Universitat de les Illes Balears

DEPARTAMENTO DE QUÍMICA

DOCTORADO EN CIENCIA Y TECNOLOGÍA QUÍMICA

Exploiting novel automated analytical methodologies for the monitoring of environmental organic pollutants, and its potential incorporation to environmental monitoring regulations

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2012

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Palma de Mallorca, 3 de Septiembre de 2012

Dr. Víctor Cerdà Martín

Dr. Rafael Forteza Coll

A mis padres, Luis y Mercedes.

(To my Parents)

AGRADECIMIENTOS

Echando la vista atrás, sin duda un importante desafío al que me enfrento en esta memoria corresponde a la parte de agradecimientos. Han sido años de grandes cambios, de mucho trabajo y en los que han intervenido muchas personas en mi vida, tanto personal como investigadora. Espero ser capaz de mostrar la gratitud que les debo a todos de igual forma que la siento:

Al Ministerio de Ciencia e Innovación de España, por haberme otorgado una beca pre doctoral y una ayuda para una estancia en Copenhague, sin la cual no hubiera podido optar al título de Doctor.

Al Consell Insular de Mallorca, por la financiación a través de diversos proyectos para el análisis de compuestos orgánicos volátiles.

A la Universidad de las Islas Baleares y la Universidad de Copenhague, por permitirme desarrollar mi labor investigadora en sus centros.

Al Dr. Víctor Cerdà, jefe del grupo de Química Analítica, Automatización y Medioambiente, por haber confiado en mí hace cuatro años dándome un lugar en el que crecer como investigador.

Al Dr. Rafael Forteza, por estos cuatro años de aprendizaje, y de los cuales además me llevo una amistad sincera que espero dure para siempre.

A todos los trabajadores de las empresas participantes en nuestros proyectos: TIRME, EMAYA y LABAQUA, con especial aprecio a la Dra. Amalia Cerdà, Xisco Amaya y Gonzalo del Valle de TIRME y a la Dra. Dolores Mateo de EMAYA, por sus horas de trabajo, ayuda y asesoramiento, siempre ofreciendo su mejor versión.

A la Dra. Kristine A. Krogh y demás miembros del laboratorio de Advanced Drug Analysis de la Facultad de Ciencias Médicas y de la Salud de la Universidad de Copenhague: Martin, Søren, Gitte, Frederik, Bjarne, Susanne, Jesper, Keneth y compañía. Por haberme enseñado tanto, y haber tenido la suerte formar parte de un grupo de trabajadores y personas extraordinarias. Mi casa es vuestra casa.

Y por supuesto a mis compañeros de laboratorio, a los que espero no haber cansado con mis canciones, bailes y chistes. No escribo el nombre de todos porque son tantos que me perdería: cantidad de compañeros, doctores, becarios, profesores y técnicos, sin olvidar los innumerables visitantes que han pasado por nuestro grupo a lo largo de estos años. A pesar de haber sido durante mucho tiempo el “bicho raro de los malos olores”, han sido años llenos de recuerdos imborrables que han dado lugar a algunas grandes amistades y que han provocado en mí una maravillosa evolución personal fruto de tanta buena gente conocida. Todos vosotros habéis aportado algo

positivo a mi vida. Ojalá el sentimiento sea mutuo.

A todos vosotros os doy las gracias más sinceras por todos los momentos vividos, las enseñanzas y recuerdos que me llevo.

En la parte personal, han sido cuatro años cargados de emociones y sentimientos enfrentados. Muchas personas nos han dejado, llenando este camino de obstáculos que uno, por fuerza, aprender a esquivar.

Gracias a mi madre Mercedes, mis hermanos, Luis, Guillermo, Miguel y Pablo, a Adriana y mis sobrinos Iker y Miguel, por ser parte de mí a pesar de los pesares, levantándonos juntos las veces que hayamos podido caer. La familia no se elige, y a mí me ha tocado una de las buenas.

Esta Tesis Doctoral ha sido el fruto de un trabajo constante y difícil, casi siempre en solitario y sin recompensas, que no hubiera sido posible sin tres de las mejores personas que hay en este Mundo. Quiero terminar mis agradecimientos con ellas porque son las más especiales:

Dr. Erland Björklund, aquel que un día el destino colocó en la mesa de al lado, y sin buscarlo se convirtió en la persona que me ha orientado, enseñado y dirigido en el mundo de la investigación, siendo además un gran amigo en los momentos difíciles. Muchas gracias a ti, Erland, y a Karin y al resto de "mi familia sueca". Como siempre te digo: "*eres como el cuarto hermano mayor que nunca tuve…*".

Dr. Fernando Maya, la persona a la que más debo en este laboratorio, compañero de tantas aventuras que uno ya pierde la cuenta y, seguramente, la persona más preparada para la investigación que conozco. Su marcha del laboratorio para ir con la élite dejó un hueco que no se va a llenar, así que no pierdo la esperanza de seguir compartiendo laboratorio en el futuro. Gracias "compadre" por llenarme todos los vasos "medio-vacíos".

Y por último y más importante, mi mujer, Isabel, mi otro yo, la mejor persona que pude encontrar, la que ha compartido conmigo cada momento sin esperar nada a cambio, y con la que espero llenar de vidas nuestro futuro. Es sin duda la que mejor conoce el esfuerzo que ha supuesto esta Tesis para mí y la que más la ha sufrido junto a mí. Gracias. Te quiero.

Esta Tesis va dedicada a la memoria de mi Padre, Luis, quien se empeñó en complicarme los dos últimos años y al que tanto echamos de menos.

ACKNOWLEDGEMENTS

Looking back over the years, one big challenge that I face in this PhD Thesis certainly arises from the acknowledgments part. These have been years of great changes, a lot of work and where many people get involved in my life, both personal and researcher. I hope to be able to show the gratitude that I owe them all in the same way as I feel it:

Spanish Ministry of Education and Sciences, for giving me a pre-doctoral scholarship and the financial support that helped me to make a stay in Copenhagen, essential to go for the PhD Degree.

Consell Insular de Mallorca for the financial support on the identification of volatile organic compounds

Dr Victor Cerdà, head of the Analytical Chemistry, Automation and Environment Group, for trusting me four years ago by giving me a place where to grow as a researcher.

Dr. Rafael Forteza, for these four years of learning which took me a sincere friendship which I hope will last for many years.

All employees of the companies participating in our projects: TIRME, LABAQUA and EMAYA. A special appreciation goes to Dr. Amalia Cerdà, Xisco Amaya and Gonzalo del Valle from TIRME, and Dr. Dolores Mateo from EMAYA, for their labour time, always offering help and advice with the best of their professionalism.

Dr. Kristine A. Krogh and other members of the Advanced Drug Analysis Laboratory, Faculty of Medical Sciences and Health, University of Copenhagen: Martin, Søren, Gitte, Frederik, Bjarne, Susanne, Jesper, Kenneth, and so on; for having taught me so much as part of a group of extraordinary people. My home is your home.

To my lab mates, who I hope will not be tired with my songs, dances and jokes. I do not write the list of names of all of them since there are so many that I would get lost: colleagues, professors and technicians, also mentioning the countless visitors who have passed through our group over the years. Despite having been long time the "freak of bad odours", these have been years full of unforgettable memories that have led to some great friendships and have caused me a wonderful fruit of personal growth owing the so many good people met along the way. I wish the feeling is reciprocal.

To all of you I thank you sincerely for all the moments experienced, knowledge and memories that I take with me.

On the personal side, these four years have come full of emotions and mixed

feelings. Many people have left us, filling the course with obstacles that I had to learn how to avoid.

Thanks to my mother Mercedes, my brothers, Luis, Guillermo, Miguel y Pablo, Adriana and my nephews Iker and Miguel, for being always a part of me, raising us up together as often as we could fall. Families cannot be chosen, and I got one of the good.

This Doctoral Thesis has been the fruit of constant and hard work, often alone and without rewards. Ii would not have been possible without three of the most incredible people that live in this World. I want to finish the acknowledgments with them as long as they are the most important:

Dr. Erland Björklund, that the fate one day placed on the table next to mine and, without trying, became the one who guided, taught and directed me, furthermore becoming a friend in the hard times. Thank you very much to you, Erland, and Karin and the rest of my *Swedish family*. As I like to say, "*You are like the 4th big brother I never had…*"

Dr. Fernando Maya, the person to whom I owe the most in this laboratory, fellow of so many stories and the person most incredibly prepared for the research that I know. His departure left a hole in the lab that has not been filled yet, but I do not lose any hope to keep on sharing laboratory in the future.

And finally and most importantly, my wife, Isabel, my other self, the best person I could find, which has shared with me all this time without expecting anything in return. She is undoubtedly the one who knows best the effort that has brought this thesis to me. Thank you. I love you.

This Thesis goes dedicated in loving memory of my father, Luis, who tangled me the last two years and whom we all deeply miss in our lives.

RESUMEN

Las actividades humanas llevan asociadas, en la mayoría de los casos, la emisión a gran escala de contaminantes (muchos de ellos compuestos orgánicos) que suponen un peligro inminente para la salud humana y el medioambiente. Alrededor de 100 000 productos químicos han sido catalogados hasta el día de hoy, siendo a priori todos ellos potencialmente susceptibles de generar peligro a corto, medio o largo plazo. Sólo un pequeño porcentaje de estos compuestos ha sido estudiado para la evaluación de los daños en humanos o en el medioambiente. Se puede considerar que se desconocen los impactos reales de la gran mayoría de estos compuestos.

El seguimiento de los niveles de concentración ambiental de los contaminantes mediante la monitorización periódica es el método más empleado actualmente para conocer el estado de polución (degradación) de un determinado medioambiente. En función de los niveles de contaminación medidos se deben tomar las medidas efectivas pertinentes para reducir dichas emisiones y restablecer el medioambiente dañado lo más rápido posible. Estas medidas efectivas deben reflejarse en leyes de protección ambiental que restrinjan las actividades humanas contaminantes y favorezcan las actividades sostenibles con el medioambiente. A pesar de los avances en investigación en el campo de la química analítica y sus aplicaciones ambientales, muy escasos compuestos son todavía considerados contaminantes prioritarios, y por tanto, el número de compuestos reglamentados en leyes que regulan sus emisiones (fijando valores umbral de emisión) se limita a menos de un centenar. Los intereses económicos actuales no permiten que los avances científicos en el campo de la protección medioambiental sean aplicados en medidas efectivas que repercutan en el bienestar del conjunto de la sociedad, y en general sólo se actúa en caso de catástrofes ambientales.

Por este motivo, se han desarrollado varios métodos analíticos en nuestro grupo para la valoración de los niveles de emisión y la concentración ambiental de una serie de compuestos orgánicos considerados peligrosos en el medioambiente de Mallorca que, en muchos casos, no están contemplados en ningún tipo de legislación de protección ambiental.

La parte experimental de la Tesis doctoral se divide en dos secciones. La primera parte, más extensa, se centra en el desarrollo de un método analítico para la determinación de compuestos orgánicos volátiles, para una posterior evaluación de las emisiones y concentraciones ambientales de diversas instalaciones de tratamiento de residuos urbanos en Mallorca. La segunda parte está enfocada en la determinación de

fármacos de consumo humano en el medioambiente acuático de Mallorca, justificando las fuentes concretas de emisión de cada compuesto detectado.

En primer lugar se desarrolló un método analítico para determinar múltiples compuestos orgánicos volátiles en muestras gaseosas. El método estaba basado en la cromatografía gaseosa con posterior detección por espectrometría de masas, *GC-MS* según su acrónimo inglés. Para la extracción y preconcentración de los analitos de interés se utilizaron trampas adsorbentes (dentro de las técnicas de extracción en fase sólida) con posterior desorción térmica (*TD*, acrónimo inglés). Para la calibración analítica del método se implementó y optimizó un nuevo procedimiento basado en la volatilización de patrones líquidos previa a la interacción sobre los sólidos adsorbentes que mejora los factores de respuesta y la reproducibilidad del método.

En segundo lugar, se aplicó el método de desorción térmica – cromatografía gaseosa – espectrometría de masas (*TD-GC-MS*) para calcular las emisiones totales de 42 compuestos orgánicos volátiles en el mayor vertedero de residuos sólidos urbanos de Mallorca. En el mismo estudio se llevó a cabo una evaluación de los niveles de olor por olfatometría dinámica de las muestras (mediante un laboratorio externo acreditado) para encontrar una correlación positiva entre niveles de olor y composición del aire. De este modo se podrían identificar algunos compuestos de la muestra como marcadores de olor

En tercer lugar, se analizaron diferentes plantas de tratamiento de residuos sólidos urbanos aplicando el método analítico *TD-GC-MS* para la caracterización de 93 compuestos orgánicos volátiles emitidos en cada una de las plantas. Mediante tratamiento estadístico de los datos, incluyendo un análisis de componentes principales y un análisis de clústeres, se evaluaron las diferencias entre las distintas muestras, correlacionando de manera clara cada muestra con su composición química, asignándola a su planta de origen. Este nuevo método permite la identificación del origen de una muestra desconocida, mostrándose especialmente útil para episodios de olor cercanos a las plantas de tratamiento estudiadas.

En último lugar se optimizó y aplicó un método analítico de cromatografía líquida de alta presión con detección por espectrometría de masas en tándem, *HPLC-MS*^{2} según su acrónimo inglés, para conocer el grado de contaminación ambiental acuático en Mallorca a causa del uso de fármacos en humanos. En este mismo estudio se describen las vías de contaminación seguidas por este grupo de contaminantes orgánicos polares, desde su uso como fármacos medicinales o su eliminación en vertederos, hasta los acuíferos subterráneos, el mar o Parques Naturales. Los analitos de interés fueron extraídos de las muestras acuosas mediante una extracción en fase sólida convencional.

ABSTRACT

Human activities have associated, in most of cases, the large-scale emission of pollutants (involving thousands of different organic compounds) that pose imminent danger to environment and human health. About 100 000 chemicals have been catalogued to date, being a priori all potentially susceptible to generate risks in the short, medium or long-term. Only a small proportion of these compounds has been studied to assess real damages in humans or the environment. One can consider that the current real impact of the majority of these chemicals still remains unknown.

Tracking of environmental concentrations levels of pollutants by the periodic monitoring evaluation is nowadays the main scheme used to determine the pollution state (degradation level) of a specific ambient. Appropriate effective measures should be taken, on the basis of the measured levels, to reduce contaminant emissions and restore the damaged environment as soon as possible. These measures must be reflected in novel environmental protection laws restricting pollutant human activities and promoting the sustainable ones. Despite advances in analytical chemistry and environmental research, very few compounds are still considered priority pollutants, and therefore the number of compounds being actively regulated within environmental legislation governing their emissions (setting threshold values) is limited to less than one hundred in Spain and many other EU and non EU Countries. Current economic interests do not allow scientific advances in the environmental protection field to be implemented on the welfare of the whole society. In most cases these environmental measures are merely adopted after environmental disaster.

For this reason, several analytical methods have been developed in our group for assessing emission rates and environmental concentration levels of a broad variety of organic compounds considered potentially hazardous in the environment of Mallorca, which in many cases do not fall within any kind of environmental protection regulation.

The experimental part of this Doctoral Thesis is divided into two sections. The first one, more extensive, focuses on the development of an analytical method for the determination of volatile organic compounds, for further evaluation of the emissions and environmental concentration levels in diverse municipal solid wastes' treatment plants and disposal landfills. The second part is focused on the determination of pharmaceuticals for human consumption in the aquatic environment of Mallorca, justifying particular emission sources

First of all, we developed an analytical method to determine multiple volatile organic compounds in gaseous samples. The method was based on gas chromatography with

subsequent detection by mass spectrometry (GC-MS). For the extraction and clean-up of the analytes of interest were used sorbent traps (included within solid phase extraction techniques) with subsequent thermal desorption (TD). For analytical calibration of the method it was implemented and optimized a novel procedure based on the volatilization of liquid standards prior to the solid adsorbent interaction, which improves the response factors and reproducibility of the method.

Secondly, we apply the method of thermal desorption - gas chromatography - mass spectrometry (TD-GC-MS) to calculate overall emissions of 42 VOCs in the largest municipal solid waste landfill in Mallorca. In the same study was carried out an assessment of odour levels by dynamic olfactometry of the collected samples (by an external ISO accredited laboratory) with the goal to find a positive correlation between odour units and air composition. Thus certain compounds could be identified in the sample as markers of odour.

In the third work, several industrial facilities (treating different fractions of municipal wastes) were analysed by applying the TD-GC-MS method for the characterization of 93 volatile organic compounds emitted in each of the plants. By a statistical treatment of data, including principal component analysis and cluster analysis, we evaluated the differences between samples, correlating each sample clearly with their chemical composition, enabling the assignation to the facility of origin. This new method allows the identification of an unknown origin of one polluted ambient air, being particularly useful when odorant episodes occur near the studied treatment plants.

Finally, it was optimized and implemented an analytical methodology based on high pressure liquid chromatography with tandem mass spectrometry detection (HPLC-MS^2), to ascertain the extent of water pollution in Mallorca because of the use of medicines in humans. In this study are described the contamination routes followed by this group of polar organic pollutants, from their use as medicines or landfill disposals to groundwater aquifers, sea or Natural Parks. The analytes of interest were extracted from the aqueous samples by a solid phase extraction

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CHAPTER 1

GENERAL INTRODUCTION

GENERAL INTRODUCTION

In all likelihood, the World currently faces the worst global environmental pollution situation ever. Human activities have had a continuous critical impact at all the environmental levels: atmosphere, lithosphere and hydrosphere. By definition, *pollutant* (or *contaminant)* is any substance which may harm humans, animals, vegetation or material. Many socioeconomic factors have contributed decisively up to the present situation. One example among many is about the contamination derived from the constant increase of the worldwide energy production, to completely supply the increasing necessities of the consumer society. This situation involves massive use of fossil fuels or radioactive matter to supply energetic demands for industrial processes, transport use, etc. Indeed, all these industrial developments have come with undesired high prices: air pollution, massive generation of wastes, overexploitation of natural resources, destruction of biodiversity, poisoning of fresh water reservoirs or climate changes are some evidences, and it might continue to a nearly endless list of medium and long-term consequences. Human health and environment are nowadays unquestionably affected by worldwide contamination.

Natural ecosystems are dynamic environments, entangling broad biological, chemical, and geological cycles in constant transformation (Figure I), and environment pollutants may participate actively into changing processes. Once they reach the environment, pollutants can transform in multitude of sub-products, spread or distribute randomly, and/or accumulate either in specific areas or regularly along ecosystems. The interconnection between adjoining ecosystems aggravates the global environmental pollution problem, since specific local changes, even in a small scale, may result in severe unexpected consequences which might lead to a situation of no return. One worldwide known example was described in 2004 about the unexpected annihilation over up to 95% of vulture's population in Pakistan, due to liver failure as a consequence of the ingestion of diclofenac residues, originally used for veterinary medicine in several animals [1]. It evidenced that medicines may have unknown mechanisms of action, and many similar cases might be happening worldwide concerning other chemicals, even though there were no evidences.

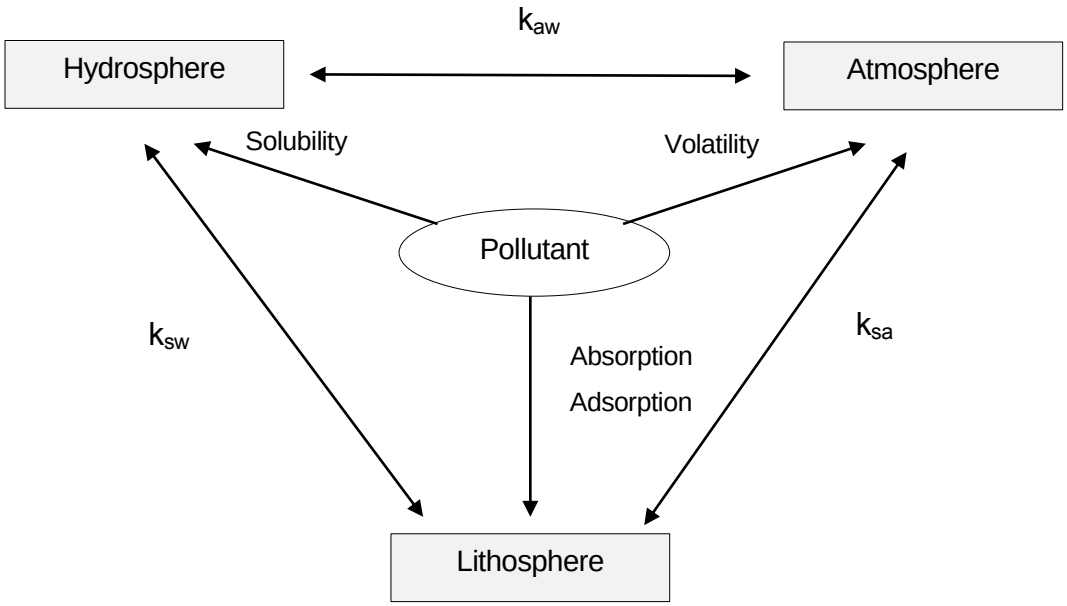


Figure I. Distribution pathways of the pollutants in the environment. Pollutant's coefficient rate: K_{aw}, between air and water; K_{sw}, between soil and water; K_{sa}, between soil and air

As it seems evident, to comprehensively understand the seriousness of the situation, environmental pollution evaluations need a global long-term point of view. The real impact of certain pollutants might not be detected in a short or medium-term, thus the dangers might be wrongly estimated. Another critical factor arises from the difference in the time-scale of bio-geological natural processes compared to human's time-scale. Frequently natural cycles are not able to amend existing environment pollution levels in a time-scale valid for humans, looming threatening implications. In this sense, the only way to completely remove contamination would be by stopping contaminant activities. However, the "industrial stop" is not possible at all, so the best alternative is the implementation of restrictive laws regulating human activities with the aim to protect environment and human health. Only this new legal framework would lead to unpolluted environmental situations.

Environmental protection must be accomplished working on several different areas, covering from the local to global perspectives. Only by joining forces in all areas can be achieved optimal environmental conditions. Improvements must be focused on research, education, reduction and legislation.

Research. As backbone of the human development, this is assumed the most important area of action to amend environmental pollution. Two are the main goals: stop releasing contaminants, and remove the existing pollutants from the environment.

On one hand, environmental friendly (sustainable) technologies must be developed and implemented worldwide to substitute at all levels current contaminant industries and technologies (e.g. transports, industrial processes, energy generation, chemicals, waste treatments, recycling, etc.). It is necessary to investigate alternative green and sustainable processes to substitute the current ones.

On the other hand, further comprehensive studies must be carried out to better understand the real impacts of current pollution levels over environment and human health. Short, medium and long-term evaluations (e.g. risk assessments, occurrence studies, modelling of pollution paths, etc.) must be carried out to in order to develop novel technologies which enable the elimination of pollutants to move back to the desired clean environments (free of any contamination).

Education. Another important field of action must rely upon the raising of public awareness about the severe damage we are causing to environment, and the threat of long-term irremediable consequences. It is especially unavoidable in those countries in process of development, where industrial improvements are still on time to be environmental sustainable. It is evident that the higher the public awareness on contamination and its consequences, the less the pollution levels, either at local or national frameworks. Economy cannot be the top priority of any society above environment protection. Public environmental educational programmes must be implemented to make population aware that economy must be a tool, not the objective itself.

Reduction. World's global demands and consumption rates must be inexorably reduced to reach a balanced situation between the total human consumption with the sustainable amount the Earth can safely provide us. This is in direct relationship to the research field, since better developed technologies would help us in saving raw materials even though human demands were not decreased.

The other imperative need is the reduction of all kind of wastes (solid, liquid and gaseous). Waste treatment and disposal planning in many industrialized countries (included Spain) are currently based on three principles, namely the three '*R*': Reduction, Reuse and Recycle of residues. However, looking back with perspective, we can clearly realize that this system is vulnerable and can easily fail. In practice, almost every responsibility relies on the final users, and few if any restrictions are given to manufacturing companies. The reduction of residues must start from the design and the elaboration of any product, establishing beforehand feasible reuses or recycling paths.

Legislation. As long as research draws the pathways to reach efficient environmental protection by the use of sustainable technologies, legislative frameworks are the necessary tool forcing all the parts to follow the marked route. Legislation is the

glue that fixes every piece in the puzzle.

Governments in force must unavoidably establish appropriate laws, governing and establishing the cooperation framework between the different mentioned areas, where protection of environment and human health must be the top priority above all other social factors, leaving no room for ambiguities. International collaboration is also completely necessary

Besides the risks over human health and environment, appropriate environmental legislations would help to save money, so important in the current global financial crisis. Only in EU countries, the cost of the industrial air pollution has been estimated over €169 billion in 2009 (see section 1.1.1). These costs are estimated for a specific area of the World. What about overall costs including water and soil in the whole World? "Environmental friendly" can also mean "economical friendly".

Environmental monitoring

Environmental directives covering periodical monitoring of pollutants in Europe are one of the most restrictive and comprehensive in the World. European Union adopted in 1993 the European Environmental Agency (EEA) and the European Environment Information and Observation Network (EIONET) [2]. These two agencies are responsible of helping the Community and Member Countries make informed decisions about improving the environment and integrating environmental considerations into economic policies moving towards sustainability.

Environmental protection has been notably improved since EEA and EIONET were created, owing the unification of the different criteria governing every country. However European environment is still too far from a "total protection" situation, and even further from their rehabilitation. There are many lacks in the environmental laws regarding monitoring regulations.

Nearly 100.000 chemicals have been inventoried, and 500 to 1000 are added every year to the list [3]. The major part of these chemicals has not been evaluated for risk assessment, neither in the environment nor in humans. Very few of them are legislated in environmental directives to be periodically monitored to verify its concentration within stated limit thresholds.

In the last 20 years, i.e. since EEA and EIONET were created, the improvements in analytical instrumentation (e.g. selectivity, sensitivity, ease and speed) and sample clean-up and extraction techniques, in parallel with the development of powerful computers and statistical modelling tools, enabled easy and fast analysis of multiple compounds embedded inside very complex matrices (e.g. environmental soil, air and water). Multitude of new chemicals can be currently evaluated in the environment

through a wide list of suitable and verified methodologies. Regretfully, these advances have not been implemented into efficient and strict laws and novel contaminants are continuously emerging every year.

There is a rising concern about organic chemicals in the environment. For example, the US–EPA bibliographic database of pharmaceuticals and personal care products (PPCPs) [4] lists over 6500 relevant studies in scientific journals and books since 1999, however it is a double-edged sword. While this certainly shows an on-going escalation in publishing activity, it does not tell us if these works have targeted the most pressing needs, if they are being actively used to inform decision making, or whether they are resulting in useful outcomes for society. The ultimate destination for organic pollutants research might be only evident in the larger context involving a truly holistic examination of the complete life cycles of the chemicals. Despite the wealth of published data, little has yet proved of use of major number of organic compounds in actual implementation of system redesigns that are more sustainable or even for informing regulatory deliberations.

We have expounded along this general introduction about the backbone guidelines which may lead us to a safe environment. The focus of this Doctoral Thesis (comprehensively described in Chapter 2) is the development and application of reliable analytical methodologies to determine a group of organic compounds in the environment, meeting the requirements to be immediately implemented in more restrictive environmental monitoring regulations.

Volatile organic compounds (VOCs) and human medical pharmaceuticals residues (pharmaceutically active compounds, PhACs) were analysed in environmental samples of relevant interest. An overview of these sub-sets of organic compounds, including recent trends in the analytical techniques, sample extraction techniques, environmental occurrence and fate is described along this introductory Chapter 1.

1.1 DETERMINATION OF VOLATILE ORGANIC COMPOUNDS IN THE AIR.

This Doctoral Thesis is firstly focused on the atmospheric pollution of volatile organic compounds (VOCs), thus there is a comprehensive description of VOCs behaviour in the atmospheric environment along this introduction, as well as the major recent trends in the determination and quantification of VOCs in the air.

Volatile Organic Compounds are one of the most common organic pollutants in the environment. They encompass a diverse group of organic chemicals with different structure and properties such as alkanes and alkenes, aldehydes and ketones, acids, esters and ethers or aromatic and halogenated compounds, and other natural compounds like isoprene and terpenes. Table 1.1-1 shows several examples of VOCs with some of their most frequent uses.

A high vapour pressure is the common characteristic to all of them. The IUPAC *(International Union of Pure and Applied Chemistry)* do not provide a unique definition for VOCs, however in some reports [5] they mention the European Union definition, adopted by the European Environment Agency (EEA) [6]:

- "Volatile organic compound (VOC) means any organic compound, excluding methane and carbon dioxide, having at 293.15 K a vapour pressure of 0.01 kPa or more, or having a corresponding volatility under the particular condition of use."

Other EU definitions [7] reported VOCs as

- "Any organic compound having an initial boiling point less than or equal to 250°C measured at a standard pressure of 101,3 kPa".

The United States Environmental Protection Agency (US-EPA or EPA) also defines VOCs as [8]:

- "Any compound of carbon, excluding carbon monoxide, carbon dioxide, carbonic acid, metallic carbides or carbonates, and ammonium carbonate, which participates in atmospheric photochemical reactions" .

Thousands of compounds are estimated to be included among VOCs. Their emissions are distributed along atmosphere, water and soil and sediments. Notwithstanding, these liquid organic compounds, according to each individual vapour pressure value (vapour pressure of the liquid, P_L, *Eq. 1, page 12*, are essentially in the gaseous phase, so the atmosphere is the main receptor of the emitted VOCs. They can also be discharged through any kind of waste water effluents upon hydrosphere and soils (e.g. municipal wastewater, municipal or industrial solid wastes). Pollution pathways may not be considered static; nevertheless VOCs exchanges between reservoirs are frequent, especially for those of the most persistent compounds.

Atmospheric pollutants are transferred to soil and water through deposition, either with or without rain.

Table 1.1-1 Examples of VOCs and main emission sources and/or applications.

Type of substance	Compound	Formula	Emission/application
Aromatic Hydrocarbons	Benzene	C_6H_6	Traffic
	Toluene	C_7H_8	Lacquers, dyes
	Xylenes	C_8H_{10}	paints, traffic
Aliphatic Hydrocarbons	n-Hexane	Various C_6H_{14}	Lacquers, adhesives
Halogenated Hydrocarbons	Dichloromethane	CH_2Cl_2	Solvents, paints
	Chlorobenzene	C_6H_5Cl	Dry cleaning, rubbers
	Tetrachloroetylene	C_2Cl_4	Plastics
Alcohols	Methanol	CH_3OH	Organic synthesis
	Ethanol	C_2H_5OH	Drinks
Esters	Ethyl acetate	$CH_3COOC_2H_5$	Lacquers, solvents
Ketones	2-Butanone	$CH_3COC_2H_5$	Lacquers, resins
Ethers	Ethyl tert-buthyl ether	$CH_3OC(CH_3)$	Oxygenated fuels
Amides	Dimethylformamide	$HCON(CH_3)_2$	Plastics

1.1.1 POLLUTION IN THE ATMOSPHERIC ENVIRONMENT

Atmosphere is the gaseous layer around the Earth rising up to 10000 km height. Its current chemical composition is the result of hundred millions of years of evolution on Earth. It is structured in several stratums, divided one another according to gas density and temperature criteria. Every stratum has different chemical compositions and so different physicochemical processes takes place [9]. The lowest stratum, namely *troposphere*, which covers up to 12 km above sea level, becomes the most important fraction since it is the one supporting life on Earth. Its composition can be considered rather constant (except water vapour). It is estimated that 80% of the total atmospheric gases are comprised within the tropospheric stratum, including the major percentage of the organic pollutants emitted to the atmosphere. The gases in the *troposphere* can be listed, according to each relative contribution [9] as:

- *Major gases*: N_2 (78,08%) and O_2 (20,95%)
- *Minor gases*: Ar (0,934%) and CO_2 (0.035%)
- *Noble gases*: Ne (0,0018%), Kr (0,00114%), He (0,0052%) and Xe (0,00009%)
- *Trace gases*: compounds either from biogenic or anthropogenic origin, in a much lower proportion. They may be organic like CH_4 and $CHCl_3$ or inorganic like NO_x, SO_2 and CO.
- *Water vapour*: its proportion may vary between 0,1 to 5% according to local meteorological conditions.

Despite the relative contribution of trace gases might seem low compared to N_2 and O_2, these are the main responsible of pollutant impacts, since their presence in the atmosphere are altering the biochemical natural cycles slowly established along the evolution progress.

Organic compounds present in the atmosphere are partitioned between gas and particle phases [10-12] and the phase in which a chemical exists in the atmosphere can significantly influence its dominant tropospheric removal process(es) and lifetime [11]. For partitioning proceeding by surface adsorption, gas/particle partitioning depends on the liquid-phase (or sub-cooled liquid-phase) vapour pressure, P_L, at the ambient atmospheric temperature, the surface area of the particles per unit volume of air, ϑ, and the nature of the particles and of the chemical being adsorbed. The fraction of the chemical present in the particle phase, φ, depends on these parameters through an equation of the form [10, 11]:

$$\varphi = c\vartheta / (c\vartheta + P_L) \quad (1)$$

where c is a parameter which depends on the chemical being adsorbed and on the nature of the particle. To a first approximation, chemical compounds with liquid-phase vapour pressures of $P_L<10^{-6}$ Pa ($<10^{-8}$ torr) at the ambient atmospheric temperature are present in the particle phase, and those with values of $P_L>1$ Pa ($>10^{-2}$ torr) at the ambient atmospheric temperature exist essentially totally in the gas-phase [11, 13] and are commonly named volatile organic compounds (VOCs). Chemicals with intermediate values of P_L are present in both the gas and particle phases and are often termed semi-volatile organic compounds (SOCs or SVOCs). Because of the variation of P_L with temperature, for a given particle surface area a decrease in ambient atmospheric temperature will increase the fraction of the SOC present in the particle phase.

The need to improve air quality has been long recognized. In modern times the disaster in the fluorine intoxication in Meuse Valley (Belgium) in 1930 [14] and the London's deadly smog in 1952 [15] killed thousands of people in Europe. Many other environmental pollution disasters have taken place worldwide, and Bhopal Disaster in 1984 might be the worst episode ever [16]. These disasters prompted the adoption of air quality legislations. In the last decades a variety of laws have been enacted at the local, national and EU levels, as well as through international conventions, such as the European Nations Convention on Long-range Transboundary Air Pollution (UNECE-CLTRAP, see section 1.1.5.1 [17]).

In Europe, policies and actions implemented at different levels have greatly reduced anthropogenic emissions and exposure in the last decades; however many air pollutants have not been evaluated ever, while some other still harms environment and human health. Emissions of acidifying pollutants have been reduced, but atmospheric nitrogen oversupply still threatens biodiversity in sensitive terrestrial and water ecosystems. Nowadays, the movement of atmospheric pollution between continents attracts increasing research and political attention.

