

## “Investigation of Protonation Constants of L-Tyrosine in DMF and EG-Water Mixtures by Spectrophotometric Method”

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**Abstract:** Method of static UV-VIS spectrophotometry were applied for the determination of protonation constants of values of L-Tyrosine were determined in Dimethylformamide(DMF) and Ethylene Glycol(EG) - water mixtures (0–60% v/v) at 303.0 K at an ionic strength of 0.16 M. The log K values were found to be an increase with increase of the organic solvent content. Distribution of species, protonation equilibria and effect of influential parameters on the protonation constants have also been presented.

**Key words:** L-Tyrosine, Dimethylformamide, Ethylene Glycol, Protonation constant, UV-VIS spectrophotometry

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### I. Introduction:

L-Tyrosine is usually absorbed in the proximal small intestine. Any L-tyrosine reaching the large intestine is decarboxylated to tyramine, a biogenic amine, in the human gut. Inadequate degradation (detoxification) of formed tyramine by the gut monoamine oxidases can lead to tyramine entering the systemic circulation. Tyramine acts as a vasopressor [1-2]; it is known to be a cause of migraine headaches in humans [3]. Very recently, for a single oral administration in healthy individuals, a no observed adverse effect level (NOAEL) of 200 mg tyramine/person has been proposed, based on a literature survey [4]. In contrast, individuals with reduced monoamine oxidase activity may suffer hypertension after ingestion of < 5 mg tyramine [5]. Intellectual deficit problems seem to occur when human neonates receive abnormally high quantities of L-tyrosine [6].

L-Tyrosine (International Union of Pure and Applied Chemistry (IUPAC) name (2S)-2-amino-3-(4-hydroxyphenyl)propanoic acid, Chemical Abstracts Service (CAS) No 660-18-4) has a molecular weight of 181.2 g/mol; its molecular formula is C<sub>9</sub>H<sub>11</sub>NO<sub>3</sub> and its molecular structure is given in Fig. 1.

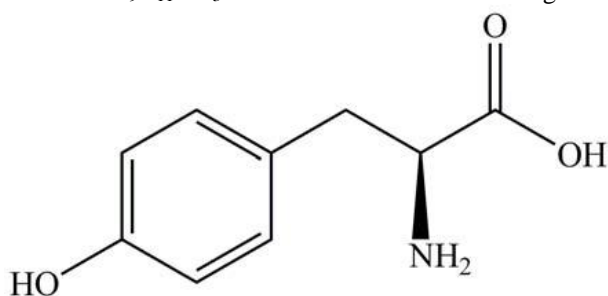


Figure: 1 Molecular structure of L-tyrosine

The logK<sub>1</sub> values are related to the attachment of H<sup>+</sup> to the phenolic oxygen in L-tyrosine. The logK<sub>2</sub> value corresponds to the attachment of a proton to the -NH<sub>2</sub> in L-tyrosine. The logK<sub>3</sub> values are the smallest and are thought to correspond to the protonation of carboxyl groups.

Protonation constant is the equilibrium constant for the addition or release of proton to a charged or uncharged ligand depending on the availability of hydrogen ions (protons) in natural waters and biofluids. The protonation constant of organic molecule plays a basic role in many analytical procedures and has been shown to affect mobility, toxicity and the pharmaceutical properties of organic acid and base [7].

Ethylene glycol is a colorless, practically odorless, low-volatility, low-viscosity, hygroscopic liquid. It is completely miscible with water and many organic liquids. Ethylene glycol (EG)—the simplest diol—was first developed in 1859 by a French chemist—Charles-Adolphe Wurtz—via saponification of ethylene glycol diacetate with potassium hydroxide [8-9].

N, N-Dimethylformamide (DMF) was first prepared in 1893 by the French chemist Albert Verley. It is a compound formed by the substitution of the hydroxyl group of formic acid with dimethyl amino group and the

molecular formula HCON(CH<sub>3</sub>)<sub>2</sub>. It is a clear, transparent, high-boiling point liquid with a light amine flavor and a relative density of 0.9445 (25°C). It is soluble in water and most organic solvents [10] that used as a common solvent for chemical reactions. The aim of the present work was the determination of protonation constants of L-tyrosine using the Spectrophotometric method.

### II. Materials and Methods:

0.05 mol L<sup>-1</sup> solution of L-tyrosine (Himedia, India) was prepared in deionised triple-distilled water by maintaining 0.05 mol L<sup>-1</sup> concentration of hydrochloric acid to increase the solubility. Dimethylformamide and Ethylene glycol (Merck, India) were used as Solvents.

2 mol L<sup>-1</sup> Sodium Chloride (Merck, India) was prepared to maintain the ionic strength. The UV-visible spectra were taken using a Shimadzu SP65 UV Visible spectrophotometer in

200-800 nm range using a 1.0 cm quartz cell path length at a controlled temperature of 25±0.1 °C with a Cole-Parmer bath.

The reaction medium is one of the most important influencing factors in determining the equilibrium constants. Many workers were of the opinion that both electrostatic and non-electrostatic effects should be considered even in the case of simple acido-basic equilibria, one dominates the other, depending upon the nature of solute and solvent [11-13]. The solvent effect on protonation constants could be explained on the basis of dielectric constant of the medium, solvent structure, preferential solvation and microscopic parameters.

