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An added value for forensic analysis

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Large sample neutron activation analysis avoids representative sub-sampling and sample preparation difficulties: an added value for forensic analysis.

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Abstract

A crucial part of any chemical analysis is the degree of representativeness of the measurand(s) in the test portion for the same measurands in the object, originally collected for investigation. Such an object usually may have either to be homogenized and sub-sampled, or digested/dissolved. Any of these steps introduce sampling errors, risk of contamination or loss of the measurand(s). Neutron (and photon) activation analysis and prompt gamma analysis have the capabilities of analyzing large objects or samples without the need of any pre-treatment, i.e., intact 'as received', with masses varying from tens of grams to tens of kilograms, and with any type of (irregular) shape. The basic concept of neutron activation analysis and prompt gamma analysis are shortly revisited and the scope of application of the large sample analysis with these technique are elaborated on with an outlook for use in forensic studies, including the analysis of medicinal products and drugs of abuse.

Keywords
Homogenization, representativeness, neutron activation analysis, large samples, prompt gamma analysis, medicinal products, drugs of abuse.

1. Introduction

The interpretation of measurement results requires knowledge of the degree of representativeness of the measurand in the test portion for the corresponding measurand in the originally collected material. A sample is denoted to be 'representative' when it can be expected to exhibit the average properties of the material, environment or population it was taken from [1]. This is a common and recognized issue in both analytical chemistry and forensic science. A good example is any large amount of drug of abuse seized by Law Enforcement Agencies [2]. Drugs of abuse can be analyzed to measure the percentage of the active ingredient or to obtain the elemental profile with the aim to infer about a possible common source of seized samples [3].

Whenever the analysis of large samples is possible, it is much easier to get representative sampling results e.g., for the analysis of large batches of drugs of abuse. The trace elements of such samples would be very useful to infer about their possible common source.

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The ultimate test portion to be analyzed for element profiling is often much smaller than the amount of material collected, varying from a few milligrams to a few grams of solids or in the range of a few mL in the case of liquids. An indication of the typical test portion sizes routinely measured in the most common analytical techniques is given in Table 1.

Table 1: Typical sizes of the test portions handled in several multi-element analysis techniques [4]

Analysis technique	Solid material mass used or prepared to test portion	Volume used as test portion
Atomic Absorption Spectroscopy (AAS)	typically 1 - 2 g dissolved; maximum approximately 10 g	10 - 20 µL
Inductively Coupled Plasma Spectroscopy (ICP)	typically 1 - 2 g dissolved; maximum approximately 10 g	Approximately 500 µL
X-ray Fluorescence Spectroscopy (XRF)	Typically up to 10 g	
Instrumental Neutron Activation Analysis (INAA)	typically approximately up to 500 mg	1 to 50 mL

There is even a tendency going to smaller test portions like in solid state atomic absorption spectrometry, laser-induced breakdown spectrometry, laser-ablation ICP and in total reflection X-Ray fluorescence spectrometry where microgram amounts are measured.

