Available online at www.ijpsdr.com
International Journal of Pharmaceutical Sciences and Drug Research 2010; 2(1): 45-47

Research Article ISSN 0975-248X

Atomic Absorption Spectrometric Method for Estimation of Diclofenac sodium and Mefenamic acid in Pharmaceutical Formulations

Sunil Jawla[1*], Sandeep Jain[2]

[1]*I. T. S. Paramedical College (Pharmacy), Delhi-Meerut Road, Murad Nagar, Ghaziabad, Uttar Pradesh-201 206, India*
[2]*Dept. of Pharmaceutical Sciences, G. J. University of Science and Technology, Hisar, Haryana-125001, India*

ABSTRACT
Diclofenac sodium and Mefenamic acid have been quantified in tablet dosage form by atomic absorption spectrometry (AAS). These methods are based on formation of the metal complexes of Diclofenac sodium and Mefenamic acid with cupric chloride and cobaltous chloride. The first method is based on reaction of both the drugs with cupric chloride to give light blue colored metal complexes, which are then extracted with dichloromethane and digested with 0.1 M nitric acid. Both the drugs are indirectly estimated via determination of copper content in the formed complexes by AAS. The second method is based on the formation of pink colored complexes of both the drugs with cobaltous chloride. These metal complexes are extracted with dichloromethane and estimated via determination of cobalt content in the formed complexes after digestion with 0.1 M nitric acid by AAS.

Keywords: Cupric chloride, Cobaltous chloride, Atomic absorption spectrometer, Mefenamic acid and Diclofenac sodium.

INTRODUCTION

Diclofenac sodium and Mefenamic acid are widely used pharmaceutical compounds. They inhibit arachidonic acid metabolism by cyclo-oxygenase (COX). Diclofenac is unique among the NSAIAS (nonsteroidal anti-inflammatory agents) as it possesses three possible mechanisms of actions; inhibition of the arachidonic acid cyclo-oxygenase system (3-1000 times more potent than other NSAIAS), inhibition of the lipo-oxygenase pathway, and inhibition of arachidonic acid release and stimulation of its reuptake. It is indicated for the treatment of rheumatoid arthritis, osteoarthritis and ankylosing spondylitis. Hence approved as an anti-inflammatory agent; for several uses, in United States. Mefenamic acid in a dose of 250mg is superior to 600mg of aspirin as an analgesic. It has lower incidences of GIT (gastrointestinal tract) bleeding compared to aspirin. It has been approved for use in the management of primary dysmenorrheal. [1-2]

Several methods like Spectrophotometric [3-6], HPLC [7-10], HPTLC [11-12], Colorimetric [13-14], Spectrofluorimeteric [15-16], Capillary Electrophoresis [17-18] and GC [19-20] have been reported for quantitative estimation of Diclofenac sodium and Mefenamic acid.

***Corresponding author: Mr. Sunil Jawla,**
I. T. S. Paramedical College (Pharmacy), Delhi-Meerut Road, Murad Nagar, Ghaziabad, Uttar Pradesh-201 206, India; **Mob. No.:** +919456039139
E-mail: suniljawla777@gmail.com

Reactions of the investigated drugs with cupric chloride and cobaltous chloride have not been examined before. The present methods are simple, sensitive, accurate and economical for routine quality control analysis of both the drugs.

MATERIAL AND METHODS

All the analysis has been carried out on Atomic absorption spectrometer (GBC Aventa 935 plus), UV/ VIS spectrophotometer (EZ 301 Perkin Elmer) and FTIR spectrometer (Test scan Shimadzu FTIR 8000 series). Pure samples of Diclofenac sodium and Mefenamic acid were kindly supplied by Jagsonpal Pharmaceutical. Ltd. (India) and P & B Laboratories Pvt. Ltd. (India) respectively.

Standard stock solutions of both the drugs; containing 0.5 $mgml^{-1}$ were prepared in methanol. Each was further diluted to five dilutions ranging from10 to 250 μgml^{-1} with distilled water.

Preparation of standard curves

In cupric chloride method; 1 ml of each dilution was transferred to 10 ml volumetric flasks. Added 5 ml (1 %) cupric chloride solution and shaken vigorously for 15 minutes. All volumes were made up to mark with distilled water. Transferred quantitatively to separating funnels and extracted with (3×10 ml) dichloromethane. These dichloromethane extracts were evaporated and digested with 10ml (0.1 M) nitric acid. Aspirated the acid extracts directly in the atomic absorption spectrometer and measured their

absorbance at 324.8 nm for copper. Standard curves were generated for both the drugs by using regression analysis (Table 1).