### III. Results and Discussion:

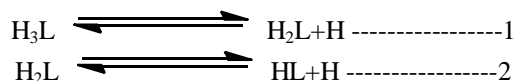
#### Method of Protonation Constant Calculation

All calculations were done by our computation program based on the following assumption. In each point of titration curve of weak base by strong acid the following equation must be satisfied

$$\frac{a \cdot c - [H^+] + K_b / [H^+]}{c} = \frac{\sum_{i=1}^n i \prod [K_i [H^+]]^i}{1 + \sum_{i=1}^n \prod [K_i [H^+]]^i}$$

where *c* is the overall base concentration, *K<sub>i</sub>* is the successive protonation constants, *a* is the titration fraction, *K<sub>s</sub>* is the ionic product of solvent, [H<sup>+</sup>] is the equilibrium concentration of hydrogen ions, and *n* is the number of protons which can be attached to the base molecule.

The results of species and Step-wise protonation constants of L-tyrosine in DMF- and EG-water mixtures along with some important statistical parameters are given in Table-1.



**Table: 1 Step-wise protonation constants of L-tyrosine**

%V/V	LogK	
	LH	LH <sub>2</sub>
	<b>DMF</b>	
0.0	9.30	15.90
10	9.22	15.82
30	9.17	15.80
50	9.15	15.77
	<b>EG</b>	
0.0	9.30	15.90
20	9.08	15.84
40	9.14	15.77
60	9.02	15.68

Typical spectrophotometric parameters of L-tyrosine in DMF - water and L-tyrosine in EG - water are given in Table 2 and 3.

**Table: 2 Parameters L-tyrosine in 0–50% v/v DMF - water.**

v/v DMF	L-tyrosine			
	0	10	30	50
λ <sub>max</sub> (nm)	280	280	280	280
Abs	0.601	0.670	0.634	0.650

**Table: 3 Parameters L-tyrosine in 0–60% v/v EG - water.**

v/v EG	L-tyrosine			
	0	20	40	60
$\lambda_{max}$ (nm)	280	280	280	280
Abs	0.601	0.713	0.786	0.802

The absorption spectra of ligand(L-tyrosine) in 0–60% v/v DMF and EG- water media is given in Fig. 2 and 3, and Distribution diagrams of L-tyrosine in DMF and EG-water mixtures in Fig. 4

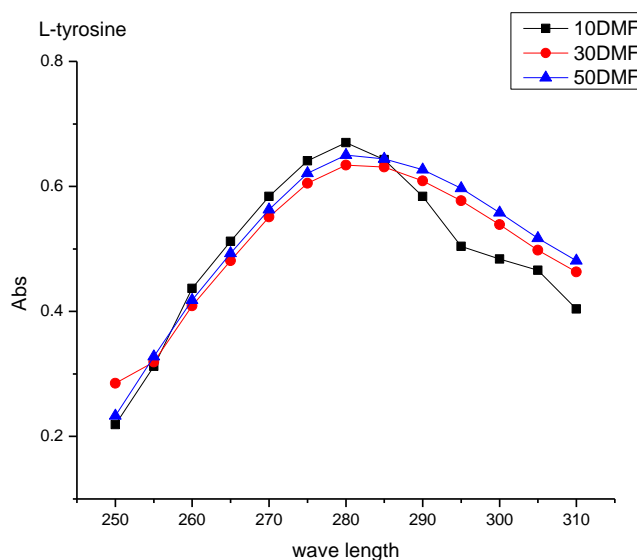


Figure: 2 Absorption spectra of L-tyrosine in 0–50% v/v DMF - water.