Air pollutants, such as carbon monoxide (CO), sulphur dioxide (SO_2), nitrogen oxides (NO_x), volatile organic compounds (VOCs), ozone (O_3), heavy metals, and respirable particulate matter ($PM_{2.5}$ and PM_{10}), differ in their chemical composition, reaction properties, emission, time of disintegration and ability to diffuse in long or short distances. Air pollution has both acute and chronic effects on human health, affecting a number of different systems and organs. It ranges from minor upper respiratory irritation to chronic respiratory and heart disease, lung cancer, acute respiratory infections in children and chronic bronchitis in adults, aggravating pre-existing heart and lung

disease, or asthmatic attacks. In addition, short- and long-term exposures have also been linked with premature mortality and reduced life expectancy. Table 1.1-2 summarizes harmful effects of some regulated air pollutants on human health, the environment and the climate changes.

Besides this group of organic chemicals there is a vast list of other toxic organic compounds, classified as persistent organic pollutants (POPs) [18]. They persist in the environment for long periods of time, and their effects are magnified as they move up through the food chain (bio-magnification). They include pesticides, polychlorinated dibenzo-dioxins (PCDDs), polychlorinated dibenzo-furans (PCDFs), polychlorinated biphenils (PCBs), polycyclic aromatic hidrocarbons (PAHs), chlorofluorocarbons (CFCs), and a wide list of emerging contaminants. There is a vast bibliography available regarding analytical methodologies, environmental occurrence and fate, toxicity, etc. for this groups of POPs [19, 20].

Environmental pollution also generates high costs to any society. A 2011 report from the European Environmental Agency (EEA) estimated the costs of air pollution up to €169 billion [21]. The contaminants with the most elevated costs are (in decreasing order): dioxins and furans, PAHs, benzene, heavy metals, particulate matter (PM), nitrogen and sulphur oxides (NO_x and SO_x), ammonia, some VOCs and CO_2. In the same report is stated that half of the total damage cost was caused by just 191 facilities. It is an extra guideline to efficiently aim the efforts to mostly reduce air pollution: “global perspective, local actions”.

Table 1.1-2 Effects of regulated air pollutants on human health, the environment and the climate.

Pollutant	Health Effects	Environmental effects	Climate effects
Particulate matter (PM)	Can cause or aggravate cardiovascular and lung diseases (e.g. reduced lung function, asthma attacks, chronic bronchitis, susceptibility to respiratory infections), heart attacks and arrhythmias. Can affect the central nervous system, the reproductive system and cause cancer. The outcome can be premature death.	Can affect animals in the same way as humans. Affects plant growth and ecosystem processes. Can cause damages and soiling of buildings, including monuments and objects of cultural heritage. Reduced visibility	Climate effects vary depending on particle size and composition: some are reflective and lead no net cooling, while other absorbs solar radiation leading to warming. Can lead to changed rainfall patterns. Deposition can lead to changes in surface albedo.
Ozone (O_3)	Irritates eyes, nose, throat and lungs. Can destroy throat and lung tissues, leading to decrease in lung function; respiratory symptoms, such as coughing and shortness of breath; aggravated asthma and other lung diseases. Can lead to premature mortality.	Damages vegetation by injuring leaves, reducing photosynthesis, impairing plant reproduction and growth, and decreasing crop yields. Ozone damage to plants can alter ecosystem structure, reduce biodiversity and decrease plant uptake of CO_2	Ozone is greenhouse gas contributing to warming of the atmosphere
Nitrogen oxides (NO_x)	NO_2 can affect the liver, lung spleen and blood. Can aggravate lung diseases leading to respiratory symptoms and increased susceptibility to respiratory infection.	Contributes to the acidification and eutrophication of soil and water, leading to changes in species diversity. Enhances sensitivity (such as drought) on vegetation. Act as a precursor of ozone and, particulate matter, with associated environmental effects. Damages buildings.	Contributes to the formation of ozone and particulate matter, with associated climate effects

Sulphur oxides (SO_x)	Aggravates asthma and can reduce lung function and inflame the respiratory tract. Can cause headache, general discomfort and anxiety.	Contributes to the acidification of soil and surface water. Contributes indirectly to the transformation of mercury to bioaccumulative methyl-mercury, which is toxic. Causes injury to vegetation and local species losses in aquatic and terrestrial systems. Contributes to the formation of inorganic particulate matter with associated environmental effects. Damages building materials.	Contributes to the formation of sulphate particles, cooling the atmosphere.
Carbon monoxide (CO)	Can lead to heart disease and damage to the nervous system (e.g. personality and memory changes, mental confusion and loss of vision). Can cause headache, fatigue and dizziness.	may affect animals in the same way as humans, although concentrations capable of causing these effects are unlikely to occur in the natural environment, except in extreme events such as forest fires	Contributes to the formation of greenhouse gases such as CO_2 and ozone.
Heavy metals	Can affect almost every organ and system, especially the nervous system. Can cause premature birth, impaired mental development and reduced growth.	Bioaccumulates and adversely impacts both terrestrial and aquatic systems. Effects on animal life include reproductive problems and changes in appearance or behaviour. Very toxic to aquatic life.	No specific effects
Benzene and Benzo(α)pyrene	A human carcinogen, which can cause leukaemia and birth defects. Can affect the central nervous system and normal blood production, and can harm the immune defence	Has an acute toxic effect on aquatic life. It bioaccumulates especially in invertebrates. Leads to reproductive problems and changes in appearance or behaviour. It can damage leaves and cause death in plants.	Greenhouse gas contributing to the warming of the atmosphere. It also contributes to the formation of ozone and secondary organic aerosols.

1.1.2 EMISSION SOURCES OF VOCs TO THE ATMOSPHERE

In former times, the origins of VOCs emissions were biological and geological natural processes, such as microorganism degradation products or vegetation and volcanoes emissions. However this equilibrium started to be altered in 20th century with the industrial revolution and the massive use of chemicals and fossil fuels. Hence, in parallel with fast industrial developments there was the increasing emission of VOCs to the environment.

Organic compounds in the atmosphere are in general in the trace levels, being methane (CH_4) the most abundant. The anaerobic degradation of organic matter by means of some microorganisms is the main source of methane. Atmospheric methane concentrations are increasing at a 1% rate annually, from 1,5ppm in the 1980s to 1,75ppm in the 1990s [22], estimated over 2 ppm in the 2010-2020 decade. Therefore, VOCs are also known as non-methane volatile organic compounds (or NMVOCs). According to potential emission sources, VOCs can be classified as anthropogenic VOCs (AnVOCs), when released by human activities; and biogenic VOCs (BVOCs) when emitted by natural bioprocesses without direct human participation. Methane (CH_4) is the most abundant primarily emitted from agriculture (from ruminants and cultivation), whereas non-methane volatile organic compounds (or NMVOCs) are mainly emitted from transportation industrial processes and use of organic solvents.

1.1.2.1 ANTHROPOGENIC VOCs

Aromatic hydrocarbons are greatly released to the environment by human activities, especially through fuel combustion processes. Benzene, toluene, ethylbenzene and xylenes, namely BTEX, represent one of the major known threats in the present to environment and human health owing high emission rates and great toxicity. The higher concentrations have been measured at industrial and urban areas; however concentrations may sensitively vary according to local atmospheric conditions. Halogenated compounds (e.g. dichloromethane, chloroethylene) are other frequent anthropogenic pollutants, with an increasing emission rate in the last century since they are massively used as solvents and in the industry.

Oxygenated volatile organic compounds encompass a wide range of compounds: ketones, aldehydes, esters, ethers, alcohols, carboxylic acids, etc. Aldehydes are one of the most important groups since they are primary contaminants, directly emitted by biogenic and anthropogenic sources, but also secondary contaminants as intermediate reaction products, with a key role in the generation of oxidative compounds [23, 24].

Anthropogenic emissions are estimated and published in European countries since 1990, according to United Nations Convention on Long-Range Transboundary Air Pollution [17] (UNECE-CLRTAP, Section 1.1.5.1). Figure 1.1-1 shows the average contribution made by different sectors to emissions of non-methane volatile organic compounds (NMVOCs) for 32 European Countries in the year 2009 [25].

It is very important to remark that the computation of total emissions is, in general, based on certain arbitrary values specified in the emission inventory guidebook [25], but not with a real evaluation of occurrence levels. Principal emission source is the use as solvent and products (35,8%), followed by industrial processes (15,1%) and commercial, institutional and households uses (15,4%). Total VOC emissions in Spain are reported every year included in the annual emission inventory [26].

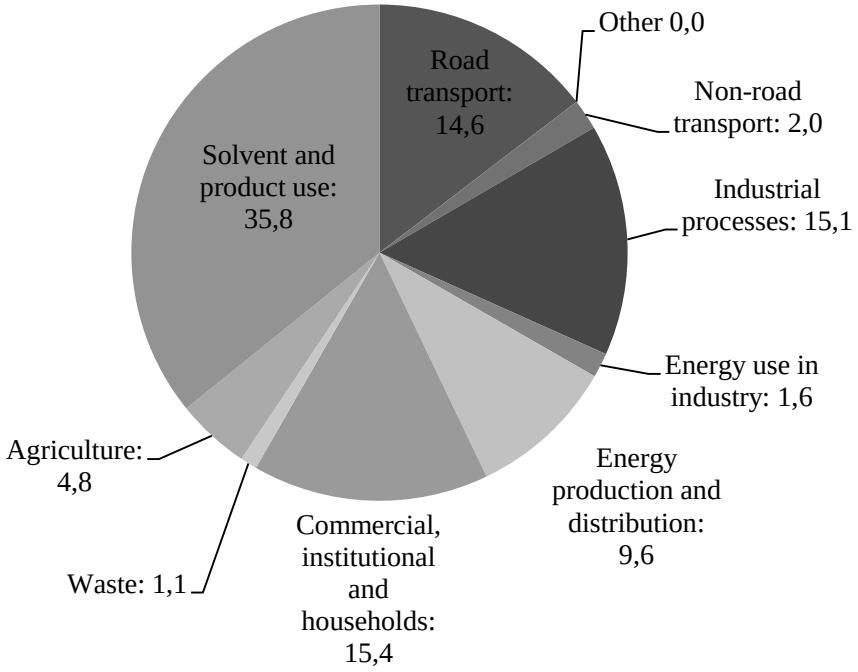


Figure 1.1-1 Contribution made by different sectors to emissions of non-methane volatile organic compounds (NMVOCs) for EU-32

The total estimation of VOCs in Spain was 678,7 Gg in the last official reported year 2009. This estimative corresponds over 1000 tons of VOCs $year^{-1}$ km^2 in the Spanish territory (assuming 500 000 km^2 of territory). It is really disturbing the fact that such amount of VOCs can be released to the atmospheric environment every year with the Governmental European, National and local benevolence.

European emissions of NMVOCs have shown a significant decrease over 33% in for the period 1990-2009 [27]. The decline in emissions has primarily been due to

reductions achieved in the road transport sector due to the introduction of vehicle catalytic converters and carbon canisters on petrol cars, for evaporative emission control driven by tighter vehicle emission standards, combined with limits on the maximum volatility of petrol that can be sold in EU Member States, as specified in fuel quality directives. The reductions in NMVOC emissions have been enhanced by the switching from petrol to diesel cars in some EU countries, and changes in the 'Solvents and product use' sector (a result of the introduction of legislative measures limiting for example the use and emissions of solvents, see Section 1.1.5.1). Figure 1.1-2 shows the contribution made by each sector to the total change in non-methane volatile organic compounds (NMVOC) emissions between 1990 and 2009. Figure 1.1-3 shows percentage of change in non-methane volatile organic compound (NMVOC) emissions for each sector between 1990 and 2009.

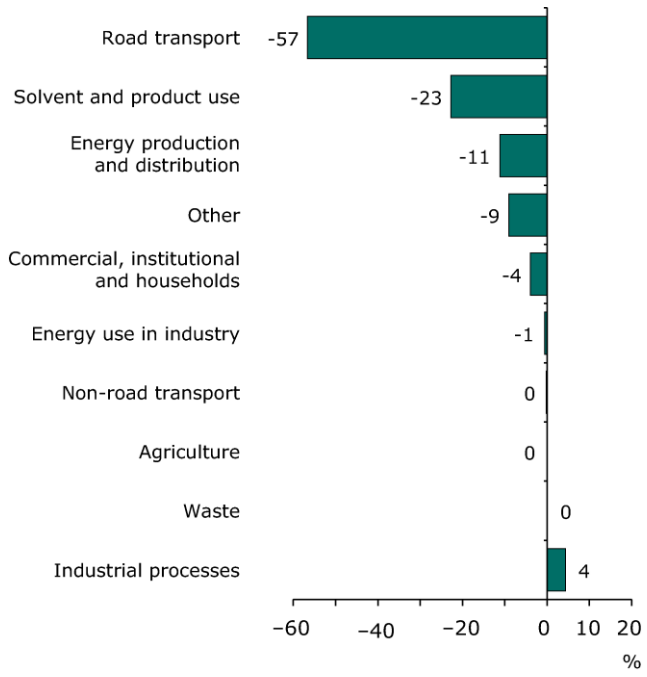


Figure 1.1-2. Relative variation on individual contributions to total VOC emissions for the period 1990-2009

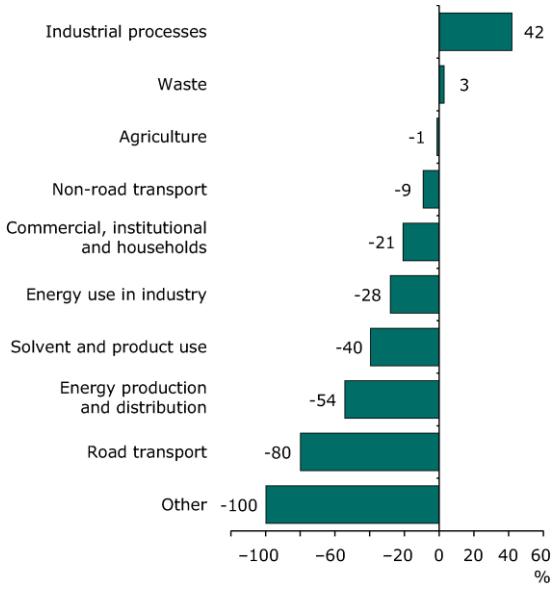


Figure 1.1-3 Changes in non-methane volatile organic compound (NMVOC) emissions for each sector between 1990 and 2009.

1.1.2.2 BIOGENIC VOCs

Great amounts of non-methane organic compounds are also emitted into the atmosphere from biogenic sources, mainly from vegetation. These organic compounds include isoprene, $C_{10}H_{16}$ monoterpenes, $C_{15}H_{24}$ sesquiterpenes, and a number of oxygenated compounds including methanol, hexene derivatives, 2-methyl-3-buten-2-ol, and 6-methyl-5- hepten-2-one. Some examples are reported in Table 1.1-3.

Natural emissions have been sometimes estimated about 30% of overall VOCs emissions [22] . Green plants emit high amounts of isoprene and terpenes (like limonene, cymene or myrcene), which largely contribute to the concentration of VOCs in rural areas. Guenther et al. estimated total worldwide emission in 1150 Tg $year^{-1}$, composed of 44% isoprene, 11% monoterpenes, 22.5% other reactive VOC, and 22.5% other VOC [28]. In a more recent study, Karl et al. [29] estimated European emissions of BVOCs in 12 Tg $year^{-1}$. Tropical woodlands (rain forest, seasonal, drought-deciduous, and savannah) are estimated to contribute with half of global biogenic VOC emissions. Croplands, scrublands and other woodlands contribute 10–20% apiece.

Notwithstanding, the wide variety of uncontrollable factors (e.g. life stage of the plant, weather conditions, season of the year) combined with the lengthy list of compounds comprised among VOCs, the estimation of emissions may steer to an unaffordable challenge [30]. Furthermore, it is a big challenge to determine the concentration of all the

VOCs in the environment since there are hundreds (even thousands) of them present in the air. Periodic monitoring of the environmental occurrence of individual VOCs, instead of the total sum, looms the best option to understand emissions for an efficient control.

Table 1.1-3 Calculated atmospheric lifetimes of biogenic volatile organic compounds

Biogenic VOC	Lifetime for reaction with		
	OH	**O_3**	**NO**
Isoprene	1.4 h	1.3 day	1.6 h
Monoterpenes			
Camphene	2.6 h	18 day	1.7 h
2-Carene	1.7 h	1.7 h	4 min
3-Carene	1.6 h	11 h	7 min
Limonene	49 min	2.0 h	5 min
Myrcene	39 min	50 min	6 min
cis-/trans-Ocimene	33 min	44 min	3 min
α-Phellandrene	27 min	8 min	0.9 min
β-Phellandrene	50 min	8.4 h	8 min
α-Pinene	2.6 h	4.6 h	11 min
β-Pinene	1.8 h	1.1 day	27 min
Sabinene	1.2 h	4.8 h	7 min
α-Terpinene	23 min	1 min	0.5 min
γ-Terpinene	47 min	2.8 h	2 min
Terpinolene	37 min	13 min	0.7 min
Sesquiterpenes			
β-Caryophyllene	42 min	2 min	3 min
α-Cedrene	2.1 h	14 h	8 min
α-Copaene	1.5 h	2.5 h	4 min
α-Humulene	28 min	2 min	2 min
Longifolene	2.9 h	>33 day	1.6 h
Oxygenates			
Acetone	61 day	>4.5 year	>8 year
Camphor	2.5 day	>235 day	>300 day
1,8-Cineole	1.0 day	>110 day	1.5 year
cis-3-Hexen-1-ol	1.3 h	6.2 h	4.1 h
cis-3-Hexenyl acetate	1.8 h	7.3 h	4.5 h
Linalool	52 min	55 min	6 min
Methanol	12 day	>4.5 year	2.0 year
2-Methyl-3-buten-2-ol	2.4 h	1.7 day	7.7 day
6-Methyl-5-hepten-2-one	53 min	1.0 h	9 min

1.1.2.3 ENVIRONMENTAL EFFECTS

Volatile organic compounds play an important role in the atmospheric chemistry and the climate, while being simultaneously impacted by chemical and climate changes. VOCs contribute to the formation of fine particulate matter ($PM_{2.5}$) through oxidation reactions with hydroxyl radical, and to the formation of tropospheric ozone (O_3) through photochemical reactions in the presence of nitrogen oxides (NO_x). $PM_{2.5}$ and O_3 are both criteria pollutants, making VOC emissions, and the various anthropogenic factors affecting them, an important factor in the evaluation of current and future air quality scenarios. [24]

The *mean life (or lifetime)*, defined as the period of time on which one compound remains in a specific environmental reservoir, may greatly differ one another between VOCs [22]: some can be transformed in few minutes whereas some others may have long-term decomposition up to hundreds of years (the most persistent). The potential removal and transformation processes for VOCs are wet and dry deposition, photolysis, reaction with the hydroxyl (OH) radical, reaction with the nitrate (NO_3) radical, and reaction with ozone (O_3). Reaction with chlorine (Cl) atoms may also be important in, for example, coastal areas [31]. For most VOCs, dry and wet deposition is probably of minor importance, though these physical removal processes could be important for the chemically long-lived methanol and for certain VOC reaction products. Because of absorption of short-wavelength solar radiation by O_2 and O_3 in the stratosphere, photolysis in the troposphere requires the VOC to absorb radiation of wavelengths $\geqslant$290 nm and is expected to be potentially important for carbonyls and organic nitrates (and hence for many of the VOC reaction products). The processes leading to the presence of O_3, OH radicals and NO_3 radicals in the troposphere are briefly discussed below.

1.1.2.3.1 VOCs are ozone precursors.

The initial reactions of OH radicals, NO_3 radicals and O_3 with NMVOCs have been elucidated over the past decades [24, 32, 33] and the reactions of BVOCs have been previously reviewed by Atckinson and Arey Calogirou et al. [34, 35]. Ozone emissions and reaction mechanisms with VOCs have been studied since long ago [36-38]. In Table 1.1-3 are summarized atmospheric lifetimes of some BVOCs as ozone precursors. From a global environmental point of view, photochemical reactions involving O_3 generation are the most important, since VOCs accumulation in the air alters the natural ozone photochemical cycle.

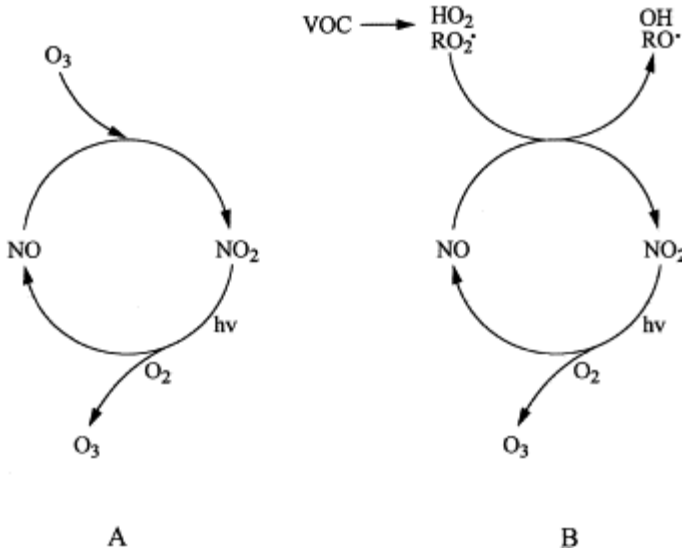


Figure 1.1-4 Schematics of the reactions involved in NO-to-NO_2 conversion and O_3 formation in (A) natural NO–NO_2–O_3 systems in the absence of VOCs, and (B) NO–NO_2–O_3 systems in the presence of VOCs.

In this natural cycle (Figure 1.1-4 A), O_3 is generated and degraded in parallel to the NO-NO_2 photochemical cycle. This is a process with a null net product, summarized into the following reactions [24]:

$$NO_2 \xrightarrow{hv} NO + O \quad (2)$$

$$O + O_2 \rightarrow O_3 \quad (3)$$

$$NO + O_3 \rightarrow NO_2 + O_2 \quad (4)$$

Atmospheric VOCs, especially hydrocarbons, enable additional oxidation steps from NO to NO_2 (Figure 1.1-4 B). The principal competitive chain reaction starts when a VOC radical (VOC: hydrocarbon, RH) reacts with an OH* radical followed by an oxidation step with O_2:

$$RH + OH^{\circ} \rightarrow R^{\circ} + H_2O \quad (5)$$

$$R^{\circ} + O_2 \rightarrow RO_2^{\circ} \quad (6)$$

The new radical can continue through two different mechanisms, according to VOC nature, to generate a NO_2 molecule:

$$RO_2^{\circ} + NO \rightarrow NO_2 + RO^{\circ} \quad (7)$$

or

$$RO_2^{\circ} + O_2 \rightarrow HO_2^{\circ} + (\text{carbonilic compounds}) \quad (8)$$

$$HO_2^{\circ} + NO \rightarrow NO_2 + HO^{\circ} \quad (9)$$

In consequence, assuming the overall mechanism of RO^* radicals, each RH (VOC) free radical in the troposphere may produce two molecules of O_3:

$$RH + 4O_2 \rightarrow 2O_3 + H_2O + (\text{carbonilic compounds}) \quad (10)$$

Furthermore, during the ozone photolysis it is produced hydroperoxid radical (HO_2^*) as secondary product, which in turn leads to regeneration of NO_2 and HO^*, hence being an autocatalytic cycle on which several radical species may continue the chain reaction.

Ozone is not naturally degraded, and it accumulates in the atmosphere. There have been reported ozone levels on polluted areas (urban and industrial areas) ranging 2-100 times higher than rural areas [39]. Notwithstanding, tropospheric ozone concentration may depend on a wide set of factors, such as solar radiation and concentration of trace gases, since O_3 is involved in many reactive mechanisms. A global balance of O_3 stated by Peña-Creciente [40], reported an idea of all these mechanisms (Figure 1.1-5), providing evidences over the critical importance of tropospheric photochemical processes among the generation mechanisms, and thus the anthropogenic contribution by massive VOCs emissions.

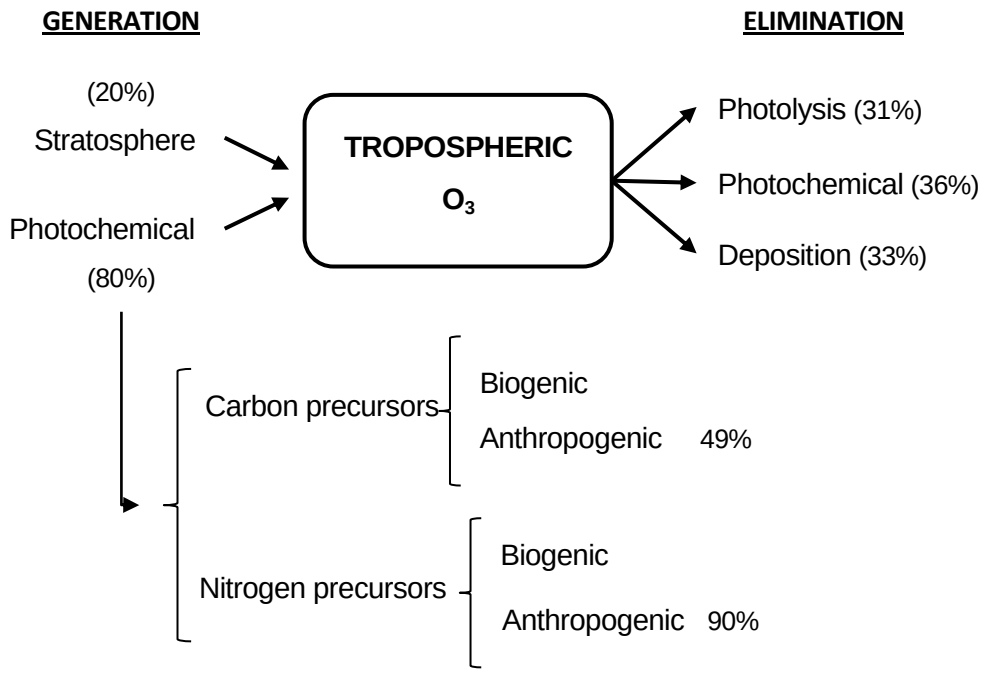


Figure 1.1-5 Total balance of tropospheric ozone

The potential of each VOC to behave as ozone precursor may sensitively differ one another, owing big differences in individual physicochemical properties of VOCs. The capability to act as an O_3 precursor depends on the reactivity grade with OH^* radicals, the mean life in the atmosphere, emission rates and punctual concentrations in the air. The Photochemical Ozone Creation Potential (POCP) is the parameter used to classify VOCs ozone creation capability according to its physicochemical properties.

POCPs are calculated on the basis of a photochemical path modelling [41]. According to this procedure (11) the increase of ozone levels for each VOC (under controlled conditions) is rated by the increase of ozone levels for ethane (assumed as one of the BVOCs with the highest potential as ozone precursor). A POCP value of 100 has been adopted for ethane to normalize the scale. Table 1.1-4 summarizes POCPs estimated for some VOCs [42, 43].

$$POCP_{VOC} = \frac{O_3 \text{ generated by VOC}}{O_3 \text{ generated by ethene}} \cdot 100 \qquad (11)$$

Table 1.1-4 POCPs estimated for some VOCs

Compound	POCP	Compound	POCP
Ethane	14,0	Ethylbenzene	80,8
Propane	41,1	o-Xylene	83,1
n-Butane	59,9	m-Xylene	108,8
n-Pentane	62,4	p-Xylene	94,8
n-Hexane	64,8	Styrene	7,7
n-Heptane	77,0	n-Propilbenzene	71,3
n-Octane	68,2	Isopropylbenzene	74,4
n-Decane	68,0	1,2,3- Trimethylbenzene	124,5
Ethene	100,0	1,2,4- Trimethylbenzene	132,4
Propene	107,9	1,3,5-Trimethylbenzene	129,9
1-Butene	113,2	o-Ethyltoluene	84,6
2-Butene	99,3	1,1,1-Tricloroethane	0,2
2-Pentene	95,3	Trichloroetene	7,5
1-Pentene	104,1	Tetrachloroethene	3,5
Isoprene	117,8	1,1-Dichloroethene	23,2
Benzene	33,4	cis-Dihcloroethene	17,2
Toluene	77,1	trans-Dichloroethene	10,1

1.1.2.3.2 Photochemical Smog

One consequence of the hazardous combination of O_3, NO_x, solid particles in suspension in air and specific climatologic conditions is the phenomena commonly named *smog* (*smoke* + *fog*). It was firstly described in the 1950s [36, 37], as the combination of carbon and sulphuric particles emitted in industrial areas from the petrol or carbon combustions. Under these conditions, the emitted sulphur oxides (SO_x) turned into small drops of sulphuric acid, were mixed with the high amounts of solid particles in the air, produce a toxic and dense fog, with severe health effects on humans and buildings. This is known as **Industrial *Smog***, and was usual during certain period of time at very industrialized Cities (e.g. London, Chicago). Nowadays, industrial facilities and processes are developed with appropriate cleaning systems to prevent the release into the environment of smog precursor particles. However it still may be a severe problem in some Asian cities where environment protection is not a priority.

It is evident, however, that a wide list of cities present types of smog pollution even though no petrol or carbon industries are present nearby. That smog is known as **photochemical *smog***, and it is generated by the photochemical reactions involved in the O_3 cycles already mentioned [44]. Under the presence of NO_x, O_3 and VOCs, photochemical reactions produce a large list of secondary minor compounds, such as acrolein, formaldehyde and peroxyacetyl nitrates (PAN). If sulphuric and nitrogen compounds are also present in the atmosphere (acids, oxides, nitrates, etc.) they condense in small particles producing a dense and toxic aerosol in the ambient air.

Photochemical *smog* is usual in areas with high amounts of petrol vehicles, which emit both the necessary hydrocarbons and oxides to start photochemical reactions under solar radiation. Hot and dry climates increases O_3 photochemical reactions and aggravate smog effects.

1.1.2.4 HUMAN HEALTH EFFECTS

As far as humans are concerned any pollutant may cause or contribute to an increase in mortality or serious illness or may pose a present or potential hazard to either human health or the environment. The determination of whether or not any substance poses a risk to humans is based on clinical, epidemiological, and/or animal studies which demonstrate that exposure to a substance is associated with health effects. A group of compounds covering so wild wide range of chemical features also presents a wide range of effects on human health, from the extremely hazardous to

those with no known effects. However it can be stated that any VOC may be harmful to human health, either short or long term, as it may accumulate in the body over time [45, 46].

In the context of human health, “risk” is the probability that noxious health effects may occur. The strength of such damages depends on many factors, including time and level of exposure, individual sensitivity or pollution pathways. VOCs are generally introduced in the body through the respiratory tract by direct exposure, attacking and/or accumulating specially in the lungs. Diffusion of VOCs through parenteral ways may also be an important pathway. The main parts of studies regarding risk assessment are indoor evaluations, since VOCs concentration are in general higher than outdoors and easier to measure [47-54]. In the year 2008 Butt et al. reviewed the fundamentals of risk assessment evaluations of landfill disposal sites [55].

The US-EPA has compiled a list of the 188 most hazardous contaminants in the air [56], most of them classifiable among the group of VOCs. In 2011, US-EPA published a report of the 177 air toxics included in the 2005 national-scale assessment [57]. That risk characterization considers the risk of both cancer and noncancerous effects from inhalation of 139 of these air toxics (the subset of pollutants with health data based on chronic exposure). The purpose of this national-scale assessment is to understand these cancer risks and noncancerous health effects in order to help the EPA and others to identify pollutants and source categories of greatest potential concern, and to set priorities for the collection of additional information to improve future assessments. The assessment represents a "snapshot" in time for characterizing risks from exposure to air toxics. The national-scale assessment is not designed to characterize risks sufficiently for it to be the sole source for regulatory action. In this study US-EPA assessed 80 of the air toxic as carcinogenic according to carcinogen risk assessment guidelines [58]: 10 carcinogenic to humans, 53 likely carcinogenic for humans, 16 suggestive evidence of carcinogenic potential.

Nowadays there are enough relevant available research studies regarding potential risks, so it is necessary to appropriately aware population about the risks that entails air pollution, including which ones are present in the air, which the concentrations and which the severity of effects on human health. The European Environmental Agency is working since 2003 in the HEAL project (Health and Environmental Alliance), a non-for-profit organisation addressing to [59]: (1) strengthening and utilizing the knowledge on environment and health links to promote and support precautionary policy-making; (2) mobilising multidisciplinary constituencies for advocacy on environment and health issues; and (3) ensuring the organisation’s sustainability as an effective and influential representative of civil society.

US-EPA is working towards the same direction through the Integrated Risk Information System (IRIS) [59], a human health assessment program that evaluates information on health effects that may result from exposure to environmental contaminants. Through the IRIS Program, EPA provides high-quality science-based human health assessments to support the Agency's regulatory activities. The IRIS database is web accessible and contains information on more than 550 chemical substances which are known to be harmful. Very comprehensive information about individual VOCs can be found in both EEA-HEAL and EPA-IRIS. Furthermore, US-EPA has developed a generic list of publications to meliorate indoor air quality and minimize risks inside American homes [60].

In light of this evidences it looms imperative the implementation of restrictive laws in order to: (1) reduce emissions of VOCs to the environment, and (2) control pollution levels by periodic individual monitoring of compounds.

1.1.3 ODORANT POLLUTION

In the last decades there has been an increasing concern regarding the “odorant pollution”. Emission of chemicals to the environment, besides environmental and health risks, generate annoyance to the population, up to the situation of extremely severe levels, having a great impact in the quality of life. Living in clean and pleasant environments is one of the basic requirements of any inhabitant; therefore emissions must be properly controlled

Chemicals in the air are the one producing odours, either in gas phase or in suspension. Once they reach the olfactory system, multiple reactions over the neuronal system produce the odorant sensation. Odorant characterisation of a sampled matrix thus might be carried out, however owing the extremely complex composition of environmental gas samples and the unknown interactions within the olfactory system; it is not possible to make reliable analysis of odours nowadays without the use of subjective odorant measurements made by trained human panellists.

1.1.3.1 ODOUR AS ANALYTE

The European standard method EN13725:2003 [61] is the reference methodology for the determination of odorant emissions in the EU. In this report European Odour Unit (OU_E) is defined as the amount of odorant substances that, evaporated in 1 m^3 of neutral gas in normal conditions, generates a physiological response -equivalent to a reference value- in the 50% of a set number of expert human panellists.

The reference measurement is accepted as the odour of 132 µg of n-butanol (CAS 17-36-3), which vaporized inside 1 m^3 of neutral gas has a set concentration of 40 ppbv. By means of this reference, odour measurement was thus traceable to mass and volume international system units. Odour concentration is defined as the number of odorant units per cubic meter of a gas under normal conditions ($OU_E\ m^{-3}\ N$). The odour intensity is a parameter that enables differentiation of chemicals, as long as different chemicals show different odour intensities, i.e.

Odour intensity may be determined as stated in the standard report of the American Society for Testing Materials (ASTM) E544-99 [62] within a static 8-points scale, according to the Odour Intensity Reference Scale. However, odour perception is a psychophysical magnitude, i.e. it describes a relationship between a physical stimulation (one odour) with the intensity of the perception from one observer (trained human panellists), so a static scale is not always usable to quantify OUs. For this purpose other measurements are often used. This is the case of the Odour Threshold Values (OTVs),

defined in the EN-13725 as the detectability of any odorant substance. By this new definition, chemical substances are classified according to each individual physicochemical property, where some compounds cannot be detected even at very high concentrations and vice versa. Several different guides have evaluated odour thresholds in water and air (see Chapter 3).

