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Review

New trends in quantification of acrylamide in food products

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ABSTRACT

Methods applied in acrylamide quantification in foods have been reviewed in this paper. Novel analytical techniques like capillary electrophoresis (CE), immunoenzymatic test (ELISA) and electrochemical biosensors, which can replace traditional methods like high performance liquid chromatography (HPLC) and gas chromatography (GC) were presented. Short time of analysis and high resolution power of electrophoretic techniques caused that they became routinely used in food analysis apart from high performance liquid chromatography and gas chromatography. Application of modern chromatography methods like ultra performance liquid chromatography (UPLC) in acrylamide quantification considerably shortened the time of analysis and decreased the consumption of indispensable reagents. The most promising approaches to acrylamide quantification in foods are electrochemical biosensors and immunoenzymatic tests. In contrast to chromatography and electrophoretic methods they require neither expensive equipment nor time consuming sample preparation and allow for fast screening of numerous samples without the usage of sophisticated apparatuses. Because of many advantages such as miniaturization, rapid and simple analysis, and high sensitivity and selectivity, biosensors are thought to replace conventional methods of acrylamide quantification in food.

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Contents

1. Introduction

Acrylamide is a chemical compound produced in industrial scale through catalyzed hydrolysis of acrylonitrile. It has been used for almost 60 years in synthesis of modified polyacrylamides which found multiple applications in various branches of industry including manufacturing of plastics, pigments, glues, cosmetics and cement binders [1,2]. These substances have been also used as coagulants in wastewater and sewage treatment [3]. Polyacrylamide became one of the most useful laboratory tools which involve application SH groups selective modification, gel electrophoresis of proteins and nucleic acids and immobilization of enzymes and microbial cells [1,5].

In April 2002 the Swedish State Agency on Food and researchers from Stockholm University informed that large amounts of acrylamide were found in certain thermally processed foods. This finding attracted attention all round the world because in 1994 acrylamide was classified by the International Agency for Research on Cancer as probably carcinogenic to humans [2,4,6–8]. The long-term exposition to acrylamide causes the damage of central and peripheral nervous system in humans and other animals [9,10]. Acrylamide was also found to be a genotoxin with mutagenic and carcinogenic activities to animals (because it causes gene mutations and changes in chromosomes) [11–13].

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Since the appearance of large acrylamide amounts, during thermal processing of foods rich in carbohydrates at temperature above 120 °C, was confirmed, researchers have tried to explain the mechanism of this phenomenon [14]. It was revealed that Maillard reactions generating compounds responsible for smashing taste, aroma and color of foods are coupled with formation of acrylamide from asparagine and reducing sugars [15]. Currently it is well known that this compound is also one of triacylglycerols thermal degradation products taking place during food processing at very high temperature. The intensity of acrylamide formation in foods containing asparagine and reducing sugars depends on initial concentrations of these precursors and their ratio as well as on temperature and duration of thermal treatment, water activity and pH [16–18].

The highest amounts of acrylamide are generated through frying of potatoes, roasting of coffee and cocoa beans, baking of bread and cakes, thermal processing of cereals and meat roasting [15,19–21].

Information about an acrylamide occurrence in foods and the knowledge of its harmful impact on human health was the statement of the Joint Expert Committee of FAO/WHO on Food Additives (JECFA) revealing that the toxicological threat caused by intake of acrylamide with food cannot be excluded [22]. In consequence, certain strategies aimed at reducing acrylamide content in thermally processed foods were proposed and search into suitable analytical procedures concerning the control of thermal food processing and acrylamide concentration monitoring in foods was intensified [3,9,23–25].

Advanced methods of acrylamide quantification are necessary to accurately assess the human exposure to this harmful compound [26,27]. The need of acrylamide and its adducts quantification in order to intensify epidemiologic studies was emphasized at the meeting of European Food Safety Authority (EFSA) in 2008 [28]. Due to the increasing knowledge about mechanisms of toxic, also mutagenic and carcinogenic impact of acrylamide on human organisms the newly developed research methods aim not only at monitoring of biomarkers of exposition to acrylamide but also at making diagnosis related to the level of risk caused by this exposition [26,28–30]. HPLC–MS/MS and immunoenzymatic tests are particularly suitable for quantitative determination of adducts formed by acrylamide and its metabolite glycidamide with hemoglobin or DNA, and metabolites secreted with urine like mercapturic acid, which can be regarded biomarkers of exposition to acrylamide [3,30–35]. Direct detection of DNA damage caused by formation of adducts of acrylamide and its metabolite with DNA is conducted by using electrochemical biosensors and UV–vis spectrophotometers [36].

Moreover, procedures of acrylamide quantification in foods must yield reliable quantitative data and should be inexpensive, convenient and rapid [37,38]. It is obvious that to obtain accurate and reproducible results sample collection and preparation before instrumental analysis must be conducted with sufficient precision [39,40]. However, an official method of acrylamide quantification in food has not been hitherto recommended [39]. Because of acrylamide presence in numerous food products, in last year's multiple studies aimed at validation of applied analytical methods used to detect and quantify this compound were conducted [39,40]. Recently performed studies focus on the improvement of existing techniques of quantitative acrylamide analysis and development of novel ones which should be quick, simple, inexpensive, effective, safe and reliable [40,41]. Efforts on standardization of methods used to detect and quantify acrylamide in foods have been continued. An official method of acrylamide quantification in foods is believed to be established in the end of 2013 by the European Committee of Normalization (Comité Européen de Normalisation, CEN) [42].

Selection of an appropriate research methodology is mostly based on the type of food product (sample matrix) and acrylamide structure and properties. Its quantification in food is difficult because of the low molecular mass (71.08 Da) [43], high polarity, very good water solubility (215.5 g/100 mL), high reactivity, and low volatility [8,37,44,45]. Besides, because of the lack of sufficiently strong chromophore groups (conjugated double or triple bonds, aromatic rings) in acrylamide molecules, and the lack of natural fluorescence it cannot be measured by using spectrophotometric UV detectors [46,47]. Quantification of acrylamide in complex matrices, rich in interfering compounds is also very difficult. Furthermore, amounts of this compound are usually minimal and therefore sample preparation consisting in concentration of acrylamide and removal of interfering compounds is the crucial step in its analysis [43,48].

Currently, acrylamide has been quantified in various foods by using chromatography techniques like gas chromatography (GC) or liquid chromatography (LC), and selective and specific detectors. Another useful technique for acrylamide determination can be capillary electrophoresis (CE). Also bioanalytical methods, such as immunoenzymatic tests and biosensors were found to be sufficiently sensitive and selective [15,48–50].

2. Sample preparation

Accurate quantification of acrylamide contained in foods by using modern techniques of chromatography and electrophoresis requires complete and laborious isolation of this analyte and purification from co-extractable substances which can interfere with its assay. Moreover, sample preparation procedure often involves both analyte extraction from food matrix and its derivatization which improves precision of analysis. In view of the complex character of food matrices, isolation of individual substances is extremely difficult for the analyst [39,48,51].

