TRACE ELEMENT IMPURITY DETERMINATION IN ASPIRIN TABLETS BY INAA

Erik K. MIYOSHI and Mitiko SAIKI
Instituto de Pesquisas Energéticas e Nucleares, IPEN-CNEN/SP, Avenida Professor Lineu Prestes no. 2242, Cidade Universitária, CEP 05508-000, São Paulo, SP, Brazil. Email: mitiko@ipen.br

Aspirin or acetylsalicylic acid (ASA) is one of the most widely consumed drugs in the world as an analgesic, antipyretic, anti-inflammatory and due to its anti-platelet effect. It is one of the safest and least expensive pain relievers available in pharmacies, drugstores and food stores under different dosages, forms and brands. With the increasing use of remedies containing ASA several types of this product are present in drugstores. The determination of trace element in aspirin tablets is of great interest since they may contain, in addition to aspirin, coloring and flavoring agents, binders, pH stabilizing buffers or effervescent inducing compounds. This study presents results obtained in the analyses of six samples of aspirin tablets acquired in São Paulo city, Brazil in order to evaluate other elements than those included in the formulation that may cause undesirable side effects.

Aspirin tablets were ground in an agate mortar for the analyses. The analytical methodology used in this study was instrumental neutron activation analysis (INAA). Aliquots of about 180 mg of each aspirin sample weighed in polyethylene involucres were irradiated in the IEA-R1 nuclear research reactor along with the synthetic element standards. Synthetic standards were prepared by drying multielement or single element standards of appropriate concentrations pipetted onto small sheets of Whatman No. 40 filter paper. Irradiations of 16 h under a thermal neutron flux of about 4×10^{12} n cm^{-2} s^{-1} were performed. Samples and standards were measured twice, after about 4 and 12 days of decay times using an HGe detector coupled to a gamma ray spectrometer. The radioisotopes were identified according to their half-lives and gamma-ray energies and, the element concentrations were calculated by comparative method.

To evaluate the precision and the accuracy of the results certified INCT-MPH-2 Mixed Polish Herbs was analyzed. Data obtained in this analysis presented in Table 1 indicate good precision and good agreement with the certified values. The relative standard deviations of the results were lower than 9.2 % and relative errors varied from 0.9 to 11.5 %. The standardized difference or Zscore values[2] obtained for most of the elements analyzed were |Zscore| <2, indicating that our results are satisfactory and are within the ranges of certified data at the 95% confidence level.

The concentration ranges of the elements Br, Ca, Co, Cr, Fe, K, La, Na, Sc and Zn determined in six samples of aspirin are presented in Table 2. For some samples, not all these elements were detected due to their low concentrations or to interferences Detection limit values were evaluated according to Currie criteria[3] in a sample of aspirin and were included in this Table.

The highest concentration of Na was found in Effervescent aspirin and of Br, Co and Cr in Buffered one. The sample generic ASA presented high levels of Ca and Zn. Toxic elements such as As, Cd, Cu, Hg and Sb were not detected in the six aspirin samples analyzed. The findings of this study suggest an evaluation of whether or not to prescribe some aspirin brands presenting high level of Na to hypertensive individuals.

The study also showed that INAA is a valuable tool to analyze pharmaceutical products due to its simplicity, precision and accuracy of the results and mainly due to the possibility of simultaneous determination of several elements present in a large range of concentrations

Table 1. Element concentrations obtained in the analysis of INCT-MPH-2 Mixed Polish Herbs certified reference material

Element	This work				Values of Certificate[1]
	Mean±SD	RSD %	Er, %	Zscore	
Br. mg kg^{-1}	8.04±0.65	8.1	4.2	0.5	7.71±0.61
Ca, %	1.09±0.07	6.3	0.9	0.1	1.08±0.07
Co, µg kg^{-1}	235±22	9.2	11.5	1.0	210±25
Cr, mg kg^{-1}	1.83±0.16	8.7	8.3	1.1	1.69±0.13
Fe, mg kg^{-1}	535±22	4.2			(460)*
K, %	1.96±0.06	3.1	2.6	0.4	1.91±0.12
La, µg kg^{-1}	559±47	8.4	2.1	- 0.3	571±45
Na, mg kg^{-1}	402±11	2.6			(350)
Sc, µg kg^{-1}	124.7±5.9	4.8	1.4	0.2	123±9
Zn, mg kg^{-1}	35.2±0.7	2.0	5.1	0.8	33.5±2,1

Mean±SD = Arithmetic mean and standard deviation; RSD= Relative standard deviation; Er = relative error; *- Numbers in parentheses indicate informative values

Table 2. Element concentration ranges obtained in six aspirin samples

Elements	Range	Detection limit
Br. µg kg^{-1}	82.2 - 709	6.9
Ca, mg kg^{-1}	34.6 - 8028	14.3
Co, µg kg^{-1}	7.5 - 12.5	3.3
Cr, µg kg^{-1}	33.6 - 658	18.6
Fe, mg kg^{-1}	0* - 3.88	2.1
K, mg kg^{-1}	6.12 – 10.7	1.9
La, µg kg^{-1}	0* – 22.7	1.01
Na, mg kg^{-1}	12.2 - 12350	0.03
Sc, µg kg^{-1}	0* - 3.2	0.5
Zn, mg kg^{-1}	1.3 -4.9	0.3

0* - indicates that the element was not detected in some samples

References

1. INSTITUTE OF NUCLEAR CHEMISTRY AND TECHNOLOGY, Polish Certificate Material, Mixed Polish Herbs (INCT-MPH-2), 2002.
2. P. BODE, C. P. van Dijk. J. Radional. Nucl. Chem., 215(1997)87.
3. L. A. CURRIE, Anal. Chem. 40(1968)586.

Acknowledgements:

To CNPq and FAPESP for the financial support.

12687