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A sensitive spectrophotometric determination of ammonium molybdate as a residual catalyst in tinidazole bulk in parts per million levels

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Abstract

Tinidazole[2,] is used as an antiprotozoal and amoebic. It is manufactured by condensation of 2 methyl 5 Nitro Imidazole followed by oxidation with hydrogen Peroxide using Ammonium Molybdate as a catalyst. Trace level of this catalyst as residual molybdenum may remain in the product. The residual Molybdenum content of bulk samples of Tinidazole is determined by colorimetric procedure. The method is based on principle that in acid solutions. In the presence of a suitable reducing agent such as stannous chloride, Thiocyanate gives an orange red colour with Molybdenum. This coloured compound, which is a Thiocyanate complex of Quinquevalent Molybdenum, is extracted into Amyl alcohol and determined spectrophotometrically.

Beer's law was obeyed in the concentration ranges 2.0 to10.0 ppm .The sensitivity of the method surpasses that of the reported spectrophotometric methods. The method was successfully applied for the determination of Ammonium Molybdate in Tinidazole (Bulk) as residual catalyst in Parts per Million Level.

Key Words: Spectrophotometry, Tinidazole, Bulk.

Introduction

A Sensitive Spectrophotometric method for determination of Ammonium Molybdate as Residual catalyst in Tinidazole (Bulk). Ammonium Molybdate is used as catalyst in Oxidation reaction in manufacturing the Tinidazole.(Bulk). Several methods[3,4,5] are cited

in literature for determination of assay by Ultra Violate spectroscopy[7,8], related substances by High Performance Liquid Chromatography but no literature was available to determine the ammonium Molybdate as residual catalyst in Tinidazole (Bulk) and we succeeded in developing a simple, rapid and accurate spectrophotometric procedure for the determination of ammonium Molybdate as residual catalyst in Tinidazole (Bulk) in Parts per Million Level.

Experimental

Instrumentation and reagents

A Unicam SP 500 Series 2, with 1.0 cm matched quartz cells was used for electronic spectral measurements. Chemicals required for analysis like Sodium Molybdate AR, Hydrochloric acid AR, Stannous Chloride (SNCl2), Potassium Thiocyanate AR, Iso Amyl Alcohol AR were purchased from M/s S.D.Fine Chem. Ltd. India.
Distilled water was used for the preparation of all aqueous solutions.

General procedure

Preparation of standard Molybdenum solution

Weight accurately 0.252 gms of Sodium molybdenum ($Na_2MoO_4.2H_2O$) into a 1 Litre volumetric flask and dissolve in 100 ml Water. Dilute to volume, stopper and shake. Dilute 10 ml of this solution to 1 Litre with water (solution A). 1 ml of this solution contains 1 mg of Molybdenum

Preparation of calibration curves

Transfer 2.0, 4.0, 6.0, 8.0, 10.0 ml of Aliquots of solution A, each separately to 100 ml separating funnel and treat each one as follows:
Add 200 ml of water, 4 ml of concentrated hydrochloric acid, 10 ml of 2% w/v solution of stannous chloride solution, 5 ml of 10% w/v solution of Potassium thiocyanate and sufficient water. To yield a final volume of about 50 ml shake for 1 minute and stand for 5 minutes to allow the colour produced to reach maximum intensity. Add 10 ml of Amyl alcohol. Shake and allow the layer to separate. Run off the lower aqueous layer and discard. Transfer the Amyl alcohol layer to A 10 ml Centrifuge tube and Centrifuge for 5 minutes to obtain a clear solution. Measure the absorbance of this solution in a 1 cm cell at 466 nm against a reagent blank prepared by taking reagents alone through above procedure.
Plot the standard absorbance Vs weight of Molybdenum in mg.

Procedure for tinidazole samples

Weight accurately about 2 g of Tinidazole sample in to a 50 ml volumetric flask and add 8 ml of concentrated HCl and 30 – 40 ml of water. Shake to dissolve and dilute to volume with water. Pipette 25 ml of this solution in to a 100 ml separating funnel the preparation of standard curve as given, 10 ml of 2% w/v solution of stannous chloride solution, 5 ml of 10% w/v solution of Potassium thiocyanate and sufficient water. To yield a final volume of about 50 ml shake for 1 minute and stand for 5 minutes to allow the colour produced to reach maximum intensity. Add 10 ml of Amyl alcohol. Shake and allow the layer to separate. Run off the lower aqueous layer and discard. Transfer the Amyl alcohol layer to A 10 ml Centrifuge tube and Centrifuge for 5 minutes to obtain a clear solution. Measure the absorbance of this solution in a 1cm cell at 466 nm against a reagent blank prepared by taking reagents alone through above procedure.

