Sequential determination of cadmium and lead in organic pharmaceutical formulations using high-resolution continuum source graphite furnace atomic absorption spectrometry

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ABSTRACT

This paper proposes a method using high resolution continuum source graphite furnace atomic absorption spectrometry (HR CS GFAAS) for the sequential determination of cadmium and lead in organic pharmaceutical formulations. The temperature program for cadmium was established employing the pyrolysis and atomization temperatures of 800 °C and 1400 °C, respectively, and the atomization temperature of 2000 °C for lead, being that the pyrolysis temperature for lead is the same used for the cadmium atomization. The analytical measures were performed using the primary lines for cadmium (228.802 nm) and (217.001 nm) for lead. The absorbance signals obtained were quantified by peak area using 3 pixels for both analytes, utilizing as chemical modifier an acid mixture palladium-magnesium. Employing the optimized conditions, the method allows the sequential determination of cadmium and lead, with limits of detection and quantification of 4 and 13 ng g^{-1} for cadmium and 49 and 165 ng g^{-1} for lead, respectively. The characteristics masses were also calculated, being 1.6 pg for cadmium and 12.4 pg for lead. The precision expressed as relative standard deviation (%RSD) were 5.0% for cadmium and 6.2% for lead, determined by ten replicates of a sample solution with cadmium and lead contents of 38 and 303 ng g^{-1}, respectively. The method accuracy was evaluated and confirmed by analysis of two certified reference materials of leaves furnished by National Institute of Standards and Technology (NIST). Furthermore, addition/recovery tests were also performed using three different real samples. The recoveries obtained varied from 94 to 114%, it confirming the method accuracy. The method was applied for the determination of cadmium and lead in ten different pharmaceutical formulations and the analyte concentrations found in the samples varied from 16 to 51 ng g^{-1} for cadmium and of 179 to 318 ng g^{-1} for lead, being that for six samples the lead contents were lower than the limit of quantification (165 ng g^{-1}) and for three samples the cadmium concentrations were lower than 13 ng g^{-1}. All samples were also analyzed employing inductively coupled plasma mass spectrometry (ICP-MS) and the results obtained are agreement with those achieved by HR CS GFAAS.

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1. Introduction

The presence of metals and metalloids in pharmaceutical formulations comes from impurities derived from raw materials, as well as contamination due to: transport and storage of raw materials, and also metal catalysts employed in the syntheses of some drugs [1,2]. Generally, the concentrations of these elements are low and analytical methods with great sensitivity (low limits of quantification) are required for these determinations. Thus, the development of analytical methods to determine impurities in medicine samples is notably necessary. A preconcentration procedure using thiourea immobilized silica was proposed for determination of lead and cadmium in pharmaceutical products by inductively coupled plasma optical emission spectrometry [3]. Ferreira et al. determined lead in aluminum and magnesium antacids using electrothermal atomic absorption spectrometry [4]. Flores evaluated sample digestion methods for the determination of toxic elements in tricyclic active pharmaceutical ingredients by ICP-MS [5]. Santos et al. determined mercury in iron supplements used for the treatment of anemia [6]. Rosolina et al. proposed a direct method for determination of cadmium and lead in pharmaceutical ingredients using anodic stripping voltammetry [7].

High resolution continuum source atomic absorption spectrometry (HR CS AAS) has several advantages over conventional atomic absorption spectrometry (AAS). Among these, there is the ability to multi-elemental determinations established by simultaneous or sequential methods. The simultaneous determinations require that all the lines of the elements that will be determined should be on the same spectral

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Table 1
Temperature program established for the sequential determination of cadmium and lead in medicine samples by HR-CS GF AAS.

Stage	Temperature/°C	Ramp/°C s^{-1}	Hold time/s	Ar flow rate/L min^{-1}
Drying 1	100	3	20	2.0
Drying 2	120	5	10	2.0
Pyrolysis	800	300	10	2.0
Atomization of Cd	1400	3000	5	0.0
Cooling stage and change of wavelength				
Pyrolysis[a]	800	300	1	2.0
Atomization of Pb	2000	3000	5	0.0
Clean	2450	500	4	2.0

[a] This pyrolysis step is not necessary for the sequential determination, but is required by the software of the equipment.

window of the detector. Also, the pyrolysis temperature is determined by the most volatile element and the atomization temperature is established considering the most refractory element. By other hand, for the sequential determinations to two elements, the thermal program is established by the pyrolysis and atomization temperatures for the most volatile element and the atomization temperature for the most refractory element. In this case, the pyrolysis step of the second element occurs during the atomization step of the first element [8,9]. This way, several analytical strategies have been proposed employing HR CS AAS for determination of two or more elements using sequential or simultaneous approach [8–21]. High-resolution continuum source graphite furnace atomic absorption spectrometry (HR CS GFAAS) allowed the sequential determination of cadmium and chromium in biomass samples and their ashes [10]. Antimony and lead were sequential determined in pewter alloys using high-resolution continuum source flame atomic absorption spectrometry (HR CS FAAS) [11]. Krawczyk et al. proposed a solid phase system employing multiwalled carbon nanotubes for preconcentration and sequential determination of iron and zinc in water samples by HR CS GFAAS [12]. Guerrero et al. proposed a preconcentration procedure using solid phase extraction for sequential determination of antimony, bismuth, tin and mercury employing HR CS AAS [13]. Silva et al. developed a sequential direct method for the determination of cadmium, cobalt, copper, iron, manganese, sodium, nickel, lead and zinc in ethanol fuel using HR CS FAAS [14]. Gomez-Nieto et al. established a method for the fast sequential multi-element determination of eleven elements in environmental samples [15]. Other method was proposed for the sequential determination of lead and cadmium in water samples after a preconcentration step utilizing multiwalled carbon nanotubes as solid sorbent. The quantification was performed by HR-CS GFAAS using the lines 228.8018 nm for cadmium and 283.3060 nm for lead [16]. Vale et al. proposed a multi-elemental method for the sequential and simultaneous determination of cadmium, chromium, iron and aluminum in soil samples. Firstly cadmium was determined in the line 228.802 nm. Afterward chromium, iron and aluminum were quantified simultaneously using the lines

