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Direct Analysis of Samples of Various Origin and Composition Using Specific Types of Mass Spectrometry

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ABSTRACT

One of the major sources of error that occur during chemical analysis utilizing the more conventional and established analytical techniques is the possibility of losing part of the analytes during the sample preparation stage. Unfortunately, this sample preparation stage is required to improve analytical sensitivity and precision. Direct techniques have helped to shorten or even bypass the sample preparation stage; and in this review, we comment of some of the new direct techniques that are mass-spectrometry based.

The study presents information about the measurement techniques using mass spectrometry, which allow direct sample analysis, without sample preparation or limiting some pre-concentration steps. MALDI – MS, PTR – MS, SIFT – MS, DESI – MS techniques are discussed. These solutions have numerous applications in different fields of human activity due to their interesting properties. The advantages and disadvantages of these techniques are presented. The trends in development of direct analysis using the aforementioned techniques are also presented.

KEYWORDS

Desorption electrospray ionization–mass spectrometry; direct sample analysis; matrix assisted laser desorption ionization–mass spectrometry; proton transfer reaction–mass spectrometry; selected ion flow tube–mass spectrometry

Introduction

Human activities contribute to the formation of numerous pollutants that are released into the environment, increasing human impact on it. The growing concentrations of pollutants from human activities have a negative effect on both animate and inanimate components of the environment. Undertaking effective actions aimed at a reduction of pollutants emissions requires constant monitoring of the most important sources of emission, which include industrial plants, refineries, farms, municipal services and many more. It is possible to obtain information about the type of pollutants and their concentrations owing to the use of a broad spectrum of analytical methods, in which various analytical techniques are used at the stage of analyte detection, identification and determination. (Nicell, 2009; Baltrenas et al., 2013). Figure 1 presents a classification of the most often used analytical methods according to their degree of automation.

Manual analytical methods are usually time- and labor-consuming. It is very difficult to achieve high precision, so these solutions are more and more often replaced by instrumental methods. These methods make it possible to obtain information about both average and instantaneous values of concentrations of determined compounds. The methods based on direct analyte measurement seem to be a very advantageous solution – in this way, one eliminates all the procedures connected with preparation of samples and their preliminary separation.

A pursuit for more precise description of the environment condition imposes a challenge on the analytical chemist as far as determination of wide range of analytes in the complex matrix samples is concerned. Currently, there are two dominant approaches to measurement of the analytes present at low concentration level in the investigated samples:

- utilization of more sensitive, selective, specific detectors,
- introduction of analyte isolation/enrichment stage prior to the final measurement.

Mass spectrometers coupled with different techniques of analyte ionization allow skipping the sample pre-preparation stage and they offer the option of direct subjection of the sample to the final measurements.

This results in the fact that the analyst's work becomes less time- and control-consuming. Moreover, one can avoid many inconveniences and problems connected with the operations and activities performed during preparation of a sample for analysis. It can be concluded with high certainty that the final result of analysis would be encumbered with lower error or uncertainty. Table 1 presents the techniques, other than mass spectrometry, which allow performing the final measurement without the need of preliminary preparation of the sample.

Mass spectrometry – basic information

Mass spectrometry is one of the most important instrumental techniques used to identify the chemical structure of many

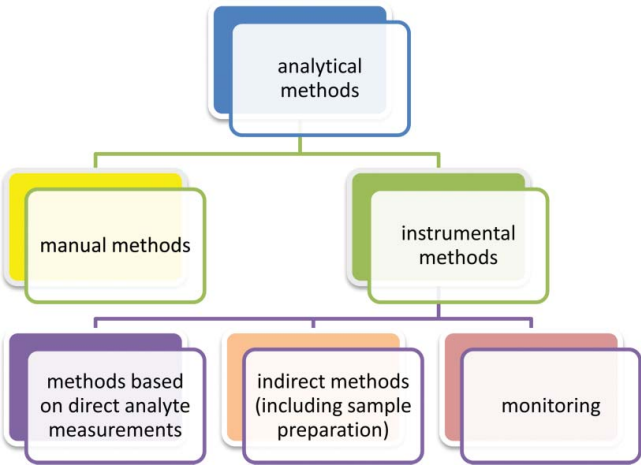

Figure 1. Classification of analytical methods depending on degree of automation.

different compounds. A very important role is played out by different variations of mass spectrometric-based techniques that can be all included under the umbrella of direct analysis. Depending on the type of ions formed as a result of analyte decomposition, which are to be recorded in the mass spectrum, it is possible to use various scanning modes: Precursor Ion Scan, Product Ion Scan, Neutral Loss and Single/Multiple Reaction Monitoring. The selection of an appropriate scanning mode makes it possible to obtain information about a specific group of compounds that are present in the sample in the entire range of concentrations. The sensitivity of a mass spectrometer has a direct influence on the sample preparation procedure – the greater the spectrometer sensitivity is, the more possible it is to limit the stages related to the minimization of matrix influence on the final result of the analysis.

One of the most practical solutions of mass spectrometry is its combination with the chromatographic techniques (liquid or gas chromatography) for analysis of mixture composition. In this way, a separation technique is coupled with the possibility of identification of a broad spectrum of chemical compounds (Gebicki et al., 2016). The chromatographic techniques paired with mass spectrometry find application in various research areas such as pharmacology, anti-doping control, biotechnology, toxicology, biochemistry, control of foodstuff quality, environmental protection or research connected with development of the so-called "-omics" sciences (Ibáñez et al., 2013; Sahil et al., 2011; Bujak et al., 2014; Soler et al., 2008).

Table 1. Direct measurement techniques used during tests of samples of various material objects.

Acronym	Full name
ISE	Ion Selective Electrodes
(I)NNA	(Instrumental) Neutron Activation Analysis
GF AAS	Graphite Furnace Atomic Absorption Spectroscopy
QF AAS	Quartz Furnace Atomic Absorption Spectroscopy
FTIR	Fourier Transformation Infrared
NMR	Nuclear Magnetic Resonance Spectroscopy
LIBS	Laser-Induced Breakdown Spectroscopy
XRF	X-Ray Fluorescence
ED-XRF	Energy-Dispersive X-Ray Fluorescence
RS	Raman Spectroscopy
SERS	Surface Enhanced Raman Spectroscopy
LIBS	Laser-Induced Breakdown Spectroscopy
IMA	Immunoanalysis
ELISA	Enzyme Linked Immunosorbent Assay
LIF	Laser-Induced Fluorescence
EPR	Electron Paramagnetic Resonance Spectroscopy
ESR	Electron Spin Resonance Spectroscopy
MSDV	Mass Spectrometry Difference Variance

Obtaining better performance parameters, such as higher sensitivity, accuracy or resolution, is possible due to the introduction of various modifications in the mass spectrometer design. One of such solutions consists of the application of tandem mass spectrometry where a single analyzer is replaced with a two-analyzer system. Such a solution allows monitoring of the fragmentation reaction of selected ions, which makes it possible to determine the structure of individual chemical compounds more accurately. Furthermore, quantitative determination of analytes present in the samples with a very complex matrix, which is used, for example, in proteomic studies aimed at determination of the peptide amino acid sequence is possible. The most often used configuration of mass analyzers includes triple quadrupole (QqQ) and quadrupole and time of flight analyzer separated by a quadrupole collision cell (QqTOF) (Luzardo et al., 2015; Rodríguez-Carrasco et al., 2014).

In some cases, it is not the analyzer that is modified but the chromatographic module itself, which can be exemplified by a multi-dimensional gas or liquid chromatography (GC–GC–MS, LC–LC–MS). Such an approach offers the possibility of obtaining a high degree of separation of the analytes, which are characterized by a varied degree of polarity, volatility or chirality, via appropriate selection of two different chromatographic columns. In recent years, these techniques have been becoming more and more important, which can be evidenced by their application in, among other things, the assessment of food product quality, biotechnology and medicine (Dymerski et al., 2015; Risticevic et al., 2012; Dymerski et al., 2016; Omar et al., 2012; Sampat et al., 2015; Król-Kogus et al., 2014; Regalado et al., 2014; Wang et al., 2016; Brasseur et al., 2012; Focant et al., 2013; Brasseur et al., 2016).

One of the main limitations of the chromatographic techniques coupled with mass spectrometry is the lack to ensure the possibility of monitoring samples with minimal or no preparation preceding the analysis (Smith and Španěl, 2015b). One of the directions for mass spectrometry development is a search for the instrumental solutions that ensure the possibility of conducting direct research with minimal or without sample preparation for analysis. The authors of this study would like to present the latest solutions in mass spectrometry, which allow direct analysis of the samples of various chemical composition and origin.

