Alma Mater Studiorum Università di Bologna
Archivio istituzionale della ricerca

New polluting metals. Quantification in herbal medicines by voltammetric and spectroscopic analytical methods

(Article begins on next page)

18 August 2024

1   **NEW POLLUTING METALS.**

2   **QUANTIFICATION IN HERBAL MEDICINES BY**

3   **VOLTAMMETRIC AND SPECTROSCOPIC ANALYTICAL METHODS**

4

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17

18   **Abstract**

19   A new application of voltammetric techniques in stripping mode to the quantitative determination of

20   metals belonging to the platinum group (PGM) in herbal medicines, at the ultra-trace level, is

21   reported. Pd (II), Pt (II) and Rh (III) are determined by means of square-wave adsorption voltammetry

22   (SWAdSV); Os (VIII) and Ru (III) are determined through catalytic square-wave voltammetry

23   (SWCV); Ir (III) is determined through the application of square-wave catalytic adsorption

24   voltammetry (SWAdCSV). In all the applied methods, a conventional three-electrode voltammetric

25   cell is employed, which sees the presence of a suspended mercury-drop electrode (HMDE) or a glassy

26   carbon electrode (GCE) as working electrodes for the determination of Ir (III). The auxiliary electrode

27   was a platinum electrode, and an $Ag\,|\,AgCl\,|\,KCl_{satd.}$ electrode was employed as reference electrode.

28   Validation of the analytical procedure here proposed has been achieved using reference standards:

29   NIST-SRM 1570a (Spinach Leaves) and NIST-SRM 1573a (Tomato Leaves), both added with pure

30   metal standards, obtaining more than good precision values and better than the limits set for the

31   validation of quantitative methods. Following the verification of the validity of the procedure

32   indicated here, commercially available herbal medicines, based on *Eucalyptus globulus,*

33   *Harpagophytum procumbens* DC and *Taraxacun officinale weber*, were analyzed. Standard samples

34   were also analyzed by atomic absorption spectroscopy in order to have a reference technique for

35   validating the entire procedure.

36

37

38   **Keywords**: PGMs, Voltammetry, Spectroscopy, Herbal Medicines.

39

1. INTRODUCTION

In recent years, the Scientific Community has paid increasing attention to metals belonging to the platinum group (PGM), especially in the environmental field and following the increase in their concentration in this type of matrices. This effect is attributable to the use of these metals in various anthropic sectors such as the production of industrial catalysts, anticancer drugs, jewelry, and use of autocatalytic converters. This last element, especially linked to the incorrect "stop and go" use of these converters, with consequent deterioration and abrasion, implies a significant release into the environment of airborne particulate matter characterized by high content of PGM and is currently the most relevant source of contamination by PGM. The increase has been all the greater since the transition from platinum, palladium and rhodium-based catalysts to the increasing use of iridium, ruthenium and, above all, osmium [1].

The main problem observed with PGMs is their persistence in the environment, with serious damage to food safety. This is above all linked to the fact that they have a tendency to bioaccumulation in all environmental matrices (plants, terrestrial and aquatic organisms) thus representing a way of entry into the food chain. Human beings, as the final element of this supply chain, therefore represent the subjects most exposed and at risk, especially in light of the toxicity of PGMs in their various bioavailable forms [2]. What has been observed so far certainly finds reason to exist in the normal food chain, but the growing use of food supplements entails the need to monitor these PGMs also in these products, even if currently the Scientific Community does not yet consider them in this sense.

Food supplements, encompassing a wide range of products ranging from vitamins and minerals to herbal agents (remedies and medicines based on herbs), various extracts and enzymes, require constant evaluation and quality control to ensure that toxic levels fall within acceptable limits. In this context, medicinal herbs are certainly a significant component of the market, if not the dominant one. Herbal medicines are currently referred to as "*products of plant origin used for*

65 *medicinal and/or nutritional purpose*s", encompassing a large range of products, from herbal teas to

66 products for nutritional-care and body-care.

67   Despite herbal medicines can be considered not dangerous to health, being derived from

68 natural products, unfortunately there is currently not much scientific evidence to support this general

69 belief. While synthetic products can be purified and stabilized in their formulations, with a defined

70 dosage to obtain the therapeutic effect and minimizing the adverse effects, herbal medicines are

71 difficult to standardize due to raw extracts containing different active ingredients (phytocomplex).

72 This is above all linked to the fact that different pharmacologically active ingredients are present in

73 the phytocomplex, often similar to synthetic compounds but potentially showing a greater number of

74 adverse effects [1, 3-4].

