

The Effect of Dielectric Constant On The Kinetics of Reaction Between Plasma Albumin And Formaldehyde In Ethanol- Water Mixtures.

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Abstract

This study determined the effect of increased concentration of ethanol solution on the rate of the reaction between plasma albumin and formaldehyde. It was design to investigate the kinetics of reaction between plasma albumin and low concentrations of formaldehyde under pseudo-first order conditions of formaldehyde. The reaction was studied at constant conditions at various dielectric constants and temperatures of 1%, 5%, 15%,20% and 20⁰C 25⁰C, 30⁰C and 37⁰C respectively. The rate constant as a function of different permittivity in ethanol-water mixtures was determined at constant conditions. The dielectric constant of the reaction medium was altered by the addition of the varying amounts of ethanol – water mixtures (1- 25% v/v) in a cuvette and the absorption of 0.51×10^{-4} mol dm⁻³ plasma albumin and 0.27×10^{-1} formaldehyde- plasma mixtures at 235 nm were measured. The values of dielectric constants for different aqueous ethanol- mixtures were taken from literature. The values of rate constants of the reaction of between plasma albumin and formaldehyde were found to decreased with the increase in the concentration of ethanol and the reaction was a second order or bimolecular . The Activation energy and the thermodynamic parameters (Gibbs free energy, enthalpy and entropy changes of the reaction) decreased with decrease in dielectric constant of the medium, that is with increase in the proportion of the ethanol component in the solvent mixtures. The dependence of $\ln k_2$ vs. reciprocal dielectric constant ($1/D$) of this reaction was found be linear with three linear portions indicating three zones, that is three mechanistic changes. Also the correlations between $\ln k_2$ and the mole fractions of water and ethanol (χ_{H_2O} and χ_{EtOH}) have shown that there was an increase in rate of the studied reaction in water but a decrease in rate in ethanol mole fraction. This leads us to suggest that the reaction rates were slowed by progressive addition of ethanol . A steady decrease in rate constant with decrease in dielectric constant values was observed with a statistically significant p-value = 0.0013 on a two tailed correlation analysis at 95% confidence assurance.

Key Words; dielectric constant, kinetics , plasma albumin, formaldehyde , ethanol- water mixtures.

Introduction

The dielectric constant of a solvent roughly provides a measure of the solvent's polarity. A dielectric constant below 15 is usually considered non-polar. Basically, the dielectric constant can be thought of as the solvent's ability to reduce the internal charge of the solvent. The hydrogen atom in a polar protic solvent is reported to be highly positively charged, and it can interact with the anionic nucleophile which would negatively affect an bimolecular nucleophilic substitution reaction(SN²), but it does not affect an unimolecular nucleophilic substitution (SN¹) reaction because the nucleophile is not a part of the rate-determining[1]. Hence it found that the higher the dielectric constant the more polar the substance and in the case of S_N1 reactions, the faster the rate. Polar protic solvents are known to actually speed up the rate of the unimolecular substitution reaction because the large dipole moment of the solvent helps to stabilize the transition state. The highly positive and highly negative parts interact with the substrate to lower the energy of the transition state. Since the carbocation is unstable, anything that can stabilize this even a little will speed up the reaction [1].

Solvents used in substitution reactions were found to inherently determine the nucleophilicity of the nucleophile. This fact has become increasingly more apparent as more reactions are performed in the gas phase. As such, solvent conditions significantly affect the performance of a reaction with certain solvent conditions favouring one reaction mechanism over another. For S_N1 reactions the solvent's ability to stabilize the intermediate carbocation is of direct importance to its viability as a suitable solvent. The ability of polar solvents to increase the rate of S_N1 reactions is as a result of the polar solvent's solvating the reactant intermediate species, i.e., the carbocation, thereby decreasing the intermediate energy relative to the starting material [2].