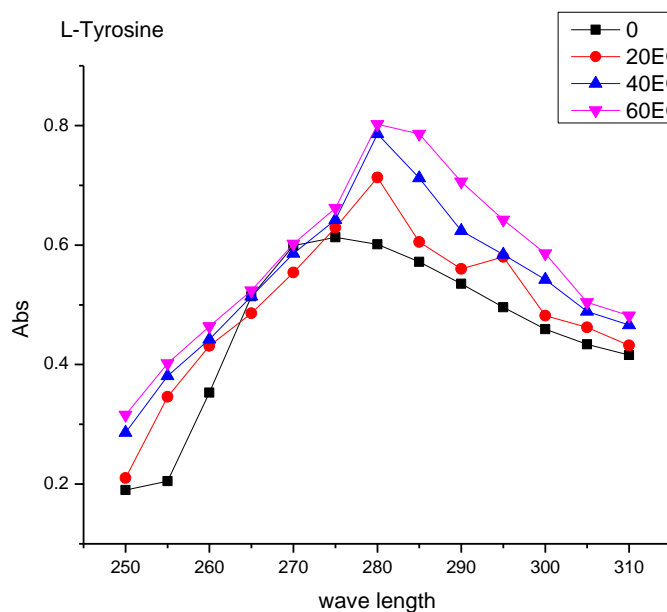
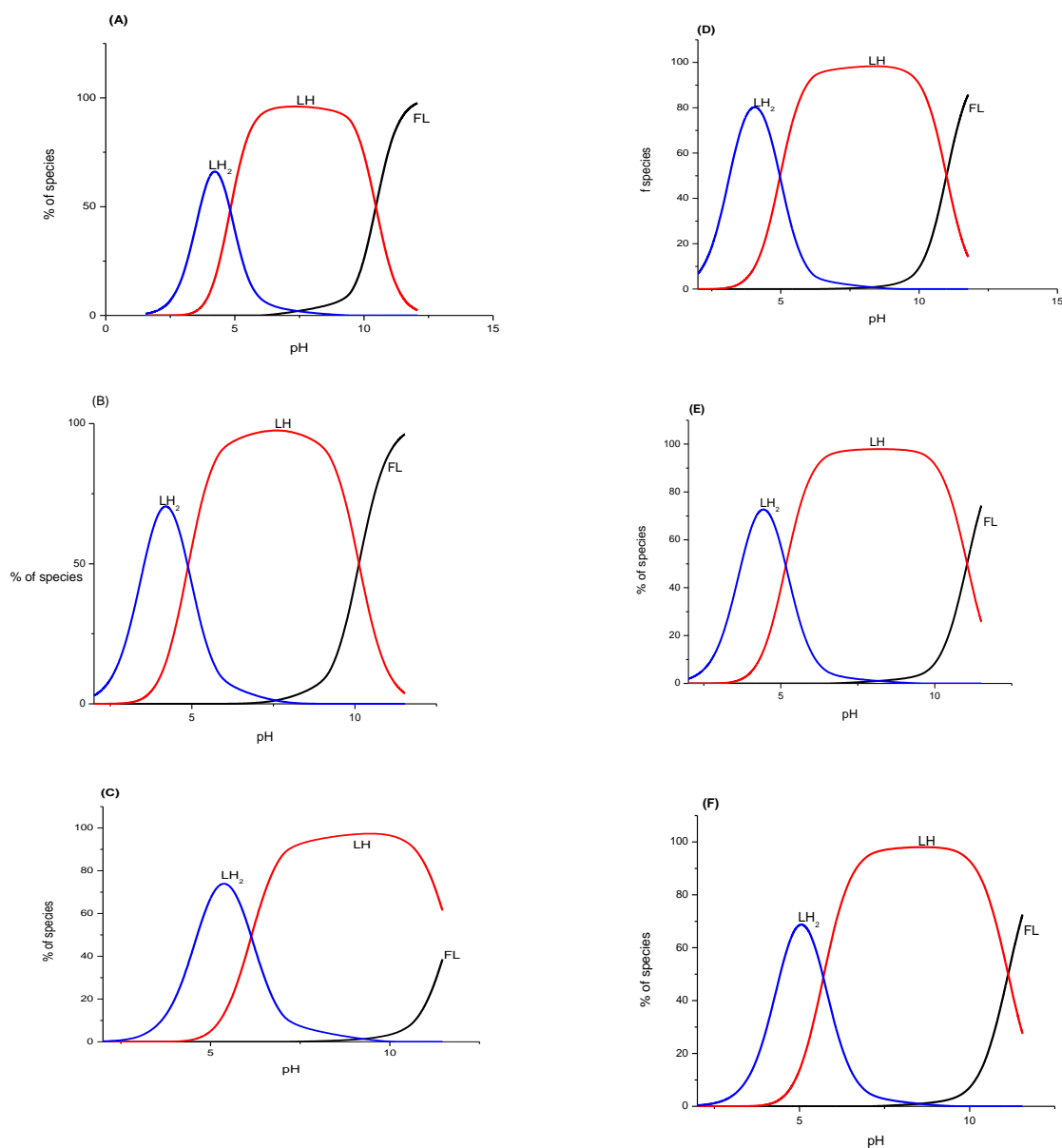


Figure: 3 Absorption spectra of L-tyrosine in 20–60% v/v EG- water.



**Figure: 4** Distribution diagrams of L-tyrosine in (A) 10.0 (B) 30.0 (C) 50.0 (% v/v) DMF-water mixtures (D) 20.0 (E) 40.0 (F) 60.0 (% v/v) EG-water mixtures.

#### IV. Conclusions:

1. The investigation by the biomimetic studies indicates the pH ranges of protonation equilibria of Tyro in both DMF- and EG- water mixtures.
2. The log values of protonation constants of Tyro increase linearly with decreasing dielectric constant of DMF-water and EG-water mixtures. This indicates the dominance of electrostatic forces in the protonation-deprotonation equilibria.
3. Protonation Equilibria of L-Tyrosine in DMF and EG water mixtures. The protonation constants of L-tyrosine, The  $\log K_1$  values are related to the attachment of  $H^+$  to the phenolic oxygen in L-tyrosine. The  $\log K_2$  value correspondsto the attachment of a proton to the  $-NH_2$  in L-tyrosine. The  $\log K_3$  values are the smallest and are thought to correspond to theprotonation of carboxyl groups.
4. Overlapping of the formation curves indicates that no condensed product is formed.

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