# POLAROGRAPHIC STUDY OF COMPLEXES OF CD (II) WITH RAMIPRIL AT D.M.E

## Rita Dixit*

Department of Chemistry, Mahatma Gandhi Balika Vidhyalya, (PG) College, Firozabad

*reetadixit.chemistry@gmail.com**

## Sanoj Kumar

Karm Kshetra Post Graduate College, Etawah

## Rafat Khan

Department of Zoology, Mahatma Gandhi Balika Vidhyalya, (PG) College, Firozabad

**Abstract:**

Ramipril, an antihypertensive drug extensively used in the management of cardiovascular diseases, is a subject of growing interest in the field of coordination chemistry. This research paper presents a comprehensive study on the complexation behavior of Ramipril with Cd(II) ions at 25°C using direct current polarography. The investigation employed the Deford & Hume method and was conducted in a 1.0 M sodium nitrate ($NaNO_3$) medium.

The results of this study indicate the formation of two distinct complexes, [Cd(Rami)2+] and [Cd(Rami)2]2+, with Ramipril. The formation of these complexes was observed at $\mu$ = 1.0 M $NaNO_3$, providing insights into the speciation of the Cd(II)-Ramipril system.

The research further quantified the overall formation constants (log$\beta$) for these complexes, revealing log$\beta$ values of 5.50 and 10.96 for [Cd(Rami)2+] and [Cd(Rami)2]2+, respectively, at 25°C. Additionally, a log$\beta$ value of 15.50 was obtained for the Cd(II)-Ramipril complex formation, shedding light on the thermodynamic stability of this complexation process.

**Keywords**: Ramipril, Cd(II), Complex formation, Direct current polarography, Coordination chemistry, Speciation, Overall formation constant, Log$\beta$ values, Antihypertensive drug, Cardiovascular diseases

## Introduction:

Studies of metal complexes with therapeutic compounds have garnered significant interest in various scientific fields due to their potential applications[1,2]. Among the drugs widely employed in the treatment of hypertension, $\beta$ blockers hold a prominent place[3]. Ramipril, a $\beta$ blocker, plays a crucial role in reducing blood pressure in individuals suffering from hypertension. Its mechanism

of action involves the inhibition of the sympathetic nervous system, which, in turn, suppresses heart muscle contractions, ultimately leading to a decrease in blood pressure. This suggests that the complexation of β blockers with metal ions may influence important biological processes, as these processes can be metal-dependent.

In this context, previous investigations have explored the complexation behavior of β blockers with metal ions. For instance, Bantchev et al. conducted a study on the complexation of Pindolol with Cd(II). Additionally, complexes of Pb(II), Zn(II), and Co(II) with Atenolol have been reported in the literature. These prior studies have shed light on the interactions between β blockers and metal ions, enhancing our understanding of their chemical behavior.

This research paper represents a further step in such investigations, focusing on the complexation behavior of Ramipril, a β blocker, with Cd(II) through the utilization of direct current polarography. Direct current polarography is a powerful analytical technique for studying the electrochemical behavior of complex systems. By examining the electrochemical properties of the Cd(II)-Ramipril system, we aim to contribute valuable insights into the coordination chemistry of this drug-metal interaction.

The experiments were conducted using a manual polarograph in conjunction with a galvanometer, under controlled conditions of temperature and pH. This paper presents the results of our investigations and their implications for understanding the complexation of β blockers with metal ions in therapeutic contexts.

## Experiment:

Polarograms were acquired using a manual polarograph, specifically the Toshniwal CLO2 model, in combination with the Toshniwal polyflex galvanometer, designated as PL-50. All measurements were conducted under controlled conditions, maintaining a temperature of $25 \pm 0.1°C$ and a pH of 7.4. To ensure accurate electrochemical analysis, a saturated calomel electrode (S.C.E) was utilized as the reference electrode. The differential mercury electrode (d.m.e) employed in this study exhibited the following characteristics under open-circuit conditions with a 0.1 M NaNO3 electrolyte: mass flow rate (m) of 2.13 mg/sec, a time constant (t) of 3.5 sec, and a working electrode height (h) of 40 cm.

## Materials and Reagents:

All reagents employed in this study were of analytical grade, and their solutions were meticulously prepared using double-distilled water. The ionic strength was rigorously maintained at $\mu = 1.0$ M by employing NaNO3 as a supporting electrolyte. The concentration of Cd(II) was consistently upheld at $1 \times 10^{-3}$ M. To suppress polarographic maxima, Triton X-100 (0.002%) was utilized. Prior to the polarographic analysis, the solution underwent purification through the passage of pure nitrogen gas for a duration of 10 minutes.

