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Determination of pK and Log K values of tramadol hydrochloride with Cu(II), Co(II) and Fe(II) metal ions

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Abstract
$\bar{n}_A$ and $\bar{n}$ values, pK and log k of tramodol hydrochloride with Cu(II), Co (II) and Fe(II) metal ions at 0.2 M ionic strength in water were determined by potentiometricaly. Irving–Rossotti titration technique was used for determination of stability constants. 1:1 complexes were formed in present investigation in between tramodol hydrochloride (TH) and Cu (II), Co (II) and Fe(II) metal ions.

Keywords: Tramodol hydrochloride (TH), stability constant, potentiometric measurements

1. Introduction
Tramadol hydrochloride is used in a form of an ingredient in multi-agent topical gels, creams and solutions for nerve pain, rectal foam, concentrated retention enema and a skin plaster (transdermal patch) quite similar to those used with lidocaine, it is weak μ-opioid receptor agonist that induces serotonin release and inhibits uptake of norepinephrine [1, 2]. Drug has a wide range of application including treatment of rheumatoid arthritis, restless legs syndrome, motor neuron disease and fibromylgia. It is classified as the central nervous system drug [3-5] because of hallucinations, agitation, fever, nausea fainting, convulsions, skin rash, shallow breathing, weak pulse. Metabolism of drug directly depends on stability of the molecule. Stability of molecules can be easily determined from the values of stability constants, which can be easily determined with potentiometry. Formation of complex can be determined from values of stability constants, hence pH-metric investigation have various significances in life, medicinal and pharmaceutical, agricultural and industrial sciences. Nitrogen and oxygen containing molecules are used as drugs [6-7]. Many researchers determined $\bar{n}_A$, $\bar{n}$, pK and log K of various ligands containing N, S, O heteroacycls and heterocycles and benzenoids in different solvents and their systems at different molar concentrations and temperatures [8-15]. Hence, stability constant of complexes formed by interactions of tramadol hydrochloride were studied with Cu(II), Co (II) and Fe(II) metal ions at 0.2 M ionic strength potentiometrically in water.

2. Materials and Method
Nitrate salts of Cu(II), Co(II) and Fe(II) were taken. Tramadol hydrochloride denoted as TH. Stock solutions were prepared in water. In the present investigation Irving and Rossotti method was used. pH-Metric titrations were carried out in 100 ml Pyrex glass beaker by maintaining a constant temperature at 32^0C. Nitrogen gas was bubbled during titration, pH meter readings were only taken after gas bubbling and magnetic stirring were stopped. In these potentiometric titrations it was observed that first reading decreases and then increases, increased in the reading indicated the end point. Complete titration required near about one hour. Titrations of (i) free acid (0.01 M), (ii) free acid (0.01 M) and ligand (20 x 10^{-4}M) and (iii) free acid (0.01 M), ligand (20 x 10^{-4}) and metal ion (4 x 10^{-4}M) were carried out against aqueous 0.1N NaOH solution. In all titrations readings were recorded after addition of 0.2 ml solution. Graph of volume of alkali added against pH were plotted.

3. Results and discussion
$\bar{n}_A$ and $\bar{n}$ values were determined by using following expressions.

$$\bar{n}_A = \gamma - \left\{ \frac{(V_2 - V_1)(N + E^0)}{(V^0 + V_1)T_L^0} \right\}$$

where, V^0 is the initial volume of the solution. E^0 and T_L^0 are initial concentrations of mineral acid and ligand respectively. V_1 and V_2 are volumes of alkali of normality N during acid and ligand titration at given pH. 'γ' is replaceable proton from ligand. $\bar{n}_A$ Values were determined at 32 (±1) °C in E^0=1x10^{-2} M, T_L^0 = 20 x 10^{-4} M, V^0 = 50 ml, N = 0.2 N respective ratios of solutions.

Plots between volume of NaOH and pH of solution were used to determine proton-ligand stability constant. Horizontal difference (V_2-V_1) was measured accurately between titration curves of free acid and acid+ligand. It was used to calculate formation number $\bar{n}_A$ at various pH values and fixed ionic strength μ = 0.2 M using equation 2.

Data of $\bar{n}_A$ obtained at various pH along with horizontal difference for some representative systems are represented in Table 1. Metal–ligand formation number ($\bar{n}$) was determined using equation. Where, notations have same meaning as given in earlier equation. Horizontal difference (V_3-V_2) between metal complex (A+M+L) and reagent (A+L) curve were used for determination of $\bar{n}$ values. $\bar{n}_A$ and $\bar{n}$ values obtained during study are given in Table-1

$$\bar{n} = \frac{(V_3 - V_2) \times ((N + E^0)}{(V^0 + V_2) T_M^0}$$

Table 1

	$\bar{n}_A$ Values			$\bar{n}$ Values		
Sr. No.	TH-Cu(II)	TH-Co(II)	TH-Fe(II)	TH-Cu(II)	TH-Co(II)	TH-Fe(II)
1	0.5823	0.79886	0.59848	0.9148	0.9162	0.8743
2	0.5414	0.59771	0.49665	1.1493	1.1787	1.1792
3	0.5053	0.49761	0.43700	1.3412	1.4512	1.3140
4	0.3732	0.49761	0.43700	1.6128	1.5363	1.3140
5	0.3746	0.43808	0.39771	1.6492	1.6264	1.8248
6	0.1893	0.39886	0.35854	1.7712	1.7758	2.0541

pK values of TH were calculated by half integral method and point wise calculation method is given in Table-2

Table 2

System	Method		
	Half Integral	Point wise	Diffrence
Cu(II)-L_5	2.5198	2.0667	±0.4531
Co(II)-L_5	2.8197	2.648	±0.1717
Fe(II)-L_5	2.3198	2.4824	±0.1626

log K obtained during study was given in Table-3.

Table 3

System	Log K_1	Log K_2	Δ Log K	Log K_1/Log K_2
TH+Cu(II)	3.9972	2.5200	1.4772	1.58619
TH +Co(II)	3.9972	2.8199	1.1773	1.417497
TH +Fe(II)	3.8971	2.3200	1.5771	1.679784

4. Conclusion

The order of pK values of ligand give attributed toward removal of hydrochloride from ligand and having good activity to form more stable complex. pK value of TH is good for stable complexation. Observation of Table-3 showed that less difference between log K_1 and log K_2 values indicates complex formation between metal ion and ligand occurring simultaneously and 1:1 complexation occurs in between to above metal ions and TH. Values of log K_1 and log K_2 show stability of complexes. For TH values of log K_1 and log K_2 is higher with Fe(II) complex than Cu(II) and Co(II) complexes. Fe(II) forms more stable complex with TH than Co(II) and Cu(II) metal ions.

5. References

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