Huges [3] however found that the case for S_N2 reactions is quite different, as the lack of solvation on the nucleophile increases the rate of an S_N2 reaction. In either case (S_N¹ or S_N²), the ability to either stabilize the transition state (S_N¹) or destabilize the reactant starting material (S_N²) acts to decrease the ΔG^\ddagger of activation and

thereby increase the rate of the reaction. This relationship is according to the equation $\Delta G = -RT \ln K$ (Gibb's free energy). The rate equation for S_N^2 reactions are bimolecular being first order in nucleophile and first order in reagent. The determining factor when both S_N^2 and S_N^1 reaction mechanisms are viable is the strength of the nucleophile. Nucleophilicity and basicity are linked and the more nucleophilic a molecule becomes the greater is the nucleophile's basicity. This increase in basicity causes problems for S_N^2 reaction mechanisms when the solvent of choice is protic. Protic solvents react with strong nucleophiles with good basic character in an acid/base fashion, thus decreasing or removing the nucleophilic nature of the nucleophile. It is important to note that solvent effects as well as steric effects both affect the relative reaction rates; however, for demonstration of principle for solvent polarity on S_N2 reaction rates, steric effects may be neglected. There are two major factors affecting the reactivity of a specific amino acid side chain toward a reagent that under ideal conditions reacts with it. These are; effects on the pK of the reacting group (which affects its nucleophilicity), and steric effects. The reaction between plasma albumin and formaldehyde an aprotic solvent in water ethanol solutions is essential since formaldehyde will undergo addition reactions with most protic solvents and is a good hydrogen bond acceptor [4]. A study by [5] found that Apolar solvents did not solubilise denatured proteins, but low solubilizing powers were observed for polar, aprotic solvents. Heat denaturation was observed to result in the formation of large intermolecular aggregates, in which, for ovalbumin and lysozyme, were formed by intermolecular S-S bonds, but for bovine serum albumin involved intermolecular iso peptide bond This study therefore investigated the effect of increase in the concentration of ethanol in a solution on the rate of the reaction partly denatured plasma albumin and formaldehyde The study was also aimed at ascertaining the molecularity this reaction from the results and to shed more light on this important reaction that is often found to occur in alcoholic systems.

Materials and Method

The reaction was studied at constant conditions at various dielectric constants and temperatures of 1%, 5%, 15%, 20% and 20°C, 25°C, 30°C and 37°C respectively. The rate constant as a function of different permittivity in ethanol-water mixtures was determined at constant conditions. The dielectric constant of the reaction medium was altered by the addition of the varying amounts of ethanol – water mixtures (1- 25% v/v) in a cuvette and the absorption of 0.51×10^{-4} mol dm⁻³ plasma albumin and 0.27×10^{-1} formaldehyde- plasma mixtures at 235 nm were measured. Rate was measured in (1% to 25% v/v) Ethanol- water mixtures. The values of dielectric constants for different aqueous Ethanol- mixtures were taken from literature [6, 7]. Triplicate values were taken in each case to obtain the pseudo-first and second order rate kinetics from a plot of $\ln(A_t - A_\infty)$ versus time. The Eyring plots, that $\log k_2/T$ vs $1/T$ for different dielectric constant were plotted and the thermodynamic parameters were calculated from the relation $\ln(k_2/T) = -\Delta H^\ddagger/RT + \Delta S^\ddagger/R + 23.8$ while the activation energy was calculated by using the expression $E_a = \Delta H^\ddagger + RT$ [8,9]. (The values of the thermodynamic parameters energy were determined as a function of dielectric constant of medium the results recorded. Also the values of the second order rate constant $\log k_2$ were plotted against reciprocal dielectric constant to obtain the relation of the change in dielectric constant and the rate of the reaction between plasma Albumin and Formaldehyde.

Results and Discussions

Tables 1-11 and Fig. 1 - 8 provide the data for rate constant of plasma albumin and formaldehyde reaction at various compositions of ethanol in water solution. The values of rate constants were found to decreased with the increase in the concentration of ethanol, this deviation from the Bronsted theory is in accordance to the literature [9]. The reason for such behaviour is reported to be due to the greater influence of ionic orientation for regulating the reaction rate. The probability of ideal orientation is found to be maximum at extreme dilution and higher value of dielectric constant. The probability of formation of a more polar transition state is favourable in a medium of high dielectric constant [9].

The values of energy of activation other thermodynamic parameters as a function of dielectric constant of medium at varying temperatures are as given in Table 10. The activation energies and the other thermodynamic parameters were found to be effected by solvent medium. All the parameters, activation energy the other thermodynamic parameters (Gibbs free energy, enthalpy and entropy changes of the reaction) decreased with decrease in dielectric constant of the medium, that is with increase in the proportion of the ethanol component in the solvent mixtures. This behaviour is reported to be in accordance with the idea of solvation of activated complex [10].