75   Another element not to be overlooked is that, to date, there is no real regulation for the

76 production of herbal medicines, combined with the fact that they can be purchased without a

77 prescription. In light of these regulatory deficiencies, international organizations like WHO (World

78 Health Organization and FDA (US Food and Drug Administration) simply recommend to check for

79 the quantity of toxic heavy metals in medicinal plants, starting from raw materials. Only for some of

80 these metals the upper-threshold admissible limits are defined: 1.0 ppm for mercury; 10.0 ppm for

81 lead; 0.3 ppm for cadmium; 10.0 ppm for arsenic [5-6]. For all other metals, a real decision has not

82 been evaluated and/or taken, yet; probably this happens because, in many cases, these metals are

83 considered micronutrients and consequently their potential harmfulness is not adequately taken into

84 account when they are assumed in large quantities.

85   In the analysis of metals, the most widely used instrumental technique is certainly the

86 electrothermal atomic absorption spectroscopy (ET-AAS) [7-9], especially in the configuration that

87 envisages the graphite furnace (GF-AAS) as an atomization device. In the literature there are some

88 works [10, 11] in which the herbal medicine fingerprint is obtained using this technique, which can

89 then be processed using chemometric approaches to investigate their origin [12], or the possible

90 evaluation of fraud [13].

In recent years, a line of research has been expanded in our laboratories that includes investigating new approaches to quantitatively determine PGMs in environmental and food samples [14-30] through the application of such spectroscopic techniques, and only recently to quantify toxic metals in matrices characterizing such categories of samples [8 and bibliography, 31 and bibliography].

In this context, especially considering the lack of studies relating to the voltammetric determination of PGMs in herbal medicines, we wanted to develop a procedure to meet the needs related to the quality control and characterization of these matrices. This paper presents studies and results related to the following voltammetric techniques: square wave adsorbent stripping voltammetry (SWAdSV) [Pd (II), Pt (II), Rh (III)], square-wave catalytic voltammetry (SWCV) [Ru (III), Os (VIII)] and square-wave catalytic adsorbent stripping voltammetry with (SWAdCSV).

2. EXPERIMENTAL

2.1 Instrumentation

The acquisition of voltammograms was performed by a Multipolarograph AMEL Mod. 433 (Milan, Italy). The measuring cells (three-electrode set-up) is structured in the case of iridium with a working electrode consisting in a glassy-carbon electrode (GCE, AMEL, Milan; 7.065-mm^{2}surface area). For all the other PGMs herein considered, a stationary HMDE was used. In all cases, Ag│AgCl│KCl$_{satd.}$ was the reference electrode and a platinum-wire electrode was the auxiliary electrode. The Teflon voltammetric cell was rinsed many times before carrying out measurements, in order to prevent contamination. This procedure was performed as follow: *i)* a first rinsing with supra-pure HNO$_3$ 69%$_{w/w}$, diluted 1:1 with water obtained by a Milli-Q deionizing system (Millipore, Darmstadt, Germany); *ii)* the cell was rinsed many times using Milli-Q water.

Disposable plastic tips were used for the standard additions. The solutions were previously thermostated at $20.0\pm0.5°C$ and treated by pure N$_2$ for 5 min to remove oxygen. During the measurements, solutions were kept under nitrogen. The magnetic stirring (with Teflon-coated

117   magnetic stirring bar) was constantly maintained during the purge step. For the analyses here

118   presented, the supporting electrolytes and the voltammetric parameters are reported in Table 1 and

119   Table 2.

120

121   **Table 1.** Instrumental details for Pd(II), Pt(II), Rh(III) by SWAdSV and Pb(II) by SWASV.
122   Supporting electrolytes: HCl 0.15 mol L^{-1} + dimethylglyoxime $1.9 \cdot 10^{-4}$ mol L^{-1} [Pd(II)] and HCl 0.15
123   mol L^{-1} + dimethylglyoxime $1.9 \cdot 10^{-4}$ mol L^{-1} + formaldehyde 0.65 mmol L^{-1} + hydrazine (formazone
124   complex) 1.25 mmol L^{-1} in HCl 0.15 mol L^{-1} [Pt(II) and Rh(III)].
125

126   **Table 2.** Instrumental parameters for Ru(III) and Os(VIII) by SWCV, and Ir(III) by SWAdCSV.
127   Supporting electrolytes: acetate buffer 0.5 mol L^{-1} pH 4.9 + NaBrO$_3$ $7.3 \cdot 10^{-2}$ mol L^{-1} [Os(VIII),
128   Ru(III)], and acetate buffer 0.5 mol L^{-1} pH 4.9 + NaBrO$_3$ $7.3 \cdot 10^{-2}$ mol L^{-1} + cetyltrimethylammonium
129   bromide $4.9 \cdot 10^{-5}$ mol L^{-1} + KCl 0.25 mol L^{-1} [Ir (III)].

