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# Evaluation of Electro analytical Behaviour of Famotidine in the Presence of Nickel by Differential Pulse Polarography

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## ABSTRACT

Famotidine (3-[[[2-[(Aminoiminomethyl) amino] - 4thiazolyl] methyl] thio]-N-(aminosulfonyl) propanimidamide) is a histamine H2 Receptor antagonist that is a highly effective human gastric acid secretion inhibitor. Differential pulse polarography (DPP) is used to study the electrochemical properties and quantitative analysis of famotidine on mercury electrodes. The optimum experimental parameters for the differential pulse polarography (DPP) method were: current range 10uA, data acquisition fast, scan rate: 6mV/sec, drop time: 1sec, scan type: forward, pulse amplitude: 100mV. The linearity for famotidine in HPLC and DPP was found in the concentration range of 1 to 8 µM and 10 to 100 µM respectively. The correlation coefficient values for HPLC and DPP were 0.998 and 0.996 respectively. Limit of detection values for HPLC and DPP were found to be 0.3659 µM and 9.7615 µM respectively. Limit of quantification for HPLC and DPP was found 1.2196 µM and 32.23 µM respectivelyFrom the statistical analysis of the proposed technique, the differential pulse polarography method is more sensitive than the HPLC method.

**KEYWORDS:** Metallopharmaceutical, Famotidine, palaeography, electrochemical.

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## 1. INTRODUCpTION

Famotidine (FAM) (**Fig. 1**) is chemically (3-[[[2-[(Aminoiminomethyl) amino] - 4thiazolyl] methyl] thio]-N-(aminosulfonyl) propanimidamide).It is commonly used to treat peptic ulcer disease and gastroesophageal reflux disease. Famotidine is a histamine H2 receptor antagonist that blocks the action of histamine on gastric cells and reduces acid production.

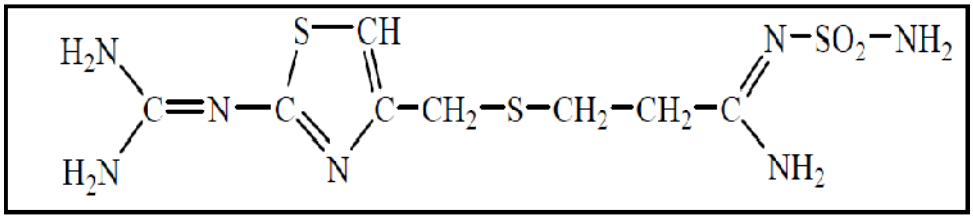


**Figure1: Chemical Structure of Famotidine**

Several techniques including HPLC[1], HPTLC[2], capillary electrophoresis [3], differential pulse voltammetry [4], potentiometric titration [5], polarography [6], chemiluminescence spectroscopy [7] and fluorescence spectrophotometry [8] have been used to determine the dosage form in pharmaceutical formulations. Some of these methods have sufficient sensitivity to determine lower concentrations of drugs; however, many of these techniques have drawbacks in terms of simplicity, cost effectiveness, and accessibility. Differential pulse polarography is characterized by fast speed, simplicity, accuracy and the required instruments are inexpensive. Therefore, it is an important alternative to other analytical techniques and has significant advantages in terms of cost analysis. Considering the great advantages of DPP, we studied the electrochemical characterization of famotidine in the presence of nickel in DPP.

## 2. MATERIALS AND METHOD

### *2.1 Chemicals*

Analytical reagent grade famotidine was used and the solution was prepared in HCl using double distilled water. The purity of the reference standard was famotidine 99.9. Nickel sulfate (Merck), KCl, HCl, NaOH, phosphoric acid, boric acid, acetic acid, sodium acetate, etc., all of which were of analytical grade and were purchased from the local market. Distilled water was used throughout the work. All other reagents used were of analytical grade and could be used without further purification.

### *2.2Preparation of Standard Solutions*

A stock solution of famotidine (1x $10^{-3}$ M) was prepared by dissolving an appropriate amount of the drug in 0.001 M HCl. The absorbance of these stock solutions was measured using ultraviolet-visible (UV/VIS) spectrophotometer and the concentrations of selected ligand were calculated. The

measurements of these drug stock solutions were carried out monthly by keeping under cool condition for stability study.

### *2.3 HPLC Studies Famotidine*

Approximately 40 mg of famotidine was accurately weighed and transferred to a 25 ml volumetric flask. This was dissolved in 15 ml of methanol, made up to volume with methanol and sonicated for 8 minutes. Thus, a working standard solution of 100 µg/ml strength was prepared. From the dilution, 10, 20, 40, 60 and 80 µg/ml were prepared in a 10 ml volumetric flask containing methanol. From each diluted solution, 20 µl of the sample was injected into the column at a flow rate of 1.0 ml / min. Each sample was injected into the column 3 times and the corresponding chromatogram was obtained.