Another problem encountered when electrophoretic methods are used in acrylamide quantification in foods is the need of sample desalting because ions released from the salt impair migration of macro-ions. High salt concentrations can cause the damage of the equipment used in analyses and make retention times irreproducible. Also the peaks corresponding to particular compounds can be wider [52,53]. Separation of acrylamide from other substances extracted from food is laborious and might lead to its losses and therefore considerable amounts of internal standards are added. Therefore, only a few laboratories are equipped with appropriate and high-performance analytical apparatuses which are applicable to acrylamide determination [15,51].

Like in traditional assays also in bioanalytical methods procedures of sample preparation consist in selective extraction of analytes by means of liquid–solid phase extraction, protein precipitation (PP), purification by solid phase extraction (SPE) and dissolving in an appropriate buffer solution [54–56]. Quantification of acrylamide in foods by using biosensors requires only simple procedures of sample preparation before the assay. Preparation of food samples consists in extraction and defatting of tested material by using water and hexane and in purification of resulting extracts by using Carrez reagents [57]. The clean-up of the extracts is necessary like in traditional analytical procedures. This protocol of sample preparation requires only small amounts of reagents including toxic organic solvents, efficiently removes matrix components and ensures high recovery of quantified compounds [57–59]. When acrylamide content is determined by immunoenzymatic method (ELISA) sample preparation may require also derivatization by using 3-mercaptobenzoic acid apart from acrylamide isolation and removal of matrix components before the analysis [60]. Recently, Quan et al. [61] developed a fast and simple technique of sample preparation which does not require the time consuming steps of extract clean-up and derivatization. This method consists in two

fold extraction of the analyte with phosphate buffered saline (PBS). Its advantage is the low consumption of reagents and simplicity because the samples are only shaken and centrifuged [56]. This makes the analysis inexpensive. However, results of immunoenzymatic tests can be affected by matrix composition [56,62]. The same buffer solutions can be used to eliminate matrix interference through interactions with the interfering compounds lowering or even completely eliminating their impact on the analyte. The elimination of matrix effects can be also achieved by preparing calibration solutions containing food sample matrix dissolved in the solvent [56,61,63]. However, the quantified substances cannot be contained in these calibration solutions.

Methods of acrylamide isolation depend on food composition. Usually, the sample preparation procedure involves traditional extraction in the liquid–solid system. Various variants of this technique are used prior to acrylamide analysis by either traditional (LC, GC and CE) or immunological methods, or by using biosensors. For instance, extraction can be intensified by ultrasounds, accelerated by a solvent (ASE – accelerated solvent extraction) or conducted by using a supercritical fluid (SFE – supercritical fluid extraction) [63,64]. ASE method consists in extraction of analytes by using minor amounts of a solvent. This process is conducted at elevated temperature and pressure [38,65]. Therefore, solvents consumption in ASE method is very low while acrylamide extraction from various food samples is efficient [66–68]. The disadvantage of this method is formation of acrylamide from precursors present in tested samples (e.g. cocoa, powdered milk) taking place during extraction at elevated temperature, and incomplete extraction of the analyte from these samples which in consequence can lead to false assay results [69,70,71]. The most commonly used solvent for acrylamide extraction is water, less frequently used are mixtures of polar organic diluents. Because the yield of extraction is decreased by high fat content, foods rich in fat are additionally defatted by using hexane, cyclohexane or toluene [43]. The liquid supercritical carbon dioxide (CO_2) is used as a solvent in SFE procedure. This technique does not cause degradation of analytes, is fast, highly efficient in fat removal and highly selective, and does not use toxic solvents. However, it is expensive [63,66].

Clarification is applied to remove interferential substances. Proteins are precipitated with acetonitrile, methanol, ethanol, sodium chloride or Carrez reagents (potassium ferricyanide (II) and zinc (II) sulfate (VI) [72–74].

Because of the low selectivity of extraction resulting extracts are additionally purified by means of solid phase extraction (SPE), most often on modified silica gel and polymeric matrices packed in SPE columns [44,75,76]. Clean-up of acrylamide-containing extracts by means of SPE prior to chromatography, electrophoretic or biological assay eliminates multiple interfering compounds and increases precision and accuracy of instrumental analyses. The newer version of classic SPE method is dispersive solid phase extraction (dSPE), also named QuEChERS method (Quick, Easy, Cheap, Effective, Rugged and Safe) [77]. In this procedure the bed of sorbent is replaced by sorbent particles which are added to the solution of a sample [54]. This technique is based on extraction by using organic solvents such as acetonitrile, ethyl acetate and acetone, fractionation with magnesium sulfate ($MgSO_4$) and sodium chloride (NaCl), and dSPE clean-up [76,78,79]. Despite of mentioned above SPE advantages also liquid–liquid extraction is carried out to increase acrylamide concentration in water extracts. The liquid–liquid extraction (LLE) and SPE techniques are relatively fast processes, however, to achieve the desired detection level, the organic solvent must be evaporated which is time consuming and can lead to losses of compounds to be quantified. Besides, to avoid any interference caused by solvent desorption only high purity solvents are used to extract compounds of interest, which generates additional costs of analysis [66,80,81].

One of modern isolation techniques applicable to compounds which are strongly bound with the matrix is the matrix solid phase dispersion method (MSPD) consisting in simultaneous extraction and purification of a sample. Sample preparation is a critical step of the whole analysis. MSPD has been increasingly used in isolation of drugs, pesticides and diverse natural food components. According to Dias Soares et al. [82] MSPD can be also applied to extract acrylamide from various foods and partially clean-up the extract through dispersion on the solid phase (C_{18}) followed by acrylamide elution [83]. MSPD increased the sensitivity of analysis, decreased consumption of organic solvents and shortened the time of extraction. Furthermore, problem caused by formation of emulsion, which is often encountered in liquid–liquid extraction, was omitted [23,80].

Different methods of samples preparation for chromatography analysis were published. One of the newest methods of sample preparation before chromatography analysis is solid phase micro extraction (SPME). SPME allows isolation of a substance from liquid and gaseous samples based on its separation between a matrix and a stationary phase coating a thin glass or quartz fiber [84]. There are two types of microextraction techniques: from the headspace (HS-SPME) or direct immersion (DI-SPME). This method has been increasingly used in isolation of acrylamide and its derivatization because of the short time of extraction and very small volumes of organic solvents [85].

The time consuming, multi-stage preparation of samples before acrylamide quantitative determination by chromatography or electrophoresis techniques caused that some fast, easy to perform, sensitive and inexpensive analytical methods were developed. Although classical extraction methods such as LLE and SPE have been commonly used, the newer procedures like SFE, dSPE, MSPD and SPME become increasingly popular because they offer savings of chemical compounds and faster sample preparation before the analysis.