130

131   An Atomic Absorption Spectrometer by Perkin-Elmer (Mod. A-Analyst 100 with deuterium

132   background-corrector, Autosampler AS-72 and graphite furnace model HGA 800), was used for the

133   acquisition of ET-AAS measurements. The light sources were Lumina hollow-cathode lamps for

134   single-element measurements (Perkin-Elmer, USA), while the steps of ashing and atomization

135   (different from element to element) were set up as reported in the literature [32]. Table 3 reports the

136   instrumental parameters, optimized in the present work.

137

138   **Table 3**. Instrumental details for Pd(II), Pt(II), Ir(III), Os(VIII), Rh(III) and Ru(III) by GF-AAS.
139   Injected volume: 20 μL. Argon flow: 60 mL min^{-1} only in the atomization step, 300 mL min^{-1} in all
140   other steps. For all the elements no matrix modifier is employed.

141

142   *2.2 Reagents and Reference Solutions*

143   Chemicals at suprapure-grade (Merck, Darmstadt, Germany) were used in this work, while a

144   Milli-Q system was use to obtain demineralized water. Reference standard solutions were obtained

145   starting from acidic standard solutions: Ir(III), Pd(II), Pt(II), Rh(III), Ru(III) (1000 mg L^{-1}, Merck,

146   Darmstadt, Germany). Osmium tetroxide solution in water (4%$_{w/w}$, Sigma-Aldrich, Darmstadt,

147   Germany) was used as starting standard solution. In order to optimize the instrumental parameters,

148 two reference materials were used as standard: NIST-SRM 1570a (Spinach Leaves) and NIST-SRM

149 1573a (Tomato Leaves) (National Institute of Standards and Technology, Gaithersburg, MD, USA).

150

151 *2.3 Sample Preparation*

152   The standard reference materials (NIST-SRM 1570a and NIST-SRM 1573a) and the herbal

153 medicines (*Eucalyptus globulus, Harpagophytum procumbens DC* and *Taraxacum officinale Weber*)

154 were solubilized by an acidic attack using a mixture of HCl, HNO_3 and H_2SO_4 .

155   The vegetables were accurately weighed (order of magnitude: 1 g), and put in a 25-mL Pyrex-

156 tube for digestion, and a solution containing 4 mL HNO_3 69%$_{w/w}$, 4 mL HCl 37%$_{w/w}$ and 5 mL H_2SO_4

157 96% $_{w/w}$ was added. Then a Vigreux column condenser was connected to the tube , and the tube was

158 inserted into a cold block digester (appositely homemade); finally, the temperature was progressively

159 raised up to 150°C and maintained at this final temperature for 2 h to achieve the mineralization.

160 After this step, the content was dried, cooled, and dissolved in Milli-Q water (25 mL) or in 25 mL of

161 the supporting electrolyte.

162

163 *2.4 Voltammetric procedure for Pd(II)-Pt(II)-Rh(III)*

164   The voltammetric procedure for Pd(II)-Pt(II)-Rh(III) consists in two steps: *i)* 10-mL sample

165 aliquot of HCl 0.15 mol L^{-1} + dimethylglyoxime (DMG) $1.9 \cdot 10^{-4}$ mol L^{-1} aqueous reference solution

166 or solutions obtained in the mineralization step were transferred into the voltammetric cell; de-

167 aeration was achieved by bubbling water-saturated pure N_2 for 5 min. The determination of Pd(II)

168 was carried out by SWAdSV; *ii)* 0.5 mL of formaldehyde $1.37 \cdot 10^{-2}$ mol L^{-1} + hydrazine (formazone

169 complex) $2.63 \cdot 10^{-2}$ mol L^{-1} in HCl 0.15 mol L^{-1} solution (final concentration: formaldehyde = 0.65

170 mmol L^{-1} and hydrazine = 1.25 mmol L^{-1}) were added. The determination of Pt(II) and Rh(III) was

171 carried out by SWAdSV.

