



Study on detection methods for methyldopa in biological samples

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Abstract

Methyldopa (MDOP) is a catecholamine derivative which is used as an old antihypertensive agent in the treatment of mild to moderate hypertension. It is converted to α -methyl norepinephrine in adrenergic nerve terminals, and its antihypertensive action appears to be due to stimulation of central α -adrenoreceptors by this agent. Therefore, determination of this drug is very important. In this article the studies of detection methods for MDOP in biological samples in recent years are reviewed.

Keywords: Methyldopa; MDOP; catecholamine; determination; detection

1. Introduction

Methyldopa (MDOP), known as (2-amino-3-(3,4-dihydroxy-phenyl)-2-methyl-propanoic acid), is a catecholamine derivative and used as an old antihypertensive agent in the treatment of mild to moderate hypertension. Hypertension is a highly prevalent worldwide disease, constituting one of the main risk factors for cardiovascular morbidity and mortality [1-3]. Although the mechanism of antihypertensive action of MDOP has yet to be conclusively demonstrated, MDOP has been shown to cause a net reduction in the tissue concentration of serotonin, dopamine, norepinephrine, and epinephrine. MDOP works by relaxing blood vessels, which reduces blood pressure and allows blood and oxygen to circulate more freely around the body [4-6]. Therefore, determination of this drug is an important feature in pharmaceutical and clinical procedures. In this paper, the attributes of different analytical technique for the determination of MDOP in biological samples in recent years are reviewed.

2. Analytical Methods

2.1. Spectrophotometric method. High sensitivity, sufficient accuracy, simplicity, speed and the necessity of less expensive apparatus make spectrophotometric

method as an attractive method for the determination of MDOP in samples with different matrices such as biological and pharmaceutical samples. Currently, the combination of a flow-based technique such as flow injection analysis, with spectrophotometric detection methods increase the automation degrees and sample throughput for analysis of MDOP in various samples [7,8].

Ribeiro *et al.* [9] proposed a flow-injection spectrophotometric procedure for MDOP determination in pharmaceutical preparations. The determination was based on formation of a yellow product after complexation of MDOP with molybdate. Under optimal conditions, Beer's law was obeyed in a concentration range of 50–200 mg l^{-1} MDOP. The analytical results obtained in commercial formulations by applying the proposed flow-injection analysis method were in good agreement with labeled values and those obtained by the Brazilian Pharmacopoeia procedure at 95% confidence level.

Gadkariem *et al.* [10] developed a new, simple and low cost spectrophotometric method for the determination of MDOP in pharmaceutical preparations. The method was based on the coupling of MDOP with 2,6-

dichloroquinone-4-chlorimide. The absorbance maximum of the resulted colored product was at 400 nm. Beer's law was obeyed in concentration range of 4–20 µg/ml MDOP. The correlation coefficient was found to be 0.9975. The limit of detection and limit of quantification were 1.1µg/ml and 3.21µg/ml, respectively. The work included the study of the possible interference of hydrochlorothiazide found in combination with MDOP tablets. The method was validated and results obtained for the assay of two different brands of MDOP tablets were compared with the colorimetric method.

Upadhyay *et al.* [11] described a simple, sensitive, extractive spectrophotometric method for determination of MDOP in both pure form and in pharmaceutical formulations. The method was based on the reaction of diazotized *p*-aminoacetophenone with MDOP in basic medium to yield an orange-yellow-colored product having an absorption maximum at 440 nm. The orange-colored species was extracted in isopentanol. The colored species obeyed Beer's law in the range of 0.05–0.5µg/mL. Common excipients did not interfere with the proposed method. The proposed method offered the advantages of simplicity and higher sensitivity over the other existing methods.

2.2. HPLC method. High-performance liquid chromatography (HPLC) is a powerful tool that enables the separation of complex mixtures into individual components, and is a highly sensitive and reproducible analytical technique. In recent years, HPLC has been combined with many sensitive detection techniques and has experienced continuous improvement of stationary phases, which have improved its sensitivity and specificity. HPLC is currently widely used for the analysis of drugs and dosage forms with respect to quality control, quantitative determination of active ingredients and impurities, monitoring drug blood concentration in patients, and bioequivalence assessment [12,13].

