*Research Article*

# Validation and comparative electrochemical analysis of aspirin in formulation

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**Abstract**

**Objective:** The objective of the work is to develop a simple precise, rapid accurate, sensitive and comparative electrochemical titrimetric method for quantitative determination of aspirin in pharmaceutical dosage form. **Material and methods:** The titration was carried out using standardized 0.1 M sodium hydroxide against formulated aspirin sample and all the results were statistically validated. Here Potentiometric and Conductometric titration method were used. **Results and Discussion:** The proposed potentiometric method was found to be precise with % RSD <1 (n = 5) as the method showed strict linearity ($r^2$ > 0.99) in between 100-200 mg of drug substance weight. The percentage recovery of aspirin in the optimized method was found to be lies in between 97 % to 101 %. The proposed conductometric method was found to be precise with % RSD >1 (n = 6). The method showed strict linearity ($r^2$ > 0.99) between 100-200 mg of drug substance weight. The percentage recovery of aspirin in the optimized method was almost 100% to the corresponding 100 and 300 mg of the drug. **Conclusion:** Potentiometric method was seems to have more effective one rather than the conductometric method one as aspirin can be assayed electrochemically with in concentration range with this validated method that was optimized without the effect of excipients.

***Keywords*:** Validation, Titration, Potentiometric method, Conductometric method, precision, Percentage recovery.

## Introduction

Aspirin, also known as acetylsalicylic acid (ASA), is a medication used to treat pain, fever, or inflammation. In potentiometric titration the potential of an indicator electrode is measured as a function of the volume of titrant added. The equivalence point of the reaction will be reach by a sudden change in potential in a plot of e.m.f reading against the volume of titrant solution. In this method a pH meter can be used having an indicator electrode or glass electrode (give reference). The electrical current through a chemical cell is carried out by the ionic species in the solution conductometrically. The ease with which current is conducted through a solution (under the influence of potential difference applied across two electrodes) is mainly depends upon the concentrations and kind of ions in the solution. If two suitable electrodes are present in a solution and potential difference is applied across those electrodes then current will flow through the solution. During progress of a conductometric titration changes in the conductivity of the solution usually occur and at the end point involving neutralization or precipitation reaction the conductivity of the solution will be minimum. The equivalence point may be located graphically by plotting the change in conductance as a function of the volume of titrant added. The term 'titrimetric analysis' or volumetric analysis refers to quantitative chemical analysis carried out by determining the volume of a solution of accurately known concentration which is required to react quantitatively with a measured volume of a solution of the substance to be determined (Bagchi et. al., 2016).

In this study the comparative electrochemical method was developed by using linearity, accuracy and precision as parameters which were statistically validated.

## Chemical assay

A chemical assay, as studied under the branch of chemistry called analytical chemistry, is divided into qualitative (identity) analysis and quantitative (amount of substance) analysis. Some of the methods used in qualitative analysis include extraction, distillation, precipitation and other methods that determine physical and chemical properties. Quantitative analysis involves the measurement of the isolated volume or weight of the substance. A chemical assay also utilizes instruments and techniques, such as

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spectroscopy, chromatography and electrophoresis, to measure the physical quantities of the analyte.

**Validation Parameters - Assays**

USP General Chapter 1225, as well as the ICH Guideline for Industry (Text on Analytical Procedures), provide cursory descriptions of typical validation parameters, how they are determined, and which subset of each parameter is required to demonstrate validity, based on the method's intended use. For example, it would be inappropriate to determine limits of detection or quantisation for an active ingredient using an assay method intended for finished product release. However, if the method was intended to detect trace quantities of the active ingredient for purposes of a cleaning validation study, then knowledge of the detection and quantification limits are appropriate and necessary. For this reason, validation of each assay or test method should be performed on a case-by-case basis, to ensure that the parameters are appropriate for the method's intended use. This is even more important when validating stability-indicating assay methods, because these validations are more complex - for example, they may require forced degradation, samples spiked with known degrades, literature searches, etc.

**Material and methods**

**Materials**

Potassium Hydrogen Phthalate and Ethanol were required and it was purchased from Merck India Pvt. Ltd. Also Sodium hydroxide was required as it was purchased from Loba Chem Pvt. Ltd. Dilution has been carried by using ethanol.