Direct analysis of samples using mass spectrometry technique

Since the appearance of mass spectrometry among the techniques used for identification and quantitative determination of various substances present in the surrounding environment, numerous attempts have been made to develop new solutions that would allow selective determination of analytes in the shortest time and with as few

operations related to sample preparation as possible. As a result, a lot of new solutions appeared, which are used in the research related to environmental protection (determination of the content of volatile organic compounds (VOCs) in water, soil and air samples), the assessment of the quality of food products (testing the chemical composition of selected food products, determination of changes in their composition depending on storage conditions) or medical diagnostics (determination of potential markers of digestive or respiratory diseases). Figure 2 presents the most important moments in development of the techniques using mass spectrometry allowing direct sample analysis, while Figure 3 shows the most popular solutions nowadays (Gohlke and McLafferty, 1993; Bauer 1995; Lindinger et al., 1998; Smith and Španěl, 2015b; Park et al., 2015; Nefliu et al., 2008; Alexander et al., 2003; Armstrong et al., 2001).

The device solutions, which are referred to in Figure 3, are based on the utilization of various processes and phenomena that ensure the possibility of the selective release of individual compounds directly from the surface of the sample and their transition to the ionized form. A key role is played by such factors as laser radiation and the presence

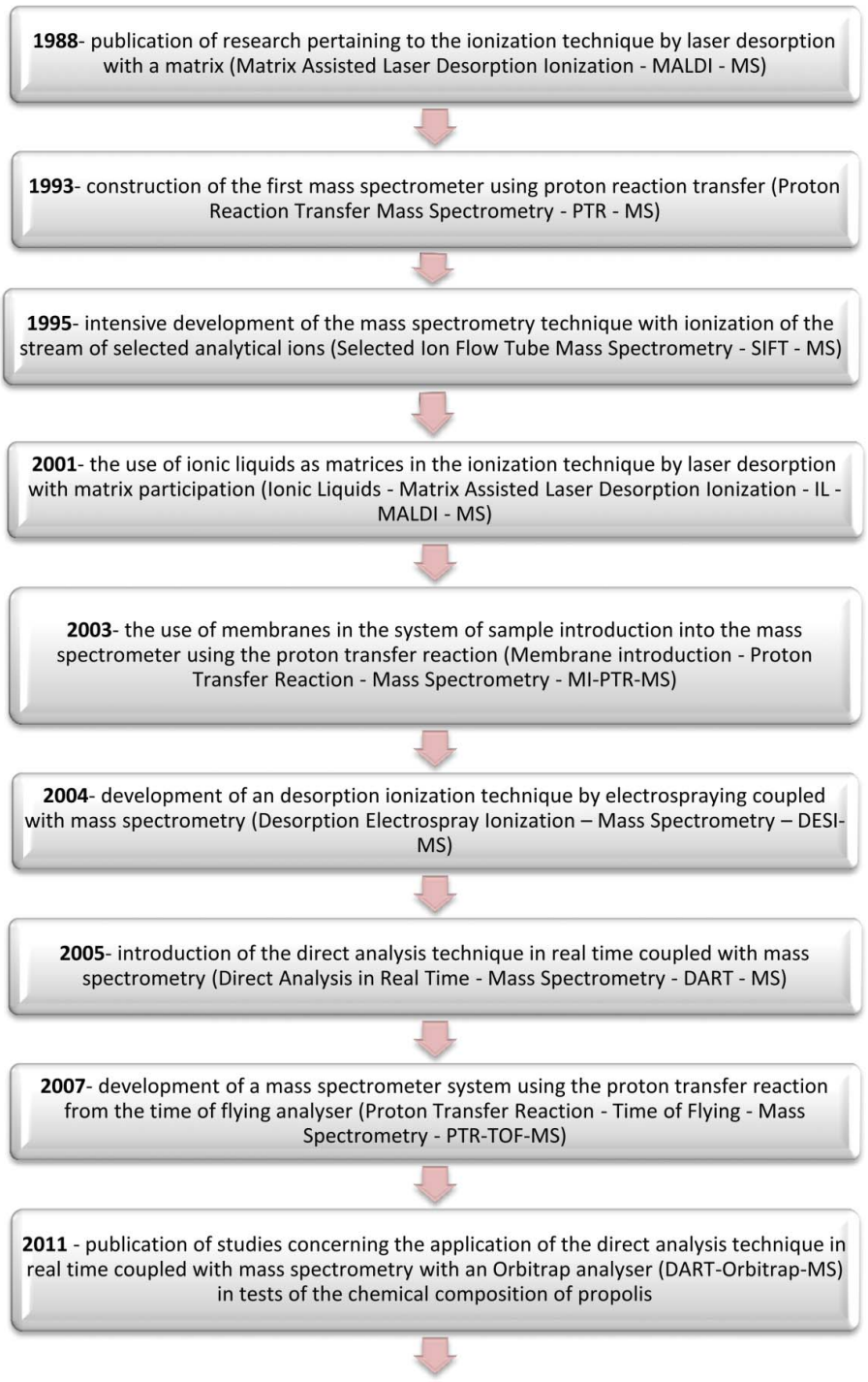

Figure 2. Milestones in the development of direct measurement techniques based on mass spectrometry.

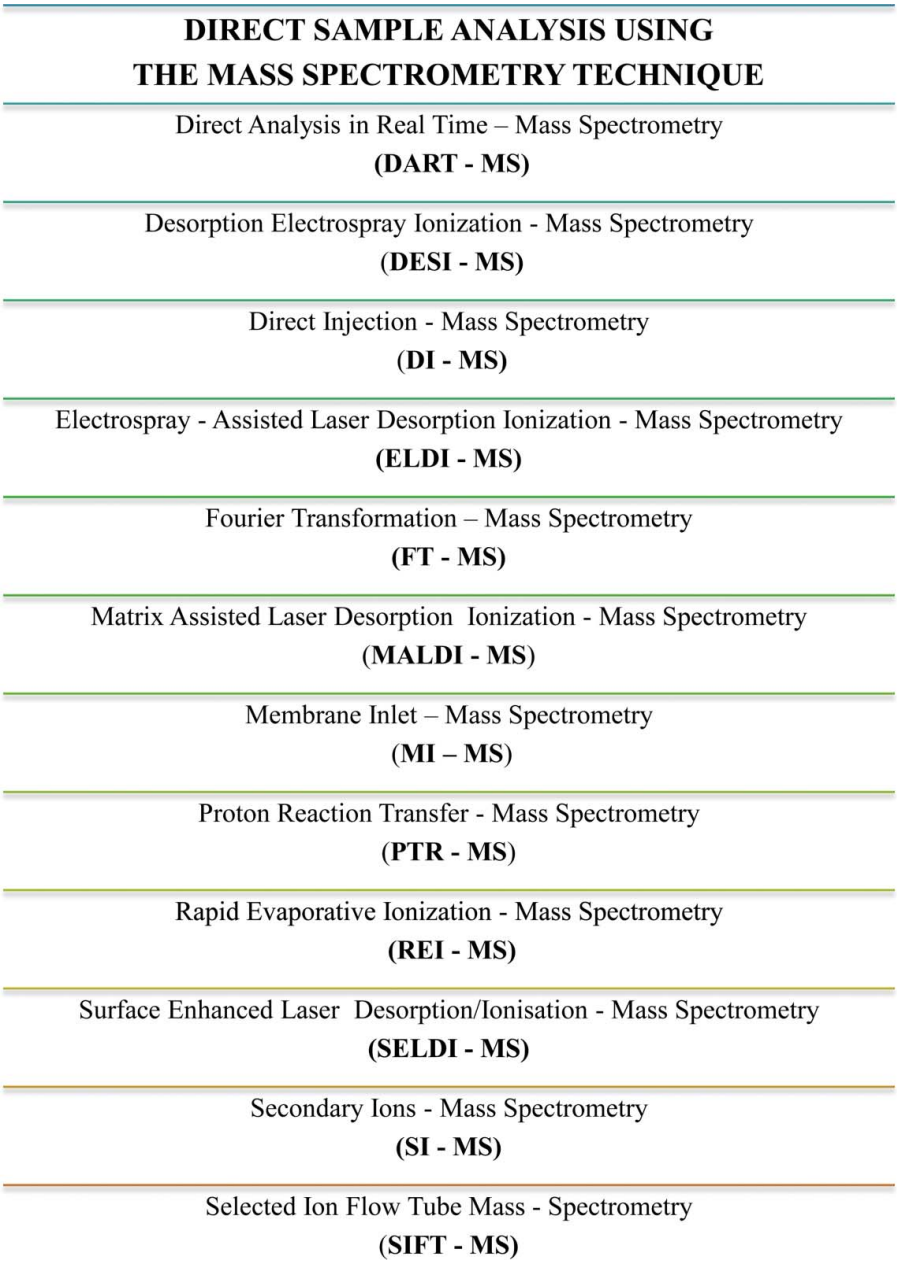

Figure 3. Selected technical solutions in mass spectrometry allowing for direct sample analysis without chromatographic separation prior to analysis by mass spectrometry.

of additional chemical compounds enhancing the ionization process. In this way, much more advantageous resolution parameters are obtained than when the chromatographic techniques are coupled with the mass spectrometer. Simultaneously, the time of a single analysis is reduced as there is no need for preliminary separation of analytes in the chromatographic column. One of the characteristics of these devices is the possibility of determination of the analytes that occur in samples at the level of traces and ultra-traces, which is an enormous advantage as compared to the other analytical techniques (electrochemical, spectrophotometric or chromatographic ones). Only selected examples of direct measurement techniques utilizing different ionization mechanisms have been discussed in the next part of this article. In the authors' opinion, they can become the starting point for the development of new device solutions in the future.

