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Review

Multidimensional Chromatography and Its Applications in Food Products, Biological Samples and Toxin Products: A Comprehensive Review

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Abstract: Food, drugs, dyes, extracts, and minerals are all made up of complex elements, and utilizing unidimensional chromatography to separate them is inefficient and insensitive. This has sparked the invention of several linked chromatography methods, each of them with distinct separation principles and affinity for the analyte of interest. Multidimensional chromatography consists of the combination of multiple chromatography techniques, with great benefits at the level of efficiency, peak capacity, precision, and accuracy of the analysis, while reducing the time required for the analysis. Various coupled chromatography techniques have recently emerged, including liquid chromatography–gas chromatography (LC–GC), gas chromatography–gas chromatography (GC–GC), liquid chromatography–liquid chromatography (LC–LC), GCMS–MS, LCMS–MS, supercritical fluid techniques with chromatography techniques, and electro-driven multidimensional separation techniques. In this paper, the different coupled chromatography techniques will be discussed, along with their wide spectrum of applications for food, flavor, and environmental analysis, as well as their usefulness for the pharmaceutical, color, and dyes industries.

Keywords: chromatographic techniques; industrial application; efficiency; food; environmental analysis

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1. Introduction

Owing to the difficulties in separating complex mixtures, multidimensional chromatography through the combination of different chromatography has emerged as a key strategy to overcome such obstacles. From a conceptual point of view, paper chromatography was used to pioneer two-dimensional chromatography for the separation of 22 amino acid hydrochlorides [1,2]. Later, two-dimensional thin-layer chromatography (2D-TLC) and two-dimensional gas chromatography (2D-GC) were introduced in early 1978. In the same year, Erin and Frei introduced two-dimensional liquid chromatography defining online and offline approaches. This technique was considered very useful due to its ability to separate, as well as its speed and efficiency [3].

For the separation of complex mixtures, multidimensional chromatography employs a varied composition of the mobile phase and the stationary phase or separation mechanism, in which the effluent is transferred after initial separation to another column for the final separation, ultimately increasing the efficiency of separation of the analytes [4]. Among other key aspects, this is a sophisticated approach for separating mixture components that

incorporate several different procedures. The great difference between one- and multi-dimensional chromatography is better separation. It uses similar principles as that of the traditional chromatographic technique, with the advancement of the use of a combination of different chromatographies.

With evolving advanced analytical techniques, the speed of separation, selectivity, precision, and accuracy is highly increased, owing to the use of different mobile phases, particles of different sizes, column temperature, pH, etc. To carry out such analysis, different chromatographic techniques, including liquid chromatography–gas chromatography (LC–GC), liquid chromatography–liquid chromatography (LC–LC), GCMS–MS, LCMS–MS, and electrophoresis–liquid chromatography, have been extensively used for pharmaceutical and environment applications, as well as in the food, dye, and color industries.

This review aims to provide an overview of the different coupled chromatography techniques, and their spectrum of applications for food, flavor, and environmental analysis, as well as their usefulness for the pharmaceutical, color, and dye industries.

2. Materials and Methods

The operation of multidimensional chromatography is composed of different types, as there is the coupling of various techniques in a single separation unit. The basic principle involved in complex separation depends on the implemented separation method. The coupling of different techniques is of interest for different analytes, and they retain the same. Some of the coupled techniques for multidimensional separation are discussed below.

2.1. Liquid–Gas Chromatography

The need to analyze complexes, such as food products, medicines, fossil fuels, etc., is important in separation techniques. Through using very efficient methods and specialized detectors, this may be achieved. However, the single separation technique cannot meet the need for high efficiency and specificity, and thus, it has been replaced by multidimensional chromatography. This approach makes the process of complexes' separation easier than the single separation unit [5].

Liquid chromatography coupled with gas chromatography (LC–GC) uses the selectivity of LC and the high efficiency and selectivity of GC [6]. The combined advantages of both separation units were utilized for the separation of the complexes. The offline approach is usually applied for coupling, as it is easy but laborious and time-consuming. The online approach is very expensive, accurate, requires fewer samples, and is fast, despite requiring an advanced set-up with skilled handling [7]. The main problem with the online approach is that both separation units operate in different physical states [8].

2.1.1. Transfer Techniques

Various transfer techniques can be used for the transfer of eluent from one system to another. It can be a direct approach or an indirect approach for both the normal phase and the reverse-phase eluent. Transfer techniques greatly depend on the nature of the eluent [9].

2.1.2. Retention Gap Technique

The retention gap technique is used for the qualitative and quantitative approach to complex compound separation containing volatile substances. The specific approach is for introducing the LC eluent into the GC unit at a temperature below the boiling point of the eluent. The volatile compounds are reconcentrated, forming a thick layer of retaining stationary phase ahead of the analytical column due to the solvent effect. This allows the momentum of volatile compounds through the column, which is referred to as the retention gap technique [10,11].

2.1.3. Loop-Type Interfaces

Loop-type interfaces are essential for the analysis of highly volatile compounds due to their simplicity and transfer of very large amounts of solvent. Briefly, the solvent is

introduced at or above the boiling point from LC units. The short retention gap and fast evaporation of the solvents make it superior to the other techniques. The only disadvantage of the system is that it leads to the loss of volatile compounds [12].

2.2. Gas Chromatography–Multidimensional High Resolution (GC–MHR)

Multidimensional high resolution coupled to a GC column is used for the separation of complexes in industry and environmental analysis. The main purpose of coupling is to increase the peak capacity of the separation unit and the speed of analysis. The first approach of GC-coupled columns was used in crude oil and refinery products in 1960, aiming to achieve a high degree of deconvolution with the two-column system [13].

In two-dimensional GC, the analyte is subjected to two or more separation steps that are mutually independent in their selectivity, and the components are separated throughout the analysis. The main goal of this procedure is to achieve a high peak capacity, despite it depending on the individual column peak capacity. The eluent from the primary column is re-analyzed through a second column with differing selectivity [14].

Two-dimensional GC has been used extensively for the separation of highly complex molecules, where GC columns provide a high peak capacity of up to 1000 with theoretical plates as high as those found in [15]. Although high peak capacity alone is not enough, selectivity also plays an important role in separating molecules such as gasoline. In a normal approach, the analyst will increase the length of the column or decrease the inner diameter of the column. This does not satisfactorily enhance the separation of the complex, but the two-column approach does. The second column differs in selectivity and hence peak capacity is increased. The greater the orthogonality between the stationary phase selectivity in each dimension of a multidimensional GC separation, the greater the peak capacity improvement [11].

Industry-pioneered high-throughput single-compound analysis with the 2D-GC. In this technique, the primary column behaves very similarly to the LC column, where pre-fractionation is just the primary goal, so that the two carry out the separation. The pre-column has advanced the GC application, where it is used for the detection of complexes in high-molecular-weight species [16].

2.3. Two-Liquid Chromatography Coupled System

High-performance liquid chromatography has been used extensively in the field of biochemistry, analytical units, food industries, etc. Although its impact is enormous, it has a limitation when applied to complex mixtures [17]. These problems can be overcome by using columns of high efficiency and good gradient elution order. Another approach is to introduce multidimensional separation, where two LC columns are linked together through an online or offline approach. The online approach is automated, very specific, and accurate for its application [18], whereas the offline approach is easy but laborious and prone to contamination. One distinction between two-column LC and two-dimensional LC is that it is completely automated, and two columns may have the same or different lengths and stationary-phase compositions. Two separate criteria have been used to define multidimensional LC separation, as follows:

(1) For a multidimensional system, the first criterion is that the sample components must be displaced by orthogonal separation processes;
(2) For the second condition, it is not permissible to mix components that have been separated by more than one separation dimension.

The eluent from the first column is routed to the second column for further separation in a multidimensional LC unit. This new technique uses an online approach rather than the usual two-dimensional LC approach and hence differs from the previous system. A new elution order sees the most retained compounds removed first, followed by the least [19]. Usually, the first column has mid-selectivity, while the second column is highly selective for the separation and contributes to the reverse elution order.

2.4. Coupled Supercritical Fluid Techniques with Chromatography Techniques

There are two main types of supercritical fluid techniques, i.e., supercritical fluid chromatography (SFC) and supercritical fluid extraction (SFE). The latter helps in extracting the component from the mixture quickly, whereas traditional methods used take several days to extract. There are many types of chromatographic techniques that have been coupled with SFE [20,21].

2.4.1. SFE–GC

SFE–GC is the most investigated system and has direct application, as the extracted analyte is fed to the GC column for quantification. A column or spitless injector is being used as the interface, where the end restrictor of SFE is introduced into the GC unit using the cryogenic technique for trapping. The programmed temperature injector is also used as an interface where evaporation takes place [12,22].

The most important application of this technique is that it is used in multicomponent molecules where the organic components are extracted through the SFE and are directed toward the GC unit for their detection. These extractions took several days using traditional systems and are laborious and time-consuming, and with SFE they can be completed within 1 h [23].

2.4.2. SPE–SFE–GC

Solid-phase extraction and SFE are sample pre-treatment steps, with both having different approaches in their application. SPE is used for the extraction of the analyte from the aqueous or biological matrix, whereas SFE is used for the extraction of an organic molecule from the solid matrix [24].

The online coupling of these techniques provides direct exposure for utilizing all the benefits. Briefly, the SPE cartridge is conditioned, washed, and loaded with the sample along with the analyte elution. These eluents are further separated by loading into SFE units and followed by GC measurement to understand the complete profile of analytes [25].

2.4.3. SFE–SFC

SFE–SFC is one of the most widely coupled and extensive easy techniques, as it does not require any modification while coupling. Both the systems utilize CO_2 for the extraction solvent, as well as a mobile phase later. Extracted analyte from SFE is directly transferred to the SFC unit for its separation and quantification [26].

2.5. Electro-Driven Multidimensional Separation

Multidimensional chromatography is used for the separation of complex components using different separation mechanisms. Conversely, the electro-driven separation technique adds benefits to the system through charged amino acids, and nucleic acids in the matrix are separated through it [27].

A comprehensive system combination becomes very easy when orthogonality becomes essential for increased sensitivity and selectivity. The two techniques differ in their separation systems, where one separates with electro-driven mechanics while the other separates in retention capacity [28].

The heart-cutting pattern is used for analyte processing in which the elute from the first unit is subsequently examined by the second unit, where both systems vary in selectivity [11]. As long as the resolution of the separation unit is not disturbed or affected, the peak capacity of the unit can be termed as the product of the individual peak capacity of each unit.

In the non-comprehensive system, both systems are different in their separation mechanism as well as elution order and do not affect each other. Both systems, i.e., electrophoresis and LC, have complete orthogonality, but resolution was lost during system hyphenation, which is one of the major drawbacks of using a non-comprehensive system [29].

Many of the electro-driven separations were coupled using different separation techniques linked together, such as:

(a) Reverse-phase high-performance liquid chromatography–capillary electrophoresis microcolumns;
(b) Capillary zone electrophoresis–microcolumn size exclusion chromatography;
(c) Reverse-phase high-performance liquid chromatography–capillary electrophoresis in a single capillary;
(d) Fast capillary zone electrophoresis with packed capillary reverse-phase high-performance liquid chromatography;
(e) Reverse-phase liquid chromatography–capillary zone electrophoresis–three-dimensional size-exclusion chromatography is some of the techniques used.

2.6. Three-Dimensional Liquid Chromatography (3D-LC)

Three-dimensional liquid chromatography (3D-LC) is a technique for integrating three distinct LC technologies to simplify proteomics digest materials. Moreover, 3D-LC systems may be implemented either online or offline. All three dimensions in an ideal 3D-LC system would be orthogonal to one another.

2.6.1. Online Systems 3D-LC

Certain online 3D-LC systems have been developed in an attempt to reduce the amount of time spent on each sample, the amount of labor needed, and the total number of steps. They often have more sophisticated technology but a lower sample size. Yates' team built a 3-phase MudPIT column filled with RP-SCX-RP after creating MudPIT as the first 2D-LC system. It is possible to claim that this is the first 3D-LC arrangement utilized for proteome study [30]. Some organizations have constructed online 3D-LC platforms by modifying HPLC/UPLC system configurations, which is an alternative to packing 3-phasic columns [31–33].

2.6.2. Offline Use of 3D-LC Systems

MudPIT was the basis for several early 3D-LC systems, with slight modifications. The bulk of them used a combination of SCX and RPLC approaches. Two RPLC systems are utilized in pH-varying conditions (typically high and low pH) [34,35]. Various 2D-LC HILIC-RPLC systems have been developed into 3D techniques due to their efficacy [36].

In offline 3D-LC systems, the nonspecific adsorption of samples to tubes or other surfaces, in addition to unnecessary sample handling, is a typical source of sample loss. They often need a large number of peptide-level samples [37]. As a consequence, some investigations have merged the fractionation and sample preparation processes into a single instrument. Stage Tips, in-StageTip (iST), 3D-SISPROT, and mixed-mode SISPROT (Table 1) are all examples of integrated devices that may decrease sample loss, operate with a little amount of material, and provide very efficient digestion and fractionation [37–39].

2.6.3. Online–Offline 3D-LC Systems in Combination

A hybrid online/offline configuration is necessary to carry out a 3D-LC method. The sample is either pre-fractionated using the first dimension before an online 2D-LC separation, or it is fractionated using the online 2D-LC platform and then separated using the third dimension combined with MS/MS analysis.

3. Multidimensional Applications

3.1. Foods, Flavors, and Fragrances

Natural complex mixtures are constituents of food, flavor, and fragrance products, with analysis of these matrices being carried out in [40] (Figure 1 and Table 1).

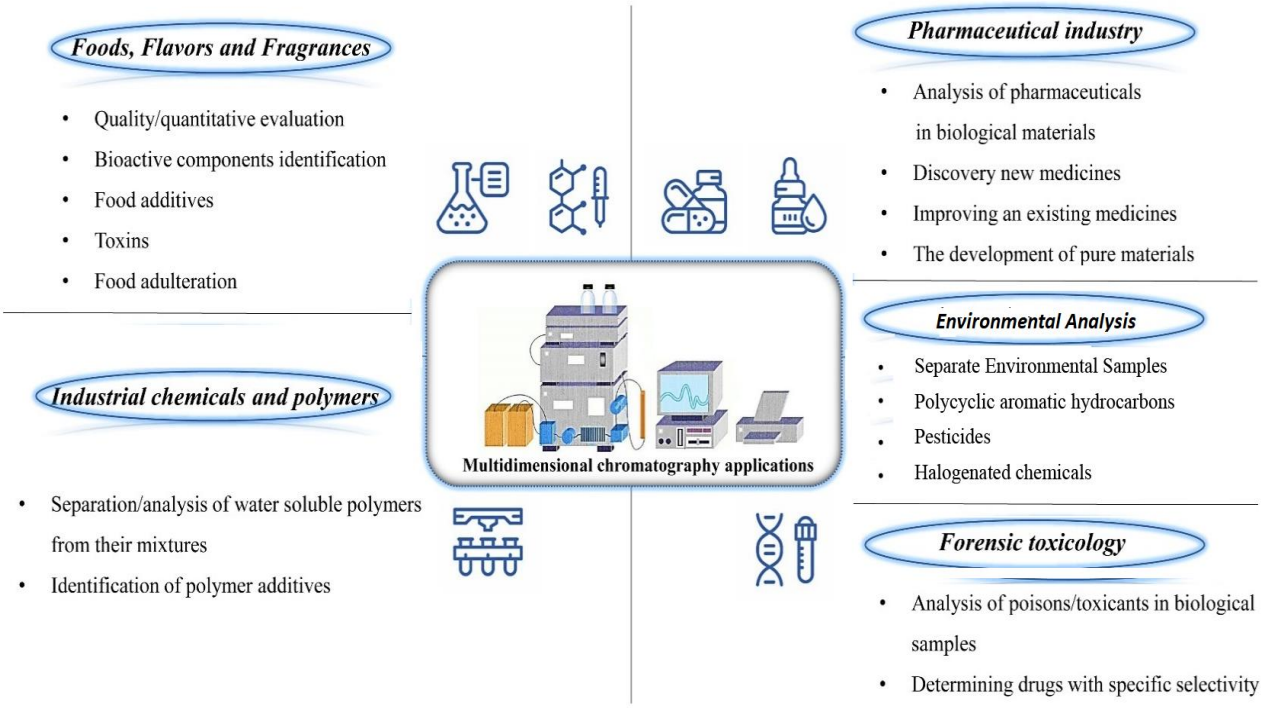

Figure 1. Representative scheme with the most important applications of multidimensional chromatography.

- Qualitative and/or quantitative determination of certain classes of constituents;
- Quality and authenticity control of the product;
- Adulteration or contamination detection.

One-dimensional chromatography does not provide sufficient selectivity for the separation of the complex, as there are problems of overlapping peaks, variation in selectivity, or even when the components are present in trace amounts, hampering the selectivity [41,42]. On the contrary, multidimensional chromatography provides an advanced pre-separation effect before analyte separation and quantification, ultimately overcoming the problems related to peak overlapping and trace element detection [43,44].

3.1.1. Gas Chromatography (GC–GC or MDGC)

A large number of food products, flavorings, and fragrances consist of chiral compounds that, on detection, present overlapping peaks and selectivity problems. The distribution of enantiomers is useful for the identification of adulterants, controlling the fermentation process and storage effects. GC–GC can be used for the enantiomeric determination of these products, but pre-selection is crucial due to overlapping peaks. The pre-chiral columns are being used before the main chiral column just to avoid overlapping peaks. This method is used to determine products' authenticity [45].

3.1.2. High-Performance Liquid Chromatography (MD–HPLC)

Multidimensional HPLC has high separation power; hence it is used for the separation of complex molecules [18,46]. Heart-cut, on-column concentration, or trace enrichment are different types of techniques used to promote the application of multidimensional HPLC [47]. Using multidimensional HPLC, the researchers have been able to determine the levels of complex B vitamins in protein food, on-column vitamin concentrations in food matrixes, molasses sugars, malathion in tomato plants, lemonin in grapefruit peels, and other polar pesticides, with detection limits being as low as 0.1 g/L [48,49].

3.2. Biomedical and Pharmaceutical Applications

Multidimensional chromatography is used widely in the field of the biomedical and pharmaceutical industry due to the complex nature of the analyte and decreased amount present in the biological matrix [50–52] (Figure 1). High selectivity and accurate systems are needed with high reliance to determine such compounds [53,54].

LC is well established in these industries and very well adopted, so LC remains a component for separation and quantification purposes, along with other systems. Online and offline approaches are being used for coupling systems, where the online approach provides greater accuracy and precision along with shorter analysis time [55].

Charged, polar, thermolabile, non-volatile, and high-molecular-weight compounds are just some of the clinically relevant chemicals that can be directly examined by LC. Antibiotics, retinoids, methotrexate, codeine, psilocin, and almokalant have all been studied using this method, as well as anabolic steroids, morphine, and clozapine [56].

3.3. Industrial Chemicals and Polymer Applications

Industrial chemicals and associated materials have also been subjected to multidimensional chromatography analysis (Figure 1). Coal tar, antiknock additives in gasoline, light hydrocarbons, trihaloalkanes and trihaloalkenes in industrial solvents, soot, particle extracts, and different industrial compounds that may be found in gasoline and oil samples have been studied via multidimensional chromatography [57].

The rapid identification of polymer additives, such as antioxidants, lubricants, flame retardants, waxes, and UV stabilizers was made possible by a multidimensional system using capillary SEC–GC–MS [58]. Chemical additives, such as hydrocarbons and alcohols, for example, may not only be analyzed in the context of polymer chemistry but also in the context of food chemistry using the same methodologies. The study of polyaromatic hydrocarbons in food oils has also proven very important. Moreover, a polystyrene matrix has been employed for the investigation of polymer additives using SEC and GC [59].

3.4. MDC in Environmental Analysis

Environmental analysis relies heavily on multidimensional chromatography. The wide range of polarity of the constituents and a large number of isomers or congeners with similar or equal retention properties make it impossible to separate environmental samples using a single chromatographic approach (Table 1). Polycyclic aromatic hydrocarbons (PAHs), pesticides, and halogenated chemicals are all persistent organic pollutants that can be found in the air, water, soil, and sediment, and multidimensional chromatography has been used to analyze such contaminants [60]. Among them are polychlorinated dibenzo-dioxins, dibenzofurans, polychlorinated biphenyl, terphenyls, naphthalene, alkanes, organochlorine insecticides, and the brominated flame retardants, polybrominated biphenyls and polybrominated diphenyl ethers, which are some of the most representative [61].

3.5. Forensic Toxicological Applications

Analyses in forensic and toxicological sciences involve the identification of complexes that signal sickness, poisons, and a wide range of unlawful acts as examples [62] (Figure 1). Tissues, urine, plasma, serum, hair, arson debris, and fragments of other objects are often discovered to contain analytes [63,64]. For such purposes, LC–GC has been used for the analysis of numerous toxic complexes in biological samples, such as plasma and tissues, whereas GC–GC has been used for complex samples with exceptional selectivity. For example, organic pesticides and polychlorinated biphenyls (PCBs) may be separated and analyzed using online LC–GC, which can also be used for lipid matrices. In addition, the analysis of illicit growth hormones in corned beef can be performed using LC linked to two-dimensional GC [65]. Specifically, LC–LC has found its extensive use for the analysis of biological matrices, while GC–GC has special applications in determining drugs with specific selectivity. More recently, micellar HPLC has been used for the analysis of cardiovascular drugs from urine [66].

Multidimensional LC has also been used to determine ursodeoxycholic acid and its conjugates in serum, while multidimensional GC is used to separate derived urinary organic acids that are indicative of metabolic diseases, phenylketonuria, tyrosinemia, and others. Additionally, two-dimensional GC is used for the determination of 2,2,3,3,4,6-hexachlorobiphenyl in milk [67]. Food products often contain complex matrix interferences, such as emulsifiers, thickeners, stabilizers, pigments, antioxidants, and others, making it difficult to analyze the analytes of interest. As such, multidimensional GC coupled with infrared or mass spectroscopy may be used to improve the outcomes (Figure 1 and Table 1) [68].

Table 1. Utilization of multidimensional chromatography in food products, biological samples, industrial, environmental, and toxins.

Sample	Solvent System	Analytes	Operation Mode	Refs.
Fish and chicken	Acetonitrile	Enrofloxacin	SPE–HPLC	[69]
Pig urine, human plasma, and Smashed shrimp samples	Water, methanol, and acetonitrile	Bisphenol A	C18 SPE–HPLC	[70]
Wheat, barley, potato, and carrots	Acetonitrile and acetic acid	Fenuron	HPLC–DAD	[71]
Baby food, chicken meat, vegetables (carrots, tomatoes, green beans, onions, peas, and leeks), potatoes puree, and olive oil	Formic acid and acetonitrile	Quinolones and fluoroquinolones	SAX or MIP cartridges- HPLC	[72]
Soy samples	Acetonitrile	Parabens	Off-line MISPME by GC-FID	[73]
Corn	Water and Acetonitrile	Phenylurea herbicides	HPLC–MISPE	[74]
Pork and chicken	Acetonitrile	Sulfonamides	SPE–HPLC	[75]
Egg, honey, duck, and lobster samples	Methanol: acetonitrile	Tetracycline	LC-tMS-MISPE	[76]
Milk	Acetic or trichloroacetic acid	Chloramphenicol	Voltammetry	[77]
Coffee	Acetic or trichloroacetic acid	Benzo[a]pyrene	HPLC–FLU	
Citrus fruits	Acetonitrile, sodium dihydrogen Phosphate	Thiabendazole	CE MISPE	[78]
Potato, corn, pea,	Toluene in acetonitrile	Triazines	SPE-PIP	[79]
dried milk, condensed milk, and dried cheese	Solvents for solubility	Melamine, cyanuric acid	DART–TOFMS, LC–MS/MS and ELISA	[80]
Human growth hormone	Ammoniumacetate (AmAc), pH 6.8 solution at 20 mM concentration	Reslizumab, bevacizumab	EC-IEX-UV-nMS system	[81]
Peptides mapping tryptic digest	D1 mobile phase: (A) 10 Mm CH3COONH4 in H2O v/v (pH 9); (B) 10 mM CH3COONH4in H2O/ACN 10:90, v/v (pH 9). D2 mobile phase: (A) 0.1% TFA in H2O v/v (pH 2); (B) 0.1% TFA in H2O/ACN 10:90, v/v (pH 2).	Amino acids. α-Casein and dephosphorylated α-casein	2D LC system in which RPLC × RPLC system, coupled to PDA and MS detection.	[82]
Saccharomyces (yeast protein)	Four buffer solutions: Buffer A (2% ACN), buffer B (80% ACN), buffer C (250 mM ammonium acetate/2% ACN), and buffer D (2 M ammonium acetate/2% ACN) with each 0.1% formic acid	Soluble, urea-solubilized, and SDS-solubilized proteins	RP1-SCX-RP2 microcapillary column and an LCQ Deca XPMS/ Online	[83]
S. cerevisiae and *E. coli*	Isocratic-acetonitrile and KCl each with 20 mM ammonium formate at pH 10	Tryptic peptides	3-D RP-SAX-RP and RP-RP-LCQ/ Online	[84]
HEK 293T cell lysates	Buffer solutions with various pH 12, 6, 2 with variance 7-35% con Buffer	Peptides	SAX-based SISPROT/ Off-line	[85]
Tryptic digest of whole Jurkat cell lysate	Water and acetonitrile with gradient system with each 0.1% HFBA	Peptides	LC-MS/MS (TripleTOF 5600)/Offline	[86]
Mouse brain cell proteome digest	Water and acetonitrile with gradient system with each 0.1% FA and ammonium acetate solution (pH 2.88)	Peptides	SCX-RPLC-CZE-MS/MS/ Combined	[87]

Table 1. *Cont.*

Sample	Solvent System	Analytes	Operation Mode	Refs.
Breath of healthy smokers and non-smokers, and patients with COPD	-	13 VOC and NSCLC	GCMS HP 6890 GC coupled with an HP 5973 mass selective detector	[88]
Human urine	-	Aromatic amines	GC–MS/MS Agilent 7890-7000 C GC–MS/MS	[89]
Microwave and conventional oven food contact material	-	Fatty foods—microwave meals,	GC–MS_EI	[90]
	Water (A) and acetonitrile (B), both with 0.1% formic acid (+), and 0.16 M ammonium hydroxide (-)	Roasting meat and poultry	LC–MS_ESI	[90]
Tuna fish muscle and wastes	-	Lipid extract	QqQ MS,	[91]
Tuna β-actin	0.1% TFA in water and 0.1% TFA in water: ACN	Peptides	RP-UPLC with ESI-ion trap-TOF MS/MS	[91]

4. Conclusions

Multicomponent mixtures are essential parts of food products, drugs, flavoring agents, and dyes. The need for analysis for these products requires high hyphenation and advanced techniques to ensure proper quantification, which is not achieved through using a single separation unit. In this way, multidimensional chromatography has emerged as a strategy with multiple advantages, leading to high peak capacity, increased speed of analysis, high throughput, and increased efficiency and accuracy. Different chromatography techniques are coupled together with different modes of operation and different selectivity for analytes. Coupling LC with GC is used in an online and offline approach, where LC column selectivity and GC high efficiency confer a marked benefit to the final analysis. In this coupling, the process is independent concerning the columns, and separates each elution band with high resolution. Columns in 2D and 3D, where the first columns have low selectivity compared to the second and third ones, result in a reversion in elution order. As the number of columns increase, the resolution in separation changes and is dependent on the type, the volume of the sample, and the phase of the column. Other techniques, such as supercritical fluid coupled with chromatography and electro-driven techniques, have also been used for the extraction of analytes from mixtures, either through partition or the electric moment of the system's component ions followed by quantification using chromatographic techniques.

From a technical–practical point of view, and owing to the markedly advanced mechanisms, ease of handling, robustness, and high-throughput capacity, multidimensional chromatography has been widely used in the field of the food, flavor, oil, mineral and pharmaceutical industries, and even in environmental analysis, with promising results.

With multiple applications in the biological, food product, and hormonal fields, and in the toxin analysis of MDC, it must be extended to analyze and understand forensics, therapeutic drug monitoring, and biochemical analysis for various disease pattern applications.

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