**Instrument and Apparatus required**

A GOLD model 533 pH meter with Glass electrode and a simple weight machine from EAGLE were used. From the instrument the potential reading was noted which having the unit called Milli volt (mV). All the glass apparatus that were used are made of BOROSILICATE GLASS and were properly calibrated.

**Potentiometric titration**

Titration no 1: Standardization of 0.1 M NaOH solution was performed with potassium hydrogen phthalate (KHPhthalate) by using potentiometric method where ethanol was used as solvent.

Titration no 2: Assay of Aspirin solutions (Tablet) was performed by using Potentiometric method and the results were validated by using different parameters (linearity, accuracy and precision) statistically. The results were obtained by using 50, 100, 150, 200, 250, 300 mg of powdered tablet and the results were statistically validated.

**Results and discussion**

**Potentiometric method**

The method was followed by using formula from according to I.P. as:

1 ml 0.5 M of NaOH is equivalent to 0.04504 gm of Aspirin.

Actual strength found during the experiment was 0.15 M.

**Linearity**

The linearity of an analytical procedure is its ability (within a given range) to obtain test results, which are directly proportional to the concentration (amount) of analyte in the

**Table 1.** Linearity of Aspirin (Powdered Tablet)

| 50 mg | | 100 mg | | 150 mg | | 200 mg | | 250 mg | | 300 mg | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Vol. of NaOH(x) | mV(y) | Vol. of NaOH(x) | mV(y) | Vol. of NaOH(x) | mV(y) | Vol. of NaOH(x) | mV(y) | Vol. of NaOH(x) | mV(y) | Vol. of NaOH(x) | mV(y) |
| 0 | 260 | 0 | 192 | 0 | 232 | 0 | 251 | 0 | 268 | 0 | 273 |
| 5 | 110 | 5 | 53 | 5 | 104 | 5 | 100 | 5 | 114 | 5 | 112 |
| 10 | 73 | 10 | 9 | 10 | 29 | 10 | 53 | 10 | 63 | 10 | 93 |
| 15 | -133 | 15 | -127 | 15 | -127 | 15 | -132 | 15 | -163 | 15 | -144 |
| 20 | -144 | 20 | -140 | 20 | -140 | 20 | -140 | 20 | -168 | 20 | -156 |
| 25 | -156 | 25 | -168 | 25 | -168 | 25 | -155 | 25 | -180 | 25 | -160 |
| 30 | -160 | 30 | -169 | 30 | -175 | 30 | -160 | 30 | -210 | 30 | -170 |

**Table 1.** Continue….

| Wt.(mg) | Wt. (gm) | x1(initial vol. of NaOH) | x2(final vol. of NaOH) | y1(mV of x1) | y2(mV of x2) | y(mV at end point) | x(end point) ml | Wt. (gm) | % assay |
|---|---|---|---|---|---|---|---|---|---|
| 50 | 0.05 | 10 | 15 | 73 | -133 | 0 | 11.772 | 0.1590612 | 158.12233 |
| 100 | 0.1 | 10 | 15 | 9 | -127 | 0 | 10.331 | 0.1395909 | 109.59088 |
| 150 | 0.15 | 10 | 15 | 29 | -127 | 0 | 10.929 | 0.1476792 | 98.452821 |
| 200 | 0.2 | 10 | 15 | 53 | -132 | 0 | 11.432 | 0.154475 | 77.237514 |
| 250 | 0.25 | 10 | 15 | 63 | -163 | 0 | 11.394 | 0.1539531 | 61.581239 |
| 300 | 0.3 | 10 | 15 | 93 | -144 | 0 | 11.96202532 | 0.1616309 | 53.876962 |

