



Micro Determination of Furosemide Pure and Some of its Pharmaceutical Preparations with Ammonium Hexanitratocerate (IV) Reagent

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ABSTRACT

A new method has been developed for the micro determination of furosemide pure and some of its pharmaceutical preparations by using Ce(IV) reagent as oxidant. The method is simple, accurate, sensitive and gives reproducible results within $\pm 1\%$ error. Effects of different variables have been studied and SD & CV calculated. Recovery experiment is carried out by standard drug addition method. A probable reaction mechanism has also been suggested. Interference of various ions has been studied.

Key words : Determination, furosemide, Ce(IV), Micro methods.

INTRODUCTION

A furosemide¹⁻¹¹ is an agent with increase the volume of urine extracted by the kidneys. In the healthy subject the amount and content of the urine is automatically adjusted to maintain the water and electrolytic status of the body at an almost constant level. Regulation of this function is performed by the posterior, pituitary gland and its associated hypothalamus. These all diuretics are administered orally because of the great medicinal importance. The analysis and the assay

of diuretics need prime attention. Taking advantage of the presence of benzene ring in all these compounds. A survey of literature reveals that very few methods are available for microdetermination of diuretic drugs. Singh¹² and Pathak¹³ determined diuretic drugs in microgram quantities using NBS, NBSA and BrCl in acetic acid medium respectively.

Assay of pure samples and their pharmaceutical preparation viz tablets & injection was achieved by recommended procedure with an error not exceeding +1%.

MATERIAL AND METHODS

Reagent and Solution

0.1M Ammonium hexanitratocerate (IV) (AnalaR, B.D.H.) :13.90g Ammonium hexanitrotocerate (IV) was accurately weighed and dissolved a minimum amount of 0.5 N nitric acid in a 250ml volumetric flask and make upto mark with same solvent.

0.025M Ferrous ammonium sulphate

2.4508 g of ferrous ammonium sulphate (AnalaR, B.D.H.) was accurately weighed and dissolved in minimum amount of distilled water in a 250ml volumetric flask, 10ml of 4M sulphuric acid was added to it and the solution was made up to the mark with distilled water.

0.001M ferroin

Ferroin 0.001M (1,10 Phenanthranine-ferrous sulphate complex) solution is prepared by diluting 0.025M, B.D.H. indicator solution with distilled water.

1M Sulphuric acid

1M solution of sulphuric acid (V/V) was prepared by diluting (AnalaR, B.D.H.) sample in distilled water.

Pure drugs

Accurately weighed 50 mg of amount and dissolved in a minimum amount of 6 N, NaOH solution and then make upto the mark with distilled water in 50ml volumetric flask. Tablets were well powdered equivalent to about 50 mg of pure drug was dissolved in a minimum amount of 6 N, NaOH. After dissolution the solution were filtered and then make upto the mark with distilled water in 50 ml volumetric flask.

Incase of injection

Volume equivalent to 50ml of pure sample was measured accurately and mixed with minimum amount of 4N, NaOH and now the container are made upto the volume in 50ml volumetric flask with distilled water.

Procedure

Aliquots containing 1-10 ml of the sample were taken in 100ml Erlenmeyer flask followed by

the addition of 10 ml of 0.1M Ce(IV) reagent. The reaction mixture was shaken and allow to react for 10 minutes. The reaction was quenched by adding 10ml of 1M sulphuric acid solution and contents shaken for a minute. The unconsumed Ce(IV) was titrated against 0.025 M ferrous ammonium sulphate using ferroin as an indicator. A blank experiment was also run under identical conditions using all the reagent except the sample. Recovery of the sample was calculated with the difference in readings of Fe(II) used for blank and the sample.

$$\text{Mg of sample} = \frac{M \times N \times (V_B - V_S)}{n}$$

Where

- M = Molecular wt. of the sample
 N = Normality of Fe (II) solution
 V_B = Volume of Fe(II) consumed to titrate the blank experiment (ml)
 V_S = Volume of Fe(II) consumed to titrate the sample solution (ml)
 n = Stoichiometry (number of moles of Ce(IV) reagent consumed for one mole of sample)

RESULTS AND DISCUSSION

Aliquots containing 1-5mg drug were allowed to react with a known and excess of Ce(IV) reagent for various lengths of time and the unconsumed reagents were back titrated. The reacting ratio (moles of Ce(IV) per mole of drugs) was calculated for each test and plotted against reaction time. It was found that all the drugs required 10 minutes reaction time for complete the reaction.

Since there is no evidence in literature for getting oxidative reaction of the furosemide, looking the structure of furosemide, it is clear that it has a benzene nucleus to which a furan ring is attached through $-\text{CH}_2-\text{NH}-$ group. The benzene ring has also got a Carboxyl group $-\text{CO}_2-\text{NH}_2$ group and chlorine atom at ortho, meta and para position to NH_2 group respectively. In the present reaction, it is assumed that the furosemide ring break into part giving rise benzene & furan nuclei. The over all reaction may be written as below :

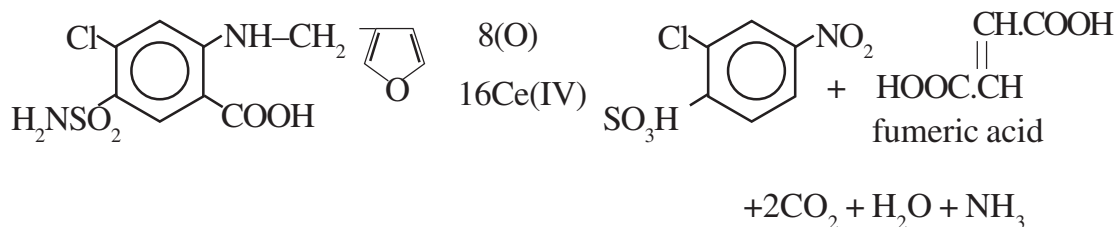


Table 1: Microdetermination of furosemide with Ce(IV) reagent

Sample	Amount taken(mg)	Stoichiometry	Amount found (mg)	Error %	S D	CV
1. Furosemide	1.0040	16	0.9980	- 0.60	0.042	0.4194
	3.0114		3.0400	+ 0.95		
	5.0190		5.0425	+ 0.47		
2. Lasix (Tab.)	1.0035	16	1.0072	+ 0.37	0.0223	0.7380
	3.0120		2.9900	- 0.73		
	5.0205		5.0438	+ 0.46		
3. Lasix (Injection)	1.0038	16	1.0600	+ 0.22	0.0039	0.3886
	3.0105		2.9810	- 0.98		
	5.0165		4.9920	- 0.49		
4. Diural (Tab.)	1.0032	16	0.9982	- 0.50	0.0042	0.4294
	3.0150		3.0598	+ 0.82		
	5.0290		5.0378	+ 0.57		
5. Diural (Injection)	1.0021	16	0.9952	+ 0.29	0.0032	0.6542
	3.0054		3.0200	+ 0.49		
	5.0250		5.0528	+0.45		

The above reaction product satisfy the stoichiometry ratio of furosemide with Ce(IV) reagent. In final reaction products the presence of fumeric acid also support the hypothesis. Assay of

pure sample of furosemide & their pharmaceutical preparations viz tablets and injection was achieved by recommended procedure with an error not exceeding + 1%.

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