### *2.4 DPP Studies of Ni (II)-famotidineComplex*

To measure the complexation of Ni(II) with famotidine, an electrochemical cell was assembled with 10 mL of a sodium acetate buffer pH 5.00 ± 0.10 containing 0.1 M KCl in deionized water. Then, the solution was thoroughly washed with pure nitrogen for 10 minutes. The polarograms were recorded in the following order: pure support electrolyte after addition of Ni(II) and after addition of each famotidine.

## 3. INSTRUMENTATION

For DPP measurements, the Polarographic analyser model CL-362 supplied by Elico Ltd of Hyderabad was used. Mercury was added as a working electrode, saturated calomel was used as a reference, and platinum wire was used as an auxiliary electrode. A UV-VIS spectrophotometer, PerkinElmer Lambda 25, was used for spectrophotometric analysis in a 1 cm quartz cell. The pH measurement was carried out with the help of an Elico pH meter. Quantitative HPLC was performed on a gradient high pressure liquid chromatography (Perkin Elmer HPLC 1100).

## 4. RESULTS AND DISCUSSION

### *4.1 High Performance Liquid Chromatography (HPLC)*

An RP-HPLC method was proposed as a suitable method for evaluating famotidine in pharmaceutical dosage forms. Good separation was achieved using a C18 column. The chromatographic conditions are adjusted to provide good assay performance. The method involves a mobile phase consisting of methanol-water (80:20, v/v) completed at 270 nm. The retention time was 3.3 minutes, the flow rate was 1 mL min-1, and the injection volume was 10 µl. The total running time measured was 10 minutes. The mobile phase was selected after multiple trials using other

solvent combinations. The mobile phase selection is based on peak parameters (symmetry, tailing), run time, ease of preparation and cost. **Figure 2.** Shows a typical chromatogram obtained from the analysis of standard famotidine using the proposedmethod.

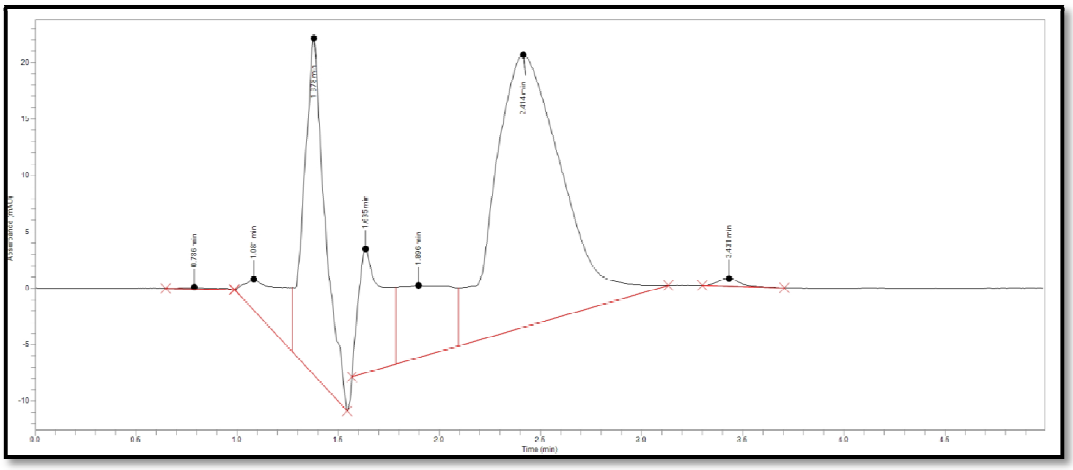

**Figure 2. Chromatogram of Famotidine in Methanol-water (80:20, v/v)**

## *4.2 Differential Pulse Polarography*

The electrochemical behavior of famotidine and zinc on DME was investigated by differential pulse polarography before quantitative determination. DPP curves were recorded in different supporting electrolytes. The results obtained (Figure 3) show that acetate buffer pH 5.0 containing 1.0 M KCl is the best medium for the detection and quantification of famotidine and nickel on mercury electrodes.