Emara *et al.* [14] developed and validated a simple, rapid and environment-friendly direct injection HPLC method for the determination of MDOP in human serum. The method was based on cleanup and separation of MDOP from serum by mixed-mode liquid chromatography using a single protein-coated TSK gel ODS-80 TM analytical column. Solid-phase extraction and HPLC separation were carried out simultaneously with a green mobile phase consisting of acetate buffer at a flow rate of 1 mL/min and at room temperature. The eluent was monitored at emission and excitation wavelengths of 320 and 270 nm, respectively. A calibration curve was linear over the range of 0.1–30 mg/mL with a detection limit of 0.027 mg/mL. This online solid-phase extraction method was successfully applied to real samples obtained from patients receiving MDOP therapy.

Emara *et al.* [15] developed and validated a new rapid time-overlapping HPLC method using coupled-column double-injection technique with fluorescence detection to determine MDOP in human urine. The method was based on injecting a new sample onto the second column before finalizing the cleanup and the re-equilibration of the first column for the former sample. A combination of isocratic and gradient elution was employed according to a pre-set program. The calibration curve was linear over the concentration range of 0.1–40µg/mL MDOP. The overall mean recoveries were in the range of 98.29–101.39%. The applicability of the method was successfully evaluated by monitoring the incremental urinary excretion of MDOP in human urine over 12 hr after a single oral administration of 250 mg.

Bahrami *et al.* [16] described a simple and ultra rapid HPLC method coupled with alumina extraction and fluorescence detection for determination of MDOP in human serum. The drug and an internal standard were adsorbed onto alumina and eluted using acidic methanol. The eluate was directly injected onto ODS reverse phase column using a mixture of phosphate buffer containing triethylamine and methanol at a flow rate of 2.1 ml/min as the mobile phase. The limit of quantification was evaluated to be 20 ng/ml. Validity of the method was studied and the method was precise and accurate with a linearity range from 20 ng/ml to 5000 ng/ml. This method has been used in a randomized crossover bioequivalence study of two different MDOP preparations in 24 healthy volunteers.

2.3. Electrochemical method. Electrochemical methods have attracted more attention in recent years to monitor electroactive species, such as drugs and metabolites in biological fluids due to their simplicity, accuracy and lower cost without requiring complex sample pretreatment. MDOP is a catecholamine derivative, which are aromatic vic-diols and can be oxidized electrochemically to o-quinones. But ordinary electrochemical methods usually have not enough selectivity and sensitivity for analysis in complex matrix such as pharmaceutical and biological samples. Various methods are used to modify the surface of electrodes which can increase sensitivity and selectivity of the electrochemical sensors [17,18].

Perez-Mella *et al.* [19] modified a glassy carbon electrode with carbon nanotubes and the ionic liquid *N*-butyl pyridinium trifluoromethyl methanesulfonate for the determination of MDOP in urine samples. MDOP exhibited a well-defined anodic signal over a broad pH range of 2–10 and the peak current increased approximately 100 fold over that of the unmodified electrode. Accordingly, they proposed a novel method for the determination of MDOP using differential pulse voltammetry. The peak current was linear over a MDOP concentration range from 21 to 2111 ngmL⁻¹, and the detection and quantitation limits were 6.9 ngmL⁻¹ and 7.4

ngmL⁻¹. The method was applied to determine the excretion profile of MDOP in urine without sample pretreatment.

Salmanipour *et al.* [20] reported the determination of MDOP for a carbon nanotube (CNT) modified carbon-paste electrode and ferrocene (FC) electrocatalyst. The cyclic voltammetric results indicated that the CNT and FC system could remarkably enhance electrocatalytic activity toward the oxidation of MDOP. This enhancement led to a considerable improvement of the anodic peak current for MDOP, and allowed the development of a highly sensitive voltammetric sensor for the detection of MDOP in real samples. Under optimized conditions on the sensor, the proposed method showed a wider dynamic range in comparison to other reported electrochemical methods, with a detection limit of $0.08 \pm 0.002 \mu\text{M}$. In addition, the proposed method was able to determine MDOP in the presence of folic acid.

Molaakbari *et al.* [21] used a carbon paste electrode modified with TiO₂ nanoparticles and ferrocene monocarboxylic acid to prepare a novel electrochemical sensor for seeking new electrochemical performances for the detection of MDOP in the presence of folic acid and glycine. Under the optimum pH of 7.0, the oxidation of MDOP occurred at a potential about 160 mV less positive than that of the unmodified carbon paste electrode. The response of catalytic current with MDOP concentration showed a linear relation in the range from 2.0×10^{-7} to 1.0×10^{-4} M with a detection limit of 8.0×10^{-8} M.

