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(54) METHOD AND APPARATUS FOR MASS ANALYSING A SAMPLE

(57) The invention relates to a method for mass analysing a sample, the method including the steps of in an ion source (2), generating in a plasma torch (4) of the ion source (2) a plasma from a plasma gas and inserting the sample into the plasma for ionising the sample to ions; transferring the ions from the ion source (2) to a mass analyser (5); obtaining at least one mass spectrum of the ions with the mass analyser (5); wherein the plasma gas includes at least 10 weight percent oxygen, preferably at least 15 weight percent oxygen, particular preferably at least 20 weight percent oxygen, most preferably at least 23 weight percent oxygen. Furthermore, the invention relates to an apparatus (1) for executing the method according to the invention, wherein the apparatus (1) includes an ion source (2) for ionising the sample to ions, wherein the ion source (2) includes a plasma torch (4) for generating in the plasma torch (4) a plasma from a plasma gas, wherein the sample is ionisable to the ions by inserting the sample into the plasma, a mass analyser (5) for obtaining at least one mass spectrum of the ions, the mass analyser (5) being fluidly coupled to the ion source (2) for receiving the ions from the ion source (2) for obtaining the at least one mass spectrum from the ions, wherein the plasma gas includes at least 10 weight percent oxygen, preferably at least 15 weight percent oxygen, particular preferably at least 20 weight percent oxygen, most preferably at least 23 weight percent oxygen.

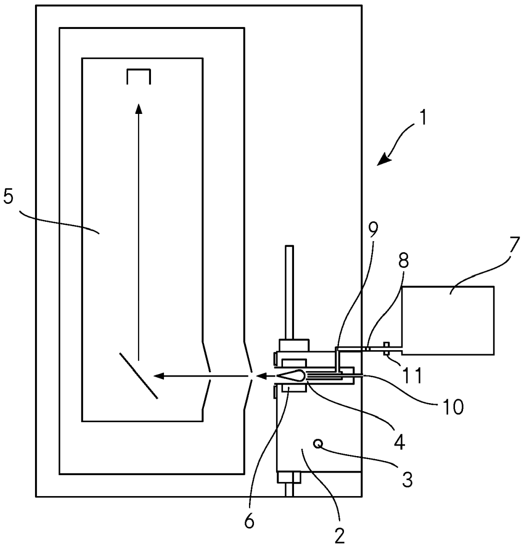

Fig. 1

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Description

Technical Field

[0001] The invention relates to a method for mass analysing a sample and an apparatus for executing the method.

Background Art

[0002] Methods an apparatuses for mass analysing a sample are known. One example is described in EP 3 890 449 A1 of Tofwerk AG, where the described apparatus includes a microwave driven plasma ion source for ionising a sample to be ionised to sample ions. Thereby, in a plasma torch of the microwave driven plasma ion source, a plasma is generated from a plasma gas and the sample is inserted into the plasma for ionising the sample to ions. Furthermore, the ions are transferred from the microwave driven plasma ion source to a mass analyser of the apparatus and at least one mass spectrum of the ions is obtained with the mass analyser. Thereby, according to EP 3 890 449 A1, the plasma gas contains a Nitrogen content from 80 volume percent to 100 volume percent or an argon content from 0.9 volume percent to 100 volume percent.

[0003] Mass spectra obtained with such known methods and apparatuses for mass analysing a sample however show rather broad peaks of noble gases, in particular of Argon, Krypton and Xenon, which are present in the plasma gas unless highest purity Nitrogen is used as plasma gas. The use of such highest purity Nitrogen as plasma gas however makes the operation of the known methods and apparatuses very cost intensive. Thus, the known methods and apparatuses are either very costly in operation or do not enable proper detection and quantification of elements having mass to charge ratios in the range of the mass to charge ratios of noble gases, in particular of Argon, Krypton and Xenon.

[0004] In the present text, the unit Th is used for indicating the mass to charge ratio of ions and is used in the mass spectra shown in the figures. Th is the abbreviation of Thomson, wherein one Thomson is one unified atomic mass unit divided by one elementary charge. One unified atomic mass unit is $1.66053906660 \times 10^{-27}$ kg, while one elementary charge is $1.602176634 \times 10^{-19}$ C.

[0005] In the present text, the formulation "and/or" is occasionally used for linking two features. This formulation is to be understood as either one of the two features or both of the features. Thus, "A and/or B" is to be understood as three equivalent options, wherein one option is A, another option is B and yet another option is both A and B.

Summary of the invention

[0006] It is the object of the invention to create a method and an apparatus for mass analysing a sample pertaining to the technical field initially mentioned, that enable a cost effective operation and which enable a proper detection and quantification of elements having mass to charge ratios in the range of the mass to charge ratios of noble gases, in particular of Argon, Krypton and Xenon.

[0007] The solution of the invention is specified by the features of claim 1. According to the invention, the method includes the steps of: in an ion source, generating in a plasma torch of the ion source a plasma from a plasma gas and inserting the sample into the plasma for ionising the sample to ions; transferring the ions from the ion source to a mass analyser; obtaining at least one mass spectrum of the ions with the mass analyser; wherein the plasma gas includes at least 10 weight percent oxygen, preferably at least 15 weight percent oxygen, particular preferably at least 20 weight percent oxygen, most preferably at least 23 weight percent oxygen, preferably with respect to the total weight of the plasma gas.

[0008] The apparatus for executing the method according to the invention for mass analysing a sample includes an ion source for ionising the sample to ions, wherein the ion source includes a plasma torch for generating in the plasma torch a plasma from a plasma gas, wherein the sample is ionisable to the ions by inserting the sample into the plasma, a mass analyser for obtaining at least one mass spectrum of the ions, the mass analyser being fluidly coupled to the ion source for receiving the ions from the ion source for obtaining the at least one mass spectrum from the ions, wherein the plasma gas includes at least 10 weight percent oxygen, preferably at least 15 weight percent oxygen, particular preferably at least 20 weight percent oxygen, most preferably at least 23 weight percent oxygen, preferably with respect to the total weight of the plasma gas.

[0009] It is irrelevant, whether the oxygen is present in the plasma gas as pure oxygen or whether the oxygen is present in the plasma gas as being part of other compounds that are present in the plasma gas. In one example, the oxygen is present in the form of oxygen molecules consisting of two oxygen atoms bound together. In another example, the oxygen is present in the plasma gas by being oxygen atoms being bound with two hydrogen atoms to water molecules. Thus, in this example, the oxygen is present in the plasma gas because water vapour is present in the plasma gas. In yet another example, the plasma gas comprises carbon dioxide and thus comprises oxygen. In yet another example, the plasma gas comprises carbon monoxide and thus comprises oxygen. The oxygen can also be present in the plasma gas in parts or entirely in one or more of the before as example mentioned and other, not before as examples mentioned forms. Thus, the formulation according to which the plasma gas includes at least a certain amount of weight percent oxygen preferably refers to the weight percentage of oxygen atoms in the plasma gas. Therefore, advantageously, the weight percentage of oxygen in the plasma gas is determined by considering a reference volume of plasma gas and by determining the summed weight of the oxygen atoms in this reference volume and by determining the weight of the plasma gas in this reference volume, wherein the weight percentage of oxygen in the plasma gas is the summed weight of the oxygen atoms in this reference volume multiplied by hundred and divided by the weight of the plasma gas in this reference volume.

[0010] In this sense, in the present text, a weight percentage of a particular substance in the plasma gas is preferably the weight percentage of the particular substance with respect to the total weight of the plasma gas. In other words, a weight percentage of a particular substance in the plasma gas is advantageously determined by considering a reference volume of plasma gas and by determining the summed weight of the respective particular substance in this reference volume and by determining the weight of the plasma gas in this reference volume, wherein the weight percentage of this respective particular substance in the plasma gas is the summed weight of the respective particular substance in this reference volume multiplied by hundred and divided by the weight of the plasma gas in this reference volume.

[0011] Due to the oxygen content in the plasma gas of at least 10 weight percent oxygen, preferably at least 15 weight percent oxygen, particular preferably at least 20 weight percent oxygen, most preferably at least 23 weight percent oxygen, some elements being part of the sample oxidise during ionisation and are thus detected in an oxidised state, while other elements which are part of the sample are still detected in their pure, unoxidised state. For example, with the method according to the invention, Uranium is detected in its oxidised state UO_2 and is thus found at 270 Th in the mass spectra. The detection efficiency is thereby about the same as for pure Uranium when pure Nitrogen is used as plasma gas. On the other hand, as compared to the use of pure Nitrogen as plasma gas, with the method according to the invention, Indium is still detected with a high efficiency in its pure state of In at 115 Th, while Cobalt is still detectable at 59 Th.

[0012] As compared to mass spectra obtained with a plasma gas including Nitrogen with less than 5 weight percent oxygen, in particular obtained with a plasma gas being a pure Nitrogen plasma gas, mass spectra obtained with a plasma gas including at least 10 weight percent oxygen, preferably at least 15 weight percent oxygen, particular preferably at least 20 weight percent oxygen, most preferably at least 23 weight percent oxygen, show considerably reduced characteristic peaks of Argon at about 40 Th, Krypton at about 80 Th and Xenon at about 130 Th. Furthermore, as compared to mass spectra obtained with a plasma gas which consists to more than half of Argon and includes less than 5 weight percent oxygen or which even consist of pure Argon, mass spectra obtained with a plasma gas including at least 10 weight percent oxygen, preferably at least 15 weight percent oxygen, particular preferably at least 20 weight percent oxygen, most preferably at least 23 weight percent oxygen, show considerably reduced characteristic peaks of Argon atoms (Ar) at about 40 Th and Argon ions (Ar_2) at about 80 Th.