By means of this dynamic olfactometry standard method (EN 13725:2003) European Council has established odorant limit values for a set of activities, including waste treatments, industrial facilities, etc [61].

Some important drawbacks of this technique are the elevated expenses which involve these measurements, the difficulty that entails and the fact of being a subjective simulation. Because of that, with the purpose to simplify the olfactometry technique, some studies tried to correlate odour units and chemical composition (concentrations) with partial success. In Chapter 3 (Section 3.1.2 and 3.1.3) there is a description of the recent trends about the correlation between odour units and the composition of VOCs.

1.1.4 CHROMATOGRAPHIC TECHNIQUES FOR THE DETERMINATION OF VOCs IN AIR.

The analysis of VOCs in the environment air is challenging from various perspectives:

(i) VOCs are, in general, embedded in complex volatile mixtures of gases, commonly with solids and liquids in suspension;

(ii) Their concentrations may evolve rapidly with time; and,

(iii) They may be present on a wide range of concentration, usually in trace levels.

As trace compounds, VOCs concentrations in the ambient air are typically in the order from ng m^{-3} to mg m^{-3}, besides severely polluted effluents or indoor closed areas with a heavy VOC source (i.e. industrial facilities). This important issue makes VOCs analyses conditional on: (a) the use of very sensitive analytical techniques and (b) the need of extraction and clean-up step prior to the analysis. Some other critical factors determine the best analytical methodologies for VOCs quantification in the air.

Owing the extremely wide range of different compounds included among VOCs, with different physicochemical properties and different effects on human health and environment, it is a priority to quantify them individually. It is necessary the use of an appropriate separation technique to characterize air chemical composition on the basis of individual concentrations. Chromatographic techniques perform the most efficient separation. Due to VOCs high vapour pressure, gas chromatography (GC) is the selected analytical separation technique usually adopted by analysts. Capillary columns (typical inner diameters ranging from 150 to 350 µm) currently provide the best separation efficiency, enabling the detection of hundreds of different VOCs in one single run in a relative short time. Yassa et al., for example, analysed 190 VOCs in the air in 30 minutes [63].

Different instrumentation may be coupled to GC for the analytical detection of VOCs, depending on the chemical properties of the analytes being measured. Some detectors enable good sensitivity but non-selectivity to VOCs. Flame Ionization Detector (*FID*) and Photoionization Detector (*PID*) are specific for compounds with organic carbon and hydrogen, and Electron Capture Detector (*ECD*) and Electrolytic Conductivity Detector (*ELCD*) are specific for halogenated compounds. These detectors do not provide any qualitative information about analytes. In this sense the most capable detection method is the Mass Spectrometry Detection (*MSD* or *MS*) which also provides structural information of the molecules. Due to the mentioned features, gas chromatography separation technique coupled with mass spectrometry detection, hereafter GC-MS, is

the recommended technique for VOCs analyses in mainly every environmental standard report, including US-EPA compendium of methods TO 14A, TO 15 y TO 17 [8, 64, 65] and some EEA directives , as it is further explained in section 1.1.5.1.

1.1.4.1 SAMPLING AND EXTRACTION TECHNIQUES

Sampling techniques are one of the key points of all environmental analyses, regardless the compound analysed. In general, they must be selected in order to satisfy several critical features [66]:

- Sampled aliquot must be representative of the (average) matrix composition of the sample.
- Sample matrix cannot be altered during the procedure.
- Ease and speed.
- Capable to be performed in-situ under field conditions.

The specific case focused in this Thesis, the analyses of VOCs in air samples, requires a extraction step owing the low concentrations in the environment. It is usually recommended to combine sample collection and extraction into one single when it is feasible. Given the complexity and variability of organic vapours in air, no one sampling approach suits every monitoring scenario. As it has been stated before, it is necessary to measure the concentration of each individual chemical. Overall or total VOC (TVOC) data - such as that generated by direct read-out detectors– does not give sufficient information to allow an accurate assessment of the total risks associated with a given atmosphere.

The most usual collection techniques in the field sampling of VOCs in the air are: (1) cryogenic techniques, (2) whole air collection techniques, (3) sample collection using solid sorbents and (4) on-line continuous sampling. These techniques have been extensively reviewed during the last years [67-73] and are explained in this section. Other on-line non-chromatographic techniques are described in section 1.1.4.5. A summary of the principal advantages and drawbacks of each technique is further showed in Table 1.1-6.

1.1.4.1.1 Cryogenic sampling techniques

Cryogenic extraction, passing an air flow through a cooled tube usually filled with glass beads, remains one of the typical VOC enrichment methods for air samples. It is not a very common technique, but some applications where this technique is combined

with canister sampling are reported in the last years for analysis of indoor environments [74], the lower troposphere [75, 76], and (sub)urban environments [77-79] (canisters, see Section 1.1.4.1.2.2). Removal or control of water vapour is essential for suitable cryogenic extraction [78] to avoid water crystals.

Farrell and Pacey developed a novel technique Dispersive Vapour Extraction (DVE) [80], on which less than 1.0 mL of a volatile solvent was vaporized inside a flask containing gaseous mixture. The flask was then cooled under running tap water for 2–3 min to induce condensation of the vapour and co-extraction of the VOCs from the headspace using solid-phase microextraction (SPME, see section 1.1.4.2.5.1).

Other novel in-line sampling device developed by Wang et al. [81] improves the canister-cryogenic extraction in two main features: (1) minimizes cryogenic gas consumption, and (2) reduces the extension of the sampling time to approximately one hour to improve the hourly representations.

1.1.4.1.2 Whole air collection

Collecting air in a sampling container is the simplest way to collect atmospheric air. The samples are usually further analysed using gas chromatography, by direct injection or, more frequently, in combination with an extraction step. This technique presents some advantages over sorbent methods as it allows, for example, whole-air sampling, avoiding the breakthrough of target compounds and eliminating the need for thermal or solvent desorption. It also provides multiple aliquots for replicate analysis and time-integrated samples can be obtained using controlled-flow pumps with bags or metal containers. Several types of containers can be used: gas-tight syringes, glass bulbs, especial bags, or metal containers, although the most widely used are plastic bags and stainless-steel containers (canisters) [82]. The U.S. Environmental Protection Agency (US-EPA) adopted two evacuated canister methods to determine VOCs (TO-14A [64] and TO-15 [65]). This sampling method has been widely used for air toxics monitoring [83-85].

1.1.4.1.2.1 Sampling bags

Plastic bags are simple to use, inexpensive and commercially available in various sizes, normally from 500 mL to 100 L. Plastic bags may be reused after cleaning by repeatedly filling the bag with pure nitrogen or ultrahigh purity air, and evacuating them with slight negative pressure, however it is not a frequent procedure and they normally are for single-use purposes. Several materials are commercially available: Haral®, Saran®, Tedlar®, Teflon®, Nalophan®, etc. Many of them are usable for dynamic

olfactometric measurements, and recommended in the official European method for determination of odours by dynamic olfactometry EN-13725 [61], owing the low odour background emitted which reduces interferences in the odour sensorial detection.

As principal drawback, some bags are also permeable to certain chemicals, and losses of significant amounts of sample have been observed when they have been stored for prolonged periods [86, 87]. A disadvantage of using Tedlar® and Nalophan® bags is that compounds may not remain stable for more than 24-48 hours [82]. Moreover, Tedlar® bags can allow humidity to diffuse when relative humidity levels differ between the inside and outside. A double layer Tedlar bag has been designed with a drying agent between the two films to limit the impact of external humidity on a low-humidity sample [88].

The commercially available sampling bags are provided empty (vacuum), and must be filled up by the "lung principle" procedure. (Figure 1.1-6). By this procedure the bags are kept inside a vessel which can be hermetically closed. A pump removes the air from the vessel, creating an overpressure which fills the bag with connected with the exterior air by a sampling probe.

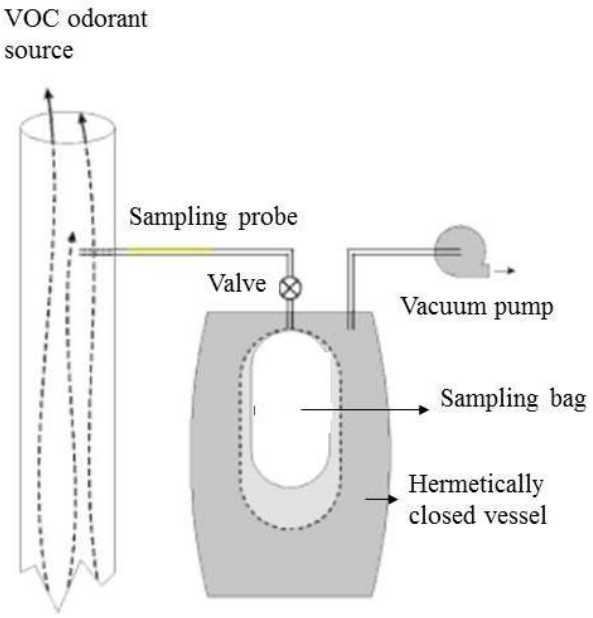


Figure 1.1-6 Schematic depiction of the "lung principle" procedure to fill up sampling bags

1.1.4.1.2.2 Canisters

Unlike the plastic bags, the principle disadvantages of using metal canisters are the high initial cost. Wang et al. [89] have reviewed evacuated canister methodology to

determine VOCs in ambient air. A canister is a cylinder or sphere, in general made of stainless steel, which is usually provided with a valve which controls the speed and the filling time. Thus the canister may be filled rapidly, 5 or 10 s without restriction (direct filling) or can be filled at a constant rate over a controlled period of time, typically 24 h to calculate average daily concentrations (restricted passive filling). Another possibility is to fill it using a pump, namely active or pressurized sampling, which increases the sample volume. The canister sampling method is contained in the method TO 14A of the US-EPA. This technique has great advantages, such as the ability to analyse compounds with a wide range of volatilities or highly reactive compounds that degrade when working with solid sorbents. Furthermore, it prevents the effects of other pollutants such as O_3, NO_x and SO_2, which can oxidize the solid adsorbents and the retained compounds. The main disadvantage of canisters is the relative high prizes compared to other sampling techniques, since in most cases it is necessary extra equipment for automating the concentration of analytes prior to chromatographic separation and also remove water and oxidizing gases which can interfere in the analysis. On the other hand we must add the cost of the canisters and the cleaning procedure. This process is critical in this type of techniques since a poor cleaning of the canister may cause carryover of consecutive samples. Usual cleaning procedure is done by passing high flow of inert gas (N_2) and heating within 80 - 120°C.

In whole air sampling, an intermediate step for the VOC extraction is frequently carried out prior to analytical detection [67]. Either sorbent or cryogenic trapping can be used to do this [82, 87, 89]. The US-EPA TO- 14A and TO-15 methods establish the use of a cryogenic trap. Solid phase microextraction (SPME) has also been used to preconcentrate analytes from air collected in containers [90]. Also, Mangani et al. [91] used “cold” solid-phase microextraction to preconcentrate compounds from air samples collected into stainless-steel canisters using sub-ambient temperatures to enhance the retention capability of the SPME fiber.

A big challenge is removing water from the sample, which, although is an advantage in the case of Summa canisters, where water enhances the stability of collected VOCs, it can also interfere with subsequent analytical techniques. Some problems resulting from humid air streams include loss of VOCs in condensed water, blockage of cryogenic traps through the formation of ice, variability in GC retention time by overloading and damaging the stationary phase, and deterioration of the mass spectrometer ion source due to ionization of H_2O. Some techniques for removing water vapour include drying using desiccants, adsorbents, cryocondensation and permeation [89]. The US-EPA TO-14A method calls for use of a Nafion dryer upstream from the trap.

1.1.4.2 ENRICHMENT INTO SOLID SORBENTS

This is a well-established sample preparation technique for VOCs in air [68, 92]. The VOC fraction of the sample is collected exclusively by trapping them through the adsorption or reaction of VOCs upon solid sorbent surfaces, either by active or passive sampling. These procedures are included among the Solid Phase Extraction (SPE) techniques. These SPE techniques enable:

- Determination of either individual or total concentrations.
- Enable non-solvent techniques, since elution may be made by controlled thermal desorption.
- Sorbent regeneration and re-use.

1.1.4.2.1 Active methods

Active sampling consists of pumping a defined volume of air through a bed of sorbent(s) in a tube where analytes are retained. Active sampling with sorbents is the most versatile option, and several official reports have been established based on this technique, such as US-EPA TO- 17 [8], ASTM D-6196 [93] , NIOSH 2549 [94] and ISO 16017-1,2 [95, 96]. Standard tube characteristics have also been defined: 3.5 inches long and ¼ inch external diameter, which can sample efficiently at flow-rates ranging from 10 to 200 mL min^{-1}. Stainless steel sorbent tubes (Figure 1.1-9, page 42) are adapted to thermal desorption automatic units (see Section 1.1.4.3). In active sampling, flow rates can vary from 10 to 1000 mL min^{-1}, collecting sample volumes ranging from 0.1 to 150 L [68].

Tubes filled with solid sorbents have been the most used strategy to monitor VOCs in ambient air. A broad list of examples is given along Chapter 3 (Section 3.1).

Even though the use of individual solid sorbent is a common procedure, if analytes in a broad volatility range are determined, it is often useful to select more than one adsorbent, combining different materials with complementary features, arranged in order of increasing adsorbent strength for sampling, to achieve best results. These tubes are commonly named *sorbent traps*. In this case, it is especially important that the sampling direction starts from the weakest to strongest sorbent, to keep the less volatile compounds from being irreversibly retained in the strongest sorbent. If desorption of analytes is carried out by controlled thermal desorption, the carrier gas must flow towards the opposite direction (strongest to weakest sorbents) as is indicated in Figure 1.1-9. Several of the most common sorbents with some of their main features described in sections 1.1.4.2.3 and 1.1.4.2.4 are summarized in Table 1.1-5.

1.1.4.2.2 Passive methods

Analyte enrichment in passive samplers [97-100] results from the diffusion of analytes from the immediate surroundings to the inside of the sampler, where they are trapped on the surface or in the bulk of the solid sorbents. As long as the organic compounds have affinity for the sorbent, a concentration gradient can be established to favour diffusion of the contaminant from air to the sorbent. The layer of solid sorbent is covered with a barrier material, whose outer surface is exposed to the contaminated air. The barrier is a semi-permeable membrane or a layer of plastics drilled with many small parallel holes. Fick's law of diffusion describes the principle of passive-sampler operation, which is detailed in the literature [97]. Briefly, Fick's first law can be explained by the equation [87]:

$$m/(tA) = D(C_a - C_f)/L \qquad (12)$$

where m is the mass of substance that diffuses (µg), t is the sampling interval (s), A is the cross-sectional area of the diffusion path (cm^2), D is the diffusion coefficient for the substance in air ($cm^2\ s^{-1}$), C_a is the concentration of substance in air (µg cm^{-3}), C_f is the concentration of the substance above the sorbent, assumed to be 0, and L is the diffusion path length (cm).

Assuming that adsorbents act as a perfect sink (C_f = 0), Equation (1) can be simplified to:

$$m/(t \cdot C_a) = D \cdot A/L \qquad (13)$$

The term "$m/t\ C_a$" is uptake rate or sampling rate. Theoretically, this is constant for an analyte and a type of sampler. Once it has been determined, it can be used to calculate ambient concentration C_a from a measured mass of analyte. Figure 1.1-8 shows the process of diffusion. The experimental approach involves experimental determination of uptake-rate coefficients based on exposure of the sampler to standard gas mixtures in exposure chambers [97]. European Committee for Standardization developed European Standard EN 13528-1,2 [101, 102] to set the requirements in the use of passive sampling for gases and vapours monitoring.

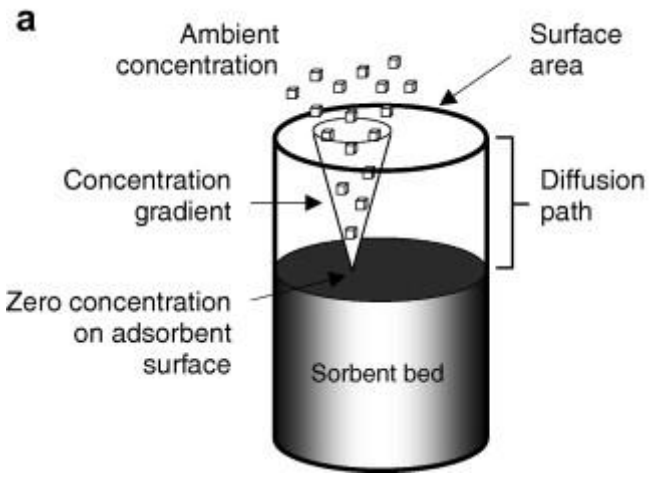


Figure 1.1-7 Diffusion process [67]

Conventional passive samplers fall into two main geometrical categories (see Figure 1.1-8):

- *Axial*, which are characterized by a long axial diffusion path and a low cross-sectional area; and,
- *Radial*, which have a diffusion path parallel to the cartridge radius and a greater cross-sectional area, allowing higher uptake rates.

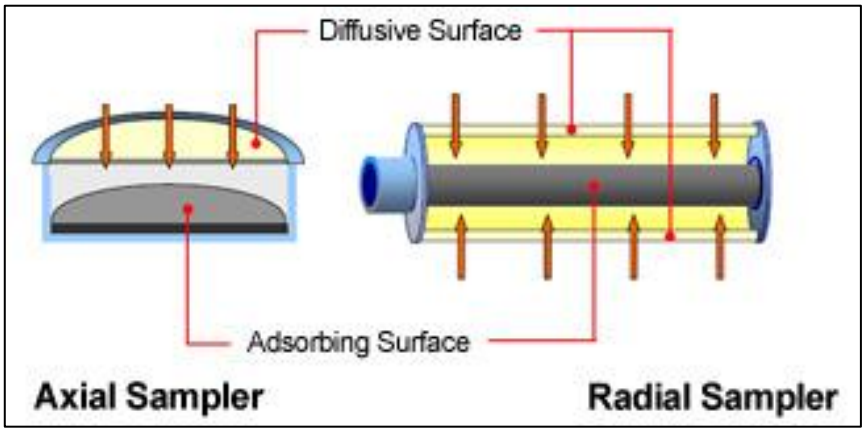


Figure 1.1-8 Different passive samplers axial and radial [103]

Different types of passive samplers are commercially available and have been used for the determination of environmental VOCs. Radial passive samplers are commercially available as Radiello (FSM, Padova, Italy). These samplers have 100 times more area than axial samplers, reducing sampling times. They are also compatible with TD instrumentation. Radiello samplers have been widely evaluated for use in monitoring benzene, toluene, ethylbenzene, and xylenes (BTEX) and VOCs by many authors [104-

107]. The blank values and analytical recovery of VOCs trapped in Carbograph 4 and released by TD was in accordance with European Standard EN 13528-2 requirements [102], and uncertainty for benzene to be 20%. Compared with dynamic techniques, passive samplers offer some advantages (e.g., elimination of portable pumps and flow-meter). Relatively small and simple, passive samplers can be left unattended for long-time exposures. Moreover, they are suitable for the determination of time-weighted-average concentration based on exposure time only, without knowing the sample volume. However, passive sampling is unsuitable for monitoring short-term variations in analyte concentration.

Passive enrichment is sensitive to temperature fluctuations and air movement, and the efficiency of a passive sampler can be influenced by not only factors such as sampler storage, exposure, storage after exposure and desorption of analytes, but also by the sampler design [98]. The limitations of passive samplers include problems of contamination and artefact formation. These are more pronounced than for active samplers because longer sampling periods are required, due to the very low uptake rates. Due to the characteristics mentioned above, diffusive sampling has been mainly used to monitor indoor atmospheres in risk assessment studies.

Data obtained from passive samplers are often verified by comparison with data obtained by a reference method, which is most commonly a dynamic technique [105]. Bruno et al. [107] evaluated Radiello for its potential for BTEX monitoring with subsequent TD. They found low blank values and good storage stability of sorbent cartridges.

1.1.4.2.3 Solid sorbents

Sorbent-packed tubes and focusing traps that are compatible with thermal desorption typically contain between 1 and 4 sorbents arranged in order of increasing sorbent strength from the sampling end. There are a general range of factors to consider when selecting suitable sorbents or sorbent combinations including [71, 108]:

- ***Strength of the sorbent*:** The sorbent or sorbents selected must be sufficiently ‘strong’ to retain target analytes during sampling/concentration, but weak enough to release them efficiently during the thermal desorption phase. Sorbent strength is usually measured in terms of retention or breakthrough volumes. Standard air monitoring methods are a good source of validated retention and breakthrough volume information for a wide range of common

sorbent/sorbate combinations and describe how these values can be determined experimentally.

Selection of sorbents of appropriate strength allows quantitative retention and release of compounds ranging from C_2 hydrocarbons to semi-volatiles such as PCBs, phthalates and PAHs without exceeding optimized tube/trap dimensions and without requiring liquid cryogen coolant.

- ***Hydrophobicity*:** If a large amount of water is retained on the tube and not selectively eliminated prior to analysis, it can adversely affect. Most common weak- and medium strength sorbents are very hydrophobic, thus their sorbent strength is not compromised even when sampling at high (>80%) relative humidity. However, most strong sorbents comprise some form of carbonised molecular sieve and, in this case, sorbent strength can be reduced by as much as a factor of 10 at 90% relative humidity [70].
- ***Inertness*:** some sorbents contain chemically active materials. This is especially true of carbon blacks, many of which derive originally from natural charcoals and contain trace metals. These sorbents are in many cases unsuitable for labile (reactive) species like some sulphured compounds, terpenes or amines.
- ***Mechanical strength (friability)*:** Graphitised carbon blacks are extremely friable and prone to the formation of fines. Care should be taken not to over compress these sorbents during tube packing and to avoid sharp knocks once the tubes are packed. As the carbon packing ages, the formation of fines may increase tube impedance (back pressure) beyond the limit of some pumps.
- ***Mesh size*:** Within the 30–80 mesh range, sorbent particle size does not play a critical role in sorbent selection because analyte retention volumes will remain constant as the particle size increases up to a limit of 5 particles across the internal diameter of the sorbent tube/trap.

There is nowadays a long list of commercially available sorbents, covering a wide range of features. Table 1.1-5 shows some of the most usual adsorbents in environmental evaluations and some their particular features.

Table 1.1-5 Most frequently used TD compatible adsorbents in the clean-up and extraction step of VOCs in air and their main features, sorted in ascending order of sorbent strength [67, 71, 87, 108, 109].

Sorbent	Strength	Max. Temp.	Features
Quartz wool	Very weak	>450°C	Very inert, non-water retentive
Carbograph 2TD Carbopack C Carbotrap C	Weak	>450°C	Hydrophobic Minimal artefacts (>0,1ng) Friable. 40/60 mesh recommended to minimise back pressure
Tenax TA	Weak	350°C	Hydrophobic Low inherent artefacts Inert - suitable for labile components
Carbograph 1TD Carbograph B Carbotrap	Weak/medium	>450°C	Hydrophobic Minimal artefacts (>0,1ng) Friable. 40/60 mesh recommended to minimise back pressure
Chromosorb 102	Medium	225°C	Hydrophobic High inherent artefact levels (10-50 ng/component) Inert - suitable for labile components
PoraPak Q	Medium	250°C	Hydrophobic High inherent artefact levels (10-50 ng/component) Inert - suitable for labile components
HayeSep D	Medium	290°C	Hydrophobic High inherent artefact levels (10-50 ng/component) Inert - suitable for labile components
Carbograph 5TD	Medium/strong	>450°C	Hydrophobic High inherent artefact levels (10-50 ng/component) Friable. 40/60 mesh recommended to minimise back pressure

Sorbent	Strength	Max. Temp.	Features
Carbopack X	Medium/strong	>450°C	Hydrophobic High inherent artefact levels (10-50 ng/component) Friable. 40/60 mesh recommended
Carboxen 1000	Very strong	>450°C	Inert, not hydrophobic Individual artefacts below 0,1 ng Must be conditioned slowly Significantly water retentive - do not use in humid conditions
Carbosieve SIII	Very strong	>450°C	Minimal (>0,1 ng) artefacts Inert - suitable for labile components Significantly water retentive - do not use in humid conditions

1.1.4.2.4 Multi sorbent tubes

If a wide volatility range of compounds is to be monitored, it is often necessary to pack a tube with more than one sorbent material, arranged in order of increasing strength from the sampling end (Figure 1.1-9). Note that, in the case of multi-sorbent tubes and traps, it is even more critical than normal to use back flush desorption – i.e. the flow of gas through the tube/trap during desorption must be the reverse of the air/gas flow during sampling. Higher boiling analytes are thus retained by and desorbed from the weaker front sorbent(s) without coming into contact with the stronger sorbents behind. These tubes can only be used in the active sampling procedure.

Key issues to consider in relation to sorbent selection for multi sorbent tubes include:

- The volatility range of the target compounds for a quantitative retention and efficient desorption of each.
- Sorbent compatibility – the temperature required for conditioning the most thermally-stable sorbent must not exceed the maximum temperature limit of any other sorbent in the tube.
- Stability during storage. Loosely bound analytes can migrate from weak to strong sorbents within a multi-sorbent tube during storage.

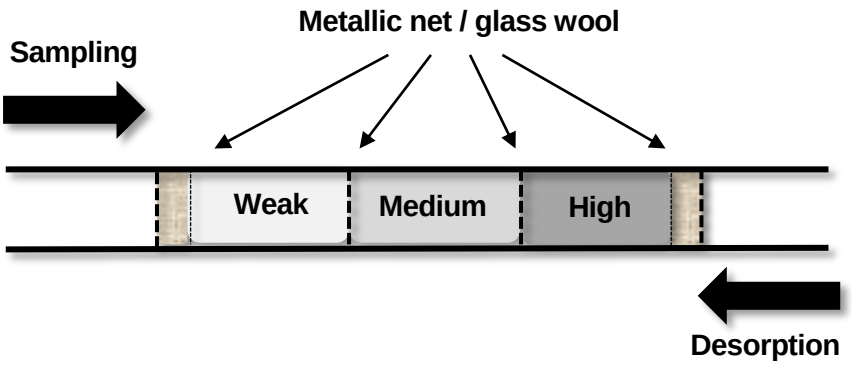


Figure 1.1-9 Schematic sorbent distribution and flow direction using multi sorbent tubes.

Research into multi-sorbent tube combinations is on-going in order to extend the application range even further and better define the working limits (storage times, safe sampling volume, etc). Some examples of common combinations are widely used in environmental analyses as follows:

The namely "universal" tubes [71] have been reported as the most broadly applicable combination of sorbents into one single tube, including one weak sorbent Tenax® TA, plus an intermediate Carbopack® or Carbopack®, and finally the strongest molecular sieves Carboxen® or Unicarb®. It offers quantitative retention of compounds ranging in volatilities from C_2 to n-C_{26}. However, carbon-based sorbents are not completely inert, and some labile analytes, such as sulfur compounds, can be degraded

Wide list of combinations have been evaluated regarding the type of analytes studied [71, 110]. Solid sorbents must be combined according to individual features (Table 1.1-5) to optimize VOCs quantitative retention. There is a vast number of studies with different combinations. As examples, Kuntasal et al. [111] used Tenax TA and Carbopack B to collect 102 individual VOCs ranging from C5 to C12. Tubes filled with Carbotrap, Carbopack X and Carboxen-569 were used by Ribes et al. [23] to trap isocyanates, isocyanato- and isothiocyanatocyclohexane, among other VOCs.

1.1.4.2.5 Extraction techniques into solid sorbents.

Besides active and passive sampling, some other techniques have been developed based on the solid sorbent enrichment techniques (solid phase extraction, SPE) in the last decades for the monitoring of VOCs in air. The most extended technique is the solid-phase microextraction (SPME). A brief description of SPME and related techniques used for VOCs analysis in air is exposed in this section.

1.1.4.2.5.1 Solid Phase Mictroextraction (SPME)

Since its introduction in 1990ies [112], hundreds of manuscripts including some excellent recent review articles [113-119] deal with both fundamentals and applications of this attractive sample extraction technique. This technique has been used in the VOCs analyses since then, and nowadays is one of the most used SPE for environmental characterisation. As a general description, SPME (or fibre SPME) is based on the equilibrium partitioning of target analytes between the sampled matrix and a stationary phase, coated on a fused silica fibre. Analytes are retained upon the solid sorbents while the SPME fibre is exposed to sample matrix (Figure 1.1-10).

Despite the wide application potential of SPME and its numerous advantages over more conventional extraction techniques, it suffers some main limitations [139,140]. First, the small volume of sorbent coated on a SPME fibre (usually less than 1 mg) results in a rather limited sorption capacity. Second, the fragility of the fused-silica rod needs a careful handling during the extraction and desorption steps, and limits the lifetime of the fibre. Third, bleeding of the SPME coating into a GC injector and sample carry-over are sometimes difficult to avoid.

We should note that the calibration method for SPME is an important factor for on-site application. Because of the difficulties in adding internal standards and control of agitation of the matrix in on-site sampling, it is necessary to develop new calibration methods. Some reviews have discussed in detail the characteristics of traditional and novel kinetic calibration methods [114, 119].

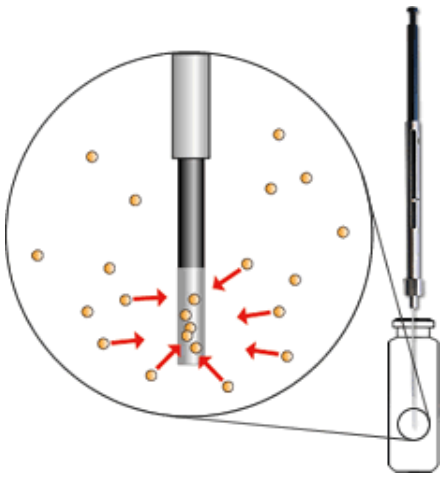


Figure 1.1-10 Schematic depiction of SPME fibre interaction with the sample matrix

The principal advantages of this technique include [120] a solvent free technique, fibres are reusable, small size (portable device), and do not disturb equilibrium of the sample during the study. SPME also enables solid fibre in-situ derivatization to improve the selectivity over the retention of analytes. SPME, in combination with GC and HPLC, has been reported for the analysis of VOC in indoor air [121, 122], gaseous industrial effluents [123, 124], and the lower troposphere [91, 125], with LODs typically below 1 ng L^{-1}. Some advantages and drawbacks are summarized in Table 1.1-6.

Table 1.1-6 General advantages and disadvantages of sample and extraction techniques for the analysis of VOCs in air matrices.

Technique	Advantages	Disadvantages
Whole-air techniques (e.g.: canisters)	Easy to use Whole-air collection No breakthrough volume No desorption needed Enables use of several aliquots Lower limits of detection	High costs of canisters Hard to clean, possible carry-over between samples Unstable, some plastics may not properly retain VOCs along the time Passivation steps when using canisters Further extraction steps are mandatory (e.g. SPME) ozone and humidity interactions may provoke losses of VOCs
Solid sorbents	A long list of sorbents commercially available High concentration capacity	Necessity of conditioning step prior to each analysis some sorbents may be too inert Blank interferences and irreversible adsorptions Need of flow-meters and pumps
Active sampling upon solid sorbents	A wide range of VOCs may be analysed owing different sorbent combinations Simple calibration procedure (compared to passive sampling) Automated analysis Humid traps may avoid water interferences Enable the use of cryogenic traps Simple and small	Possible analyte losses Not usable for variations within short periods of time

Technique	Advantages	Disadvantages
Passive sampling into solid sorbents	No pumps or flow-meters needed Enable measurements of average concentrations Enable thermal desorption Long list of sampling devices commercially available	Lower concentration capacity compared to active sampling Need to determine enrichment factors Not always enable automation Sensitive to changes on temperature and air streams More contamination problems and artefact generation than active sampling
Membrane extraction	High enrichment factor high sensitivity Non-solvent technique Enable automated analyses Enable on-line analyses	Long-time sampling periods are needed
SPME	Portable Fast and simple, integrating sample-extraction steps Enables derivatization on the SPME fibre Low cost	Artefact formation with competitive (ad)sorption effects Small volume of sorbent coated provides limited enrichment factor compared to sorbent tubes Fragile fibre storage before and after sampling May provide high inaccuracy Bleeding of the SPME coating to GC and possible sample carry-over

1.1.4.2.5.2 Solid Phase Microextraction based techniques

More recently, a list of innovative extraction devices has been introduced. Kataoka [126] reviewed and classified the different techniques developed in the last decade . Duan et al. focused on recent developments in microextraction techniques for on-site sampling and sample preparation besides fibre SPME, including stir-bar sorptive extraction (SBSE), thin-film microextraction (TFME) and different types of in-needle SPME [118]. A schematic diagram of the diverse techniques is presented in Figure 1.1-11. Some of the extraction procedures are described in Figure 1.1-12.

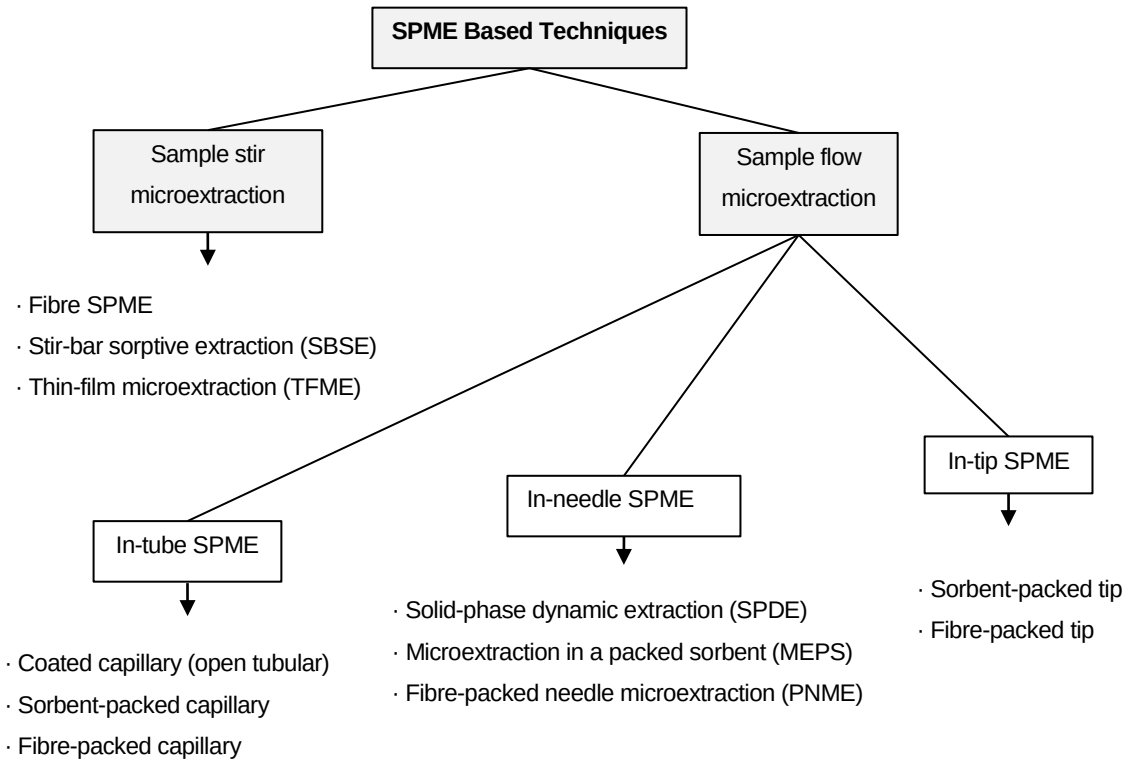


Figure 1.1-11 Classification of SPME based techniques used in air matrix samples.