Matrix-assisted laser desorption ionization – mass spectrometry

The MALDI – MS (matrix-assisted laser desorption ionization – mass spectrometry) technique is one of many solutions using mass spectrometry, in which analyte ionization takes place as a result of the transfer of energy from the previously prepared intermediate matrix, on which the sample is applied to the analyzed substances. During the transition of the neutral molecules into the ionized form, no fragmentation of the obtained ions occurs, which is observed in many other ionization techniques used in mass spectrometry (Emonet et al., 2010; Brasseur et al., 2014; Kanerva et al., 2013).

The device used for conducting analyses using the MALDI – MS technique consists of three basic elements; the first of them is the source of ions, in which the transition of the neutral

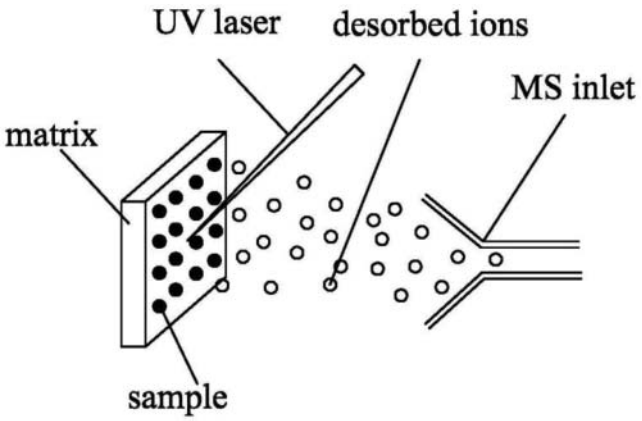

Figure 4. Diagram of the MALDI – MS system.

molecules to the ionized form occurs. For this purpose, the N_2 gas laser is directed to the previously prepared sample applied on the matrix, which causes the release of ions from the sample. At the sample preparation stage, it is necessary to dissolve it in a volatile solvent and in the previously selected matrix solution. While selecting the latter, one must ensure that it has a high level of radiation absorption from the wavelength range used during the measurement. Individual matrix components should be selected in a way that considerably facilitates analyte ionization with simultaneous limitation of the ionization process of the molecules from the matrix material. The correctly selected solution makes it possible to obtain high-quality mass spectra (Kafka et al., 2011).

The ions released from the sample are directed into the analyzer where they are separated on the basis of individual numerical mass to charge values (m/z). The last element of the entire system is the detector, where task involves recording of the ions that reach it from the analyzer (De Carolis et al., 2014; Macha and Limbach, 2002). Figure 4 presents a general diagram of the MALDI – MS technique (Sturtevant et al., 2015).

The selection of a matrix used in the MALDI – MS technique is a very important stage. So far, no methodology has been developed that could be used to identify the matrix composition and makes it possible to obtain a full spectrum of information about a sample. The appropriate choice of matrix composition strongly depends on the sample properties. Typically, one of the best methods involves optimization of the experimental conditions. However, the MALDI – MS matrices should

- be soluble in analyte-compatible solvents,
- be able to isolate analytes,
- absorb the laser wavelength,
- initiate selectively co-desorption of analyte,
- promote analyte ionization,
- be stable during ionization process.

While determining the analytes with small molecules (and the MALDI – MS technique is mostly used for determination of such molecules), the most frequently used matrices include α-cyano - 4-hydrocycinnamic acid, 2,3-dihydroxybenzoic acid, pyridine-2-carboxylic acid or 2,5-dihydroxybezoid acid (De Carolis et al., 2014; Bechara et al., 2012; Borisov et al., 2013; Yang et al., 2013; Kim et al., 2016; Park et al., 2015; Shahnawaz et al., 2015). An interesting solution and, at the same time, an alternative for the organic matrices that can be characterized by significant interactions with determined analytes are undoubtedly the matrices which include carbon nanotubes (Cegłowski et al., 2013; Shi et al., 2012), metal oxides (McAlpin & Voorhees, 2013; Sonderegger et al., 2011) and graphene (Zhang et al., 2011).

The ionic liquids (ILs) are used as the matrix components in the MALDI – MS technique. Application of these chemical compounds allows obtaining homogenous mixtures and higher stability of vacuum as opposed to the solid matrices. Higher peak intensity and lower limit of detection are also available when the ILs are utilized in the matrix. Another advantage of the ILs is their good solubility in a number of organic, inorganic and polymeric compounds. Both cation and anion part of the IL must be tailored to particular analysis. In case of the MALDI – MS technique, the ionic matrix must exhibit significant absorbance at desired wavelength. If the liquid does not fulfill the aforementioned requirements, it is ineffective as the MALDI – MS matrix. Selection of suitable IL is time-consuming and currently constitutes the biggest inconvenience in the field (Chan et al., 2009; Meriaux et al., 2010; Abdelhamid, 2015; Shrivas & Tapadia, 2015; Koel, 2005). Table 2 presents the examples of various substances, including the ILs, which are used as matrices together with the groups of compounds that have been determined using them in the research conducted up to date.

Determination of peptides, drugs or lipids in biological samples can be performed using mass spectrometry imaging with MALDI ionization (MALDI – MSI). MALDI is the most widely applied ionization technique in MSI for many various analytes. Typically, a sample section is coated with matrix solution; then the analytes are extracted with solvent and they become co-crystalized with the matrix. Ionization of the analytes takes place by irradiation of the sample with a UV laser. In MALDI – MSI, the most popular matrices are 2,5-dihydroxybenzoic acid (DHB), α-cyano-4-hydroxycinnamic acid (CHCA) and sinapinic acid. A different approach to matrix selection has been developed based on the classical Brønsted–Lowry acid–base theory. These matrices employ an "ionless matrix" (1,8-bis (dimethylamino)naphthalene (DMAN), which produces ions referred by the authors as "no matrix-related interfering" as opposed to the conventional matrices used in MALDI – MS (Shroff et al., 2009). MALDI – MSI is a highly sensitive technique for determination of metabolites, lipids, pharmaceuticals or peptides; however, it involves the possibility of presence of the spectral peaks derived from the matrix with the same mass range as the spectral peaks from the analyzed compounds. In order to solve this problem, MS/MS can be applied in most MALDI – MS experiments, allowing absolute identification and quantification of the analytes (Prideaux and Stoeckli, 2012).

Despite the broad range of modifications and applications in various areas of research, the MALDI – MS technique has also some limitations which can affect the final results of analysis. One of the major problems is a choice of suitable chemical reagent needed to prepare the matrix. Usually, most matrices can generate ions from their surface (by UV laser), which are present in a mass spectrum in low mass region (up to ca. 500 m/z). The signals from these ions are very intensive and

Table 2. Examples of various substances used as matrices in the MALDI – MS technique.