[0013] Thus, the method and apparatus according to the invention have the advantage that with a cost effective operation, a proper detection and quantification of elements having mass to charge ratios in the range of the mass to charge ratios of noble gases, in particular of Argon at about 40 Th, Krypton at about 80 Th and Xenon at about 130 Th, is enabled.

[0014] Advantageously, the plasma gas includes at least 70 weight percent Nitrogen. Thereby, it is irrelevant, whether the Nitrogen is present in the plasma gas as pure Nitrogen molecules or whether the Nitrogen is present in the plasma gas as being part of other compounds that are present in the plasma gas. The plasma gas including at least 70 weight percent Nitrogen has the advantage that, since bottled Nitrogen can be purchased for considerably less money than other bottled gases like for example Argon, executing the method according to the invention and operating the apparatus according to the invention is considerably less expensive. Furthermore, a plasma gas including at least 70 weight percent of Nitrogen and including at least 10 weight percent oxygen, preferably at least 15 weight percent oxygen, particular preferably at least 20 weight percent oxygen, most preferably at least 23 weight percent oxygen has the advantage that it can easily and cheaply be obtained from the atmospheric air surrounding the apparatus according to the invention. Thereby, for obtaining the plasma gas, no Nitrogen enrichment is required. Thus, no generator is required for obtaining purified Nitrogen gas from atmospheric air which means that no Nitrogen enriched gas supply from atmospheric air is required since the composition of the atmospheric air can be used unchanged as plasma gas. Thus, no gas-selective filtration membrane or pressure-swing adsorption of oxygen by use of a suitable sorbent such as a carbon molecular sieve is required for obtaining the plasma gas from atmospheric air.

[0015] Preferably, the plasma gas is atmospheric air. Thereby, it is irrelevant whether the atmospheric air is at atmospheric pressure when being fed as the plasma gas to the plasma torch of the ion source for generating the plasma from the plasma gas or whether the atmospheric air is compressed or at a lower pressure than atmospheric pressure when being fed as the plasma gas to the plasma torch of the ion source for generating the plasma from the plasma gas.

[0016] The plasma gas being atmospheric air has the advantage that the plasma gas can easily and cheaply be obtained from the atmospheric air surrounding the apparatus according to the invention. The apparatus can therefore be easily operated in the field, in particular far from bottled plasma gas supply infrastructures, like for example at remote places. In the same sense, the method according to the invention can be executed independent of a constant supply of bottled plasma gas which enables applications of the method in the field, in particular far from bottled plasma gas supply infrastructures, like for example in remote places.

[0017] Thus, particular preferably, the plasma gas being atmospheric air is air obtained from a surrounding of the apparatus. In a variant, however, the plasma gas being atmospheric air can be air obtained from far from the apparatus. For example, the plasma gas being atmospheric air can be bottled plasma gas obtained at a plant where the plasma gas is bottled and then transported in bottles to the apparatus for executing the method.

[0018] Advantageously, aerosol particles are filtered out of the atmospheric air before the atmospheric air is fed as the plasma gas to the plasma torch of the ion source for generating the plasma from the plasma gas. Thereby, it is irrelevant whether the aerosol particles are solid particles, liquid particles or a combination of solid particles and liquid particles. Preferably, the aerosol particles are filtered out of the atmospheric air with a filter. In this case, the apparatus according to the invention advantageously includes the filter for filtering the aerosol particles out of the atmospheric air.

[0019] Filtering out the aerosol particles of the atmospheric air before the atmospheric air is fed as the plasma gas to the plasma torch of the ion source for generating the plasma from the plasma gas has the advantage that background signal of aerosol particles included in the plasma gas is avoided in the mass spectra. This avoidance of background signal has the advantage that a quantitative analysis of the sample is enabled. This is advantageous independent of the type of sample which is mass analysed. Even in case the sample itself is atmospheric air including discrete particles and/or discrete droplets, in particular aerosol particles, entrained in the atmospheric air, the filtering out of the aerosol particles of the atmospheric air being the plasma gas has the advantage that a quantitative analysis of the sample is enabled because the sample can be introduced into the plasma in a controlled manner for being ionised such that the amount of sample introduced into the plasma and ionised by the plasma is known, enabling the quantitative analysis of the atmposheric air with the entrained discrete particles and/or discrete droplets, in particular aerosol particles.

[0020] Alternatively, no aerosol particles are filtered out of the atmospheric air before the atmospheric air is fed as the plasma gas to the plasma torch of the ion source for generating the plasma from the plasma gas. This has the advantage that the method can be executed in a simpler manner and the apparatus can be operated in a simpler manner. For example, in case bottled atmospheric air is used as plasma gas, the step of filtering the atmospheric air obtained from bottles is not required because the bottled atmospheric air can for example be filtered already when being obtained in the bottles.

[0021] Independent of whether aerosol particles are filtered out of the atmospheric air before the atmospheric air is fed as the plasma gas to the plasma torch of the ion source for generating the plasma from the plasma gas or not, the atmospheric air being the plasma gas is advantageously atmospheric air that is compressed, in particular to at least 2 bar, particular preferably to at least 3 bar, and fed as the plasma gas to the plasma torch of the ion source for generating the plasma from the plasma gas. Thus, the plasma gas is advantageously fed as compressed atmospheric air to the plasma torch of the ion source for generating the plasma from the plasma gas. This has the advantage that supplying the ion source with plasma gas is simplified.

[0022] In an advantageous variant, the atmospheric air that is compressed, in particular to less than 10 bar, particular preferably to at less than 5 bar, and fed as the plasma gas to the plasma torch of the ion source for generating the plasma from the plasma gas. This has the advantage that a simple commercially available compressor can be used for compressing the atmospheric air.

[0023] Advantageously, the atmospheric air is compressed with a compressor. In this case, the apparatus advantageously includes the compressor for compressing the atmospheric air, in particular to at least 2 bar, particular preferably to at least 3 bar, before feeding the atmospheric air as the plasma gas to the plasma torch of the ion source for generating the plasma from the plasma gas. Particular advantageously, the compressor is for compressing atmospheric air being air obtained from a surrounding of the apparatus. This has the advantage that the apparatus can easily be operated from an infrastructure for supplying bottled plasma gas. Thus, the apparatus can be operated very cost effective and the method can be executed very cost effective.

[0024] In a variant, however, the compressor may be separate from the apparatus, which means the apparatus can go without compressor for compressing the atmospheric air before feeding the atmospheric air as the plasma gas to the plasma torch of the ion source for generating the plasma from the plasma gas. An example of this variant is the case where the plasma gas is obtained from bottles.

[0025] In an alternative, the atmospheric air being the plasma gas is not compressed before being fed as the plasma gas to the plasma torch of the ion source for generating the plasma from the plasma gas.

[0026] Preferably, the plasma gas being atmospheric air includes 1.2 weight percent or less of water vapour, preferably 0.9 weight percent or less of water vapour, particular preferably 0.6 weight percent or less water vapour, more preferably 0.29 weight percent or less water vapour, most preferably 0.07 weight percent or less of water vapour when being fed to the plasma torch of the ion source for generating the plasma from the plasma gas. Thereby, it is irrelevant whether the atmospheric air is at atmospheric pressure when being fed as the plasma gas to the plasma torch of the ion source for generating the plasma from the plasma gas or whether the atmospheric air is compressed or at a lower pressure than atmospheric pressure when being fed as the plasma gas to the plasma torch of the ion source for generating the plasma from the plasma gas.

[0027] At a temperature of 20°C and a pressure of 1 bar, 1.2 weight percent of water vapour in atmospheric air corresponds to a relative humidity of 80%, while 0.9 weight percent of water vapour in atmospheric air corresponds to a relative humidity of 60%, while 0.6 weight percent of water vapour in atmospheric air corresponds to a relative humidity of 40%, while 0.29 weight percent of water vapour in atmospheric air corresponds to a relative humidity of 20%, while 0.07 weight percent of water vapour in atmospheric air corresponds to a relative humidity of 5%. Thus, the relative humidity of the atmospheric air, in particular before being compressed, determined at a temperature of 20°C and a pressure of 1 bar is preferably 80% or less, particular preferably 60% or less, more preferably 40% or less, even more preferably 20% or less, and most preferably 5% or less.

[0028] Alternatively, the plasma gas being atmospheric air includes more than about 1.2 weight percent or less of water vapour when being fed to the plasma torch of the ion source for generating the plasma from the plasma gas. In one example, the plasma gas being atmospheric air includes 1.35 weight percent of water vapour when being fed to the plasma torch of the ion source for generating the plasma from the plasma gas. At a temperature of 20°C and a pressure of 1 bar, 1.35 weight percent of water vapour in atmospheric air corresponds to a relative humidity of 90%. In another example, the plasma gas being atmospheric air includes 1.5 weight percent of water vapour when being fed to the plasma torch of the ion source for generating the plasma from the plasma gas. At a temperature of 20°C and a pressure of 1 bar, 1.5 weight percent of water vapour in atmospheric air corresponds to a relative humidity of 100%.

[0029] In case the atmospheric air being the plasma gas is atmospheric air that is compressed, in particular to at least 2 bar, particular preferably to at least 3 bar, and fed as the plasma gas to the plasma torch of the ion source for generating the plasma from the plasma gas, the compressed atmospheric air is advantageously dried with an air drier before being fed as the plasma gas to the plasma torch. In this case, the apparatus advantageously includes the air drier for drying the compressed atmospheric air before being fed as the plasma gas to the plasma torch of the ion source for generating the plasma from the plasma gas.