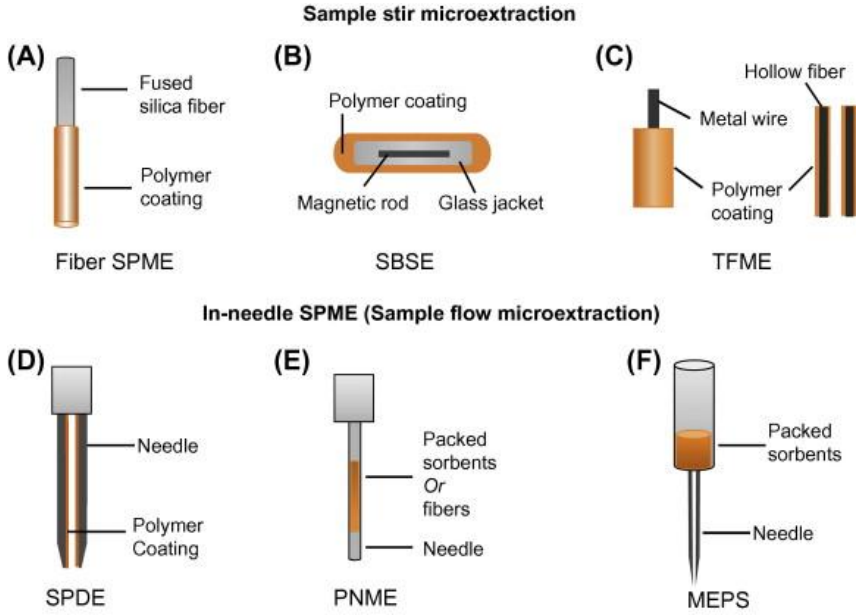


Figure 1.1-12 Schematic extraction procedure of some SPME based techniques. (A) Fibre SPME; (B) stir bar sorptive extraction (SBSE); (C) thin-film microextraction (TFME); (D) solid phase dynamic extraction (SPDE); (E) fibre-packed needle microextraction (PNME); and (F) microextraction in a packed sorbent (MEPS).

1.1.4.3 DESORPTION TECHNIQUES

The second step of any extraction technique regards on the elution of the retained analytes. Therefore it is also a key point on sample treatment [66], since it is necessary to optimize any elution step to satisfy reliability and traceability of analyses. VOCs are mainly eluted by two techniques: extraction using liquid solvents (solvent desorption, SD) and extraction by volatilisation of the retained compounds under controlled heating conditions (thermal desorption, TD). An overview of the most relevant features from both desorption techniques is presented in this section.

1.1.4.3.1 Solvent Desorption

Solvent extraction allows longer sorbent beds, higher flow rates and larger total-sample volumes than thermal desorption (TD). It is often used for processing passive samplers, and is the best technique for thermally-labile compounds. Furthermore, samples can be analysed repeatedly, and no expensive equipment is required. However, the sample is diluted, and can be contaminated by the solvent. Trace analysis may require solvent evaporation, which can lead to losses of the most volatile compounds.

Analytes are extracted from the adsorbent with a low boiling solvent -e.g., dichloromethane or carbon disulphide (CS_2). CS_2 is the most common solvent used for solvent desorption owing good solubilisation properties for many analytes, and a very low response on a flame ionization detectors (FID) [67]. However, it poses a serious risk to human health (analysts) and the environment. Also, compounds with low boiling points can evaporate due to the adsorption heat released during desorption.

Elbir et al. [127] extracted 60 VOCs trapped in activated carbon by adding 1 mL of CS_2, using a ultra-sonication bath with further centrifugation to obtain a clear phase at the top. Martins et al. [128] desorbed BTEX from coconut shell charcoal by transferring the sorbent bed to vials and adding 1 mL of CH_2Cl_2 with agitation. Pressurized liquid extraction technique (PLE) has been applied by Campos-Candel et al. [129] to extract BTEX from activated charcoal using acetonitrile as extraction solvent, obtaining recoveries >90% for all the compounds. This technique furthermore allowed the use of closed stainless-steel vessels that avoid the risk of airborne contamination, thus eliminating worker exposure to the solvent.

1.1.4.3.2 Thermal Desorption

Due to the low concentrations of analytes, samples taken from relatively unpolluted environments cannot normally be analysed using solvent desorption without additional sample concentration, and a procedure involving concentration, dilution and re-concentration is unwieldy in practice and prone to errors [92]. Thermal desorption (TD) is a solvent-free method that works excellently with GC separation.

TD offers the advantage of lower LODs. This is because the sample can be completely transferred to the chromatographic column with no elution, and because it avoids the presence of a solvent peak, which may mask analyte peaks. It also prevents analyte losses by minimizing sample manipulation and risks of contamination due to solvents. The main disadvantage of TD is the initial cost of the commercial equipment [130]. Another drawback is sample consumption in a single analysis, although modern TD equipment incorporates design modifications to allow re-collection of split samples in a fresh tube.

This technique is commonly used for volatile chemical analysis, being the method of choice to determine VOCs in the major part of studies of urban and industrial air, indoor and workplace atmospheres and other atmospheres (e.g., those influenced by waste emissions).

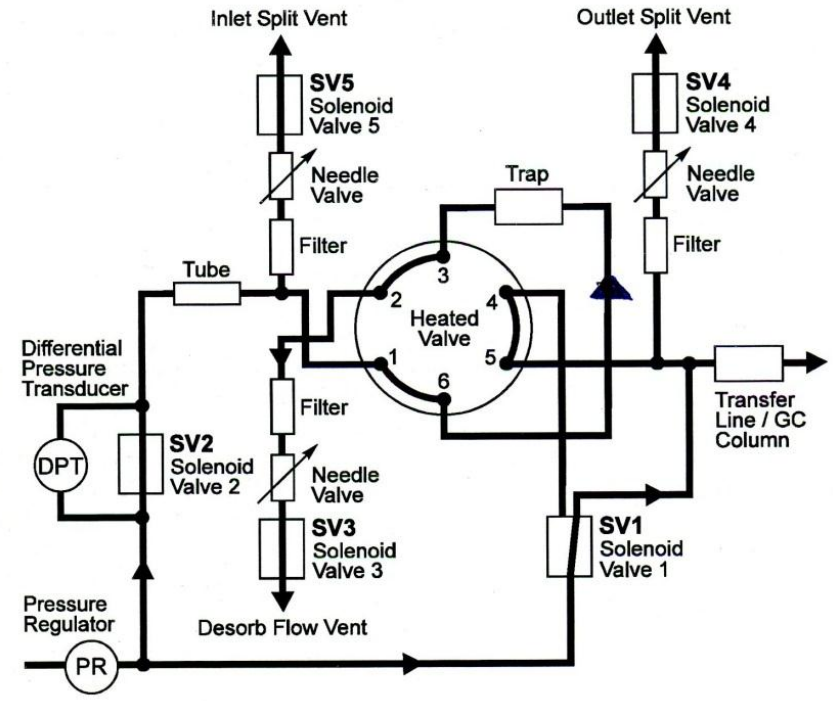
In some cases, analytes can be too strongly adsorbed. This occurs frequently with polar solutes and strong adsorbents (e.g., activated carbon). The analysis of thermally-

unstable compounds is critical because of the risk of degradation. Furthermore, the adsorbents used in TD must be thermally stable to avoid artifact formation. The most frequent adsorbents used in TD are Tenax®, Chromosorb®, and graphitized carbons (e.g., Carbotraps® and Carboxens®). Activated charcoal and silica gel are not appropriate for TD, since their high surface activity can lead to sample degradation at elevated temperatures.

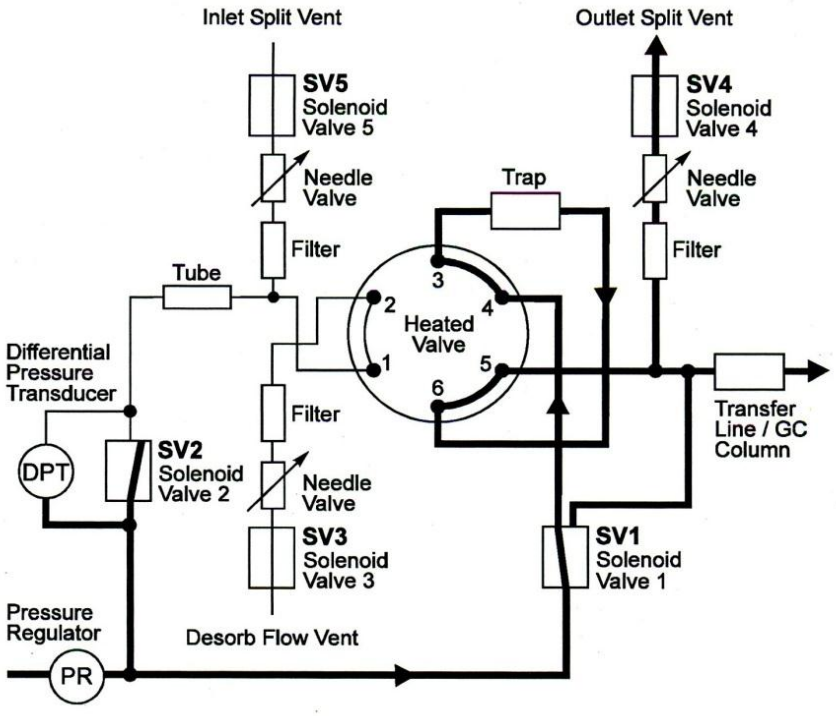
Kornacki et al. [131] observed that graphitized carbons (e.g., Carbopack X, Carbograph 5TD and Carbotrap B), used to enrich samples of C_3 and C_4 alcohols produced experimental artefacts, and, after TD, recoveries were low, with the appearance of aldehydes and ketones in the chromatograms. In another study [132] the same authors state that preliminary experiments should be performed to determine recovery, for example, mimicking as exactly as possible the conditions that occur during real sampling. It is absolutely essential to use air as a matrix for standards, because degradation of analytes results from reactions involving oxygen chemisorbed on the activated adsorbent surface. However, polymeric adsorbents (e.g., Tenax TA and Chromosorb 106) do not exhibit such oxidative properties. The principal adsorbents used in the TD clean-up step of VOCs have been reviewed [71, 108], and their principal characteristics were explained in Table 1.1-5 (section 1.1.4.2.3).

When sampling with sorbent tubes, the adsorbent may be thermally desorbed directly into the GC. However, this is not a rapid process and it would create a broad initial band in the capillary GC column, drastically reducing resolution. Consequently, a two-stage TD process with a focusing step is necessary. Analytes are desorbed and re-collected on the same kind of cooled secondary sorbent trap. This, in turn, is rapidly heated to inject the analytes into the column in a narrow plug. Oxygen and water are also purged from the sorbent tube before desorption, using dry carrier gas at ambient temperature. Figure 1.1-13 shows a double-step automated TD flow manifold.

Packed and capillary traps are most commonly used as cold traps. Capillary traps have the same characteristics as columns [130], and they are usually constructed with fused silica with 0.2–0.53 mm i.d. and 40 cm length. Their main advantage is that the flow required to desorb analytes is fully compatible with GC capillary-column flows. Packed traps usually need split valves to adapt both flows, but they can take a greater load of analytes. These traps are usually quartz tubes that are filled with a sorbent or a mixture of them, and their common dimensions are 10 cm length and 2–3 mm i.d.



(A)



(B)

Figure 1.1-13 Flow diagrams of the Perkin-Elmer ATD 400 automated unit. Two-steps thermal desorption system: (A) Primary in-tube desorption, and (B) secondary cold-trap fast desorption [133].

The low-flow cold trap, which is a Perkin-Elmer (Waltham, Massachusetts, USA) modification of packed traps, allows suitable concentration and subsequent desorption of the compounds at flows more compatible with capillary columns. This reduces the split ratio, and also the amount of analytes vented, which leads to improved LODs. Fernádez-Villarrenaga et al. [130] compared the desorption of VOCs from two kinds of cold traps: standard packed and low flow. In the low-flow trap, they observed high significance of the desorption flow of tube and trap. The use of the low-flow cold trap enhanced sensitivity and improved LODs by more than 50%.

Short-path TD, patented by Scientific Instrument Services, Inc. (Ringoes, N.J., U.S.A.), is a TD system that sits directly on top of the GC injection port. Due to the short path of sample flow, these systems eliminate transfer lines, which are easily contaminated by samples, and optimize delivery of samples to the GC injector via the shortest path possible. The liquid-N_2-cooled cryofocussing trap is mounted in the GC oven, just below the injection port and around a short (5 cm) section of the capillary column. A small outboard power supply and controller unit is mounted alongside the GC [111, 134].

Temperature-programmed desorption (TPD) has also been applied. In this case, organic compounds trapped in a solid adsorbent are released into the analytical instrument by means of a controlled temperature gradient slower than other trapping techniques. This makes the solid sorbent act as an analytical separation column. The sorbent can be any sort of solid adsorbent used to trap organic compounds from air samples. Ketola et al. [135] used TPD with a mixture of Tenax TA and HayeSep D to analyse 17 polar and non-polar compounds in the same run.

Although TD is routinely used in conjunction with GC (TD-GC), this technique has been combined with SIFT-MS (see Section 1.1.4.5.5) to quantify volatile compounds (specifically xylene and toluene) more quickly than TD-GC and with no need for calibration standards. Due to the robustness of SIFT-MS analysis in the presence of water vapour and other major components of air, it is not necessary to purge the tubes to remove these constituents during the TD cycle, so reducing TD-cycle time.

1.1.4.4 ON-LINE GC-MS METHODOLOGIES

On-line chemical analysis is becoming more important due to growing knowledge of the toxicity of VOCs and the increase of environmental legislation driven by the rising of public awareness from Environmental Agencies about environmental dangers. On-line analysis is useful to study variations in the levels of atmospheric pollutants, and for real-time detection of occasional high levels. It provides rapid results that can be beneficial

for speedy, appropriate response to a problem when one is detected. It is therefore an assessed analytical technique in fixed and remote air-quality-control stations.

There is a critical need for instrumentation that can be used to carry out automated and on-line or on-site analysis rapidly and provide accurate information on a continuous basis. In general, spectroscopic techniques are ideal for on-line process monitoring because of their short analysis times. Currently, Fourier-transform infrared spectrometry (FTIR), X-ray fluorescence spectrometry (XRF), and MS are used for continuous, online monitoring [135]. Band overlap requires a separation step, and, for this purpose, GC is an excellent technique for on-site environmental monitoring. Portable GCs have also been developed as a simpler and less expensive alternative to laboratory models [136].

Interference from moisture that commonly exists in air samples, the presence of interferences in complex matrixes, and the low levels of VOCs in environmental air require extraction, whereby analytes are first separated from the environmental matrix. In a continuous, on-line application, separation also has to be carried out continuously.

1.1.4.4.1 On-line sorbent trapping

There has been much effort to develop an on-line sorbent trap system that enabling near-real-time measurements in ambient air and gaseous samples. On-line sorbent extraction has the advantage of reducing errors resulting from reactions that degrade the samples during storage.

Cryogenic trapping (*cryotrapping*) devices have been developed to the on-line sorbent analyses. Qin et al. developed a Perkin-Elmer system coupled to a GC with an adapted standard TD unit [137]. A double stream FID detector was used to analyse C_2-C_5 VOCs and C_6-C_{10} VOCs separately. Cryotrapping is not suitable for very humid samples and the use of microtraps has been evaluated [138, 139]. More recently Peng et al. developed a extraction device [140] which enabled the analysis of five C_2-C_4 hydrocarbons in the air in less than 40 min with a single cryogenic step into a sorbent microtrap.

Breakthrough of volatile compounds and quantitative desorption of large molecules are the major issues for microtraps, which are prone to low breakthrough volume as they contain a small quantity of adsorbent. A larger diameter trap with more adsorbent reduces breakthrough, but generates broad injection bands that reduce chromatographic resolution [136, 139].

Some on-line BTEX analysers are commercially available. These are special automatic portable GCs designed to measure selected organic compounds in situ. Air is pumped through a cold trap filled with a sorbent to trap BTEX. The trap is then heated

and the VOCs are transferred by carrier gas to the GC with flame ionisation detector (FID) or photoionization Detector (PID) for the analytical detection [87].

1.1.4.4.2 Membrane extraction with a sorbent interface (MESI)

This technique, developed by Segal et al. [141], combines a hollow-fibre membrane module, with a cryofocusing and TD sorbent interface, and a capillary GC. The membrane is in direct contact with the sample. Analytes of interest diffuse across the membrane and are collected in the cryogenic trap. A heat pulse desorbs analytes to the GC column using a narrow concentration pulse.

This technique, using a sorbent microtrap of Tenax and Carboxen, was later combined with a portable micro-GC system [142] for on-site monitoring. A PDMS non-porous membrane was selected, providing rapid transport of analytes due to the high rate of diffusion, and preventing water and other polar matrices from entering the system. The sorbent trap replaced the GC injector, and the design of the trap was modified to enhance extraction of analytes.

The system allowed semi-continuous monitoring of samples, and increased the sensitivity of the micro-GC system by a factor of more than 100 by adding the MESI system. In order to eliminate the inconvenience of concentrating water on the sorbent trap, a water trap was placed in the system between the membrane module and the sorbent interface. This system was also used to monitor acetone, benzene, toluene and ethylbenzene in laboratory air [142].

1.1.4.5 ON-LINE NON-CHROMATOGRAPHIC METHODS

Even though very valuable and, in many cases, indispensable for environmental monitoring, GC-MS methodologies present some limitations. GC-MS are not designed to examine the temporal changes of VOCs in fast processes (i.e. for time resolutions of a few seconds to sub-second time scales). Even when using high-speed gas chromatography [143], the time resolution of GC-based methods is at best in the minute range, and sampling and pre-treatment steps (as stated along the introduction) very often introduce time averages of the concentration of the measured mixture. Because of these limitations, other methods have been developed over the years to complement GC-based methods with simplified, high sensitivity, fast and direct on-line monitoring of VOCs, with a high (even sub-second) time resolution. These methodologies encompass a diverse group of techniques based on Direct Injection Mass Spectrometry (DIMS) without conventional gas chromatography.

DIMS based methodologies (sometimes referred as direct air-sampling mass spectrometry, DS-MS) have been greatly developed in the last years. While they all share the fact that sample gas is directly introduced into the device, they vary significantly in terms of sampling, inlet and ionization/detection principles. Some features of these techniques were recently described and compared [72, 144, 145]. Even though these are recently developed methodologies, they provide advantages in several fields and open a plethora of new possibilities in VOCs characterization. Some fields of application are:

- Monitoring VOCs in exhaled human breath as a non-invasive technique in the diagnosis of pathologies.
- Homeland security. DIMS can be used to detect traces of explosives and chemical-warfare agents.
- In-situ control of industrial processes, quality improvement, and monitoring of harmful emission.
- Agro-industry and food science and technology. Rapid measurements on food quality.
- Possibility of rapid onsite monitoring of VOCs, at concentrations that can negatively affect air quality or even induce health risks.
- Also the need of portable, rapid and high-sensitivity techniques to assess indoor exposure to VOCs is becoming increasingly urgent as new materials and electronic devices are introduced into our life.

An overview of the most important DIMS based methodologies is described in this section. There are included the most relevant methodologies, including: (1) membrane introduction mass spectrometry, (2) differential optical absorption spectrometry, (3) low pressure and ambient pressure chemical ionisation tandem mass spectrometry analysers, (4) and two different ion-flow drift-tube techniques, proton transfer reaction and selected ion flow tube mass spectrometry.

1.1.4.5.1 Membrane introduction mass spectrometry (MIMS)

In membrane-introduction mass spectrometry (MIMS), one side of a thin membrane, typically polydimethylsiloxane (PDMS), is directly exposed to the vacuum of the ion source of the MS. Exposing the other side of the membrane to the sample enable organic compounds to permeate the membrane wall. This is followed by diffusion in the gas phase to the ion source. Since the flow of the analyte matrix through the membrane is proportionally smaller than the flow of the desired organic analytes, analyte

enrichment is obtained. This provides very sensitive levels of detection, as low as ng m^{-3} in air. Figure 1.1-14 shows a MIMS set-up. Principles and developments of MIMS were reviewed by Ketola et al. [146, 147].

When determining VOCs in air samples, membrane extraction is particularly attractive for continuous monitoring applications due to its improved selectivity and the enrichment power of the membranes, minimized solvent use, and the automation potential (since the membrane allows continuous, on-line extraction and stripping of trace VOCs from the environmental matrix) [148]. The sample can continuously flow through or over the membrane, and the analytes can selectively permeate through the membrane. Near-quantitative removal of VOCs from the feed stream may be possible [68].

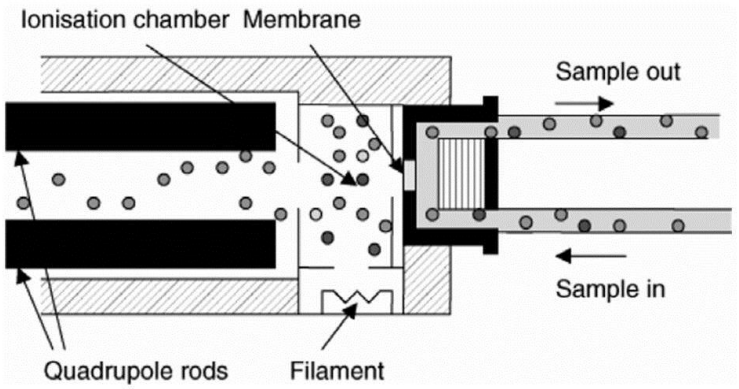


Figure 1.1-14 Schematic depiction of MIMS set-up [146]

1.1.4.5.2 Differential optical absorption spectrometry (DOAS)

The principle of the DOAS technique is based on the differential absorption of light by chemical compounds at specific wavelengths. DOAS, first described by Platt et al. [149], has been applied in field studies of VOCs in ambient air all over the world. DOAS instruments have been used for near real-time continuous monitoring of aromatic hydrocarbons (mainly BTEX) in urban air [150, 151]. DOAS combines advantages of fast response time (60 sec analysis in continuous mode) with low limits of detection (LOD = 2.6 µg m^{-3} for benzene). Disadvantages include optical interference from oxygen, ozone and several hydrocarbons [152]. . Due to the disadvantages, its use is not very extended nowadays

1.1.4.5.3 Low-pressure and atmospheric-pressure chemical ionization tandem mass spectrometry analysers (LPCI-MS^2 and APCI-MS^2)

These systems have been used to determine VOCs in atmospheric air operating on the principles of tandem mass spectrometry (MS/MS or MS^2). The sample is introduced into the mass spectrometer, where it ionizes at low pressure (in the LPCI-MS^2) [153] or atmospheric pressure (in APCI-MS^2) [154]. Ionization of analytes takes place as a result of a flow of protons between the analyte molecules and the N_2^+, O_2^+, NO^+, $(H_2O)_n^+$, and H^+ ions generated during corona discharge inside the spectrometer. The high value of the proton-activity coefficient (PA) means hydronium chlatrates (these subsequently dissociate into H_3O^+ ions) are mainly responsible for the ionization of analytes:

$$(H_2O)_n H^+ + VOC \rightarrow VOCH^+(H_2O)_m + (n-m)\,H_2O \qquad (14)$$

The frequency of collisions between H_3O^+ ions and analyte molecules increases with the pressure; a greater ionization efficiency is thus characteristic of APCI-MS^2 [153]. The ions produced are then separated by the MS analyser on the basis of their mass-to-charge ratio. If ionization takes place at atmospheric pressure (APCI-MS^2), data can also be gathered with the aid of a cold ion trap (CIT).

APCI-MS^2 analysers are routinely used to determine VOCs in atmospheric air. But, in the presence of water vapour, which prevents collisions between hydronium ions and analyte molecules during solvation (thus retarding ionization) APCI-MS^2 systems are not recommended to determine BTEX compounds in atmospheric air; gas analysers based on atmospheric pressure photoionization (APPI), instead of chemical ionization, are further sensitive for this particular purpose [145, 154].

1.1.4.5.4 Proton transfer reaction – mass spectrometry (PTR-MS)

This technique, with the next SIFT-MS, belongs to the *selected ion-flow drift-tube* (SIFDT) techniques, which measures ion-molecule reactions. In these techniques a kind of ion source produces reactant ions (A^+) that, in contact with the neutral reactant species (R) in the sample, generate reaction products (with their energetic, E, and thermodynamic, T, parameters) by a constant coefficient rate (k):

$$A^+ + R \xrightarrow{k} Products\,(E, T) \qquad (15)$$

The idea then arose to choose a reaction with a known k value, and to calculate the concentration of a VOC from the intensities of the measured final products and the parent ion. The original review of Lindinger [155] presents a clear description of PTR-MS

fundamentals and potential. More recent reviews are those of Blake et al. [156] and de Gouw and Warneke [157] for atmospheric applications.

The modus operandi of PTR-MS is the chemical ionization, by proton transfer, of a gas sample inside a drift tube. The proton source is normally H_3O^+. The fixed length of the drift tube provides a fixed reaction time for the ions as they pass along the tube: the ion residence (i.e. reaction time) time can be measured or it can be calculated from ion transport properties. If the proton donor concentration is largely unchanged by the addition of an analyte sample, the measurement of the ion signal ratio (proton donor)/ (protonated acceptor) allows the absolute concentration of the acceptor molecules to be calculated from a simple kinetic analysis. Consequently, by combining reaction kinetics with mass spectrometry, it is possible to both identify and quantify individual organic gases on a relatively short time scale and with a sensitivity that can reach well into the ng m^{-3} mixing regime.

The main constituents of a PTR-MS apparatus are the ion source, a reaction region and a mass analyser [155]. In most apparatus, the H_3O^+ primary-ion beam is produced by a hollow-cathode ion source. It presents some advantages because of the high intensity and relatively high purity of the primary H_3O^+ ion that allows the injection of the primary-ion beam directly into the reaction chamber without prior mass selection. The reason for this is that most of the ions produced in the plasma source react in cascades of reactions finally to produce H_3O^+, with the noteworthy exception of some residual O_2^+ [155] . This simplifies system realization and allows for better sensitivity. Alternative designs of the source have been tested to reduce impurities and back streaming from the reaction chamber at the cost of sensitivity [144]. More recently, other ions have been studied and, recently, a marketed commercial system allows for rapid switching between different ions: H_3O^+, NO^+ and O_2^+ [158].

1.1.4.5.5 Selected-Ion-flow-tube mass spectrometry (SIFT-MS)

Mainly developed by Španěl and Smith, they reviewed the fundamentals and several applications in 2005 [159]. Further applications and recent developments (e.g., compact SIFT-MS apparatus) have been reviewed [160]. This technique, like PTR-MS, belongs to the *selected ion-flow drift-tube (*SIFDT*)* group*.*

In SIFT-MS, the parent ions are generated by microwave plasma or by an electron-impact ion source, and the primary ions are selected by a quadrupole mass filter. This allows the selection, in principle, among many positive and negative parent ions and the production of a pure parent-ion beam. However, in DIMS monitoring of VOCs, it is convenient to select parent ions in such a way that they do not react with standard air

constituents. This factor limits practical applications to the same ions than PTR-MS: H_3O^+, NO^+ and O_2^+, however being possible, in particular cases, the use of other ions (e.g., OH^+) [161].

1.1.5 ENVIRONMENTAL LEGISLATION IN FORCE ON ATMOSPHERIC POLLUTANTS

This section describes the principal environmental laws and regulations in the local framework studied in this Thesis. The importance arises in policies and measures in force that have affected the changes, i.e. improvements, in the air quality and impact situation during the period in the context of this research.

It is necessary to know beforehand the hierarchical order of competences over the decision of implementing new environmental laws. Mallorca local regulations are based on Spanish national regulations, which in turns are based on the EU directives decided by the European Councils. Therefore EU commissions enact the guiding legal framework for all 27 EU-Countries.

Even though many other Countries (e.g. USA, Canada or Japan) have developed and implemented environmental protective laws for the regulation of the emissions of VOCs in their territories, this introductory section focuses on the legal framework in which this research: the European and the Spanish National regulations.

1.1.5.1 EU FRAMEWORK

The EU has developed a series of six Environment Action Programmes (EAPs) [162], starting in 1973. The 5th EAP (1993–2000) and 6th EAP (2002–2012) are the ones most relevant for the period addressed here, while the 6th EAP also looks ahead towards 2020. The 5th EAP, under the theme of 'air pollution' concentrated on acidification and air quality, with particular attention given to:

- A strategy to ensure that critical loads of acidifying, eutrophying and photochemical air pollutants are not exceeded;
- Establishing or amending air quality objectives for a few specific pollutants;
- Developing common procedures for assessing and monitoring of air quality.

The 6th EAP, under the theme 'environment and health and quality of life', in particular its Article 7 on air quality, states that: 'development and implementation of the measures in Article 5 in the transport, industry and energy sectors should be compatible with and contribute to improvement of quality of air'. Further measures envisaged are:

- Improving monitoring and assessment of air quality, including the deposition of pollutants, and the providing information to the public, including the development and use of indicators;
- A thematic strategy to strengthen a coherent and integrated policy on air pollution to cover priorities for further actions, the review and updating where appropriate of air quality standards and national emission ceilings with a view to reaching the long-term objective of no-exceedence of critical loads and levels, and the development of better systems for gathering information, modelling and forecasting;
- Adopting appropriate measures concerning ground-level ozone and particulates;
- Considering indoor air quality and the impacts on health, with recommendations for future measures where appropriate.

Thus, the 5th EAP and 6th EAP set the scene for developing specific policies and directives to control air pollution and improve air quality in the last two decades.

During the 1990s, the EU developed and adopted a series of directives on air quality management and assessment, setting e.g. some air quality limits and target values, and methods to monitor and assess air quality. These directives have paved the way for the exchange of data on air quality and station networks that has enabled the overview of European air quality presented in this introductory chapter.

The setting of health-related air quality limit and target values specified in the air quality directives benefited from the work and studies carried out under the Clean Air for Europe (CAFE) Programme , in cooperation with the World Health Organization (WHO), on the health effects of air pollutants.

The 6th EAP specified that the Commission should develop thematic strategies on a series of themes, including air pollution. The Thematic Strategy on Air Pollution was formulated as the final result of the CAFE Programme. It considers the complex interaction between pollutants, impacts and pollutant receptors (both humans and nature)

It deals with particulate matter in air, acidification, eutrophication and ground-level ozone, and impacts on human health, nature and biodiversity, materials and crops. The Strategy sets goals for reduced impacts on human health and the natural environment in 2020. AS it can be extracted from the 6th EAP, VOCs are not yet considered priority pollutants in the same way as PM, O_3, NO_x or SO_x, even though it is estimated that every year millions of tons are emitted to the European atmospheric environment. Since the 6th EAP draws the environmental protection path until 2020, it is loomed an

inefficient decrease over the European VOC emissions.

Hereby a summary of regulations is briefly described. The complete set of regulations is available in the EU Council website.

1.1.5.1.1 Regulations of emissions from the road traffic sector

The Euro standards have regulated emissions from motor vehicles since about 1970, through the so-called ECE R15/01-15/04 regulations for gasoline powered passenger cars. Since roughly 1990 the work was continued under the EU umbrella, using the so-called Euro 1–4 regulations for light-duty vehicles (gasoline and diesel powered) and the similar Euro I–IV regulations for heavy-duty diesel engines in trucks and buses, during the period 1992–2005. The further Euro 5/V and Euro 6/VI regulations took effect in 2009.

1.1.5.1.2 Petrol vapour recovery directives

The **Stage I Petrol Vapour Recovery Directive** (1994/63/EC) aims to prevent emissions to the atmosphere of volatile organic compounds (VOC) during the storage of petrol at terminals and subsequent distribution to service stations. It entered into force on 20 December 1994. The Directive contains measures that terminals should employ such as floating roofs and reflective coatings to reduce evaporative losses from storage tanks. In addition when petrol is loaded onto tankers and transported to service stations the Directive ensures that any vapours are recovered and returned to the tanker or terminal. Directive has influenced VOC emissions since about 2000.

The **Stage II Petrol Vapour Recovery Directive** (2009/126/EC) aims to ensure the recovery of petrol vapour that would otherwise be emitted to the air during the refuelling of vehicles at service stations. The minimum level of recovery of the systems employed should be 85 %. New service stations should comply with the directive from 2012. All stations with a throughput greater than 3 000 m3/year must comply by end-2018 at the latest. The Directive has not yet had any measured effect on VOC emissions in Europe.

1.1.5.1.3 Directives on fuel quality

The **Sulphur Contents of Liquid Fuels Directive**, 1999/32/EC regulates the sulphur limits in fuel oils, establishing the limits for sulphur in 1% by weight for heavy fuel and 0.10% by weight in gas oil.

The **Fuels Quality Directive** (2003/17/EC) amends the previous fuels directive (98/70/EC). It regulates the contents of sulphur, lead and benzene in motor fuels, as well

as other fuel quality parameters. The limit set in this Directive for benzene and PAHs are:

- For benzene in petrol, 1 % v/v;
- For PAH in diesel fuel, 11 % m/m.

The direct consequence by improving the quality of fuels is the reduction of VOC emissions derived from the traffic and transport uses, estimated over 16% of total VOC emissions in Europe (Figure 1.1-1, page 17).

1.1.5.1.4 Regulation of industrial emissions

Directive 2010/75/EU aims to recast the seven existing directives related to industrial emissions into a single clear and coherent legislative instrument. This includes the IPPC Directive, the LCP Directive, the Waste Incineration Directive, the Solvents Emissions Directive and three directives on titanium dioxide. The Commission proposed that minimum emission limit values in certain industrial sectors should be tightened (particularly for large combustion plants where progress to reduce pollution is considered insufficient).

The above legal instruments are briefly described below in chronological order:

The **Solvents Directive** (1999/13/EC) regulates the use of solvents and sets limits on emissions of VOC due to the use of organic solvents in certain activities and installations. The expressed objective of the Directive is to limit the formation of ozone in air. The list of activities and uses of solvents regulated by the Directive includes adhesive coating and other coating activities, dry cleaning, manufacturing of varnishes, adhesives, inks, pharmaceuticals, printing, surface cleaning, vehicle refinishing, wood impregnation and other. The Directive estimates emission limit values for waste gases or per volume of product, and requires a solvent management scheme for each activity.