In cobaltous chloride method; 1 ml of each dilution was transferred to 10 ml volumetric flasks. Added 5 ml (1 %) cobaltous chloride reagent and heated at 60°C for 15 minutes. Added 1ml (0.5 %) triethanolamine reagent and made volume up to mark with distilled water. Transferred quantitatively to separating funnels and extracted with (3×10 ml) dichloromethane. Dichloromethane extracts were evaporated and digested with 10 ml (0.1 M) nitric acid. Aspirated the acid extracts directly in the atomic absorption spectrometer and measured their absorbance at 240.7 nm for cobalt. Standard curves were generated for both the drugs by using regression analysis (Table 2).

Table 1: Quantitative parameters for the determination of Diclofenac sodium and Mefenamic acid with cupric chloride method

Bulk drug	Linearity range observed (μgml^{-1})	Intercept	Slope	Correlation Coefficient
Diclofenac sodium	1.5-22.5	0.024	0.016	0.998
Mefenamic acid	2.5-23.0	0.013	0.017	0.996

Table 2: Quantitative parameters for the determination of Diclofenac sodium and Mefenamic acid with cobaltous chloride method

Bulk drug	Linearity range observed (μgml^{-1})	Intercept	Slope	Correlation Coefficient
Diclofenac sodium	1.2-21.0	0.051	0.032	0.998
Mefenamic acid	3.0-24.5	0.084	0.021	0.997

Table 3: Determination of the Diclofenac sodium (D) and Mefenamic acid (M) in tablets by cupric chloride method

Sample	Label Claimed (mg / tablet)	Amount Found (mg/ tablet)	%age of Label Clamed Found	Coefficient of Variation*	Percentage Recovery
Brand I (D)	50	50.17	100.34	0.42	100.37
Brand II (D)	50	49.88	99.76	0.39	99.67
Brand III (D)	50	50.37	100.74	0.87	100.53
Brand IV (M)	500	500.70	100.14	0.37	100.26
Brand V (M)	500	501.90	100.38	0.68	100.21
Brand VI (M)	500	499.20	99.82	0.57	99.46

*Mean of three estimations

Table: 4 Determination of Diclofenac sodium (D) and Mefenamic acid (M) in tablet dosage form by cobaltous chloride method

Sample	Label Claimed (mg / tablet)	Amount Found (mg/ tablet)	%age of Label Clamed Found	Coefficient of Variation*	Percentage Recovery
Brand I (D)	50	49.92	99.84	0.82	99.85
Brand II (D)	50	50.14	100.28	0.68	100.30
Brand III (D)	50	49.87	99.74	0.87	99.87
Brand IV (M)	500	502.20	100.44	0.73	100.76
Brand V (M)	500	499.80	99.96	0.48	99.56
Brand VI (M)	500	501.30	100.26	0.55	100.47

*Mean of three estimations

Preparation and analysis of tablet sample solution

Twenty tablets were weighed and crushed to fine powder separately for Diclofenac sodium and Mefenamic acid. Weighed accurately an amount of the powdered tablets equivalent to 10 mg of each drug, shaken with (3×10 ml) methanol; filtered and washed. Reduced the volume of the solvent up to about 6 ml by evaporation. Transferred quantitatively into 10 ml volumetric flasks and completed to volume with distilled water. Made suitable dilutions to carry out analysis by AAS (Table 3 & 4).

RESULTS AND DISCUSSION

Pharmaceutical analysts are now using metal ions for the estimation of different pharmaceutical formulations by applying AAS. It provided an indirect method for determination of the investigated drugs. In cupric chloride method; Diclofenac sodium and Mefenamic acid can be determined in the concentration ranges 1.5-22.5 and 2.5-23.0 μgml^{-1} with mean percentage recovery of 100.19 ± 0.47 % and 100.31 ± 0.79 % respectively. In cobaltous chloride method; Diclofenac sodium and Mefenamic acid can be measured in the concentration ranges 3.5-21.0, 3.0-24.5μgml^{-1} with mean percentage recovery of 99.92 ± 0.15 % and 100.26 ± 0.76 % respectively in cobaltous chloride method. Linearity is obeyed in both the methods in the given concentration ranges. These methods were also applied to pharmaceutical formulations of both the drugs as shown in Table (3 & 4) along with recovery studies.

These methods can be employed for routine analysis of Diclofenac sodium and Mefenamic acid in quality control laboratories. Hence the aim of development of simple, precise, sensitive and economical methods gets fulfilled.