172

173 *2.5 Possible interference from Pb(II) and Zn(II) in quantifying Pd(II) and Pt(II) by voltammetry*

174   In the experimental conditions applied herein for the Pd(II), Pt(II) and Rh(III) determination,

175   also Pb(II) and Zn(II) show voltammetric peaks (-0.485 and -0.877 V *vs.* Ag│AgCl│KCl$_{satd.}$,

176   respectively). Hence, there is a possible interference with Pd (II) and Pt (II) (-0.343 and -1.027 V

177   *vs.* Ag│AgCl│KCl$_{satd.}$, respectively), involving in two possible interference cases: Pd(II)-Pb(II) and

178   Pt(II)-Zn(II). Figure 1 reports the voltammetric peak due to Pb (II), which shows very low

179   reversibility degree in the employed supporting electrolyte. However, it is worth pointing out that this

180   element, when present at very high concentration ratios ($c_{Pb(II)} : c_{Pd(II)} > 650$ µg g^{-1}), certainly could

181   be a possible interfering species in the Pd(II) voltammetric determination.

182

183   **Figure 1**. Square-wave adsorptive stripping voltammogram: determination of Pd(II) in the presence
184   of Pb(II) in *Taraxacun officinale weber*. Supporting electrolyte: HCl 0.15 mol L^{-1} + DMG 1.9·10^{-4}
185   mol L^{-1}. Peak 1 corresponds to Pd(II); peak 2 corresponds to Pb(II).
186   Experimental conditions: see Table 1
187

188   Similarly, Zn(II) may interfere during Pt(II) quantification, showing a voltammetric peak at –

189   0.877 V *vs.* Ag│AgCl│KCl$_{satd.}$ (Figure 2). Again, the Zn(II) electrode process shows a low

190   reversibility degree in the employed supporting electrolyte, and the interference can observed only in

191   the case of very high concentrations ratios ($c_{Zn(II)}:c_{Pt(II)} > 750$ µg g^{-1}).

192
193   **Figure 2**. Square-wave adsorptive stripping voltammogram: determination of Pt(II) and Rh(III) in
194   the presence of Zn(II) in *Taraxacun officinale weber*. Supporting electrolyte: HCl 0.15 mol L^{-1} +
195   DMG 1.9·10^{-4} mol L^{-1} + formaldehyde 0.65 mmol L^{-1} + hydrazine (formazone complex in 0.15 mol
196   L^{-1} HCl) 1.25 mmol L^{-1}. Peak 1 corresponds to Zn(II), peak 2 corresponds to Pt(II), peak 3
197   corresponds to Rh(III). Experimental conditions: Table 1.
198

199   *2.6 Voltammetric procedure for Ir(III), Os(VIII) and Ru(III)*

200   The voltammetric procedure for Ir(III)-Os(VIII)-Ru(III) is carried out two steps:

201   *i*) 10-mL sample aliquots of acetate buffer 0.5 mol L^{-1} pH 4.9 + NaBrO$_3$7.3·10^{-2} mol L^{-1} aqueous

202   reference solution, or of solutions obtained in the mineralisation step containing acetate buffer 0.5

203   mol L^{-1} pH 4.9 + NaBrO$_3$ 7.3·10^{-2} mol L^{-1}, were transferred into the voltammetric cell; de-aeration

204 was kept for 5 min by bubbling water-saturated pure N_2. The determination of Os(VIII) and Ru(III)

205 was performed by SWCV with HMDE electrode

206 *ii*) HMDE electrode was replaced with GCE electrode, in the same voltammetric cell; then, 1 mL of

207 cetyltrimethylammonium bromide (CTAB) $5.98 \cdot 10^{-4}$ mol L^{-1} (final CTAB concentration $4.9 \cdot 10^{-5}$ mol

208 L^{-1}) and 1 mL of KCl 3.0 mol L^{-1} (final KCl concentration 0.25 mol L^{-1}) were added for the

209 quantification of Ir(III) by SWAdCSV.