Also a report by [11] showed that using the logarithm of a reaction rate constant versus the reciprocal of the dielectric constant one may determine whether the reaction mechanism is changed, modifying the dielectric constant equation of the binary mixtures due to the changes in its composition. According the authors a range of

solvent composition in which the equations of logarithm of a reaction rate constant versus the reciprocal of the dielectric constant are linear is called “zone”. A solvent composition in which a zone finishes and another zone initiates is called “mechanism change point.” The dependence of $\ln k_2$ vs. reciprocal dielectric constant ($1/D$) of this reaction was found be linear as shown in Fig.5 with three linear portions indicating three zones, three mechanistic changes.

The correlations between $\ln k_2$ and the mole fractions of water and ethanol (χ_{H_2O} and χ_{EtOH}) have shown that there was an increase in rate of the studied reaction in water but a decrease in rate in ethanol mole fraction. This leads us to suggest that the reaction rates were slowed by progressive addition of Ethanol as presented in Fig 6 and 7. A steady decrease in rate constant with decrease in dielectric constant values was observed with a statistically significant p-value of 1.000 on a two tailed correlation analysis at 95% confidence assurance and result was also presented as in Table 11 and Fig. 8.

Conclusion

The values of rate constants were found to decreased with the increase in the concentration of ethanol, this deviation from the Bronsted theory is in accordance to the literature [10]. The reason for such behaviour is reported to be due to the greater influence of ionic orientation for regulating the reaction rate. The probability of ideal orientation is found to be maximum at extreme dilution and higher value of dielectric constant. The probability of formation of a more polar transition state is favourable in a medium of high dielectric constant [10]. The activation energies and the other thermodynamic parameters were found to be effected by solvent medium. Activation energy the other thermodynamic parameters (Gibbs free energy, enthalpy and entropy changes of the reaction) decreased with decrease in dielectric constant of the medium, that is with increase in the proportion of the ethanol component in the solvent mixtures. This behaviour is reported to be in accordance with the idea of solvation of activated complex [10]. The dependence of $\ln k_2$ vs. reciprocal dielectric constant ($1/D$) of this reaction was found be linear as shown in Fig. 5 with three linear portions indicating three zones, three mechanistic changes.

The correlations between $\ln k_2$ and the mole fractions of water and ethanol (χ_{H_2O} and χ_{EtOH}) have shown that there was an increase in rate of the studied reaction in water but a decrease in rate in ethanol mole fraction. This leads us to suggest that the reaction rates were slowed by progressive addition of ethanol. A steady decrease in rate constant with decrease in dielectric constant values was observed with a statistically significant p-value = 0.0013 on a two tailed correlation analysis at 95% confidence assurance. his study therefore investigated the effect of increase in the concentration of ethanol in a solution on the rate of the reaction partly denatured plasma albumin and formaldehyde The study also found that the studied reaction second order reaction in ethanol-water systems.

Competing Interests:

The Authors wish to declare that there are no conflicts of interest associated with this work.

Authors' Contributions:

Professor Uzairu,A; H.O Kwanashie, H.O, and Idris , S. O conceived and designed the research as well as carefully proof read the the manuscript. Ugye, T. J performed the analysis and prepared the draft manuscript.

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Table 1 Experimental results of the rate constants of reaction of plasma Albumin and formaldehyde at varying dielectric constants and temperature in [Ethanol-water] mixtures and $T= 20 - 37^{\circ}\text{C}$ at constant conditions, $\lambda_{\text{max}} = 235 \text{ nm}$, $\text{pH} = 7 \pm 3$

%Ethanol	Rate constant $k_2 \text{ mol}^{-1} \text{ s}^{-1}$ at different temperatures $^{\circ}\text{C}$			
	20	25	30	37
1	2.93	2.74	2.67	2.63
5	2.44	2.41	2.33	1.96
15	2.89	2.74	2.48	2.22
20	2.81	2.67	2.59	2.22

Table 2 Experimental Results of Pseudo - first order and second order rate constants at $2.7 \times 10^{-1} \text{ mol/dm}^3$ HCHO of formaldehyde with Plasma albumin reaction at different temperatures and Ethanol-water mixtures

Ionic strength = 0.5		1%Ethanol –water mixture				
K	k_{obs}	k_2	$1/T \times 10^{-3}$	$\log k_2$	k_2/T	$\log (k_2/T)$
293	0.079	2.93	3.41	0.467	0.010	-2.000
298	0.074	2.74	3.36	0.438	0.0092	-2.036
303	0.072	2.67	3.30	0.427	0.0088	-2.056
310	0.071	2.63	3.23	0.420	0.0085	-2.071

