Synthetic Bioactive Compounds and Chromatography

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Natural and synthetic bioactive compounds occur in foods in small quantities and represent a wide group of chemical compounds. Because of the complexity of food matrices, the separation and next accurate determination of their bioactive constituents with different chemical structure requires an universal analytical methodology like liquid and gas chromatography or combination of both chromatographic techniques.

Keywords: bioactive compounds ; food ; separation techniques ; liquid chromatography ; gas chromatography

1. Introduction

Food samples are very complex mixtures consisting not only of naturally occurring bioactive compounds with beneficial role on human health like for example vitamins, minerals, antioxidants but other substances coming from agrochemical treatments i.e., pesticides as well as promotors animals growth or veterinary drugs. Therefore monitoring the level of different veterinary drugs or organic pesticides coming from agrochemical treatments in food and food products could ensure the safety of potential consumers. Natural and synthetic bioactive compounds occur in foods in small quantities and represent a wide group of chemical compounds. Because of the complexity of food matrices, the separation and next accurate determination of their bioactive constituents with different chemical structure requires an universal analytical methodology like liquid and gas chromatography or combination of both chromatographic techniques.

For this fact, this article reviews new strategies including advanced equipment and validation parameters of liquid and gas chromatography methods dedicated for the identification and quantitative analysis of natural and synthetic bioactive compounds occurring in food and food products within the period of 2019–2021 (January). Special attention is given to optimization including the validation process of chromatographic analysis performed by using thin-layer chromatography (TLC), high-performance liquid chromatography (HPLC), and gas chromatography (GC) coupled with different detection modes ((TLC-UV/Vis, TLC-densitometry, HPTLC-MS, HPLC-UV/Vis, HPLC-DAD(PDA), HPLC-MS, HPLC-MS/MS, HPLC-TQ-ESI-MS/MS, GC-MS , GC-MS/MS, GC-CPI-MS/MS)) as well as the combined chromatographic techniques e.g., HPLC/GC that may be valuable for the separation, screening, quantitative determination or evaluation of certain physicochemical and pharmacological properties of many including the newly developed natural and synthetic bioactive compounds in food and food products.

2. Thin Layer Chromatography

Liquid chromatography, including thin-layer chromatography, along with other chromatographic techniques, is one of the most popular methods used in the current analysis of bioorganic and bioinorganic compounds in different including food samples [1][2][3][4][5][6][7][8][9][10][11][12][13][14].

The recently published papers indicate that thin-layer chromatography was successfully used for the quantification of selected antibiotics, alkaloids, aromatic amines, and gallic acid in food [1][2][3][4]. [2] shows a rapid and sensitive HPTLC method with densitometry for the quantification of trigonelline content as important bioactive constituent of Arabic coffees at the level of ng/spot [2]. Another study [3] indicates the use of HPTLC-DPPH (high-performance thin-layer chromatography coupled with the use of 2,2-diphenyl-1-picrylhydrazyl) method for rapid and simple screening of antioxidant constituents i.e., gallic acid in honey, in natural food products. Another study describes a novel and fully validated HPTLC-MS method for the rapid identification and determination of toxic aryl azo amines in food matrices.

Another authors; Turkmen and Kurada [6] confirmed the utility of HPTLC on silica gel 60F254plates with densitometric measurements to asses next toxic compound, namely patulin as contamination of fruit-based baby foods in Turkey.

In the vast majority of analyzes, fatty acids are investigated using the GC technique as fatty acid methyl esters. However, Dąbrowska et al. [7] developed a TLC method in combination with densitometry for the determination of omega-3 fatty acids: linolenic (ALA), docosahexaenoic (DHA), and eicosapentaenoic acids (EPA) in 15 dietary supplements and 5

cooking products.

Some studies indicate the important role of TLC and HPTLC methods as comprehensive techniques for the detection and identification of pesticides and the toxicity caused by these compounds [8][9][10][11][12][13][14]. Several new chromogenic reagents have been reported in the literature such as diphenylamine reagent for detection of organochloro insecticide endosulfan [8], stannous chloride and hydrochloric acid (reducing reagent) followed by a sodium nitrite in hydrochloric acid (coupling reagent) and β-napthol in sodium hydroxide for the detection of herbicide oxyfluorten [9], chloranil reagent with nitric acid for detection of organophosporus insecticide monocrotophos [10], 4-amminoantipyrene reagent with potassium ferricyanide for detection and identification of 2,4-dichlorophenol, an intermediate of 2,4-D (2,4-dichlorophenoxyacetic acid) herbicide [11], cupric acetate reagent for detection of organophosphate insecticide profenofos [12], and cobalt thiocyanate reagent for detection of organophosporus herbicide glyphosate [13]. [14] developed an HPTLC method for the determination of residues of various pesticides in brinjal samples from a market of Pakistan. The authors showed that HPTLC can be an alternative method to HPLC for the detection of pesticide residues.