Absorbance a

Transfer the remaining 25 ml of the test solution to a 100 ml separating funnel and sufficient water to give a volume of about 50 ml. Extract this solution with 10 ml of Amyl alcohol, centrifuge as above and determine the absorbance in A2 cm cell at 466 nm against Amyl alcohol as blank = Absorbance B.

Absorbance to Molybdenum = Absorbance A – Absorbance B.

From the calibration curve obtain the weight of Molybdenum present in final solution (x mcg).

Calculations

$$\text{PPM of Molybdenum} = \frac{\text{X mcg x } 2^{*}}{\text{Wt. of Tinidazole in gms}}$$

2* is weight of sample taken as 2 gm as directed in procedure.

Note- The standard curve is linear below 50 mcg but is not completely reproducible, varying slightly with age of the reagents. Therefore the standard curve should be constructed from standard run alongside the samples being

Results and discussion

The Method described here in very rapid , versatile and selective This system is readily available and easy to operate, and reproduces the results with less than 1 % Relative

standard deviation when compared with two different analyst. Linearity over the range of 2 ppm to 10ppm is also linear.

Here in the second step of manufacturing Ammonium Molybdate is used as catalyst for Oxidation. When Ammonium Molybdate get in to reaction it because of highly acidic nature of reaction mass Ammonium Molybdate goes in to reaction as Molybdic Acid and get determined as Molybdenum.

Optical characteristics and validation of the method

Table 1 shows Reproducibility data of said method.

Sr. No	Expected Mo Content in PPM	Actual results of Analyst 1 (In PPM)	Actual results of Analyst 2 (In PPM)
1	10	9.9	10
2	10	9.9	10
3	10	10.1	10.1
4	10	10.0	9.9
5	10	10.0	10.0
6	10	9.9	9.9
Average		9.966667	9.983333
Standard Deviation		0.074536	0.068718
Relative Standard Deviation		0.75%	0.69%
Limit		Max. 10.0 %	Max 10.0%

The accuracy and precision of the method were checked by analysing 6 replicate samples within the Beer's law. Values of RSD were 0.75 %. The lower values of RSD indicate the good precision and reproducibility of the method.

The limit of quantitation (LOQ) was determined by taking the ratio of the standard deviation of the blank with respect to water and the slope of the calibration curve multiplied by the factor 10. This means that LOQ is approximately 3.3 times greater than LOD.

Applicability of the method

The applicability of the proposed spectrophotometric procedure[1,9] for the determination of Ammonium Molybdate as residual catalyst in Tinidazole Bulk. Ammonium Molybdate content as residual catalyst was determined in various batched manufactured by using Ammonium Molybdate as catalyst in Oxidation stage in Tinidazole manufacturing. The

calibration curves showed a linear response over the range of concentrations used in the residual catalyst determination procedures. The RSD values in the range to 0.75 & 0.69 for the reproducibility results when analysed by two different analyst. This reproducibility studies show that the method is precise and accurate. The precision and accuracy of the method was further compared statistically. At a 95% confidence level, the calculated t-values and F-values do not exceed the tabulated values.

Conclusion

The method is simple reproducible fast and accurate for determination of Ammonium Molybdenum as residual catalyst in Tinidazole Bulk. This method is also useful in analysing the Ammonium Molybdate raw material

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References

1. M.W. Miller, H.L. Howes, Jr., R.V. Kasubick and A.R. English, J. Med. Chem. 13, 849 (1970).
2. Remington's Pharmaceutical Sciences, 18*th* Edition., Mack Publishng Co., Easton, 1228-1230 (1993).
3. Indian Pharmacopoeia, Controller of Publications, New Delhi, 1, pp. 488 and 2, pp. 764 (1996).
4. British Pharmacopoeia, HM Stationery , London, pp. 98, 893,1814 and 1815 (1998).
5. United States Pharmacopoeia, 24, NF 19, US- Pharmacopoeial Convention, Rockville, MD, 1104 {1106 (2000).
6. T.P. Gandhi, P.R. Patel, V.C. Patel and S.K. Patel, J. Inst. Chem. 56, 127-128 (1984).
7. N.M. Sanghavi, N.G. Joshi and D.G. Saoji, Indian J. Pharm. Sci., 41, 226-228 (1979).
8. O.S. Kamalapurkar and C. Menezes, Indian Drugs*;* 22, 164 (1984).
9. M.L. Lopez, F.J.L. Vazquez and P.L. Lopez-de-Alba, Anal. Chem. Acta, 340, 241-

244 (1997).
10. R.G. Bhatkar and S.K. Chodankar, Indian J. Pharm. Sci. 42, 127-129 (1980).
11. P. Nagaraja, K.R. Sunitha, R.A. Vasantha and H.S. Yathirajan, J. Pharm. Biomed. Anal., 28, 527-535 (2002).
12. D. Channe Gowda and Shankare Gowda, Ind. J. Chem. 39B, 709-711 (2000).

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