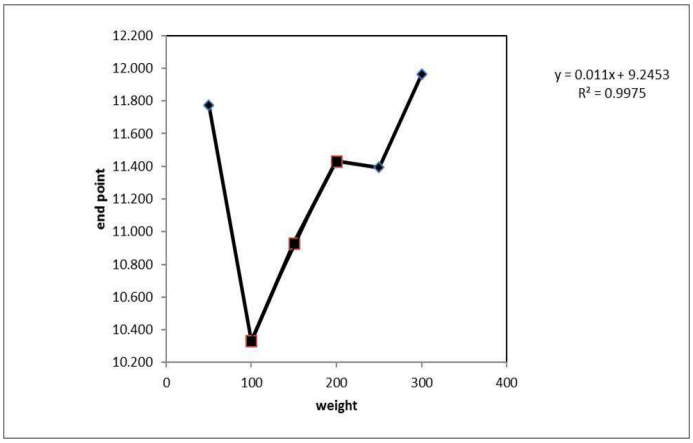


**Figure 1.** Linearity graph of Aspirin

Within a range of 100-200 mg powdered tablet the process was

sample. In order to determine the quantity of any analyte present in unknown sample, some kind of relationship (mathematical/empirical) between concentration and response was essential where response should be directly proportional to the concentration (Tewari et. al., 2017).

**Accuracy**

The accuracy of an analytical procedure express closeness of agreement between the values, which is accepted either as a conventional true value or an accepted reference value and the value can be found.

**Evaluation**

At each concentration level % mean recovery, SD and % RSD were calculated.

**Acceptance criteria**

Assay recovery should be between 98%-102%. A simple logic behind this performance characteristic was whether the procedure was capable of estimating a true value or not (Tewari et. al., 2017).

**Precision**

Precision is the measurement of how close the data values to each other for a number of measurements under the same analytical conditions. Precision may be considered at three levels according to ICH.

System Precision

Precision under same operative conditions (within a laboratory over a short period of time using the same analyst with the same equipment) was determined. Mean, SD and %RSD were calculated from data. The system precision is checked by using standard chemical substance to ensure that the analytical system is working properly. In this retention time and area of six determinations is measured and % RSD should be calculated.

Method Precision

**Table 2.** accuracy of Aspirin (Powdered Tablet)

| 50 mg | | 100 mg | | 150 mg | | 200 mg | | 250 mg | | 300 mg | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Vol. of NaOH(x) | mV(y) | Vol. of NaOH(x) | mV(y) | Vol. of NaOH(x) | mV(y) | Vol. of NaOH(x) | mV(y) | Vol. of NaOH(x) | mV(y) | Vol. of NaOH(x) | mV(y) |
| 0 | 237 | 0 | 242 | 0 | 268 | 0 | 251 | 0 | 253 | 0 | 261 |
| 5 | 1 | 5 | 2 | 5 | 65 | 5 | 84 | 5 | 95 | 5 | 100 |
| 10 | -100 | 10 | -298 | 10 | -245 | 10 | -55 | 10 | 85 | 10 | 93 |
| 15 | -147 | 15 | -293 | 15 | -261 | 15 | -132 | 15 | -255 | 15 | -261 |
| 20 | -144 | 20 | -290 | 20 | -267 | 20 | -140 | 20 | -261 | 20 | -263 |
| 25 | -156 | 25 | -282 | 25 | -271 | 25 | -155 | 25 | -268 | 25 | -268 |
| 30 | -160 | 30 | -297 | 30 | -272 | 30 | -160 | 30 | -275 | 30 | -271 |

**Table 3.** % Recovery

| actual wt(mg) | x1(initial vol. of NaOH) | x2(final vol. of NaOH) | y1(mV of x1) | y2(mV of x2) | y(mV at end point) | x(end point) ml | Wt. got (mg) | % recovery |
|---|---|---|---|---|---|---|---|---|
| 50 | 10 | 15 | 1 | -297 | 0 | 10.01678 | 70.16168 | 140.3234 |
| 100 | 10 | 15 | 22 | -298 | 0 | 10.34375 | 99.88636 | 99.88636 |
| 150 | 10 | 15 | 55 | -245 | 0 | 10.91667 | 151.9697 | 101.3131 |
| 200 | 10 | 15 | 99 | -255 | 0 | 11.39831 | 195.755 | 97.8775 |
| 250 | 10 | 15 | 80 | -120 | 0 | 12 | 250.4545 | 100.1818 |
| 300 | 10 | 15 | 103 | -100 | 0 | 12.53695 | 299.2678 | 99.75593 |

The result found to be accurate at 100-300 mg of powdered tablet.