Matrix	Symbol	Analytes	Ref.
		CONVENTIONAL MATRIXES	
α-cyano-4-hydroxycin-namic acid	CCA	peptides	Zabet-Moghaddam et al. (2006)
α-cyano-4-hydroxycin-namic acid with pyridine	CAA-Py	peptides	Zabet-Moghaddam et al. (2006)
a-cyano-4-chlorocinnamic acid	CCICA	peptides	De Ceglie et al. (2015)
α-cyano-4-hydroxycinnamic acid	CHCA	gangliosides	Chan et al. (2009)
		proteins and peptides	Crank and Armstrong (2009), Duan et al. (2009), Shrivas et al. (2013)
		oligosaccharides	Mank et al. (2004)
		phospholipids	Benabdellah et al. (2009), Shrivas and Tapadia (2015b)
		phosphorylated peptide	Kang et al. (2007)
		lipopeptides, surfactins	Debois et al. (2014)
2,5-dihydroxybenzoic acid	2,5-DHB	gangliosides	Chan et al. (2009)
		oligosaccharides	Fukuyama et al. (2008), Gao et al. (2015), Mank et al. (2004)
		lipids	Meriaux et al. (2010)
		phospholipids	Benabdellah et al. (2009), Li et al. (2005), Shrivas and Tapadia (2015b)
		triacylglycerols	Horn et al. (2014), Vanhercke et al. (2014)
		polymers	Veličkovic et al. (2014)
2,6-dihydroxyacetophenone	2,6-DHAP	lipids	Meriaux et al. (2010)
isoliquiritigenin (4,2,4-trihydroxychalcone)	ISL	oligosaccharides	Yang et al. (2011)
		IONIC LIQUIDS MATRIX	
1-methylimidazolium -cyano-4-hydroxycinnamate	[BMIM]CHCA	gangliosides	Chan et al. (2009)
		highly-sulfated oligosaccharides	Tissot et al. (2007)
cyno-4-hydroxycinnamic acid-butylamine	CHCAB	oligosaccharides	Mank et al. (2004)
		phospholipids	Shrivas and Tapadia (2015b)
2,5-dihydroxybenzoic acid butylamine	DHBB	oligosaccharides	Mank et al. (2004)
1,1,3,3-tetramethylguanidium salt of α-cyano-4-hydroxycinnamic acid	G_2CHCA	oligosaccharides	Fukuyama et al. (2008)
1,1,3,3-tetramethylguanidium salt of p-coumaric acid	G_3CA	oligosaccharides	Fukuyama et al. (2008)
N-isopropyl-N-methyl-N tert-butylammonium α-cyano-4-hydroxycinnamate	IMTBA CHCA	proteins and peptides	Crank and Armstrong (2009)
3,5-dimethoxycinnamic acid triethylamine	SinTri	oligosaccharides	Mank et al. (2004)
tributylamine and α-cyano-4-hydroxycinnamic acid	TBA-CHCA	phospholipids	Calvano et al. (2012)

they can suppress other signals in this region of mass spectrum. Sometimes, generation of ions from the matrix is more intensive than from the sample and the final mass spectra contain erroneous information. There are also many other limitations in MALDI – MS, such as risk of fragmentation of molecules during their ionization, suppression of ionization or limitation of mutual ionization of molecules (Macha and Limbach, 2002; Kafka et al., 2011; Kaletaş et al., 2009).

Proton transfer reaction – mass spectrometry

Proton transfer reaction – mass spectrometry (PTR – MS) technique is another solution that has been finding more and more applications in recent years. It is used in a wide range of scientific and technical fields including

- medicine,
- biotechnological application,
- industrial process monitoring,
- atmospheric and environmental chemistry,
- food and atmospheric science.

PTR – MS is a powerful tool for direct, rapid and highly sensitive determination of VOCs and biogenic volatile organic compounds (BVOCs) concentration in real time (Ellis and Mayhew, 2014). This technique, classified as one of the most established direct injection mass spectrometry techniques, is based on the conversion of the neutral molecules to the ionized form as a result of the proton transfer occurring during the reaction between them and hydronium ions generated inside the device in an ion source by a hollow cathode discharge on water vapor (Blake et al., 2009; Ammann et al., 2004). High intensity and relatively high purity of the primary H_3O^+ ions allow the injection directly into the drift tube without prior mass selection (Biasioli et al., 2011).

The principle of operation of the device presented in the form of a diagram in Figure 5 is based on three most important phases (Blake et al., 2009). In the first of them, as a result of

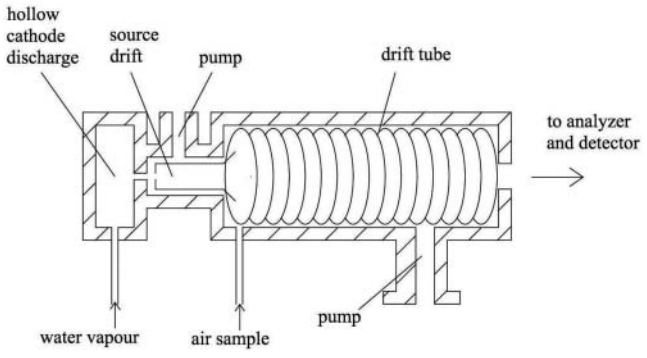

Figure 5. Diagram of the PTR – MS system.

electrode processes, water vapor molecules react with electrons. A range of ions generated react with each other and become a source of high purity hydrogen ions (the purity exceeds 99%) (Cappellin et al., 2013).

$$e^- + H_2OaH_2O^+ + 2e^-$$
$$H_2O^+ + H_2OaH_3O^+ + OH$$

In the second stage, the previously obtained stream of hydronium ions reacts with the molecules present in the sample injected in the drift tube. During this reaction, the proton is transferred to the determined analytes, which is presented by the reaction equation below.

$$H_3O^+ + RaRH^+ + H_2O$$

In the last stage, the previously formed ions are directed into the mass analyzer, owing to which it is possible to separate them according to their mass to charge ratio.

Proton transfer reaction takes place only in case of the compounds, for which the numerical value of proton affinity (PA) is higher than for the water molecule, for which PA = 691 kJ/mol. An analysis of the data contained in Table 3, that summarizes the numerical values of this parameter for the selected chemical compounds present in the air, shows that for the majority of them PA is higher than for water and, as a result, these compounds can be determined using the PTR – MS technique. The substances such as oxygen or nitrogen, which are present in the air, are characterized by lower numerical values of the PA parameter than water; thus, there is no risk that their presence in the air might affect the final result of the analysis through the generation of redundant reaction products. It is also possible to determine a large number of compounds for which PA < 691 kJ/mol – it can be achieved by employing other ions, e.g. NO2+, O2+ or Kr+ as a medium used during the proton transfer reaction with switchable reagent ions (PTR – SRI – MS). Using this system allows detection of important compounds, such as carbon oxide, carbon dioxide, sulphur dioxide, acetylene and propane, that are not detectable with the use of hydronium ions as the reagent ions in this technique. Different precursor ions enable, in some cases, separation of isobaric compounds, which significantly increases the range of possibilities of this technique (Jordan et al., 2009; Lindinger et al., 2001).

Table 3. Numerical values of the PA parameter for selected chemical compounds (Lindinger and Hansel, 1997; Lindinger et al., 2001; Zhao and Zhang, 2004).

Compound name	Molecular formula	Molecular mass [g/mol]	Proton affinity (PA) [kJ/mol]	Proton affinity (PA) [kcal/mol]
CHEMICAL COMPOUNDS WITH PA<PA_{H2O}				
hydrogen	H_2	2	422.37	100.9
methane	CH_4	16	560.92	132.0
nitrogen	N_2	28	493.95	118.0
carbon oxide	CO	28	593.02	141.7
ethane	C_2H_6	30	596.00	142.4
oxygen	O_2	32	421.11	100.6
carbon dioxide	CO_2	44	540.83	129.2
propane	C_3H_8	44	626.00	149.6
water	**H_2O**	**18**	**691.53**	**165.2**
CHEMICAL COMPOUNDS WITH PA>PA_{H2O}				
ammonia	NH_3	17	854.36	204.1
formaldehyde	CH_2O	30	713.29	170.4
methanol	CH_4O	32	754.74	180.3
hydrogen sulphide	H_2S	34	712.45	170.2
acetonitrile	C_2H_3N	41	779.43	186.2
acetaldehyde	C_2H_4O	44	768.97	183.7
ethanol	C_2H_6O	46	776.92	185.6
formic acid	CH_2O_2	46	748.46	178.8
acetone	C_3H_6O	58	812.50	194.1
trimethylamine	C_3H_9N	59	942.27	225.1
1-propanol	C_3H_8O	60	786.97	188.0
acetic acid	$C_2H_4O_2$	60	784.04	187.3
1-butanol	$C_4H_{10}O$	74	789.48	188.6
benzene	C_6H_6	78	750.55	179.3
toluene	C_7H_8	92	784.46	187.4
aniline	C_6H_7N	93	883.00	210.9
phenol	C_6H_6O	94	817.53	195.3
styrene	C_8H_8	104	839.71	200.6
benzaldehyde	C_7H_6O	106	834.27	199.3
o-xylene	C_8H_{10}	106	899.15	214.8
indole	C_8H_7N	117	934.32	223.2
acetophenone	C_8H_8O	120	861.48	205.8
naphthalene	$C_{10}H_8$	128	803.29	191.9

Originally, a quadrupole mass spectrometer was the main type of analyzer in the PTR – MS instrument. This solution provided good response time and high sensitivity but mass resolution was limited only to the nominal mass. Recently, PTR – MS has been coupled with time-of-flight (TOF) or ion trap (IT) mass analyzers, which offers greater possibilities of precise determination of mass of numerous chemical compounds present in real samples. In the quadrupole mass analyzer, only a single mass value can be analyzed at the time instant, while with the IT it is possible to accumulate all ions simultaneously and the losses are limited (Cappellin et al., 2013). PTR – TOF – MS achieves the same sensitivity as the quadrupole-based version of this technique. Furthermore, the TOF mass analyzer offers several advantages – larger mass range, higher time resolution or much higher mass resolution and mass accuracy (Biasioli et al., 2011).

