethanol in the reaction media and with increase in temperature of the reaction from 20 to 40°C. Regarding the changes in the structure of water, it is obvious that in presence of ethanol and with rise in temperature, water components of the reaction media, changes its structure from bulky to dense form.



Such findings and inferences have been reported earlier by Kumar & Singh et al.¹⁷ and also recently by Madhu & Singh et al¹⁸

Table – VI

Values of the slopes of the plots of log k versus log [H₂O] at different temperatures

Temperature	Slope - I When log[H ₂ O] value is below 1.475	Slope - II when log[H ₂ O] value is above 1.475
20°C	0.930	1.341
25°C	0.755	1.292
30°C	0.594	0.929
35°C	0.457	0.787
40°C	0.329	0.329

Solvent effect on Thermodynamic Activation Parameters of the Reaction:

For better study of the effects of solvent, the thermodynamic activation parameters, such as enthalpy of activation ΔH^* , entropy of activation ΔS^* and free energy of activation ΔG^* were taken into account as they have great significance. These parameters evaluated using Wynne-Jones and Eyring⁵ equation have been recorded in Table -VII. In order to highlight the effect of solvent concentration on these thermodynamic parameters more clearly, ΔH^* , ΔG^* and ΔS^* values were plotted against mol % of ethanol.

The values of ΔG^* recorded in Table -VII obviously indicate that the variation in ΔG^* is small and it increases from 82.54 to 84.92 kJ/mol with change of proportion of ethanol from 20 to 80% (v/v) at 30°C slowly with gradual addition of the organic content in water. The small but considerable increase in ΔG^* and non-linear variation in ΔH^* and ΔS^* curves with the increasing mol% of ethanol are indication of specific solvation taking place in the process of activation as already reported by Elsemongy et al.¹⁹, Saville & Hudson et al.²⁰ and Tomilla & mevikallio²¹ Simultaneous increase in ΔG^* , ΔH^* and ΔS^* values with increasing.

Table- VII

**Consolidated Values of Activation Parameters (ΔH^* , ΔG^* and ΔS^*) of water-EtOH
the reaction in system at different temperatures.**

ΔH^* and ΔG^* in kJ/mol, ΔS^* in J/K/mol

% of EtOH (v/v)	Mole% of EtOH	ΔH^* in kJ/mol	20°C		25°C		30°C		35°C		40°C	
			ΔG^*	ΔS^*	ΔG^*	ΔS^*	ΔG^*	ΔS^*	ΔG^*	ΔS^*	ΔG^*	ΔS^*
20%	7.17	103.65	83.15	69.99	82.69	70.36	82.24	64.68	82.4	69.53	81.92	69.45
30%	11.69	107.61	83.63	81.86	83.29	81.63	82.52	81.67	82.52	81.47	82.08	81.56
40%	17.07	111.71	84.08	94.29	83.66	94.12	82.79	94.15	82.79	93.87	82.26	94.06
50%	23.59	118.17	84.66	114.38	84.13	114.24	83.03	114.30	83.03	114.08	82.43	114.16
60%	31.06	124.94	85.18	135.68	84.57	135.48	83.30	135.48	83.30	135.20	82.60	135.25
70%	41.87	132.28	85.81	185.59	85.10	158.24	83.61	158.48	83.61	158.01	82.80	158.06
80%	55.85	142.59	86.73	190.64	85.83	190.31	84.07	158.24	84.07	190.00	83.13	189.97

mol % of ethanol in the reaction media are only possible when the extent (degree) of enhancement in ΔS^* values is less than that in ΔH^* values and from this, it may be inferred that in alkali catalysed hydrolysis of Methyl nicotinate in aquo-ethanol media, ethanol acts as entropy controller and enthalpy dominating solvent. Such inferences have also been found in support of the recently reported views Sushma & Singh et al²².

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