2.4. Other methods. In addition to these main approaches mentioned above for MDOP detection, still a few special techniques with high sensitivity have been applied. Tubino *et al.* [22] proposed a reliable and very simple kinetic method for the determination of MDOP in pharmaceutical preparations. Wang *et al.* [23] developed a simple capillary electrophoresis method for the determination of levodopa and MDOP in human serum. Talebpour *et al.* [24] developed a method utilizing NMR spectroscopy to confirm the identity and quantity of levodopa, carbidopa and MDOP in human serum and pharmaceutical preparations. Ribeiro *et al.* [25] described a very simple and rapid quantitative reflectance spot test procedure for the determination of MDOP in pharmaceutical formulations.

3. Conclusion

MDOP is one of the most important drugs used for treatment of high blood pressure. A change in the concentration of this drug in the body may influence the bioavailability and biopharmaceutical properties of the pharmaceutical preparation and subsequently, their magnitude of action. Therefore, in order to achieve a better curative effect and a lower toxicity, it is very important to rapidly control the content of MDOP and

impurities in biological fluids and pharmaceutical formulations [26,27]. This review has highlighted the significant developments in rapid and alternative techniques for the detection of MDOP in recent years. We believe the development of MDOP sensors with better sensitivity and specificity, lower cost, simplicity, along with in vivo analytical technique is still the future effort.

Acknowledgments

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References

- [1] Vahedi J, Karimi-Maleh H, Baghayeri M, Sanati AL, Khalilzadeh MA, Bahrami M. A fast and sensitive nanosensor based on MgO nanoparticle room-temperature ionic liquid carbon paste electrode for determination of methyl dopa in pharmaceutical and patient human urine samples, *Ionics* 2013; 19(12):1907-1914.
- [2] Gholivand MB, Amiri M. Highly sensitive and selective determination methyl dopa in the presence of ascorbic acid using OPPy/TY/Au modified electrode, *J Electroanal Chem* 2013; 694:56-60.
- [3] Shahrokhian S, Rastgar S. Electrodeposition of Pt-Ru nanoparticles on multi-walled carbon: Application in sensitive voltammetric determination of methyl dopa, *Electrochim Acta* 2011; 58:125-133
- [4] Ghoreishi SM, Saeidinejad F, Behpour M, Masoum S. Application of multivariate optimization to electrochemical determination of methyl dopa drug in the presence of diclofenac at a nanostructured electrochemical sensor, *Sens Actuator B: Chem* 2015; 221:576-585.
- [5] Gupta VK, Khosravi S, Karimi-Maleh H, Alizadeh M, Sharafi S. A voltammetric sensor for determination of methyl dopa in the presence of hydrochlorothiazide using Fe:Co nanoalloy modified carbon paste electrode, *Int J Electrochem Sci* 2015; 10(4):3269-3281.
- [6] Shahrokhian S, Saberi RS, Kamalzadeh Z. Sensitive electrochemical sensor for determination of methyl dopa based on polypyrrole/carbon nanoparticle composite thin film made by in situ electropolymerization, *electroanalysis* 2011; 23(9):2248-2254.
- [7] Chamsaz M, Safavi A, Fadaee J. Simultaneous kinetic-spectrophotometric determination of carbidopa, levodopa and methyl dopa in the presence of citrate with the aid of multivariate calibration and artificial neural networks, *Anal Chim Acta* 2007; 603(2):140-146.