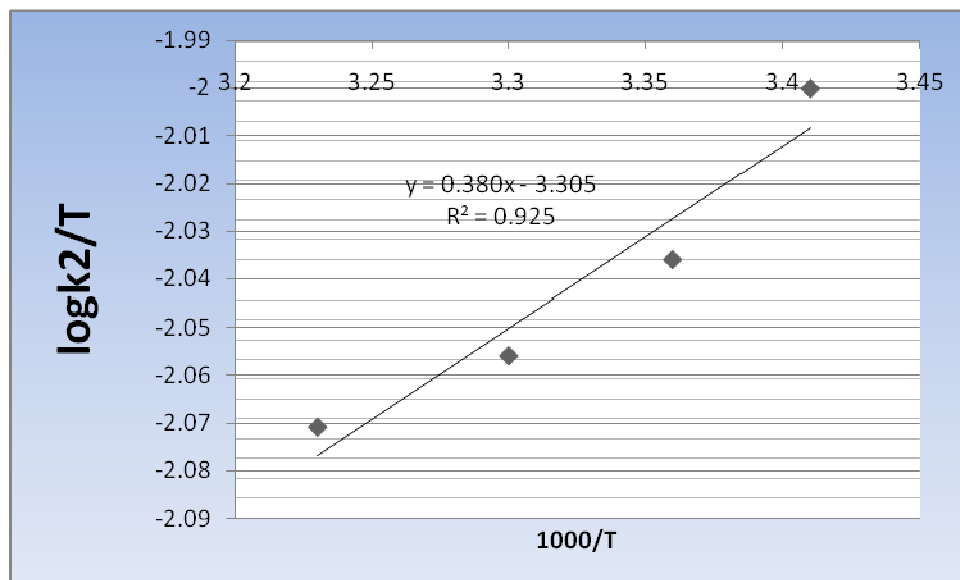


Figure 1 Eyring Plot of $\log k_2/T$ versus $1/T$ at 1% ethanol-water mixture

Table 3 Thermodynamic Parameters (ΔG , ΔH^\ddagger and ΔS^\ddagger) and Ea for the Reaction of formaldehyde with plasma Albumin in 1%(Ethanol water) mixture at different temperatures(20⁰C,25⁰C,30⁰C and 37⁰C.

[HCHO] moldm ⁻³	Ea (kJmol ⁻¹)	ΔG^\ddagger (kJmol ⁻¹)	ΔH^\ddagger (kJmol ⁻¹)	ΔS^\ddagger (Jmol ⁻¹ K ⁻¹)
2.7 x10 ⁻¹	1.89	66.880	-0.951.	-225.351

Table 4 Experimental Results of Pseudo - first order and second order rate constants at 2.7 x 10⁻¹ mol/dm³ HCHO of formaldehyde with Plasma albumin reaction at different temperatures and 5% Ethanol-water mixture

Ionic strength = 0.5		5.0 %Ethanol –water mixture					
K	k _{obs}	k ₂	1/T x10 ⁻³	logk ₂	k ₂ /T	log (k ₂ /T)	
	293	0.066	2.44	3.41	0.387	0.0083	-2.081
	298	0.065	2.41	3.36	0.382	0.008	-2.097
	303	0.063	2.33	3.30	0.367	0.0077	-2.114
	310	0.053	1.96	3.23	0.292	0.0063	-2.201