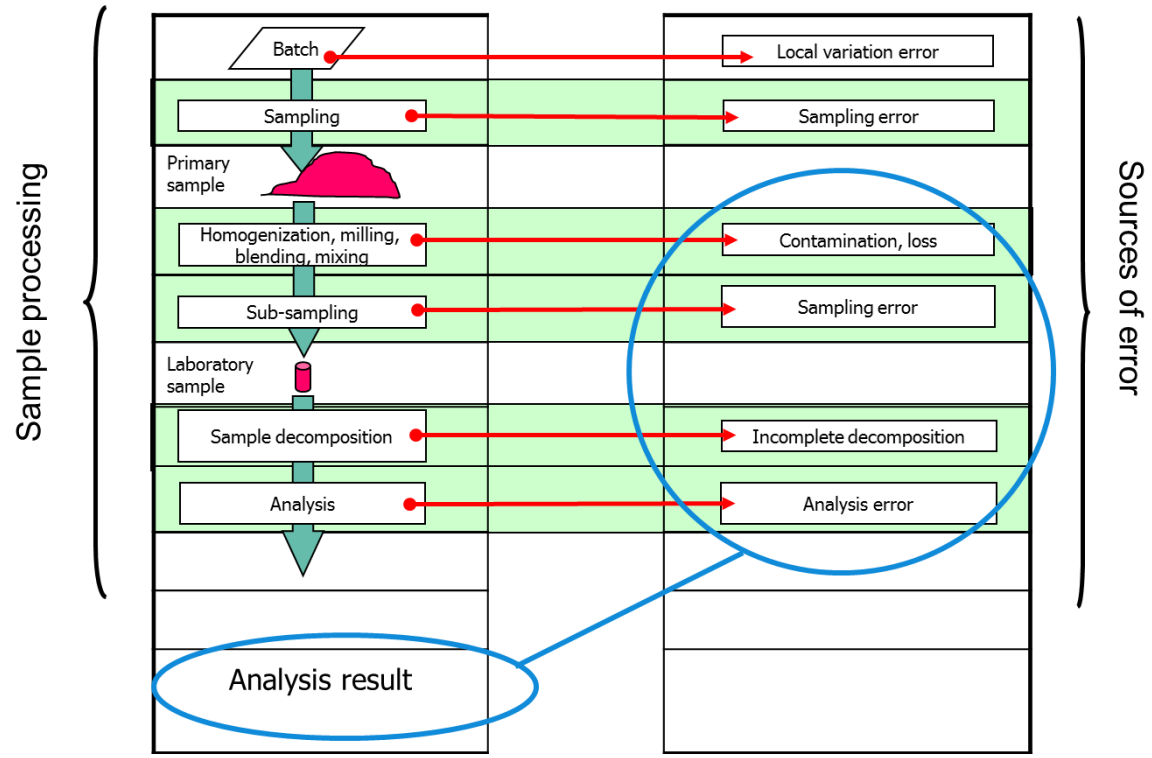
Analysts may be confronted with the necessity of collecting large amounts of material to ensure representativeness of the population under study. As an example, Ramsey and Boon [5] elaborated on the occurrence of hot spots of Pb in a contaminated area (which could reflect a forensic investigation in case of illegal dumping) and concluded that, for reaching a 10 % expanded uncertainty of the mean of replicates, a minimum mass of 7 kg should be collected (and analyzed). There are many more such examples published in which, using Ingamell's sampling constant, indication were obtained that the minimum test portion size to be analyzed should be in order of several tens of grams up to even tens of kilograms [6-7].

An indication of the representativeness may, to some extent, be achieved by replicate sub-sample analyses assuming sufficient material is available. Another approach is to homogenize the collected material (both for solids and liquids) or even dissolute solids[2]. Homogenization not only physically destroys the evidence but additionally introduces the potential risk of contamination or element loss by incomplete digestion.

Solids, and to some extent liquids, can also be analyzed for chemical element composition without sub-sampling and even without test portion preparations (such as drying, milling, sieving, homogenizing), thus circumventing the representativeness problems. X-ray fluorescence analysis can in principle be applied for this if the interest is limited to the composition of the surface layer of intact materials. Neutron activation analysis (NAA) allows for bulk analysis; NAA is one among the few analytical techniques[3] in which there are no physical boundaries for the size of this test portion, and in principle samples of any size (from microgram to multiple kilograms), any physical shape and state (solid, liquid) can be processed for assessment of its element content within the technique's analytical capabilities. Analysis of large samples 'as collected', and without further sample preparation, reduces also the number of sources of error in the procedure (Figure 1).

[2] Homogeneity is defined as 'the degree to which a property or substance is randomly distributed throughout the material' [2].

[3] The other techniques are prompt gamma analysis and photon activation analysis [8]. Large sample prompt gamma analysis can equally well be applied using the same neutron source(s) as for neutron activation analysis. The number of facilities for (large sample) photon activation analysis is, however, much smaller than for large sample NAA.