3. Liquid chromatography

Liquid chromatography is one of instrumental analysis techniques. LC is commonly used in separation and quantification of compounds which are well soluble in water and nonvolatile because they sometimes cause analytical problems in gas chromatography procedures [72,86]. Determination of the acrylamide concentration is most often assayed by high performance liquid chromatography (HPLC) coupled with mass spectrometry (MS) [81,87–89]. In some cases also spectrophotometric detectors with a diode matrix UV-DAD were used [72,90–92]. LC is one of most rapidly developing techniques of instrumental analysis [93]. Some new solutions such as smaller size of particles (1–2 μm) of column matrices and construction of chromatographs which can work under much higher pressures compared to the traditional HPLC systems gave rise to the development of ultra performance liquid chromatography (UPLC) [93–95]. The improvement of traditional HPLC systems can be also achieved by using columns with fused bed instead of pre-packed columns because it improves the system's resolution [93].

The ultra performance liquid chromatography (UPLC) which is an alternative to the conventional HPLC requires higher pressures and lower flow rates. UPLC allows better separation of mixture components in the shorter time and with high sensitivity [97–99]. Such a separation is achievable by using the reversed-phase column BEH C_{18} (150 mm × 2.1 mm, 1.7 μm) with much thinner film than in typical HPLC columns [94]. Chromatographic separation of acrylamide on a traditional column filled with particles having diameter of 5 μm suffers from weak retention and separation of polar compounds like acrylamide and deformation of the shape

of peaks [44,72,73,100–102]. Application of UHPLC method solved these problems because it improved the analyte peak symmetry [94,97]. Besides, the smaller size of bed particles (1.7 μm) renders the analysis faster but not less efficient [93,97,103,104]. Other points worthy of emphasis in this connection are UPLC advantages which include minimized volumes of solvents used in separations resulting from low flow rates (0.2 ml min^{-1}), substantially shorter time of separation compared to traditional liquid chromatography techniques, more symmetric peaks of separated compounds and considerably smaller sample volumes [104]. Therefore UPLC is particularly well suited to multiple routine analyses. However, chromatograms obtained by UPLC usually contain more peaks corresponding to co-extractable food matrix components than chromatograms of the same tested samples but obtained by conventional HPLC, and finally the interpretation of results may be more difficult [16,94,98,105–107]. The removal of unwanted interfering compounds from samples and effective separation of peaks enables to obtain a separate peak of the analyte which is not overlapped by peaks of matrix components [93,105,107]. The disadvantage of this new technique is the need of application of new pumps that produce much higher pressure compared to HPLC systems [40,97–99].

Like HPLC systems also UHPLC systems used in quantification of acrylamide are usually equipped with tandem mass spectrometer (MS) as a detector [93]. Mass spectrometers are frequently used in identification of compounds separated by gas or liquid chromatography. They are particularly useful when trace amounts of substances to be assayed are contained in complex matrices [41]. MS detectors are both universal and selective [72]. Liquid chromatography coupled with tandem mass spectrometry (LC–MS/MS) is particularly well suited to analyses of polar compounds such as acrylamide which are not sufficiently volatile to be quantitatively determined by gas chromatography coupled with mass spectrometry (GC–MS). LC–MS/MS enables omitting of time consuming step of derivatization which is necessary before GC–MS separation. Therefore, sample preparation is simpler and shorter [73,87]. In mass spectrometers equipped with triple quadruple analyzers (QqQ) selected ions separated in the first analyzer are then fragmented again and the resulting daughter ions are analyzed in the second mass analyzer. It differs from the mode of function of ion traps (IT) which is periodical. One cycle comprises the selection of the ion to be fragmented, the process of collision with gas atoms and analysis of fragment ions, and takes place in a single chamber [108,109].

Mass detectors used in qualitative and quantitative UHPLC assays of acrylamide are usually triple quadruple analyzers while systems with ion trap are not used so frequently because they are thought to be characterized by higher detection levels, lower precision of mass measurement and worse reproducibility [40,88,93,94,97,110–112]. However, analytical systems based on ion traps are superior when the high sensitivity in the "full scan" mode and high scanning rates are necessary [112,113]. Besides, mass spectrometers equipped in triple quadruples are more expensive compared to those equipped with ion traps [114]. Both types of analyzers are low resolution systems. There are also hybrid analyzers (hybrid quadruple linear ion trap (QqLIT)) which display both the high sensitivity of quadruple and the capacity of ion trap. The ion which is selected in the quadruple analyzer is then fragmented in the ion trap [112,113]. Also high resolution analyzers like the time of flight analyzer (TOF) can be used in tandem systems. The function of TOF consists in the measurement of time between the moment of ions acceleration by an electric impulse and the moment of their detection in connection with the quadruple (QqTOF) [111]. These devices enable determination of elementary composition of mixtures derived through ions collision and acquisition of information about their structure based on fragmentation of analyzed ions and a significantly higher mass resolution than quadrupole analyzers. [107,112,115]. Most popular ionization methods used in LC–MS systems include electrospray ionization (ESI) and chemical ionization under atmospheric pressure (APCI), which are regarded as "mild" ionization techniques enabling detection of even very polar substances whose analysis is difficult [87].

In LC–MS/MS systems, identification and quantification can be conducted through monitoring of selected reactions (MRM) taking place in mass spectrometer equipped with the triple quadruple or ion trap [111]. High selectivity and specificity of this recording method ensures excellent sensitivity and renders this method most suitable in quantitative assays [87–89].

Literature survey provides evidence that UHPLC technique conducted in the reversed phase system combined with the tandem mass spectrometry can be successfully used as an alternative to the traditional HPLC–MS/MS technique [97,98,105]. There are many reports demonstrating that UHPLC–MS/MS is well suited to acrylamide analysis because it is characterized by the high reproducibility, selectivity and sensitivity of measurements [40,97,98,105]. Levels of detection (LOD) and quantification (LOQ) of UHPLC–ESI-MS/MS technique were for the analyzed material (potato chips) of 1 and 3 μg kg^{-1}, respectively [94].

Methods enabling simultaneous analysis of more than one chemical compound have been also recently developed [40,96]. Such analyses are particularly difficult because physicochemical attributes of chemical compounds are structure-dependent. Nielsen et al. [96] developed the method enabling simultaneous quantification of acrylamide and its precursors in foods. They used for this purpose LC–MS/MS technique in the reversed phase and quantified apart from acrylamide also asparagine, fructose, glucose and sucrose. This method enables simultaneous quantification of acrylamide, simple sugars and sucrose (a non-reducing disaccharide). Levels of detection of acrylamide and asparagine in wheat bread were of 0.013 and 1.8 mg kg^{-1}, respectively [96]. Zhang et al. [40] improved the earlier method through application of UHPLC–MS/MS technique and achieved the considerably higher sensitivity apart from quick and simple sample preparation and short time of analysis. Their method enables quantification of acrylamide and its precursors. The application of UHPLC–MS/MS in this analysis may contribute to explaining mechanisms of appearance and disappearance of acrylamide in foods [40,96].