[0030] Alternatively, the compressed atmospheric air is not dried with an air drier before being fed as the plasma gas to the plasma torch. In this case, execution of the method is simplified. In the same sense, alternatively, the apparatus goes without the air drier for drying the compressed atmospheric air before being fed as the plasma gas to the plasma torch of the ion source for generating the plasma from the plasma gas.

[0031] As an alternative to the before mentioned variants, the plasma gas is not atmospheric air. Even more, alternatively, the plasma gas includes less than 70 weight percent Nitrogen.

[0032] Advantageously, the ion source is a microwave driven ion source, wherein the plasma is generated from the plasma gas by means of microwaves. Such ion sources have the advantage that they are very effective in generating a plasma from Nitrogen. Thus, the ion source being a microwave driven ion source, wherein the plasma is generated from the plasma gas by means of microwave, has the advantage that the use of a plasma gas including at least 70 weight percent Nitrogen, in particular that the use of atmospheric air as plasma gas, is readily enabled.

[0033] An example of such a microwave driven ion source is described in EP 3 890 449 A1 of Tofwerk AG. However, the ion source can be any other microwave driven ion source or can be no microwave driven ion source.

[0034] In case the ion source is a microwave driven ion source, the microwaves can be used directly and/or indirectly to generate the plasma from the plasma gas. In either case, the ion source advantageously includes a microwave generator for generating the microwaves. Thus, in a first preferred variant, the plasma gas is exposed to the microwaves generated by the microwave generator for generating the plasma from the plasma gas. In this first variant, in an example, the ion source is a microwave induced plasma ion source. In a second preferred variant, the microwave driven plasma ion source comprises a microwave resonator, wherein the microwave resonator is exposed to the microwaves generated by the microwave generator such that the microwave resonator generates an electromagnetic field due to a resonant behaviour of the microwave resonator when being exposed to the microwaves, wherein the plasma gas is inductively coupled to the electromagnetic field generated by the microwave resonator for generating the plasma from the plasma gas.

[0035] In either of these variants, the microwaves are the electromagnetic waves of radio frequency electromagnetic radiation in the microwave range. This microwave range is advantageously the range of electromagnetic radiation having a frequency in the range from 30 MHz to 3 GHz, more preferably from 45 MHz to 3 GHz, most advantageously from 30 MHz to 300 MHz, in particular 45 MHz to 300 GHz, or from 300 MHz to 3 GHz. In an example, the radio frequency of the radio frequency electromagnetic radiation is 2.45 GHz.

[0036] In an alternative to these variants, the ion source is an inductively coupled plasma ion source (ICP) which includes a coil arranged around the plasma torch, wherein a high frequency voltage is applied to the coil for generating a high frequency electromagnetic field in the plasma torch for generating the plasma from the plasma gas. Thereby, in an example, the high frequency is 27.12 MHz.

[0037] Independent of whether the ion source is a microwave driven plasma ion source, an inductively coupled plasma ion source or any other type of ion source, the ion source advantageously includes a plasma gas inlet for inserting the plasma gas into the plasma torch for generating the plasma from the plasma gas. Furthermore, the ion source advantageously includes a sample inlet for inserting the sample into the plasma for ionising the sample to the ions.

[0038] Preferably, the sample includes at least one element with a mass to charge ratio of around 40 Th, around 80 Th, and/or around 130 Th. As compared to mass spectra obtained with a plasma gas including Nitrogen with less than 5 weight percent oxygen, in particular obtained with a plasma gas being a pure Nitrogen plasma gas, mass spectra obtained with a plasma gas including at least 10 weight percent oxygen, preferably at least 15 weight percent oxygen, particular preferably at least 20 weight percent oxygen, most preferably at least 23 weight percent oxygen, show considerably reduced characteristic peaks of Argon at about 40 Th, Krypton at about 80 Th and Xenon at about 130 Th. Furthermore, as compared to mass spectra obtained with a plasma gas which consist to more than half of Argon and less than 5 weight percent oxygen or which even consist of pure Argon, mass spectra obtained with a plasma gas including at least 10 weight percent oxygen, preferably at least 15 weight percent oxygen, particular preferably at least 20 weight percent oxygen, most preferably at least 23 weight percent oxygen, show considerably reduced characteristic peaks of Argon at about 40 Th. Thus, elements with a mass to charge ratio of around 40 Th, around 80 Th, and around 130 Th can be detected better with the present invention where the plasma gas includes at least 10 weight percent oxygen, preferably at least 15 weight percent oxygen, particular preferably at least 20 weight percent oxygen, most preferably at least 23 weight percent oxygen. Consequently, the method is advantageously employed for mass analysing samples including at least one element with a mass to charge ratio of around 40 Th, around 80 Th, and/or around 130 Th. Advantageously, the sample includes at least one of Calcium, Selenium, Bromine, Tellurium and Barium. Alternatively, however, the sample does not include any of Calcium, Selenium, Bromine, Tellurium and Barium.

[0039] In a preferred variant, the sample includes at least one element with a mass to charge ratio of around 40 Th, in particular Calcium. Since Calcium ions are found in mass spectra at about 40 Th, this enables an improved detection of Calcium. Consequently, the method is advantageously used for detecting Calcium, in particular determining the amount of Calcium, in the sample. This has the advantage that the sensitivity for determining the calcium content in the sample is increased as compared to the use of Argon or Nitrogen, in particular pure Nitrogen generated with a generator, as plasma gas.

[0040] Advantageously, the sample includes biological cells and/or body fluids. Thereby, the biological cells are procaryotic cells, like bacteria or archaea, or eukaryotic cells, like single celled protozoa and slime moulds, or cells of multicellular organisms like fungi, plants and animals, in particular human cells. Body fluids are liquids from within an animal body or a human body, like intracellular fluid and extracellular fluid, in particular interstitial fluid like lymphatic fluid, or transcellular fluid and intravascular fluid like blood. Since Calcium is an important part of biological cells and body fluids, the method enabling an improved detection of the Calcium content in the sample improves the sensitivity of the analysis of such samples. In particular in case the plasma gas includes at least 70 weight percent Nitrogen besides the at least 10 weight percent oxygen, preferably at least 15 weight percent oxygen, particular preferably at least 20 weight percent oxygen, most preferably at least 23 weight percent oxygen, like in case where the plasma gas is atmospheric air, the additional advantage of an improved detection rate of Iron is achieved as compared to the use of a plasma gas consisting to at least its half of Argon because no peaks of ArO at about 56 Th appears in the mass spectra which could interfere with the peaks of Iron at about 56 Th. Consequently, in case the plasma gas includes at least 70 weight percent Nitrogen, in particular in case the plasma gas is atmospheric air, Calcium as well as Iron which are both important components of biological cells and body fluids can be very well be detected. Thus, advantageously, in a method for analysing a sample including biological cells and/or body fluids, the method according to the invention is employed, wherein the plasma gas includes advantageously at least 70 weight percent Nitrogen, particular preferably wherein the plasma gas is atmospheric air. Thus, in this method for analysing the sample including the biological cells and/or body fluids, the sample is mass analysed, wherein the method includes the steps of: in an ion source, generating in a plasma torch of the ion source a plasma from a plasma gas and inserting the sample into the plasma for ionising the sample to ions; transferring the ions from the ion source to a mass analyser; obtaining at least one mass spectrum of the ions with the mass analyser; wherein the plasma gas includes at least 10 weight percent oxygen, preferably at least 15 weight percent oxygen, particular preferably at least 20 weight percent oxygen, most preferably at least 23 weight percent oxygen. This enables to detect Calcium in the sample and determine its content in the sample. Advantageously, the plasma gas thereby includes at least 70 weight percent Nitrogen. Particular advantageously, the plasma gas is atmospheric air. This method or analysing a sample including biological cells and/or body fluids has the advantage that Calcium as well as Iron which are both important components of biological cells and body fluids can be very well be detected and their content in the sample can be determined. Of course, this method for analysing a sample including biological cells and/or body fluids which employs the method according to the invention can be executed with the herein described apparatus for executing the method according to the invention.

[0041] In the method according to the invention, independent of whether the sample includes biological cells and/or body fluids or not, in a preferred variant, the sample includes at least one element with a mass to charge ratio of around 80 Th, in particular Selenium and/or Bromine.

[0042] Independent of whether the sample includes biological cells and/or body fluids or not, in a preferred variant, the sample includes at least one element with a mass to charge ratio of around 130 Th, in particular Barium and/or Tellurium. Since Barium ions are found in mass spectra at about 130 Th, this enables an improved detection of Barium. Consequently, the method is advantageously used for detecting Barium, in particular determining the amount of Barium in the sample. Since the isotope pattern of Barium in mass spectra resembles the isotope pattern of Xenon more than the isotope pattern of Tellurium in mass spectra resembles the isotope pattern of Xenon, the method is particular advantageously used for detecting Barium, in particular determining the amount of Barium, in the sample. As shown in the table in Figure 3, Barium is better detectable with the method according to the present invention than in case where the plasma gas is pure Nitrogen generated with a generator.

