IJPSR (2017), Vol. 8, Issue 2 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 30 July, 2016; received in revised form, 19 September, 2016; accepted, 26 September, 2016; published 01 February, 2017

MICRO-COULOMETRIC ESTIMATION OF NITROFURANTOIN

Sushil B. Kapoor [*1], Parmanand M. Shende [2] and Dilip B. Patil [3]

Arts [1], Commerce and Science College, Tukum, Chandrapur- 442401, Maharashtra, India.
Dr. Ambedkar Arts [2], Commerce and Science College, Chandrapur-442401, Maharashtra, India.
Govt. Institute of Science [3], Nagpur-440001, Maharashtra, India.

Keywords:

Nitrofurantoin, Micro-Coulometry, Statistical Analysis, Microgram Level Estimation, Potentiostat

Correspondence to Author:
Dr. Sushil B. Kapoor

Assistant Professor
Arts, Commerce and Science College, Tukum, Chandrapur-442401, Maharashtra, India.

Email: kapoor.sushil2012@gmail.com

ABSTRACT: The objective of the present work was to set up micro-coulometric technique in the laboratory and estimate microgram level quantity of nitrofurantoin in the pharmaceutical tablets. A simple, sensitive, and reproducible manually operated microcoulometric technique has been successfully used for the estimation of nitrofurantoin in pharmaceutical tablets. A potentostat and coulometric cell was used in the technique. A coulometric cell was consist of mercury pool electrode, spiral silver electrode, and saturated calomel electrode. The accuracy of the current was 1µA and applied potential was 0.001 volt against SCE. Further, the prepared tablet solution of nitrofurantoinin ammonia buffer of pH 9.0 was estimated and statistical analysis of the data were carried out. Polarogram of the nitrofurantoin in ammonia buffer of pH 9.0, shows that six electrons are involved in the reduction of nitrofurantoin. The lowest limit of estimation of nitrofurantoin was 15ug. The reprodusability of estimation i.e. relative root mean square error(RMSE) was less than 2µg. The recovery was 100 ± 5%.

INTRODUCTION: Nitrofurantoin [1-{(5-nitro-2-furyl) methylideneamino} imidazolidine-2, 4-dione] is a nitro furan-derivative. It is used in human [1, 2] to treat Urinary tract infection and effective against common urinary tract pathogens, which includes *E. coli, E. cocci, Klebsiella* and *E. bactor*. It is bacteriostatic at low concentrations and bactericidal at higher concentrations [3, 4]. It acts by absorbing through gastrointestinal tract in the proximal small intestine [5]. Mostly the bioavailability of this drug increases when taken with food [6].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.8(2).799-03

Article can be accessed online on: www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.8 (2).799-03

Nitrofurantoin is commercially available in different dosage forms and can be administered as tablet. Various advanced methods are available for its assay in dosage forms and in biological fluids [7-19]. These includes stripping voltammetry [7-13], high performance liquid chromatography [14-17], LC-MS [18, 19], Liquid-Liquid extraction [15, 19] and flow injection analysis [20].

Although various advanced methods are available for estimation of Nitrofurantoin, they are costly and out of reach of small educational institutions. The objective of the present work is to develop a manually operated micro-coulometric method for the routine estimation of Nitrofurantoin in pharmaceutical tablets. Among all other methods, micro-coulometry is the dominant one. This is because it is independent of temperature and depends only on the amount of species of interest.

Nitrofurantoin is choosen because it is electro reducible and hence amenable to micro-coulometric determinations. This method is simple, cheap, accurate, prone to less errors and reproducible.

MATERIALS AND METHODS:

Materials: All the chemicals used for the preparation of solutions and buffer were of analytical grade. Mercury employed was purified by reported method [21] and the silver spiral used was electronalytically pure. Acetic acid was obtained from May and Baker. Potassium chloride, sodium acetate were from Sarabhai M chemicals, Baroda, India. N, N-Dimethyl formamide of Excelar Grade from Glindia Ltd, Mumbai, India. Nitrofurantoin tablets were purchased from local pharmacies in Nagpur city, India by APS Biotech Pvt. Ltd. Utterakhand, India.

A $5.0x10^{-3}$ M Nitrofurantoin [22] solution was prepared in 40% N,N-dimethylformamide containing ammonia buffer of pH 9.0. The content of Dimethyl formamide was maintained at 1% by volume in the reaction mixture.

pH measurement were carried out with digital pH meter model L1-120 from Elico Pvt. Ltd., Hyderabad, India.

