Micro determination of some diuretic drugs with ammonium hexanitratocerate(IV) reagent

Shamshad Ahmad Khan[1] and Jaya Srivastava[2*]

[1]Department of Chemistry, D.A.V.P.G College Siwan-841226(Bihar),India

[2]Research Scholar, Department of Chemistry, J.P University Chapra(Bihar),India

[*]Corresponding author: E-mail: j.srivastava002@gmail.com

ABSTRACT

A new method has been developed for the micro determination of some diuretic drugs by using ammonium hexanitratocerate(IV) reagent as oxidant. Diuretics are a class of drugs that increase the flow of urine. Diuretics work by removing sodium and chloride from the body in the urine and the sodium and chloride in turn draw excess water from the body. In the present paper quick and convenient method has been developed for micro determination of some diuretic drugs within accuracy of ± 1% solution of Ce(IV) reagent. A probable reaction mechanism has also been suggested.

Key words: Ce(IV), furosemide, hydrochlorothiazide, micro determination.

INTRODUCTION

Diuretics are drugs that increase secretion of excess water and salt that accumulates in tissue and urine. An excess quantity of intercellular fluid is formed in the organism as a result of an inability of the kidneys to release sodium ions fast enough to ensure that a sufficient quantity of water is excreted along with them. Therefore, efficacy of a diuretic depends first and fore most on its ability to release sodium ions from the body, since they are accompanied by an osmotically equivalent amount of water that is released from interstitial fluids. A large number of chemically related compounds exhibit diuretic effects. Diuretics also are useful in edema caused by renal dysfunction. Diuretics are used to lower urinary calcium excretion, making them useful in preventing calcium- containing kidney stones. Diuretics are used as the sole therapeutic agents to treat hypertension. Diuretics can also be used in combination with antihypertensive drugs to treat more several forms of hypertension. Loop diuretics are the most potent diuretics as they increase the elimination of sodium and chloride. The high efficiency of loop diuretics is due to the unique site of action involving the loop of Henle in the kidneys.

Furosemide

It is a patent, oral, white crystalline diuretic possessing a halogenated ring common to thiazide diuretics. It is chemically represented as 4-chloro-N-furfuryl-5-sulfamoyl anthranilic acid. It produces more chloride loss than sodium loss and it depress both urinary dilution and concentration mechanism. Furosemide is a potassium-

wasting diuretic, which acts by reducing the reabsorption of salts in the blood, leading to their excretion in urine. The drug is well absorbed from the gastro-intestinal tract and is excreted rapidly, largely unchanged both by glomerular filtration and tabular secretion. The unset action is quick and the duration is short. It is a powerful diuretic its unintelligent action can precipitate serious electrolyte and water disturbances due to loss of Na, K,Cl and water. A patient may complain of weakness, fatigue, dizziness, cramps and orthostatic hypertension can occur. The drug can precipitate hepatic cone in the presence of liver diseases.

Ethacrynic acid

It is an unsaturated ketonic derivative of an aryloxy acetic acid. It has been used successfully in the management of cardiac and renal oedema. It has been effective in cases, refractory or irresponsive to other diuretics. It is effective in many patients who have significant degrees of renal insufficiency. In both animals and man ethacrynic acid causes a marked increase in excretion of sodium and chloride ions and of water. This effect is seen under condition of hydopenia as well as hydration. The experimental studies indicated that ethacrynic acid influence both the diluting and the concentrating mechanism of the kidney. By inhibiting active sodium reabsorption in the ascending limb of the loop of Henle as well as else where in the nephron. It reversibly depresses the preparation of the diluting mechanism and diminishes increasing solute gradient of the kidney from cortex to medulla. The net effect is the excretion of a large amount of virtually the isosmotic urine.

Thiazides

Chlorothiazide and poly thiazide are chemically referred as 6-chloro-7-sulphonyl-1,2,4-benzothiadiazine-1,1-dioxide and 2-methyl-3-thiatrifluoropropyl-1,2,4-benzothiadizine-1,1-dioxide. These diuretics provide the means of treating nephrogenic diabetes insipidus and that are strongly indicated when arterial disease develops in patients which the pituitary form of diabetes insipidus. These all diuretics are administered orally or forally 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, the use of use of bromine monochloride has been made for their quantitative evaluation. In the present paper pure samples and their pharmaceutical preparation viz tablets and injection was achieved by recommended procedure within accuracy of ± 1%.

MATERIALS AND METHODS

Chemicals and Reagents

All the starting materials and solvents used in this research were of analytical grade and were used in reaction as received without further purification. Ammonium hexanitratocerate(13.90g) was accurately weighed and dissolved a minimum amount of 0.5 N nitric acid in a 250 ml volumetric flask and make up to mark with same solvent.

0.025M Ferrous ammonium sulphate

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

0.001M Ferroin

0.001M ferroin solution was prepared by diluting 0.025M, B.D.H indicator solution with distilled water.

1M Sulphuric acid

1Molar solution of sulphuric acid was prepared by diluting sample in distilled water.