The **Waste Incineration Directive** (2000/76/EC) repealed former directives on the incineration of hazardous waste (Directive 94/67/EC) and household waste (Directives 89/369/EEC and 89/429/EEC) and replaced them with a single text. The aim of the Waste Incineration Directive is to prevent or reduce as far as possible negative effects on the environment caused by the incineration and co-incineration of waste. In particular, it should reduce pollution caused by emissions into the air, soil, surface water and groundwater, and thus lessen the risks that these pose to human health. This is to be achieved through the application of operational conditions, technical requirements, and emission limit values for incineration and co-incineration plants within the EU.

The Waste Incineration Directive sets emission limit values and monitoring

requirements for pollutants to air such as dust, nitrogen oxides (NO_X), sulphur dioxide (SO_2), hydrogen chloride (HCl), hydrogen fluoride (HF), heavy metals, dioxins and furans and some heavy methals, but not specifically for VOCs.

Most types of waste incineration plants fall within the scope of the Waste Incineration Directive, with some exceptions, such as those treating only biomass (e.g. vegetable waste from agriculture and forestry).

The Waste Incineration Directive makes a distinction between:

- Incineration plants, which are dedicated to the thermal treatment of waste and may or may not recover heat generated by combustion;
- Co-incineration plants, such as cement or lime kilns, steel plants or power plants whose main purpose is energy generation or the production of material products and in which waste is used as a fuel or is thermally treated for the purpose of disposal.

The **Large Combustion Plants** (**LCP) Directive** (2001/80/EC) regulates emissions of acidifying pollutants, particulate matter and ozone precursors from large combustion plants for heat end energy production. The Directive sets emission limit values (ELVs) for sulphur dioxide (SO_2), nitrogen oxides (NO_X) and dust (Total Suspended Particles, TSP), which vary according to the age of the plant, the fuel used and the plant capacity (see EEA Technical Report No 8/2010).

The **Paints Directive** (2004/42/CE) establishes limit values for the maximum VOC contents of decorative paints and vehicle-refinishing products, to limit the emissions of volatile organic compounds, amending also the Solvents Directive concerning vehicle-refinishing products. It has two phases for the implementation of stricter limits on VOC contents in products, Phase I to be implemented by 1 January 2007 and Phase II by 1 January 2010.

The original **Integrated Pollution Prevention and Control (IPPC) Directive** was adopted on 24 September 1996, and has since been adapted four times, until the present version, adopted on 21 December 2007 (2008/1/EC). It regulates basically all industrial plants, including energy production, metals production, mineral industries, chemical industries, waste management and other sectors. The air pollutants addressed are SO_2, NO_x, CO, VOC, metals, dust, asbestos, chlorine, fluoride, arsenic, cyanides and other carcinogenic and mutagenic compounds and some specific dioxins.

In the Directive, the concept of 'best available techniques' or BAT plays a central role. In this context:

- 'techniques' include both the technology used and the way in which the installation is designed, built, maintained, operated and decommissioned;

- 'available' techniques are those developed on a scale that allows application in the relevant industrial sector, under economically and technically viable conditions, taking into consideration the costs and advantages, whether or not the techniques are used or produced inside the Member State in question, and as long as they are reasonably accessible to the operator;
- 'Best' means most effective in achieving a high general level of protection of the environment as a whole.

Authorities are also obliged to set up a system of issuing integrated permits that will lead to the implementation of BAT in new and existing plants.

1.1.5.1.5 Directive on national total emissions

The National Emissions Ceiling Directive (**NEC Directive**), adopted on 23 October 2001, sets upper limits for each Member State for the total emissions in 2010 of the four main pollutants responsible for acidification, eutrophication and ground-level ozone pollution (sulphur dioxide, nitrogen oxides, volatile organic compounds and ammonia). It leaves it largely to the Member States to decide which measures — on top of Community legislation for specific source categories — to take in order to comply.

1.1.5.1.6 Long-range Transboundary Air Pollution (LRTAP) Convention

The long-range transport of air pollution is an important factor affecting ecosystems and the human population. The United Nations Economic Commission for Europe (UNECE) Convention on Long-range Transboundary Air Pollution (LRTAP) [17] aims to reduce and prevent air pollution. In addition to the EU legislation listed above the LRTAP Convention has a number of legally binding protocols, covering specific categories of air pollutants.

The Task Force on Emission Inventories (TFEI) was initiated in 1991 following agreement by the Executive Body for the Convention on Long-Range Transboundary Air Pollution. The TFEI Secretariat is currently provided by the United Kingdom and is supported by the other signatories to the Convention including the European Community, through the European Commission and the European Environment Agency (EEA).

The TFEI is designed to assist in:

- The evaluation of the emission inventory requirements of the Co-operative Programme for Monitoring and Evaluation of Air Pollutants in Europe (EMEP);
- Ensuring an adequate flow of reliable information to support the work under the Convention;
- Accounting for the emission data needs of other relevant bodies under the Executive Body.

The objectives of the TFEI are therefore:

- To provide a technical forum to discuss, exchange information and harmonise emission inventories including emission factors, methodologies and guidelines;
- Conduct in-depth evaluation of emission factors and methodologies in current operation and
- co-operate with other international organizations working on emission inventories with the aim of harmonising methodologies and avoiding duplication of work.

The TFEI meets these objectives through the holding of an annual meeting, the publication of a guidebook and through the operation of a number of expert panels. The first annual meeting of the TFEI was held in London in May 1992. In 1993 the TFEI agreed a specification for the EMEP/EEA Emission Inventory Guidebook (the 'Guidebook'). The first edition of the Guidebook was subsequently completed in 1996 and published and distributed by the EEA. The latest version was published in 2009 [25].

1.1.5.1.7 Spanish Framework

Spanish Environmental Ministry adopted in 2007 the Law 34/2007 "about Air Quality and Atmosphere protection". It amended existing regulations regarding air pollution recasting them into a single and clear one.

Regretfully, and even though there have been reported clear evidences on human and environmental hazardous effects, the Spanish government only meets the minimum requirements set by the EU, and has not developed more restrictive laws regarding VOCs. Only two directives set a limit value over two specific industrial processes:

- Stage I Petrol Vapour Recovery Directive 94/63/EC, which amended the Spanish *Real Decreto 2102/1996.*

- Solvents Directive 1999/13/EC, adapted in Spain as *Real Decreto 117/2003*.

1.1.5.2 CONSIDERATIONS ABOUT ENVIRONMENTAL MONITORING REGULATIONS OF VOCs

VOCs emissions in Spain are reported every year (among other regulated air pollutants) in the Spanish Inventory of Emissions [26] obeying to National Emission Ceiling (NEC) Directives. The Guidance Document for the implementation of the European Pollutant Release and Transfer Register (E-PRTR) is the backbone guideline to implement the UNECE PRTR Protocol at the EU level [163]. In this guidance document there are described the standard methodologies to measure, calculate or estimate NMVOCs emissions. The European standard method EN 13649:2001 to measure VOCs concentrations in air [164] is based on the use of activated carbon with further solvent desorption and gas chromatography. Notwithstanding, European Committee for Standardisation (CEN) nowadays also suggests other international standard methods: EN ISO 16000:2006- parts 5, 9, 10 and 11; and EN ISO 16017:2003 parts 1 and 2.

As it was previously mentioned in section 1.1.2.1, Spanish NMVOCs emissions (and many others in Europe) are estimated on the basis of arbitrary selected values, specified in the TFEI emission inventory guidebook [25]. By this procedure, it is assumed a bias between estimated and real emissions. Even though there are several suitable techniques which enable reliable, fast and robust techniques for VOCs determination in air (as we have shown in this chapter), legal regulations do not force to characterize real emissions in the air, and simple estimation of VOCs are valid, thus adopted as common procedure.

Extra efforts have to be done in this field in order to effectively reduce emissions of VOCs to the environment. As it has been mentioned, an average of 1 ton Km^{-2} is estimated to be emitted in Spain every year. This issue is not tolerable if the society wants to ever reach a safe environment. Moreover, as long as emission focuses of VOCs are not homogenously spread over the territory but localized in specific areas (industries, landfills, big cities, etc.), these zones are expected to be continuously under severe pollution levels. Updated environmental occurrence data is needed to understand emission patterns and act in consequence to efficiently reduce emissions.

1.2 DETERMINATION OF PHARMACEUTICAL RESIDUES IN WATER

In the last years, a wide number of organic pollutants known as emerging contaminants (ECs) are receiving increasing concern in the scientific community. ECs encompass a broad category of chemicals currently not included in routine monitoring programmes (EU framework) but which could pose a significant risk requiring regulation, depending on their potential (eco)toxicological and health effects and on their levels in the (aquatic) environment. This definition would mean that the substances:

- Could have been around for a long time, or been invented quite recently;
- Could be any type of chemical, not necessarily in the categories we might tend to think of (pharmaceuticals, personal care products, nano-compounds);
- (If they pose a risk) must have slipped through the regulatory net, or not been subject to a regulatory check when first produced or used, perhaps because they occur naturally.

Essentially, they share the characteristic that we are only just becoming aware that they might pose a risk. In that respect, environmental agencies sometimes suggest that it would be more correct to name them as "contaminants of emerging concern", but "emerging contaminants" is a convenient short form. Nevertheless, as a general assumption, every chemical substance poses a significant effect either in humans or in the environment. However, not all of them will produce noticeable impacts in short-term.

Richardson and Ternes review [165] has included the most well-studied emerging organic contaminant groups including, among others, artificial sweeteners, nanomaterials, perfluorinated compounds (PFCs), pharmaceuticals and personal care products (PPCPs), steroid hormones, drinking water disinfection byproducts (DBPs), sunscreens/UV filters, brominated flame retardants (including polybrominated diphenyl ethers), benzotriazoles, naphthenic acids, antimony, siloxanes, musk, algal toxins, perchlorate, ionic liquids, dioxane and pesticide transformation products.

The widespread production and use of organic ECs without corresponding occurrence evaluations and monitoring had an increasing contribution to environmental pollution in the last decades. As stated in the beginning of this introduction, 100.000 chemicals are registered in the USA and Europe [3], therefore we can assume that the major part of them are polluting the environment out any kind of control. Since pharmaceuticals are the primary focus of this Thesis with the already stated VOCs, they are discussed in this chapter in more detail. Hundreds of publications are available regarding the rest of emerging contaminants. Some of them may be found in Richardson and Ternes review [165], since it summarizes the most relevant reviews in ECs analysis in water since 2009.

Human exposure is generally of key concern for these contaminants precisely because of their widespread applications. Some of these ECs are also reported to be endocrine disrupting compounds (EDCs) [166]. According to the US-EPA definition, EDCs are exogenous agents that interfere with the production, release, transport, metabolism, binding, action, or elimination of the body natural hormones, which are responsible for the maintenance of homeostasis and the regulation of developmental processes. EDCs can include manmade chemicals such as pesticides and plasticizers, natural chemicals found in plants (phytoestrogens), pharmaceuticals, and hormones that are excreted in animal or human waste [167]. EDCs are not defined by their chemical nature, but rather by their biological effects.

In September 2009 the US-EPA published its final list (Contaminant Candidate List 3 – CCL3) of unregulated emerging organic contaminants with potential to present health risks via drinking water exposure. The final CCL 3 includes 104 chemicals or chemical groups and 12 microbiological contaminants [168]. Contaminant Candidate List 4 (CCL4) is under current development requesting any newly available information that was not considered in the development of the CCL3. Much work is still needed to understand real risks about the compounds listed amongst the 100.000 registered chemicals.

1.2.1 PHARMACEUTICALS AND PERSONAL CARE PRODUCTS (PPCPs)

PPCPs are a broad group of thousands of chemicals belonging to a wide spectrum of chemical classes, and this larger group is often sub-divided into two more inclusive groups, pharmaceutically active compounds (PhACs) and personal care products (PCPs). Pharmaceuticals group (PhACs) include all of the prescription and over-the-counter pharmaceuticals consumed for purposes of human and veterinary health care as well as all other drugs, whether therapeutic or recreational. Personal care products (PCPs) include many of the chemicals found in beauty and personal hygiene products such as cosmetics, fragrances, etc. It is estimated that approximately 3.000 different substances are used as pharmaceutical ingredients, including among others painkillers, antibiotics, antidiabetics, contraceptives, antidepressants, etc. However, only a very small subset of these compounds has been investigated in environmental studies so far. Table 1.2-1 shows several groups of pharmaceuticals already detected in the environment and some examples of each group.

Besides pharmaceuticals, the other important group of contaminants included in the list of emerging organic contaminants is the group of ingredients widely known as personal care products (PCPs). In recent years there has been growing interest in the determination of this group. Several personal care product ingredients have been among the most commonly detected compounds in environmental samples. It is continuously increasing the concern about environmental fate and the potential effects of synthetic organic chemicals used in soaps, lotions, toothpaste and other personal care products. Of particular concern are compounds that are environmental persistent, bioaccumulate, or have a designed bioactivity. There are different groups of PCPs such as synthetic musk fragrances, antimicrobials, sunscreen agents, insect repellents and preservatives, among others.

PCPs are not studied in the experimental part of this Doctoral Thesis; however they are included in some discussion sections as well as other organic emerging contaminants, assuming that they may have similar environmental behaviour than the pharmaceuticals studied in this Thesis, following similar or equivalent pollution pathways.

Since this Doctoral Thesis is focused on environmental evaluations (occurrence, fate and pollution pathways), additional information -e.g. therapeutic use, individual physicochemical properties and structure, mechanisms of reaction, etc. – are only displayed if needed along this introductory section

Table 1.2-1Examples of pharmaceuticals studied in environmental samples

Group	Examples
Quinolones (Antibiotic)	Ciprofloxacin Ofloxacin Norfloxacin
Macrolides (Antibiotic)	Clarithromycin Erythromicin Tylosin
Tetracyclines (Antibiotics)	Tetracycline Oxitetracycline 4-epitetracycline
Sulfonamides (Antibiotics)	Sulfadiazine Sulfamethoxazole Sulfathiazole
Diuretics	Furosemide Hydrochlorthiazide
β-Blockers	Atenolol Enalapril Metoprolol
Proton pump inhibitors	Omeprazole ranitidine
Psychoactive	Carbamazepine Diazepam Oxazepam
Nonsteroidal anti-inflammatory	Ibuprofen Diclofenac Naproxen
Bronchodilators	Salbutamol Terbutalin
Lipid regulators	Bezafibrate Gemfibrozil
Antitumorals	Cyclophosphamide Methotrexate
Phosphodiesterase type V inhibitors	Sildenafil Vardenafil Tadalafil
Contrast products	Iopromide

1.2.2 POLLUTION IN THE AQUATIC ENVIRONMENT

After use or intake by humans or animals (in veterinary medicine), PPCPs may follow different pathways to reach the environment [169-171]. Nowadays it is estimated that the major part of pharmaceuticals in the environment were excreted by human or animal waste or rinsed from the body. Human residues are mainly flushed down drains and into sewer systems to eventually arrive at wastewater treatment plants (WWTPs). Current wastewater treatment methods are not efficient at removing all PPCPs and their metabolites, and therefore many of them are consequently released back into the aquatic environment through the WWTPs effluents. Other veterinary residues may reach environment by its use as manure. As seen in Figure 1.2-1, the potential exposure ways of PPCPs to the environment include WWTP effluents, sludge, and waste disposal.

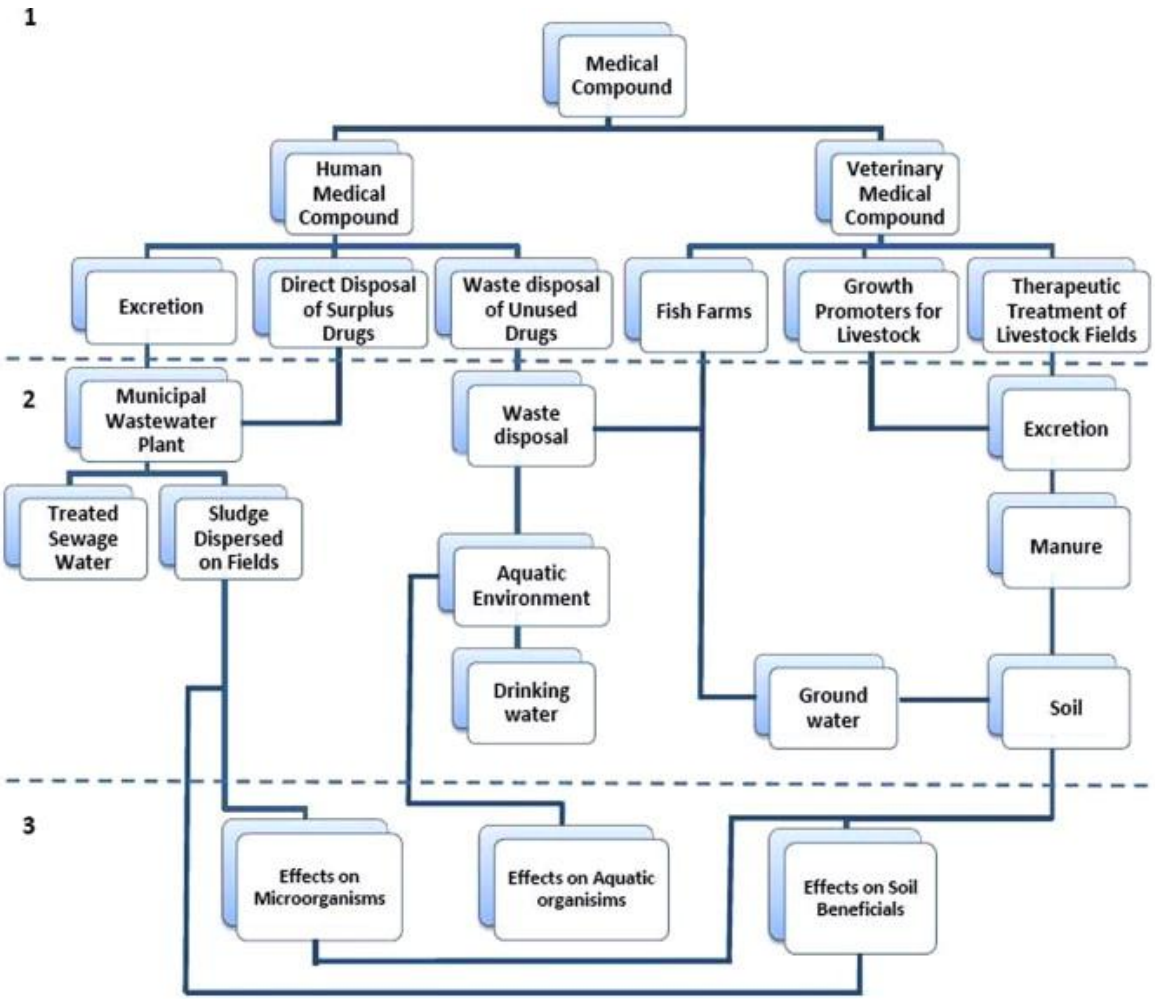


Figure 1.2-1 Occurrence and environmental effects of pharmaceutical wastes (1 – exposure, 2 – fate, and 3 – environmental effects) [169-171]

Studies regarding the fate of PPCPs in sewage (both sewage water and sludge) have been conducted in numerous countries worldwide, including EU countries, USA, Canada, Asian countries, etc. Although the exact fate and effect of medical substances in the water environment is not easy to predict, anticipated exposure routes are as schematized in Figure 1.2-1.

1.2.2.1 EMISSION SOURCES OF PHARMACEUTICALS INTO THE AQUATIC ENVIRONMENT

PhACs are continually released into the environment in large quantities from a wide number of small sources, including human and animal excretion in urine and faeces, manufacturing residues, hospital and landfill disposal and subsequent leaching or disposal of unused pharmaceuticals. In addition, occurrence of pharmaceuticals in a specific environment may depend on many factors, e.g. production rate, human or animal intake dose, frequency of use, metabolic pathways or the efficiency of disposal processes [172, 173].

As stated above, wastewater treatment has become nowadays one of the most critical environmental issues regarding water. In Europe it has been experienced a very significant increase in the number of WWTPs to meet the quality standards stipulated in the European Council Directives (Directives 91/271/EEC and 98/15/EEC).

In general, re-use of wastewater and sludge is encouraged, since it represents a long-term solution to fulfil increasing water demands and reduce environmental impact of wastewaters, as long as the quality of the final re-used qualities do not represent any threat to health or environmental protection requirements. Current EU legislation regulates the agricultural use of sewage sludge based only on the concentration of toxic heavy metals and nutrients. However, following measures from the European Commission beginning in 1999 [174], although emerging organic contaminants were not included - the third draft of a future Sludge Directive contained a proposal to limit values of several organic contaminants [175], such as dioxins, PAHs or PCBs. Specific regulations concerning PPCPs in environmental waters are still in process of implementation in the EU.

Studies of contaminant toxicity in public water systems, which may lead to adverse health effects, are needed to guide actions taken by regulatory authorities. Although many regulations are already in place to protect the public, there is a need to constantly update these, based upon the existence of new knowledge. Similarly, water treatment practices are designed to protect human health, but their performance also needs to be

continually re-evaluated and optimized, based upon new research results. The levels of these compounds found in effluents show that they may be only partially removed during conventional treatment, before WWTP-treated effluents are discharged into aquatic environment. Since it is known that PPCPs are present in the environment and might cause adverse impacts, it has been studied the efficacy of different ways to remove pharmaceuticals from reclaimed wastewater. Consequently, while some earlier treatments remain effective today, the elimination prerequisites have also increased significantly in more recent times, and additional treatment objectives have been added. Treatment processes must be closely linked with the water quality objectives and standards established by local and National regulatory authorities.

Many of the new treatment technologies being developed are designed to address the health and environmental concerns raised by the findings of recent research. Although removal of PPCPs was not the initial objective of WWTPs, facilities must be designed with the capability to be updated with new procedures in the future dealing with new emerging contaminants. Furthermore, as long as recent developments of more sensitive analytical techniques enable the detection of new chemicals, some previously undetected contaminants are in the research spotlight. The elimination efficiency of any WWTP is directly related to its design. Although new treatment techniques are in constant development, the adoption and implementation into WWTPs facilities needs long and costly procedures, so upgrade of WWTPs is not frequent.

WWTPs apply primary (physico-chemical separation processes), secondary (microbial biodegradation), and usually tertiary (advanced) treatments prior to the discharge into aquatic environment. During wastewater treatment, a redistribution of PPCPs will occur between the dissolved fraction and the solids and soils (primary or secondary sludge, see Figure 1.2-1). In accordance, release of PPCPs to the environment will occur not only by final effluents but also with sludge's disposal. As it was already mentioned, excess sewage sludge is commonly used in the EU as a fertilizer in agriculture. There is a wide list of available bibliography addressing this topic [176, 177].

In general, primary treatments in WWTPs consists of physico-chemical processes, including filtration, sedimentation, coagulation, and flocculation. Secondary treatments are designed to degrade organic matter through the use of microorganisms. Biological degradation and transformation take place aerobically through biological oxidation in activated sludge, through the use of trickling filters, or in anaerobic sludge digesters. Tertiary treatments use physical, biological, and chemical processes as an extra step to further reduce pollutants not degraded during the secondary treatment. Tertiary treatment also provides better quality of effluents by reducing odours and coloration.

These treatments often include the application of chlorine and/or other chemicals to oxidize remaining organic matter. Some advanced treatments have recently been evaluated, including membrane processes (microfiltration, ultrafiltration, nanofiltration, and reverse osmosis), advanced oxidation processes (AOPs) and adsorption into granular activated solid sorbents. Some recent studies reviewed the different methods used for the removal of pharmaceuticals and TPs from wastewater [178-181].

Wide number of studies detected PPCPs (and many other ECs) in the WWTPs effluents, due to inefficient removal during the treatment processes. Several studies reported bad removal rates, with the consequent release of these pollutants into the environment [182, 183]. Therefore, the need for new directions and considerations in wastewater treatment is evident. Regretfully, some major treatment plants are still using only limited physico-chemical processes, which unfortunately produce only undesired low removal efficiencies for PPCPs. Comprehensive assessments of the resulting health and environment effects, as well as community concerns about these effects, are therefore becoming increasingly important in the field of wastewater management.

1.2.2.2 PHARMACEUTICAL'S TRANSFORMATION PRODUCTS (TPs)

The occurrence or fate of PhACs residues in environmental waters has been categorized in three principal transformation pathways from the active former prescribed structure [171]: (1) ultimate mineralization; (2) partial biodegradation (i.e. partly retained in sediment) and (3) conversion to more hydrophilic but persistent metabolites (i.e. end up in receiving water bodies).

While most organic contaminants are entering the wastewater influent without being metabolized, pharmaceuticals are frequently transformed in the body and a combination of non-altered pharmaceuticals and their metabolites are excreted by humans [184]. Microbial transformation products of pharmaceuticals and hormones can also be formed during biological treatment of wastewaters, from contact with sediment and soils, as well as during bank filtration. Furthermore, TPs can be formed by UV irradiation in surface waters and during oxidative treatment processes, such as ozonation and chlorine disinfection. Figure 1.2-2 shows some schematic trends of the transformation processes of different PhACs.

Even though TPs have gained increasing interest as water contaminants, only a few studies have investigated the formation and fate of biological TPs of pharmaceuticals in contact with biologically active matrices, such as activated sludge or sediments. One

reason is the challenge of structural elucidation of TPs occurring at low concentrations in complex environmental matrices. Sophisticated analytical techniques are needed, such as hybrid high-resolution mass spectrometry and nuclear magnetic resonance (NMR) [185]. Although the target compound is known, with a few exceptions of very simple reactions (e.g., hydrolysis of amides and esters), quadrupole-MS and even high resolution-MS are often not sufficient to obtain or confirm chemical structures of TPs. The TP structure suggestions based on exact masses and mass fragments have to be confirmed by alternative analytical methods or chemical reactions specifically altering the new functional moieties formed.

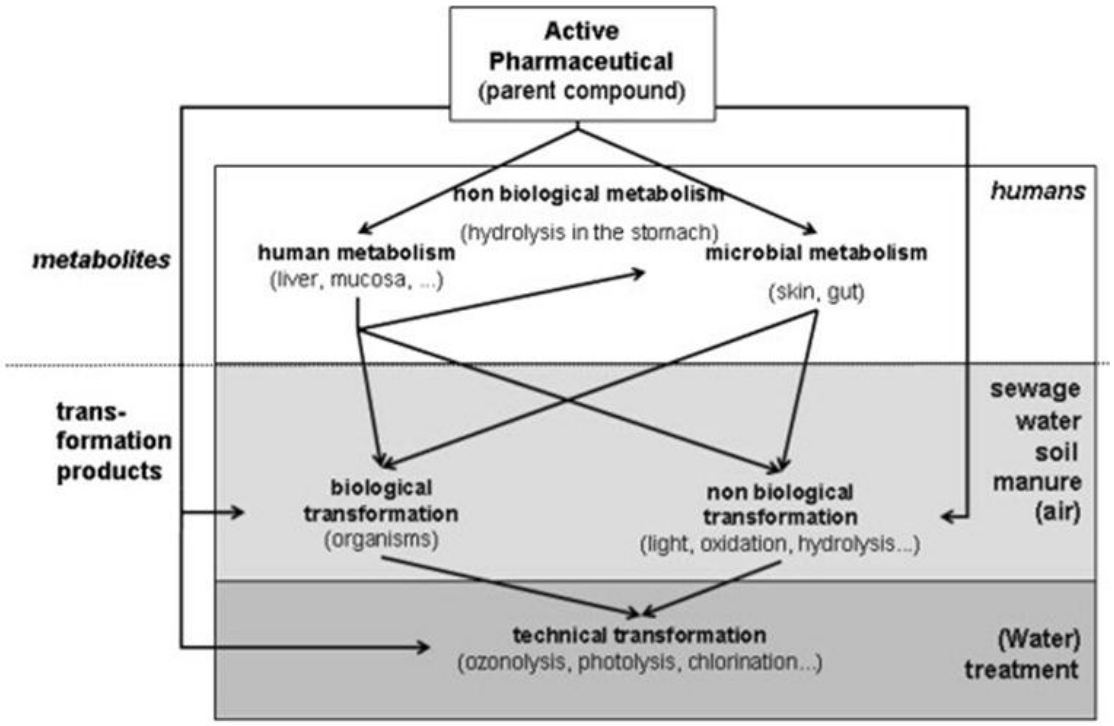


Figure 1.2-2 Metabolites and transformation products pathways (TPs) [184]

Potential analytical methods include a wide variety of currently available NMR techniques or, to a much less extent, infrared (IR) spectroscopy. However, a drawback of both techniques is the elevated quantity and the high purity needed for isolated standards. In those cases, where no authentic standard is available and only MS spectra of TPs have been obtained, we might better define the suggestions of the chemical TP structures as “tentative identifications” unless further plausibility criteria are fulfilled, confirming the proposed chemical structures. A complete overview of the

literature regarding the detection and identification of pharmaceutical TPs until 2008 was provided by Celiz et al [186].

Several recent studies indicated that the majority of pharmaceutical TPs formed under aerobic conditions have a slightly modified molecular structure featuring increased polarity, due to the introduction of hydroxyl, carboxyl, or keto moieties [187, 188]. On the basis of the similarity of their molecular structure to the parent compound, a significant number of TPs are expected to possess comparable biological activity as their chemical precursors [189]. However, the enhanced polarity improves the permeability of these compounds for several water treatment processes such as adsorptive filtration (e.g., activated carbon), underground soil passage, or bank filtration. Consequently, the likelihood increases that TPs are contaminating groundwater and drinking water [190].

1.2.3 CHROMATOGRAPHIC TECHNIQUES FOR THE DETERMINATION OF PHARMACEUTICALS IN WATER

Environmental analysis of pharmaceuticals in water matrices has a common background with the analysis of VOCs in environmental air matrices (see Section 1.1.3). The analysis of pharmaceuticals in the environment water is thus challenging from similar perspectives:

(i) Are in general embedded within very complex mixtures of liquids, also with solids and gases either in solution or suspension;

(ii) Their concentrations may evolve rapidly with time; and,

(iii) May be present on a wide range of concentrations, commonly in the trace levels

As trace compounds, pharmaceutical's concentrations in the aquatic environment are typically in the order from pg L^{-1} to µg L^{-1}. This issue makes PhACs analyses conditional on: (a) the use of very sensitive analytical techniques and (b) a clean-up and extraction step prior to the analytical detection. Some other critical factors determine the best analytical methodologies for pharmaceutical's quantification in the water.

Owing the extremely wide range of different compounds included among PhACs, with different physicochemical properties and different effects on human health and environment, it is important to quantify them individually. It is necessary the use of an appropriate separation technique to characterize water chemical composition on the basis of individual concentrations. Chromatographic techniques do provide the most efficient separation, becoming especially important when multiple compounds are to be detected.

With some exceptions, PhACs tend to be polar, non-volatile, and thermally labile. For these compounds gas chromatography without a prior derivatization step is not a suitable technique. liquid chromatography thus presents a great advantage here, since a derivatization step is not required. Undoubtedly however, the main advances in improving sensitivity and specificity in environmental analysis of pharmaceutical residues has been due to the application of mass spectrometry (MS) and tandem mass spectrometry (MS-MS or MS^2). Specifically, MS-MS is today the technique of choice for the identification of a broad range of PhACs in environmental samples.

An overview of the most relevant methods and the new trends in the determination of PhACs in environmental waters are presented. However, facing the huge number of studies regarding the analysis of PPCPs (up to 7000 publications listed in the US-EPA [4]) only the most relevant articles published in the most important Scientific Journals are overviewed.

1.2.3.1 EXTRACTION TECHNIQUES

Pharmaceuticals in the aquatic environment are present at trace levels, typically in the order from pg L^{-1} to few µg L^{-1}. Analysis of organic compounds at trace levels in the environment (like PPCPs or VOCs) requires sensitive, robust and fast analytical techniques. As it was stated in Section 1.1.4.1, and similarly to VOCs determination in air, sampling and extraction techniques for PhACs in water must satisfy some relevant criteria. Environmental water sampling is, in general, less challenging than environmental air sampling, hence common sampling procedure involves the collection of environmental water into clean glass vessels (equivalent to "whole air" collection techniques of VOCs). However, environmental water samples, in general, involve more complicated clean-up and extraction procedures than environmental gas samples.

In the last years a wide list of clean-up and extraction techniques have been developed and applied for the determination of PPCPs in water samples (as well as soils and sludge samples). The most widely used are based on solid phase extraction (SPE), owing the wide list of solid sorbents commercially available, which simplifies working operations –enables on-line automated methods [191]- , but may generate elevated solvent residues. One important recent trend is the development of techniques involving the concept "green chemistry", reducing the amount of solvent used [192].

This section shows an overview of the most important extraction techniques, suitable for the monitoring of organic PhACs in the environmental water samples: (1) solid-phase extraction (SPE), (2) stir bar sorptive extraction (SBSE), (3) liquid-phase microextraction techniques (LPME), and (4) solid-phase microextraction (SPME). These techniques have been comprehensively reviewed in the last years [119, 165, 172, 181, 192-194]. Basic principles of SBSE and LPME and related techniques are briefly described in this section. SPE and SPME have been previously described in this introductory Chapter (Section 1.1.4.1).

1.2.3.1.1 Stir bar sorptive extraction (SBSE)

Stir bar sorptive extraction (SBSE), introduced in 1999 [195], was developed with the aim to overcome some of the limitations of the solid sorbent techniques, in particular those involving SPME and small volumes of sorptive material [196]. The technique is based on sorptive extraction, whereby the solutes are extracted into a polymer coating on a magnetic stirring rod. The extraction is controlled by the partitioning coefficient of the solutes between the polymer coating and the sample matrix, as well as by the phase ratio between the polymer coating and the sample volume.

In practice, the stir bar used in SBSE is introduced into the water sample to extract the analytes into the coating polymer over a period of time. Several parameters should be optimized, such as agitation speed, sample volume, pH, extraction time, or ionic strength. After extraction, the stir bar is removed, and the analytes are recovered from the sorbent by desorption, either thermal (TD) or liquid (LD). With the thermal method, the stir bar is introduced into a glass tube, which is then placed in a thermal desorption unit installed on a GC system [197]. When a liquid desorption approach is used, the stir bar is used to stir the solvent, which is suitable for the target analytes, and this extract is then injected into the LC or GC unit [198].