The scientific literature cited and discussed above indicates that TLC/HPTLC can be successfully used to detect and quantify a wide variety of synthetic and natural classes of bioactive compounds occurring in food and food products. There are many reports in the scientific literature combining TLC with a densitometry. However, there is an increase of works linking TLC with MS. Therefore, it seems that in the next few years there should be more scientific papers using TLC/MS.

3. Column Liquid Chromatography

Extensive review of literature published in the two last years indicates that high-performance liquid chromatography (HPLC) with different detection systems such as ultraviolet detector (HPLC-UV), photodiode array detector (HPLC-PDA), or coupled to mass spectrometry or tandem mass spectrometry called as HPLC-MS and HPLC-MS/MS respectively is a powerful analytical tool with many applications including food analysis [15][16][17][18][19][20][21][22][23][24][25][26][27][28][29][30][31][32][33][34][35][36][37][38][39][40][41][42][43][44][45][46][47][48][49][50][51][52][53][54][55][56][57][58][59][60][61][62][63][64][65].

Due the widespread use of agricultural chemicals in food production, people are exposed to low levels of pesticide residues through their diets. Because the organic pesticides usually exist in very small amounts in food samples and have different chemical structure containing, for example, triazine, imidazolinone, phenyluracyl, or macrocyclic lactone structure, thus there is a need to develop efficient and sensitive CLC systems for the simultaneous determination of compounds that are dangerous to human health, present in food and food products which belong to one of the presented groups as well as to various groups (i.e., multiclass pesticides) The current literature review indicates that validated high performance liquid chromatography is a powerful analytical technique used to determine many single or multi-class pesticides present in different food matrices. Because of its high selectivity and sensitivity, HPLC and UHPLC in combination with MS/MS have mostly been used in this field especially to determine the insecticides and herbicides belonging to organophosphorus compounds, imidazolinone and pyridine carboxylic acid derivatives, and in study of samples containing multiclass pesticides [15][16][17][18][19][20][21][22][23][26][29][30][31][32][33].

However, owing to the new SPE (solid phase extraction) systems consisting novel polymers as adsorbents e.g., porous organic polymer Car-DMB, Py-DMB HCP (heterocyclic hypercrosslinked polymer), HPLC analysis further allows the quantification of some pesticides in food samples at concentrations of ng/g [24][27]. In addition, the HPLC-MS/MS methods with electrospray ionization (ESI) and quadrupole trap (QTRAP) in multiple reaction monitoring (MRM) mode have been also employed in the analysis of various pesticides [22][23][29][33]. Whereas UHPLC-Q Orbitrap-ESI-MS/MS has been applied for the determination of highly polar pesticides and contaminants (glyphosate, aminomethyl phosphonic acid (AMPA), phosphonic acid, fosetyl-Al, chlorate, and perchlorate) in processed fruits, vegetables, and infant foods [21].

Studies [18][32] indicate that chiral LC-TQ-ESI-MS/MS and UPLC-TQ-ESI-MS/MS in MRM mode have been successfully applied to the simultaneous enantioselective determination of chiral pesticides in different vegetables and fruits. Martínez et al. [26] determined 27 acidic herbicides and 8 phytohormones in fruits and vegetables using UHPLC-TQ-ESI-MS/MS technique in the MRM mode.

Several papers created during the last two years [34][35][36][37][38][39][40] demonstrate the importance of different CLC procedures to determine selected veterinary drugs in animal food and food products belonging to various groups including non-steroidal anti-inflammatory agents (NSAIDS), some antibiotics, and others according to EU Commission Decision 2002/657/EC requirements [34] to guarantee food safety.

Whereas, LC-MS/MS methods with triple quadrupole (TQ), electrospray ionization (ESI) in multiple reaction monitoring (MRM) mode have been used for the determination of multiclass NSAIDs in meat of swine, chicken, eggs, and bovine [36][37][39]. Developed chiral UHPLC-TQ-ESI-MS/MS in MRM mode have been successfully applied to the simultaneous determination of four profens enantiomers including naproxen, carprofen, indoprofen, and flurbiprofen in fish tissues [38]. The obtained LODs and LOQs for each enantiomer ranged from 1 to 8 ng/g and 2 to 10 ng/g, respectively [38].

Kurjogi et al. [48] applied an HPLC-UV for the detection of antibiotics in milk samples originating from the dairy herds located in India. Similarly, Dinh et al. [49] elaborated QuEChERS-LC-MS/MS clean up method with UHPLC-MS/MS for the analysis of sulfonamides and potentiators, macrolides, lincosamides, quinolones and fluoroquinolones, nitrofurans, nitroimidazoles, chloramphenicol, triphenyl-methane dyes, teracyclines, and metabolites in cultured and wild seafood sold (in red-meat fish, white-meat fish, and shrimp).

Studies confirm the vital role of HPLC with diode array detection method and mass spectrometry for the analysis of some steroids in current residual food analysis of meat products and eggs coming from farmed animals, thus to control steroids in meat [41][42]. A reliable and sensitive UHPLC-MS method was also constructed by Han and Liu to detect 17 endogenous and exogenous steroid hormones including estrogens, androgens, glucocorticosteroids, and mineralocorticosteroids in Antarctic krill (Euphausia superba Dana) [43].

Another study shows the utility of HPLC with MS/MS based on the operation of a triple quadrupole (LC-ESI-MS/MS) for quality control of the species of meat or products by determining the presence of thermostable dipeptides (e.g., anserine, carnosine and balenin) [50].

Some studies demonstrate the important role of HPLC with UV, DAD, or FL detector as well as UHPLC-MS/MS in the study of patulin (mycotoxin) and related compounds in fruits e.g., mangoes, apples, grapes, oranges, and fruit products (juices and drinks) for children [51][52][53][54][55][56][57]. In this case C18 column and different usually binary mobile phases consisting, for example, of eluent A: 10 mM ammonium acetate in water and eluent B: 10 mM ammonium acetate in methanol [51] or acetonitrile-water [53] with gradient elution have been successfully applied. These methods allowed determining patulin at different levels given in µg/mL or µg/kg [51][52][53][54][55][56][57].

Several authors have also described the analytical methodologies based on HPLC to characterize the food composition i.e., to detect especially a new bioactive compounds with nutritional value and a proper biological activity, for example, antioxidant properties that are present in vegetables and fruits consumed in various countries. Developed methods are necessary to control the quality/authenticity of food and have been carried out by researchers during the last two years.

Numerous studies indicate that HPLC is the method of choice due to its precision and sensitivity for the determination and quantification of natural as well as synthetic antioxidants in various food/food products [44][45][46][58][59][60][61][62][63]. The main group of antioxidants investigated were phenolic compounds, especially phenolic acids, catechins, and flavonoids. [44] developed and validated an HPLC-DAD method for the identification of selected synthetic phenolic antioxidants (SPAs) in chewing gum, noodle, snacks, nut, chocolate, fruit juices, coffee, oat, and biscuits. [58] shows the utility of this technique for the determination of phenolic acids (16) and flavonoids (14) profiles in honey samples, thus for quality control of honey.

Gbylik-Sikorska et al. [45] developed for the first time an UHPLC-MS/MS method for the estimation of the pharmacokinetic parameters of quercetin in milk samples of dairy cows.

A few papers indicate the HPLC studies of different phenolic compounds in green coffee and the fruits of the three European plum cultivators [46][59].

Pepe et al. [60] undertook the study of the composition of polyphenols (26) and anthocyanins (12) found inCitrus sinensisandVitis vinifera. RP-UHPLC-PDA combined with LCMS-IT-TOF (ion trap-time of flight mass spectrometer) was used in analysis of polyphenols and anthocyanins. HPLC with UV-Vis detection was also used for the determination of anthocyanin in skins and seeds of five Greek red grape varieties [61].

Similar study by means of HPLC-MS/MS method was performed to estimate the contents of some antioxidant components in grapevine seedsVitis viniferaL cultivated in Italy [62]. The results of chromatographic analysis confirmed the presence of nine major flavonoids (apigenin, astragalin, hyperoside, isorhamnetin, kaempferol, myricetin, quercetin, quercitrin, and rutin) and two procyanidins (procyanidin A2and procyanidin B) in the studied extracts.

Carotenoids and polyphenols were evaluated and quantified by HPLC-DAD and UHPLC-Q-Orbitrap HRMS, respectively, in two-pigmentedLactuca sativa L. var.[63]. Separation and quantification of carotenoids were performed by HPLC-DAD on C18 column. Polyphenols analysis was performed by UHPLC-Q-Orbitrap HRMS on biphenyl column. LODs and LOQs of

analyzed compounds were in the range of 0.03–0.05 and 0.10–0.16 ng/g, respectively.

Another author Cirilli et al. [64] investigated iberin (an isothiocynate with chemoprevention of different tumors) in natural products and in different food supplements. Analysis was performed by UHPLC-PDA-ESI/MS. Three degradation products of iberin were identified, namely: thiourea, methyl thiocarbamate, and ethyl thiocarbamate.

Summarizing, it can be stated that the studies described above confirm that validated high-performance liquid chromatography methods coupled with DAD, UV-Vis, MS/MS, and HPLC-TQ-ESI-MS/MS are the powerful tools in analysis i.e., separation, identification, and quantification of different natural and synthetic bioactive compounds occurring in food and food products for different purposes, i.e., authenticity and safety of food and food products.

It was stated that examined by column liquid chromatography bioactive compounds in food samples belonged to different chemical classes e.g., steroids, phenolic compounds, variety antibiotics (fluoroquinolones, tetracyclines, β-lactams), organophosphorus, phenyluracyl or triazines pesticides, and others. Therefore, both the factors, chemical diversity and the complexity of investigated mixtures, i.e., the kind of studied matrix were the biggest challenges in the case of HPLC technique and were accurately described in this review paper. A broad variety of packing material of column including a new one such as molecularly imprinted magnetic polymers as well as modern extraction systems like solid-phase extraction and salting-out extraction combined with switchable-hydrophilicity solvent liquid–liquid microextraction to sample preparation allow separation and quantification of new bioactive compounds like synthetic antioxidants or trace levels of different chemical groups of pesticides simultaneously (i.e., multiclass pesticides) in food. The use of chiral stationary phases improves the separation and determination of the selected stereoisomers (S- and R-form) of some imidazolinonen herbicides in food samples (e.g., soybean, peanut, wheat, maize, rice) and some NSAIDs belonging to profens

Properly validated for optimal conditions HPLC method by means of DAD (PDA) and UV-Vis detector with gradient elution program makes this technique enough sensitive for the quantitative determination of different bioactive compounds including the selected pesticides and drugs in food samples in μg/mL or ng/g, respectively.

4. Gas Chromatography

Recent literature review shows that gas chromatography coupled to single or tandem mass spectrometric approaches (GC-MS, GC-MS/MS) served as an efficient tool for the determination of various organic compounds in food samples. GC was used to quantify: 200 multiclass pesticides in fruits [66]; 14 lipophilic pesticides in raw propolis [67]; 5 organophosphorus pesticides (OPPs) in fruit juice and water [68], endocrine disrupting chemicals (EDCs) i.e., alkylphenols; 4 phenylphenols, bisphenol A; 7 parabens; 11 OPPs and triclosan in different cereal-based foodstuffs [69]; 4 isomers of hexachlorocyclohexane; 6 pyrethroid pesticides i.e., bifenthrin, fenpropathrin, cyhalothrin, cyfluthrin, cypermethrin, deltamethrin in milk [70]; 133 multiclass pesticides in pericarpium citri reticulatae (chenpi) [71]; 5 NSAIDs i.e., ibuprofen, paracetamol, diclofenac, naproxen, ketoprofen; 3 natural estrogens i.e., estrone, 17β-estradiol, estriol in MusselsMytilus edulis trossulus[72] , glyoxal and methylglyoxal in different alcoholic beverage and fermented foods [73], essential fatty acids in cereals and green vegetables [74], and fatty acids in grilled pork [75].

Crude fat, total saturated acids, and totaltransfatty acids in home meal replacements, and restaurant foods were analyzed using GC-FID Total crude fat contents were 0.61 ÷ 6.75 g/100 g, and 0.22 ÷ 5.69 g/100 g for home meal replacements and restaurant foods, respectively. Totaltransfatty acids contents were 0.0 ÷ 0.11 g/100 g, and 0.0 ÷ 0.07 g/100 g for home meal replacements and restaurant foods, respectively [76]. The authors of the study compared the total fatty acid concentration (saturated, unsaturated, omega-3, omega-6, the ratio of saturated and unsaturated, omega-3/omega-6 fatty acids and trans fatty acids) [77].

Study [78] shows the applicability of GC-MS analysis for identification of chemical components with different activity including antioxidant properties of varieties, not well described in literature, of edible plants and fruits cultivated in different countries. GC-MS was successfully applied for the separation and identification of chemical components with antioxidant activity such as different phenolic acids from citrus fruits cultivated in India i.e., grapefruits. The major components found were: limonene, methyl-cyclohexane, hexane-3-one, 3-hexanol, 2-hexanol, myrcene, sabinene, nonanal, neral, geranyl acetate, ostole. These compounds might contribute to the antioxidant activity of the juice and oil [78].

The reviewed papers confirm that gas chromatography has recently been used to study food and edible plants (the contents of pesticides, endocrine disrupting chemicals, NSAIDs, natural estrogens, glyoxal, methylglyoxal, fatty acids, compounds with antioxidant properties, such as e.g., flavonoids, phenolic compounds). The most commonly used gas chromatography was combined with a mass spectrometer or a dual mass spectrometer with electrospray ionization (GC-

EI-MS, GC-EI-MS/MS). The presented papers show the utility of this technique for both, i.e., residue analysis of multiclass pesticides and NSAIDs simultaneously in food and food products as well as for the determination of new antibacterial and antitumor agents in edible plants.

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