4. Gas chromatography

Quantitative assays of acrylamide contained in foods or its derivatives were also performed by gas chromatography coupled with mass spectrometry (GC/MS) with or without derivatization process. Application of chromatographic techniques combined with mass spectrometry (MS) allows the simultaneous separation of the isolated from matrix compound and quantitative determinations execution [71,87,116,117].

The most popular method of acrylamide derivatization is its bromination before the analysis [48,116]. This technique is highly selective and improves precision of assays, it also effectively compensates for difficult and time-consuming derivatization process [71,87,117–120]. Another method of acrylamide derivatization consists in its silylation followed by solid phase microextraction (SPME) which can be used in analysis of polar and non-polar compounds in gases, liquids and solids [66,74,85].

Most frequently used detectors are mass spectrometers with high resolving power which can record signals generated by selected fragmentation ions (SIM) [121]. A compromise between the high selectivity of analyzed compounds separation and costs of the investment and operational is GC systems equipped with detectors with the double fragmentation of tested compound (GC–MS/MS). This solution is the newer variant of apparatuses

equipped with ion traps which can register ions formed through secondary multiple collisions with helium atoms. Under optimum working conditions GC–MS/MS systems can show the similar selectivity and level of detection as magnetic systems GC–MS with the high resolving power [116,122,123]. In MS/MS technique the number of additional peaks which make interpretation of chromatograms more difficult is lesser which improves the selectivity of assays. The lowering of chromatograms background and in consequence the increase of the signal value to the noise ratio enables detection of lower acrylamide levels in foods [117]. Results which have been obtained to date indicate that application of SPME to prepare samples that are further analyzed by GC coupled with MS enable accurate identification and quantification of acrylamide in foodstuff [48,74].

The main drawback in GC–MS without derivatization is the lack of characteristic ions in mass spectrum of underivatized acrylamide and interference caused by matrix composition [75,116,124]. In connection with high background noise a low limit of detection is impossible to obtain. Application of gas chromatography coupled with tandem mass spectrometry GC–MS/MS allows to decrease the interference which results in a larger area under the peak corresponding to acrylamide. Values of LOQ and LOD in the GC–MS/MS method for baby food are below 5 $\mu g\,kg^{-1}$ and 1.5 $\mu g\,kg^{-1}$, respectively [71].

Another technique which was found to be useful in determination of acrylamide content is direct solid phase microextraction (DI-SPME) conducted without derivatization. In this method acrylamide is quantified by GC–PCI–MS–MS in the system of monitoring of selected reactions (SRM). This method enables detection of acrylamide in concentration of 0.1 $\mu g\,L^{-1}$ water sample [85].

Other detectors used in a tandem with gas chromatographs to quantify acrylamide are: flame-ion detectors (FID) or electron capture detectors (ECD) [75,87,120]. GC–ECD with prior derivatization by $KBrO_3$ and KBr method was used to determine amounts of brominated acrylamide derivative in fried foods. Electron capture detectors are selective and very sensitive. They are commonly used in quantitative assays of polychlorinated biphenyls, pesticides and other chlorinated compounds. For GC–ECD method, values of LOD and LOQ for potato crisps, potato chips, fried chicken wings, were around 0.1 $\mu g\,kg^{-1}$ and 3 $\mu g\,kg^{-1}$, respectively, which provides evidence of good precision of this relatively new method. Besides, the cost of instruments in GC–ECD system is lower compared to GC–MS/MS while their sensitivity is comparable [120].

A new promising method of acrylamide quantification in foods is based on application of gas chromatography and a highly selective and sensitive nitrogen phosphorus detector (NPD) which is very well suited to analyses of compounds containing atoms of nitrogen and phosphorus [125]. The presence of nitrogen atom in acrylamide molecule makes it measurable by NPD detector. El-Ghorab et al. [125] used the method of head space solid phase microextraction (HS-SPME) and then GC–NPD in quantification of acrylamide generated in model systems by Maillard reactions. Kim et al. [37] formulated a method of acrylamide quantification in samples of fried potatoes, in which they used both GC and NPD. Advantages of this technique comprise simple sample preparation and relatively short time of the whole analysis. Presented results of assays provided evidence that the proposed procedure offered not only the simple sample preparation and fast analysis but was also characterized by sufficiently high precision and sensitivity rendering GC–NPD method useful in acrylamide quantification in foods [37].

5. Capillary electrophoresis

Another group of separation techniques used in acrylamide quantification is based on electrophoresis. Capillary electrophoresis (CE) is a relatively new and still developing, analytical method employed in acrylamide assays in foods. CE is a universal and rapid technique enabling resolution of mixtures of substances, and the simultaneous resolution of polar and nonpolar compounds [52]. The essence of CE is components separation from analyzed samples which takes place in a filled with a buffer solution having the defined pH value quartz capillary (25–75 μm, 50–100 cm) [126]. Charged compounds which are dissolved in the electrolyte migrate to electrodes at different rates when a high voltage is applied [43,127,128]. Thus the resolution of mixture components is driven by high voltage [129,130].

An interesting variant of CE is micellar electrokinetic chromatography (MEKC) which enables separation of charge and uncharged compounds that can undergo ionization due to a change in pH [129,130]. Their separation is based on distribution between the water buffer phase and the pseudo-stationary phase made of micelles [43,53]. Because acrylamide is a polar uncharged compound and cannot move in electric field the rate of its migration depends only on the coefficient of separation between the micelles and water buffer solution. MEKC allows separation and quantitative assay of virtually all chemical compounds soluble in water. Detectors which are used in quantitative analysis of acrylamide by CE technique are usually UV spectrophotometers equipped with a diode matrix (DAD). Another solution is an application of capillary electrophoresis coupled with MS. For this reason some scientists have attempted to use MECK in quantitative analysis of acrylamide in foods [43,131]. Drawbacks of the first MECK techniques were the very low sensitivity and selectivity [132]. In subsequent years the MECK–UV–vis method was improved and enabled content determination in potato chips [43]. This technique is characterized by the low detection limit and can be used to estimate trace amounts of acrylamide in complex matrices. In terms of efficiency and selectivity MEKC is comparable to HPLC [43,127,133].