The main advantages are the easiness of its application and the possibility of automations with thermal desorption. The principal drawback is that the only commercially available fibre is the non-polar polymer polydimethylsiloxane (PDMS), and it is sometimes needed to develop novel in-house stir bar coatings to improve recoveries, adding extra valuable time to the analysis,

1.2.3.1.2 Liquid-phase microextraction (LPME)

As reviewed by Sarafraz-Yazdi et al. [199], liquid-phase microextraction (LPME) was introduced in order to overcome the problems that could occur with the use of SPME fibres. Because of its advantages in terms of high enrichment, efficient sample cleanup, and low consumption of organic solvent, substantial interest has been devoted to LPME in recent years. Some applications of this method for analysis of environmental waters have been recently reviewed [200, 201]. In hollow-fibre membrane liquid-phase microextraction (HF-LPME), target analytes are extracted from aqueous samples and transferred into a supported liquid membrane (SLM). They are then sustained in the pores in the walls of a small porous hollow fibre. Zhang et al. [100] reported on their pioneering use of dynamic HF-LPME, combined with a port derivatization of the compounds with trimethylanilinium hydroxide (TMAH), followed by GC-MS analysis. They applied this technique to determine four pharmaceuticals (ibuprofen, ketoprofen, naproxen, and clofibric acid) in waste and tap waters.

Another of the main methodologies that has evolved from liquid phase microextraction, and which has received increasing attention in recent years, is dispersive liquid-liquid microextraction (DLLME). The advantages it offers include ease of operation, low cost, and a high enrichment factor. There are still few reports on studies using DLLME to determine PhACs. However, one that can be mentioned was published by Du et al. [82], who determined, for the first time, estrone and 17β- estradiol in water samples, using DLLME and LC with a variable-wavelength detector. Their

recovery levels in spring, tap, and river waters ranged from 90% to 94% for estrone, and from 84% to 112% for 17β-estradiol. Their results showed that the various matrices had little effect on the efficiency of DLLME enrichment.

A new direction for LPME has been developed and is referred to as electromembrane (EME). This novel system combines the technical setup used in LPME with known principles for electroextraction, which force the extraction process with an applied potential difference across the membrane. Fontana et al. [202] successfully applied EME to determine trace levels of acidic and basic PhACs in waters. Only 10 min of extraction time and 50 µL of organic solvent (octanol) were needed under ideal conditions, making this technique very interesting for the environmental monitoring of a few number of specific compounds

1.2.3.2 GAS CHROMATOGRAPHY

As mentioned above, GC may be a suitable technique for determination of volatile pharmaceuticals in environmental waters, commonly hyphenated with MS or MS-MS detection, which are selective enabling the use of library searching on the basis of the m/z ions. However it presents a major drawback, since PhACs are tending to be polar, common procedure is the introduction of a derivatization step prior to injection, in order to adapt analytes' polarity, volatility and thermal stability to GC features.

In Table 1.2-2 there is a list of different analytical methods developed for the analysis of PhACs in water samples with the most relevant features in every case.

In accordance, GC techniques are not the most appropriate techniques for the environmental analysis (with monitoring purposes) of PhACs, since there are a limited number of compounds suitable to be determined by GC. As we state in the next section, LC better meets the requirements to be used as analytical methods for the environmental monitoring of PhACs.

Table 1.2-2 Overview of relevant analytical methods based on GC-MS applied for determination of PhACs in water

Analytes	GC technique (analyser)	Extraction technique (derivatization agent)	Ref.
Hormones, anti-inflammatories, illicit drugs	GC-MS (Q)	SPE (BSTFA)	[203]
Hormones, anti-inflammatories	TD-GC-MS (Q)	SBSE (in-situ BSTFA)	[197]
Lipid regulators, β-blockers, anti-inflammatories	PTV-GC-MS (Q)	SBSE (MTBSTFA)	[204]
Hormones, endocrine disrupting compounds	GC-MS (Q)	SPME (on fibre BSTFA)	[205]
Anti-inflammatories, analgesics	GC-MS (Q)	SPE (MTBSTFA)	[206]
Lipid regulators, anti-inflammatories, endocrine disrupting compounds	GC-(NCI)MS (Q)	SPE (PFBBr and PFBOCl)	[207]
97 organics (lipid regulators, anti-inflammatories, analgesics, anti-depressants)	GCxGC-MS (TOF)	SPE (TMSH)	[208]
Lipid regulatirs, anti-inflammatories	PTV-GC-MS	SPE (MTBSTFA)	[209]
Lipid regulators, anti-inflammatories, analgesics, caffeine, hormones	GC-MS^2 (IT)	SPE (TMS and TMS-oxime)	[210]
Anti-epileptics, anti-inflammatories, stimulants	GC-MS^2 (IT)	SPE (no derivatization)	[211]

1.2.3.3 LIQUID CHROMATOGRAPHY

Owing the physicochemical characteristics of PhACs, liquid chromatography (LC or HPLC, high-performance liquid chromatography) is the most widely used separation technique, overcoming the principal drawbacks of the GC. Liquid chromatography is a relative simple, robust and effective technique for organic polar and non-volatile compounds like PhACs [212]. LC is typically hyphenated to mass spectrometry detection (LC-MS) or tandem mass spectrometry detection (LC-MS/MS or LC-MS^2) with electrospray ionisation (ESI) or atmospheric pressure ionisation (API) interfaces.

This technique also presents some challenges in the analysis of environmental water samples. The principal is the compromise situation involving the column separation

efficiency and the time of analysis. Recent trends in LC techniques are using analytical columns packed with smaller sized particles (commonly 1.7 µm in diameter vs. 4 to 5 µm), enabling better separation efficiency due to an increase on the number of theoretical plates, reducing the time of analysis. This technique is called Ultra high-performance liquid chromatography (UHPLC). As a counterpoint, the smaller size of particles generates an outstanding increase of pressure in the system, thus special equipment is needed, capable to run under thousands of psi (up to 15000 psi).

The liquid chromatography characteristics allows the potential hyphenation with the flow injection based techniques, e.g. flow injection analysis (FIA) or sequential injection analysis (SIA), for the complicated clean-up and extraction step(s), enabling on-line analytical methodologies, really adequate for the (constant) monitoring of environmental levels of PhACs.

Table 1.2-3 shows a summary of different analytical methodologies for the determination of PhACs based on LC-MS with the extraction technique.

Table 1.2-3 Overview of relevant analytical methods based on LC-MS for determination of PhACs in wastewater and natural waters

Analytes	LC technique (MS analyzer)	Extraction	Ref.
Hormones	LC-UV	DLLME	[213]
Hormones	LC-DAD	SBSE	[198]
Hormones	LC-UV	On-line SPE	[214]
Ilicit drugs and metabolites	LC-MS^2 (QqQ)	SPE	[215]
Fluoroquinolones	LC-MS^2 (QqQ)	In-tube SPME	[216]
Sulfonamides, tetracyclines, analgesics and hormones	LC-MS^2 (QqQ)	SPE	[217]
Carbamazepine, sulfonamides, lipid regulators, anti-inflammatories	LC-MS^2 (QqQ)	SPE	[182]
Analgesics and non-steroidal anti-inflammatories (NSAIDs), lipid regulators, psychiatric drugs, anti-histaminics, anti-ulcer agent, antibiotics and β-blockers	LC-MS2 (QqQ)	SPE	[218]
Analgesics, anti-inflammatories, lipid regulators, psychiatric drugs	UHPLC-MS^2 (QqQ)	SPE	[219]

Analytes	LC technique (MS analyzer)	Extraction	Ref.
Antibiotics (quinolones, sulfonamides, diaminopyrimidine)	UHPLC-MS^2 (QqQ)	SPE	[220]
Ranitidine, carbamazepine, trimethoprim, psychiatric drugs	UHPLC-MS^2 (QqQ)	SPE	[221]
Antiepileptics, lipid regulators, analgesics, β-blockers, antiinflammatories, illicit drugs	UHPLC-MS^2 (QqQ)	SPE	[222]
Ilicit drugs and metabolites	HILIC-MS^2 (QqQ)	SPE	[223]
Benzodiazepines, sulfonamides, macrolides, tetracyclines, anti-epileptics	LC-MS^2 (QqLIT)	SPE	[224]
Analgesics, anti-inflammatories, lipid regulators, antibiotics	LC-MS^2 (QqLIT)	SPE	[225]
β-blockers	LC-MS^2 (QqLIT)	SPE-MIP	[226]
Macrolides	LC-MS^2 (QqLIT)	On-line SPE	[227]
Analgesics, antiinflammatories, lipid regulators, cholesterol lowering statin agents, psychiatric drugs, anti ulcer histamine H2 receptor antagonist, antibiotics, β-blockers	UHPLC-MS^2 (Q-TOF)	SPE	[228]

1.3 REFERENCES

[1] J.L. Oaks, M. Gilbert, M.Z. Virani, R.T. Watson, C.U. Meteyer, B.A. Rideout, H.L. Shivaprasad, S. Ahmed, M.J. Iqbal Chaudhry, M. Arshad, S. Mahmood, A. Ali, A. Ahmed Khan, Nature, 427 (2004) 630-633.
[2] European Council. COD 2007/0235. Regulation (EC) No 401/2009 of the European Parliament and of the Council of 23 April 2009 on the European Environment Agency and the European Environment Information and Observation Network (latest version), 2009.
[3] D.C.G. Muir, P.H. Howard, Environmental Science & Technology, 40 (2006) 7157-7166.
[4] US-EPA, Pharmaceuticals and Personal Care Products (PPCPs): Relevant Literature (a comprehensive database of literature references compiled and maintained by CG Daughton and MST Scuderi; first implemented 19 February 2008), 2010.
[5] R. Heinrich-Ramm, M. Jakubowski, B. Heinzow, J. Molin Christensen, E. Olsen, O. Hertel, Pure Appl. Chem., 72 (2000) 385-436.
[6] EEA, Proposal for a Council Directive on limitation of emissions of volatile organic compounds due to the use of organic solvents in certain industrial activities. 96/0276 (SYN) Article 2, 1996.
[7] EEA, Directive 2004/42/CE of the European Parliament and of the Council of 21 April 2004 on the limitation of emissions of volatile organic compounds due to the use of organic solvents in certain paints and varnishes and vehicle refinishing products and amending Directive 1999/13/EC, 2004.
[8] US-EPA, Method TO-17. Determination of Volatile Organic Compounds in Ambient Air Using Active Sampling Onto Sorbent Tubes, 1999.
[9] S.E. Manahan, Fundamentals of environmental Chemistry. , USA, 2001.
[10] J.F. Pankow, Atmospheric Environment, 21 (1987) 2275-2283.
[11] T.F. Bidleman, Environmental Science & Technology, 22 (1988) 361-367.
[12] A. Finizio, D. Mackay, T. Bidleman, T. Harner, Atmospheric Environment, 31 (1997) 2289-2296.
[13] S.J. Eisenreich, B.B. Looney, J.D. Thornton, Environmental Science & Technology, 15 (1981) 30-38.
[14] K. Roholm, The Journal of Industrial Hygiene and Toxicology, 19 (1937) 126-137.
[15] Greater London Authority, 50 years on the struggle for air quality in London since the great smog of December 1952, Ed. Greater London Autorithy, City Hall, 2002.
[16] R. Varma, D.R. Varma, Bulletin of Science, Technology & Society, 25 (2005) 37-45.
[17] UNECE. Convention on Long-range Transboundary Air Pollution, 1979.
[18] M. Kampa, E. Castanas, Environmental Pollution, 151 (2008) 362-367.
[19] S. Harrad, Persistent Organic Pollutants, John Wiley & Sons, Ltd, 2010.
[20] A. Schecter, L. Birnbaum, J.J. Ryan, J.D. Constable, Environmental Research, 101 (2006) 419-428.
[21] EEA,Technical Report No 15/2011. Revealing the costs of air pollution from industrial facilities in Europe, 2011.
[22] P. Ciccioli, Chemistry and analysis of volatile organic compounds in the environment. Ed. J. Blackie Academic & Professional, UK, 1993.
[23] A. Roger, Atmospheric Oxidation, in: Handbook of Property Estimation Methods for Chemicals, CRC Press, 2000.
[24] R. Atkinson, Atmospheric Environment, 34 (2000) 2063-2101.

[25] EEA, Co-operative Programme for Monitoring and Evaluation of Air Pollutants in Europe (EMEP). Atmospheric emission inventory guidebook, 2009.
[26] Unidad de Información Ambiental Estratégica. Inventario de emisiones a la atmósfera de España. Serie 1990-2009 (In spanish). 2011.
[27] EEA, Data on emissions of air pollutants submitted to the LRTAP Convention, 2011.
[28] A. Guenther, C.N. Hewitt, D. Erickson, R. Fall, C. Geron, T. Graedel, P. Harley, L. Klinger, M. Lerdau, W.A. McKay, T. Pierce, B. Scholes, R. Steinbrecher, R. Tallamraju, J. Taylor, P. Zimmerman, J. Geophys. Res., 100 (1995) 8873-8892.
[29] M. Karl, A. Guenther, R. Köble, A. Leip, G. Seufert, Biogeosciences, 6 (2009) 1059-1087.
[30] J.H. Schween, R. Dlugi, C.N. Hewitt, P. Foster, Atmospheric Environment, 31, Supplement 1 (1997) 199-215.
[31] K.W. Oum, M.J. Lakin, D.O. DeHaan, T. Brauers, B.J. Finlayson-Pitts, Science, 279 (1998) 74-76.
[32] R. Atkinson, Journal of Physical and Chemical Reference Data, 26 (1997) 215-290.
[33] J.G. Calvert, R. Atkinson, J.A. Kerr, S. Madronich, G.K. Moortgart, T.J. Yarwood, The Mechanisms of Atmospheric Oxidation of the Alkenes. Oxford University Press, 2000.
[34] R. Atkinson, J. Arey, Accounts of Chemical Research, 31 (1998) 574-583.
[35] A. Calogirou, N.R. Jensen, C.J. Nielsen, D. Kotzias, J. Hjorth, Environmental Science & Technology, 33 (1998) 453-460.
[36] A.J. Haagen-Smith, M.M. Fox, Indian Enginering Chemistry, 48 (1956) 1484.
[37] A.J. Haagen-Smith, M.M. Fox, Journal of Air pollution Control Association, 4 (1954) 105-109.
[38] P.A. Leighton, Photochemistry of air pollution, New York and Loncdon Academic Press, 1961.
[39] M. Climent Bellido, Aspectos químicos de la contaminación atmosférica (In Spanish), Ed. University of Cordoba, 1996.
[40] R.M. Peña Creciente, Contribución al estudio de compuestos oxidantes en el entorno de una central térmica (in spanish), PhD Dissertation in Chemistry Dpt., University of Santiago de Compostela. 1997.
[41] M.E. Jenkin, K.C. Clemitshaw, Atmospheric Environment, 34 (2000) 2499-2527.
[42] M.E. Jenkin, S.M. Saunders, M.J. Pilling, Atmospheric Environment, 31 (1997) 81-104.
[43] V. Fernández-Villarrenaga Martín, Desarrollo de metodologías para el análisis de compuestos orgánicos volátiles (COV) en matrices ambientales (in spanish), PhD Dissertation in Chemistry Dpt., University of A Coruña, 2002.
[44] A. Whittaker, K. BéruBé, T. Jones, R. Maynard, R. Richards, Science of The Total Environment, 334–335 (2004) 435-445.
[45] S. Sironi, L. Capelli, P. Céntola, R. Del Rosso, M. Il Grande, Atmospheric Environment, 39 (2005) 5387-5394.
[46] L. Vilavert, M. Nadal, M. Figueras, J. Domingo, Environmental Science and Pollution Research, 19 (2012) 96-104.
[47] M.M. Renfrew, Journal of Chemical Education, 67 (1990) A241.
[48] T. Ohura, T. Amagai, X. Shen, S. Li, P. Zhang, L. Zhu, Atmospheric Environment, 43 (2009) 6352-6359.
[49] E. Uhde, T. Salthammer, Atmospheric Environment, 41 (2007) 3111-3128.

[50] S.-C. Lee, H. Guo, W.-M. Li, L.-Y. Chan, Atmospheric Environment, 36 (2002) 1929-1940.
[51] K.B. Hoddinott, A.P. Lee, Chemosphere, 41 (2000) 77-84.
[52] H. Guo, S.C. Lee, L.Y. Chan, W.M. Li, Environmental Research, 94 (2004) 57-66.
[53] D. Arslanbas, H. Pekey, B. Pekey, Z. Bulut Bozkurt, G. Dogan, M. Civan, Ö. Oguz Kuntasal, G. Tuncel, in: 2nd International Conference on Air Pollution and Control (CAPAC-II), Antalya (Turkey), 2011.
[54] C. Jia, S. Batterman, C. Godwin, Atmospheric Environment, 42 (2008) 2083-2100.
[55] T.E. Butt, E. Lockley, K.O.K. Oduyemi, Waste Management, 28 (2008) 952-964.
[56] US-EPA, Technology Transfer Network: Air toxics website, 2012, http://www.epa.gov/ttn/atw/188polls.html..
[57] US-EPA, 2005 National-Scale Air Toxics Assessment, 2011, http://www.epa.gov/ttn/atw/nata2005/.
[58] US-EPA, Guidelines for Carcinogen Risk Assessment, 2005. Risk Assessment Forum Editor, Washington , DC.
[59] US-EPA, Integrated Risk Information System (IRIS), 2012, http://www.epa.gov/iris/.
[60] US-EPA, A Guide to Indoor Air Quality, http://www.epa.gov/iaq/pubs/index.html.
[61] European Committe for Standardization, EN-13725. Air quality: determination of odour concentration by dynamic olfactometry, 2003.
[62] American Society for Testing Materials (ASTM), Standard Practice for Referencing Suprathreshold Odour Intensity., 1999.
[63] N. Yassaa, B.Y. Meklati, E. Brancaleoni, M. Frattoni, P. Ciccioli, Atmospheric Environment, 35 (2001) 787-801.
[64] US-EPA, Method TO 14A. Determination Of Volatile Organic Compounds (VOCs) In Ambient Air Using Specially Prepared Canisters With Subsequent Analysis By Gas Chromatography, 1999.
[65] US-EPA. Method TO-15. Determination of Volatile Organic Compounds (VOCs) In Air Collected In Specially-Prepared Canisters And Analyzed By Gas Chromatography Mass Spectrometry (GC/MS), 1999.
[66] J. Pawliszyn, H.L. Lord, Handbook of sample Preparation. Ed. Whiley-Blackwell, 2010.
[67] M.R. Ras, F. Borrull, R.M. Marcé, TrAC Trends in Analytical Chemistry, 28 (2009) 347-361.
[68] K. Demeestere, J. Dewulf, B. De Witte, H. Van Langenhove, Journal of Chromatography A, 1153 (2007) 130-144.
[69] J. Dewulf, H. Van Langenhove, G. Wittmann, TrAC Trends in Analytical Chemistry, 21 (2002) 637-646.
[70] E. Woolfenden, Journal of Chromatography A, 1217 (2010) 2674-2684.
[71] E. Woolfenden, Journal of Chromatography A, 1217 (2010) 2685-2694.
[72] S. Król, B. Zabiegała, J. Namieśnik, TrAC Trends in Analytical Chemistry, 29 (2010) 1092-1100.
[73] S. Król, B. Zabiegała, J. Namieśnik, TrAC Trends in Analytical Chemistry, 29 (2010) 1101-1112.
[74] L.-L. Hsieh, C.-C. Chang, U. Sree, J.-G. Lo, Water, Air, & Soil Pollution, 170 (2006) 107-121.
[75] M. Gautrois, T. Brauers, R. Koppmann, F. Rohrer, O. Stein, J. Rudolph, Journal Geophysical Research, 108 (2003) 4393.

[76] M. Das, D. Kang, V.P. Aneja, W. Lonneman, D.R. Cook, M.L. Wesely, Atmospheric Environment, 37 (2003) 2269-2277.
[77] M. Colón, J.D. Pleil, T.A. Hartlage, M. Lucia Guardani, M. Helena Martins, Atmospheric Environment, 35 (2001) 4017-4031.
[78] N. Ochiai, S. Daishima, D.B. Cardin, Journal of Environmental Monitoring, 5 (2003) 997-1003.
[79] C.-C. Chang, U. Sree, Y.-S. Lin, J.-G. Lo, Atmospheric Environment, 39 (2005) 3187-3190.
[80] E.S. Farrell, G.E. Pacey, Talanta, 82 (2010) 739-744.
[81] J.-L. Wang, C.-C. Chang, K.-Z. Lee, Journal of Chromatography A, (In press).
[82] D. Wang, C. Austin, Analytical and Bioanalytical Chemistry, 386 (2006) 1089-1098.
[83] C. Hung-Lung, H. Ching-Shyung, C. Shih-Yu, W. Ming-Ching, M. Sen-Yi, H. Yao-Sheng, Science of The Total Environment, 381 (2007) 200-211.
[84] Y.L. Zhang, H. Guo, X.M. Wang, I.J. Simpson, B. Barletta, D.R. Blake, S. Meinardi, F.S. Rowland, H.R. Cheng, S.M. Saunders, S.H.M. Lam, Journal Geophysical Research, 115 (2010) D15309.
[85] I.J. Simpson, N.J. Blake, B. Barletta, G.S. Diskin, H.E. Fuelberg, K. Gorham, L.G. Huey, S. Meinardi, F.S. Rowland, S. A., A.J. Weinheimer, M. Yang, D.R. Blake, Atmospheric Chemistry and Physics., 10 (2010) 11931-11954.
[86] P. Mochalski, B. Wzorek, I. Śliwka, A. Amann, Journal of Chromatography B, 877 (2009) 189-196.
[87] A. Kumar, I. Víden, Environmental Monitoring and Assessment, 131 (2007) 301-321.
[88] S. Cariou, J.-M. Guillot, Analytical and Bioanalytical Chemistry, 384 (2006) 468-474.
[89] D. Wang, C. Austin, Analytical and Bioanalytical Chemistry, 386 (2006) 1099-1120.
[90] M.R. Ras, R.M. Marcé, F. Borrull, Talanta, 77 (2008) 774-778.
[91] G. Mangani, A. Berloni, M. Maione, Journal of Chromatography A, 988 (2003) 167-175.
[92] M. Harper, Journal of Chromatography A, 885 (2000) 129-151.
[93] American Society for Testing Materials (ASTM), D-6196. Standard Practice for Selection of Sorbents, Sampling, and Thermal Desorption Analysis Procedures for Volatile Organic Compounds in Air, 2009.
[94] National Institute for Occupational Safety and Health, NIOSH-2549. Volatile Organic Compounds (Screening) 1996.
[95] International Standarisation Organisation, ISO 16017-1. Indoor, ambient and workplace air -- Sampling and analysis of volatile organic compounds by sorbent tube/thermal desorption/capillary gas chromatography -- Part 1: Pumped sampling, 2000.
[96] International Standarisation Organisation, ISO 16017-2. Indoor, ambient and workplace air -- Sampling and analysis of volatile organic compounds by sorbent tube/thermal desorption/capillary gas chromatography -- Part 2: Diffusive sampling, 2000.
[97] J. Namieśnik, B. Zabiegała, A. Kot-Wasik, M. Partyka, A. Wasik, Analytical and Bioanalytical Chemistry, 381 (2005) 279-301.
[98] M. Partyka, B. Zabiegała, J. Namiésnik, A. Przyjazny, Critical Reviews in Analytical Chemistry, 37 (2007) 51-78.
[99] S. Seethapathy, T. Górecki, X. Li, Journal of Chromatography A, 1184 (2008) 234-253.

[100] L. Tuduri, M. Millet, O. Briand, M. Montury, TrAC Trends in Analytical Chemistry, 31 (2012) 38-49.
[101] European Committee for Standarization, EN 13528-1:2002. Ambient air quality. Diffusive samplers for the determination of concentrations of gases and vapours. Requirements and test methods. General requirements, 2002.
[102] European Committee for Standarization, EN 13528-2:2002. Ambient air quality. Diffusive samplers for the determination of concentrations of gases and vapours. Requirements and test methods. Specific requirements and test methods, 2002.
[103] Sigma-Aldrich, in http://www.sigmaaldrich.com/analytical-chromatography/air-monitoring/passive-sampling.html.
[104] H. Plaisance, P. Desmettres, T. Leonardis, A. Pennequin-Cardinal, N. Locoge, J.C. Galloo, Journal of Environmental Monitoring, 10 (2008) 517-526.
[105] C. Cocheo, C. Boaretto, D. Pagani, F. Quaglio, P. Sacco, L. Zaratin, D. Cottica, Journal of Environmental Monitoring, 11 (2009) 297-306.
[106] A. Pennequin-Cardinal, H. Plaisance, N. Locoge, O. Ramalho, S. Kirchner, J.-C. Galloo, Talanta, 65 (2005) 1233-1240.
[107] P. Bruno, M. Caselli, G. de Gennaro, M. Solito, M. Tutino, Waste Management, 27 (2007) 539-544.
[108] K. Dettmer, W. Engewald, Analytical and Bioanalytical Chemistry, 373 (2002) 490-500.
[109] K. Dettmer, W. Engewald, Chromatographia, 57 (2003) S339-S347.
[110] N.A. Martin, N.L.A.S. Barber, J.K. Black, R.P. Lipscombe, C.A. Taig, Atmospheric Environment, 41 (2007) 7666-7671.
[111] Ö.O. Kuntasal, D. Karman, D. Wang, S.G. Tuncel, G. Tuncel, Journal of Chromatography A, 1099 (2005) 43-54.
[112] C.L. Arthur, J. Pawliszyn, Analytical Chemistry, 62 (1990) 2145-2148.
[113] G. Vas, K. Vékey, Journal of Mass Spectrometry, 39 (2004) 233-254.
[114] G. Ouyang, J. Pawliszyn, TrAC Trends in Analytical Chemistry, 25 (2006) 692-703.
[115] E.E. Stashenko, J.R. Martínez, TrAC Trends in Analytical Chemistry, 23 (2004) 553-561.
[116] A. Prieto, O. Basauri, R. Rodil, A. Usobiaga, L.A. Fernández, N. Etxebarria, O. Zuloaga, Journal of Chromatography A, 1217 (2010) 2642-2666.
[117] M.T. Tena, J.D. Carrillo, TrAC - Trends in Analytical Chemistry, 26 (2007) 206-214.
[118] C. Duan, Z. Shen, D. Wu, Y. Guan, TrAC Trends in Analytical Chemistry, 30 (2011) 1568-1574.
[119] G. Ouyang, J. Pawliszyn, Analytica Chimica Acta, 627 (2008) 184-197.
[120] J. Pawliszyn, B. Pawliszyn, M. Pawliszyn, The Chemical Educator, 2 (1997) 1-7.
[121] J. Nicolle, V. Desauziers, P. Mocho, Journal of Chromatography A, 1208 (2008) 10-15.
[122] R. Barro, J. Regueiro, M. Llompart, C. Garcia-Jares, Journal of Chromatography A, 1216 (2009) 540-566.
[123] C. Domeño, F. Martínez-García, L. Campo, C. Nerín, Analytica Chimica Acta, 524 (2004) 51-62.
[124] F.V. Parreira, C.R. de Carvalho, Z. de Lourdes Cardeal, Bulletin of Environmental Contamination and Toxicology, 70 (2003) 0957-0963.
[125] E. Davoli, M.L. Gangai, L. Morselli, D. Tonelli, Chemosphere, 51 (2003) 357-368.
[126] H. Kataoka, Analytical and Bioanalytical Chemistry, 396 (2010) 339-364.

[127] T. Elbir, B. Cetin, E. Cetin, A. Bayram, M. Odabasi, Environmental Monitoring and Assessment, 133 (2007) 149-160.
[128] E.M. Martins, G. Arbilla, G.F. Bauerfeldt, M.d. Paula, Chemosphere, 67 (2007) 2096-2103.
[129] A. Campos-Candel, M. Llobat-Estellés, A. Mauri-Aucejo, Talanta, 78 (2009) 1286-1292.
[130] V. Fernández-Villarrenaga, P. López-Mahía, S. Muniategui-Lorenzo, D. Prada-Rodríguez, E. Fernández-Fernández, X. Tomàs, Analytical Letters, 37 (2004) 3313-3330.
[131] W. Kornacki, P. Fastyn, J. Gawlowski, T. Gierczak, J. Niedzielski, Analyst, 130 (2005) 632-636.
[132] W. Kornacki, P. Fastyn, T. Gierczak, J. Gawłowski, J. Niedzielski, Chromatographia, 63 (2006) 67-71.
[133] Perkin-Elmer, in, Norwalk, CT, USA.
[134] C.-Y. Peng, S. Batterman, Journal of Environmental Monitoring, 2 (2000) 313-324.
[135] R.A. Ketola, J.T. Kiuru, V. Tarkiainen, J.T. Kokkonen, J. Räsänen, T. Kotiaho, Analytica Chimica Acta, 562 (2006) 245-251.
[136] J.M. Sanchez, R.D. Sacks, Journal of Separation Science, 30 (2007) 1052-1060.
[137] Y. Qin, T. Walk, R. Gary, X. Yao, S. Elles, Atmospheric Environment, 41 (2007) 6018-6032.
[138] C. Thammakhet, P. Thavarungkul, R. Brukh, S. Mitra, P. Kanatharana, Journal of Chromatography A, 1072 (2005) 243-248.
[139] J.M. Sanchez, R.D. Sacks, Journal of Separation Science, 28 (2005) 22-30.
[140] H. Peng, J. Wang, Z. Shen, D. Wu, Y. Guan, Analyst, 136 (2011) 586-590.
[141] A. Segal, T. Górecki, P. Mussche, J. Lips, J. Pawliszyn, Journal of Chromatography A, 873 (2000) 13-27.
[142] X. Liu, J. Pawliszyn, International Journal of Environmental Analytical Chemistry, 85 (2005) 1189-1200.
[143] M. Qi, X. Ge, M. Liang, R. Fu, Analytica Chimica Acta, 527 (2004) 69-72.
[144] F. Biasioli, C. Yeretzian, T.D. Märk, J. Dewulf, H. Van Langenhove, TrAC Trends in Analytical Chemistry, 30 (2011) 1003-1017.
[145] K. Badjagbo, S. Sauvé, S. Moore, TrAC Trends in Analytical Chemistry, 26 (2007) 931-940.
[146] R.A. Ketola, T. Kotiaho, M.E. Cisper, T.M. Allen, Journal of Mass Spectrometry, 37 (2002) 457-476.
[147] R.A. Ketola, J.T. Kiuru, T. Kotiaho, V. Kitunen, A. Smolander, Boreal Environment Research, 16 (2011) 36-46.
[148] N. Srinivasan, R.C. Johnson, N. Kasthurikrishnan, P. Wong, R.G. Cooks, Analytica Chimica Acta, 350 (1997) 257-271.
[149] U. Platt, D. Perner, H.W. Pätz, J. Geophys. Res., 84 (1979) 6329-6335.
[150] G. Barrefors, Science of The Total Environment, 189–190 (1996) 287-292.
[151] D. Brocco, R. Fratarcangeli, L. Lepore, M. Petricca, I. Ventrone, Atmospheric Environment, 31 (1997) 557-566.
[152] H. Skov, A. Lindskog, F. Palmgren, C.S. Christensen, Atmospheric Environment, 35, Supplement 1 (2001) S141-S148.
[153] A. Guenther, C. Geron, T. Pierce, B. Lamb, P. Harley, R. Fall, Atmospheric Environment, 34 (2000) 2205-2230.

[154] K. Badjagbo, P. Picard, S. Moore, S. Sauvé, Journal of the American Society for Mass Spectrometry, 20 (2009) 829-836.
[155] W. Lindinger, A. Hansel, A. Jordan, International Journal of Mass Spectrometry and Ion Processes, 173 (1998) 191-241.
[156] R.S. Blake, P.S. Monks, A.M. Ellis, Chemical Reviews, 109 (2009) 861-896.
[157] J. de Gouw, C. Warneke, Mass Spectrometry Reviews, 26 (2007) 223-257.
[158] A. Jordan, S. Haidacher, G. Hanel, E. Hartungen, L. Märk, H. Seehauser, R. Schottkowsky, P. Sulzer, T.D. Märk, International Journal of Mass Spectrometry, 286 (2009) 122-128.
[159] D. Smith, P. Španěl, Mass Spectrometry Reviews, 24 (2005) 661-700.
[160] P. Španěl, D. Smith, Mass Spectrometry Reviews, 30 (2011) 236-267.
[161] P. Španěl, M. Pavlik, D. Smith, International Journal of Mass Spectrometry and Ion Processes, 145 (1995) 177-186.
[162] EEA, 2012. http://ec.europa.eu/environment/archives/env-act5/envirpr.htm.
[163] European Comission, Guidance Document for the implementation of the European PRTR, 2006.
[164] European Committe for Standardization, EN-13649:2001. Stationary source emissions - Determination of the mass concentration of individual gaseous organic compounds - Activated carbon and solvent desorption method, 2001.
[165] S.D. Richardson, T.A. Ternes, Analytical Chemistry, 83 (2011) 4614-4648.
[166] I. Robinson, G. Junqua, R. Van Coillie, O. Thomas, Analytical and Bioanalytical Chemistry, 387 (2007) 1143-1151.
[167] M. Pedrouzo, F. Borrull, E. Pocurull, R.M. Marcé, Talanta, 78 (2009) 1327-1331.
[168] US-EPA, Contaminant Candidate List 3 (CCL-3), 2011, in http://water.epa.gov/scitech/drinkingwater/dws/ccl/ccl3.cfm#ccl3.
[169] T. Heberer, Toxicology Letters, 131 (2002) 5-17.
[170] B. Halling-Sørensen, S. Nors Nielsen, P.F. Lanzky, F. Ingerslev, H.C. Holten Lützhøft, S.E. Jørgensen, Chemosphere, 36 (1998) 357-393.
[171] A. Ziylan, N.H. Ince, Journal of Hazardous Materials, 187 (2011) 24-36.
[172] K.Y. Bell, M.J.M. Wells, K.A. Traexler, M.-L. Pellegrin, A. Morse, J. Bandy, Water Environment Research, 83 (2011) 1906-1984.
[173] M.J.M. Wells, K.Y. Bell, K.A. Traexler, M.-L. Pellegrin, A. Morse, Water Environment Research, 82 (2010) 2095-2170.
[174] Comission to the Council Directive and the European Parliament. Report 99752 on the implementation of Community waste legislation., 2000.
[175] European Commission, (2000).
[176] A. Nieto, F. Borrull, R.M. Marcé, E. Pocurull, Journal of Chromatography A, 1216 (2009) 5619-5625.
[177] A. Kot-Wasik, J. Debska, J. Namieśnik, TrAC - Trends in Analytical Chemistry, 26 (2007) 557-568.
[178] I. Oller, S. Malato, J.A. Sánchez-Pérez, Science of The Total Environment, 409 (2011) 4141-4166.
[179] D. Fatta-Kassinos, M.I. Vasquez, K. Kümmerer, Chemosphere, 85 (2011) 693-709.
[180] S. Judd, The MBR book. Principles and applications of membrane bioreactors in water and wastewater treatment. Ed. Butterworth-Neinemann, Oxford, UK, 2011.
[181] F.A. Caliman, M. Gavrilescu, CLEAN – Soil, Air, Water, 37 (2009) 277-303.