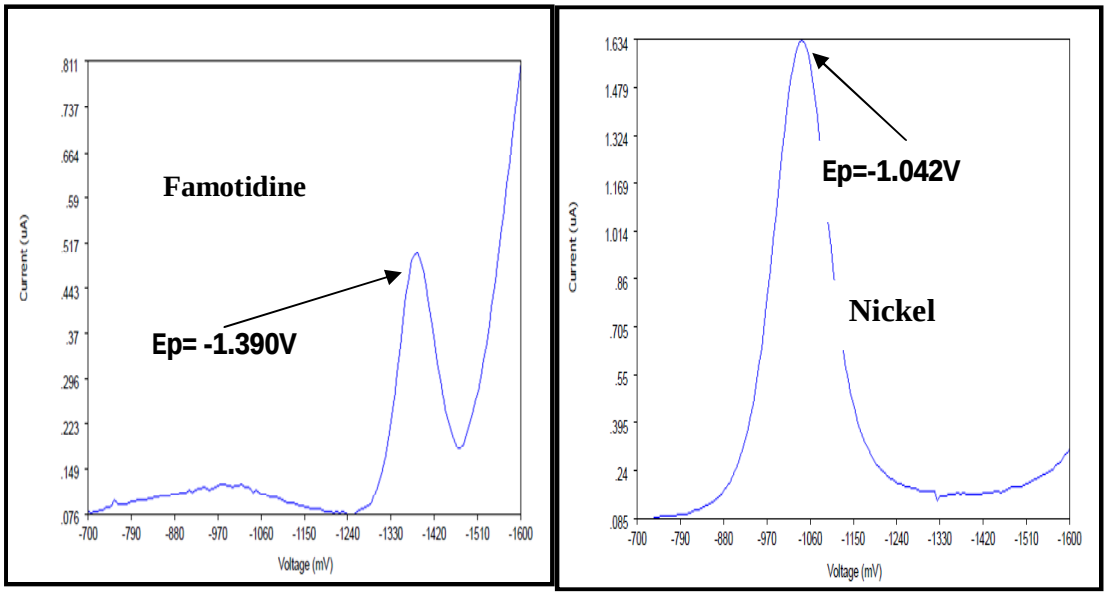


**Figure3. DPP Polarogram of Famotidine and Nickel in Acetate Buffer pH 5.0**

## *4.3 Calibration of Famotidine by HPLC Method*

Various mobile phases containing varying proportions of methanol and water were examined. The methanol:water (8:2 v / v) mobile phase was chosen as the best choice for obtaining well defined and resolved peaks. The optimum detection wavelength and quantitative wavelength used were 290 nm. The retention factor of famotidine was 0.23 ± 0.102. A representative chromatogram of the famotidine standard solution is shown in Figure 2. The linear range of famotidine in high performance liquid chromatography is 1~8μM, and the correlation coefficient is 0.998, as shown in **Figure 4.**

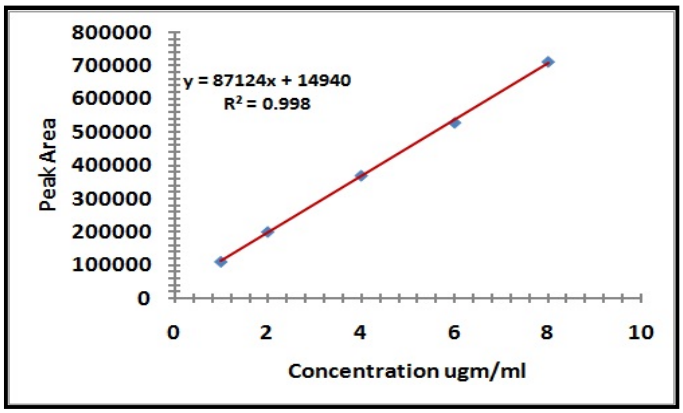


**Figure 4. Linearity Curve of Famotidine by HPLC in Methanol-water (80:20, v/v)**

## *4.4 Calibration of Famotidine by DPP Method*

The prepared famotidine stock solution in acetate buffer was further diluted to 10 mL to obtain a working standard solution having a concentration ranging from 10 to 100 μM. The peak current of the solution was measured at a peak potential of -3.752 V as a blank acetate buffer. A calibration curve for famotidine was then plotted by obtaining the peak current obtained on the y-axis and the concentration of the solution on the x-axis **(Figure. 5).** The curve shows linearity in the range of 10-100 μM with a correlation coefficient of 0.996.**(Table 2).**