210

211 *2.7 Voltammetric interference from Cu(II) and Pb(II) in the Os(VIII) and Ru(III) determination*

212 Cu(II) and Pb(II) (-0.169 ± 0.015 and -0.327 ± 0.010 V *vs.* Ag│AgCl│KCl$_{satd.}$, respectively) in

213 acetate buffer 0.5 mol L^{-1} pH 4.9 + NaBrO$_3$ $7.3 \cdot 10^{-2}$ mol L^{-1} supporting electrolyte could interfere

214 strongly with the determination of Os(VIII) and Ru(III) (-0.243 ± 0.010 and -0.023 ± 0.015 V *vs.*

215 Ag│AgCl│KCl$_{satd.}$, respectively). This phenomenon, reported in Figure 3a, is decidedly important

216 also related to the fact that Cu(II) and Pb(II), in general, are always present in all real matrices, in

217 particular the environmental ones, even if at low-concentration level. This drawback can be avoided

218 using the well-known ability of Ethylene Diamine Tetraacetic Acid (EDTA) to shift peaks toward

219 cathodic potentials if added to the voltammetric cell. In this work, Cu(II) and Pb(II) interfering peaks

220 were shifted by adding EDTA di-sodium salt, specifically: 200 μL EDTA-Na$_2$ $9.6 \cdot 10^{-3}$ mol L^{-1} were

221 added to a 10-mL sample aliquot, obtaining $1.88 \cdot 10^{-4}$ mol L^{-1} as final EDTA-Na$_2$ concentration.

222 Indeed, the EDTA-Na$_2$ presence results in a shift of potential values in the cathodic direction, either

223 for Os(VIII) and Ru(III) or Cu(II) and Pb(II) [Os(VIII): -0.096 ± 0.015; Ru(III): -0.529 ± 0.015; Cu(II):

224 -0.301 ± 0.015; Pb(II): -0.751 ± 0.010 V *vs.* Ag│AgCl│KCl$_{satd.}$]. Under these conditions, the final peak

225 position of the four elements makes it possible to achieve complete resolution (see Figure 3b), and

226 consequently the quantitative determination becomes possible.

227

228 **Figure 3**. Square-wave catalytic voltammogram: Os(VIII) and Ru(III) in presence of Cu(II) and
229 Pb(II) in *Taraxacun officinale weber*. Supporting electrolyte: acetate buffer 0.5 mol L^{-1} pH 4.9 +
230 NaBrO$_3$ $7.3 \cdot 10^{-2}$ mol L^{-1} in absence (a) and presence (b) of EDTA-Na$_2$. Peak 1 corresponds to

9

231 Os(VIII), peak 2 corresponds to Cu(II), peak 3 corresponds to Ru(III), peak 4 corresponds to Pb(II).
232 Experimental conditions: see Table 2.
233

234 As for Ir(III) (see Figure 4), EDTA-Na$_2$ seems to slightly change the position [Ir(III) peak

235 potential in presence of EDTA-Na$_2$ 1.88·10^{-4} mol L^{-1}: +0.623±0.015 V vs. Ag│AgCl│KCl$_{satd.}$; Ir(III)

236 peak potential without EDTA-Na$_2$: +0.609±0.010 V vs. Ag│AgCl│KCl$_{satd.}$], keeping the peak height

237 practically unchanged. Following these experimental observations, several elements can be smoothly

238 determined by the procedure suggested here.

239

240 **Figure 4**. Square-wave adsorptive catalytic stripping voltammogram: determination of Ir(III) in
241 *Taraxacun officinale weber*. Supporting electrolyte: acetate buffer 0.5 mol L^{-1} pH 4.9 + NaBrO$_3$
242 7.3·10^{-2} mol L^{-1} + CTAB 4.9·10^{-5} mol L^{-1} + KCl 0.25 mol L^{-1}. Experimental conditions: see Table 2.
243

244 **3. RESULTS AND DISCUSSION**

245 *3.1 Aqueous Reference Solutions*

246 The calculation of limits of detection (LOD) (Table 4) was performed according to IUPAC

247 by the "3 σ approach", were σ is the observed standard deviation. LODs were calculated in the

248 aqueous reference solution and in the digestates obtained from standard reference materials. LODs

249 were calculated as (K $s_{y/x}$)/b [33-34] (K=3), where $s_{y/x}$ is the standard deviation of regression and b is

250 the slope of the analytical calibration function. When voltammetry was used, LODs were obtained

251 directly in the real matrices (Table 4); in fact, the standard addition method was applied to create the

252 analytical calibration model. For each analyte, linearity was explored through regression models of

253 voltammetric signal *vs.* metal concentration in aqueous reference solution with the instrumental

254 details reported in Tables 1 and 2. The linearity of the model was demonstrated in the range from

255 LOQs up to 10.0 µg L^{-1}. Determination coefficients R^2 were always higher than 0.9989.

256

257 **Table 4.** Limits of detection of Ir(III), Os(VIII), Pd(II), Pt(II), Rh(III), Ru(III), in aqueous
258 reference solutions and in solutions from reference materials. Experimental values are calculated as
259 the mean of 5 independent determinations. The confidence level was 95 %.