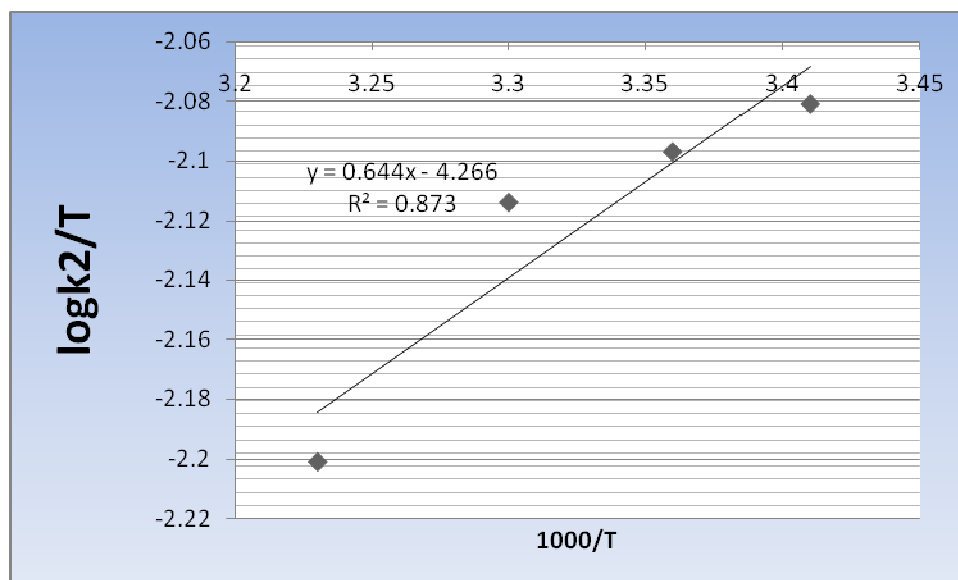


Figure 2 Eyring Plot of $\ln k_2/T$ versus $1/T$ at 5% ethanol-water mixture

Table 5 Thermodynamic Parameters (ΔG^\ddagger , ΔH^\ddagger and ΔS^\ddagger) and Ea for the Reaction of formaldehyde with plasma Albumin in 5%(Ethanol water) mixture at different temperatures(20⁰C,25⁰C,30⁰C and 37⁰C

[HCHO] moldm ⁻³	Ea (kJmol ⁻¹)	ΔG^\ddagger (kJmol ⁻¹)	ΔH^\ddagger (kJmol ⁻¹)	ΔS^\ddagger (Jmol ⁻¹ K ⁻¹)
2.7 x10 ⁻¹	0.891	59.232	-1.612.	-202.139

Table 6 Experimental Results of Pseudo - first order and second order rate constants at 2.7 x 10⁻¹ mol/dm³ HCHO of formaldehyde with Plasma albumin reaction at different temperatures and 15% Ethanol-water mixture

Ionic strength = 0.5		15%Ethanol –water mixture					
K	k _{obs}	k ₂	1/Tx10 ⁻³	logk ₂	k ₂ /T	log (k ₂ /T)	
	293	0.078	2.89	3.41	0.461	0.010	-2.000
	298	0.074	2.74	3.36	0.438	0.009	-2.046
	303	0.067	2.48	3.30	0.394	0.008	-2.097
	310	0.060	2.22	3.23	0.346	0.007	-2.155

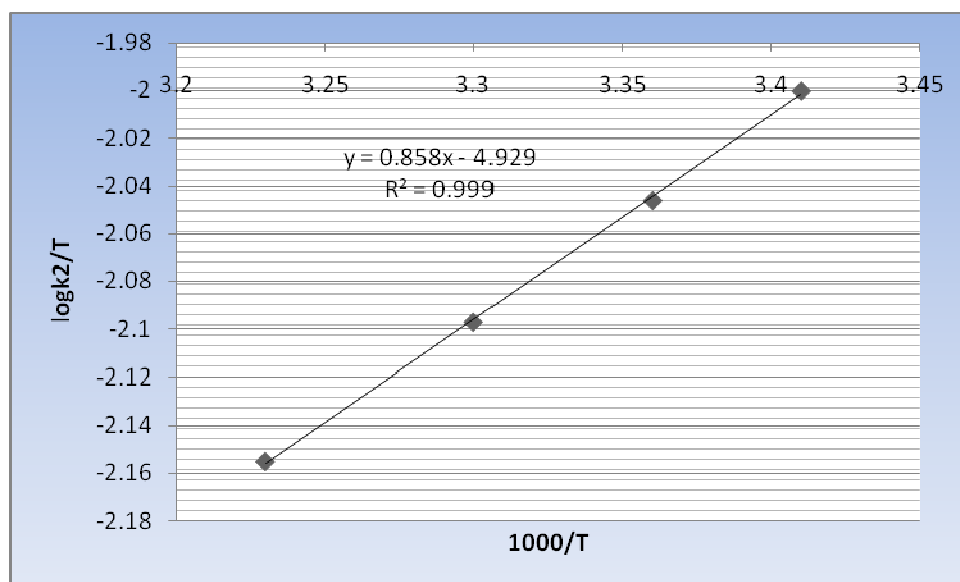


Figure 3 Eyring Plot of $\ln k_2/T$ versus $1/T$ at 15 %ethanol-water mixture

Table 7 Thermodynamic Parameters (ΔG , ΔH^\ddagger and ΔS^\ddagger) and Ea for the Reaction of formaldehyde with plasma Albumin in 15%(Ethanol water) mixture at different temperatures(20⁰C,25⁰C,30⁰C and 37⁰C