REFERENCES

1. Ronald Borne F, David Williams A. Thomas Lemake L. Foye's Principles of Medicinal Chemistry. Edn 5, Wolters Kluwer Health (India) Pvt. Ltd., New Delhi, 2002, pp. 751- 790.
2. Hardman G, Limbird Lee E. Goodman and Gilman's The Pharmacological Basis of Therapeutics. Edn 10, Mc Graw-Hill, Medical Publishing Division, New York, 2001, pp. 709-711.
3. Agatonovic-Kustrin, S, Zivanovic L, Zecevic M, Radulovic D. Spectrophotometric study of diclofenac-iron (III) complex. Analytical letters. 1997; 30(12): 2235-2249.
4. Botello JC, Perex-Caballero G. Spectrophotometric determination of declofenac sodium with methylene blue. Indian Drugs. 1995; 32 (4): 194-196.
5. Dinc E, Yucesoy C, Onur F. Simultaneous Spectrophotometric determination of mefenamic acid and paracetamol in a pharmaceutical preparation using ratio spectra derivative spectrophotometry and chemometric methods. Journal of Pharmaceutical and Biomedical Analysis, 2002; 28 (6): 1091-1100.
6. Das S, Sharma SC, Talwar SK, Sethi PD. Simultaneous spectrophotometric determination of mefenamic acid and paracetamol in pharmaceutical preparations. Analyst (London). 1989; 114 (1): 101-103.
7. Malliou ET, Markopoulou CK, Koundourellis JE. Simultaneous determination of clobutinol together with some anti-inflammatory drugs in urine by HPLC. Journal of Liquid Chromatography & Related Technologies. 2004; 27 (10): 1565-1577.
8. Sun Y, Takaba K, Kido, H, Nakashima, MN, Nakashima, K. Simultaneous determination of arylpropionic acid non-steroidal anti-inflammatory drugs in pharmaceutical formulations and human plasma by HPLC with UV detection. Journal of Pharmaceutical and Biomedical Analysis. 2003; 30 (5): 1611-1619.
9. Rouini MR, Asadipour A, Ardakani YH, Aghdasi F. Liquid chromatography method for determination of mefenamic acid in human serum. Journal of Chromatography, B: Analytical Technologies in the Biomedical and Life Sciences. 2004; 800(1-2): 189-192.

10. Cerretani D, Micheli L, Fiaschi AI, Giorgi G. High-performance liquid chromatography of flufenamic acid and mefenamic acid in rat plasma. Journal of Chromatography, B: Biomedical Applications. 1996; 678(2): 365-368.
11. Dorado P, Berecz R, Caceres MC, Llerena A. Sensitive HPTLC method for monitoring dissolution profiles of diclofenac from different tablets containing combined diclofenac and acetaminophen. Journal of Chromatography, B.Analytical Technologies in the Biomedical and Life Sciences. 2003; 89(2): 437-442.
12. Argekar AP, Sawant JG. Simultaneous determination of paracetamol and mefenamic acid in tablets by HPTLC. Journal Planar Chromatography-Modern TLC. 1999; 12(5): 361-364.
13. Mathur SC, Kumar Y, Prasad Rao PBN, Rathore ACS, Gupta YKS, A simple colorimetric estimation of diclofenac sodium in dosage forms. Indian Drugs. 1994; 31(9): 447-448.
14. El-Sherif ZA, Walash MI, El-Tarras MF, Osman AO, Colorimetric determination of two nonsteroidal anti-inflammatory drugs using p-dimethylamino cinnamaldehyde. Analytical Letters. 1997; 30(10): 1881-1896.
15. Arancibia JA, Boldrini MA, Escandar GM, Spectrofluorimetric determination of diclofenac in the presence of cyclodextrin. Talanta. 2000; 52(2): 261–268.
16. Ioannou PC, Rusakova NV, Andrikopoulou DA, Glynou KM, Tzompanaki GM. Spectrofluorimetric determination of anthranilic acid derivatives based on terbium-sensitized fluorescence. Analyst (Cambridge, U. K.). 1998; 123(12): 2839-2843.
17. Macia A, Borrull F, Aguilar C, Calull M. Improving sensitivity by large-volume sample stacking using the electroosmotic flow pump to analyse some nonsteroidal anti-inflammatory drugs by capillary electrophoresis in water samples. Electrophoresis. 2003; 24(16): 2779-2787.
18. Wei W, Ju HX. Affinity capillary electrophoresis studies on the influence of alcohols on the interaction of β-cyclodextrin with non-steroidal anti-inflammatory drugs. Chromatographia. 2003; 57(7-8): 449-453.
19. Sioufi A, Pommier F, Godbillon J. Determination of diclofenac in plasma and urine by capillary gas chromatography – mass spectrometry with possible simultaneous determination of deuterium-labelled diclofenac. J.Liq. Chromatoger. 1994; 17(5): 1065-1088.
20. Reddersen K, Heberer T. Multi-compound methods for the detection of pharmaceutical residues in various waters applying solid phase extraction (SPE) and gas chromatography with mass spectrometric (GC-MS) detection. Journal of Separation Science. 2003; 26(15-16): 1443-1450.