261 *3.2 Quality control and quality assessment*

262   Standard reference materials of Spinach Leaves and Tomato Leaves were analysed by means

263 of voltammetric and spectroscopic method for validating the whole method through the evaluation of

264 its accuracy (Table 5). Furthermore, the repeatability was evaluated as relative standard deviation

265 ($s_r\%$) [33-34], from 5 independent measurements, and always resulted better than 6%. Trueness was

266 evaluated through the relative error ($e\%$), and resulted to be on the order of 5-7%. These experimental

267 values observed for the method correspond to satisfactory accuracy.

268

269 **Table 5**. Accuracy of the analytical procedure. Experimental values are calculated as the mean of 5
270 independent determinations. The confidence level was 95%. The spiked-sample concentration was
271 always 79.5 ng g^{-1} (the addition to the Standard Reference Materials took place at the beginning of
272 digestion).
273
274
275 *3.3 Practical applications*

276   Since the quantification of PGMs in reference materials gave good accuracy, the methods

277 were applied to real samples: herbal medicines sold on the local market, and based on *Eucalyptus*

278 *globulus*, *Harpagophytum procumbens DC* and *Taraxacun officinale weber*. The section "Sample

279 Preparation" describes how samples were treated, after a preliminary step of powdering, by

280 lyophilisation and dried at 80°C for 24 h. Table 6 reports the experimental results obtained from these

281 commercial herbal medicines.

282

283 **Table 6.** Mean values of Ir(III), Os(VIII), Pd(II), Pt(II), Rh(III), Ru(III) (ng g^{-1}) for *Eucalyptus*
284 *globulus*, *Harpagophytum procumbens DC* and *Taraxacun officinale weber* sold on the market
285 (Portomaggiore, Italy). Experimental values are calculated as the mean of 5 independent
286 determinations. The confidence level was 95%.
287
288 *3.4 Comparison between spectroscopic and voltammetric measurements*

289   The results shown in Tables 5 and 6, related to the accuracy (precision and trueness) and the

290 real sample analyses, can be considered as an additional validation of the analytical method, based

291 on voltammetry, herein developed. Such a validation can be deduced from the good agreement

292   between the spectroscopic and voltammetric results. Specifically, as regards precision, trueness and

293   detection limits, no significant difference was observed between results obtained with the two

294   different techniques, and analytical performance was good in all cases. Indeed, spectroscopy was

295   taken as reference technique due to its analytical qualities: a well-established and tested robust

296   procedure, suitable for this purpose [35]. However, voltammetry shows interesting advantages with

297   respect to atomic absorption spectroscopy atomic: almost always, it allows the simultaneous

298   determination of many metals (multi-analytes procedure) in a very easy, rapid and inexpensive way.

299   In particular, the standard addition method, which may be easily applied in the herein proposed

300   voltammetric procedures, makes these procedures very rapid, even for multi-element determinations

301   in complex matrices, without renouncing to good selectivity and good sensitivity. For the sake of

302   correctness, it must be highlighted that both Inductively Coupled Plasma (ICP) and Inductively

303   Coupled Plasma-Mass Spectrometry (ICP-MS) also allow for multi-element analyses, even if ICP-

304   based spectroscopic techniques require time-consuming and expensive sample pre-treatments and

305   enrichment steps, like solvent extraction. Moreover, the instrumentation itself and its maintenance

306   are very expensive (e.g. up to 25-30 times with respect to voltammetry), especially when multi-

307   element spectroscopic determinations are performed.

308

309   **CONCLUSIONS**

310   As highlighted in this work, the method herein developed and validated represents a valid

311   procedure for the quantification of PGMs in samples of natural origin. Particularly important is its

312   effective application to natural derived products such as herbal medicines (*Eucalyptus globulus*,

313   *Harpagophytum procumbens DC* and *Taraxacun officinale weber*) for which there is currently no

314   precise legislation regarding the maximum content of heavy metals, especially for those relating to

315   the group of Platinum. The procedure described here can be a valid starting point for future

316   applications aimed at standardizing and quality control of these products increasingly used today.

317   This is all the more evident from the application of this procedure to certified reference materials,

318   through which it was possible to obtain important information about the potential of the method. The

319   analytical performances show how a simple sample preparation can be used in order to avoid

320   interferences and obtain reproducible and robust results through the application of voltammetric

321   techniques well known and widespread in the various laboratories.

322

325

326   **CONFLICT OF INTEREST**

327   The authors declare that the content of this article has no potential conflict of interest.

328

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