Int. J. Chem. Sci. : 2 (1), 2004, 62–67

ANALYTICAL UTILITY OF ATOMIC ABSORPTION SPECTROMETRY FOR THE INDIRECT DETERMINATION OF CERTAIN AMINOGLYCOSIDE ANTIBIOTIC DRUGS

S. THANGADURAI[a*], L. GIRIDHARAN[a], S. K. SHUKLA[b] and Y. ANJANEYULU[c]

[a] Department of Geology & Mining, Guindy, CHENNAI–600 032, (T.N.) INDIA

[b] Central Forensic Science Laboratory, BPR & D, HYDERABAD–500 013, (A.P.) INDIA

[c] Centre for Environment, IPGS & R, JNT University, HYDERABAD–500 028, (A.P.) INDIA

ABSTRACT

A method has been developed for the indirect determination of certain aminoglycoside antibiotic drugs viz., amikacin sulphate, gentamicin sulphate and streptomycin sulphate by Atomic Absorption Spectrometry (AAS) using carbonate as an auxiliary precipitant. The method employed is based on the reaction of these drugs with copper (II) ions under specified conditions. The common excipients used as additives in pharmaceuticals do not interface with the proposed method. The results obtained either for the pure form or in pharmaceutical formulations are accurate and precise.

Key words : Aminoglycoside antibiotic drugs, Ligand, AAS, Pharmaceuticals

INTRODUCTION

The atomic absorption spectrometric (AAS) technique has lead to the development of indirect methods of analysis of a large number of organic compounds[1–3]. Amikacin, gentamicin and streptomycin are the members of the class of aminoglycosides antibiotics. Therapeutically used aminoglycosides usually contain a 1,3– or, 1,4–diaminocyclitol[4]. The aminoglycoside antibiotics most commonly used in food producing animals are gentamicin, neomycin and streptomycin. Antibiotic residues in milk and animal tissues are traditionally determined by microbiological test. The microbiology method is lengthy and cumbersome to chemical methods in both accuracy and precision[5]. Fatalities are reported in many cases after intramascular injection of these drugs[9], when test dose is not given. Such medico–legal cases are received from modern urban areas as well as from rural areas. Recently, fatal cases owing to aminoglycoside antibiotic drug administration have also been received in the forensic laboratories.

*Corresponding author

goldaurium@yahoo.co.in (or) goldau@rediffmail.com

Maitra *et al.*[6,7] reviewed numerous methods for the determination of aminoglycoside antibiotics in biological fluids. Shaikh and Allen[8] also reviewed physicochemical methods for determining aminoglycoside antibiotics in tissues and fluids of food producing animals. Salisbury *et al.*[9] reviewed chromatographic methods for the determination of aminoglycosides in food products. Isoherranen and Soback[10] also reviewed chromatographic methods for the analysis of aminoglycosides antibiotics.

The complexation of neomycin with a number of biochemically important compounds has been reported. Reports on Zn (II) and Cu (II) complexes in solution, are available but no information can be obtained about the solid complexes of aminoglycoside antibiotics with transition divalent metal ions. The coordination chemical studies of certain aminoglycosides antibiotics with Co (II), Ni (II) and Zn (II) were carried out by Abu *et al.*[11]. The complexes were characterized by elemental analysis, conductance and magnetic moment studies as well as IR, electronic and EPR spectra in order to gain more knowledge about their structure and geometry. Based on this study we have extended our research to the other aminoglycoside antibiotics, which are structurally closely related with the neomycin. The present work describes an indirect method for the determination of aminoglycoside antibiotics viz., amikacin sulphate, gentamicin sulphate and streptomycin sulphate by atomic absorption spectrometry, based on the formation of a complex with copper (II) ion. This method was used to determine these drugs either in the pure form or in pharmaceutical formulations.

EXPERIMENTAL

Apparatus

A GBC–902 Atomic Absorption Spectrophotometer (GBC Scientific Equipment) was used for the determination of copper. Instrumental setting used were: wavelength 327.4 nm, lamp current 3.0 mA, slit width 0.5 nm, air/acetylene ratio 4:1 and burner head, 3.5 cm. A bucket type digital Remi R8C, laboratory centrifuge was used to centrifuge the residue of copper carbonate.

Reagents

All the reagents used were of analytical reagent grade where otherwise not mentioned. Distilled water was used to prepare all solutions. Freshly prepared solutions were always employed.

1000 $\mu g\ mL^{-1}$ solution of Cu and Na are prepared by accurately weighing copper sulphate and sodium carbonate. Copper sulphate solution was standardized by the recommended method[12]

because of the adsorption of Cu (II) ions in the pores of the filter paper. At lower analyte concentrations, more copper carbonate is formed, resulting in a large surface area available for adsorption, hence slightly higher concentration of analyte is recommended for the better recovery by the proposed method.

The recommended procedure of separation using the centrifuge is found to be better technique for complete recovery of the complex and the results are in good comparison with the official methods. To confirm the validity of the method, pure authentic samples of aminoglycoside antibiotics were also analyzed. Excellent recovery in these analyses shows that the method is accurate and precise. The results of analysis for commercially available dosage forms are shown in Table 1.