Further development in electrophoresis field was connected with another promising technique – the capillary zone electrophoresis (CZE) which requires acrylamide derivatization. In this technique, compounds are separated on the basis of different charge to mass ratios. Bermudo et al. [134] used CZE–FASI–UV with precolumn derivatization by using 2-mercaptobenzoic acid to determine the content of acrylamide in foods such as biscuits, crisp bread, cereal flakes, potato crisps and coffee [133,135]. To increase the sensitivity of this method the field amplified sample injection (FASI) technique was used. For crisp bread samples analyzed by this method, the value of LOD was as 3 $ng\,g^{-1}$ [133–135]. The authors provided evidence that FASI–CZE–UV could be an alternative to traditionally used acrylamide quantification methods in food analysis. Later, the same group of researchers proposed how to ameliorate this method by means of application of capillary electrophoresis coupled to the tandem mass spectrometry (FASI–CE–MS/MS). Sample preparation required derivatization by using 2-mercaptobenzoic acid [132]. The use of mass spectrometry is particularly expedient because of the universal character of these detectors [129]. Combination of FASI technique with capillary electrophoresis and tandem mass spectrometry (FASI–CE–MS/MS) yielded a sensitive and selective methodology of acrylamide identification and quantification in foods [129]. Selectivity of this method was very high. Limits of detection and quantification for bread crumb were 8 and 20 $ng\,g^{-1}$, respectively [132]. The authors showed that results obtained by FASI–CE–MS/MS technique were consistent with that obtained by LC–MS/MS.

Mass spectrometers used in combination with capillary electrophoresis are of the same type as those used in liquid chromatography systems [136]. Analyzers which are used in CE-MS systems are: single quadruples, ion traps, time-of-flight analyzers and quadruple TOF [136]. Electrospray ionization (ESI) is the most frequently applied ionization technique in systems composed of an

electrophoretic apparatus and mass spectrometer [137,140,141]. However, the presence of solid salts in buffer solutions used in capillary electrophoresis apparatuses hinders mass spectrometer analysis [138,139]. These salts cause rapid soiling of ionization chamber and slots of spectrometer analyzer while the presence of buffer solutions decreases the efficiency of ionization [52]. For this reason should use the buffers contain nonvolatile salts, like sodium phosphate, or surfactants, like SDS [141,142]. Despite these disadvantages capillary electrophoresis apparatuses are characterized by the good reproducibility of resolution results and high sensitivity [53]. This analytical method enables quantification of pikomole concentrations of chemical compounds.

Non-aqueous buffer solutions were used in novel analytical methods based on electro-migration [53,143]. The use of only organic solvents as the background electrolyte (BGE) solvents can offer significant advantages over aqueous capillary electrophoresis such as improving sensitivity and selectivity [143].

Baskan and Erim [144] developed the method of non-aqueous capillary electrophoresis (NACE) coupled with spectrophotometric UV detection at 200 nm that enables acrylamide quantification in foods. This method is based on modification of acrylamide properties. Because in water solution acrylamide molecules are polar but uncharged they do not migrate in electric field. However, in the solvent with the low pH like acetonitrile, acrylamide molecules bind protons and thereby they gain electric charge and electrophoretic mobility. NACE is more sensitive than CZE coupled with UV detection [134,144]. Because of the low detection limit (4.4 ng mL^{-1}) this method was used to quantify acrylamide in potato chips [135]. Also combination of NACE and ESI-MS/MS is thought to be a promising methodology based on application of non-aqueous buffer solutions [53].

Advantages of electrophoretic techniques are minimized volumes of samples which are required for analysis, the high resolving power, the short time of analysis, and relatively simple equipment. Besides, unlike HPLC techniques they do not require complex clean-up of samples prior to the instrumental analysis [43,145].

6. Bioanalytical methods

6.1. Immunoenzymatic test

Acrylamide quantification can be also conducted by bioanalytical methods. One of them is enzyme-linked immunosorbent assay (ELISA) in which its identification and quantitative determination is based on immunological reaction. ELISA is based on a very specific reaction between an antigen and antibody (which selectively recognizes only this antigen) [146]. This test is used to capture and detect particular antigens or antibodies in tested materials with the aid of antibodies specific to a particular antigen or specific anti-antibodies recognizing a given antibody, which are conjugated (tagged) with an appropriate enzyme [63]. Antibodies are a group of globular proteins categorized as immunoglobulins (molecular mass of 150,000 Da) that are synthesized by immune system in response to the appearance of antigens [63]. Immunoenzymatic tests are characterized by the high specificity and selectivity and enable detection of trace amounts of contaminating substances in foods [56,146]. They are used to quantify such pollutants as aflatoxins and residues of pesticides [56,61,63,147]. Immunochemical methods rely on selective binding of antibodies to organic compounds previously linked to protein molecules which elicited production of these antibodies. In consequence, the specific antibody is bound only to a protein bearing the analyte to be quantified. Quantification consists in the determination of differences in residual, unbound antibodies concentrations [146]. For this purpose, either an indicator antibody linked to an enzyme or an antibody facilitating a very specific detection without any interference with a capturing antibody is used. This effect can be achieved either by using antibodies derived from other animal species or by chemical tagging of the antibody, e.g. by linking with biotin. Usually, the activity of enzyme is determined based on absorbance measurements after conversion of its substrate into colored product of the enzyme-catalyzed reaction [63].

Application of ELISA in acrylamide quantification requires synthesis of specific antibodies which was earlier troublesome because of low molecular mass of this compound [15,148]. In general, substances with molecular mass below 1000 Da are not immunogenic and do not elicit synthesis of antibodies [15,63,147,148]. Preston et al. [60] proposed to use polyclonal antibodies for this purpose. The isolation of acrylamide binding antibodies enabled quantitative determination of acrylamide in foods. Because of the low molecular mass and the lack of strong epitope groups, acrylamide cannot elicit synthesis of specific antibodies itself however, its coupling (as a hapten) to immuno-stimulating carrier proteins was found to be an effective method of stimulation of antibodies synthesis [61,63]. Synthesis of specific antibodies capable of acrylamide binding was achieved after its derivatization by 3-mercaptobenzoic acid (Ade-3-MBA). The acrylamide derivative (Ade-3-MBA) was linked to carrier proteins such as tyreoglobulin (BTG) and human serum albumin (HSA) which were chosen because of good solubility, appropriate molecular mass and sufficient amount of functional groups which can bind acrylamide. Coupling of acrylamide derivative with these proteins is a result of Michael reaction which is based on reaction between an unsaturated compound and nucleophilic group of protein (most often amine or thiol group). The isolated immunogen is used in immunization of laboratory animals (rabbits, mice) that are producers of specific antibodies. Immunization of these animals relies on administration of several doses of the antigen with few weeks pauses because successive doses of the antigen increase the level of immune response of animal organism and intensify the synthesis and accumulation of specific antibodies in blood serum [60]. Acrylamide quantification by ELISA is based on reaction between Ade-3-MBA-HSA antigen with its antibody. Detection of the latter consists in its reaction with the additional specific antibody which is linked to horseradish peroxidase (HPR). Reaction catalyzed by this enzyme yields colored product which in turn enables measurements of absorbance at the wavelength of 450 nm [60]. This method was very specific and the detection level (LOD) of acrylamide derivative obtained by using 3-mercaptobenzoic acid in water samples was as low as 65.7 $\mu g\,kg^{-1}$ [60].