[0043] Advantageously, the sample is a sample gas with discrete particles and/or discrete droplets, in particular with aerosol particles, entrained in the sample gas. This has the advantage that the content of the discrete particles and/or discrete droplets, in particular aerosol particles, can be mass analysed in a simple and efficient manner. Thereby, the sample gas can be ambient air or any other gas. In an example, the sample gas is Nitrogen. In another example, the sample gas is helium. Independent of the type of sample gas, it is irrelevant whether the aerosol particles are liquid particles, solid particles or a combination of liquid particles and solid particles. In a particular advantageously, the sample is ambient air with discrete particles and/or discrete droplets, in particular aerosol particles, entrained in the ambient air. Aerosol particles usually have a size in a range from 10 nm to 10 μm. Aerosol particles smaller than 10 nm have a large surface to size ratio and therefore grow quickly into larger aerosol particles. Aerosol particles larger than 10 μm on the other hand become too heavy to be suspended for a long time and will eventually fall to the ground. For this reason, the typical size range of aerosol particles in a sample being an aerosol is from 50 nm to 2'000 nm or 2 μm, respectively. As compared to the aerosol, the sample being discrete particles and/or discrete droplets entrained in a sample gas is to be understood broader. Such discrete particles and/or discrete particles, respectively, entrained in a sample gas can be generated right in front of the sample intake of the ion source for example by laser ablation of some sample material. In this case, the discrete particles and/or discrete droplets, respectively, can have sizes that exceed the upper limit of 10 μm of aerosol particles and as well as sizes that fall below the lower limit of 10 nm of aerosol particles. Of course, the discrete particles and discrete droplets can have sizes like aerosol particles, too.

[0044] In case the sample is the sample gas, in particular ambient air, with the discrete particles and/or discrete droplets, in particular aerosol particles, entrained in the sample gas, the sample gas including the discrete particles and/or discrete droplets, in particular aerosol particles, respectively, are advantageously inserted into the ion source with an atmospheric sampler for inserting the sample into the plasma for ionising the sample to the ions. Thus, in this case, the apparatus advantageously includes the atmospheric sampler for inserting the sample gas, in particular ambient air, with the discrete particles and/or discrete droplets, in particular the aerosol particles, entrained in the gas into the ion source for inserting the sample into the plasma for ionising the sample to the ions. Such atmospheric samplers are known in the art.

[0045] In case the sample is a sample gas with discrete particles and/or discrete droplets, in particular aerosol particles, entrained in the sample gas, advantageously, the discrete particles and/or solid droplets, respectively, in particular the aerosol particles, are separated according to their size with an aerosol mobility spectrometer (AMS), which is also sometimes referred to as aerodynamic particle sizer, before being fed into the plasma for ionising the sample to the ions. In this case, the apparatus advantageously includes the aerosol mobility spectrometer (AMS) for separating the discrete particles and/or solid droplets, respectively, in particular the aerosol particles, before the discrete particles and/or solid droplets, respectively, in particular the aerosol particles, are fed into the plasma for ionising the sample to the ions.

[0046] Preferably, the sample is a liquid. This has the advantage that the liquid can be mass analysed in a simple and efficient manner. In this case, the sample is advantageously sprayed with a nebuliser or with a micro droplet generator and inserted into the plasma for ionisation of the sample to the ions. Thus, in this case, the apparatus advantageously includes the nebuliser or micro droplet generator for spraying the sample before inserting the sample into the plasma for ionisation of the sample to the ions. Such nebulisers and such micro droplet generators are known in the art.

[0047] Since with a micro droplet generator, droplets of a well defined size can be generated, a micro droplet generator can be used for calibrating the apparatus as known in the art. In this case, the apparatus advantageously includes a micro droplet generator for calibrating the apparatus. Thereby, the micro droplet generator can be a unit independent of one or more further units for inserting the sample into the plasma for ionisation of the sample to the ions, like the above mentioned atmospheric sampler, the above mentioned nebuliser and the above mentioned micro droplet generator. Consequently, the apparatus may include two micro droplet generators, whereof one is for inserting the sample into the plasma for ionisation of the sample to the ions, while the other one is for calibrating the apparatus.

[0048] Advantageously, the mass analyser is a time of flight mass analyser. This has the advantage that the at least one mass spectrum of the ions obtained from the sample can be obtained with the mass analyser in a very efficient and precise manner. Alternatively, however, the mass analyser is not a time of flight mass analyser. In an example of such an alternative, the mass analyser a sector mass analyser or a quadrupole mass analyser.

[0049] Independent on whether the mass analyser is a time of flight mass analyser, a sector mass analyser, a quadrupole mass analyser or any other type of mass analyser, in an advantageous variant, the ions are separated according to their mobility in an ion mobility separation chamber when being transferred from the ion source to the mass analyser. In this case, the apparatus includes an ion mobility separation chamber arranged between the ion source and the mass analyser for separating the ions according to their mobility when being transferred from the ion source to the mass analyser. This has the advantage that an improved analysis of the ions is enabled. Alternatively, however, the method goes without separating the ions according to their mobility in an ion mobility separation chamber when being transferred from the ion source to the mass analyser, and the apparatus goes without such ion mobility separation chamber. Such an alternative has the advantage that the apparatus can be constructed simpler.

[0050] Other advantageous embodiments and combinations of features come out from the detailed description below and the entirety of the claims.

Brief description of the drawings

[0051] The drawings used to explain the embodiments show:

Fig. 1	a schematic view of an apparatus according to the invention for mass analysing a sample with the method according to the invention,
Fig. 2a, b	mass spectra obtained with the apparatus when operating the apparatus without any sample being introduced into the plasma, once with pure nitrogen as the plasma gas and once with atmospheric air as the plasma gas,
Fig. 3	a table with the results of three measurements of a reference sample, whereof two measurements were obtained with the method according to the invention and one for comparison reasons was obtained with pure nitrogen as plasma gas.

[0052] In the figures, the same components are given the same reference symbols.

Preferred embodiments

[0053] Figure 1 shows a schematic view of an apparatus 1 according to the invention for mass analysing a sample with the method according to the invention. The apparatus 1 includes an ion source 2 for ionising the sample to ions. Thereby, the ion source 2 includes a plasma torch 4 for generating in the plasma torch 4 a plasma from a plasma gas, wherein the sample is ionisable to the ions by inserting the sample into this plasma. The ion source 2 further includes a plasma gas inlet 9 for inserting the plasma gas into the plasma torch 4 for generating the plasma from the plasma gas. Furthermore, the ion source 2 includes a sample inlet 10 for inserting the sample into the plasma for ionising the sample to the ions.

[0054] Besides the ion source 2, the apparatus 1 includes a mass analyser 5 for obtaining at least one mass spectrum of the ions, the mass analyser 5 being fluidly coupled to the ion source 2 for receiving the ions from the ion source 2 for obtaining the at least one mass spectrum from the ions. Thereby, the mass analyser 5 is a time of flight mass analyser. In a variant, however, the mass analyser is a sector mass analyser which uses a magnetic field for mass separating the ions spatially such that the ions reach a position sensitive detector of the mass analyser at positions which depend on the mass to charge ratio of the respective ion and thus indicate the mass to charge ratio of the respective sample ion.

[0055] In the apparatus 1 shown in Figure 1, the ion source 2 is a microwave driven plasma ion source. Thus, the ion source 2 includes a microwave generator 3 for generating microwaves for generating the plasma from the plasma gas. Thereby, in a first variant, the microwave driven plasma ion source includes a microwave resonator 6 for generating an electromagnetic field for inductively coupling the plasma gas to the electromagnetic field for the generation of the plasma from the plasma gas, wherein the microwave resonator 6 exhibits a resonant behaviour and generates the electromagnetic field when being exposed to the microwaves generated by the microwave generator 3. In a second variant, the ion source 2 being the microwave driven plasma ion source goes without the microwave resonator 6 for generating an electromagnetic field for inductively coupling the plasma gas to the electromagnetic field for the generation of the plasma from the plasma gas, wherein the microwave resonator 6 exhibits a resonant behaviour and generates the electromagnetic field when being exposed to the microwaves generated by the microwave generator 3. In this case, the plasma is generated directly be exposing the plasma gas to the microwaves generated by the microwave generator 3. Both these variants are described in more detail in EP 3 890 449 A1 of Tofwerk AG. In a third variant, which is not described in EP 3 890 449 A1 of Tofwerk AG, however, the ion source 2 is not a microwave driven plasma ion source. In this case, the ion source 2 includes the plasma torch 4 but goes without the microwave generator 3 and microwave resonator 6.

Instead of the microwave generator 3, in this third variant the ion source 2 includes a coil arranged around the plasma torch 4, wherein a high frequency voltage is applied to the coil for generating a high frequency electromagnetic field in the plasma torch 4 for generating the plasma from the plasma gas. Thereby, in an example, the high frequency of the high frequency voltage is 27.12 MHz. Commonly, such ion sources with such a coil to which a high frequency voltage is applied for generating the plasma from the plasma gas are referred to as inductively coupled plasma ion sources (ICP).

[0056] In contrast to the apparatus described EP 3 890 449 A1 of Tofwerk AG, the present apparatus 1 shown in Figure 1 includes a compressor 7 for obtaining atmospheric air from a surrounding of the apparatus 1 and compressing the atmospheric air to 3 bar before the atmospheric air is fed as the plasma gas to the plasma torch 4 of the ion source 2 for generating the plasma from the plasma gas. Thereby, the compressor 7 is fluidly coupled to the plasma torch 4 and thus to plasma gas inlet 9 of the ion source 2 for transferring the compressed atmospheric air from the compressor 7 to the plasma torch 4 to be used as the plasma gas for generating the plasma. In a first variant however, the compressor 7 is for compressing the atmospheric air to 2 bar. In a second variant, the compressor 7 is for compressing the atmospheric air to 4 bar, while in a third variant, the compressor 7 is for compressing the atmospheric air to 5 bar.