**Table 4.** Precision of Aspirin (Powdered Tablet)

| 250 mg..1 | | 250 mg..2 | | 250 mg…3 | | 250 mg…4 | | 250 mg…5 | | 250 mg…6 | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Vol. of NaOH(x) | mV(y) | Vol. of NaOH(x) | mV(y) | Vol. of NaOH(x) | mV(y) | Vol. of NaOH(x) | mV(y) | Vol. of NaOH(x) | mV(y) | Vol. of NaOH(x) | mV(y) |
| 0 | 205 | 0 | 245 | 0 | 183 | 0 | 232 | 0 | 248 | 0 | 202 |
| 5 | 100 | 5 | 122 | 5 | 120 | 5 | 122 | 5 | 126 | 5 | 112 |
| 10 | 73 | 10 | 90 | 10 | 83 | 10 | 99 | 10 | 105 | 10 | 114 |
| 15 | -244 | 15 | -256 | 15 | -261 | 15 | -238 | 15 | -212 | 15 | 63 |
| 20 | -276 | 20 | -267 | 20 | -270 | 20 | -268 | 20 | -266 | 20 | -256 |
| 25 | -278 | 25 | -267 | 25 | -279 | 25 | -270 | 25 | -279 | 25 | -268 |
| 30 | -276 | 30 | -268 | 30 | -268 | 30 | -270 | 30 | -266 | 30 | -270 |

**Table 5.** % Assay calculation

| z | x1 | x2 | y1 | y2 | y | xml(end point) | Wt. (gm) | % assay |
|---|---|---|---|---|---|---|---|---|
| 1 | 10 | 15 | 73 | -244 | 0 | 11.151 | 0.2511 | **100.45199** |
| 2 | 10 | 15 | 90 | -256 | 0 | 11.301 | 0.2545 | **101.79561** |
| 3 | 10 | 15 | 83 | -261 | 0 | 11.206 | 0.2524 | **100.94721** |
| 4 | 10 | 15 | 99 | -238 | 0 | 11.469 | 0.2583 | **103.31134** |
| 5 | 10 | 15 | 105 | -212 | 0 | 11.656 | 0.2625 | **104.99861** |
| 6 | 15 | 20 | 63 | -256 | 0 | 15.98746082 | 0.36 | 144.01505 |
| | | | | | | **Mean** | **11.357** | |
| | | | | | | **S.D.** | **0.206233099** | |
| | | | | | | **% RSD** | **1.815963346** | |

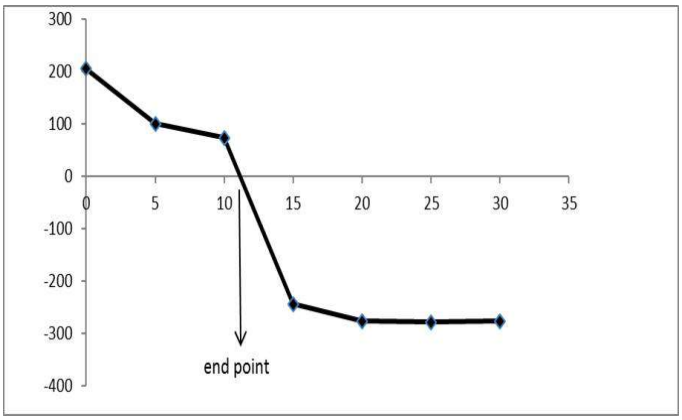


**Figure 2.** Determination of end point

In method precision, a homogenous sample of single batch should be analysed 6 times. This indicates whether a method is giving consistent results for a single batch. In this analysis the sample has been analysed six times with the calculation of %RSD.

Intermediate Precision (Ruggedness)

Precision under different laboratory conditions (within-laboratory variation, as on different days, or with different analysts, or equipment within the same laboratory) has been carried out.

Reproducibility

Precision between laboratories/intermediate precision can be considered during the standardization of a procedure before it is submitted to the pharmacopoeia. A simple logic behind this parameter was some degree of inconsistency (occurrence of random error) was allowed for every analytical measurement. But, the extent depends on steps involved (weighing, dilution etc.), technique used in other expected variables (stability) and intended use of the procedure (Tewari et. al., 2017).

