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WDXRF Spectrometry for elemental impurities analysis in drug products and dietary supplements

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Introduction

Actual regulatory requirements by the European Medicines Agency (EMA) (1) and the United States Pharmacopeia (USP) (2) for elemental impurities monitoring in drug products highlight the importance of analytical techniques able to determine the concentration of these impurities in the ppm range with a quantitative, fast and accurate analysis.

Work Purposes

- To investigated the feasibility of WDXRF for the measurement of 11 elements (Cu, Cr, Ir, Mo, Mn, Ni, Os, Pb, Pt, Rh and Ru) in drug products and dietary supplements, following the requirements set by international bodies.
- To calculate Risk assessment for non-carcinogenic effects for dietary supplements using the Hazard Index (HI) following the Environmental Protection Agency (EPA) guidelines (4).

Materials & Methods

Equipment:

4 kW WDXRF spectrometer (S4 Pioneer, Bruker AXS).

Calibration and validation: According to ICH Guidelines (3).

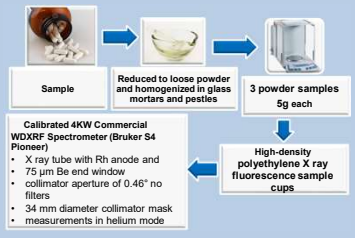
Reagents: All reagents were of high analytical grade (≥99% Reagent or Ph Eur).

Concentration ranges of calibration standards (ppm): 0-10 (Pb), 0-15 (Ir

Samples:

At least 6 concentration levels were considered for each element.

Samples: 27 drug products (6 branded, 21 generic) and 25 dietary supplements were monitored (Figure 1).



Results

Elemento	<LQ[a]	Concentração[b] (ppm)	EMA[c] limite (ppm)	>EMA limite[d]	HQ (mediana)	HQ (máx)
Ru	7	15.38 (10.05; 23.27)	10	20	n.a.	n.a.
				HI	n.a.	n.a.

Elemento	<LQ[a]	Concentração[b] (ppm)	EMA[c] limite (ppm)	>EMA limite[d]	HQ (mediana)	HQ (máx)
Cr	22	42.54 (22.19; 63.12)	25	2	3.4E-4	5.0E-4
Mn	20	99.77 (66.63; 896.08)	250	1	8.5E-3	7.7E-2
Mo	17	7.13 (5.57; 10.44)	25	0	1.7E-2	2.5E-2
Os	22	2.84 (2.19; 3.39)	10	0	n.a	n.a.
Pb	24	2.04 (1.74; 2.48)	1[e]	1[f]	6.8E-3	8.3E-3
Ru	12	14.33(10.06; 19.11)	10	13	n.a.	n.a.
				HI	3.3E-2	1.1E-1

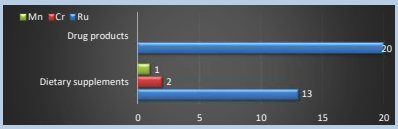
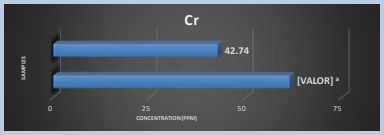
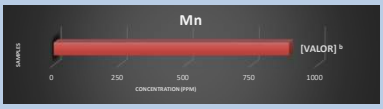
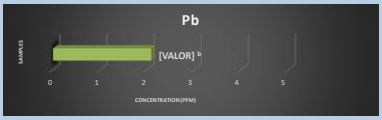


Figure 2. Number of samples with impurities above USP limits







Conclusions

- **Alternative** to the compendial
- **High levels of Cr, Mn and Pb** were measured in some of the analysed products;
- The simultaneous presence **of high levels of Pb and Mn** in the same supplement, represent a concern to human health, since both elements are neurotoxic;
- **Humans are often exposed**, by **different routes and/or sources**, to toxic elements and supplementary consumption of **Dietary Supplements** may cause **potential toxicological risks that cannot be ignored**

References
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Acknowledgements
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To the memory of late Professor José Martins dos Santos