Drugs

Tablets were well powdered equivalent to 50 mg of pure drug was dissolved in a minimum amount of 5N, NaOH. After dissolution the solution were filtered and then make up to the mark with distilled water in 50 ml volumetric flask.

Injection

50 ml of pure sample was mixed with minimum amount of 4N, NaOH and then make up to the volume in 50 ml volumetric flask with distilled water.

General procedure

For testing quantitate validity of the reaction, furosemide was choosen as the test sample. Aliquots containing different amount of the sample were allowed to react with varying concentration of ammonium hexanitratocerate(IV) reagent at room temperature and uncomposed ammonium hexanitratocerate(IV) was black titrated against Fe(II) 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 iron(II) used for blank and the sample.

Mg of sample = $M \times N \times (V_B - V_S)/ n$

Where

M = Molecular weight of the sample

N = Normality of iron(II) solution

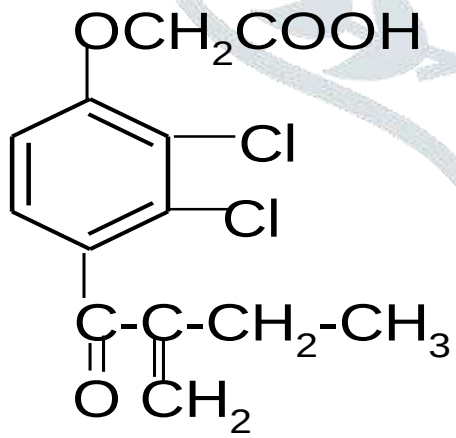
V_B = Volume of iron(II) consumed to titrate the blank experiment

V_S = Volume of iron(II) consumed to titrate the sample solution

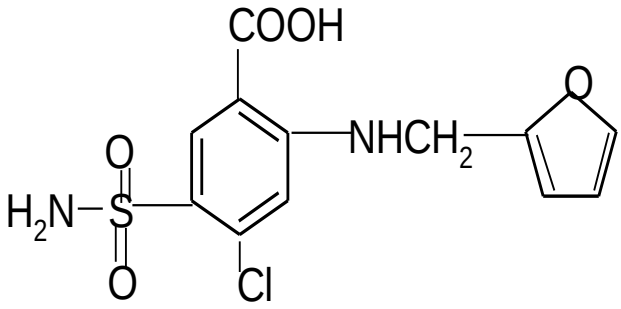
n = Stoichiometry

RESULTS AND DISCUSSION

Aliquots containing 1-5 mg drug were allowed to react with a known and excess of Ce(IV) reagent for various length of time and the unconsumed reagents were back titrated. The reacting ratio was calculated for each test and plotted against reaction time. It was observed that the recovery of the sample becomes constant within the reaction time of 30 minutes. Ethacrynic acid also requires 30 minutes for complete reaction. Thus, for general procedure a reaction time of 30 minutes was recommended. In case of thiazide derivatives similar experiment were performed and was observed that hydrochlorothiazide and chlorothiazide require 25 minutes for constant results. Whereas polythiazide get oxidized within 30 minutes. Thus, for a general procedure of estimation of thiazide a reaction time of 30 minutes was recommended. Keeping amount of furosemide and reaction time as constant the effect of varying concentration of Ce(IV) reagent was studied. Concentration was varied from 0.05M to 0.2M and the recovery of the sample was calculated. It was found that the best recovery of the sample was obtained by using 0.1M concentration of the reagent. Furosemide, an anthranilic acid derivatives is a rapid acting highly efficacious diuretic. Furosemide is classified as a loop diuretic and because of its marked efficacy as a high ceiling diuretic. Furosemide has proven more effective than other diuretics. Besides a diuretic effect, it also dilutes peripheral vessels. It is frequently used in combination with other antihypertensive drugs. The particular sulphonamide functional group containing loop diuretic drug allows the removal of extra water and salt from the body into the urine. Since there is no evidence in literature for getting oxidation reaction of furosemide. It is clear that furosemide structure has a benzene nucleus to which a furan ring is attached.



Ethacrynic acid



Furosemide

Table-1

Stoichiometric ratio of diuretic compounds in pure form and their pharmaceutical preparation with0.1M Ce(IV)reagent

Sample	Observed molar ratio of Ce(IV) per mole of compound			
Furosemide	16.0022	15.9927	16.0042	16.0058
Lasix(Tab)	16.0022	15.9938	16.0040	16.0032
Lasix(Inj)	15.9922	15.9952	16.0040	16.0032
Diural(Tab)	15.9950	15.9930	16.0034	16.0042
Diural(Inj)	15.9932	16.0040	16.0025	16.0054
Ethacrynic acid	10.0025	10.0085	10.0099	9.9954
Ethacrynic(Tab)	9.9984	10.0047	10.0038	9.9976
Chlorothiazide	7.9989	7.9951	8.0022	8.0085
Polythiazide	8.0025	**7.**9991	8.0081	7.9932
Nephril(Tab)	8.0012	8.0054	7.9976	7.9964