Zhou et al. [62] used another ELISA test (BA–ELISA) employing the system biotin–avidin and polyclonal antibodies to quantify acrylamide in foods. They used N-acryloxysuccinimide (NAS) whose structure is alike acrylamide as the antigen. It was conjugated with an immunostimulator such as bovine serum albumin (BSA) and used to stimulate synthesis of antibodies. Application of biotin–avidin system considerably increased the sensitivity of detection [62]. High sensitivity of detection is vitally important in acrylamide quantification by immunoenzymatic techniques.

The main factor affecting the sensitivity of ELISA tests is an affinity of antibodies to the antigen and the sensitivity of detection methods. Advances in immunoenzymatic methodology gave rise to application of chemiluminescence techniques which employ chemiluminescence markers (luminol) emitting light with defined wavelength in consequence of reaction that in turn enables measurements of concentration of target substance [61]. In chemiluminescence methods the antigen combines with the specific antibody linked to the HPR. Then this peroxidase catalyzes the oxidation of luminol by hydrogen peroxide giving the product with the lower energy [149]. Quan et al. [61] combined the test ELISA with enhanced chemiluminescence (ECL) to quantify acrylamide in food products such as potato crisps, instant noodles, biscuits

and cakes. They used polyclonal antibodies obtained by immunization of rabbits with N-acryloxysuccinimide (NAS) and keyhole limpet hemocyanin (KLH). Combination of ELISA with ECL instead of conventional colorimetric techniques considerably increased the sensitivity and selectivity of immune tests and eliminated the interference caused by matrix components which is encountered in analyses of potato chips and biscuits [61,149]. Chemical compounds such as acrylic acid, propanoic acid, propanamide and asparagine were used to determine the selectivity of ECL–ELISA. These assays revealed the high specificity of isolated antibodies to acrylamide. Detection limits for the tested samples of potato crisps, instant noodles, biscuits and cakes were 126, 41, 137 and 69 ng mL^{-1}, respectively [61].

Results of acrylamide quantification by immunoenzymatic techniques and HPLC were consistent [61,62]. In contrast to chromatography and electrophoretic techniques, immunoenzymatic assays require neither specialist and expensive equipment nor multi-step sample preparation, and can be used in routine analyses of multiple samples [61,146]. Additional advantages of these methods are sufficient precision, high sensitivity, low costs, short time and simplicity [56,147,150]. Because of these advantages ELISA tests can be used in acrylamide quantification in various food products [62]. The survey of literature provides evidence that modern immunochemical techniques enable rapid screening of multiple samples without the need of specialist equipment [56].

6.2. Biosensors

The novel bioanalytical technique which is used to quantify acrylamide in foods involves electrochemical biosensors. In this method analytes are quantitatively determined by using highly selective bioreceptors whose function is based on natural affinity of biologically active compounds to the substance of interest. Biosensors are a promising solution to acrylamide quantification in foods because they offer many advantages over other methods such as the relatively low price, high sensitivity and selectivity even in case of samples characterized by the complex matrix composition, as well as possibility of miniaturization which in turn enables on-line uses [151–153]. Furthermore, application of biosensors is less expensive compared to other selective methods like HPLC [154]. Biosensors are widely used in detection of pathogenic microorganisms and their toxins, and monitoring of levels of pesticides, allergens and antibiotics [151,155]. Biosensors are a group of sensors in which the analytically active, biological part (biochemical receptor) can be connected to various processors [155–157]. There are six principal types of biosensors which differ in the method of transduction of biological signal (e.g. electrochemical, optic, thermal, mass (piezoelectric), magnetic and micromechanical) [152].

During the last 10 years electrochemical techniques of detection have been gaining the increasing popularity among processing systems because of their high sensitivity, simplicity and possibility of miniaturization [154]. These techniques are based on measurements of the difference between the intensity of electric current flowing through the stationary indicator electrode and the potential of this electrode [152]. Basing on the mode of measurements of reaction effects, the electrochemical sensors fall into: potentiometric, amperometric and voltamperometric, conductometric and impedimetric [152,158,159]. Amperometric and voltamperometric techniques are most frequently used in electrochemical biosensors applied in quantification of trace amounts of acrylamide [154]. The majority of them employ methods of cyclic voltamperometry (CV) and square wave voltamperometry according to Osteryoung (OSWV) that provide information about processes of oxidation and reduction [45,57–59]. Also piezoelectric biosensors are often used in bioanalytical methods. Biological components of biosensors can be enzymes, apoenzymes, antibodies, natural receptors, whole microorganisms, fragments of tissues, single cells, DNA, and RNA [159]. Processors convert biological reaction into the biological or biochemical signal, or into the measurable electric signal, which can be further amplified and changed into the analytical signal [159]. The function of biosensors is based on specific interactions (receptor–analyte) between enzymes and their substrates, on mutual recognition of antibodies and antigens, on the accessibility of specific molecules to their receptors or on the very high affinity of nucleic acids to their complementary sequences [152,160]. Modern biosensor technologies focus on the development of tools capable of detecting numerous analytes that may be used in food analysis [152].

Many biosensors use whole microbial cells for detection of single chemical compounds and determination of their toxicity. Their application does not require complex sample preparation and various microbial cells can be used for this purpose [161]. First trials of application of these biosensors in acrylamide quantification were described by Ignatov et al. [162] who used an amperometric biosensor equipped with oxygen Clark electrode as a processor. By using this system they measured the respiratory activity of bacterial *Brevibacterium* sp. cells which was affected by the presence of acrylamide and acrylic acid in waste waters. The analytical reaction of amperometric sensor was accompanied by oxygen consumption [162,163]. The presence of analyte in sensor's cell decreased the concentration of oxygen at the surface of the sensor which in turn decreased the intensity of current in Clark electrode. In the absence of acrylamide the respiratory activity of cells was found to be the measure of acrylic acid content [164]. The sensitivity of this method is very high (10 mg L^{-1}) [162]. Its other advantages are the relatively short time of assays, simplicity of sample preparation and contribution to the development of acrylamide quantification procedures [162,165].

Recent advances in biological methods enabled construction of a new type of sensors characterized by the high sensitivity and selectivity which enabled quantification of trace amounts of acrylamide in samples containing various complex matrices [166]. Their examples are potentiometric biosensors based on ion-selective electrodes which were constructed by Silva et al. [166] who used as detectors cells of *Pseudomonas aeruginosa* displaying the activity of amidase. This enzyme catalyzes hydrolysis of acrylamide to acrylic acid and ammonium ion. Whole bacterial cells were immobilized on the surface of a polymer membrane by cross-linking with glutaraldehyde and then incorporated into the ammonium ion-selective electrode [166].