425.433 nm, 425.076 nm and 425.315 nm, respectively [17]. Others methods using sequential and simultaneous determinations include: manganese and chromium in vegetable oil and biodiesel samples [18], cadmium, iron and tin in canned food samples [19], cobalt, iron, nickel and lead in carbon nanotubes [20], cobalt, aluminum and iron in waste water [21] and etc.

Nowadays, the optimization of other methods has been often performed using multivariate methodologies [22–25]. The two-level full factorial design is the tool more employed. This allows evaluate the effects of the experimental factors and their interactions on the studied processes [24,26,27].

The present paper proposes an analytical method for sequential determination of cadmium and lead in organic pharmaceutical formulations employing HR CS GFAAS. The optimization of the pyrolysis and atomization temperatures was performed utilizing two-level full factorial design.

2. Experimental

2.1. Instrumentation

A model ContrAA 700 high resolution continuum source graphite furnace absorption atomic spectrometer from Analytik Jena AG (Jena, Germany) was used to sequentially determinate cadmium and lead in pharmaceutical samples. This spectrometer is equipped with a Xe short-arc lamp (GLE, Berlin, Germany) operating in the hot-spot mode as continuum radiation source with nominal potential of 300 W, a high resolution double Echelle monochromator and a charge-coupled device linear array detector. In addition, the equipment has a transversely heated graphite tube atomizer supplied with a MPE 60 autosampler (Analytik Jena AG) to introduce liquid samples. Pyrolytically coated graphite tube with integrated platform furnished by same manufacturer was used to sequentially atomize the elements. Argon with 99.998% purity from White Martins (Salvador, BA, Brazil) was used as the purge and protective gas with a flow rate of 2.0 L min^{-1} during all heating stages, except during atomization, when the gas flow was stopped. All sequential measurements were performed using the primary atomic absorption lines of cadmium and lead located at 228.8018 and 217.0001 nm, respectively. The absorbance signals were obtained by peak height using an integration time of 5.0 s and three pixels (pixel central plus the adjacent ones, CP $\pm$ 1) for both analytes.

As a comparative method, a mass spectrometer with inductively coupled plasma (ICP-MS) model XSeries[II] from Thermo Fisher Scientific (Bremen, Germany) was also used to determinate cadmium and lead in the medicine samples after acid digestion. This equipment has a hexapole collision cell, nickel sampler, skimmer cones and a model ASX-520 autosampler from Teledyne CETAC Technologies (Omaha, NE, USA) to automatically introduce the samples. Sample introduction was performed with concentric nebuliser and spray chamber with Peltier cooling. The operating conditions used to determinate the elements were radio frequency applied power of 1.3 kW, nebulizer gas

Table 2
Optimization of the heating program using two-level full factorial design.

Experiment	Pyrolysis temperature Cd	Atomization temperature Cd	Atomization temperature Pb	Analytical signal cadmium	Analytical signal lead	Multiple response (Cd + Pb)
1	−1 (600 °C)	−1 (1200 °C)	−1 (1800 °C)	0.0953	0.1192	1.2179
2	1 (1000 °C)	−1 (1200 °C)	−1 (1800 °C)	0.1394	0.1257	1.4969
3	−1 (600 °C)	1 (1600 °C)	−1 (1800 °C)	0.1679	0.0725	1.3414
4	1 (1000 °C)	1 (1600 °C)	−1 (1800 °C)	0.1288	0.0806	1.1748
5	−1 (600 °C)	−1 (1200 °C)	1 (2200 °C)	0.0827	0.1591	1.3823
6	1 (1000 °C)	−1 (1200 °C)	1 (2200 °C)	0.1581	0.1604	1.8019
7	−1 (600 °C)	1 (1600 °C)	1 (2200 °C)	0.1640	0.1567	1.8124
8	1 (1000 °C)	1 (1600 °C)	1 (2200 °C)	0.1272	0.1232	1.4155
CP	0 (800 °C)	0 (1400 °C)	0 (2000 °C)	0.1831	0.1709	1.9997
CP	0 (800 °C)	0 (1400 °C)	0 (2000 °C)	0.1771	0.1627	1.9197
CP	0 (800 °C)	0 (1400 °C)	0 (2000 °C)	0.1749	0.1675	1.9350