Equipment used in the present study was a manually operated potentiostat built in the laboratory with accuracy of current 1µA and applied potential 0.001 volt against saturated calomel electrode (SCE).

A coulometric cell consist of large mercury pool electrode as working electrode and bright spiral silver in separate compartment as an auxiliary electrode **(Fig.1).** The electrolyte above mercury pool was kept vigoursly stirred. Provision was made for SCE; nitrogen inlet and outlet. The current was measured with microameter to an accuracy of 1µA. From this quantity of electricity in millicoulomb could be measured and therefore microgram quantity of Nitrofurantoin could be estimated.

A supporting electrolyte of 0.1M potassium chloride solution was prepared in doubly distilled water and its final concentration in the reaction mixture was 0.01M.

Removal of Oxygen: Nitrogen from commercial cylinder was passed through two traps arranged in series, one containing acid chromous chloride and other containing pyrogallol in 30% potassium hydroxide solution [23, 24]. Then it was bubbled through doubly distilled water before passing through the solution in the coulometric cell.

Method: Number of millicoulomb at constant potential: A pre-electrolysis was carried out at a potential which was 300 mv more negative than the half-wave potential of the Nitrofurantoin in order to remove electroactive impurities present in the reaction medium. The electrolysis was continued until only small constant background current only few microampere remained. The Nitrofurantoin was introduced into the cell and electrolyzed at a potential 200 mV more negative than the half-wave potential. The current was noted down at regular interval of 10 seconds. The electrolysis was continued until the current decreased to the same value as the background current. The current versus time curve was plotted and number of millicoulomb passed was determined by evaluating the area under the curve.

Recovery: The reliability of the Nitrofurantoin estimation was established by carrying out recovery experiments. For this purpose the above procedure was repeated but with Nitrofurantoin added in known amount. By knowing the number of millicoulombs passed the amount recovered could be calculated.

Error Analysis: The root mean square error (RMSE) and relative root mean square error (RRMSE) were calculated for reproducibility and recovery experiments.

$$\text{RMSE} = \sqrt{(\text{Difference})^2/(n-1)}$$
$$= \sqrt{\Sigma Di^2/(n-1)}$$

Where, n= no. of trials carried out
Difference=Amount of Nitrofurantoin taken-Amount of Nitrofurontoin found
RRMSE=RMSE/x
X=Amount of Nitrofurontoin taken to estimate.

RESULTS AND DISCUSSION: A manually operated micro-coulometric estimation of Nitrofurantoin was carried out to determine the lowest possible amount that could be estimated

with reasonable accuracy. The number of electrons participating in reduction was also evaluated. It was found that 6 electrons are participating in the Nitrofurantoin reduction. It was observed that, the lowest limit of estimation of this compound by manually operated micro-coulometry was at least ten fold lower than that of the D.C. Polarographic lower limit of estimation.

The lowest limit of Nitrofurantoin that could be estimated was 15µg. The reproducibility was checked by repeating the estimations four times. It was found that it was reproducible with a RMSE less than 2 µg (**Table 1**). Recovery experiments were carried out by adding known amount namely18µg, 58µg and 98µg of Nitrofurantoin (**Table 2**). The results reveals that the recovery was 100±5%.

TABLE 1: ERROR ANALYSIS IN ESTIMATION OF NITROFURANTOIN

pH=9.0 Temp. = 25.0 ºC

No. of Estimations	Nitrofurantoin in 25.0 cm^3/µg	No. of millicoulombs passed	Amount of Nitrofurantoin estimated/ µg	RMSE	RRMSE
1	15	38.0	15.1	1.000	0.067
2		39.5	15.7		
3		41.0	16.3		
4		40.0	15.9		
1	30	85.0	29.0	0.687	0.023
2		86.5	29.6		
3		87.0	30.3		
4		88.0	30.9		
1	45	157.5	44.3	2.30	0.051
2		156.5	43.1		
3		159.5	45.5		
4		157.5	43.6		
1	60	231.5	60.7	1.407	0.023
2		232.5	61.4		
3		230.0	59.5		
4		233.0	61.8		

TABLE 2: ERROR ANALYSIS OF RECOVERY EXPERIMENTS FOR ESTIMATION OF NITROFURANTOIN IN 15 µg ORIGINAL SOLUTION

pH=9.0 Temp.=25.0 ºC

No. of Estimations	Amount of added Nitrofurantoin /µg	No. of millicoulombs passed	Amount of Nitrofurantoin Recovered/ µg	Percentage Recovery %	RMSE	RRMSE
1	15	47.5	18.6	103	0.768	0.038
2		46.0	17.8	98.9		
3		48.0	19.1	106		
4		47.0	18.4	102		
1	58	144.0	58.7	101	0.872	0.015
2		143.5	58.1	100		
3		145.0	59.3	102		
4		143.0	57.7	99.5		
1	98	241.5	98.9	101	1.101	0.011
2		242.5	99.5	101		
3		241.0	98.7	101		
4		240.0	97.7	100		

The results of estimation of Nitrofurantoin shows that manually operated micro-coulometry is relatively simple and yet reliable technique to estimate microgram level quantities of Nitrofurantoin. The apparatus is cheap and can be easily setup in any educational institute.