[0057] The apparatus 1 shown in Figure 1 furthermore includes a filter 8 for filtering aerosol particles out of the atmospheric air before the atmospheric air is fed as the plasma gas to the plasma torch 4 of the ion source 2 for generating the plasma from the plasma gas. This filter 8 is arranged between the compressor 7 and the ion source 2 such that in operation of the apparatus 1, the aerosol particles are filtered out of the atmospheric air before the atmospheric air is fed as the plasma gas to the plasma torch 4 of the ion source 2 for generating the plasma from the plasma gas.

[0058] Since atmospheric air provides an oxygen content of about 23.14 weight percent, the plasma gas contains at least 23 weight percent oxygen when operating the apparatus 1 with the method according to the invention. In a variant, the apparatus 1 is however operated with a generator for slightly enriching nitrogen content in the atmospheric air for being used as plasma gas. Thereby, the generator may include a compressor for compressing the atmospheric air to a pressure like 2 bar, 3 bar, 4 bar or 5 bar before feeding the atmospheric air as the plasma gas to the plasma torch 4 of the ion source 2 for generating the plasma from the plasma gas. In a first variant, the generator is operated such that the plasma gas includes 10 weight percent oxygen. In a second variant, the generator is operated such that the plasma gas includes 15 weight percent oxygen. In a third variant, the generator is operated such that the plasma gas includes 20 weight percent oxygen. In yet another variant, the apparatus 1 goes without generator and without compressor and is operated with bottled plasma gas, wherein the plasma gas includes at least 10 weight percent oxygen, preferably at least 15 weight percent oxygen, particular preferably at least 20 weight percent oxygen, most preferably at least 23 weight percent oxygen.

[0059] The plasma gas being atmospheric air includes water vapour due to the relative humidity in the atmospheric air which is obtained from the surrounding of the apparatus 1. In a first variant, where at a temperature of 20°C and a pressure of 1 bar, the relative humidity of the atmospheric air is 80%, the plasma gas includes 1.2 weight percent of water vapour. In a second variant, where at a temperature of 20°C and a pressure of 1 bar, the relative humidity of the atmospheric air is 60%, the plasma gas includes 0.9 weight percent of water vapour. In a third variant, where at a temperature of 20°C and a pressure of 1 bar, the relative humidity of the atmospheric air is 40%, the plasma gas includes 0.6 weight percent of water vapour. In a fourth variant, where at a temperature of 20°C and a pressure of 1 bar, the relative humidity of the atmospheric air is 20%, the plasma gas includes 0.29 weight percent of water vapour. In a fifth variant, where at a temperature of 20°C and a pressure of 1 bar, the relative humidity of the atmospheric air is 5%, the plasma gas includes 0.07 weight percent of water vapour. In a sixth variant, where at a temperature of 20°C and a pressure of 1 bar, the relative humidity of the atmospheric air is 90%, the plasma gas includes 1.35 weight percent of water vapour. In a seventh variant, where at a temperature of 20°C and a pressure of 1 bar, the relative humidity of the atmospheric air is 100%, the plasma gas includes 1.5 weight percent of water vapour.

[0060] In a further variant, the apparatus 1 includes an air drier 11 for drying the compressed atmospheric air before being fed as the plasma gas to the plasma torch 4 of the ion source 2 for generating the plasma from the plasma gas.

[0061] Figure 2a and 2b show mass spectra obtained with the apparatus 1 when operating the apparatus 1 without any sample being introduced into the plasma. Thus, these mass spectra have been obtained from a pure plasma. Thereby, the axis of abscissae (or x-axes) show the mass to charge ratios in Th, while the ordinates (or y-axes) show the signal intensity provided by the ion detector of the mass analyser 4, the mass analyser 4 being a time of flight mass analyser. This signal intensity is provided in voltage in the units of mV and is not yet calibrated to the number of detected ions but is nonetheless proportional to the number of ions detected. Thus, a higher signal intensity at a particular mass to charge ratio corresponds to a larger number of ions having the respective mass to charge ratio, while a lower signal intensity at a particular mass to charge ratio corresponds to a smaller number of ions having the respective mass to charge ratio. Both mass spectra shown in Figures 2a and 2b cover the range of mass to charge ratios from 10 Th to 275 Th.

[0062] The mass spectrum shown in Figure 2a has been obtained from a plasma generated from pure Nitrogen which was generated by a generator, the pure nitrogen having a purity of more than 99.99%. This mass spectrum shows clear peaks at about 40 Th originating from Argon ions, a smaller peak at about 80 Th originating from Krypton ions and a rather broad peak at about 130 Th originating from Xenon ions. The further peak at about 32 Th has not yet been assigned unambiguously to a particular ion or molecule. However, it is clearly not a peak originating from oxygen molecules O_2 since its isotopic pattern does not match the one of oxygen molecules O_2. According to the literature, Nitrogen molecules (N_2^+) provide an ionisation energy of 1’503 kJ/mol which corresponds to 15.578 eV, while Nitrogen Atoms (N^+) provide an ionisation energy of 1’402 kJ/mol which corresponds to 14.531 eV.

[0063] The mass spectrum shown in Figure 2b has been obtained from a plasma generated from atmospheric air which has been compressed with the compressor 7 to a pressure of 3 bar. In comparison to the mass spectrum shown in Figure 2a, in the mass spectrum shown in Figure 2b, the peaks at about 40 Th, about 80 Th and about 130 Th have disappeared. The very weak blurred feature which can be adumbrated at about 120 Th originates from some remaining Sn-impurities in the apparatus 1. This feature is as well present in the mass spectrum shown in Figure 2a, even though there, it is hidden in the shoulder of the Xenon-peak at about 130 Th.

[0064] The comparison of the mass spectra shown in Figures 2a and 2b indicates that with the method according to the invention and with an apparatus for executing the method according to the invention, a proper detection and quantification of elements having mass to charge ratios in the range of the mass to charge ratios of noble gases, in particular of Argon at about 40 Th, Krypton at about 80 Th and Xenon at about 130 Th, could very well be enabled while being operated very cost effective.

[0065] A reference sample was mass analysed with the apparatus 1, wherein the apparatus 1 included as the ion source 2 the microwave driven plasma ion source with the microwave resonator 6 as described above. The reference sample was a 10 ppm 29 Element ICP Calibration/Quality Control Standard sample with the product name "IV-STOCK-21" of the company Inorganic Ventures. This reference sample is a liquid solution including 10 μg/ml of each of the elements Ag, Al, As, Ba, Be, Bi, Ca, Cd, Co, Cr_3, Cs, Cu, Fe, Ga, In, K, Li, Mg, Mn, Na, Ni, Pb, Rb, Se, Sr, Tl, U, V and Zn and including 5 weight percent nitric acid. Before mass analysing the reference sample, the reference sample was diluted one hundred times with 2% HNO_3. For ionisation, this diluted reference sample was inserted into the plasma with a micro droplet generator. Thus, the diluted reference sample was sprayed with the micro droplet generator to form droplets of a known size, wherein the droplets were entrained in a stream of a carrier gas and inserted into the plasma with this stream of the carrier gas for the ionisation of the sample to the ions. In order to analyse an individual droplet of the diluted reference sample, a triggering system was employed. This triggering system was tuned to start collecting mass spectra with the mass analyser 4 before the first ions originating from the individual droplet arrived at the mass analyser 4 and to stop collecting mass spectra after the last ions originating from the respective individual droplet arrived at the mass analyser 4 and were analysed with the mass analyser 4. Thereby, the time period from starting collecting mass spectra to stopping collecting mass spectra during the mass analysis of the individual droplet was set to 1.5 ms. In order to ensure that the collected mass spectra only included information about the respective individual droplet, the mass spectra collected for the respective individual droplet were only used for further analysis in case no other individual droplet was ionised during this time period. In case another droplet was ionised during this time period, the collected mass spectra were discarded.

[0066] Once it was ensured that the mass spectra collected during the before mentioned time period of 1.5 ms included only data from ions obtained from one and the same individual droplet, the mass spectra collected during the time period from starting collecting mass spectra to stopping collecting mass spectra were integrated to a total mass spectrum for the individual droplet. These total mass spectra were then calibrated as known in the art to provide ordinates (or y-axes) indicating the ion counts. In the present case, the calibration was based on measurements of known single ions. Thereby, known single ions have been detected with the ion detector of the mass analyser and the integral of the signal of such known single ions in the mass spectra has been determined in the units of mV*ns (millivolt times nanoseconds). This integral has been considered as the detector signal per ion count. For calibrating the total mass spectra to provide ordinates (or y-axes) indicating the ion counts, the area below the mass peaks in the total mass spectra have been divided by the detector signal per ion count.

[0067] Since the droplets generated with the micro droplet generator had a known size, the volume of sample material per individual droplet was known. Thus, based on the known content of the reference sample and the diluted reference sample, it was known for each analyte in the reference sample how many atoms of this particular analyte were comprised in one individual droplet. Based on this knowledge, the responses for specific ions of the individual analytes comprised in the reference sample were determined by fitting the isotopic pattern of the respective analyte to the corresponding mass peaks in the total mass spectrum and by comparing the resulting fit with the number of atoms of the respective analyte in one individual droplet. More precisely, the responses for the individual analytes were determined for specific ions of the respective analyte. These specific ions were either the single atom of the respective analyte with one positive charge or one atom of the respective analyte oxidised with a certain number of oxygen atoms with one positive charge. In this latter case, the mass peaks of the isotopic pattern of the respective analyte were shifted in the total mass spectrum by the mass of the certain number of oxygen atoms as compared to the specific ion consisting of the single atom of the respective analyte with one positive charge.