Reports on acrylamide quantification in foods by using specific biosensors have been rather scarce. Biosensors based on cells are used not only to quantify various chemical compounds but also to determine biological effects of their presence in the natural environment such as oxidative stress, which provides more information about investigated analytes [167,168]. The exposition to a specific analyte (stressor) causes chemical or physical changes in cells. Biosensors measure these changes in the physiology or behavior of organisms which are results of the stress caused by toxic compounds [169,170]. Hasegawa et al. [167] used cellular biosensors to quantify acrylamide and to find a food product reducing or inactivating effects of acrylamide action. Acrylamide is known to be a xenobiotic causing oxidative stress in living systems. The authors used a biosensor employing transgenic bacterium *Caenorhabditis elegant* bearing fusion gene *gst-4*::*gfp* constructed from the promoter gene *gst-4* and reporter gene *gfp*. The presence of acrylamide induced the transcription of the reporter gene which in turn switched on synthesis of the easily measurable green fluorescent protein (GFP) [167].

Further advances in biosensors construction were achieved through application of acrylamide-binding tetralactam (a macrocyclic compound of Hunter–Vögtle type) as an active component of

a biosensor. Kleefisch et al. [153] used a gravimetric sensor containing tetralactam for acrylamide quantification in a gaseous phase. This sensor was built of a quartz crystal coated with tetralactam film. It was found to measure precisely the content of acrylamide at the gas–solid interface [47,153]. When the vapors from the sample interacted with the film coating the crystal, acrylamide was bound by the tetralactam and the mass of the sensor was slightly increased. This slight increase was measurable because the rise in mass of the film deposited on the surface of quartz crystal changed the frequency of its resonance vibrations [153]. Measurements of these minor frequency changes are conducted by the quartz crystal microbalance technique (QCM) [153]. The macrocyclic compound of Hunter–Vögtle type was also found to be a suitable host enabling detection of trace amounts of acrylamide (a guest) in piezoelectric sensors [59,153]. Experiments showed that this compound displayed the considerably higher affinity to acrylamide than to related compounds like acrylic acid and propionamide. Therefore, piezoelectric sensors containing tetralactam display the high selectivity and sensitivity of acrylamide measurements ($10\ \mu g\ kg^{-1}$) and are almost insensitive to changes in the relative humidity [59,153]. Despite of these advantages these biosensors are not applicable to acrylamide quantification in some sorts of food.

Methods employing hemoglobin immobilized on the surface of electrodes as a receptor of acrylamide were used as one of first to quantify this compound in water extracts from food products [57–59]. The function of biologically active receptors in biosensors is based on their natural affinity to detected substances. One of such biologically active compounds which can bind certain substances is hemoglobin [171]. Acrylamide is known to form adducts with hemoglobin. These adducts are biomarkers of exposition to this toxic compound and are generated through Michael reaction between acrylamide and valine α-NH_2 group located on N-terminus of hemoglobin polypeptide chain [57,58,171,172]. Therefore, hemoglobin can be used as a bioactive receptor of a biosensor. Stobiecka et al. [57] developed a method of acrylamide quantification involving hemoglobin immobilized on the surface of electrodes as a receptor. The function of this biosensor is based on formation of adducts between hemoglobin and acrylamide. The voltamperometric sensor was constructed from carbon paste electrodes (CPE) coated by liposomes DDAB–Hb obtained through dispersion of hemoglobin and a surfactant (dimethyldioctadecylammonium bromide, DDAB) in acetate buffer solution [173]. Formation of Hb–acrylamide adducts changes the structure and electroactivity of hemoglobin immobilized on the surface of the electrode which in turn generate the response of voltamperometric biosensor [57,59]. A consequence of an increase in the concentration of Hb–AA adducts on the surface of electrode is the irreversible reduction of Fe(III) ions to Fe(II) ions in heme, which is a prosthetic group of hemoglobin [58]. Results of voltamperometric measurements provide quantitative and qualitative information about electrochemical reactions and their outcome is the accurate information about acrylamide content in tested samples [174]. The limit of acrylamide detection in samples of potato chips by using the voltamperometric biosensor was very low ($1.2 \times 10^{-10}\ mol\ L^{-1}$) [57].

The key problem in construction of biosensors is the immobilization of biological component on the surface of signal processor ensuring the stability of this biomaterial [156,175]. Adsorption of biomolecules such as hemoglobin on the surface of electrode frequently leads to their denaturation and inactivation. Optimization of immobilization methods aiming at the stabilization of biological components of sensors used in acrylamide quantification in foods was conducted by many researchers. It was found that nanoelements like carbon nanotubes (CNT) or colloidal gold act as stabilizers of biological elements. Besides the nanotubes are thought to support electron transfer in electrochemical reactions [173]. Krajewska et al. [59] used the voltamperometric biosensor containing immobilized hemoglobin and glass carbon electrodes (GCE) modified with single wall carbon nanotubes (SWCNT) in acrylamide detection in water extracts of food products. The sensitivity of electrodes was not affected by matrix components extracted from potato chips. Measurements of acrylamide concentration were carried out by using square wave voltamperometry technique according to Osteryoung (OSWV) which was chosen because of the higher sensitivity with respect to acrylamide compared to the cyclic voltamperometry (CV) technique [59]. For this method and the sample containing the matrix of potato chips, the limit of detection was as low as $1.0 \times 10^{-9}\ mol\ L^{-1}$ [59]. In another study, these authors used in acrylamide quantification gold electrodes coated with either tetralactam or its acyclic derivative and demonstrated the usefulness of this system in acrylamide assays in aqueous solutions of matrices from potato chips [58,176]. Biosensors used by Krajewska et al. [58] were obtained by coating electrodes with probes containing the disulfide bonds capable of forming covalent Au–S bonds. Receptor molecules containing lipophilic side chains were bound by hydrophobic interactions and van der Waals bonds. This immobilization method is relatively simple and therefore it is often used in construction of biosensors based on hybridization reaction. Garabagiu and Mihailescu [177] used another method, based on formation of adducts between acrylamide and hemoglobin (redox protein) to improve the sensitivity of electrochemical biosensors. They constructed the electrochemical cell from gold nanoparticles and hemoglobin deposited onto the surface of indium–tin-oxide (ITO) glass electrode. Their Hb–GNP–ITO glass electrochemical sensor was characterized by very high sensitivity with respect to acrylamide and therefore it is well suited to quantification of low levels of acrylamide in foods (down to 10^{-8} M) [177].

Measurements conducted by using this technique usually do not require time-consuming sample preparation [57]. Advantages of biosensors are their high sensitivity and selectivity, resistance to interference caused by matrix components and very simple mode of operation making them well suited to acrylamide quantification in foods [57,178,179]. Due to these advantages biosensors are an excellent alternative to expensive and time-consuming chromatographic and electrophoretic methods [153,162]. Therefore, the dynamic development of biosensor technology enabling quantification of acrylamide in foods has been recently observed.