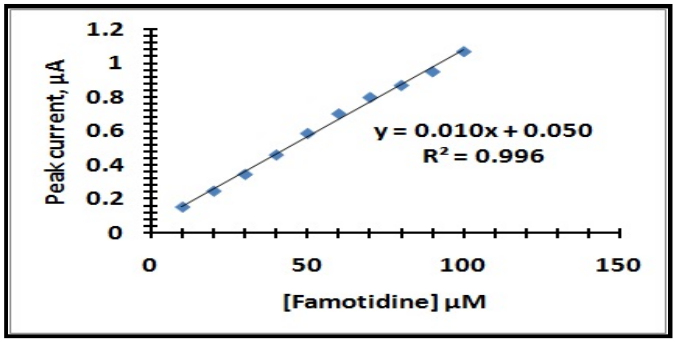


**Figure5. Linearity Curve of Famotidine by DPP in Acetate Buffer pH 5.0**

**Table 2: Linearity of famotidine by DPP in acetate buffer pH 5.0**

| Conc. ( µM) | Ip=Y | Yi=mx+b | Y-Yi | $(Y-Yi)^2$ |
|---|---|---|---|---|
| 10 | 0.150 | 0.15 | -0.006 | 0 |
| 20 | 0.244 | 0.25 | -0.007 | 3.6E-05 |
| 30 | 0.343 | 0.35 | 0.008 | 4.9E-05 |
| 40 | 0.458 | 0.45 | 0.035 | 6.4E-05 |
| 50 | 0.585 | 0.55 | 0.051 | 0.001225 |
| 60 | 0.701 | 0.65 | 0.048 | 0.002601 |
| 70 | 0.798 | 0.75 | 0.019 | 0.002304 |
| 80 | 0.869 | 0.85 | 0 | 0.000361 |
| 90 | 0.950 | 0.95 | 0.019 | 0 |
| 100 | 1.069 | 1.05 | 0 | 0.000361 |
| | | | $\sum(Y-Yi)^2$ | 0.007001 |
| | | SD | | 0.02958 |
| | | LOD | | 9.7615 µM |
| | | LOQ | | 32.23 µM |
| | | Regression equation : y= 0.010x + 0.050 | | |
| | | Regression Coefficient : $R^2$ = 0.996 | | |

## *4.5 Calibration of Nickel by DPP Method*

The prepared stock solution of Ni in acetate buffer pH 5.0 was further diluted to 10 mL to obtain a working standard solution having a concentration ranging from 10 to 100 µM. The peak current of the Ni solution was measured at a peak potential of -1.042 V as a blank acetate buffer. The linear curve and DPP Polarogram of Ni are shown in Fig. 6, and the correlation coefficient is 0.998.

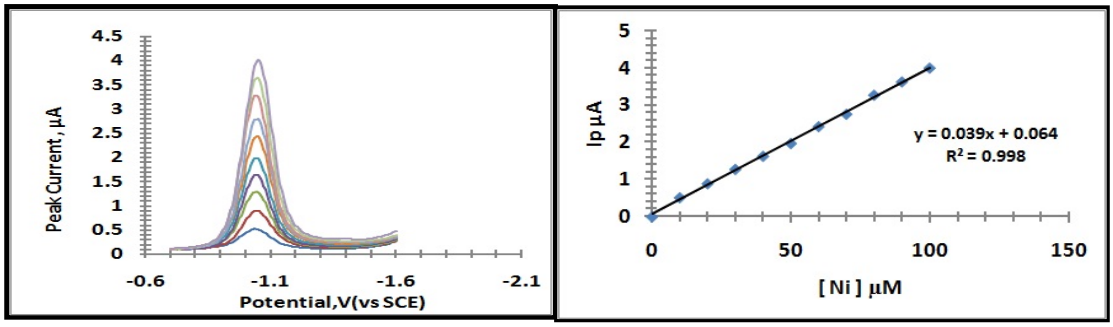


**Figure6.Differential Pulse Polarogram and Linearity of Increasing Concentration of Nickel at pH 5.0**

## 5. CONCLUSION

Both proposed techniques have been successfully developed and applied to the determination of famotidine in pharmaceutical preparations. Compare the results of the two techniques; HPLC is a more sensitive technique than the DPP method. However, HPLC techniques have disadvantages such as long analysis times; consumption of large amounts of reagents and expensive, complicated operations, high maintenance costs, expensive equipment, and experimental conditions requiring good control.

The DPP method has great potential as an alternative to this application and has been successfully developed for the determination of famotidine, nickel and its metal complexes in pharmaceutical preparations. **(Table 4)**

**Table: 4 Analytical parameters for calibration curves for famotidine and Nickel by DPP and HPLC**

| Method | Material | Regression Equation | Linearity µM | Ep (V) | LOD µM | LOQ µM | $R^2$ |
|---|---|---|---|---|---|---|---|
| HPLC | Famotidine | y = 87124x + 14940 | 1-8 | - | 0.3659 | 1.2196 | 0.998 |
| DPP | Famotidine | y= 0.010x + 0.050 | 10-100 | -1.390 | 9.7615 | 32.23 | 0.996 |
| DPP | Nickel | y = 0.039x + 0.064 | 10-100 | -1.042 | 4.8534 | 16.178 | 0.998 |

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