[0068] These responses for the specific ions of the individual analytes are indicated in the present text in the units of counts per atom of the respective analyte. Thereby, the counts per atom of the respective analyte are proportional to the integral of the area below the isotopic pattern of the respective analyte fitted to the corresponding mass peaks in the total mass spectrum and thus proportional to the signal intensity provided by the ion detector of the mass analyser 4 for the respective specific ion of the respective analyte. Due to this proportionality, the responses for different specific ions of a particular analyte as well as the responses for different analytes and the responses for one particular analyte when using different measurement settings can be compared with one another.

[0069] With the above described arrangement, a first measurement was obtained with atmospheric air obtained from the surrounding of the apparatus 1 and compressed with the compressor 7 to a pressure to 3 bar as plasma gas, wherein the carrier gas was atmospheric air obtained from the surrounding of the apparatus 1. Both the atmospheric air used as the plasma gas and the atmospheric air used as the carrier gas were filtered in order to remove aerosol particles from the atmospheric air before being used as the plasma gas and the carrier gas, respectively. Furthermore, a second measurement was obtained with atmospheric air obtained from the surrounding of the apparatus 1 and compressed with the compressor 7 to a pressure to 3 bar as plasma gas, wherein pure nitrogen gas generated with the generator was used as the carrier gas. Thereby, the pure nitrogen gas had a purity of more than 99.99%. In both this first measurement and this second measurement, the method according to the invention was employed for mass analysing the diluted reference sample. For comparison reasons, the diluted reference sample was additionally mass analysed with the apparatus 1 in a third measurement with pure nitrogen generated with the generator used as the plasma gas and as the carrier gas, wherein the purity of the nitrogen was more than 99.99%. Thus, for this third measurement, the compressor 7 was circumvented and the pure nitrogen generated with the generator was supplied to the plasma torch 4 and to the micro droplet generator for providing the plasma gas and the carrier gas.

[0070] Figure 3 shows a table with the results of these three measurements for the analytes included in the reference sample. However, since the obtained mass spectra only covered the range from 10 Th to 275 Th, Li and Be have not been visible in the mass spectra. For this reason, no data on Li and Be have been obtained and the table shown in Figure 3 does thus not contain any information about Li and Be.

[0071] The first column of the table shown in Figure 3 shows the analytes while the second column indicates the specific ion of the respective analyte for which the mass peaks of the isotopic pattern of the respective analyte have been analysed. For most analytes, the mass peaks of the isotopic pattern of the single atom of the respective analyte with one positive charge has been analysed. For Vanadium (V), however, both the mass peaks of the isotopic pattern of the single atom with one positive charge and the mass peaks of the isotopic pattern of the oxidised ion VO^+ have been analysed. Thus, in the first column of the table, the analyte Vanadium occurs twice, once indicated as "V1" for the mass peaks at about 51 Th and once indicated as "V2" for the mass peaks at about 67 Th. Similarly, for Uranium (U), the mass peaks of the isotopic pattern of the single atom with one positive charge and the mass peaks of the isotopic pattern of the double oxidised ion UO_2^+ have been analysed. Thus, the analyte Uranium occurs as well twice in the first column of the table, once as "U 1" for the mass peaks at about 238 Th and once as "U2" for the mass peaks at about 270 Th.

[0072] The results of the first measurement obtained with atmospheric air as the plasma gas and atmospheric air as the carrier gas are shown in the table in the columns with the title "air plasma (air as carrier gas)". The results of the second measurement obtained with atmospheric air as the plasma gas and pure nitrogen generated with the generator as the carrier gas are shown in the table in the columns with the title "air plasma (N2 as carrier gas)", while the results of the third measurement obtained with nitrogen generated with the generator as the plasma gas and the carrier gas are shown in the table in the columns with the title "N2 plasma".

[0073] For each one of the three measurements, the first column shows the response in units of counts per atom for the respective specific ion of the respective analyte. The second and third column however show the lower limits for the mass in fg (femtogramm) and diameter in nm (nanometer), respectively, of hypothetical particles consisting of the pure respective analyte which would still be detectable in the respective measurement when analysing the respective mass peaks of the respective analytes isotopic pattern at the position where the respective specific ion of the respective analyte is found. These lower limits indicated in the second and third columns of each one of the three measurements are estimates. They are based on an estimation of the minimum detectable signal according to formula (17) provided on page 1712 of the publication "Nomenclature in evaluation of analytical methods including detection and quantification capability" of the international union of pure and applied chemistry, published in Pure & Applied Chemistry, Volume 67, Number 10, pages 1699 to 1723, from 1995. Thus, the minimum detectable signal S_D in units of counts was estimated according to the formula $S_D = 2.71 + 3.29\sqrt{B}$, wherein B was the mean value of the background signal measured in counts.

[0074] In order to determine the hypothetical particles consisting of the pure respective analyte which would still be detectable in the respective measurement when analysing the respective mass peaks of the respective analytes isotopic pattern at the position where the respective specific ion of the respective analyte is found, the response in counts per atom indicated in the first column of the table was scaled with a scaling factor to the estimated minimum detectable signal S_D. The minimum number of atoms of the respective analyte required in the sample in order to be able to detect the respective analyte when having the measured background signal was then calculated by multiplying this scaling factor with the number of atoms of the respective analyte in one individual droplet. This minimum number of atoms was then assumed to be arranged in the sample in one hypothetical, spherical particle having the density which the respective analyte has in its pure form. The second and third columns of the three measurements shown in the table of Figure 3 indicate the mass in fg (femtogramm) and the diameter in nm (nanometer) of this hypothetical particle. This hypothetical particle is an estimate of the minimal size aerosol particles consisting of the respective analyte in order to be detectable in case individual aerosol particles entrained in a carrier gas would be to be analysed with the corresponding settings of the respective one of the three measurements shown in the table of Figure 3.

[0075] The table shown in Figure 3 illustrates that in the bigger picture, the use of atmospheric air as the plasma gas as compared to the use of pure nitrogen generated with the generator as the plasma gas does change the detectability for certain analytes considerably while maintains the detectability for other analytes almost the same. For example, the detectability of Calcium is improved when using atmospheric air as the plasma gas by a factor of about 1.7 as compared to the use of pure nitrogen generated with the generator as plasma gas. On the other hand for Vanadium, the detectability of the specific ion of the single atom with one positive charge is decreased by more than a factor of 2 to 3, while the detectability of the oxidised ion VO^+ is slightly increased. For Uranium, on the other hand, the detectability of the single atom with one positive charge and the detectability of the oxidised ion UO_2^+ are essentially swapped when comparing the use of pure nitrogen generated with the generator as the plasma gas with the use of atmospheric air as the plasma gas. These changes in detectability are caused by the oxygen content in the plasma gas. As compared to these changed detectabilites, the detectability of analytes like Natrium (Na), Aluminium (Al), Potassium (K), Rubidium (Rb), Strontium (Sr), Indium (In), Caesium (Cs), Barium (Ba), Thallium (Tl) and Lead (Pb) remains about the same.

[0076] The table shown in Figure 3 furthermore illustrates that in the bigger picture, when using atmospheric air as the plasma gas, the differences in the detectability do not change that significantly when using atmospheric air as the carrier gas as compared to the use of pure nitrogen generated with the generator as the carrier gas. Only the detectability of the specific Uranium ion being the single atom with one positive charge is decreased significantly. Thus, for most analytes, the detectability does not change considerably when the oxygen content in the plasma is changed by using the atmospheric air instead ofpure nitrogen generated with the generator as the carrier gas. Consequently, the method according to the invention with the plasma gas including at least 10 weight percent oxygen, preferably at least 15 weight percent oxygen, particular preferably at least 20 weight percent oxygen, most preferably at least 23 weight percent oxygen enables a sufficient stable detection of these analytes, even though some analytes have to been detected on the basis of their oxidised ion.

[0077] The method according to the invention can be applied to different samples. In one example, the sample is a liquid sample which is sprayed into droplets and inserted into the sample inlet 10 of the ion source 2 entrained in a carrier gas. Thereby, the sample can by sprayed into the droplets as described above with the micro droplet generator. In this case, the apparatus 1 may include the micro droplet generator. Or, the sample can be sprayed into droplets with a nebuliser. In this case, the apparatus 1 may include the nebuliser. In another example, the sample is a gas with discrete particles and/or discrete droplets, in particular with aerosol particles, entrained in the sample gas. In one example, the sample includes aerosol particles which have been generated by laser ablating a bulk sample material, wherein the aerosol particles are entrained in a carrier gas. In another example, the sample is ambient air with discrete particles and/or discrete droplets, in particular aerosol particles, entrained in the ambient air. In the latter example, the apparatus may include an atmospheric sampler fluidly couplet to the sample inlet 10 of the ion source 2 for inserting the sample into the plasma for ionising the sample to the ions.

[0078] As illustrated with the table shown in Figure 3, Calcium is considerably better detectable with the method according to the invention than with a method where pure nitrogen generated with the generator is used as the plasma gas. Thus, the method according to invention is particularly useful to mass analyse samples comprising Calcium. Samples where the Calcium content is of interest include for example biological cells and/or body fluids. Thereby, the biological cells are procaryotic cells, like bacteria or archaea, or eukaryotic cells, like single celled protozoa and slime moulds, or cells of multicellular organisms like fungi, plants and animals, in particular human cells. Body fluids are liquids from within an animal body or a human body, like intracellular fluid and extracellular fluid, in particular interstitial fluid like lymphatic fluid, or transcellular fluid and intravascular fluid like blood. In such samples, often the Iron content is of interest, too. As illustrated by the table shown in Figure 3, Iron can be reasonably well detected at 56 Th with the method according to the invention. In this context, it is to be mentioned, that with the method according to the invention, the Iron can be reasonably well detected at 56 Th since there is no peak of ArO^+ at 56 Th as would be the case if high purity Argon is used as the plasma gas and the sample includes a small amount of oxygen. Thus, the method according to the invention enables an improved detection of Calcium and of Iron in a same sample as compared to measurements with pure nitrogen generated with the generator or Argon as the plasma gas.