Sample processing
Batch
Sampling
Primary sample
Homogenization, milling, blending, mixing
Sub-sampling
Laboratory sample
Sample decomposition
Analysis
Analysis result
Local variation error
Sampling error
Contamination, loss
Sampling error
Incomplete decomposition
Analysis error
Sources of error

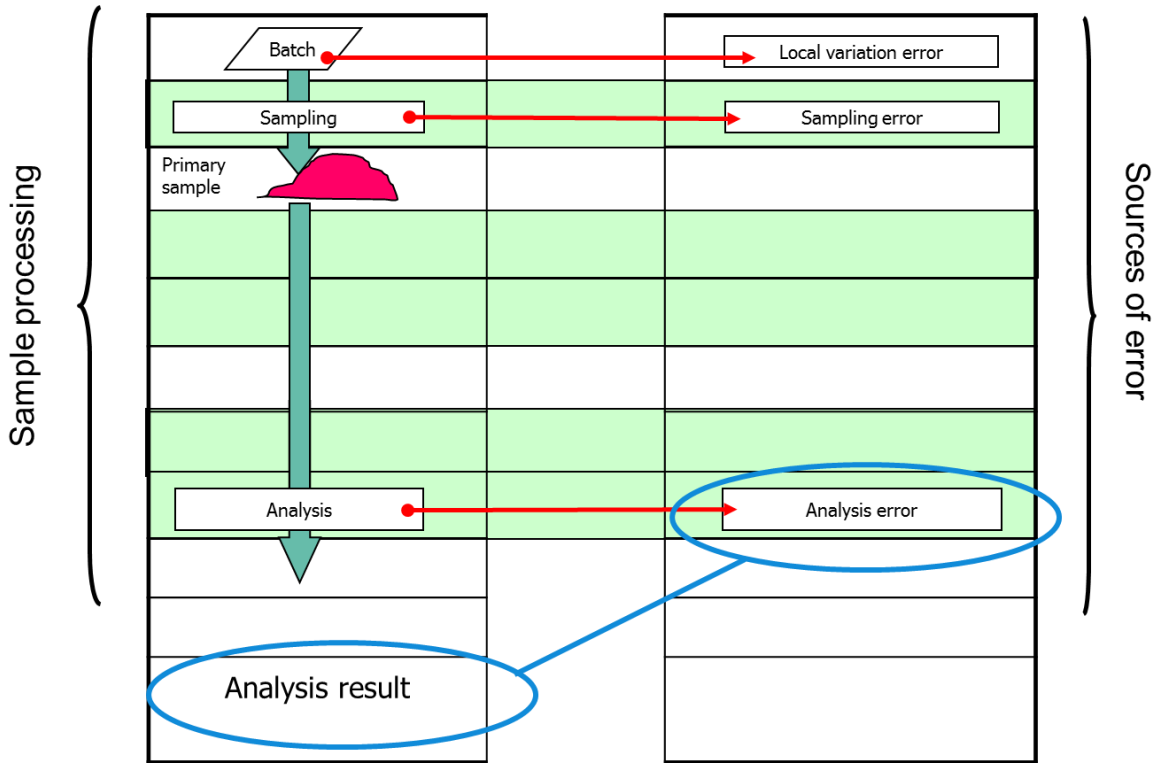

Sample processing
Batch
Sampling
Primary sample
Analysis
Analysis result
Local variation error
Sampling error
Analysis error
Sources of error

Figure 1. Schematic comparison of potential sources of error during the process from sample collection to analysis for (top) conventional analysis and (bottom) large sample NAA.

NAA has already been applied for the analysis of large objects for many decades. The methodology takes advantage of the high penetrating power of both the incoming radiation for activation (neutrons) and the outgoing radiation to be measured (gamma-rays). As such, neutron activation products can be measured in objects with dimensions of several kilograms. Anders and Briden [9] described the measurement of Oxygen in 60 g steel samples; Kim et.al. described the analysis of 250-500 mL water samples [10] and many mining and exploration companies use NAA in well-logging tools [11]. Also, the use of in-vivo NAA for measurement of major, toxic or essential elements in the human body is an example of NAA's capability to analyze objects having a mass much larger than a few grams [12]. In the 1990s, following developments by the Delft University of Technology [13-14], large sample NAA was internationally acknowledged as a unique research reactor based methodology for analysis of materials under the following constraints:

- Homogenization of solid materials - to achieve better representativeness' of a small test portion - is difficult or impossible due to material properties.
- Homogenization is unwanted since it may result in contamination of the material.
- Sub-sampling and/or homogenization is not allowed since the original materials it either too precious for removal of small pieces or should remain intact.
- Local inhomogeneities in intact materials are subject of study.