Method was found to be precised up to 5 consecutive results. So it is evident that 300mg drug was precised according to the result.

**Conductometric method**

Actual strength found during the experiment was 0.25M

The linearity of an analytical procedure is its ability (within a given range) to obtain test results, which are directly proportional to the concentration (amount) of analyte in the sample. In order to determine the quantity of any analyte present in unknown sample, some kind of relationship (mathematical/empirical) between concentration and response was essential where response should be directly proportional to the concentration (Tewari et. al., 2017).

So it is evident that within the range of 100-200 mg of drug, the method is Linear.

**Accuracy**

The accuracy of an analytical procedure express closeness of agreement between the values, which is accepted either

**Table 6.** Linearity of Aspirin (Powdered Tablet)

| 00mg: | | 200mg: | | 300mg: | | 400mg: | | 500mg: | |
|---|---|---|---|---|---|---|---|---|---|
| Vol. of NaOH(x) | mV(y) | Vol. of NaOH(x) | mV(y) | Vol. of NaOH(x) | mV(y) | Vol. of NaOH(x) | mV(y) | Vol. of NaOH(x) | mV(y) |
| 0 | 0.00097 | 0 | 0.00117 | 0 | 0.00103 | 0 | 0.00055 | 0 | 0.00173 |
| 5 | 0.148 | 5 | 0.052 | 5 | 0.0876 | 5 | 0.0421 | 5 | 0.0862 |
| 10 | 0.284 | 10 | 0.094 | 10 | 0.136 | 10 | 0.078 | 10 | 0.156 |
| 15 | 0.378 | 15 | 0.137 | 15 | 0.183 | 15 | 0.111 | 15 | 0.202 |
| 20 | 0.463 | 20 | 0.187 | 20 | 0.232 | 20 | 0.144 | 20 | 0.24 |
| 25 | 0.547 | 25 | 0.257 | 25 | 0.289 | 25 | 0.175 | 25 | 0.309 |
| 30 | 0.626 | 30 | 0.279 | 30 | 0.345 | 30 | 0.216 | 30 | 0.373 |

**Table 7.** % Recovery Calculation

| Wt. (mg) | Xml (End Point) | Wt. (gm)(x) | % Assay |
|---|---|---|---|
| 100 | 5 | 0.1126 | 112.6 |
| 200 | 10 | 0.2252 | 112.6 |
| 300 | 10 | 0.2252 | 75.06667 |
| 400 | 15 | 0.3378 | 84.45 |
| 500 | 10 | 0.2252 | 45.04 |
| Mean = 85.951333; SD = 28.349471; % RSD = 32.98317. | | | |

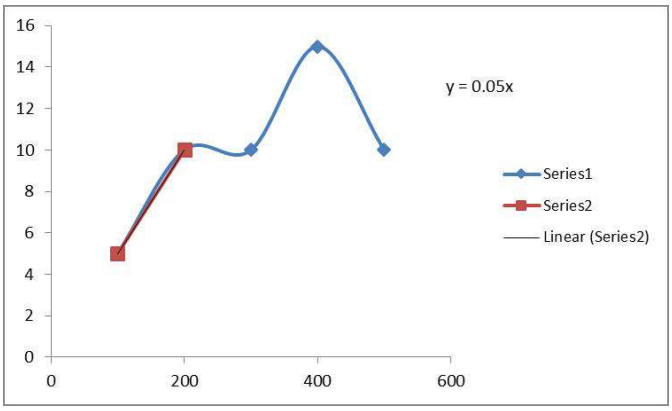


**Figure 3.** Linearity graph of Aspirin

as a conventional true value or an accepted reference value and the value can be found.

### Evaluation

At each concentration level % mean recovery, SD and % RSD were calculated.

### Acceptance criteria

Assay recovery should be between 98%-102%. A simple logic behind this performance characteristic was whether the procedure was capable of estimating a true value or not (Tewari et. al., 2017).

Hence the recovery of the aspirin came accurately at the values of **100 mg & 300 mg**.