[0079] As further illustrated with the table shown in Figure 3, Barium is slightly better detectable with the method according to the invention than with a method where pure nitrogen generated with the generator is used as the plasma gas.

[0080] In summary, it is to be noted that a method and an apparatus are provided for mass analysing a sample pertaining to the technical field initially mentioned, that enable a cost effective operation and which enable a proper detection and quantification of elements having mass to charge ratios in the range of the mass to charge ratios of noble gases, in particular of Argon, Krypton and Xenon.

Claims

1. A method for mass analysing a sample, said method including the steps of:

a) in an ion source (2), generating in a plasma torch (4) of said ion source (2) a plasma from a plasma gas and inserting said sample into said plasma for ionising said sample to ions;
b) transferring said ions from said ion source (2) to a mass analyser (5);
c) obtaining at least one mass spectrum of said ions with said mass analyser (5); wherein said plasma gas includes at least 10 weight percent oxygen, preferably at least 15 weight percent oxygen, particular preferably at least 20 weight percent oxygen, most preferably at least 23 weight percent oxygen.

2. The method according to claim 1, **characterised in that** said plasma gas includes at least 70 weight percent Nitrogen.

3. The method according to claim 1 or 2, **characterised in that** said plasma gas is atmospheric air.

4. The method according to claim 3, **characterised in that** where aerosol particles are filtered out of said atmospheric air before said atmospheric air is fed as said plasma gas to said plasma torch (4) of said ion source (2) for generating said plasma from said plasma gas.

5. The method according to claim 3 or 4, **characterised in that** said atmospheric air being said plasma gas is atmospheric air that is compressed, in particular to at least 2 bar, particular preferably to at least 3 bar, and fed as said plasma gas to said plasma torch (4) of said ion source (2) for generating said plasma from said plasma gas.

6. The method according to claim 5, **characterised in that** said atmospheric air is compressed with a compressor (7).

7. The method according to claim 5 or 6, **characterised in that** said plasma gas being atmospheric air includes 1.2 weight percent or less of water vapour, preferably 0.9 weight percent or less of water vapour, particular preferably 0.6 weight percent or less water vapour, more preferably 0.29 weight percent or less water vapour, most preferably 0.07 weight percent or less of water vapour when being fed to said plasma torch (4) of said ion source (2) for generating said plasma from said plasma gas.

8. The method according to one of claims 1 to 7, **characterised in that** said ion source (2) is a microwave driven ion source, wherein said plasma is generated from said plasma gas by means of microwaves.

9. The method according to one of claims 1 to 8, **characterised in that** said sample includes at least one element with a mass to charge ratio of around 40 Th, around 80 Th, and/or around 130 Th.

10. The method according to one of claims 1 to 9, **characterised in that** said sample includes at least one of Calcium, Selenium, Bromine, Tellurium and Barium.

11. The method according to one of claims 1 to 10, **characterised in that** said sample includes biological cells and/or body fluids.

12. The method according to one of claims 1 to 11, **characterised in that** said sample is a sample gas with discrete particles and/or discrete droplets, in particular with aerosol particles, entrained in said sample gas.

13. The method according to one of claims 1 to 11, **characterised in that** said sample is a liquid.

14. An apparatus (1) for executing the method according to one of claims 1 to 13 for mass analysing a sample, **characterised in that** said apparatus (1) includes

a) an ion source (2) for ionising said sample to ions, wherein said ion source (2) includes a plasma torch (4) for generating in said plasma torch

(4) a plasma from a plasma gas, wherein said sample is ionisable to said ions by inserting said sample into said plasma,

b) a mass analyser (5) for obtaining at least one mass spectrum of said ions, said mass analyser (5) being fluidly coupled to said ion source (2) for receiving said ions from said ion source (2) for obtaining said at least one mass spectrum from said ions,

wherein said plasma gas includes at least 10 weight percent oxygen, preferably at least 15 weight percent oxygen, particular preferably at least 20 weight percent oxygen, most preferably at least 23 weight percent oxygen.

15. The apparatus (1) according to claim 14, **characterised in that** said apparatus (1) includes a compressor (7) for compressing said atmospheric air, in particular to at least 2 bar, particular preferably to at least 3 bar, before feeding said atmospheric air as said plasma gas to said plasma torch (4) of said ion source (2) for generating said plasma from said plasma gas.

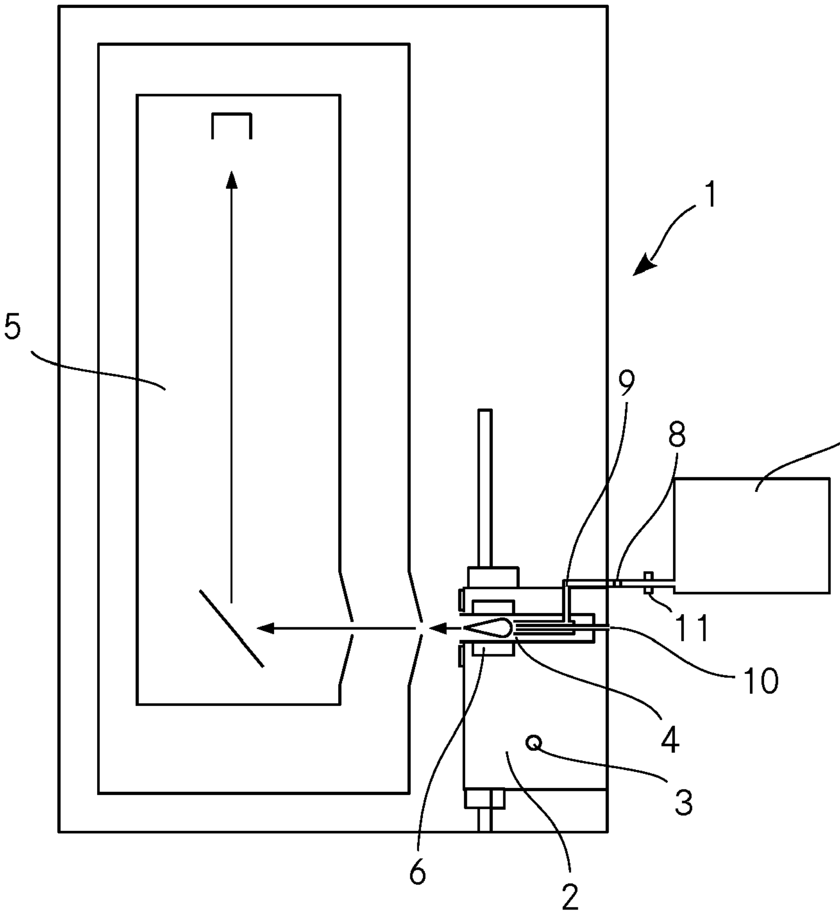
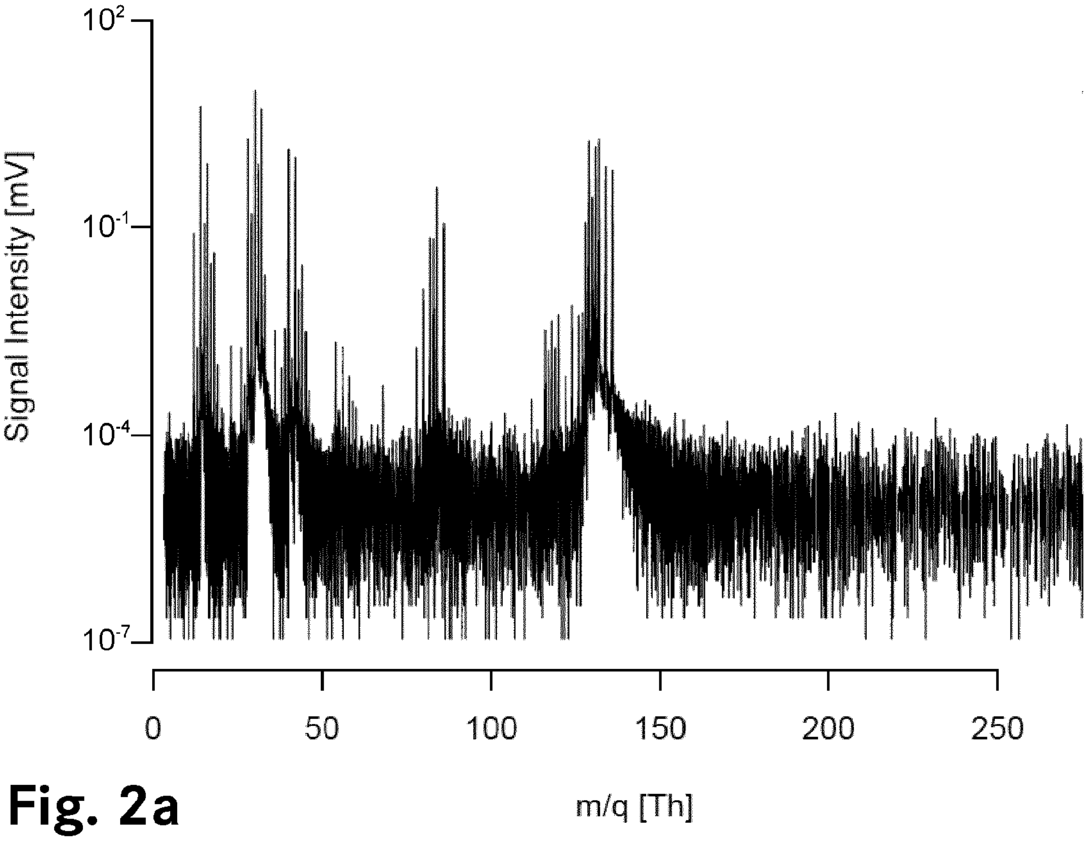
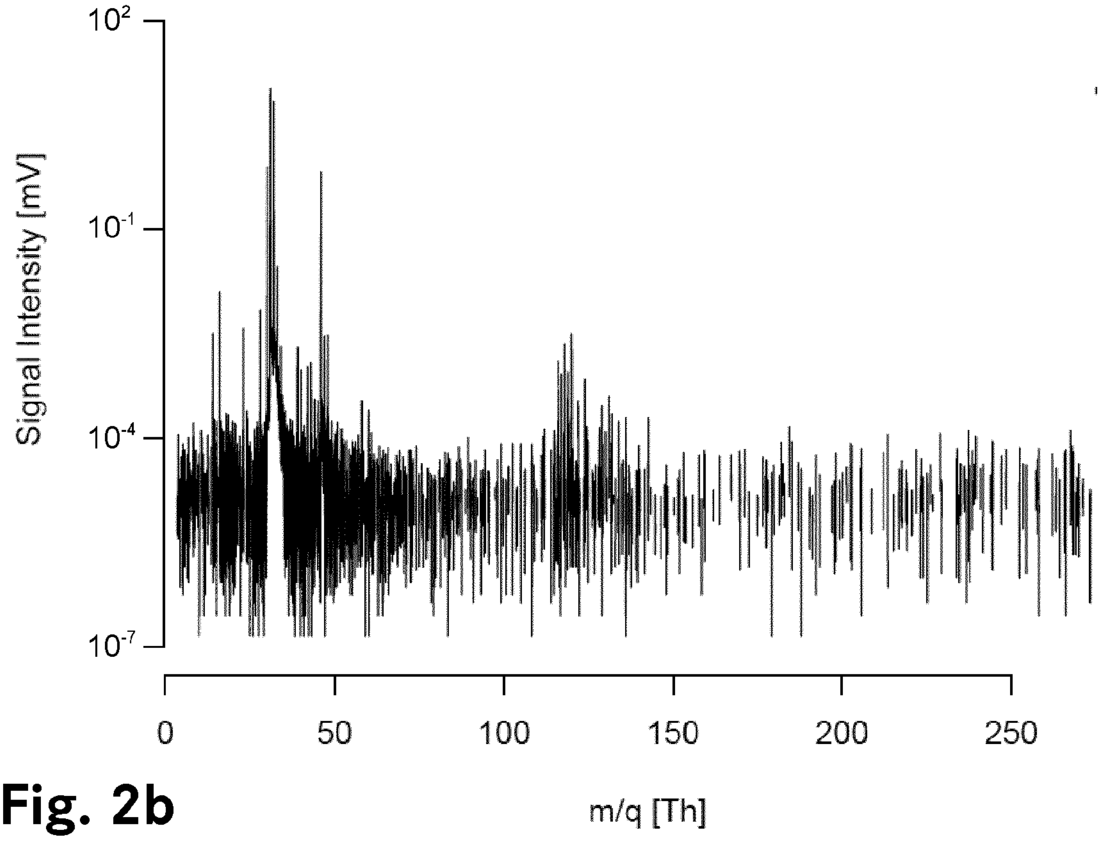