7. Conclusions

The survey of methods used in acrylamide quantification in foods demonstrates that the one universal procedure being appropriate in analysis of all types of products does not exist because protocols of sample preparation prior to the analysis are in most cases complicated and application of expensive reagents is necessary. Therefore, acrylamide concentration has been determined by relatively few laboratories, which apart from modern analytical equipment use also complex techniques of sample preparation before instrumental analyses. The necessity of acrylamide assays in foods gave rise to the development of numerous techniques and analytical methods.

Chromatography methods enable fast, accurate and reproducible determination of acrylamide. Currently apart form popular high performance liquid chromatography (HPLC) also the newer, ultra performance chromatography (UPLC) has been used. Application of newer chromatographs requires improvement of sample preparation methods and development of new conditions of the whole analysis protocol.

The rapid development of analytical techniques considerably improved precision, accuracy and sensitivity of methods used in

Table 1
Examples of analytical methods used for determination of acrylamide in foodstuff.

Matrix	Method	Sample preparation	Recovery	LOD/LOQ	Comments	Ref.
Coffee and cocoa	LC–MS/MS, ESI	Extraction with water, protein precipitation with Carrez I and II solutions, liquid–liquid Extraction with ethyl acetate, SPE with Isolute Multimode® cartridges	93–99%	LOD 10 μg kg^{-1} LOQ 20 μg kg^{-1}	Multi-step preparation, reliable and efficient analytical procedure	[81]
Tea	LC–MS/MS, ESI	Extraction with water, liquid–liquid extraction with acetonitrile with $MgSO_4$ and NaCl, SPE with Oasis MCX cartridges	74–79%	LOD 1 ng mL^{-1} LOQ 5 ng mL^{-1}	Rapid and effective pretreatment, high sensitive analytical procedure	[87]
Potato crisps	UPLC–MS/MS, ESI	Deffating with petroleum ether, extraction with 2 M NaCl in water, liquid–liquid extraction with ethyl acetate, SPE with Oasis HLB cartridges	82–99%	LOD 1 μg kg^{-1} LOQ 3 μg kg^{-1}	Simple preparation, rapid and high sensitivity analytical procedure	[94]
Deep-fried flour-based	HPLC-UV/DAD	Extraction with water, SPE with Oasis HLB SPE and Varian Bond Elut-Accucat cartridges	78–107%	LOD 6 μg kg^{-1} LOQ 23 μg kg^{-1}	Effective, simpler pretreatment, accurate and inexpensive analytical procedure	[90]
Potato chips and crisps	LC-UV/DAD	Extraction with methanol, protein precipitation with Carrez I and II solutions, SPE with Oasis HLB cartridges	93–97%	LOD 2 μg mL^{-1} LOQ 4 μg mL^{-1}	Simple, rapid preparation and inexpensive analytical procedure	[72]
French fries	GC–MS, EI	Extraction with water, SPE whit Oasis HLB and Oasis MCX cartridges, derivatization with bromination reagent (KBr, HBr, bromine water), liquid–liquid extraction with ethyl acetate, dehydrobromination with triethylamine	102–110%	LOD 5 μg kg^{-1} LOQ 10 μg kg^{-1}	Time-consuming preparation, high sensitivity analytical procedure	[117]
Tea	GC–MS, EI	Extraction with water, SPE with Isolute Multimode® cartridges, derivatization with bromination reagent (KBr, HBr, bromine water), liquid–liquid extraction with ethyl acetate	94–108%.	LOD 0.2 ng mL^{-1} LOQ 0.6 ng mL^{-1}	Time-consuming preparation, high sensitivity and accurate analytical procedure	[122]
Various foods	GC–MS, EI	Extraction with water, MSPD with C_{18} sorbent, derivatization with bromination reagent (KBr, HBr, bromine water), liquid–liquid extraction with ethyl acetate	1–7% (precision)	LOD 5.2 μg kg^{-1} LOQ 15.7 μg kg^{-1}	Simple pretreatment, high sensitive analytical procedure	[80]
Cereals	SPME/GC–MS	Extraction in acetonitryle, silylation with BSTFA, headspace sampling whit SPME fiber	102–103%	LOD 0.9 μg kg^{-1} LOQ 3 μg kg^{-1}	Simple and rapid pretreatment, specific and very high sensitive analytical procedure	[74]
Fried foods	GC–ECD	Deffating with *n*-hexane, extraction with aqueous solution NaCl, derivatization with $KBrO_3$ and KBr, and liquid–liquid extraction with ethyl acetate	87–97%	LOD 0.1 μg kg^{-1}	Simple and fast pretreatment, specific and very high sensitive and low-cost analytical procedure	[120]

Table 1 (*Continued*)

Matrix	Method	Sample preparation	Recovery	LOD/LOQ	Comments	Ref.
Potato chips	MEKC–UV–vis	Extraction with methanol, deffating with hexane, diluting with electrolyte $Na_2B_4O_7$-SDS	91–99%	LOD 0.1 μg mL^{-1} LOQ 0.33 μg mL^{-1}	Simple pretreatment, accurate and inexpensive analytical procedure	[43]
Crisp bread, biscuits and snacks	CZE–FASI–UV	Extraction with water, deffating with hexan, SPE with Strata-X-C and ENV+ cartridges, derivatization with 0.01 M NaOH and and 2-mercaptobenzoic acid liquid–liquid extraction with dichloromethane, reconstituted in water	16% (precision)	LOD 3 ng g^{-1}	Time-consuming pretreatment, very high sensitive and low-cost analytical procedure	[133]
Water	ELISA	Dissolving in DMSO and 1 M NaOH, addition cationised HSA, BTG and HRP protein, dialysis, dissolving in 0.9% NaCl, derivatization with 3-mercaptobenzoic acid,	–	LOD 65.7 μg kg^{-1}	Analytical procedure specific and inexpensive	[60]
Potato crisps	Hb–DDAB carbon-paste electrode	Extraction with water, deffating with hexane, precipitation with Carrez I and II solutions, addition 0.2 M CH_3COOH and 0.05 M NaBr, adjusted to pH 4.8 with 0.1 M NaOH	–	LOD 1.2×10^{-10} M	Very simple preparation and very good selectivity analytical procedure	[57]

acrylamide analysis. Time-consuming and multi-step procedures of sample preparation prior to acrylamide quantification by chromatography or electrophoresis techniques spurred search into development of fast, easy to use, sensitive and inexpensive analytical methods.

One of them is immunochemical analysis which is based on selective binding of antigens to be quantified by antibodies. Other promising methods involve highly specific biosensors interacting only with one substance contained in a complex matrix. Despite intensive development in this field many of presented techniques have been still tested in laboratories. Table 1 contains examples of analytical methods which have been used to quantitative analysis of acrylamide in foodstuff.

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