[HCHO] moldm ⁻³	Ea (kJmol ⁻¹)	ΔG^\ddagger (kJmol ⁻¹)	ΔH^\ddagger (kJmol ⁻¹)	ΔS^\ddagger (Jmol ⁻¹ K ⁻¹)
2.7 x10 ⁻¹	0.355	59.301	- 2.148	-202.802

Table 8 Experimental Results of Pseudo - first order and second order rate constants at 2.7 x 10⁻¹ mol/dm³ HCHO of formaldehyde with Plasma albumin reaction at different temperatures and 20%Ethanol-water mixture

Ionic strength = 0.5 moldm ⁻³		20 %Ethanol –water mixture					
K	k _{obs}	k ₂	1/Tx10 ⁻³	logk ₂	k ₂ /T	log (k ₂ /T)	
	293	0.076	2.81	3.41	0.449	0.010	-2.000
	298	0.072	2.67	3.36	0.427	0.009	-2.046
	303	0.070	2.59	3.30	0.413	0.008	-2.097
	310	0.060	2.22	3.23	0.346	0.007	-2.155

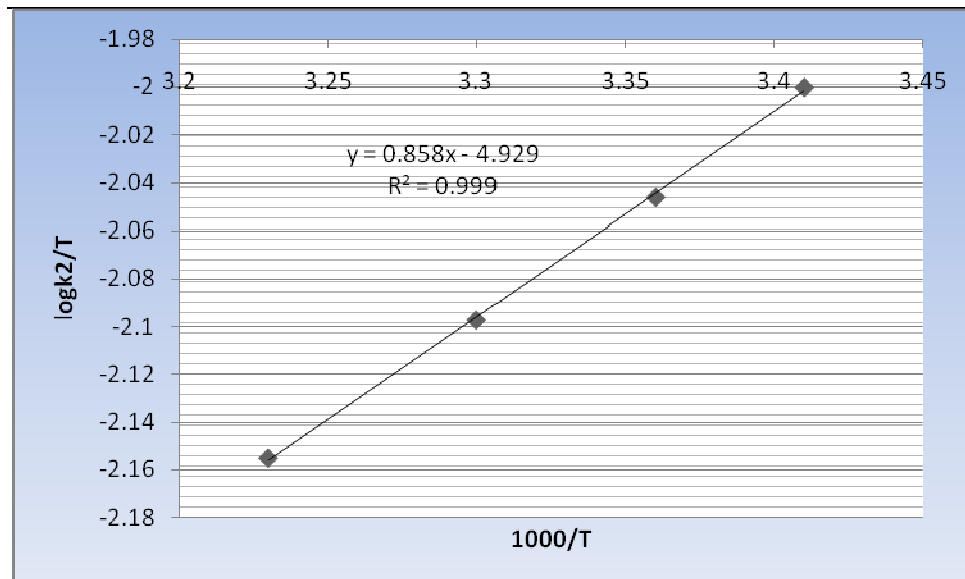


Figure 4 Eyring Plot of lnk₂/T versus 1/T at 20%ethanol-water mixture

Table 9 Thermodynamic Parameters (ΔG , ΔH^\ddagger and ΔS^\ddagger) and Ea for the Reaction of formaldehyde with plasma Albumin in 20%(Ethanol water) mixture at different temperatures(20⁰C,25⁰C,30⁰C and 37⁰C

[HCHO] moldm ⁻³	ΔE_a (kJmol ⁻¹)	ΔG^\ddagger (kJmol ⁻¹)	ΔH^\ddagger (kJmol ⁻¹)	ΔS^\ddagger (Jmol ⁻¹ K ⁻¹)
2.7 x10 ⁻¹	0.355	59.301	-2.148	-202.802

Table 10 Thermodynamics and other Parameters for Reaction in Various ethanol–Water Media. Temp. = 20 - 37°C ,ionic strength = 0.5

Solventcompost %	Ea (k Jmol ⁻¹)	ΔG^\ddagger (kJmol ⁻¹)	ΔH^\ddagger (kJmol ⁻¹)	ΔS^\ddagger (Jmol ⁻¹ K ⁻¹)
1	1.290	66.880	-0.951	-225.351
5	0.891	59.232	-1.612	-202.139
15	0.355	59.301	-2.148	-202.802
20	0.355	59.301	-2.148	-202.802
Mean	0.723	61.18	-1.715	-208.27

