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Original Article

Validated Non-Aqueous Conductometric Studies of Ibuprofen in Formulation

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ABSTRACT

Introduction: A simple precise, rapid accurate and sensitive non-aqueous conductometric titration method was developed for quantitative determination of ibuprofen from pharmaceutical dosage form. **Material and Methods:** The titration was carried out using standardized 0.1 N perchloric acid against the formulated ibuprofen solution. **Result and Discussion:** The proposed method was found to be precise with % RSD <1 (n = 5). The method showed strict linearity (r^2 > 0.99) in between 200-600 mg of drug substance weight. The percentage recovery of ibuprofen in the optimized method was found to be lies in between 98 % to 102 %. **Conclusion:** The validated method was optimized without the effect of excipients.

Key Word: Validation, Non-aqueous titration, Conductometric method, Percentage recovery, Ibuprofen.

1. INTRODUCTION

Ibuprofen is a medication in the non-steroidal anti-inflammatory drug (NSAID) class that is used for treating pain, fever, and inflammation [1].

Principle of conductometric titration

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

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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 [2].

Estimation of Validation Parameters

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 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.

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.

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.

Repeatability

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

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 equipments 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 [3].

Chemical assay [4]

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

Validation Parameters – Assays [5]

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.

2. MATERIAL AND METHODS

Materials

Potassium Hydrogen Phthalate, Acetone and glacial acetic acid were required and it was purchased from Merck India Pvt. Ltd. Also Sodium hydroxide and Perchloric acid were required as it was purchased from Loba Chem Pvt. Ltd. Dilution has been carried by using glacial acetic acid. The ibuprofen tablets were used that is known as Brufen 400 of Abbott India Ltd.

Instrument and Apparatus required

A SYSTROICS model 306 Conductivitymeter with Conductivity cell type CD-10 and a simple weight machine from EAGLE was used. From the instrument conductance reading was noted which having the unit called Millisiemens (mS). All the glass apparatus that were used are made of BOROSILICATE GLASS and were properly calibrated.

Conductometric titration

Titration no 1: Standardization of 0.1 M Perchloric acid solution was performed with potassium hydrogen phthalate (KHPhthalate) by using conductometric method where glacial acetic acid was used as solvent.

Titration no 2: Assay of ibuprofen solutions (Tablet) was performed by using conductometric method and the results were validated by using different parameters (linearity, accuracy and precision) statistically. The results were obtained by using 200, 300, 400, 500, 600 mg of powdered tablet.

3. RESULT AND DISCUSSION

According to IP

1 ml 0.1 M of $HClO_4$ is equivalent to 0.02063 gm of ibuprofen.

Actual strength found during the experiment was 0.03 M

Linearity

Table 1: Linearity calculation of Ibuprofen (Tablet)

200 mg		300 mg		400 mg		500 mg		600 mg	
Vol. of $HClO_4$	mS	Vol. of $HClO_4$	mS	Vol. of $HClO_4$	mS	Vol. of $HClO_4$	mS	Vol. of $HClO_4$	mS
0	0.00145	0	0.0194	0	0.0102	0	0.0174	0	0.0212
5	0.09	5	0.192	5	0.16	5	0.185	5	0.18
10	0.281	10	0.265	10	0.229	10	0.261	10	0.254
15	0.362	15	0.305	15	0.269	15	0.307	15	0.293
20	0.411	20	0.329	20	0.292	20	0.333	20	0.316
25	0.43	25	0.344	25	0.308	25	0.35	25	0.335
30	0.441	30	0.354	30	0.317	30	0.363	30	0.345
35	0.447	35	0.36	35	0.324	35	0.371	35	0.353
40	0.449	40	0.366	40	0.331	40	0.371	40	0.357
45	0.449	45	0.366	45	0.336	45	0.369	45	0.357
50	0.446	50	0.364	50	0.336	50	0.36	50	0.35

Table 2: % Assay Calculation

wt(mg)	wt (gm)	xml(end point)	wt (gm)	% assay
200	0.2	12.86	0.0795905	39.79527
300	0.3	24	0.148536	49.512
400	0.4	32.91	0.20368	50.919998
500	0.5	24.86	0.1538585	30.771708
600	0.6	25	0.154725	25.7875