The principles of this large sample NAA are presented below with an outlook for use in forensic studies, including the analysis of medicinal products and drugs of abuse.

2. Large samples analyzed by nuclear analytical techniques

2.1 Principle and characteristics of NAA

Neutron activation analysis is a method for the measurement of the total mass of chemical elements (in all chemical and physical forms) based upon the conversion of stable nuclei to other, mostly radioactive nuclei via nuclear reactions with neutrons, and measurement of the reaction products. The reaction products to be measured are either the radiation, released almost promptly upon neutron capture ('prompt gamma analysis'[4]) or, if the resulting new nuclei are radioactive, the radiation emitted during their decay. Gamma-radiation offers the best characteristics for the selective and simultaneous detection of radionuclides and thus of elements. The activation will result

[4] Often the term 'prompt gamma activation analysis' is used although the measurement is not based on the induced activity as is done in activation analysis.

in a mixture of radionuclides, which can be analyzed by two approaches: (i) the resulting radioactive sample is decomposed, and chemical separations are applied to obtain fractions with a few elements each: Destructive or Radiochemical Neutron Activation Analysis; (ii) the resulting radioactive sample is kept intact, and the elements are determined by taking advantage of the differences in decay rates by gamma-ray spectrometry at different decay intervals: Non-destructive or Instrumental Neutron Activation Analysis (INAA). The latter is the most common form of NAA.

The most intense source of neutrons for NAA is the nuclear research reactor but also isotopic neutron sources such as ^{252}Cf and accelerators serving as neutron generators are used for specific applications.

The metrological basis for NAA was established by the mid-to-late 1990's [15-16], although the fundamental research was largely completed earlier. In the first decade of the 21st century, it was demonstrated and internationally accepted that NAA has the potential to fulfil the requirements of a primary ratio method with evidence on the methods' metrological fundamentals including the measurement equation, the evaluation and quantitation of all sources of uncertainty and the metrological traceability of the values of the results [16-17].

The analytical characteristics of NAA can be summarized as

- Real total analysis since the test portion does not have to be dissolved. The size of test portions in NAA commonly varies from e.g. 5-10 to 200-300 mg.
- No effects of the chemical or physical state of the measurands as all phenomena (neutron activation, emission of radiation) are related to properties of the atomic nucleus. There is no difference whether an element is bound to an inorganic compound or an organic compound, or if it is present as a pure metal.
- There is no need for calibrators ('standards') which are fully commutable in chemical composition with the materials studied; no need for matrix-matching reference materials. This makes NAA very useful for analysis of materials of complete unknown elemental compositions.
- Self-validating properties resulting in a very high degree of accuracy and element specificity.
- Adequate sensitivity; typically detection limits are in the range of micrograms to nanograms or even less.
- Many adjustable experimental parameters for optimization of experimental design.
- Elements such as H, C, N, and O do not affect the determination of other elements
- Suitable for measurement of total element mass in the order of micrograms to nanograms or even less.
- Less suitable for liquids.
- Elements like H, C, N, O, Bi, Tl and Pb cannot be measured by NAA.

These characteristics make NAA especially suitable - but not limited - for analysis of the following types of materials:

- Solid materials difficult to bring completely into a solution, such as from geological origin or plastics.

- Solid materials that are easy to contaminate during preparation of the test portion, if e.g. digestion would be needed for a different analytical technique, such as ultra-pure substances, ultra-small quantities (e.g. fine dust), biological tissues and body fluids.
- Solid materials that are unique and should keep their integrity such as from forensic investigations and/or cultural/historical value.
- Solid materials of which the bulk composition has to be determined and for which surface techniques such as XRF and solid-state spectroscopic techniques (e.g. LIBS, laser ablation ICP) are therefore inadequate.

More details can be found in [16].

2.2 Large sample NAA

NAA is suitable for bulk sample analysis due to the penetrating power of the neutrons and gamma-rays involved. The intensity of the neutrons is attenuated by interaction with the nuclei of the material of the test portion as soon as the neutrons enter the test portion; the gamma-rays are attenuated by interaction with the nuclei of the test portion as soon as they are created and thus before they leave the sample to be measured. In most NAA procedures, test portions with masses up to a few hundreds of milligrams are used; for such small amounts, the neutron and gamma-ray self–attenuation effects may often be insignificant. Moreover, such small test portions can easily be encapsulated in plastic vials with a well-defined geometry for handling during irradiation and measurement.