Fig. 1



10^2
10^{-1}
10^{-4}
10^{-7}
Signal Intensity [mV]
0
50
100
150
200
250
m/q [Th]

Fig. 2a



10^2
10^{-1}
10^{-4}
10^{-7}
Signal Intensity [mV]
0
50
100
150
200
250
m/q [Th]

Fig. 2b

analyte	mass peaks of specific ion	air plasma (air as carrier gas)				air plasma (N2 as carrier gas)				N2 plasma		
		response [counts/atom]	mass [fg]	diameter [nm]		response [counts/atom]	mass [fg]	diameter [nm]		response [counts/atom]	mass [fg]	diameter [nm]
Na	[23Na]+	2.50E-08	6.37	232		2.53E-08	6.39	233		3.28E-08	4.57	208
Mg	[24Mg]+	4.93E-09	29.88	320		9.51E-09	15.62	258		3.31E-08	4.78	174
Al	[27Al]+	3.00E-08	4.53	147		3.04E-08	4.29	145		4.18E-08	3.74	138
K	[39K]+	1.12E-07	2.48	175		1.14E-07	2.56	176		1.15E-07	2.66	179
Ca	[40Ca]+	2.19E-07	1.11	111		2.19E-07	1.23	115		5.40E-07	5.98	195
V1	[51V]+	1.55E-08	15.73	170		9.15E-08	2.59	93		3.04E-07	0.81	63
Cr	[52Cr]+	7.84E-08	3.91	101		1.32E-07	2.18	83		2.97E-07	1.00	64
Mn	[55Mn]+	6.85E-08	3.77	100		1.34E-07	2.00	81		4.09E-07	0.69	57
Fe	[56Fe]+	3.09E-08	9.67	133		6.17E-08	4.99	107		3.91E-07	0.81	58
Ni	[58Ni]+	5.97E-09	75.27	253		1.27E-08	35.59	197		2.40E-07	2.03	76
Co	[59Co]+	8.72E-09	31.04	188		2.11E-08	12.99	141		2.97E-07	0.94	59
Cu	[63Cu]+	5.40E-09	80.02	257		1.17E-08	36.39	198		2.21E-07	1.89	74
Zn	[64Zn]+	1.56E-09	421.72	483		4.73E-09	128.91	325		5.89E-07	1.07	66
V2	[51V][16O]+	3.24E-08	9.75	145		3.20E-08	9.77	145		2.63E-08	12.58	158
Ga	[69Ga]+	4.07E-07	1.29	75		4.57E-07	1.18	73		6.27E-07	0.87	66
As	[75As]+	4.44E-10	782.99	639		8.15E-10	413.85	517		1.21E-07	2.97	100
Se	[80Se]+	1.48E-10	5152.63	1269		3.76E-10	1941.26	917		1.31E-07	13.07	173
Rb	[85Rb]+	9.82E-07	0.54	88		9.90E-07	0.54	88		1.04E-06	0.60	91
Sr	[88Sr]+	1.52E-06	0.32	61		1.49E-06	0.33	62		1.36E-06	0.41	67
Ag	[107Ag]+	7.18E-08	13.26	134		1.61E-07	5.81	102		1.54E-06	0.64	49
Cd	[114Cd]+	1.52E-08	124.77	302		3.71E-08	50.69	224		2.05E-06	0.96	60
In	[115In]+	2.07E-06	0.29	42		2.11E-06	0.26	41		2.58E-06	0.23	39
Cs	[133Cs]+	3.16E-06	0.19	58		3.15E-06	0.21	59		3.13E-06	0.31	67
Ba	[138Ba]+	4.31E-06	0.21	49		4.61E-06	0.19	47		4.94E-06	0.24	51
Tl	[205Tl]+	7.78E-06	0.18	31		7.56E-06	0.17	30		7.40E-06	0.19	31
Pb	[208Pb]+	2.29E-06	0.79	51		3.83E-06	0.49	44		7.29E-06	0.27	36
Bi	[209Bi]+	6.92E-07	1.37	64		1.34E-06	0.72	52		6.82E-06	0.16	31
U1	[238U]+	3.68E-10	2930.21	664		8.84E-09	127.12	233		1.30E-05	0.09	21
U2	[238U][16O]2+	6.92E-06	0.19	27		9.43E-06	0.14	24		7.59E-10	1659.39	550

Fig. 3

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EUROPEAN SEARCH REPORT

Application Number
EP 21 20 5314

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X	US 5 252 827 A (KOGA MASATAKA [JP] ET AL) 12 October 1993 (1993-10-12) * abstract * * figures 1, 2, 3a * * column 5, line 28 - column 7, line 50 * -----	1-15	INV. H01J49/10
T	JANKOWSKI KRZYSZTOF ET AL: "Recent developments in instrumentation of microwave plasma sources for optical emission and mass spectrometry: Tutorial review", JOURNAL OF ANALYTICAL ATOMIC SPECTROMETRY, vol. 28, no. 8, 5 June 2013 (2013-06-05), page 1196, XP055912289, ISSN: 0267-9477, DOI: 10.1039/c3ja50110h Retrieved from the Internet: URL:https://pubs.rsc.org/en/content/articlepdf/2013/ja/c3ja50110h> * abstract * * table 2 * * Section "1. Introduction" * * Section "8. Some applications of MWP" * -----		

TECHNICAL FIELDS SEARCHED (IPC)
H01J

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
The Hague	13 April 2022	Dietsche, Rainer

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
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D : document cited in the application
L : document cited for other reasons
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& : member of the same patent family, corresponding document

ANNEX TO THE EUROPEAN SEARCH REPORT ON EUROPEAN PATENT APPLICATION NO.

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For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

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- Nomenclature in evaluation of analytical methods including detection and quantification capability. *Pure & Applied Chemistry,* 1995, vol. 67 (10), 1699-1723 **[0073]**