[182] J.L. Zhou, Z.L. Zhang, E. Banks, D. Grover, J.Q. Jiang, Journal of Hazardous Materials, 166 (2009) 655-661.
[183] A. Jelić, M. Petrović, D. Barceló, Pharmaceuticals in Drinking Water in, Springer Berlin / Heidelberg, 2012, pp. 1-24.
[184] K. Kümmerer, Journal of Environmental Management, 90 (2009) 2354-2366.
[185] J.L. Kormos, M. Schulz, M. Wagner, T.A. Ternes, Analytical Chemistry, 81 (2009) 9216-9224.
[186] M.D. Celiz, J. Tso, D.S. Aga, Environmental Toxicology and Chemistry, 28 (2009) 2473-2484.
[187] A.H. Neilson, A.-S. Allard, Environmental degradation and transformation of organic chemicals, Boca Raton, FL, 2008.
[188] D.E. Helbling, J. Hollender, H.-P.E. Kohler, H. Singer, K. Fenner, Environmental Science & Technology, 44 (2010) 6621-6627.
[189] R. van Zelm, M.A.J. Huijbregts, D. van de Meent, Environmental Science & Technology, 44 (2010) 1004-1009.
[190] J.L. Kormos, M. Schulz, H.-P.E. Kohler, T.A. Ternes, Environmental Science & Technology, 44 (2010) 4998-5007.
[191] S. Rodriguez-Mozaz, M.J. Lopez de Alda, D. Barceló, Journal of Chromatography A, 1152 (2007) 97-115.
[192] M. Farré, S. Pérez, C. Gonçalves, M.F. Alpendurada, D. Barceló, TrAC Trends in Analytical Chemistry, 29 (2010) 1347-1362.
[193] E. Primel, S. Caldas, A. Escarrone, Central European Journal of Chemistry, 10 (2012) 876-899.
[194] A.S. Yazdi, TrAC Trends in Analytical Chemistry, 30 (2011) 918-929.
[195] E. Baltussen, P. Sandra, F. David, C. Cramers, Journal of Microcolumn Separations, 11 (1999) 737-747.
[196] F. David, P. Sandra, Journal of Chromatography A, 1152 (2007) 54-69.
[197] E. Van Hoeck, F. Canale, C. Cordero, S. Compernolle, C. Bicchi, P. Sandra, Analytical and Bioanalytical Chemistry, 393 (2009) 907-919.
[198] X. Huang, J. Lin, D. Yuan, R. Hu, Journal of Chromatography A, 1216 (2009) 3508-3511.
[199] A. Sarafraz-Yazdi, A. Amiri, TrAC Trends in Analytical Chemistry, 29 (2010) 1-14.
[200] J. Lee, H.K. Lee, K.E. Rasmussen, S. Pedersen-Bjergaard, Analytica Chimica Acta, 624 (2008) 253-268.
[201] M.Á. Bello-López, M. Ramos-Payán, J.A. Ocaña-González, R. Fernández-Torres, M. Callejón-Mochón, Analytical Letters, 45 (2012) 804-830.
[202] A.R. Fontana, R.G. Wuilloud, L.D. Martínez, J.C. Altamirano, Journal of Chromatography A, 1216 (2009) 147-153.
[203] C.-P. Yu, K.-H. Chu, Chemosphere, 75 (2009) 1281-1286.
[204] J.B. Quintana, R. Rodil, S. Muniategui-Lorenzo, P. López-Mahía, D. Prada-Rodríguez, Journal of Chromatography A, 1174 (2007) 27-39.
[205] L. Yang, T. Luan, C. Lan, Journal of Chromatography A, 1104 (2006) 23-32.
[206] A. Togola, H. Budzinski, Journal of Chromatography A, 1177 (2008) 150-158.
[207] J.-L. Zhao, G.-G. Ying, L. Wang, J.-F. Yang, X.-B. Yang, L.-H. Yang, X. Li, Science of The Total Environment, 407 (2009) 962-974.
[208] V.C. Matamoros, E. Jover, J.M. Bayona, Analytical Chemistry, 82 (2009) 699-706.
[209] C. Guitart, J.W. Readman, Analytica Chimica Acta, 658 (2010) 32-40.

[210] Á. Sebők, A. Vasanits-Zsigrai, A. Helenkár, G. Záray, I. Molnár-Perl, Journal of Chromatography A, 1216 (2009) 2288-2301.
[211] M.J. Gómez, A. Agüera, M. Mezcua, J. Hurtado, F. Mocholí, A.R. Fernández-Alba, Talanta, 73 (2007) 314-320.
[212] A.M. Comerton, R.C. Andrews, D.M. Bagley, Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences, 367 (2009) 3923-3939.
[213] X. Du, X. Wang, Y. Li, F. Ye, Q. Dong, C. Huang, Chromatographia, 71 (2010) 405-410.
[214] S. Wang, W. Huang, G. Fang, J. He, Y. Zhang, Analytica Chimica Acta, 606 (2008) 194-201.
[215] S. Castiglioni, E. Zuccato, E. Crisci, C. Chiabrando, R. Fanelli, R. Bagnati, Analytical Chemistry, 78 (2006) 8421-8429.
[216] K. Mitani, H. Kataoka, Analytica Chimica Acta, 562 (2006) 16-22.
[217] J.Y. Pailler, A. Krein, L. Pfister, L. Hoffmann, C. Guignard, Science of The Total Environment, 407 (2009) 4736-4743.
[218] M. Gros, M. Petrović, D. Barceló, Talanta, 70 (2006) 678-690.
[219] E. Gracia-Lor, J.V. Sancho, F. Hernández, Journal of Chromatography A, 1217 (2010) 622-632.
[220] F. Tamtam, F. Mercier, J. Eurin, M. Chevreuil, B. Le Bot, Analytical and Bioanalytical Chemistry, 393 (2009) 1709-1718.
[221] J.M. Conley, S.J. Symes, S.A. Kindelberger, S.M. Richards, Journal of Chromatography A, 1185 (2008) 206-215.
[222] B. Kasprzyk-Hordern, R.M. Dinsdale, A.J. Guwy, Journal of Chromatography A, 1161 (2007) 132-145.
[223] A. van Nuijs, I. Tarcomnicu, L. Bervoets, R. Blust, P. Jorens, H. Neels, A. Covaci, Analytical and Bioanalytical Chemistry, 395 (2009) 819-828.
[224] S. Grujić, T. Vasiljević, M. Laušević, Journal of Chromatography A, 1216 (2009) 4989-5000.
[225] M. Gros, M. Petrović, D. Barceló, Analytical Chemistry, 81 (2008) 898-912.
[226] M. Gros, T.-M. Pizzolato, M. Petrović, M.J.L. de Alda, D. Barceló, Journal of Chromatography A, 1189 (2008) 374-384.
[227] J. Ding, N. Ren, L. Chen, L. Ding, Analytica Chimica Acta, 634 (2009) 215-221.
[228] M. Petrovic, M. Gros, D. Barcelo, Journal of Chromatography A, 1124 (2006) 68-81.

CHAPTER 2

OBJECTIVES

OBJECTIVES

A primary objective of the research discussed in this Doctoral Thesis is to evaluate and assess the occurrence of a wide group of persistent and pseudo-persistent organic pollutants in the environment (air and water) from the region of Mallorca (Spain). Two different groups of analytes, concerning a wide subset of chemicals with little if any legal regulation, have been the focus of this Thesis: (1) volatile organic compounds (VOCs) have been evaluated in the air of several municipal solid waste treatment plants and landfills; and (2) pharmaceutically active compounds (PhACs) have been evaluated in wastewaters (treatment plants and landfill leachates) and the aquatic environment. For this purpose, novel well-developed analytical methods (based on chromatographic techniques with mass spectrometry detection) were developed and combined with diverse solid phase extraction techniques for the analytical detection of the objective organic compounds.

In parallel, the secondary objective of this Doctoral Thesis was to assess the need and/or the potential benefits owing the development of more comprehensive and restrictive (local) environmental regulations implementing the hereby assessed methods for a continuous monitoring of these relevant organic pollutants.

Analytical methods were selected with the aim of fulfilling basic requirements to enable its implementation as periodic monitoring techniques: maximum number of analytes in one single run, maximal robustness, simplicity and sensitivity, minimal consumption of reagents, waste generation, and time of analysis as well as the automation of required sample pre-treatment and applicability to real matrices and autonomous, stand-alone operation.

In order to achieve the principal objectives stated above, there were proposed some lesser specific objectives:

1. Development and optimisation of a suitable analytical method (i.e. sensible, traceable and robust over time) for the periodical (continuous) analysis of VOCs in the air, capable to analyse multiple VOCs in environmental samples without altering matrix composition.

2. Implementation and optimisation of a reliable calibration methodology using liquid standards for the analysis of VOCs in air, which reduces the inequality between (a) gaseous samples and (b) liquid standards.

3. Characterisation of the composition and concentration of multiple VOCs within the biogas emissions to the atmosphere of the principal municipal solid waste landfill in Mallorca. Estimation of landfill total emissions.

4. Development of a statistical model correlating air composition –i.e. multiple VOCs concentration – with odour measurements (carried out by dynamic olfactometry) as alternative methodology to quantify odour levels to find odour markers

5. Development of a statistical pattern recognition model enabling the classification of the air of different waste treatment facilities on the basis of their VOC composition, for a further identification of the emitting focus in the case of pollutant episodes in the nearby locations.

6. Development and optimisation of a valid analytical method (i.e. sensible, traceable and robust over time) for the analysis of multiple pharmaceuticals in different water samples (fresh water, marine water, groundwater and wastewater).

7. Evaluation of the pollution levels and the potential pollution pathways of multiple pharmaceuticals in the aquatic environment in Mallorca.

This work was incorporated into the projects of the National Plan for Science and Chemical Technology CTQ2007-64331 and CTQ2010-15541 entitled “Development of automated methods of analysis. Application to environmental monitoring plans” supported by the Spanish Ministry of Science and Technology. It contributed especially to the part of monitoring and control of organic compounds in samples of environmental interest.

The part of this work concerning determination of VOCs in the air took part into an agreement signed between University of the Balearic Islands (our Group), the Consell Insular de Mallorca (Mallorca Insular Council) and the municipal solid waste (MSW) Managing Companies in Mallorca.

CHAPTER 3

EXPERIMENTAL PART AND DISCUSSION

EXPERIMENTAL PART AND DISCUSSION

As we mentioned in the introduction, although the presence of organic contaminants in the air and water have been widely reported, information on their environmental occurrence in the Island of Mallorca is limited to three previous studies, since it does not exist a specific regulation regarding environmental monitoring of many organic pollutants. For this reason one of the objectives of this Thesis is to focus on the evaluation of some organics (VOCs and pharmaceuticals) in the environment. Thermal desorption of solid sorbents coupled to GC-MS was used to evaluate VOCs in the air, whereas solid phase extraction coupled to HPLC-ESI-MS/MS was used to evaluate pharmaceuticals in the Mallorca aquatic environment. We were encouraged to do the Thesis because of the nearly inexistent knowledge concerning the environmental pollution levels of organic compounds in Mallorca, limited to some PCBs and PAHs (see references in Sections 3.2.1.1 and 3.1.2.1).

On one hand, VOCs are ubiquitous pollutants, and the industrial processes located in Mallorca release important amounts of them to the environment. These emissions should be monitored to evaluate and prevent eventual pollutant episodes both harmful for humans and environment. Furthermore, VOCs are well known odorant compounds, and appropriate monitoring can help to identify the origin of an odorant episode in nearby inhabited areas.

On the other hand, owing the increasing use of reclaimed water for agriculture and other irrigation purposes in Mallorca (over 30% of the overall consumption), we considered the necessity to determine the concentration of pharmaceuticals in the principal wastewater treatment plants (WWTPs) effluents discharging reclaimed water to the environment. The potential pollution pathways followed by the pharmaceuticals to reach the aquatic environment were also establish in order to evaluate the fate and the potential risk of a self-contamination of natural water reservoirs due to the reuse of reclaimed wastewater.

The results reported in this Thesis provides new data which evidences the requisite of more restrictive environmental regulations in order to efficiently reduce local emissions of organic contaminants to the atmospheric and aquatic environments.

This chapter includes the experimental part and the results from different studies that have been carried out through this Doctoral Thesis. These results have been published in different scientific journals and are presented in journal paper format. Previous to each study or group of them, a brief introduction is included in which the main aim is

pointed out, as well as the novelty of the study when it was developed and some other important considerations. Even though the most important results and discussions are described in the articles, some other important discussions are briefly discussed in Chapter 4. The list of publications as a result of this Thesis is included in the Annex I of this Doctoral Thesis.

The experimental part has been divided into two sections, depending on the group of compounds measured, either VOCs or pharmaceuticals. In the biggest first Section it is developed an analytical method to determine a wide list of VOCs, and two environmental applications to characterize 42 and 93 different VOCs in the air of odorant emissions from several MSW treatment plant and MSW landfills. TD-GC-MS was the chosen technique in all the studies.

In the second Section 3.2 we developed a method based on solid-phase extraction and liquid chromatography coupled to tandem mass spectrometry by electrospray interface (HPLC-ESI-MS/MS) to determine a group of pharmaceuticals in several environmental and wastewater samples in Mallorca.

3.1 DETERMINATION OF VOLATILE ORGANIC COMPOUNDS IN THE AIR

We have mentioned along the introduction the principle characteristics of the VOCs, including the major threats for environment and human health as well as different techniques and methodologies for the determination in the atmospheric environment.

In the island of Mallorca tons of VOCs are released every year to the atmospheric environment, primarily from multitude of individually minuscule sources (especially due to the solvent use and the traffic transports). Each source contributes relatively insignificant quantities, but the combined input can yield measurable overall levels. As a counterpoint, a wide list of industrial processes located in the Island (e.g. waste management facilities, landfills, concrete manufacturing, agriculture and livestock production) emit VOCs to a lesser overall degree than traffic and solvent emissions, but can yield higher VOCs concentrations in specific areas (taking as a reference the emission inventory in the EU, page 16). Hence, VOCs emissions due to industrial processes or waste treatments in general provoke severe social awareness and annoyance, as long as emissions are punctual and can be easily allocated and reach extremely high concentration levels.

Even though analytical methodologies for the analysis of VOCs in the air have been widely described and applied worldwide (as it has been mentioned along the introductory chapter) occurrence of VOCs in the ambient of Mallorca has never been evaluated, which evidences a lack of knowledge over environmental pollution levels. In this regard, it is not possible to assess the sustainability of the existing industrial processes in order to assure a clean environment, and comprehensive analyses must be carried out.

Under this situation, it was signed a two years collaboration agreement between: (1) the *Consell Insular de Mallorca* (Mallorca's Insular Council) , (2) the Automation and Environmental Analytical Chemistry Group of the Chemistry Department of the University of the Balearic Islands (our research group) and (3) the Waste Management Companies TIRME SA and EMAYA SA. The general purposes of this collaboration were to: (i) develop a reliable analytical methodology enabling the detection and characterization of the VOCs composition of some of the potential emission focuses of VOCs located in the island due to the treatment and disposal of municipal solid wastes; (ii) find a reliable analytical methodology able to substitute the expensive and tedious odorant measurements based on the EN-13725 based upon the potential correlation of odour measurements with VOCs composition; and (iii) calculate and compare emission rates of VOCs at the different waste treatment plants.

In this section are presented the studies of a wide number of VOCs in different environmental samples, considered as important emission focus to the atmosphere.

Weighing up the possibilities, always trying to reach the main objectives stated in Chapter 2, the selection of the analytical methodology was based on different criteria:

- Capable to analyse the major number of VOCs in one single run.

- Ease and fast.
- Robust over time, suitable for monthly periodical analysis.

After an exhaustive bibliographic seek, contrasting different recommendations, a previous work was conducted testing and evaluating the best methodology for the environmental monitoring of VOCs with the instrumentation available in the laboratory group. GC was the chromatographic technique of choice with MS detection, owing the excellent selectivity and sensitivity. Different extraction methods based on the SPE and SPME techniques were evaluated combining different solid sorbents. The analytical method of choice in the studies presented in this Doctoral Thesis was finally the thermal desorption – gas chromatography – mass spectrometry (namely TD-GC-MS). Sorbent traps containing Tenax® TA and Carboxen 1000® sorbents were chosen for the preconcentration of the different compounds, and desorbed thermally by means of an automated unit. Two different sampling techniques were carried out (see sections 3.2.2 and 3.2.3) depending on the nature of the emission focus studied (emission or immission air).

The results of these studies have been published in *Chemosphere* and *International Journal of Environmental Analytical Chemistry*, while other has been submitted to the *Journal of Separation Sciences*. The complete information of the articles included in this Doctoral Thesis is detailed in Annex I.

3.1.1 IMPLEMENTATION AND OPTIMIZATION OF A HIGH-TEMPERATURE'S LOADING STRATEGY OF LIQUID STANDARDS IN THE QUANTIFICATION OF VOLATILE ORGANIC COMPOUNDS USING SOLID SORBENTS

One of the most critical concerns in any chemical analysis arises from the analytical calibration step, which determines many of the analytical features of any method (i.e. linear fit, repeatability, traceability, limits of detection, etc). It is recommended to calibrate the analytical method with standards undergoing processes the more similar as possible as the sample. However it is not always possible and frequently some restrictions are unavoidable, which limits the final analytical features.

One of the major challenges concerning the analysis of volatile compounds in air is the analytical calibration of the method. As long as samples are in the gas-phase, so the standards used for the calibration should be in the gas-phase. Final results of the analytical method will depend on analytical calibration. Unfortunately, it is well known that gas-phase standards are not always commercially available, and laboratory preparation frequently require tedious and expensive work.

In this sense, the use of liquid standards has been a common solution adopted in many technical reports and standard methods in order to save time and make the analyses easier to the analysts. As a side-effect, and as it might be foreseen, several studies have reported a systematic bias between the response factors of the standards and the gas-phase samples when liquid standards are used to calibrate a TD-GC-MS methodology with solid sorbents. Nevertheless the list of publications assessing calibration procedures is short.

In this study it has been implemented an optimized a procedure to inject liquid standards inside solid sorbent tubes for the analytical calibration of the TD-GC-MS methodology. The sorbent tubes were connected to the inlet injection port of the GC, were a temperature raised up to 300°C volatilizes the liquid standards which are transported by the carrier gas He through the solid sorbents. Compared to the non-heated standard procedure, the proposed set-up systematically increases the response factor. It also provides great robustness over time, enabling suitable determination of VOCs even though no internal standard is used in the analysed samples.

The results of this study have been submitted as full paper to the *Journal of Separation Sciences*. This calibration procedure enabled a reliable methodology which helped us to comprehensively evaluate the environmental samples which are objective of this Doctoral Thesis.

3.1.1.1 SUBMITTED ARTICLE

Implementation and optimization of high-temperature's loading strategy of liquid standards in the quantification of volatile organic compounds using solid sorbents.

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Keywords: VOC; Thermal desorption; solid sorbent; matrix effects, response factor.

Abstract

High temperature liquid standard loading strategy onto solid sorbent traps for calibration of thermal desorption-gas chromatography-mass spectrometry techniques (TD-GC-MS) for the analysis of volatile organic compounds (VOCs) is evaluated and optimized. With this proposed set-up, volatilized liquid-loaded standards interact in gas phase with solid sorbent particles. Response factor for 15 VOCs have been evaluated and compared with common strategies based on liquid matrix interactions. Using gas matrix strategy improves signal output in the range 10% to 700%. Average increase for BTEX is 480%. Reported systematic bias between liquid standards and gas samples are reduced, enhancing TD methodologies on one of its more important issues. In addition, the proposed system improves the average repeatability to a 3.2%, over 13 times some reported data. The use of an ultra-thin chromatographic capillary column of 150 µm i.d. performs better peak resolution in about 60 % the time with usual 250 µm i.d. capillary columns.

1. Introduction

Gas chromatography (GC) is the most appropriate technique to analyse volatile organic compounds (VOCs), either from biogenic or anthropogenic sources. Coupled to mass spectrometry detection (MS) compounds can be identified and quantified, being the most powerful technique for this purpose. Notwithstanding, some critical issues restrain GC-MS methodologies for quantification of VOCs in the air [1]. Typical concentrations in the ambient air are in the range from few ng m^{-3} to mg m^{-3}, so a preconcentration step prior to GC injection seems inevitable, especially in the analysis of multiple VOCs. Some new techniques have been

developed in the recent last years based on direct-injection mass spectrometry (DIMS) methodologies [2]. These methodologies have been applied to rapid monitoring and quantification of VOCs, which in combination with fast instrumentation developments open a new perspective for VOC characterization. However, these DIMS based methodologies often require a high level of speciation, so techniques based on sorption-sampling followed by thermal-desorption strategies (TD) are still prevalent and have been applied for the analysis of VOCs in environmental samples during the last decade [3, 4]. TD strategies are combined with different sample treatment methodologies, such as solid-phase microextraction (SPME) [5, 6], stir bar sorptive extraction (SBSE) [7, 8], single drop microextraction (SDME) [9, 10], liquid-phase microextraction (LPME) [11-13], headspace sorptive extraction (HSSE) [14, 15], or the most recent solid phase dynamic extraction (SPDE) [16, 17] and accelerated solid-phase dynamic extraction (ASPDE) [18, 19]. All these techniques provide good performance in terms of minimizing solvents, costs, easy-to-use, green chemistry; but present a bottleneck regarding the quantity of sorbent breakthrough volume and recovery rates. Therefore it may compromise the preconcentration step, either by increasing limits of detection or by restricting the number of VOCs adsorbed at one time. In this sense the most capable preconcentration technique is adsorption on solid sorbents followed by controlled thermal desorption [20].

A current TD limitation exists in regard to method calibration of gaseous samples. For an appropriate calibration procedure, standards must undergo exactly the same processes than samples, including matrix composition and matrix effects. Hence, the best linear fit for the quantification is expected when standards are used in gas phase. Regretfully, gaseous standards may be either expensive or not commercially available, whereas laboratory in-situ generation often requires tedious work comprising different techniques. One common alternative strategy is based on the use of liquid standards, which generally provides fast and easy treatment, compared to gas calibration standards. By this methodology, a micro drop (generally 1 to 10 µL) of liquid solution containing selected standards is loaded with a micro-syringe onto TD sorbent tubes upon the sorbent particles. Another common procedure may also be the use liquid standards in vapour phase instead of direct liquid loading of standards. The vaporisation procedure is based on carrier sweeping at lesser temperatures than compound's boiling point. As a general procedure, the sampling end of a packed sorbent tube is connected into a specific port, where an appropriate carrier gas flow is set (via a valve), sweeps the injection port and passes down through the sorbent tube to vent. The calibration solution is introduced through an injector port in the normal fashion where it vaporises and reaches the sorbent bed in the vapour phase. It is established in some technical reports from TD manufacturers [21] and also recommended in some TD-GC(MS) standard methods [22-24].

During the last years, some studies proposed and compared different calibration strategies. Martin et al. [25] concluded that gas and liquid strategies may provide same results as long as it is chosen

a suitable combination of sorbent and solvent. Therefore selection of appropriate sorbent combination is essential. A recent review [26] reported a comprehensive comparison of the most common sorbents and their chemical and physical properties, that may help analysts to select the appropriate sorbent. Demeestere et al [27] compared liquid and gaseous calibration strategies, using Tenax TA® for a set of 69 different VOCs. They reported systematic bias in the range 40-80 % for VOCs in gas matrix for the quantification with liquid phase standards, since the response factor of compounds highly depends on the sample matrix. In the same study authors recommended the use of a suitable internal standard calibration to reduce uncertainty. Kim et al. [28] obtained similar results with Tenax TA® when analysing benzene, toluene and p-xylene.

Even though vaporisation of liquid standards for the calibration procedure has been reported as a good alternative to gas standard calibration it may present some limitations. Owing the use of solvent -not present in matrices of gas samples-, it should be eliminated from the sorbent bed prior to TD, in order to simulate gaseous matrix. This step requires substantial flows of carrier in the order of 100-500 ml min^{-1} [25]. It is remarkable the lack of available studies concerning suitable sorbent-solvent combinations, currently limited to individual sorbents Tenax TA® and Carbopack X® and methanol and cyclohexane solvents, measured for a small set of VOCs [25, 26]. So then, VOCs calibration suitability using liquid standards seems to be not yet well established.

A high-temperature vaporisation strategy is proposed and evaluated in this study for the loading step of liquid standards upon solid sorbent particles (Figure 1), based on the same principles than normal GC injection. One micro drop of liquid standard solution is loaded inside the GC inlet, and so with high-temperature (300°C) standards are automatically vaporized to gas phase. An in-house designed stainless steel connector enables the joint of TD sorbent tubes directly at GC injector replacing the capillary column. Working in splitless mode, gas phase standards are carried towards TD tubes, by the inert gas, allowing the interaction standard-sorbent.

The scope of the study is to prove that our high-temperature injection method results in higher standard response factors (RF) than liquid standard strategies, defined according to IUPAC as detector sensitivity, being the signal output per unit of mass of a substance [27, 29, 30]. A second objective is to provide some evidences that with the proposed set-up it is not necessary the use of an internal standard calibration to obtain reliable quantifications. Only an appropriate instrumental control standard (ICS) is needed to compensate for MS detector variations with time.

2. Materials and methods

2.1 Chemicals

For high-temperature vaporisation strategy, 15 individual GC-MS grade standards (>99%) were provided by Sigma Aldrich and Fluka (Sigma Aldrich Quimica SA, Madrid, Spain):

tetrachloromethane, benzene, 1,2-dichlorobenzene, 1,2-dichloroethane, 2-chlorophenol, butylaldehyde, cyclohexanone, hexylaldehide, 2-butenal, styrene, ethylbenzene, toluene, o-xylene, p-xylene and p-cymene. Deuteratedp-xylene-d10 was provided by Sigma Aldrich and used as internal standard (IS). Methanol (GC residues analysis grade) was provided by Scharlau (Barcelona, Spain). Solid sorbents Tenax™ TA and Carboxen™ 1000 (both mesh 60-80) were provided by Supelco (Madrid, Spain).

In addition to the most common benzene, toluene, styrene and xylenes (so called BTEX), VOCs were selected trying to cover a wide range of volatilities, chemical groups and polarities, to assess the reliability of the procedure.

One stock solution (named A) was prepared as a mixture of the 15 individual VOCs at 1000 mg L^{-1} in methanol. Another single IS stock solution (named B) of p-xylene-d10 was prepared at 1000 mg•L-1 in methanol. For the optimisation experiments, two final working standard solutions (C1 and C2) were prepared at 20 mg $L^{-1}$and 75 mg L^{-1}, respectively, by direct dilution of stock solution A in methanol. A fixed volume of stock solution B was added to both C1 and C2, in order to obtain 50 mg L^{-1} of IS p-xylene-d10. Calibration curves of the 15 selected VOCs were checked by both loading strategies. Five solutions with different concentrations were prepared following the same procedure than solutions C1 and C2. Concentration levels were 100, 75, 50, 25 and 10 mg L^{-1}, all containing 50 mg L^{-1} of IS p-xylene-d10. All the solutions were stored at -18°C in the dark.

Tenax TA™ and Carboxen 1000™ were adopted as sorbents since it provides a good combination in sorbent strengths together with high hydrophobic properties [26] for volatile and semi volatile compounds analysis. It is an excellent combination for environmental sampling, assessed by some recent studies [31-34]. Methanol was adopted as solvent, as the recommended for Tenax TA™ [25], whereas there is no reported data for Carboxen 1000™.

TD stainless steel sorbet tubes (Perkin-Elmer, Norwalk, USA; o.d.: 6.9 mm; i.d.: 4.9 mm; length: 88.9 mm) were prepared in the laboratory according to the US-EPA TO-17 compendium of methods for determination of toxic organic compounds [22]. Tubes contained 150 mg Tenax™ TA and 100 mg Carboxen™ 1000, separated by 0.5 cm layer of silanized glass wool. Tenax™ was packed first in direction with respect to He flow when trapping (adsorption). Thermal desorption was made in the opposite direction. Sorbent tubes were conditioned at 280 °C for 180 min with He stream at 80 ml min^{-1} prior to its first use. Tubes were checked periodically to assure a flow rate within ± 5% using Mini-buck calibrator M5 (AP BUCK Inc., FL, USA)

2.2 Liquid standard loading strategies.

In order to distinguish both loading strategies, response factors with the proposed high temperature procedure is called gas strategy (gas matrix response factor, GRF), while for liquid strategy is called liquid matrix response factor (LRF)

2.2.1 Gas matrix response factor strategy (GRF).

To establish the interaction of the liquid standards in vapour phase upon sorbent particles by means of high temperature volatilisation, multimode GC injector (GC, Varian 3900, VARIAN INC., Palo Alto, USA) was equipped with a homemade steel connector (Figure 1a) as the joining point between GC inlet and sorbent tubes. Inasmuch as TD unit does the injection of the standards into capillary column, GC inlet remains free. One µL of final working standard solution (either C1 or C2) was loaded into the GC inlet by an automated sampler module (CP-8400, VARIAN INC., Palo Alto, USA) equipped with 10 µL Hamilton 700N series Microliter Syringe (Alltech). GC inlet heated at 300 ºC assured that solvent and standards were vaporized to gas phase. Immediately next, vaporized standards were thereby carried by inert gas (He) along sorbent particles, while GC split valve remained closed. Sorbent tubes were kept at room temperature during the adsorption process. He stream was set at 25 mL min^{-1} since maximum pressure achieved by the inlet was 0.5 psi, assuming that packed TD tubes involve low restrictions to carrier flow. After seven minutes tubes were removed from the homemade connector, hermetically closed with long term storage PTFE taps and placed in the thermal desorption unit (ran at the next section 2.3 specified conditions to calibrate the analytical method). TD tubes were stored inside a vessel hermetically closed, containing silica gel and charcoal to save sorbent particles from external interferences.

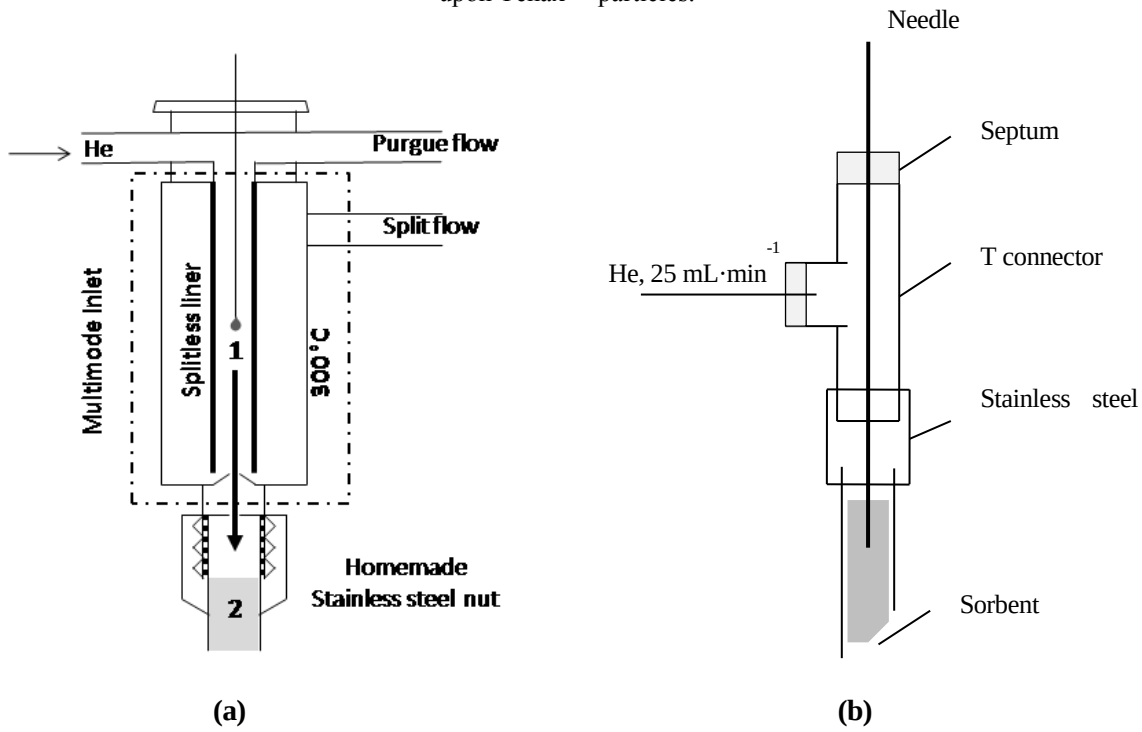
2.2.2 Liquid matrix response factor strategy (LRF).

One µL of working solution (Figure 1b) was loaded beneath glass wool directly upon sorbent surface (Tenax™) utilizing 10 µL Hamilton 800N series Microliter Syringe (Alltech™). He stream at 25 mL min^{-1} was kept for 7 minutes (in order to adopt identical conditions on both strategies, as described in section 3.1). A special T-shaped connector (Swagelok™) drove He flow through sorbent particles, with the main goal to remove the solvent [25, 33]. He flow outgoing from TD tubes was calibrated by an R-003 model rotameter (Comaquinsa, Spain).

2.2.3 Quality assurance

A second extra TD sorbent tube was connected randomly to the first sampling tube in order to check potential losses of standards in both loading strategies. Afterwards secondary tubes were ran at the same specified conditions. No positive identifications were detected either for the liquid or gas strategies.

Figure 1. (a) In-home injection set-up diagram. At first step (1), one µl of standard liquid solution is dropped (loaded) into the inlet liner at 300°C.Standards are volatilized as normal GC injection. Immediately next (2) He stream carries gas phase standards through the sorbent bed (splitless mode). (b) Diagram of manual non-heated liquid standard loading strategy. Liquid standard drop is directly loaded inside TD tubes upon Tenax™ particles.



2.3 Chromatographic analysis.

Sorbent tubes were thermally desorbed by an automated thermal desorption unit (Turbomatrix 350, PERKIN ELMER, Norwalk, USA) coupled to a gas chromatograph (GC, Varian 3900, VARIAN INC., Palo Alto, USA) with ion trap mass spectrometer detector (MSD, Saturn 2100, VARIAN INC., Palo Alto, USA) and. Instrumentation was controlled with Varian Workstation 6.9 software.

Thermal desorption of sorbent tubes was carried out in a two-step mode. In the first step, VOCs were desorbed from sorbent tubes for 5 min at 225ºC and a flow rate of 80 mL min^{-1} of He, carried through a 100 mg Tenax™ TA cryogenic internal trap, cooled at -30 ºC. Thereafter, in the second step, the trap was desorbed at 280ºC for 1 min with fast heating (900 ºC min^{-1}). After the analysis, cryogenic trap was baked at 280ºC for 30 min, to assure complete desorption of the compounds for the next run. The capillary transfer line to the GC (silica with no stationary phase, 0.32 mm i.d.) was kept at 250ºC. Prior to each use, tubes were conditioned at 280 °C for 60 min with 80 ml•min-1 He stream to avoid interferences

No organic solvent is required in sample treatment; therefore no solvent delay is needed in the detection step, allowing monitoring from the first moment. To perform a better peak resolution

one ultra-thin chromatographic capillary column (150 µm i.d.) was used. Compared to usual 250 µm i.d., chromatographic time is reduced about 40% [32].