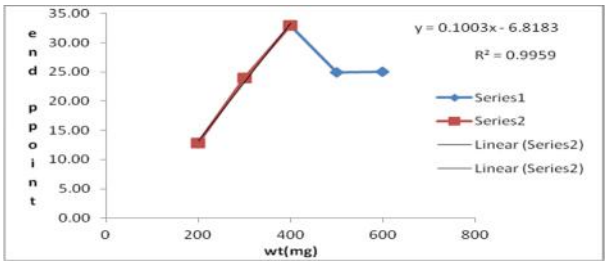

Fig 1: Linearity graph of Ibuprofen

Within a range of 200-400mg of powdered tablet the process was linear.

Accuracy

Table 3: Accuracy of Ibuprofen (Powdered Tablet)

200 mg		300 mg		400 mg		500 mg		600 mg	
Vol. of $HClO_4$	mS	Vol. of $HClO_4$	mS	Vol. of $HClO_4$	mS	Vol. of $HClO_4$	mS	Vol. of $HClO_4$	mS
0	0.00145	0	0.0194	0	0.0102	0	0.0174	0	0.0212
5	0.09	5	0.192	5	0.16	5	0.185	5	0.18
10	0.281	10	0.265	10	0.229	10	0.261	10	0.254
15	0.362	15	0.305	15	0.269	15	0.307	15	0.293
20	0.411	20	0.329	20	0.292	20	0.333	20	0.316
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40	0.449	40	0.366	40	0.331	40	0.371	40	0.357
45	0.449	45	0.366	45	0.336	45	0.369	45	0.357
50	0.446	50	0.364	50	0.336	50	0.36	50	0.35

Table 4: % Assay Calculation

actual wt. (mg)	end point	Wt. got(mg)	% recovery
200	12.86	196.194	98.0972
300	23.12	298.488	99.4959
400	32.91	396.095	99.0237
500	44.23	508.956	101.791
600	52.36	590.013	98.3355

Method was accurate in between the range of 200 to 600 mg of powdered tablet.

Precision

Table 5: Precision of Ibuprofen (Powdered Tablet)

300 mg..1		300 mg..2		300 mg..3		300 mg..4		300 mg..5		300 mg..6	
Vol. of $HClO_4$	mS	Vol. of $HClO_4$	mS	Vol. of $HClO_4$	mS	Vol. of $HClO_4$	mS	Vol. of $HClO_4$	mS	Vol. of $HClO_4$	mS
0	0.0003	0	0.0132	0	0.0136	0	0.0207	0	0.00041	0	0.0126
5	0.0797	5	0.186	5	0.21	5	0.2	5	0.1695	5	0.126
10	0.198	10	0.276	10	0.273	10	0.271	10	0.263	10	0.262
15	0.269	15	0.323	15	0.295	15	0.313	15	0.314	15	0.314
20	0.299	20	0.346	20	0.322	20	0.335	20	0.34	20	0.342

25	0.311	25	0.362	25	0.335	25	0.347	25	0.355	25	0.357
30	0.317	30	0.371	30	0.346	30	0.355	30	0.363	30	0.365
35	0.322	35	0.374	35	0.362	35	0.361	35	0.369	35	0.372
40	0.322	40	0.375	40	0.369	40	0.361	40	0.371	40	0.372
45	0.315	45	0.375	45	0.369	45	0.353	45	0.379	45	0.36
50	0.311	50	0.369	50	0.358	50	0.345	50	0.379	50	0.356

Table 6: % Assay calculation

Sl. no	xml(end point)	Wt. (gm)	% assay
1	17.12	0.1059557	0.03532
2	25.85	0.1599857	0.05333
3	17.75	0.1098548	0.03662
4	13.75	0.0850988	0.02837
5	21.8	0.1349202	0.04497
6	27.38	0.3600376	0.12001
		Mean 20.608	
		S.D 5.33153	
		% RSD 25.8707	

4. CONCLUSION

The developed method was completely validated showing satisfactory data for all method validated parameters tested. It can be conveniently used for the conductometric titration method in bulk drugs, pharmaceutical dosage form in quality control laboratory. The proposed method can analyse Ibuprofen in its pharmaceuticals forms without interference from excipients.

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