A 'large sample' in NAA is defined as a test portion in which these neutron and gamma-ray self-attenuation cannot be neglected in view of the required degree of accuracy, and/or of which the physical size requires significant corrections for its deviation from an idealistic point source geometry, both during irradiation and counting. The geometry may still be well defined, e.g., by using a 100 mL of 1 L plastic bottle for e.g. granular material, but a major attractiveness of large sample analysis is that objects of any shape can be analyzed.

The corrections for these neutron and gamma-ray self-attenuations can be applied as the related physics is fully understood [18]. Several approaches (mathematical, empirical) have been developed to correct for the deviation of the point source geometry [19-20].

An important starting point in large sample NAA is that the increase in sample mass from a few hundreds of milligrams to e.g. tens of grams or even (multiple) kilograms implies that fewer neutrons are needed for obtaining the same induced activity; the mathematical product of mass and neutron intensity (neutron flux) should be approximately the same. This also results in almost similar sensitivities as in normal (small test portion) NAA. As such, large sample NAA can be done not only with research reactors (and with derived external neutron beams) but also with the isotopic neutron sources or neutron generators.

Calibration and especially quality (trueness) control are still challenging in large sample NAA [21], but validation has shown that the degree of trueness is well under control.

The fundamentals, modes of operation and various opportunities for routine application of large sample NAA have been reviewed [22].

2.3 Prompt gamma large sample analysis

Prompt gamma analysis (PGA) is closely related to neutron activation analysis as use is made of neutron induced nuclear reactions and measurement of gamma-ray spectrometry. The difference between the techniques is that in PGA the measurement is done simultaneously with the irradiation. To this end, PGA requires an external neutron beam with a neutron intensity 5-6 orders of magnitude lower than commonly needed in NAA. The analytical characteristics of PGA are complementary to those of NAA with respect to the elements that can be measured (such as H and B), sensitivity and speed of analysis. Because of the external beam, there are fewer constraints in handling large and irregularly shaped test portions. Moreover, the PGA facility can also be used for large sample NAA by simply exposing the test portion to the neutrons and subsequently removing it from the beam for the various measurements, thanks to the intensity of the neutron beam. However, the neutron intensity may be less optimal for large sample NAA, which causes the activation duration to take much longer exposing times than the time needed for a PGA irradiation/measurement. Nonetheless, activation in a neutron beam offers a larger flexibility with respect to the size and shape of objects to be analyzed.

Prompt gamma analysis has recently been extended with simultaneous neutron imaging, which provides an opportunity for 3-dimensional quantitative trace element measurement [23-24].

3. Opportunities for forensic investigations

3.1 General

Neutron activation analysis applied in forensic investigations for many decades [25]. In 1966 and 1970 topical conferences were held on 'Forensic Activation Analysis'. Several court cases were held, mostly in the USA, in which NAA results were introduced. An impression of the materials analysed for such studies is given in Table 2 [25-26].

Table2. Examples of materials analysed with NAA for forensic studies

Hair, nail clippings
Gunshot residues, bullet lead ..JFK case…
Paint fragments
Glass fragments
Soil
Grease
Drugs (e.g., Marihuana, Heroin)
Sweat/Fingerprints
Automobile body putty and adhesive tape
Moonshine (illegal whiskey)
Galvanized wire
Paper
Diamonds

The analyses of the bullet lead fragments from the J.F.Kennedy assassination is perhaps the most well-spread example of the use of NAA for forensics [27]. Recently, the related analyses were revisited by Randich and Grant [28], who suggest that the original interpretation of the results is probably wrong due to overlooking the occurrence of an inhomogeneous distribution of the elements measured (such as Sb) and subsequent non representative sub-sampling of the test portions.

The role of NAA for forensic studies declined when competitive techniques for elemental analysis became easier available (such as AAS and ICP) and coincided with the growing interest in the use of organic and other markers rather than trace elements for characterizing substances.

Nonetheless, NAA has attractive analytical characteristics that are widely acknowledged as valuable complementary to other techniques for elemental analysis. Now, with the availability of large sample NAA, new opportunities emerge.