Table 1. Determination of aminoglycoside antibiotic drugs as copper–aminoglycoside antibiotic complex by AAS

Aminoglycoside Antibiotic Drug	Amount taken ($\mu g\ mL^{-1}$)	Amount found ($\mu g\ mL^{-1}$)	Recovery* (%)	Mean Recovery ± SD (%)	Official Method[13–15]
Amikacin sulphate	25	24.50	98.00	99.37 ± 0.97	98.3 ± 1.22
	50	50.40	100.80		
	75	74.60	99.47		
	100	99.20	99.20		
Gentamicin sulphate	30	29.20	97.33	99.08 ± 1.01	99.0 ± 1.1
	60	59.80	99.67		
	180	179.60	99.78		
	240	238.90	99.54		
Streptomycin sulphate	75	74.50	99.33	99.51 ± 0.1	100.00 ± 0.01
	150	149.20	99.47		
	225	224.30	99.69		
	300	298.60	99.53		

*Average of three determinations

CONCLUSION

The proposed method is simple, economical and precise with higher sensitivity than the official methods[13–15]. Moreover, the reproducibility of the results are superior to those obtained from other methods. Hence, this approach could also be applied to detection in drug abuse cases in forensic laboratories.

because of the adsorption of Cu (II) ions in the pores of the filter paper. At lower analyte concentrations, more copper carbonate is formed, resulting in a large surface area available for adsorption, hence slightly higher concentration of analyte is recommended for the better recovery by the proposed method.

The recommended procedure of separation using the centrifuge is found to be better technique for complete recovery of the complex and the results are in good comparison with the official methods. To confirm the validity of the method, pure authentic samples of aminoglycoside antibiotics were also analyzed. Excellent recovery in these analyses shows that the method is accurate and precise. The results of analysis for commercially available dosage forms are shown in Table 1.

Table 1. Determination of aminoglycoside antibiotic drugs as copper–aminoglycoside antibiotic complex by AAS

Aminoglycoside Antibiotic Drug	Amount taken ($\mu g\ mL^{-1}$)	Amount found ($\mu g\ mL^{-1}$)	Recovery* (%)	Mean Recovery ± SD (%)	Official Method[13–15]
Amikacin sulphate	25	24.50	98.00	99.37 ± 0.97	98.3 ± 1.22
	50	50.40	100.80		
	75	74.60	99.47		
	100	99.20	99.20		
Gentamicin sulphate	30	29.20	97.33	99.08 ± 1.01	99.0 ± 1.1
	60	59.80	99.67		
	180	179.60	99.78		
	240	238.90	99.54		
Streptomycin sulphate	75	74.50	99.33	99.51 ± 0.1	100.00 ± 0.01
	150	149.20	99.47		
	225	224.30	99.69		
	300	298.60	99.53		

*Average of three determinations

CONCLUSION

The proposed method is simple, economical and precise with higher sensitivity than the official methods[13–15]. Moreover, the reproducibility of the results are superior to those obtained from other methods. Hence, this approach could also be applied to detection in drug abuse cases in forensic laboratories.

ACKNOWLEDGMENTS

The authors are indebted to Central Drugs Laboratory, Kolkata (India) for providing gift samples of amikacin sulphate, gentamicin sulphate and streptomycin sulphate. The authors also grateful to Mr. L. Baskaran, Food Laboratory, King Institute, Chennai, India and Mr. V.M. Venkatrangam, Mrs. S. Vijaya Chitra, Mr. R. Shanmugam and Mr. T. Venugopal, Department of Geology & Mining, Chennai, India for their valuable suggestions concerning this work.

REFERENCES

1. H. Ibrahim, Microchem. J., **44**, 99 (1991).
2. S. S. Hassan, "Organic Analysis Using Atomic Absorption Spectrometry", Horwood, Chichester and Halsted Press, New York (1984).
3. A. M. EL–Brashy and S. M. AL–Ghannam, J. AOAC Int., **80**, 741 (1997).
4. Graphischer Betrieb Konrad Triltsch, Wurtzburg, Ullman's Encyclopedia of Industrial Chemistry, 5th Ed., Vol. A2, Germany (1985) p. 467.
5. D. Banes, "A Chemist's Guide to Regulatory Analysis", AOAC, Arlington, VA, (1974) p. 56.
6. S. K. Mitra, T. T. Yoshikawa, J. L. Hansen, J. Nilsson–Ehle, W. J. Palin, M. C. Schotz and L. B. Guze, Clin. Chem., **23**, 2275 (1977).
7. S. K. Maitra, T. T. Yoshikawa, C. M. Steyn, L. B. Guzeand and M. C. Schotz, Antimicrob. Agents Chemother., **14**, 88 (1978).
8. B. Shaikh and E. H. Allen, J. AOAC, **68**, 1007 (1985).
9. C. D. C. Salisbury, in H. Oka, H. Nakazawa, K. E. Hayride and J. D. Mac Neil (Editors), "Chemical Analysis for Antibiotics Used in Agriculture," AOAC International, Arlington, VA, (1995) p. 235.
10. N. Isoherranen and S. Soback, J. AOAC Int., **82**, 1017 (1999).
11. S. M. Abu–El–Wafa, M. A. El–Ries, F. M. Abou–Attia and R. M. Issa, Anal. Lett., **22**, 2703 (1989).
12. G. H. Feffery, J. Bassett, J. Mendham and R. C. Denny, "Vogel's Text book of Quantitative Chemical Analysis", 5th Edition, Addison Wesley, Longman Inc., London, (2001), p. 286.
13. The United States Pharmacopeia XX, United States Pharmacopeial Convention, Inc., Rockville, MD, (1980) p.28.

14. Code of Federal Regulations, 21:Food and Drugs, Office of the Federal Register, National Archives and Records Service, Washington, DC, (1980) p. 449.
15. H. Kubo, Y. Kobayashi and T. Kinoshita, Anal. Chem., **58**, 2653 (1986).

Accepted 10.11.2003