The lowest limit of estimation is of 15 µg to 30 µg in 25.0 cm^3. The technique is highly reproducible and accurate. The average time required for estimation in 25.0 cm^3 of sample is less than hour.

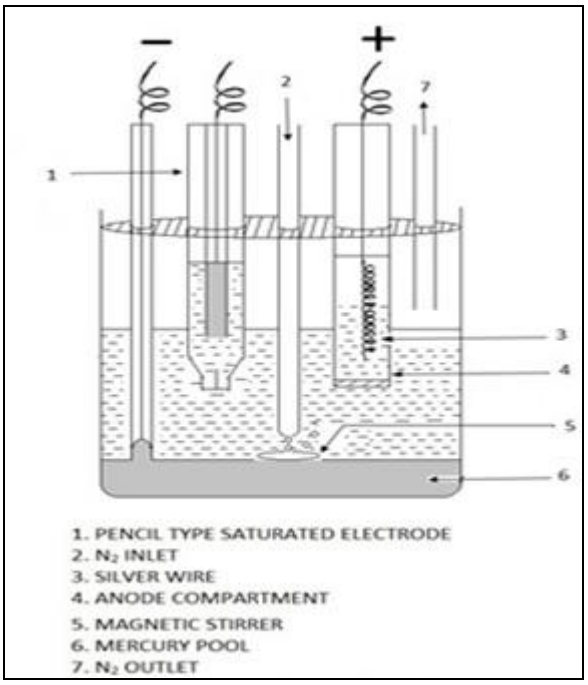

FIG. 1: COULOMETRIC CELL

CONCLUSION: The micro-coulometric technique, for estimation of microgram level nitrofurantoin, in the pharmaceutical tablets can be successfully set up in the laboratory. The technique is simple, cheap, accurate and yet reliable. The pre-estimation polarographic study showed that six electrons were involved in reduction of nitrofurantoin. The lowest limit of estimation of nitrofurantoin was 15µg in 25 cm^3. The technique was highly reproducible with RMSE less than 2µg. The time required for estimation was less than hour. The recovery of the samples were100±5%.

ACKNOWLEDGEMENT: Authors thank Director, Government Institute of Science, Nagpur for allowing to carry out the work and facilities.

CONFLICTS OF INTERESTS: All authors have none to declare.

REFERENCES:

1. D.R Guay, An update on the role of nitrofurans in the management of urinary tract infections, Drugs 61. 2001. 353-364
2. D.C. Hooper, Urinary Tract Agents: Nitrofurantoin and Methenamine, in Principles and Practice of Infectious Diseases (Eds. G. L. Mandell, J. E. Bennet and R. Dolin), Elsevier Churchill Livingstone Inc., Philadelphia2009. 515-520
3. M. Maaland, and L. Guardabassi, In vitro antimicrobial activity of nitrofurantoin against *Escherichia coli* and *staphylococcus pseudintermedius* isolated from dogs and cats, Vet. Microbiol. 151. 2011. 396-399;DOI: 10.1016/j.vetmic.2011.03.009
4. AHFS Drug Information (Ed. G.K. Mcevoy), American Society of Hospital Pharmacists, Betuerda(MD).1990. 438.
5. A. Bains, D. Buna and N.A. Hoag, A retrospective review assessing the efficacy and safety of nitrofurantoin in renal impairment, Can. Pharm. J.142. 2009. 248-252; DOI:10.3821/1913-701X-142.5.248.
6. W.A. Petri, Sulfonamides, trimethoprim, sulfamethoxazole, quinolones, and agents for urinary tract infections, in Goodman & Gilman's Pharmacological Basis of Therapeutics (Eds. L.L. Brunton, J.S. Lazo and K.L. Parker), McGraw Hill, New York, 2006.1111-1125
7. M. Khodari, HMansour, H. S. El-Din and G. Mersal, Cathodic stripping voltammetry of the antibacterial drug (nitrofurantoin), Anal. Lett. 31.1998. 251-262; DOI: 10.1080/00032719 808002043.
8. E. Hammam, Determination of nitrofurantoin drug in pharmaceutical formulation and biological fluids by square-wave cathodic adsorptive stripping voltammetry, J. Pharm. Biomed. Anal.30.2002.651-659; DOI:10.1016/S0731-7085(02)00344-8.
9. Rajeev Jain, Ashish Dwivedi and Ritesh Mishra, Journal of Hazardous Materials, vol. 169. issue 1. 2009. 667-672
10. Vinod K. Gupta, Rajeev Jain, Keishan Radhapyari, Nimisha Jadan and Shilpi Agrawal, Analytical Biochemistry .2010.doi: 10.1016/j.ab.20b.09027.
11. P.de Lima-Neto, A.N. Correia, Q.R. Portela, M.S. Juliao, G.I. Linhares Junior and J.E.S.de Lima, Talata, vol. 80 . Issue 5. 2010.1730-1736.
12. Mehmet Lutfi Yola, Nuran Ozaltin, Journal of Eletroanalytical Chemistry, vol. 653. issue 1.2011 .56-60.
13. Zuzana Krejcova, Jiri Barek and Vlastimil, Electoanalysis, 2015. 27(1) .185-192.
14. V. Arancibia, M. Valderrama, A. Madariage, M.C. Zuniga and R. Segura, Extraction of nitrofurantoin and its toxic metabolite from urine by supercritical fluids. Quantitation by high performance liquid chromatography with UV detection, Talanta2003. 61. 377-383; DOI: 10.1016/ S0039-9140(03)00276-5.
15. P. Muth, R. Metz, B. Siems, W.W. Bolten and H. Vergin, Sensitive determination of nitrofurantoin in human plasma and urine by high-performance liquid chromatography, J Chromatogr.A 729. 1996. 251-258; DOI: 10.1016/0021-9673(95)00894-2.
16. F.W Kari, R. Weaver and M.C. Neville, Active transport of nitrofurantoin across the mammary epithelium in vivo, J. Pharmacol. Exp. Ther. 280 .1997. 664-668; DOI: 0022-3565/97/2802-0664.
17. G. Merino, J. W. Jonker, E. Wagenaar, A.E. van Herwaarden and A.H. Schinkel, The breast cancer resistance protein (BCRP/ABCG2) affects pharmacokinetics, hepatobiliary excretion, and milk secretion of the antibiotic nitrofurantoin, Mol. Pharmacol. 67. 2005. 1758-1764; DOI :10.1124/mol.104.010439
18. K.K. Adkison, S. S Vaidya, D. Y. Lee, S. H. Koo, L. Li, A. A. Mehta, A.S. Gross, J. W. Polli, Y. Lou and E.J .Lee, The ABCG2 C421A polymorphism does not affect oral nitrofurantoin pharmacokinetics in healthy Chinese male subjects, BrJ. Clin. Pharmacol. 66. 2008.233-239; DOI:10.1111/j.1365-2125.2008.03184.x.

19. R.S. Patil, K.A. Chaitanya, P.V.D.L.S. Ravi Prakash and S.R. Patil, Simple rapid and sensitive method for determination of nitrofurantoin in human plasma by using liquid chromatography/tandem mass spectroscopy, Curr. Trends biotechnol. Pharm. 6 .2012. 196-203.
20. P. Salgado-Figueroa, P. Jara Ulloa, A. Alvarez-Lueje, J.A. Squella, Electroanalysis, 25, Issue 6 .2013. 1433-1438.
21. US Department of Health and Human Services, Food and Drug Administration Centre for Drug Evaluation and Researc, Guidance for Industry, Bioanalytical Method Validation, CDER, Centre for Veterinary Medicine (CVM), Rockville (MD) 2001.
22. J. Bassette, R. C. Denney G. H. Jeffery and J. Mendham "Vogels Text book of quantitative Inorganic Analysis". The English Language book Society and Longman, London, 4th edition 1982.
23. A.F. Suma, J. Pharm. Sci. 51. 1962.474.
24. A.I. Vogel, " A Text Book of Practical Organic Chemistry "The English language book Society and Longman, London, 3rd edition 1975.

How to cite this article:
Kapoor SB, Shende PM and Patil DB: Micro-coulometric estimation of nitrofurantoin. Int J Pharm Sci Res 2017; 8(2): 799-03.doi: 10.13040/IJPSR.0975-8232.8(2).799-03.