Large sample analysis is, as has been outlined in the above, particularly useful for the analysis of

- Materials that require thorough homogenization steps -and analytical verification thereof- for conventional analytical techniques to ensure representativeness of the final (small) test portion for the bulk sample it originated from. Analyzing an object as received circumvents the various laborious handling steps with implicit risks of contamination or possible element loss due to, e.g. incomplete digestion; it eliminates the need for experimental (and in principle indirect) demonstration of the representativeness - assuming there is sufficient material for preparing at least 5 replicate test portions to assess the quality of the homogenization. Soil from (suspected) contaminated areas may serve as an example but also, e.g., street samples of drugs, fire debris, glass fragments, raw materials for recycling, granular animal fodder and fertilizer may preferably analyzed in larger quantities than normally processed, e.g. tens of grams to even kilograms. Entire fragments can be analyzed without the need for pulverizing them, and neutron beams (with or without prompt gamma analysis) can be used for objects that do not fit in the regular irradiation facility.

- Materials which are not allowed to be sub-sampled because they have to remain intact, either because they are too precious or because of forensic considerations.
  Objects related to suspected manipulation or fraud of cultural and archaeological objects fit in this category. NAA has often been applied to complete bulk analysis of ancient coins (without sub-sampling) [29]. Recently it was demonstrated – via a mock-up – that entire vases can be analysed by NAA [30], see Figure 2.

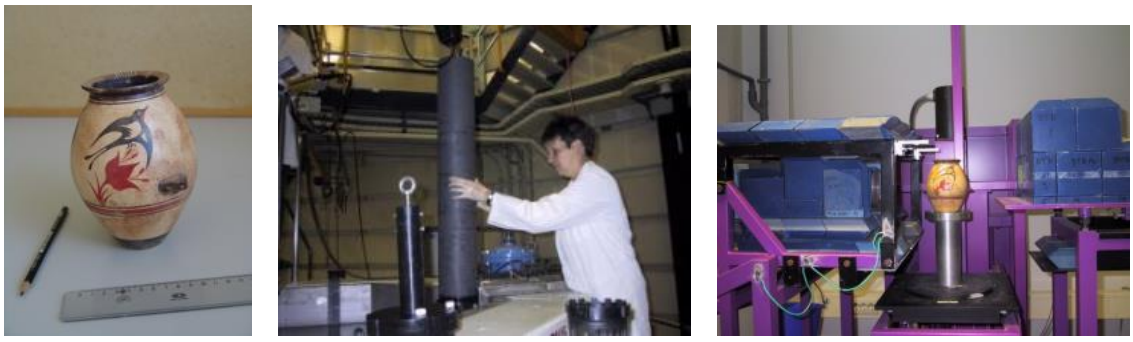


Figure 2. Example of large sample analysis. Left: mock up vase; middle: irradiation container at the facility in Delft [11] (which can handle objects up to 100 cm length and 15 cm diameter); right: neutron activated vase in the measurement facility [14].

But also fully machined objects can be analyzed as was demonstrated by Nair et.al. [31] who use the signal of an a-priori known amount (mass fraction) of a major component of the material as an 'internal standard', thus circumventing all issues such as neutron and gamma-ray self-attenuation and the correction for the deviation from the point-source geometry. They analyzed complete aluminum cladding tubes, zircaloy plates and steel plugs with masses of 2.3 g - 67 g, which are construction components of a research reactors.

- Materials that are known to be inhomogeneous and in which the (distribution of the) inhomogeneities are subject of study. For such studies, large sample NAA and/or large sample gamma analysis can be combined with neutron imaging techniques to identify the position of the inhomogeneities and quantify their amounts.

3.2 The analysis of medicinal products and drugs of abuse

The analysis of the elemental profile of drugs is important for two reasons: on one hand the search of elements with potential to be toxic at low doses, on the other hand the profiling of the material, to infer about the source.