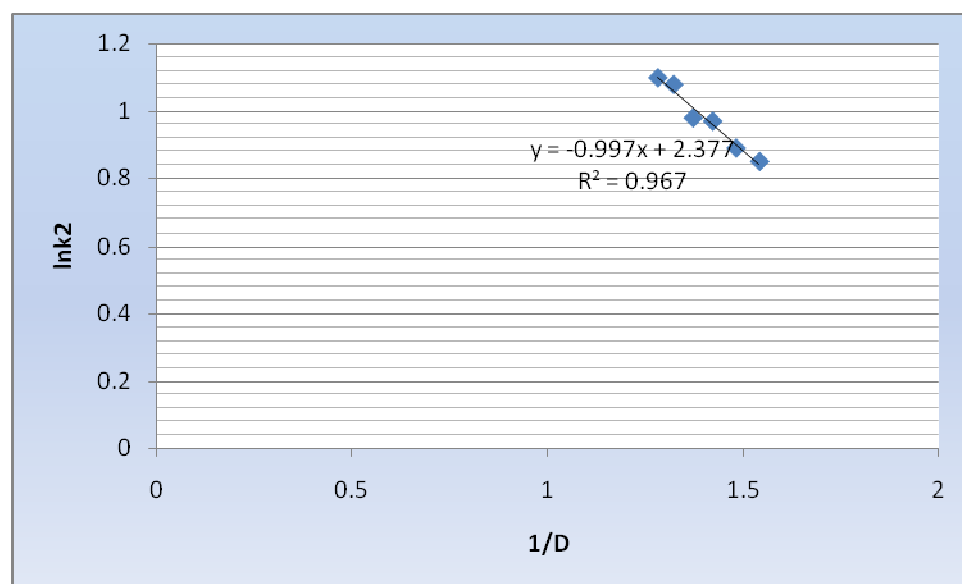


Figure 5 plot $\ln k_2$ vs, $1/D$ showing the effect of change in dielectric constants change on the rate constant on the reaction of plasma albumin with formaldehyde in ethanol-water mixtures.