Precision was evaluated with by taking 300mg of powdered drug

So it is evident that 300mg drug was precised according to the result.

### Conclusion

The developed method was completely validated showing satisfactory data for all method validated parameters tested. It was seen that both these methods were linear at 100-200 mg of drug concentration. In case of potentiometry it showed accuracy in between 100-300 mg of drug concentration where in case of conductometric it is having 100 mg and 300 mg. In case of potentiometry results were precised if we take 250 mg and in case of conductometry the precised results were found in 300 mg of drug concentration. So it can be concluded that both this electrochemical method can be conveniently used having wide range of concentration for the assay of bulk drugs as well as for pharmaceutical dosage form in quality control laboratory as the proposed method can be used to analyse aspirin in its pharmaceuticals forms without interference from excipients since potentiometric method was seems to have more effective one rather than the conductometric method one.

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**Table 8.** Accuracy of Aspirin (Powdered Tablet)

| 100mg: | | 200mg: | | 300mg: | | 400mg: | | 500mg: | |
|---|---|---|---|---|---|---|---|---|---|
| Vol. of NaOH | mV (y) | Vol. of NaOH | mV (y) | Vol. of NaOH | mV (y) | Vol. of NaOH | mV (y) | Vol. of NaOH | mV (y) |
| 0 | 0.00089 | 0 | 0.00072 | 0 | 0.00094 | 0 | 0.00076 | 0 | 0.00207 |
| 5 | 0.134 | 5 | 0.0362 | 5 | 0.7528 | 5 | 0.00092 | 5 | 0.05602 |
| 10 | 0.260 | 10 | 0.0927 | 10 | 0.09098 | 10 | 0.133 | 10 | 0.8326 |
| 15 | 0.317 | 15 | 0.152 | 15 | 0.126 | 15 | 0.162 | 15 | 0.143 |
| 20 | 0.398 | 20 | 0.229 | 20 | 0.217 | 20 | 0.215 | 20 | 0.179 |
| 25 | 0.462 | 25 | 0.318 | 25 | 0.325 | 25 | 0.243 | 25 | 0.265 |
| 30 | 0.532 | 30 | 0.467 | 30 | 0.382 | 30 | 0.283 | 30 | 0.328 |

**Table 9.** % recovery Calculation

| Actual wt (mg) | End Point (y) | Wt. got (mg)(x) | % Recovery |
|---|---|---|---|
| 100 | 5 | 100 | 100 |
| 200 | 15 | 300 | 150 |
| 300 | 15 | 300 | 100 |
| 400 | 10 | 200 | 50 |
| 500 | 15 | 300 | 60 |

**Table 10**. Precision of Aspirin (Powdered Tablet)

| S. No. | End Point | Wt. (gm) | % Assay |
|---|---|---|---|
| 1 | 21.12 | 0.105956 | 0.035319 |
| 2 | 21.05 | 0.159986 | 0.053329 |
| 3 | 20.75 | 0.109855 | 0.036618 |
| 4 | 20.47 | 0.850988 | 0.028366 |
| 5 | 21.2 | 0.13492 | 0.044973 |
| 6 | 21.38 | 0.360038 | 0.120013 |
| Mean = 20.995; S.D = 0.330015151; % RSD = 1.571874976 | | | |

**Conflicts of interest: Nil**

## References

Bagchi A, Raha A, Mukherjee P, Chokroborty S, Hossain I. 2016. Development and validation of a comparative study of standardization process between titrimetric method and a method of electrochemistry (potentiometry). International Journal of Recent Advances in Pharmaceutical Research, 6(2):19-27.

Beckett AH, Stenlake JB. 2007. Practical Pharmaceutical Chemistry. 4th Ed., Vol. I & II. CBS Publishers and Distributors, New Delhi.

Tewari A, Bagchi A, Raha A, Mukherjee P, Pal M. 2017. Preparation, Estimation and Validation of the parameters of the standard curve of Ibuprofen by comparative study. Asian Journal of Pharmacy and Pharmacology, 3(3):79-85.

Watson DG. 2012. Pharmaceutical Analysis. 3rd Ed., Churchill Livingstone, London: Harcourt Publishers Limited, Essex CM 20 2JE.