Table-2

Micro determination of furosemide with Ce(IV) reagent

Aliquots Taken(ml)	Amount Present(mg)	Reaction Time(min)	Amount Recovered(mg)	Stoichiometry	Error %	S.D	C.V
1	1.0040	30	0.9980 0.9988 1.0072	16	-0.60 -0.52 0.32	0.0042	0.4191
3	3.0114	30	3.0400 2.9820 3.0325	16	0.95 -0.98 0.20	0.0258	0.8548
5	5.0190	30	5.0425 5.0398	16	0.47 0.41	0.0012	0.0238

			5.0400		0.42		
7	7.0245	30	6.9705 7.0456 7.0480	16	-0.77 0.30 0.35	0.0273	0.3888
9	9.0350	30	9.0618 9.0620 8.9735	16	0.29 0.29 -0.71	0.0418	0.4628

Table-3

Micro determination of Lasix(Tab) with Ce(IV) reagent

Aliquots Taken(ml)	Amount Present(mg)	Reaction Time(min)	Amount Recovered(mg)	Stoichiometry	Error %	S.D	C.V
1	1.0035	30	1.0072 1.0066 0.9980	16	0.37 0.31 -0.55	0.0042	0.4184
3	3.0120	30	2.9900 3.0392 3.0272	16	-0.73 0.84 0.84	0.0223	0.7380
5	5.0205	30	5.0435 4.9398 5.0420	16	0.47 -0.94 0.44	0.0207	0.4123
7	7.0210	30	7.0478 6.9706 6.9706	16	0.38 -0.49 0.29	0.364	0.5203
9	9.0261	30	9.0618 9.0620 8.9735	16	0.29 -0.49 0.29	0.0530	0.4628

Table-4

Micro determination of Diural(Tab) with Ce(IV) reagent

Aliquots Taken(ml)	Amount Present(mg)	Reaction Time(min)	Amount Recovered(mg)	Stoichiometry	Error %	S.D	C.V
1	1.0032	30	0.9982 1.0062	16	-0.50 0.30	0.0039	0.3886

			1.0062		0.30		
3	3.0150	30	3.0598 2.9892 3.0382	16	0.82 -0.86 0.82	0.0222	0.7346
5	5.0090	30	5.0378 4.9887 5.0382	16	0.57 -0.60 0.58	0.0270	0.5379
7	7.0203	30	7.0478 6.9698 6.9778	16	0.39 -0.72 -0.68	0.0381	0.5445
9	9.0369	30	8.9721 8.9721 9.0369	16	-0.72 -0.73 0.30	0.0435	0.4832

Table-5

Micro determination of Diural(Inj) with Ce(IV) reagent

Aliquots Taken(ml)	Amount Present(mg)	Reaction Time(min)	Amount Recovered(mg)	Stoichiometry	Error %	S.D	C.V
1	1.0021	30	0.9992 1.0052 1.0000	16	-0.29 0.31 -0.21	0.0027	0.2696
3	3.0054	30	3.0200 2.9882 3.0187	16	0.49 -0.33 0.44	0.0146	0.4685
5	5.0250	30	5.0528 4.9887 5.0252	16	0.45 -0.84 0.55	0.0329	0.6542
7	7.0280	30	7.0970 7.0465 6.9718	16	0.27 0.29 -0.80	0.0358	0.5098
9	9.0297	30	8.9973 8.0000 8.0487	16	-0.36 -0.28 0.24	0.0435	0.4826

CONCLUSION

A new method has been developed for the micro determination of some diuretic drugs by using ammonium hexanitratocerate(IV) reagent as oxidant. Diuretics are a class of drugs that increase the flow of urine. Diuretics work by removing sodium and chloride from the body in the urine and the sodium and chloride in turn draw excess water from the body. The product satisfies the stoichiometry ratio of furosemide with Ce(IV) reagent. Assay of pure sample of furosemide and their pharmaceutical preparations viz tablets and injection was achieved by recommended procedure with an error not exceeding +1%.

REFERENCES

1. R. Gasa and T.L.B Springs J.Pharm.Chemother 17,442(1961).
2. United State Pharmacopeia XVIII,P.423.
3. C.F Chignell, Methods in Pharmacology 2,33, Physical methods, New yourk Meredith(1972).
4. M.A Jan and Lizzy J.Pharm. Sci62,1261(1973).
5. Kalhan and Glotter J.Ana. Chem. 31,431(1959).
6. Y.A Beltagy, A.S Issara Talanata 25(6),3496(1978).
7. I. Schire Laneet 1,174(1963).
8. A.J Moriarity Canad. Med. Assoc.J 88,97(1963).
9. Heller and Cinsburg Progress in Medicinal Chemistry. 1,132(1971).
10. B.Narayana and K. Ashwini, Ind. J.Chem. Tech. 17,150(2010).
11. N.Chuon and Pharm. Biedal. J. Sci. Scat. 94,451(1961).