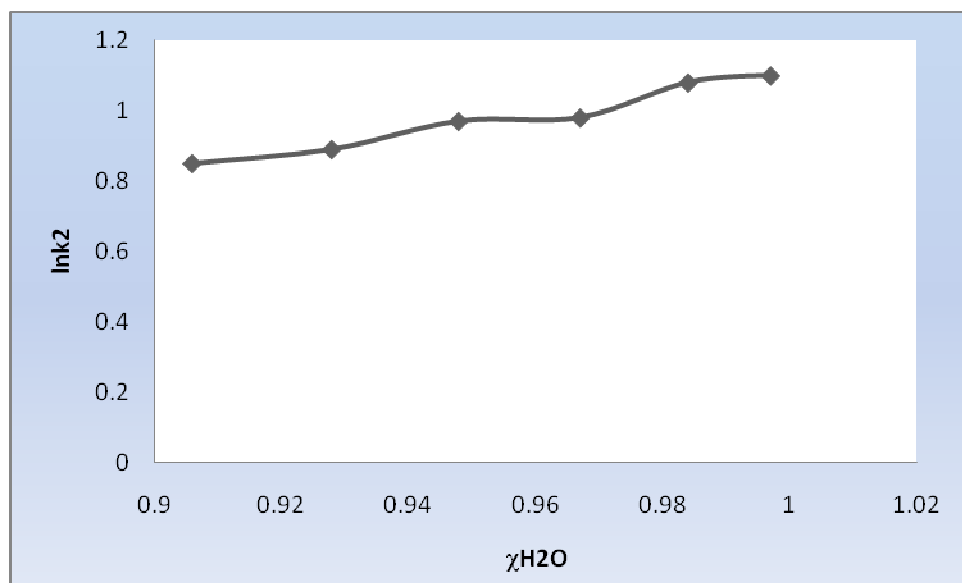


Figure 6 plot of $\ln k_2$ vs. mole fractions of water

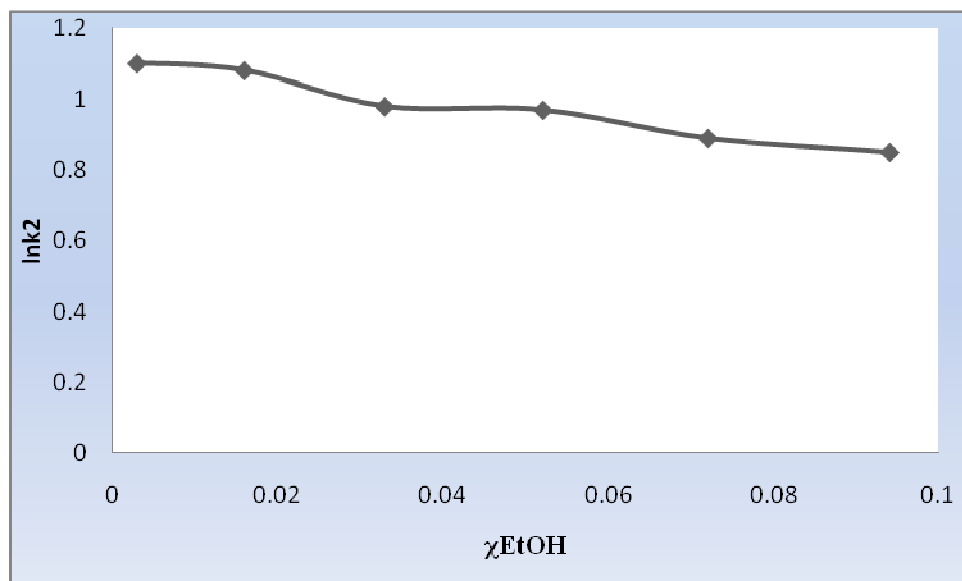


Figure. 7 plot of $\ln k_2$ vs. mole fractions of ethanol –water mixture

Table 11 Results of two tailed correlation analysis for k_2 values versus ethanol -mixtures at 95% level of assurance.

Best-fit values	
Slope	-0.02810 \pm 0.003482
Y-intercept when X=0.0	3.023 \pm 0.05273
X-intercept when Y=0.0	107.5
1/slope	-35.58
95% Confidence Intervals	
Slope	-0.03777 to -0.01844
Y-intercept when X=0.0	2.876 to 3.169
X-intercept when Y=0.0	83.14 to 157.4
Goodness of Fit	
r^2	0.9421
Sy.x	0.07080
Is slope significantly non-zero?	
F	65.14
DFn, DFd	1.000, 4.000
P value	0.0013
Deviation from zero?	Significant
Data	
Number of X values	6
Maximum number of Y replicates	1
Total number of values	6
Number of missing values	0
Runs test	
Points above line	4
Points below line	2
Number of runs	5
P value (runs test)	1.0000
Deviation from linearity	Not Significant

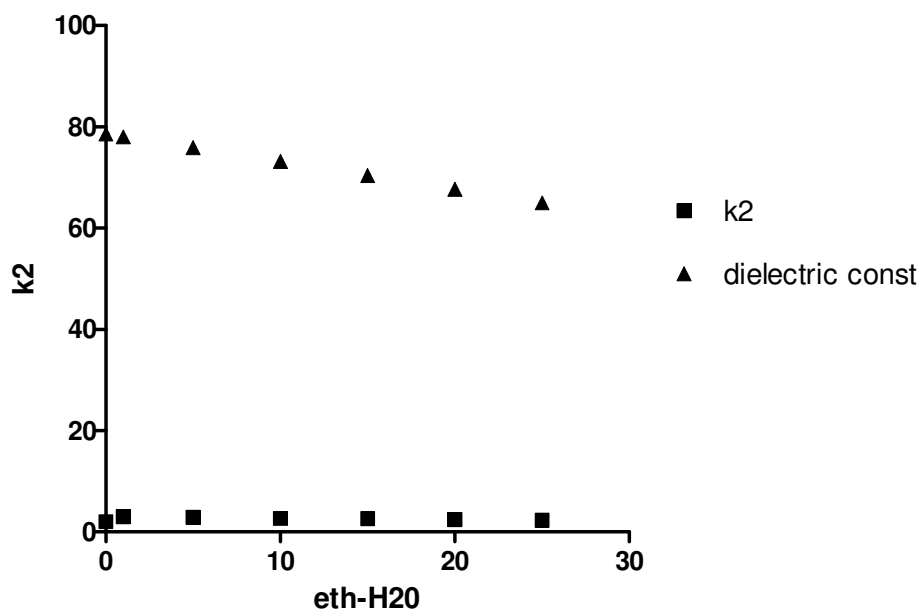


Figure 8 Correlational analysis chart of k_2 values versus dielectric constants at different ethanol-water mixtures.

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