In some cases, proton transfer reaction often results in some complication in ion chemistry in the drift tube. If any compound possesses only slightly higher PA than water (for example, formaldehyde with the PA 713.29 kJ/mol), the reaction of proton transfer from hydronium ion (which is an exothermic reaction) is reversed. The rate of both reactions is comparable and differences between them depend on the concentrations of water and analyte in the drift tube. As a result, proton transfer reaction between H_3O^+ and some compounds, like formaldehyde, is ineffective. Furthermore, H_3O^+ and RH^+ ions can cluster with water molecules in the drift tube creating $H_3O^+(H_2O)_n$ and $RH^+(H_2O)_n$ ions. Their presence in a reaction chamber is a problem because interpretation of the mass spectra is more complicated ($RH^+(H_2O)_n$ ions can interfere with the detection of higher mass species). Some of the analyzed compounds can react with $H_3O^+(H_2O)_n$ ions, but it usually depends on the humidity of the sampled air and also on the electric field and pressure in the drift tube (de Gouw and Warneke, 2007). Clustering, ions fragmentation and secondary ion–molecule reactions can have an impact on measurement of some compounds (Ambrose et al., 2010). However, the PTR – MS technique has numerous advantages like short-time response, high sensitivity and no need of calibration because concentration of the analyte can be calculated from a

ratio of ion signals and also well-known rate constants (Alexander et al., 2003).

Selected ion flow tube – mass spectrometry

Determination of VOCs, especially the ones occurring in gas matrices, is possible owing to the use of selected ion flow tube – mass spectrometry technique (SIFT – MS). This technique belongs to the solutions utilizing chemical ionization based on the reaction of selected precursor ions generated inside the device with the substances present in the analyzed sample introduced into the special reaction chamber (McEwan, 2015; Langford et al., 2014). In this way, it is possible to determine concentrations of trace and ultra-trace substances in the samples with a very complex matrix without the use of repeated external calibration (Smith and Španěl, 2015b; Prince et al., 2010; Milligan et al., 2002).

In the SIFT – MS technique, the most frequently used reaction ions include H_3O^+, NO^+ and O_2^+ ions generated in microwave discharge plasma. Before they reach the reaction flow tube, they go through the quadrupole analyzer, which is responsible for selecting appropriate ions that are then directed to the reaction chamber. In this part of the device, in the stream of a neutral carrier gas (usually helium), a range of reactions occur between the precursor ions and the analytes present in the sample gas injected through the Venturi inlet at the strictly defined time. If numerical values of the constants of rates of reactions occurring in the reaction chamber for individual ions are known, it is possible to define concentrations of individual analytes present in the sample. Additional parameters that are necessary for quantitative determination of given substances also include the time of reaction of individual ions, geometric parameters of the reaction chamber and the pressure in it. Figure 6 presents the diagram of the SIFT – MS system setup (Blake et al., 2009; Smith and Španěl, 2011; Wilson et al., 2006).

The selection of reaction ions is conditioned by the tendency for selective reaction with selected chemical compounds present in gas sample. The previously mentioned H_3O^+, NO^+ and O_2^+ ions do not react with the main gaseous components present in the air such as nitrogen, oxygen, carbon dioxide or water vapor, but they react very quickly with numerous chemical compounds undergoing quantitative and qualitative analysis in many areas of research, such as medicine or environmental protection (Španěl and Smith, 2007).

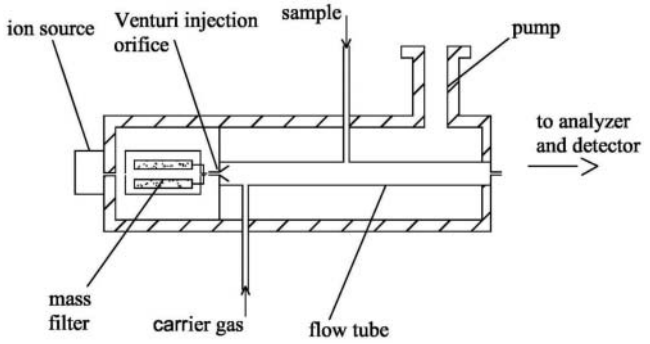

Figure 6. Diagram of the SIFT – MS system.

As opposed to the other design solutions using mass spectrometry, the SIFT – MS technique makes it possible to identify and distinguish between the chemical compounds with identical nominal mass but with a different arrangement of individual functional groups related to each other, such as acetone and propanol. It is possible that during one analysis several reaction ions can react with isobaric compounds, the result of which is completely different final products that are obtained from them, which reach the mass spectrometer analyzer (Smith and Španěl, 2011; Pysanenko et al., 2009).

There are following two main modes of operation in SIFT – MS:

- Full scan (FS) mode – when the complete mass spectrum is obtained with chosen range of ions with defined mass-to-charge ratio (m/z) for a chosen time; interpretation of the mass spectrum is based on the comparison of the product ions using the comprehensive knowledge of the ion chemistry.
- Multiple ion monitoring (MIM) mode – when the m/z values of both the products and the precursor ions can be rapidly switched; it is the more accurate analysis of the compounds present in sample when the m/z values of various product ions are recognized by the FS mode; relatively short response time of the SIFT – MS technique allows monitoring in real-time (Spanel and Smith, 2011; Smith and Španěl, 2015a).

The SIFT – MS technique is closely related to the PTR – MS technique, but SIFT – MS provides several advantages. In SIFT – MS detection, sensitivity is about two orders of magnitude higher than in PTR – MS and the ionization in the flow tube is softer (in PTR – MS – drift tube and in SIFT – MS – flow tube). In the drift tube, there is much more fragmentation of analyte ions for the same compounds than in the flow tube, and in consequence, interpretation of the mass spectra can be more difficult. This effect can be related to higher collision energies in the drift tube (0.2 eV) than the thermal collision energies (0.038 eV) in the flow tube (Blake et al., 2009). Furthermore, the switching between reagent ions in SIFT – MS is rapid as opposed to PTR – SRI – MS. As compared to SIFT – MS, in PTR – MS, it is possible to use air as a carrier and buffer gas (in SIFT – MS, it cannot be done). It is connected with the limitation of formation of adduct products due to the non-thermal conditions in the drift tube (Biasioli et al., 2011).

The SIFT – MS technique is more convenient than PTR – MS with hydronium ions as precursor ions in analysis of some compounds, such as formaldehyde or hydrogen cyanide, that have proton affinities close to that of water. In PTR – MS, where the effective temperature is much higher than in SIFT – MS (the order of 1000 K), the reactions between the protonated analyte and water in the sample take place at a much higher rate. It complicates the measurement of these compounds. In SIFT – MS, the compounds such as formaldehyde or hydrogen cyanide can be easily measured at room temperature during proton transfer reaction in the flow tube (Prince et al., 2010).

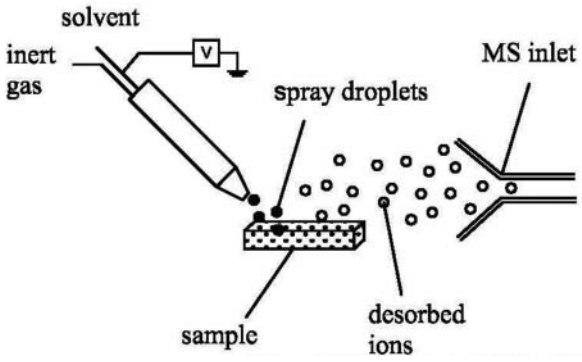

Figure 7. Diagram of the DESI – MS system.