Selected column was Varian Factor Four VF-624 (40 m x 0.15 mm x 0.84 µm), with 1 mL min^{-1} flow rate of He (carrier gas) and 1:1 split injection. Temperature program for VOC analysis was: initial temperature 35 ºC hold 3 min; 35-100 at 12 ºC min^{-1}, hold 8 min; 100-120 at 45 ºC min^{-1}, hold 7 min; 120-140 at 23 ºC min^{-1}, hold 5 min; 140-180 at 10 ºC min^{-1}, hold 0 min. Electronic ionization (EI) at 70 EV was the ionization mode. MSD was run in full scan mode within a 25-250 m/z range. Ion trap and GC/MSD interface temperatures were 200 and 240 ºC, respectively. Compounds were identified on the basis of their retention times (±0.2 min), target and qualifier ions. Three different m/z ions were selected to integrate each compound.

3. Results and discussion

3.1 Optimisation of high-temperature liquid standard loading strategy onto solid sorbent particles.

To perform suitable adsorption-desorption process with the aim to have the best gas chromatographic behaviour, some factors should be considered. First, it is necessary to assure total adsorption of loaded liquid standards onto sorbet particles. Second, the loaded volume once vaporized should not exceed inlet volume. Finally, it should be removed the solvent (methanol) but keeping constant VOCs retention onto adsorbent surface, by means of carrier flow (He)..

Based on these premises, two parameters were optimised, to find maximum VOCs recovery in combination with highest accuracy: loaded volume and time. Both working solutions (C1 and C2) were evaluated. Data was acquired by absolute peak area of each standard. Unless stated, experimental conditions were the same described in section 2.

3.1.1 Effect of loaded volume

Injected volumes over the range 1 to 5 µL were studied of both working solutions C1 (20 mg L^{-1}) and C2 (75 mg L^{-1}). As it would have been expected, integrated area data showed an increasing effect with volume. However poor average RSDs (15 compounds, n=10) within 20% - 42% were observed for volumes from 2 µL onward. Many factors might cause large uncertainty in analysis, such as incomplete retention onto sorbent owing to oversized inlet volume, or incomplete thermal desorption step due to improper TD conditions. Split discrimination during desorption due to temporarily increase the split flow relative to the desorb and or column flow [25] can be considered the principal cause of uncertainty

On the other hand, excellent average RSDs were obtained when loading 1 µL of standard: 3.2% for 20 mg L^{-1} and 2.4% for 75 mg L^{-1} (n=10). These experimental conditions provide reliable

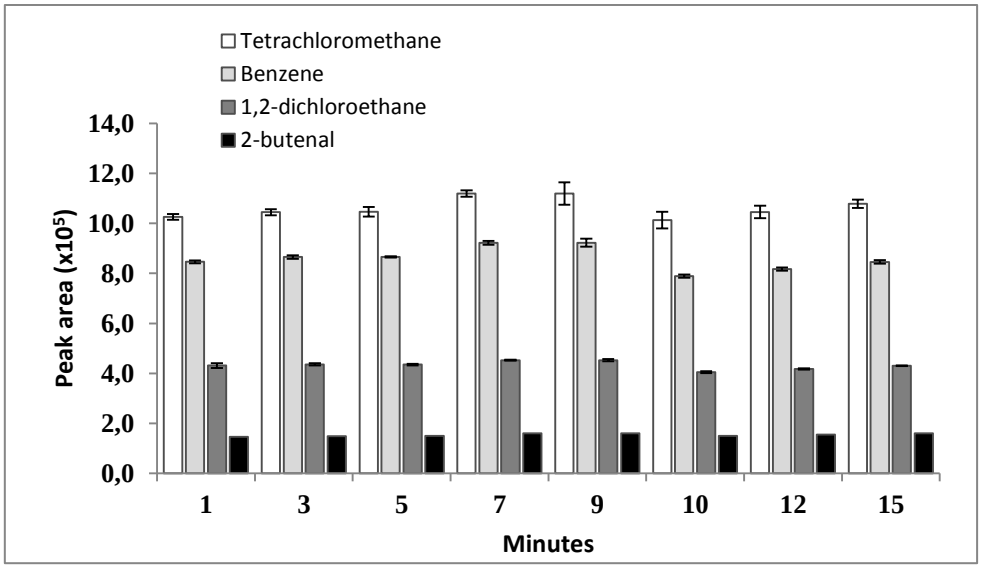
adsorption-desorption process, presenting some evidences about the complete retention of the loaded standards. Therefore 1 µL was the volume adopted for further experiments.

3.1.2 Effect of time

As it was stated, it is important that standard-sorbent interactions do not experience significant interferences or losses while connected to He stream during the solvent elimination step. Since He stream cannot be set at greater flow than 25 mL min^{-1}, time is the only factor that can be modified. Adsorption times from 1 to 15 minutes were examined. One µL of working solutions (C1 or C2) was loaded. Absolute peak area resulted constant at both concentrations. All 15 VOCs showed scarce variation below 3% (n=5) on peak area for the whole interval 1 to 15 min. As an exception, benzene and tetrachloromethane in solution C2 (75 mg L^{-1}) described somehow a maximum behaviour at seven minutes (Figure 2). Despite it is probably attributed to random variation, an adsorption time of 7 minutes was adopted for analysis.

These good results prove that liquid standards vaporized to gas-phase are properly retained onto sorbent particles, and so adsorption-desorption process is robust and provides reliable data. It also demonstrates that solvent (methanol) is completely removed prior to GC analysis; therefore elimination of solvent delay time in MS detector does not represent a risk. It is remarkable that the strategy was optimized for a specific flow of 25 mL min^{-1}. Different GCs may have different limits on flow rates which might affect to adsorption. A guideline and higher working range for the flow setting could not be evaluated.

Figure 2. Evolution of absolute peak area obtained for four significant compounds (75 mg·L^{-1}) with time, using the high-temperature gas matrix strategy.



3.2 Effect of standard matrix

The second part of the study had the goal to compare sensitivity of method regarding to standard matrix. Gas matrix response factor (GRF) were obtained with the proposed new strategy, ran at optimal conditions stated in section 3.1. Liquid matrix response factors (LRF) were obtained with the non-heated manual strategy described at section 2.2.2. One µL of working solution C1 (20 mg L^{-1}) was loaded and analysed following both strategies. Response factors for 15 selected VOCs are presented in Table 1, together with average RSD (n=10). For a more comprehensive discussion, RFs were determined on the basis of two different procedures: first, external standard procedure (ES), meaning response factor (GRF and LRF) as compound integrated area per ng loaded; second by and internal standard procedure (IS), presenting relative response factor (RGRF and RLRF) as the ration of compound integrated area to p-xylene-d10 area per ng loaded.

With our proposed strategy of high temperature vaporisation (Table 1), average GRFs systematically increase in the range from 1.1-7.2 times response factors obtained with liquid matrix adsorption (LRF), meaning that the sensitivity of the method is highly improved when compounds are retained in gas matrix. As example, compounds commonly named BTEX, raised signal output over 330%, up to 720% in the case of styrene. In addition, extremely high accuracy is obtained (2.4%), similar to average RSD obtained using IS (2.1%). On the opposite hand, liquid matrix strategy shows low accuracy, providing individual RSDs above 30%. Following that procedure, standard's drop is loaded directly upon a relative small piece of sorbent. That important feature may cause errors, including breakthrough of the sorbent or poor thermal desorption step. In that sense, the use of internal standard improves precision over 6 times, achieving some good 5.2% average RSD. Summarizing results, our developed gas matrix strategy provides overall improvement over 13 times the liquid matrix accuracy.

Quantitative analyses have been evaluated on the basis of the range of volatilities, calculated as vapour pressure in Pa at 303 K ([35]). Figure 3 shows response factor ratio between GRF and LRF ($RFR_{G/L}$) and vapour pressures for all 15 studied VOCs. No general behaviour correlating volatility with response factor has been found, thus proving that the increase is not depending on volatility of VOCs

.

Table 1. Studied VOCs and vapour pressure (Pa) calculated at 303K. Average sample response factors (GRF, LRF, peak area per ng compound loaded onto sorbent tubes) and relative standard deviation (RSD (%), n=10) for15 liquid VOCs. Relative response factors ratio (RGRF, RLRF, dimensionless) with IS peak area; Response factor Ratio (RFR, dimensionless) for GRF/LRF.

Compound	Vapour Pressure (Pa) [a]	Liquid matrix strategy				Gas matrix strategy				RFR
		ES		IS		ES		IS		
		LRF	RSD (%)	RLRF	RSD (%)	GRF	RSD (%)	RGRF	RSD (%)	G/L
1,2-dichlorobenzene	265	1547	32.2	0.85	3.7	5805	0.6	0.98	1.8	3.8
1,2-dichloroethane	12632	1469	33.2	0.79	3.0	5645	1.9	0.65	1.5	3.8
2-chlorophenol	415	1100	35.9	0.59	6.5	6306	6.2	1.37	3.8	5.7
Benzene	12030	2130	33.4	1.07	8.7	9542	1.7	1.09	2.0	4.5
Butylaldehyde	16148	553	32.9	0.3	3.3	1457	1.8	0.32	2.7	2.6
Cyclohexanone	806	919	31.4	0.51	3.2	2691	1.9	0.59	1.1	2.9
2-Butenal		222	43.0	0.13	13.2	691	2.6	0.15	3.2	3.1
Styrene	1251	2020	35.2	1.1	2.9	14631	0.4	1.67	1.7	7.2
Ethylbenzene	1689	3672	34.1	2.04	2.0	19569	1.0	2.24	1.4	5.3
Hexylaldehyde	713	603	33.5	0.34	2.8	652	6.8	0.14	2.0	1.1
o-Xylene	1161	3533	32.9	1.96	3.1	11546	0.2	1.95	0.9	3.3
p-Cymene	285	4316	32.5	2.39	2.8	25010	2.6	2.86	1.6	5.8
p-Xylene	1517	3540	34.3	1.98	2.9	11598	0.6	1.96	1.3	3.3
Tetrachloromethane	16353	732	29.3	0.36	15.6	1140	6.1	0.19	3.6	1.6
Toluene	4543	2948	34.2	1.64	4.3	16757	2.1	1.92	2.1	5.7
Average RSD			33.9		5.2		2.4		2.1	4.0[b]

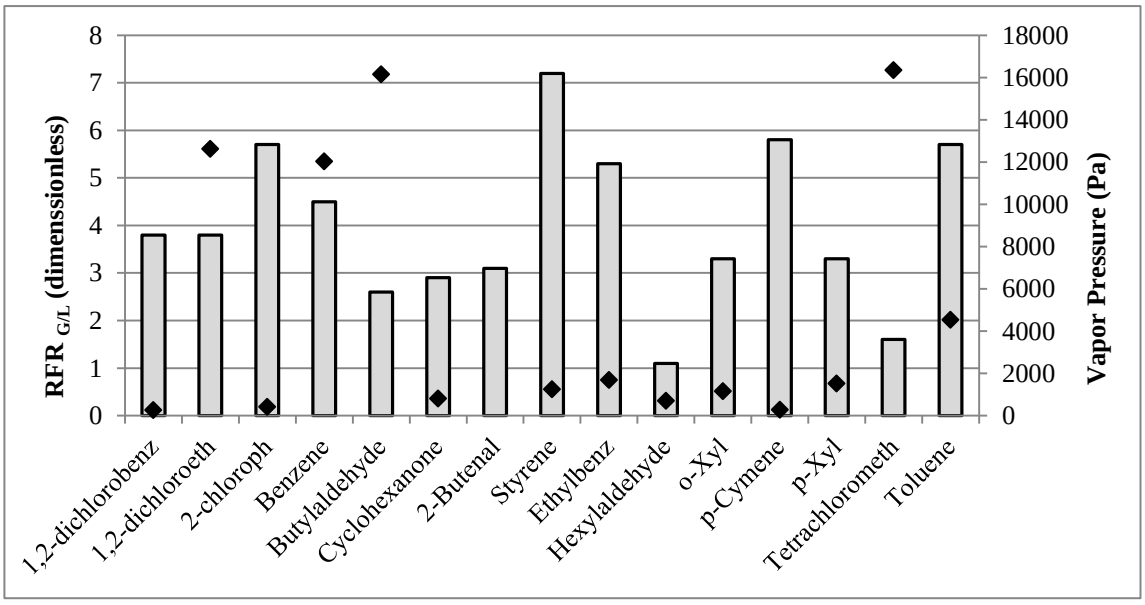
[a] Data from [35] at 303K

[b] Average RFRG/L for the 15 studied compounds.

Table 2. Slopes and determination coefficients of 15 VOCs (four calibration levels including 10, 25, 50, 75 and 100 µg·L^{-1}, n=4), by internal standard calibration (IS) and external standard calibration (ES). Limit of detection (LOD) in pg, considered as the absolute standard amount spiked into sorbent tubes in 1 µL standard mixture (dissolved in methanol).

Compound	Non-Heated liquid matrix			High-temperature gas matrix					
	IS			ES			IS		
	slope	r^2	LOD	slope	r^2	LOD	slope	r^2	LOD
1,2-dichlorobenzene	0.012	0.995	7.6	8696	0.995	22.4	0.016	0.987	5.7
1,2-dichloroethane	0.011	0.997	1.1	8067	0.980	3.2	0.011	0.995	1.1
2-chlorophenol	0.010	0.996	3.0	864	0.980	75.2	0.020	0.991	1.5
Benzene	0.016	0.991	7.6	151147	0.979	1.7	0.020	0.993	6.1
Butylaldehyde	0.004	0.986	114.1	1640	0.981	594.5	0.005	0.980	91.3
Cyclohexanone	0.006	0.997	20.3	5829	0.980	44.6	0.010	0.993	12.2
2-Butenal	0.002	0.985	121.7	864	0.970	601.9	0.002	0.970	121.7
Styrene	0.020	0.996	4.6	20629	0.971	9.5	0.028	0.990	3.3
Ethylbenzene	0.030	0.996	10.1	29555	0.976	22.0	0.040	0.993	7.6
Hexylaldehyde	0.004	0.979	60.8	2201	0.989	236.3	0.009	0.990	27.0
o-Xylene	0.026	0.997	7.0	15915	0.997	24.5	0.029	0.992	6.3
p-Cymene	0.038	0.997	2.0	36323	0.980	4.5	0.049	0.995	1.6
p-Xylene	0.028	0.987	6.0	16065	0.997	22.3	0.030	0.992	5.6
Tetrachloromethane	0.006	0.990	10.1	1255	0.989	103.6	0.020	0.994	3.0
Toluene	0.025	0.988	1.8	25263	0.977	3.9	0.034	0.993	1.3

Figure 3. Response factor ratio gas to liquid ($RFR_{G/L}$, dimensionless) detailed in bars and vapour pressures detailed in dots, for all 15 selected VOCs.



Our proposed loading strategy enhances adsorption-desorption process of liquid standards so reinforcing the idea of introducing standards in vapour phase. This discussion goes on the same direction than recent studies reported on the field. Demeestere et al. [27] concluded systematic bias from 40-70% for 69 liquid matrix standards compared with gas matrices. Also Kim et al. concluded similar results [28]. In our study we describe a strategy that systematically improves response factors for liquid standards (over 10-700%) based on high temperature standard's vaporization strategy. Thus systematic bias may be reduced, enabling more reliable models for the quantification of VOCs in gas samples. At this point some stimulating arguments may turn up, since wide number of studies in the last years have analysed VOCs in gas samples following liquid matrix loading strategies. Our proposed set-up offers new possibilities and helps to better understand VOCs behaviours inside gas samples, also by providing more reliable models on VOCs quantification.

Demeestere et al. also described average RSD up to 40% (n=5) for 69 compounds, improving a factor of 5 when using IS calibration, similar to our data. Therefore they strongly recommend the use of internal standard. With our proposed new set-up, however, response factor is decidedly increased in combination with an outstanding accuracy improvement. That new feature provides one extra advantage, since it enhances TD-GC-MS quantification by means of external standard calibration (instead of the internal standard calibration).

3.3 Evaluation of the performance of the developed strategies

To compare strategies, calibration curves were obtained by plotting the ratios of the GC integrated areas of each standard to IS vs. the concentrations of the standards (mg L^{-1}). Owing to high

repeatability of the new loading procedure, extra calibration curve was also estimated following external calibration procedure (ES) by plotting integrated areas of each standard vs. concentrations. Five solutions containing the 15 VOCs and IS with relative concentration levels of 100, 75, 50, 25 and 10 mg L^{-1} (n=4) were examined (Table 2). Obviously, slopes are sensitively higher when no IS is used. However, it is appreciated a slight lessening on the linear fit (r^2) of nine among the 15 VOCs when the calibration model is done by external standard procedure. We assume that a variation on MS output signal - not corrected by IS- adds extra error on the linear model. This issue can be corrected with the use of appropriate instrument control (ICS) standards, in order to check MS signal prior to analysis.

Detection limits of the method (LOD, pg) for all compounds (Table 2), were estimated on the basis of the mean background signal plus three times the standard deviation (LOD = mean blank + 3SD) (Table 2). The blanks consisted of 10 packed and preconditioned test tubes (280 °C, 60 min). For IS calibration LOD blank tubes were spiked with 1µL of p-xylene-d10. Values for all the compounds were within the range 1.1 – 601.9 pg as the absolute standard amount spiked into sorbent tubes in 1 µL standard mixture (dissolved in methanol). Looking into LOD data, gas matrix strategy achieves the lowest limits for all 15 VOCs. It is really interesting the fact that liquid matrix strategy using IS calibration achieves lower detection limits than gas matrix strategy using ES calibration.

Thus, based on our study where different strategies are compared, it is recommended the use of internal standard calibration procedure owing to better linear fit together with lower detection limits. However, external calibration using an appropriate ICS, which compensates random MS detector deviations, has shown reliable results, and so its potential cannot be underestimated.

4. Conclusions

This paper presents a novel strategy for the calibration procedure of TD-GC-MS methods. It is a high-temperature procedure that enables a gas matrix interaction between liquid standards and solid sorbents. With the same principle than normal GC injection, liquid standards are easily vaporized to gas phase and retained by the solid sorbents Tenax™ TA and Carboxen™ 1000. This strategy enhances the adsorption-desorption step, providing reliable data owing to a robust methodology. Two main conclusions can be drawn.

Firstly, the sensitivity of the analytical method is decidedly improved when liquid standards are vaporized to gas phase. That is exemplified from gas matrix response factors of a set of 15 selected VOCs, rising up from 1.1 to 7 times the liquid matrix response factor. Consequently, systematic underestimations derived from different matrix effects in the standard-sorbent interaction are reduced. The sensitivity increase, evaluated based on the range of volatility of

selected VOCs, does not show a general trend. No solvent (methanol) interferences have been detected in the proposed methodology.

Secondly, it is not essential to quantify by means of internal standard calibration. Repeatability of the method when liquid standards are vaporized to gas phase (2.4%-3.2%) is drastically reduced over 13 times the repeatability of standards adsorbed in liquid phase. Even so, it has been proved that the use of proper internal standard enables better detection limits of the method in addition with better linear fit for the 15 selected VOCs. This study provides a plethora of new arguments for quantification of VOC in gas samples, particularly when a vast number of VOCs wants to be analysed or no internal standards are available.

This new strategy provides excellent improvements with no extra costs, and by means of an easy and automated procedure. Therefore some inaccuracy added to the results, owing to analyst's manual sample treatment procedures, are also reduced.

Acknowledgements

Authors want to acknowledge the economic support of the Spanish Ministry of Science and Innovation by the grant BES-2008-003354, and for financial support by the Projects CTQ 2007-64331 and CTQ 2010-15541.

The financial support of the *Consell Insular de Mallorca* is also acknowledged.

[1] Dewulf, J., Van Langenhove, H., Trac-Trends Anal. Chem. 2011, 30, 935-936.

[2] Biasioli, F., Yeretzian, C., Märk, T. D., Dewulf, J., Van Langenhove, H., TrAC Trends in Analytical Chemistry 2011, 30, 1003-1017.

[3] Demeestere, K., Dewulf, J., De Witte, B., Van Langenhove, H., Journal of Chromatography A 2007, 1153, 130-144.

[4] Baltussen, E. B., Cramers, C. C., Sandra, P. S., Analytical and Bioanalytical Chemistry 2002, 373, 3-22.

[5] Nicolle, J., Desauziers, V., Mocho, P., Journal of Chromatography A 2008, 1208, 10-15.

[6] Davoli, E., Gangai, M. L., Morselli, L., Tonelli, D., Chemosphere 2003, 51, 357-368.

[7] Baltussen, E., Sandra, P., David, F., Cramers, C., Journal of Microcolumn Separations 1999, 11, 737-747.

[8] León, V. M., Álvarez, B., Cobollo, M. A., Muñoz, S., Valor, I., Journal of Chromatography A 2003, 999, 91-101.

[9] Chisvert, A., Román, I. P., Vidal, L., Canals, A., Journal of Chromatography A 2009, 1216, 1290-1295.

[10] Xiao, Q., Yu, C., Xing, J., Hu, B., Journal of Chromatography A 2006, 1125, 133-137.

[11] Liu, J.-f., Jiang, G.-b., Chi, Y.-g., Cai, Y.-q., et al., Analytical Chemistry 2003, 75, 5870-5876.

[12] Chen, S., Peng, H., Wu, D., Guan, Y., Journal of Chromatography A 2010, 1217, 5883-5889.

[13] Sun, S.-H., Xie, J.-P., Xie, F.-W., Zong, Y.-L., Journal of Chromatography A 2008, 1179, 89-95.

[14] Fries, E., Püttmann, W., Analytical and Bioanalytical Chemistry 2006, 386, 1497-1503.

[15] Callejón, R. M., González, A. G., Troncoso, A. M., Morales, M. L., Journal of Chromatography A 2008, 1204, 93-103.

[16] Lipinski, J., Fresenius' Journal of Analytical Chemistry 2001, 369, 57-62.

[17] Bicchi, C., Cordero, C., Liberto, E., Rubiolo, P., Sgorbini, B., Journal of Chromatography A 2004, 1024, 217-226.

[18] Van Durme, J., Demeestere, K., Dewulf, J., Ronsse, F., et al., Journal of Chromatography A 2007, 1175, 145-153.

[19] Pokorska, O., Dewulf, J., Van Langenhove, H., International Journal of Environmental Analytical Chemistry 2011, 91, 1206-1217.

[20] Ras, M. R., Borrull, F., Marcé, R. M., TrAC Trends in Analytical Chemistry 2009, 28, 347-361.

[21] Markes International, 2000.

[22] US-EPA, in: US-EPA (Ed.), Compendium Method TO-17, Washington, DC 1999.

[23] European Environmental Agency, 2006.

[24] International Standardisation Organisation, 2003.

[25] Martin, N. A., Barber, N. L. A. S., Black, J. K., Lipscombe, R. P., Taig, C. A., Atmospheric Environment 2007, 41, 7666-7671.

[26] Woolfenden, E., Journal of Chromatography A 2010, 1217, 2685-2694.

[27] Demeestere, K., Dewulf, J., De Roo, K., De Wispelaere, P., Van Langenhove, H., Journal of Chromatography A 2008, 1186, 348-357.

[28] Kim, K.-H., Anthwal, A., Sohn, J., Heo, G.-S., Microchimica Acta 2010, 170, 83-90.

[29] Ettre, L., Chromatographia 1994, 38, 521-526.

[30] International Union of Pure and Applied Chemistry (IUPAC), 1997.

[31] Zou, S. C., Lee, S. C., Chan, C. Y., Ho, K. F., et al., Chemosphere 2003, 51, 1015-1022.

[32] Rodríguez-Navas, C., Björklund, E., Forteza, R., Cerdà, V., International Journal of Environmental Analytical Chemistry 2012, 1-16.

[33] Dincer, F., Odabasi, M., Muezzinoglu, A., Journal of Chromatography A 2006, 1122, 222-229.

[34] Rodriguez-Navas, C., Forteza, R., Cerdà, V., Chemosphere 2012, (accepted for publication).

[35] Weast, R. C., Handbook of data on organic compounds, 1985.

3.1.2 VOLATILE ORGANIC COMPOUNDS IN LANDFILL ODORANT EMISSIONS ON THE ISLAND OF MALLORCA

Landfilling of wastes is still one of the worldwide most frequent disposal manners of solid wastes. By this practice, thousands of tons are dumped every year in localized areas, entailing an extremely hazardous risk both for human and environment. Residues may leach and reach underground water, thus contaminating the aquatic environment, but also volatile compounds are being constantly released to the ambient air, especially by the degradation of microorganisms. As it was mentioned in the introduction, transportation and migration of (organic) pollutants through interconnected environments aggravates the risks.

Municipal solid wastes in Mallorca were partially dumped to open landfills until 2010, being Son Reus the biggest one in the island. In 2008 over 200.000 tons were dumped in the Son Reus landfill, summing an overall amount of 2.600.000 tons from 1993 to 2008. As long as the surface was not covered with any kind of soil, great amounts of gases (*landfill gas* or *biogas*) were systematically emitted to the atmospheric environment of Mallorca. In this regard, only 1% of the emitted gases are VOCs, being CO_2 and CH_4 the predominant components of the biogas, mainly product of microorganisms' anaerobic degradation of wastes.

Owing the evident risks posing the landfill upon the atmospheric environment, emission rates were estimated for 42 different VOCs, including alkanes, aldehydes and ketones, aromatic compounds, alcohols, chlorinated hydrocarbons, chlorinated aromatic compounds, terpenes and reduced sulphured compounds (RSC). On the other hand, a correlation between VOCs composition and odour units (using dynamic olfactometry standard method EN -13725 by an external ISO certified laboratory) was calculated with the purpose to find a correlation model enabling identification of odour markers to simplify the expensive and tedious odour measurements procedures.

Collection of biogas inside Nalophan® bags (whole-air collection) was carried out following thoroughly EN-13725 standard method, using the "lung procedure" to fill up the bags. In order to exclusively collect the diffused emission of biogas but not the ambient air, a special hood was designed in-house. This sampling procedure enabled the estimation of emission rates both for VOCs concentration and odour units. Collected biogas was transferred by active sampling to sorbent tubes containing Tenax® TA and Carboxen® 1000 and desorbed thermally with an automated unit. The chromatographic technique applied was GC-MS with ion trap as analyser.

This study was the first application of a TD-GC-MS methodology in our group for the analysis of environmental samples. This were the first results of environmental occurrence

and emission of a wide set of VOCs in the Island of Mallorca. The work was conducted within the collaboration framework signed by the University of the Balearic Islands, *Consell Insular de Mallorca* and the MSW Managing Companies.

The results of this study were published in the *International Journal of Environmental Analytical Chemistry*.

3.1.2.1 ORIGINAL ARTICLE

C. Rodríguez- Navas, E. Björklund, R. Forteza, V. Cerdà, *Volatile organic compounds in landfill odorant emissions on the island of Mallorca*, International Journal of Environmental Analytical Chemistry, 92, 1-16 (2012)

3.1.3 USE OF THERMAL DESORPTION-GAS CHROMATOGRAPHY-MASS SPECTROMETRY (TD-GC-MS) ON IDENTIFICATION OF ODORANT EMISSION FOCUS BY VOLATILE ORGANIC COMPOUNDS CHARACTERISATION

During the last decade, the disposal manners of municipal solid wastes (MSWs) in Mallorca, adopting EU regulations, have been progressively changed from former landfilling to a combination of incineration, composting processes and bio-methane generation. Therefore a new set of facilities have been built over the last years in the same industrial area, being completely operative since 2010.

Under this new MSW processing frame, residues are classified according to its nature (organic and inorganic wastes) in order to undergo different disposal processes. In consequence the emission trends of VOCs has been changed, so different mixtures of VOCs are expected to be emitted to the ambient air depending on the nature of the incoming residues to each facility.

As it has been mentioned, VOCs are one of the principal group of chemicals regarding odour impacts, owing their low odour threshold limits. Hence odorant episodes causing annoyance to inhabited areas surrounding waste landfills or industrial areas are frequent. Regretfully it is also frequent that local councils never claim responsibilities to the industries causing the pollution, because it is difficult to identify the odorant emission focuses.

This study presents a suitable TD-GC-MS methodology followed by chemometric pattern recognition techniques which enable the classification of several different odorant emission focuses based on the characterisation of VOCs in the air. The five evaluated MSW treatment plants were: incineration plant, organic fraction classification plant, solar drying plant for wastewater sludge, and two separated premises of a composting plant for organic residues.

Immision (ambient) air was periodically collected during seven weeks by active sampling into sorbent tubes containing Tenax® TA and Carboxen® 1000. The chromatographic technique was again GC-MS (ion trap analyser) with thermal desorption through an automated unit Turbomatrix 350. Three atmospheric parameters -temperature, relative humidity and atmospheric pressure- were recorded in-situ every sampling day.

The analytical methodology was able to identify and quantify 93 different VOCs, including aromatic compounds, hydrocarbons, terpenes, phenols, aldehydes, ketones, halogenated compounds (aromatics and hydrocarbons), ethers, furanes, esthers and reduced sulphured compounds (RSCs). Three atmospheric parameters, temperature, relative humidity and atmospheric pressure, were recorded in-situ to evaluate potential relation of emitted VOcs with atmospheric conditions. Principal components analysis (PCA) was carried out with the

aim to reduce the 96 different variables (93 VOCs concentrations and the atmospheric parameters) into a lower list of principal components, PCs, independent (orthogonal) and not containing information owing the aleatory error. By means of the new PCA model, each individual sample can be classified within the facility of origin. This methodology provides a useful tool to identify emission focuses when odorant episodes are taking place.

Again, as well as the study published in section 3.2.2, this work was conducted within the collaboration framework signed by the University of the Balearic Islands, *Consell Insular de Mallorca* and the MSW Managing Companies.

The results of this study were published in *Chemosphere*.

3.1.3.1 ORIGINAL ARTICLE

C. Rodríguez- Navas, R. Forteza, V. Cerdà, *Use of thermal desorption – gas chromatography – mass spectrometry (TD-GC-MS) on identification of odorant emission focus by volatile organic compounds characterisation*, Chemosphere, (2012, *In press*),

3.2 DETERMINATION OF PHARMACEUTICALLY ACTIVE COMPOUNDS (PHACs) IN THE AQUATIC ENVIRONMENT

Contamination of waters resulting from the widespread use of pharmaceuticals has been identified as a critical environmental issue. After consumption, pharmaceutical compounds are excreted by humans and animals as parent compounds and/or metabolites and consequently enter wastewater treatment plants (WWTPs). However, it is well established that most compounds are not efficiently removed by conventional treatments and therefore eventually enter the environment [1, 2]. Hundreds of studies have reported the presence of pharmaceuticals in wastewaters, surface waters, and fresh drinking waters in USA, Australia, Japan China or European Countries [1, 3, 4]. Few studies also have reported PhACs in waste leachates [5-7]. In some cases, the presence of pharmaceuticals is studied through the presence of their metabolites (transformation products, TPs).

Although the potential footprints of many pharmaceuticals on the environment remain unclear, concerns regarding this issue continue to arise. For example, particular concern has been raised by the fact that antibiotics released to the environment may cause the development of increased resistance in naturally occurring bacterial populations [8-10].

Numerous methods have been developed for the determination of PhACs in waters. The major part of them is multi-residue analytical methods, which allow simultaneous determination of structurally diverse classes of compounds. Various techniques use solid-phase microextraction (SPME) or stir bar sorptive extraction (SBSE) for extraction of target analytes. However, solid-phase extraction (SPE) is currently the technique of choice for the determination of pharmaceutical compounds in waters [4, 11-14]. Regarding separation techniques, some authors have reported on methods using derivatization followed by gas chromatography-mass spectrometry (GC-MS) or gas chromatography-tandem mass spectrometry ($GC\text{-}MS^2$ or GC-MS/MS). However, due to the high polarity of most pharmaceuticals and hormones, liquid chromatography-mass spectrometry (LC-MS) and liquid chromatography-tandem mass spectrometry (LC-MS-MS) tend to be the preferred techniques applied.

In the Island of Mallorca (Mediterranean Sea, Spain), where PhACs are evaluated, one critical concern arises from the fact that over the 30% of the overall supply of water in Mallorca comes from treated wastewater for irrigation (not cropland) purposes. Furthermore, since other 35% of water demand (for human consumption) comes from groundwater resorvoirs, the re-use of treated wastewater poses the risk of ground contamination, producing a self-contamination cycle of the natural reservoirs. As long as re-claimed wastewater is needed to fully supply overall water demand in the Island, this risk must be evaluated in order to foresee and prevent future dangers.

In this section is presented the study focused on determination of pharmaceutical's residues in several different waters samples. A group of 27 PhACs, including antibiotics,

analgesics, anti-inflammatories, corticosteroids, tranquilizers, anti-hypertensive, β-blockers, contraceptives, anxiolytics, diuretics and antiepileptics were the targeted compounds. These particular compounds were chosen because they are all widely used and have been reported in the literature as present in wastewaters and environmental waters. The molecular structures of all of the compounds studied are illustrated in Appendix II.

The study presented used SPE as the extraction technique, which is the technique adopted because of the wide number of solid sorbents commercially available. Two different SPE procedures were carried out in the study to extract PhACs from water, according to Pérez-Carrera et al. optimized procedure [15]. Oasis® HLB and MAX were the selected sorbents combining their different adsorption features.

The chromatographic technique applied was LC-MS^2, using a triple quadrupole (QqQ) analyzer. Two different transitions were monitored for each analyte, for the quantification and corroboration of positive identifications.

The method was applied to evaluate for the first time the presence of the above listed PhACs in effluents samples from the two principal WWTPs and three municipal solid waste landfill leachates. One ground water and several marine waters (including natural parks) where compared to understand environmental pollution pathways followed by the detected PhACs around the aquatic environment in the Island of Mallorca.

The results of these studies have been submitted as full paper to the Journal *Archives of Environmental Contaminants and Toxicology.*

[1] C.G. Daughton, Environmental Toxicology and Chemistry, 28 (2009) 2490-2494.

[2] C.-P. Yu, K.-H. Chu, Chemosphere, 75 (2009) 1281-1286.

[3] US-EPA, in, 2010.

[4] S.D. Richardson, T.A. Ternes, Analytical Chemistry, 83 (2011) 4614-4648.

[5] K.K. Barnes, S.C. Christenson, D.W. Kolpin, M.J. Focazio, E.T. Furlong, S.D. Zaugg, M.T. Meyer, L.B. Barber, Ground Water Monitoring & Remediation, 24 (2004) 119-126.

[6] T. Eggen, M. Moeder, A. Arukwe, Science of The Total Environment, 408 (2010) 5147-5157.

[7] P. Buszka, D. Yeskis, D. Kolpin, E. Furlong, S. Zaugg, M. Meyer, Bulletin of Environmental Contamination and Toxicology, 82 (2009) 653-659.

[8] B. Halling-Sørensen, H.-C.H. Lützhøft, H.R. Andersen, F. Ingerslev, Journal of Antimicrobial Chemotherapy, 46 (2000) 53-58.

[9] K. Kümmerer, Journal of Environmental Management, 90 (2009) 2354-2366.

[10] P.A. Segura, M. François, C. