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A REVIEW ON GENERAL INTRODUCTION OF COMPREHANSIVE TWO-DIMENSIONAL GAS CHROMATOGRAPHY

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ABSTRACT

A comprehensive two-dimensional gas chromatography (GC×GC) is the most powerful method used for the separation of complex samples which offers reliability in quantitative and qualitative analysis, enhanced separation efficiency, information on the whole sample and its components, ability to detect low quantities. These features are essential for the analysis of complex samples, in which the number of compounds may be large or the analytes of interest are present at trace level. The aim of this work is to review the general information of comprehensive two-dimensional gas chromatography. The present review focuses on the basic principle, instrumentation of (GC×GC), and its applications. The benefits of (GC×GC) are in the analysis of complex samples easily overcome some minor drawbacks of techniques. The developed instrumentation and methodology which performs well for environmental samples, and also applied for other complex samples.

KEYWORDS: (GC×GC), 2DGC, Principle, Instrumentation, Pharmaceutical Application.

INTRODUCTION

Analysis of complex samples is very challenging when the number of compounds is larger or the analytes are present at just trace level. Traditional one-dimensional chromatographic techniques, such as gas chromatography is often fails to separate compounds well enough, and there is severe overlap of peaks results. In conventional multidimensional techniques only one or few fractions are transferred from the first to the second dimension, but in comprehensive two-dimensional techniques, the whole sample is passes through the whole system, and information is obtained on total sample.[1] A Comprehensive two-dimensional

gas chromatography (GC×GC), which is an increasingly popular multidimensional technique, was introduced in 1991. At the end of the 20th century and the beginning of the 21stcentury, the development of modulators was put into the major effort.[2]

A Comprehensive two-dimensional gas chromatography (GC×GC) is an emerging technology for the chemical separation that provides an order-of-magnitude which increase separation capacity over the traditional gas chromatography and it is capable of resolving several thousands of chemical compounds.[3, 4]

It is a modified technique used to separatethe mixtures of compounds, so that the individual components can be identified and/or quantified. Among the distinct chromatographic techniques, it occupies a prominent role due to its great separation power, flexibility, wide applications and relative simplicity.For comprehensive two-dimensional gas chromatography (GC×GC), one part must find a way to complete the first separation on first column, after that perform a second separation on a different column, while preserving the separation from the first dimension or first column. It requires more than just two columns coupled together.[5]

PRINCIPLE

A Comprehensive two-dimensional gas chromatography (GC×GC), is the best destination reached by separation science. It is categorized into the multidimensional techniques due to the association of two different mechanisms of separation. Compared to more known MDGC (Multidimensional Gas Chromatography), (GC×GC) is more "comprehensive" toward the separation involving sample analytes, in other words, it means that in (GC×GC), every portion of the eluate coming from the primary or first column(1D) undergoes a further second column (2D) separation, instead of MDGC, where the most common method was utilized which is "heart-cutting", it transfers only the selected portions of eluate from the first to the second dimension or column.[6, 7, 8, 9]

Subjecting the whole sample to a double separation process, it becomes a necessary condition forachieving a (GC×GC) separation. Also, the analytes separated in the first column must be separated when passing through the second column. These two analytical phenomena, which makes (GC×GC) a unique separation technique, and it can be achieved through "core" of all (GC×GC) instrumental set-ups, namely the modulator, which acts as a living interface between two columns or two dimensions of separation.

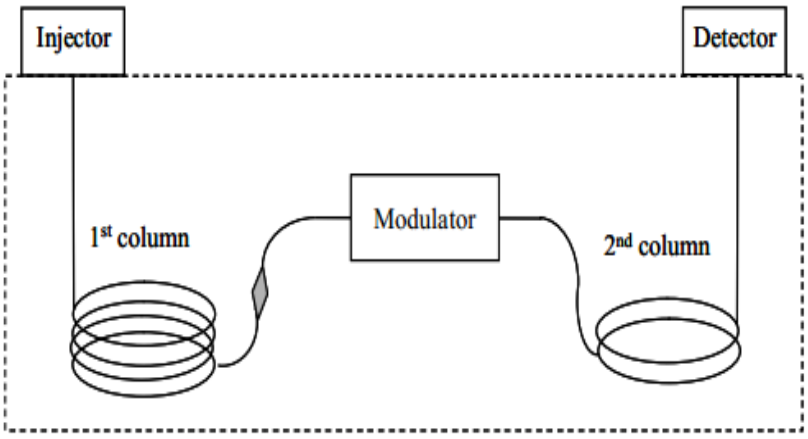

Figure 1: Schematic diagram of GC×GC apparatus.

Basically, comprehensive GC apparatus exploits the two different stationary phases in which the most common set is non-polar, with conventional dimensions, and polar, characterized by "fast" feature, located in the same or in the separate GC ovens. The modulator is placed between the first column (1D) exit and the second column (2D) inlet, and its functions are to isolate, trap, focus and reinject the bands of first column eluate into the second column. Samples are normally injected to the head of 1D column, it undergoes separation, and then, by means of modulator, analytes are diverted to the second dimension, where it undergoes further separation. Finally, they reach to the detector, which is located at the exit of the 2D column.

The comprehensive transfer of a primary column eluting peak into the secondary column can be achieved with an adequate modulation time, which is time employed by modulator for sampling or trapping and releasing 1D peak. Mostly, the modulation time being in order of seconds is just not sufficient to transfer an entire peak, but the more reasonably slices of it, generate a series of 2D retention times. Such a separation mechanism, it adds a new dimension to thevisual information which can be obtained by the analyst, the (GC×GC) chromatogram.[10, 11]

INSTRUMENTATION

Basically, a comprehensive 2D GC exploits the same type of instrumentation utilized in monodimensional gas chromatography, with the novel introduction of modulator within its apparatus. The apparatus is composed of the GC injector, the primary column, the modulator, the secondary column and the detector etc.[12]

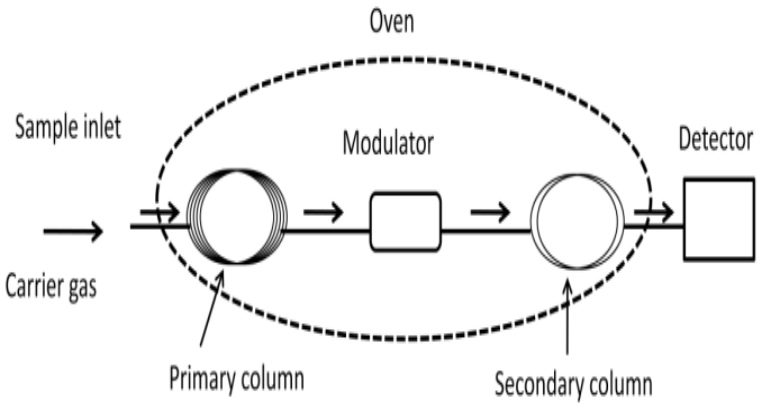

Figure 2: Schematic diagram of GC×GC apparatus.

Columns can be placed in the same GC oven or in two separate GC ovens; the latter option seems to be preferred when it asking for two independent temperature controls. In fact, as it will be explained ahead in following sections, the two columns are coated with the different types of stationary phase, hence; thelimits of operating temperatures is very often vary from each other. Anticipates also how cryogenic modulators generally work: a double pulsed cold jet of a cooling gas (liquid carbon dioxide or nitrogen) is sprayed on analytes eluting from the first dimension. The alternation of two cold jets in the two different sites at the beginning of second columnworks as a “trap and release” tool. Column set mostly utilized, it is based on a conventional-bore column as the first dimension, and a narrow-bore column as the second one.[13]

Instrumentation part contains

A. Mobile Phase

B. Stationary Phase

C. Pressure Regulator

D. Sample Injector Port

E. Column

F. Modulator

G. Detector

A detailed description of each instrumental part of GC×GC instrument will be now given.

A. Mobile phase: The Carrier gas act as a mobile phase and it supplied in stainless steel tanks with a high pressure and the purity of gas should be very high. The gas must be inert.

The purpose of acarrier gas is to transport sample through the column to the detector. Selecting the proper carrier gas is very important in whole operation because it affects both the column and the detector performance. The viscosity of gas dictates the inlet column pressure. The ratio of the carrier gas viscosity to the diffusion coefficients of sample components should be as small as possible. In this respect, hydrogen is best choice, followed by helium. Gas like Argon and Nitrogen are also used. The purity of carrier gas should be at least 99.995 %. Impurities such as water or oxygen can cause detector and column deterioration. Flow meter and Pressure regulator are required to control flow rate of the gas.[14, 15]

B. Stationary phase: The Stationary phase for gas chromatography can be silica gel, glass beads or alumina. For the analysis of very low molecular weight compound such as water for alcohol, molecular sieves or the group of porous polymer made from divinely benzene and styrene.

The Stationary phase for gas liquid chromatography isdiacetomaceous earth which is made by acid or base to remove impurities and then surface can be activated. Glass beads can be used as solid support. Liquid can be coated that is 1 to 5 % by compounds which are retained slightly. Liquid is used are silicon polymer with phenylcyano groups are introduced to influence selectivity and polarity. Ethylene glycol polymers can be used for separation of polar compounds such as alcohol. Non polar liquid phase can be used for non polar sample and polar liquid phase can be used for polar sample. Liquid phase should be stable. It should have low vapor pressure at the operating temperature.[16]

C. Pressure regulator: It is used to control the pressure of gas so that it can be compatible with the instrument. Carrier gas having pressure 40-80 psi passed through flow controller to adjust flow rate of gas. The Main instrument which is contained within thermostatted chamber is capable of maintaining the temperature raging from ambient to as high as 400° C.

D. Sample injection port: It is a small chamber separately heated to a temperature slightly above then that of the column. Here, sample is vaporized before entering to the column. The sample is introduced through silicon septum or self sealing rubber using micro syringe into flowing gas. (M.P). Sample can be solid which dissolved in liquid, pure liquid or it can be pure gas.[17]

E. Column: GC×GC chromatographic separation is the combination ofthe two different mechanisms which is the combination of two columns which are different in both the nature of the stationary phase and dimensions. The choice of most proper column set is a hard task for the GC×GC users, if one considers that, on this fundamental decision it depends on the success of this separation.[18]

Columnswhich are used in GC×GC separationcanbedividedintothe several categoriesaccordingto their polarity. The non polar group includes100% dimethylpolysiloxane and low phenylmainly5%phenylcolumns can be used.Mid-polarcolumns, it includeshigh phenylthat is 35-50% phenylandlowcyano that is 6-14%cyanocolumns can be used. Polarcolumns, itincludeshighcyanomore than 50%cyanoandtrifluoropropylandpolyethyleneglycol columns can be used.Specialcolumnsare representedbyliquid crystal and chiralphasecolumnsandby set where two different columns are coupled together.

GC×GC separation studies says that the most common column in the first dimension is a non polar column containing either 5% (di)phenyl–95% (di)methylpolysiloxane or100% dimethyl polysiloxane. Most common columns in second dimension are semi-polar column which contain 50% phenyl and 50%methylpolysiloxane or polar column containing 100% polyethylene glycol. The Cyano columns are the third most common column choice for the second dimension. Lately, the semi-polar–non-polar column combinations have become popular column, although the idea of using column in this order is not new now.[19]

The length of the first column is usually 20-30 m and the inner diameter of column is usually 0.25 mm and the film thickness is usually 0.25µm. Generally the second column is typically shorter that is 1m and the inner diameter of second column is narrower which is around 0.1 mm and the stationary phase is thinner which is around 0.1µm.

Although GC×GC separation set-ups typically consist of one first dimension and one second dimension column, sometimes two second dimension columns have been used.[20]

The carrier gas flow and the oven temperature ramp is very important feature for the GC×GC analysis. Generally the two columns are placed in the same GC oven. Placing the second column into the separate GC oven allows independent temperature programming for separation. The linear temperature programming with isothermal steps at the beginning and end of the program are usually applied. The ramp is 2–5 °C/ min.

GC×GC column with different inner diameters are connected in a series, volumetric flow through the columns is same but the average linear velocities differs. In the basic column set-ups, the two columns cannot be operated at optimum flow but the compromises have to be made. In this separation one column should be operated closed to its optimum flow conditions, while a sub optimum separation is accepted on other column. The use of narrow bore second column that is 0.05 mm or even 0.10 mm could result in very high velocity and therefore loss of plates.[21]

F. Modulator

An essential part of any GC×GC separation system is the modulator working between columns. Analytical conditions for analysis must be carefully adjusted to achieve a good separation.

The main function of the modulator is to collect and transfer the fractions from the first dimension to the second dimension column.

Modulator works throughout the analysis, it transfers the whole sample from the first to the second dimension column separation. The modulation period, which is the fraction transfer interval, is short, usually from 3 to 6 s. In view of its essential role is often called the heart of a GC×GC separation system.

Modulator is categorised into

1. Thermal Modulator

a. Heated Modulator

b. Cryogenic Modulator

2. Valve Modulator

The brief description of this is given below.

1. Thermal Modulator

When there is comparison with the valve modulators, an important benefit of the thermal modulators, bothcryogenic and heated is that they concentrate fractions before their introduction to thesecond dimensional column separation. Injection band widths have been estimated to vary fromaround 10 to 60 ms, while detectionband widths vary from around tens to hundreds of millisecond.[22, 23]

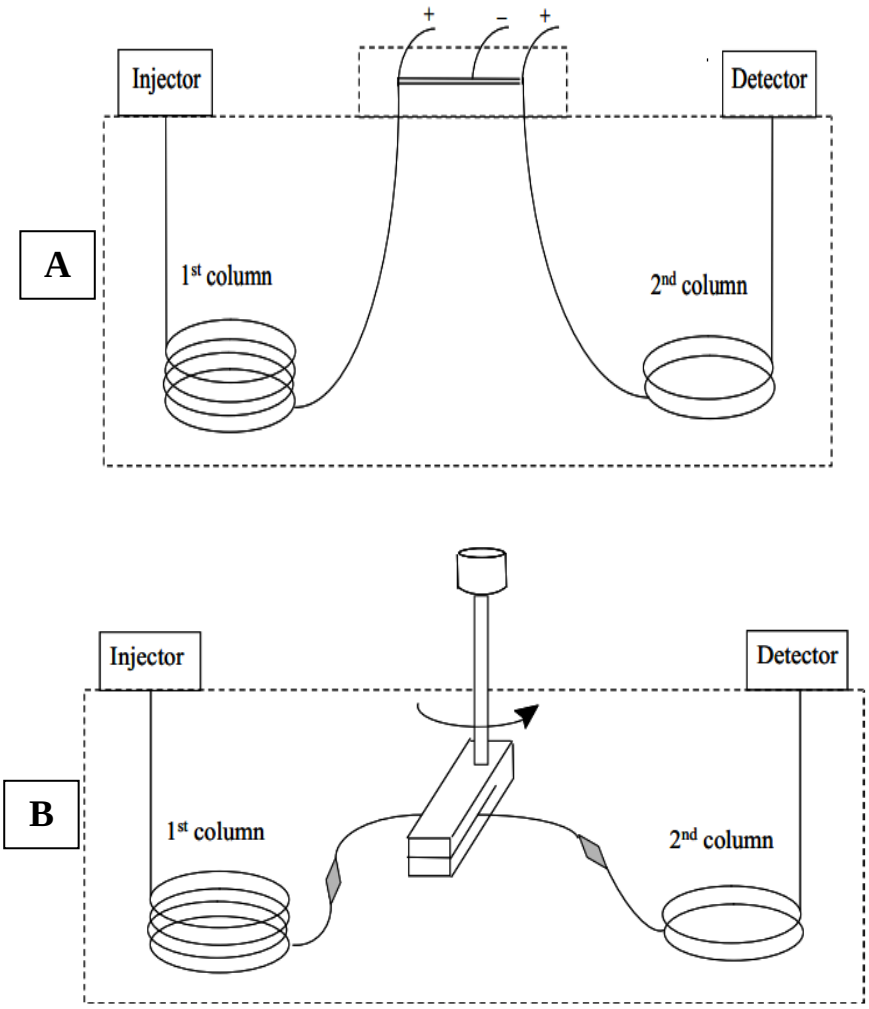

Figure 3: Schematic diagram of GC×GC instrument with thermal modulators: (A) two-stage thermal modulator and (B) Sweeper.

The first modulator in GC×GC analysis was a two-stage thermal modulator (Figure 3A), while first commercial thermal modulator was a rotating slottedheater also known as the Sweeper (Figure 3B). The application rangesof the Sweeper modulator is from C9 to C30,[24]it can be extended ton-alkane C40, but thethin film modulator tube is need to be heated in an independent temperature zone. There are other designs based on thermal effects, which are the singlestage thermal modulator, thermal array modulator and electrically heated, air-cooled modulator.[25, 26]

The widest variety of the modulators is found among cryogenic thermal modulators, which rely on carbon dioxide or liquid nitrogen as trapping coolant. When there is nitrogen, additional heating is required to desorb the analytes from the trap, and for carbondioxide, heated oven air is required. An important drawback of the cryogenic modulatorsis relatively large consumption of coolant.

The first cryogenic modulator was introduced in 1990s. The effectiveness of thisdevice was initially demonstrated as a solute trapping device and thenthat was adopted in GC×GC.[27] This first device is known as longitudinally modulated cryogenicsystem (LMCS) and, the name indicates, it moves longitudinally along the columnup and down, to perform the modulation (Figure 4A). The application range is from C8 to40.

A variety of other device in-house built and modified cryogenic modulators have beenpresented including the semi rotating cryogenic modulators developed in this study.In modifiedLMCS, the coolant is directly sprayed on the column instead of spraying into a separatecylinder as in the original version. Application range was up to C40. After thesetwo non-moving designs which are dual andsingle jet modulators were introduced. In dual-jet modulator (Figure 4B), twofixed jets alternately sprays carbon dioxide onto the columns. Application range ofthe modulator is from C8 to C30. In the single jet modulator, one fixed jet sprayscarbon dioxide onto the columns.[28]

After that new design was introduced. It was based on liquid nitrogencoolingand capable of trapping the volatiles such as propane.Commercial modulators include the quad-jet and the loop modulators. All these modulators can use the liquid nitrogen fortrapping analytes. The application range is from C5 to C 30, while the loop modulator is from C4 to C47.[29]

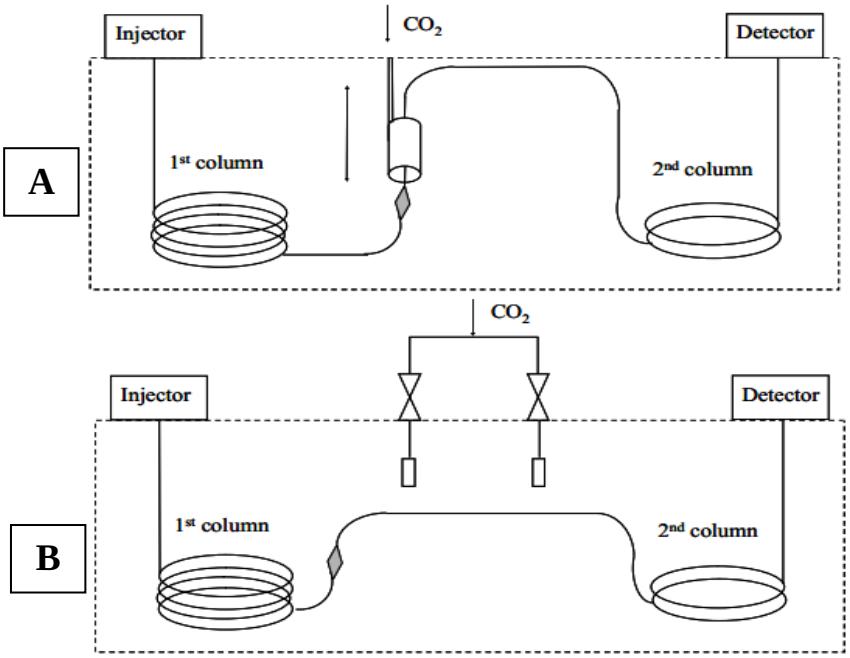

Figure 4: Schematic diagram ofGC×GC instrument with cryogenic modulators: (A) longitudinally modulatedcryogenic system (LMCS) (B) dual-jet modulator

2. Valve Modulator

The valve modulator features a multi-port valve, which directs effluent from the first tothe second dimension column. The fractions which are collected and transferred by valve are notconcentrated, but the valve can operate at a high speed. In many designs only a part ofthe sample is transferred from first to second column separation. Besides the basicconstructions of modulator, there are high temperature valves which are differential flow modulation and stop-flow modulation systems. Recently, new development is totaltransfer system including a total-transfer valve and the flowswitching devices have been introduced.Figure 5presents aschematic diagram of a valve-based GC×GC system.[30, 31]

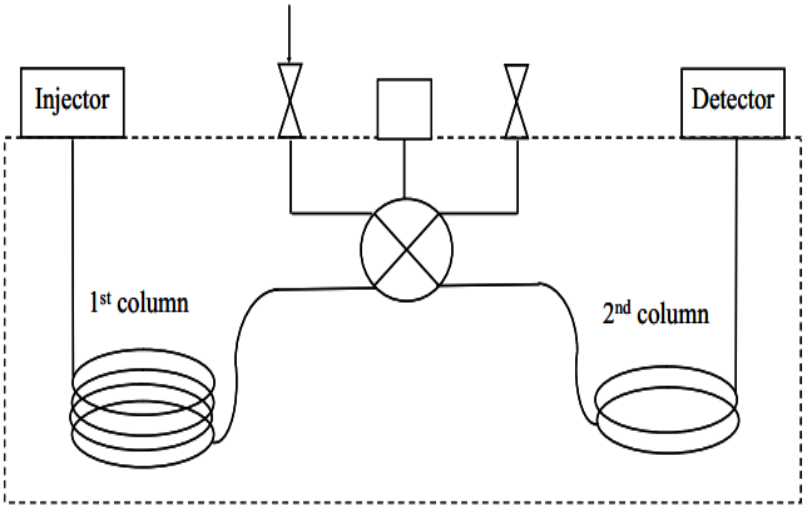

Figure 5: Schematic diagram ofGC×GC instrument with a valve-type modulator.

G. Detector: From the GC×GC analytical instrumental description, it is easy to understand that the main requirement of GC×GC detector is speed of acquisition. If, there is a lack of sensitivity and selectivity could be somehow compensate by the enhanced power of the comprehensive GC×GC separation, on the other hand the very fast practically isothermal, the 2D separations of modulated peaks requires acquisition rates of at least 100 Hz. In fact, the 2D peak widths at the base range from around 50 to 200 ms. Basically, the great part of commonly used GC detectors have been adapted to GC×GC system as well, in many applications.[32]

The most popular detectors in comprehensive GC, since its introduction, it has certainly been the Flame Ionizes Detector (FID). It isthe universal detector, which is also characterized by small internal volume. It has been proved to be efficient not only for quantitative purposes, but also for the peak identification due to the structure retention relationships on the two

dimensional plot.[33] It must be recalled that the detector FID gives the response proportional to the number of carbon present in molecules that are ionized and burned out. For this reason, the FID has been an elective detector in the petrochemical analysis, where predominant components which are hydrocarbons. For instance, GC×GC FID, which gives a better performance than PIONA that is, paraffin, iso-paraffin, olefins naphthenes, and aromatics analyzer. In another studies, GC×GC-FID demonstrated to be more effective than the LC-GC in the group type quantization of heavy gas oils, with the final improvement of detection limits.[34, 35]

Electron Capture Detector (ECD) is another detector used for many GC×GC applications. It isvery sensitive to halogenated compound; it is an electron emitter which attracts the high electron affinity molecules. This detector is specifically designed for some samples such as herbicides, pesticides, and more in general, compounds are having halogens in their structure. However, ECD is usually characterized by slow acquisition rate, and hence it is not suitable for GC×GC analysis. To overcome from this drawback was the development of miniaturized ECD (mECD),characterized by smaller internal volume and higher acquisition speed (50 Hz). Although improvedmECD demonstrated to be less effective than the FID detector, especially because of the two dimensions band broadening was observed. Now, mECD is relegated to analysis of organohalogens, so that to have the highly selective detector.

Atomic Emission Detector (AED) is falls into a group of elements selective detectors, due to thecapability to determine up to 24 elements, such as C, S, N, Pb, H, etc. It works through the formation of the plasma which atomizes the samples, causing emission of atomic spectra. Although very selective, but this detector fail in acquisition speed, which is only 10 Hz. Nevertheless, some researcher groups applied AED to the analysis of petroleum and crude oil by products, concluding the sensitivity of this detector toward S containing compounds was very good. But in this case, band broadening resulted to be very important drawback.[36]

Another detector used is SulphurChemiluminescence Detector (SCD). It emphasized that the interest of GC×GC users toward specific elements of sulphur has to be attributed to its presence in many sample types such as petrochemicals. The SCD apparatus consists of plasma burner, which produceschemiluminescent species throughthe quite complex combustion reaction. Basically, the SCD signal derives from formation of SO_2which generates the light when falling back into a neutral state. Compared to AED, SCD possessesthe higher acquisition speed (100 Hz). Unfortunately, cell volume is bigger (ca. 500

mL); consequently band broadening remains the disadvantage of such detectors. However, more than physical dimensions of the detector, it is an electronic system which affects the speed of band broadeningandacquisition.[37]

The further elements selective detectors have been utilized in comprehensive GC, which is Nitrogen Chemiluminescence Detector (NCD). Due to the higher acquisition speed, comparable to that of FID, this detector has demonstrated good performance in the analysis of dieselsamples, and in particular nitrogen-containing compounds group type analysis. The basic principle of operation is very similar to those of SCD, with main difference being the excited species (NO_2). GC×GC NCD is the promising technique for the nitrogen speciation in diesel samples, provide more reliable results compared to the monodimensional GC NCD. An overestimation of the carbazole/acridine group (51% vs. 34%) and an underestimation of quinoline/indoles were observed in these, when comparing data obtained from GC-NCD and GC×GC-NCD, respectively. Above these, it is worthy to remember that an interest of petrochemical research towardnitrogen containing compound is due to their catalyst poisoning character.[38, 39]

The use of another selective detectors cannot be neglected, namely the Nitrogen Phosphorous Detector (NPD), which is more correctly named Thermo Ionic Detector (TID) because of ionization mechanism. It is very similar to FID detector, with a difference that there is noflame working as a source, but alkali salt inside ceramic cement matrix. Theoretically, the NPD is very suitable for GC×GC separations, due to its high acquisition speed, which is up to 200 Hz. In fact, it can be successfully applied to analysis of methoxypyrazines in wine, gives better results compared to the Time of Flight TOF MS.[40]

However, an acquisition speed is not the only parameter, which positively affects a GC×GCseparation. In NPD, the gas flows (H_2, air, N_2) have to be adjusted in order to optimize not only the peak widths but also the peak symmetry.

Applications

Comprehensiveness: In contrast to conventional multidimensional chromatography in which only one or few fractions are transferred from the first to the second column, in GC×GC the whole sample is subjected to the second column separation.

This provides comprehensive information on the entire sample and its components.

It enhanced the separation efficiency through increased peak capacity.

It has capability to detect low quantities.

It increases the chromatographic resolution by using multi-columns.

Other applications are Target-compound analysis, group-type separation, and fingerprinting. All three types can be qualitative or quantitative. Non-target analysis, that is identification of unknowns, can be added to the list as the fourth type of application.

GC×GC is currently used in the analysis of petrochemical, food, environmental, biological, essential oil and cosmetic samples.

It is used in elucidation of sensory active compounds including aroma, taste, and texture by means of sample constituents such as physicochemical properties.

Trace analysis in the petroleum industry.

It also used in measurement of volatile organic species in ambient air.

Used for the analysis and quality assessment of alcoholic beverages.[41]

CONCLUSION

GC×GC separation technique have proven to be one of the most successful separation techniques which provide high separation and sensitivity in the analysis of complex samples. Use of one dimension gas chromatographic separation technique in analysis of sediment and aerosol extracts resulted in the severe overlaps of target analytes with the matrix compounds. GC×GC MS provide more reliable identification than GC MS to improved massspectral quality. Concentration of fractions through cryogenic modulation increasesthe peakintensities allowing the detection of lower quantities than in one dimension gas chromatography. One drawback ofGC×GC is relatively tedious data analysis, which is more time consuming thanGC and which requires the special software. The further disadvantage is the consumption ofcoolant requires with cryogenic modulator. Advantages of GC×GC neverthelesseasily outweigh its disadvantages, particularly in trace analysis of highly complexsamples. In summary, the instrumentationof this study proves highly useful inanalysis of environmental samples and it would besuitable for analysis of other several types of complex samples as well.

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