- [8] Ribeiro PRD, Duarte RM. Development and validation of a simple spectrophotometric method for the determination of methyl dopa in both bulk and marketed dosage formulations, *Braz J Pharm Sci* 2014; 50(3):573-582.
- [9] Ribeiro PRS, Neto JAG, Pezza L, Pezza HR. Flow-injection spectrophotometric determination of methyl dopa in pharmaceutical formulations, *Talanta* 2005; 67(1):240-244.
- [10] Gadkariem EA, Ibrahim KEE, Kamil NAA, Haga MEM, El-Obeid HA. A new spectrophotometric method for the determination of methyl dopa, *Saudi Pharm J* 2009; 17(4): 289-293.
- [11] Upadhyay K, Asthana A, Tamrakar RK. Extractive spectrophotometric determination of alpha-methyl dopa in bulk dosage and in its formulations, *Res Chem Intermed* 2015; 41(8):5521-5528.
- [12] Ye NS, Gao T, Li J. Hollow fiber-supported graphene oxide molecularly imprinted polymers for the determination of dopamine using HPLC-PDA, *Anal Methods* 2014; 6(18):7518-7524.
- [13] Capone DL, Ristic R, Pardon KH, Jeffery DW. Simple quantitative determination of potent thiols at ultratrace levels in wine by derivatization and high-performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS) analysis, *Anal Chem* 2015; 87(2):1226-1231.
- [14] Emara S, Masujima T, Zarad W, Kamal M, Fouad M, El-Bagary R. An eco-friendly direct injection HPLC method for methyl dopa determination in serum by mixed-mode chromatography using a single protein-coated column, *J Chromatogr Sci* 2015; 53(8):1353-1360.
- [15] Emara S, Masujima T, Zarad W, Kamal M, Fouad M, El-Bagary R. A combination of isocratic and gradient elution modes in HPLC with the aid of time-overlapping process for rapid determination of methyl dopa in human urine, *J Liq Chromatogr Relat Technol* 2015; 38(2):153-162.
- [16] Bahrami G, Kiani A, Mirzaeei S. A rapid high performance liquid chromatographic determination of methyl dopa in human serum with fluorescence detection and alumina extraction: application to a bioequivalence study, *J Chromatogr B* 2006; 832(2):197-201.
- [17] Tajik S, Taher MA, Beitollahi H. First report for simultaneous determination of methyl dopa and hydrochlorothiazide using a nanostructured based electrochemical sensor, *J Electroanal Chem* 2013; 704:137-144.
- [18] Rezaei B, Askarpour N, Ensafi AA. Adsorptive stripping voltammetry determination of methyl dopa on the surface of a carboxylated multiwall carbon nanotubes modified glassy carbon electrode in biological and pharmaceutical samples, *Colloid Surf B-Biointerfaces* 2013; 109:253-258.
- [19] Perez-Mella B, Alvarez-Lueje A. Development of a carbon nanotube modified ionic liquid electrode for the voltammetric determination of methyl dopa levels in urine, *Electroanalysis* 2013; 25(9):2193-2199.
- [20] Salmanipour A, Taher MA, Beitollahi H. Voltammetric behavior of a multi-walled carbon nanotube modified electrode-ferrocene electrocatalyst system as a sensor for determination of methyl dopa in the presence of folic acid, *Anal Methods* 2012; 4(9):2982-2988.
- [21] Molaakbari E, Mostafavi A, Beitollahi H. First report for voltammetric determination of methyl dopa in the presence of folic acid and glycine, *Mater Sci Eng C-Mater Biol Appl* 2014; 36:168-172.
- [22] Tubino M, Batista DCDV, Rodrigues JAR. Kinetic method for the determination of alpha-methyl dopa in pharmaceutical preparations: Analytical procedure and reaction mechanism considerations, *Anal Lett* 2006; 39(2):327-339.
- [23] Wang C, Wang Z, Han DD, Hu YX, Zhao J, Yang XM *et al.* Simultaneous determination of levodopa and methyl dopa in human serum by capillary electrophoresis, *Chin J Chromatogr* 2006; 24(4):389-391.
- [24] Talebpour Z, Haghgoo S, Shamsipur M. H-1 nuclear magnetic resonance spectroscopy analysis for simultaneous determination of levodopa, carbidopa and methyl dopa in human serum and pharmaceutical formulations, *Anal Chim Acta* 2004; 506(1):97-104.
- [25] Ribeiro PRS, Pezza L, Pezza HR. Determination of methyl dopa in pharmaceutical formulations by combined spot test-diffuse reflectance spectroscopy, *J Braz Chem Soc* 2006; 17(4):674-679.
- [26] Fouladgar M, Karimi-Maleh H. Ionic liquid/multiwall carbon nanotubes paste electrode for square wave voltammetric determination of methyl dopa, *Ionics* 2013; 19(8):1163-1170.
- [27] Mohammadi SZ, Beitollahi H, Jasemi M, Akbari A. Nanomolar determination of methyl dopa in the presence of large amounts of hydrochlorothiazide using a carbon paste electrode modified with graphene oxide nanosheets and 3-(4-Amino-3-hydroxy-biphenyl-4-yl)-acrylic Acid, *Electroanalysis* 2015; 27(10):2421-2430.

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