Desorption electrospray ionization – mass spectrometry

One of the most breakthrough device solutions based on mass spectrometry, which has been elaborated during the development of direct measurement techniques is the desorption electrospray ionization – mass spectrometry (DESI – MS). In this design solution, both the phenomenon of molecule desorption from the sample surface and simultaneous molecule ionization are used. This solution proved excellent during the research aimed at determination of pesticides, toxins or food additives where the previously known techniques had not made it possible to obtain satisfactory results (Nielen et al., 2011; Wang et al., 2013; Suni et al., 2011).

Figure 7 presents a diagram of the DESI – MS spectrometer design (Farré and Barceló, 2013). Ions are released from the sample surface as a result of directing a stream of spray gas onto it at an appropriate angle. The gas contains an appropriately selected solvent (the most often used solvents are methanol/water or acetonitrile/water with the addition of methane or acetic acid). As a result of contact of the sprayed solvent drops with the sample surface, ions are released. Then, they are directed to further elements of the spectrometer.

Selection of the optimal conditions of analysis using the DESI – MS technique requires taking into account many parameters such as

- the composition of solvent spray,
- the flow rate of solvent,
- the solvent spray pressure,
- geometrical parameters:
  - the angle, at which it is directed to the surface of the sample,
  - the angle between the sample surface and the ion transmission line into the spectrometer,
  - the emitter tip-to-surface distance,
  - the sniffer-to-surface distance,
  - the emitter tip-to-sniffer distance.

It is very important to determine the correlation between the values of these parameters and the result obtained during the analysis in the form of the mass spectra of individual analytes. The range of processes occurring on the surface of the sample during ion release is very complex, and it has not been determined in an unambiguous manner so far. It is supposed that while moisturizing of the sample with solvent drops, selected analytes are dissolved in it and next, as a result of its evaporation, the release of molecules in the ionized form is observed (Nielen et al., 2011; Takats, 2004; Suni et al., 2012).

The DESI – MS technique is widely used for imaging of surfaces, including biological tissues. The DESI – MS imaging experiment is based on direct scanning of the unmodified sample surface in two directions (x and y) with a striking spray of charged droplets. As a result, characteristics of the specific ions can be presented in two-dimensional images illustrating their abundance. The DESI – MS imaging can provide information about spatial distribution of various compounds including many classes of lipids: fatty acids (FA), sphingolipids (SP), glycerophospholipids (GP), glycerolipids (GL) and sterol lipids (ST) (Eberlin et al., 2011; Dill et al., 2009).

Solvent system (physical and chemical properties and composition) can have effect on desorption and ionization processes in the DESI – MS analysis. For example, acid modifier such as acetic acid or formic acid addition to conventional solvent system in DESI – MS (acetonitrile or methanol with water) is commonly used in analysis of polar lipids (Manicke et al., 2009; Wiseman et al., 2005). In many cases, DESI – MS with conventional solvent system without any acid modifier was also successfully performed for lipids. The addition of dimethylformamide (DMF) to a mixture methanol: water can be used to obtain distinctive lipid profiles from a mouse brain section with higher intensity signals for the compounds of low molecular weight than in the case of using a mixture methanol: water without DMF. An increase in desorption ionization signal can be greatly enhanced by the application of surfactants in order to manipulate surface tension of DESI spray solution (Badu-Tawiah and Cooks, 2010). The ability to modify the composition of the main components of solvents gives great possibilities for analysis of many biological samples, in particular, proteins, lipids and phospholipids.

One of the common problems related to the DESI – MS analysis is ionization from sample surface. Addition of salts can be helpful in promoting ions formation. This phenomenon was exploited for determination of such phospholipids as choline in positive or negative modes depending on the types of adducts (sodium or acetate adducts) (Paglia et al., 2010). In the cases when some molecules are not easily ionized by DESI – MS, a reactive DESI – MS experiment can be used. In the reactive DESI – MS experiment, some reagents are added to the solvent spray so that chemical reactions between them and specific compounds or functional groups within the sample can significantly facilitate ionization process. This modification can be used for analysis of anabolic steroids in urine (Huang et al., 2007) or counterfeit drugs (Nyadong et al., 2007).

DESI – MS does not require matrix preparation (as opposed to MALDI – MS) and it is conducted at atmospheric pressure under ambient conditions. The short time of a single analysis is a significant improvement as compared to the traditional mass-spectrometric-based separation techniques such as GC–MS or LC–MS techniques. Like every analytical technique, DESI – MS has numerous disadvantages such as quantification – sample surface can significantly affect the signal intensity. The other problem can be ion suppression or enhancement. The results of analysis, especially for complex mixtures, are resolved by MS/MS or data processing. Nevertheless, the DESI – MS technique, as a new method for rapid surface analysis, has

numerous applications in many areas including forensics (Wiseman et al., 2005; Ifa et al., 2007; D'Agostino et al., 2006; Jackson and Attalla, 2010), metabolomics (Pan et al., 2007; Kauppila et al., 2006; Fernández et al., 2006), proteins (Shin et al., 2007; Myung et al., 2006), imaging (Wiseman et al., 2006; Van Berkel and Kertesz, 2006), pharmaceutics (Williams et al., 2006; Leuthold et al., 2006; Weston et al., 2005; Chen et al., 2005) and characterization of natural products (Chen et al., 2005; Takats, 2004).

Table 4 presents the most important information about the techniques described in this article (Kertesz and Van Berkel, 2008; Schmitz et al., 2008; Prince et al., 2010; Bain, 2007; Maher et al., 2014; Sulzer et al., 2014; Miao and Chen, 2009) as well as their advantages and disadvantages.

Presented techniques based on mass spectrometry are only selected examples of many different solutions, the number of which is still increasing. One of the techniques worth mentioning is direct analysis in real tme – mass spectrometry (DART – MS). It was introduced in 2005, shortly after implementation of DESI – MS. The principle of operation of the DART – MS technique is based on ionization of neutral molecules of an analyzed sample due to interaction between hot gas stream (mainly helium) or plasma generated at an ion source and the sample surface (Gross, 2014; Hajslova et al., 2011). Similarly to the DESI – MS technique, ionization of the sample in DART – MS occurs upon atmospheric pressure. In many cases, both techniques are complimentary as far as polarity or molecular mass of measured compounds are concerned (Castro-Puyana and Herrero, 2013). The limitations of one technique can be a starting point for elaboration of new solutions. Such tendency is also observed for direct measurement techniques utilizing mass spectrometry, which is manifested by numerous solutions implemented during recent years.

Direct mass spectrometry techniques in analytical studies

One of the most frequently occurring problems during research is the necessity of preliminary separation of the analytes, especially for the biological samples characterized by a complex matrix composition. This stage takes a lot of time; however, it is necessary in the majority of studies that are currently conducted. New device solutions, which allow direct sample analysis, are more and more attractive and accordingly the number of their practical applications is growing. These techniques, also the ones based on mass spectrometry, are commonly used nowadays in the research on the quality of numerous foodstuffs, medical diagnostics and the assessment of pollutant emissions in various areas. Table 5 presents the examples of the application of direct measurement techniques described in the previous part of this study in various research areas.

The concept of green analytical chemistry in mass spectrometry techniques

Recently, one of the major aspects of designing new technical solutions is reduction of time and cost of analysis while preserving optimal separation parameters. This approach is highly desirable, but in most cases very difficult to achieve. Hence, scientists try to find a compromise. Moreover, more and more attention is paid to environmental protection issues in terms of new measurement techniques taking 12 principles of green chemistry into account (Garrigues et al., 2010; Armenta et al., 2008). The following principles may be invoked to define the main points of green analytical chemistry:

- Performing analysis with the use of direct measurement techniques.
- Reduction or elimination of the chemical substances such as reagents and organic solvents from analytical procedures.
- Elimination of highly toxic environmental reagents.
- Minimization of energy consumption.
- Reduction of derivatization.
- Reduced emissions of vapors and gases as well as liquid and solid waste.
- Proper management of analytical waste.
- Increased safety of the operation (Gałuszka et al., 2013; Tobiszewski and Namieśnik, 2012).

This idea, which was developed in 2000 (Namieśnik, 2000), has aroused increased interest among chemists.

The examples of activities focused on implementation of green chemistry principles in trace analytics engulf the following:

- Possibly widespread utilization of direct analytical techniques. They allow measurement of analytes in the sample without a need of its pre-preparation.
- A decrease in size of the samples subjected to analysis (a decrease in scale of determination). Reduction of cost connected with purchase of high-purity reagents.
- *In situ* analysis. Obtaining analytical information in real time or with the minimum time delay.
- Introduction of the solvent-free sample preparation techniques into analytical practice.
- A decrease in energy consumption per analysis or per measured component.