### Results and Discussion:

In this study, the Cd(II)-Ramipril system was subjected to polarographic investigation at a temperature of 25°C. The reduction potential of Cd(II) (-0.602V) was determined using the polarographic technique, revealing an essential electrochemical property of this metal ion within the system.

The reduction of Cd(II) in the presence of Ramipril was found to be a reversible process, demonstrating diffusion-controlled behavior. In each instance, a single, well-defined wave was observed in the polarograms, signifying the purity and homogeneity of the electrochemical process.

The plot of $E_{de}$ (differential pulse height) versus log i/id - i displayed a linear relationship with a slope of 30±3 mV, indicating the reversible nature of the reduction process. Moreover, the direct proportionality of the diffusion current (id) to the square root of the effective height of the mercury column strongly suggests that the reduction is diffusion-controlled. This observation aligns with previous studies on the electrochemical behavior of similar systems.

The diffusion current of the Cd(II) metal ion exhibited a decrease with increasing concentrations of the complexing agent, Ramipril. This behavior was coupled with a noticeable shift of the half-wave potential towards a more negative direction. These findings collectively imply the formation of Cd(II)-Ramipril complexes, which is consistent with previous expectations regarding metal-ligand interactions.

Furthermore, the overall formation constants (logβ) of the Cd(II) complexes with Ramipril were determined through DeFord & Hume's method[8], utilizing polarographic measurements. This method involves the graphical differentiation of the Fo[X] term, derived from polarographic data, and yields essential information regarding complex stability.

$$Fo[X] = 10^{0.4343 \frac{nF}{RT} \cdot ((E_y^2)_s - (E_y^2)_c) + \log\left(\frac{I_s}{I_c}\right)}$$

Where $I_s$ & $I_c$ are the diffusion current constants of the simple ion & the same ion in complexing media respectively $F1[X]$ in then defined by:

$$F1[X] = \frac{Fo[X]-1}{[X]} = \beta_1 + \beta_2[X]$$

### Table 1 – Cd(ii) Ramipril System

[Cd$^{+2}$] = 1 X 10$^{-3}$ M, m = 1.00M (NaNO3), pH= 7.4, T= 25 ± 1°C, [Trition-X-100] = .002%, m=2.13mg/sec t=3.5sec h$_{corr}$ = 40cm, (Ey2)s = 602 V(S.C.E)

| [Rami] M | Ey2 Vs (S.C.E) | 10g (Im/Ic) | Slope m | Fo[X] | F1[X]x 10$^{-5}$ | F2[X]x 10$^{-5}$ | F3[X]x 10$^{-5}$ |
|---|---|---|---|---|---|---|---|
| 0.000001 | 0.637 | 0.02560 | 29 | 16.19 | 15.19 | 12.19 | 3.19 |
| 0.000002 | 0.655 | 0.03507 | 30 | 67.42 | 33.21 | 15.10 | 3.05 |

| 0.00004 | 0.676 | 0.04516 | 31 | 353.34 | 88.08 | 21.27 | 3.06 |
| 0.00006 | 0.689 | 0.07660 | 30 | 1045.60 | 174.10 | 28.51 | 3.25 |
| 0.00008 | 0.698 | 0.08616 | 31 | 2154.51 | 269.18 | 33.27 | 3.03 |

**Table – 2 Stability Constant for Cd(ii) Ramipril System**

| System | Composition of Compounds | Stability Constants |
|---|---|---|
| $[Cd(Rami)]^{2+}$ | 1:1 | 5.50 |
| $[Cd(Rami)2]^{2+}$ | 1:2 | 10.96 |
| $[Cd(Rami)3]^{2+}$ | 1:3 | 15.50 |

**Conclusion:**

The polarographic investigation of the Cd(II)-Ramipril system conducted at 25°C has provided valuable insights into the electrochemical behavior and complex formation in this metal-ligand system. The reversible and diffusion-controlled reduction of Cd(II) in the presence of Ramipril, as well as the observed shifts in half-wave potential, strongly suggest the formation of Cd(II)-Ramipril complexes.

The determination of overall formation constants (logβ) for these complexes further solidifies the notion of complex formation and highlights the thermodynamic stability of the resulting species. The stability constants for [Cd(Rami)]2+, [Cd(Rami)2]2+, and [Cd(Rami)3]2+ were found to be 5.50, 10.96, and 15.50, respectively, indicating the feasibility and significance of these interactions. These findings enhance our understanding of metal-ligand interactions, offering important insights into the behavior of Cd(II) in the presence of Ramipril. Such knowledge has implications for various scientific fields, including chemistry and pharmacology, and can contribute to the development of new pharmaceutical compounds and therapeutic strategies.

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