Inorganic impurities are not only important to infer about drug origin, traffic routes, clandestine laboratories and methods of drug preparation, but they can be toxic even at low levels, and hence should be closely monitored to ensure safety of human health in any product available to the public. Since 1990s many scientists tested a lot of technique, including NAA, AAS (Atomic Absorption Spectroscopy), ICP-AES (Inductively Coupled Plasma-Atomic Emission Spectrometry) and ICP-MS (Inductively Coupled Plasma-Mass Spectrometry) on samples of drugs of abuse. In current years the increasing diffusion of fake or illegal pharmaceutical products is requiring an analytical approach close to the one developed in cases of drugs of abuse, to protect public health.

More than 50 years ago NAA was used to analyse trace element in drugs samples [32], e.g. to obtain information on the mass fractions of several toxic elements (Hg, Cd, As, Se, Sb, U and Th) in radiopharmaceuticals [33].

In a recent review [34] it was reported the trends of the analysis of metal impurities in pharmaceuticals products. ICP-MS was proposed in the 2000s to provide rapid, sensitive, precise, simple, and element-specific, from semi-quantitative to quantitative alternative to the United States Pharmacopeia (USP) and European Pharmacopeia (EP) heavy metals tests for pharmaceutical

material [35]. In 2007 ICP-MS was the most used method to find the metal elements in drugs and pharmaceutical material [36]. ICP-MS today shows high sensitivity, accuracy and precision, and have the flexibility to handle many other analytical tasks in pharmaceutical production control and research, but this technique suffers of representativeness issue when applied to illegal products, not produced with the quality standards of the legal pharmaceutical factories.
Recently, LA-ICP-MS (Laser Ablation-Inductively Coupled Plasma-Mass Spectrometry) was proposed to simplify sample preparation procedures, to use smaller sample size and amount, to minimize potential polyatomic interferences and to diminish contamination problems compared to ICP-MS method [37]. This tendency to smaller samples brings a critical issue of representativeness, being more serious when analyzing products manufactured by illegal production.

Dams et al. reviewed [38] in 2001 a variety of analytical techniques for the characterization of street **heroin** samples, including AAS and ICP-MS. In AAS few elements were found (Zn, Fe). Some years before, Infante et al. [39] studied 198 illicit **heroin** samples from Andalusia (southern Spain) to determine the contents of various metals (Cd, Ca, Cu, Fe, Mn and Zn) by AAS. Cadmium and, to a lesser extent, zinc, copper, and iron, are among the metals detected in heroin that can increase the inherent toxicity of the drug.

ICP-MS was used to analyse 96 illicit heroin samples seized in 2013–2014 to determine 16 inorganic elements at μg/kg (parts-per-billion, ppb) level and to study the clustering outcome by Principal Component Analysis (PCA) [40]. Bora et al. [41] have analysed 44 illicit heroin samples from Southeast Anatolia, Turkey by electrothermal AAS (Cd and Pb) and ICP-AES (Al, Ba, Ca, Cu, Fe, Mg, Mn, Zn). It has been found that the most abundant element was calcium.
Zhang et.al. [42] measured fifteen trace elements in illicit heroin by neutron activation analysis. By statistical analysis it was possible to group the sixty-two analysed heroin samples in two clusters (Region A and Region B samples) and it was concluded that it is possible to use this method to obtain information about their geographical origins.

Elemental analysis was tested not only on drugs of abuse of natural origin but also on synthetic drugs. It was determined the trace elements in opium, hashish and ecstasy pills using NAA and Proton Induced X-ray Emission (PIXE) [43]. PIXE analysis showed that samples contain various elements including Mg, Al, Si, P, S, Cl, K, Ca, Ti, Fe, Cu, Zn, Rb and Sr.

Considering **ecstasy** tablets, the performances of ICP-MS and ICP-AES to analyse the metal elements were compared on tablets coming from different police seizures in Switzerland [44]. 25 elements were screened by ICP-AES whereas most of the periodic table was screened by ICP-MS. It was shown that the ICP-MS is more sensitive than ICP-AES for inorganic analysis of ecstasy tablets. Waddell et al. [45] used ICP-MS to analyse ecstasy (3,4-Methylenedioxymethamphetamine,**MDMA**) tablets. The generated data were analysed using different statistical techniques to provide linkage information from seizure to seizure. Koper et al. [46] described how the elemental analysis can discriminate **MDMA** powders (57 samples) from illicit production sites and MDMA tablets (97 samples) taken from large seizures (over 500 tablets) in the Netherlands. Elements mostly present in high concentration (>100 $mg.kg^{-1}$) were measured with ICP-AES (such as Al, Ca and Mg), elements that are mostly present in the lower or mid-range concentration range (<100 $mg.kg^{-1}$) were analysed with ICP-MS. In both techniques the elements Cu, Zn and Pt were measured in very high concentrations.

The graphite furnace atomic absorption spectroscopy (GFAA) was tested to analyse **ecstasy tablets**. Among 6 elements measured in ecstasy tablets (Cu, Mg, Ba, Ni, Cr and Pb) Ba was the only one offering discrimination between the two ecstasy seizures [47].
Marumo et al. [48] classified seized **methamphetamine** samples in Japan using ICP-MS and AAS to obtain impurity profiling, providing very useful information on drug intelligence.
ICP-MS was also used to detect metal elements related to two synthetic routes to produce illicit **methylamphetamine**, Moscow and hypophosphorous [49].
Finally, in 2015 the metal elements in **illicit spice** samples were determined. These are synthetic cannabinoids (SCs), marketed as legal marijuana alternatives in Europe in the early 2000s. Twenty-nine samples from street in Ankara (Turkey) were analysed by ICP-MS [50]. In this work, the trace element contents in the analysed samples were below the limit values determined by the WHO.

Neutron activation analysis is, without doubt, complementary to techniques such as ICP-MS for measurement of chemical elements in drugs of abuse and associated pharmaceutical products, as is demonstrated in the few examples reproted above. However, there is shockingly little attention paid in these and other papers to the degree of homogeneity of the samples collected and the representativeness of test portions. Detection limits, precision and demonstration of degree of trueness are primarily highlighted. In some papers, the authors reported that material has been 'homogenized', without mentioning the validation thereof. In other cases analysis of replicates is reported, without providing clarity if these are replicate test portions taken from the (homogenized ?) sample or replicate analyses of the same test portion. The observed variance -which is relevant for further interpretation of the data- may be attributed to analytical and sampling errors [51]. The analytical ability of some techniques (such as ICP-MS) to reach substantial lower detection limits than before is a valuable asset in the characterization of materials, but at the same time the sampling error related to the representativeness in the measurement of smaller mass fractions increases.

3.3 Availability of facilities for large sample analysis and limitations

Facilities for large sample NAA and large sample prompt gamma analysis are already available in several countries. The International Atomic Energy Agency (IAEA) facilitated a co-ordinated research project from 2009-2012 on the implementation of research reactor based facilities and methodologies for the analysis of large sample. This project resulted in operational facilities in Brazil, Egypt, Ghana, India, Japan (neutron beam based), Malaysia (neutron generator based), Peru (neutron beam based), Romania, Russian Federation, Syrian Arab Republic, Thailand and USA. Typical object sizes that can be analyzed vary from volumes of a few cubic centimeters to several tens of liters. A report on these large sample facilities, the methodologies applied and validation thereof is in preparation [52].

The induced radioactivity in the samples upon exposing the objects with neutrons limits its handling to authorized radiological workers at locations with a related safety regime. However, the induced activity decays and the object may be safely released again after a certain period (which may vary

from a few days and months up to a year or more) that sometimes can be even well be estimated before an irradiation is considered.

4. Conclusions

A crucial part in the interpretation of results from chemical analysis is the assessment if the measured components of the test portion, collected from an object under investigation, are representative for the components in this object. If the object is large enough, the results from replicate test portion analyses may indicate this degree of representativeness. There is ample evidence that the degree of representativeness -at a given degree of confidence- can only be achieved by analyzing test portions exceeding in size the capabilities of most analytical techniques. Analysis of such test portions and even the entire object of study can be nowadays carried out by applying the principles of neutron activation analysis, prompt gamma analysis and photon activation analysis, without sub-sampling.

Large sample neutron activation analysis is a method built on the methodology of 'normal' neutron activation analysis.

Large sample neutron activation analysis is not commonly available and requires access to a nuclear analytical laboratory with access to the facilities of a nuclear research reactor or other source of neutrons but the physics of this technique is fully understood and it has been demonstrated that the degree of trueness and metrological traceability of the values of the measurement can meet the highest international metrological requirements.

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