Mass spectrometry techniques presented in this article provide the capability of environmental-friendly analysis. Application of these techniques allows reduction of solvent and reagent consumption during sample preparation. In the MALDI – MS technique, it is necessary to prepare the matrices supporting an ionization process, but in this step, typical organic solvents can be replaced by environmental-friendly reaction media – the ILs. While designing analytical procedures, it is possible to modify the main properties of the ILs depending on the experiment in order to reduce formation of waste. That is why ILs are called "designing solvents" (Tobiszewski et al., 2010; Armenta et al., 2015). Furthermore, the MS-based techniques allow rapid, online, direct analysis in real time without time-consuming chromatographic separation, which is more green alternative than the other techniques such as gas chromatography or spectrophotometry techniques. Despite many advantages related to the presented techniques, in analytical practice, there is usually a need to compromise between the principles of green chemistry and the performance parameters (Armenta and de la Guardia, 2015).

Developmental tendencies of direct mass spectrometry techniques

The development of the measurement techniques coupled with mass spectrometry resulted in the appearance of new device and

Table 4. The most important information on described measurement techniques.

Name	Principle of operation	Compounds for analysis	Performance parameters	Advantages	Disadvantages
Matrix Assisted Laser Desorption Ionization – Mass Spectrometry (MALDI – MS)	Neutral molecules undergo transition to the ionized form as a result of energy transfer from the intermediate matrix selected so as to ensure very fast and effective ionization of compounds contained in the matrix.	Determination of proteins, peptides and other biologically active molecules in biological samples.	• resolution – 5000–20000 (fwhm) • sensitivity at the ppm level • response time <100 ms • range of analyzer masses – 1–400000 amu • linear range of the detector response – no data	• broad range of chemical compounds that can be included in the matrix • possibility of determining a broad range of chemical compounds with diverse properties • relatively simple interpretation of obtained mass spectra	• it is necessary to use solvents for matrix preparation • risk of mutual ionization inhibition by various analytes present in the sample • high cost of devices • possibility of formation of ions from the matrix that are not formed as a result of analyte transformation
Proton Reaction Transfer – Mass Spectrometry (PTR – MS)	A technique in which analyte ionization takes place as a result of the proton transfer reaction to neutral molecules from ions generated inside the device (usually the hydronium ion).	Volatile organic compounds in samples of various origins (mostly biological, medical and environmental) determination in air.	• resolution – 1500–6500 (fwhm) • pptv order sensitivity • response time <100 ms • range of analyzer masses – 1–1000 amu • linear range of the detector response – 1 pptv – 0.5 ppmv	• real-time measurement • short time of single analysis • no need to prepare sample before determination	• mostly for compounds with the value of the PA parameter higher than water (alternative – PTR-SRI-MS) • high cost of devices • problems with distinguishing compounds with the same molecular mass
Selected Ion Flow Tube – Mass Spectrometry (SIFT – MS)	Ionization occurs as a result of reaction between selected precursor ions generated inside the device and selectively introduced into the reaction chamber and molecules of determined substances, which are present in the analyzed sample.	Volatile organic compounds that are present in environmental and medical samples, determination of the quality of food products and the quality of indoor and outdoor air.	• resolution – 1000–5000 (fwhm) • sensitivity at the ppt level • response time – 20ms • range of analyzer masses – 10–400 amu • linear range of the detector response – 0.5 ppt – 50 ppm	• possibility of determining compounds with the same molecular mass • possibility of determining compounds occurring in the sample at trace concentration levels • possibility of performing real time measurements	• high cost of devices • tendency for selected precursor ions to combine with water molecules present in the sample • possibility of losing a part of the analytes as a result of diffusion processes occurring in the reaction chamber
Desorption Electrospray Ionization – Mass Spectrometry (DESI – MS)	The release of analytes occurs as a result of the action of drops of solvent sprayed in the carrier gas stream on the sample surface; the ions formed in this way are directed to the spectrometer.	Determination of compounds from the group of amino acids, proteins, lipids in samples with correct matrices (forensics, analysis of drugs, explosives).	• resolution – 1000–5000 (fwhm) • sensitivity at the ppm level • response time <100 ms • range of analyzer masses – 50–80000 amu • linear range of the detector response – no data	• possibility of determining small molecules • relatively short time of single analysis • possibility of broad selection of parameters depending on the type of determined substances	• necessity to optimize a large number of parameters • risk of formation of ions, which come only from charged solvent drops • high cost of devices • lack of full understanding of the ionization mechanisms on the sample surface

Table 5. The use of direct measurement techniques based on mass spectrometry in various research areas.

Technique	Scope of research	Ref.
Matrix-assisted laser desorption ionization – mass spectrometry	Detection of the presence of Streptococcus agalactiae bacteria in pregnant women.	Ábrók et al. (2015)
	Identification of fungi from Candida family.	Angeletti et al. (2015)
	Identification of phosphatidylcholine and lysophosphatidylcholine in horse serum samples.	Angelini et al. (2014)
	Tests of membrane protein solubility in selected surfactant solutions.	Bechara et al. (2012)
	Structural analysis of glycerin alkoxylates.	Borisov et al. (2013)
	Quality control of selected sports supplements containing protein substances.	De Ceglie et al. (2015)
	Determination of the degree of fructan polymerization present in samples of selected plants.	Evans et al. (2015)
	Determination of the origin of meat from various animals.	Flaudrops et al. (2015)
	Testing chemical compositions of selected paints and acrylic emulsions.	Hoogland and Boon (2009)
	Identification of yeasts of clinical origin.	Jamal et al. (2014)
	Detection of presence of selected antibiotics in fresh milk samples.	Kim et al. (2016)
	Determining characteristics of the products obtained as a result of styrene polymerization reactions.	Kim et al. (2013)
Desorption electrospray ionization – mass spectrometry	Determining characteristics of phospholipids present in the lung tissue of mice.	Basile et al. (2011)
	Qualitative analysis of lipids in biological samples.	Eberlin et al. (2011)
	Determination of atrazine content in cabbage leaves.	Zhang et al. (2009)
	Detection of clenbuterol in urine samples.	Lin et al. (2008)
	Determination of lipids and phospholipids in mouse–pancreas, rat–brain and metastatic human-liver adenocarcinoma tissue.	Wiseman et al. (2005)
	Detection of phosphocholine and sphingomyelins in the Artery Plaque Tissue.	Manicke et al. (2009)
	Analysis of urine metabolites in patients with inborn disorders of metabolism.	Pan et al. (2007)
	Identification of alachlor, atrazine and DEET (N,N – dimethyl-m-toluamid) in samples of various origin.	Mulligan et al. (2006)
	Detection of some metabolites (dehydroepiandrosterone (DHEA), b-estradiol, dobutamine, acetaminophen in urine.	Kauppila et al. (2006)
	Direct chemical analysis of inks from 10 different blue ballpoint pens.	Ifa et al. (2007)
	Direct analysis of a variety of compounds relevant for toxicological screening purposes.	Leuthold et al. (2006)
Selected ion flow tube – mass spectrometry	Quantitative determination of acetonitrile in samples of exhaled air and in the headspace of urine.	Abbott et al. (2003)
	Measurement of selected bacterial cells in the blood.	Allardyce et al. (2006), Scotter et al. (2006)
	Determination of selected characteristics of odorous substances used for the production of cosmetic products.	Heynderickx et al. (2013a)
	Determination of emission levels of odorous substances generated at animal farms.	Heynderickx et al. (2013b)
	Assessment of the cell oxidation process occurring in beef samples.	Olivares et al. (2012)
	Determination of selected isobaric compounds in atmospheric air samples with a high moisture content and in exhaled air.	Pysanenko et al. (2009)
	Determination of emission levels of volatile organic compounds from selected fungus species.	Scotter et al. (2005)
	Measurement of concentrations of selected chemical compounds present in pig excrement and urine samples.	Smith et al. (2000)
	Determination of volatile organic compounds produced by microorganisms present in urine.	Storer et al. (2011)
	Assessment of the quality of oils of various origin and composition.	Davis and McEwan (2007), Davis et al. (2005)
Proton transfer reaction – mass spectrometry	Identification of selected chemical compounds from the monoterpene group present in atmospheric air.	Ambrose et al. (2010)
	Qualitative and quantitative analysis of air from mixed deciduous forest areas.	Ammann et al. (2004)
	Identification of volatile organic compounds emitted as a result of leaf damage.	Fall et al. (1999)
	Detection of potential liver disease biomarkers in samples of exhaled air.	Fernández del Río et al. (2015)
	Real-time analysis of volatile organic compounds present in exhaled air.	Herbig et al. (2009)
	Determination of the carbon dioxide in exhaled air.	Keck et al. (2008)
	Analysis of chemical composition of selected saffron species.	Masi et al. (2016)
	Identification of pyrogenic volatile organic compounds released into the surrounding area during the biomass combustion processes.	Brilli et al. (2014)
	Classification of selected species of uniflorous and multiflorous honeys.	Kuś and van Ruth (2015), Schuhfried et al. (2016)
	Description of characteristics of selected dairy products with various fat content.	Soukoulis et al. (2012)
	Identification of volatile organic compounds from various apple cultivars.	Cappellin et al. (2012)
	Identification of volatile organic compounds released during the burning of beans from selected coffee varieties.	Charles et al. (2015), Gloess et al. (2014)
	Analysis of the chemical composition of various kinds of wines.	Lasekan and Otto (2009), Romano et al. (2014)

methodological solutions, which allow real-time analyses. The possibility of regulation of selected parameters of individual elements of the measurement system, such as the intermediate matrix in the analyte ionization process (MALDI – MS), the type of reaction ions (SIFT – MS) or the selection of the solvent sprayed on the sample surface (DESI – MS), allows determination of the broad spectrum of chemical compounds with various physicochemical properties (polarity, volatility, PA).

The development of new analytical techniques in mass spectrometry is related, among other things, to the application of desorption and electrospraying processes of liquid medium near the surface of the analyzed sample in an electric field, which allows obtaining highly selective analytes in an ionized form (Ibáñez et al., 2013; Huang et al., 2011). For this purpose, the attempts were made to find appropriate materials, which could fulfill the role of the ionization process initiator that, under adopted conditions, would not generate additional ions that could falsify the obtained results of analysis. Matrix-assisted laser desorption ionization (MALDI – MS) proved to be one of such solutions, which is used especially for determination of various substances in biological samples. This solution, despite a range of applications, does not allow selective separation of numerous chemical compounds, especially the ones, which are characterized by a low size of molecules due to the possibility of creating competitive ions, which originate from the matrix. In the recent years, the attempts were made to replace the previously prepared matrix with other materials that could generate additional ions to a much lower degree.

One of the alternatives for the matrices used in the MALDI – MS technique is silica substrates characterized by varied surface porosity. They play the key role in mass spectrometry with nanostructure initiation (Nanostructure Initiator – Mass Spectrometry (NI – MS)) (Miura et al., 2012). The release of analytes from the sample and their transition to the ionized form takes place as a result of catching the determined substances by the solution applied on the porous silica substrate and next irradiation with a laser beam, which makes it possible to direct the formed ions into the mass spectrometers. A very important stage, which is indispensable before proper analysis, is the silica substrate preparation (Calavia et al., 2012; Gao et al., 2016; Lee et al., 2012). For this purpose, a small fragment of silica wafers is immersed in the solution of an appropriate liquid medium and next, after the fixed time, the silica plate is rinsed and dried with the application of liquid nitrogen. Afterwards, it is etched using an ethanol solution of hydrofluoric acid HF, sprayed with additional ingredients, e.g. $AgNO_3$. Then the obtained substrate is incubated at approx. 90–100°C. Depending on the origin and type of the sample, individual substrate preparation stages can be subjected to various modifications. The factors such as etching process conditions, substrate structure or sample deposition technique may significantly influence on the final result of determination. The NI – MS finds a growing number of applications, especially in the research concerning the determination of selected chemical compounds in biological samples (Patti et al., 2010; Greving et al., 2011).

Another device solution in mass spectrometry is laser ablation electrospray ionization – mass spectrometry (LAESI – MS). The use of the laser impulse (mid-infrared – mid-IR) allows evaporation of the entire water present in the sample, which enables the transition of its single molecules into the gaseous state (Nemes et al., 2008; Nemes and Vertes, 2007). These molecules collide with charged solvent drops sprayed over the sample surface. In this way, the ions originating from the sample are formed and directed to the mass spectrometer (Deimler et al., 2014; Shrestha et al., 2013). Due to the short time of single analysis, this technique allows monitoring of changes occurring within the sample. Owing to its high sensitivity and no necessity to prepare the sample before the analysis, this technique is more and more often used, e.g. in medical diagnostics (Beach et al., 2014).

In recent years, mass spectrometry with paper spray ionization – mass spectrometry (PSI – MS) has been enjoying a growing interest among numerous analytical techniques aimed at increasing separation efficiency of mass spectrometry. In this technique, the analyte ionization takes place on a specially prepared paper substrate, usually triangular, with one of the peaks directed toward the mass spectrometer inlet (Espy et al., 2012; Wang et al., 2010; Wang and Lai, 2015; Klampfl and Himmelsbach, 2015). As a result of the voltage applied and the sprayed stream of the appropriately selected solvent, ions are released from the samples that were previously applied onto the substrate. The mechanism of the ionization process occurring on such a substrate has not been explained in an exhaustive manner; yet, just like the influence of many parameters, such as the type of the paper used, its size, composition and the volume of the sprayed solution or the value of the voltage applied. The PSI – MS allows analyses of e.g. blood samples, agricultural products or explosives (Wang et al., 2013; Shi et al., 2015). This technique can be modified by direct spraying of the solvent on the sample surface without application of a special substrate. This solution was used for the development of leaf spray – mass spectrometry (LS – MS). The ions are released directly onto leaf fragments of the tested plant (Liu et al., 2011; Liu et al., 2016; Malaj et al., 2012; Sarkar et al., 2012; Tadjimukhamedov et al., 2012). It can be supposed that during the next years another techniques will be developed that will allow much more specific analysis of a broad range of chemical compounds.

Summary

Mass spectrometry is a commonly used analytical tool that allows determination of a large number of chemical compounds, which are present in various real-time samples. Although it is mostly associated as one of the possible solutions regarding detection in the chromatographic techniques – both liquid and gas chromatography, its enormous potential has resulted in the development of many new solutions. Some of them – for example, the mass spectrometry technique with a membrane inlet – have been known for a long time and are commonly used, e.g. in the determination of VOCs in the samples of various origin and composition. However, a range of new solutions are being created, which is exemplified by DESI – MS or the similar technique of DART – MS. These techniques allow direct analysis of the surface of various materials such as pieces of clothing, medication, including medication intended for disposal or samples of materials of biological origin.

The described techniques allow detection of a majority of pollutants occurring in the environment in liquid, solid and gas matrices. In the case of many other techniques (UV-VIS spectrophotometry, electrogravimetry, spectrofluorometry), it is necessary to transfer the sample into the solution, which significantly influences on the range of possible applications. The techniques described above are characterized by the lack of need for sample preparation, which is connected with omission of such stages as dilution of solid samples in the solution, mineralization or derivation processes, which are often the cause of errors, e.g. during chromatographic analyses. Examination of the influence of the matrix on the final result of analysis is also an important element of the analytical procedure. In the case of the techniques described above, it is possible to control the relevant parameters to minimize the contributions from other compounds that may be present. The introduced modifications do not influence the possibility of determination of analytes at a trace level nor lengthen the time of sample preparation. These factors are in MALDI – MS, the matrix composition and in SIFT – MS, it is the selection of the precursor ion.

Instrumentation development of new mass spectrometry techniques creates tremendous opportunities for rapid, non-invasive analysis of sample in a short time, at a high level of concentration and with minimal sample preparation prior to the MS analysis. Availability of an increasing number of new techniques also means a number of challenges related to identification, understanding of the ionization mechanism of each molecule, quantification and finally data interpretation. In many cases, it is difficult to find a correlation between the type of sample (e.g. surface properties such as porosity, density) and the signal obtained. Another problem is fragmentation of molecules during proton transfer reaction, formation of adduct products or ions clustering, which can make mass spectrum interpretation difficult. These and other problems related to the MS techniques are very important points in terms of development of new solutions allowing analysis in real time with higher procession, accuracy and sensitivity.

The methodological solutions regarding mass spectrometry described in this study confirm the enormous possibilities of this technique as an analytical tool, which allows comprehensive sample analysis. Its development will progress for many years to come and, as a result, it will be possible to perform a lot of complex analyses under favorable separation conditions. In the future, further methodological solutions can be expected, which will be aimed at a reduction of the time of single analysis, the possibility of determining a larger number of compounds at the same time, minimizing the influence of the analyzed sample background, obtaining more advantageous separation parameters and eliminating or minimizing the sample preparation stages before determination. It seems highly likely that there will be an increase in the number of research areas, in which mass spectrometry could begin to play a very important role. With time, it could become the basic technique for many determinations in several research areas, for which other solutions may not be used due to their numerous limitations.

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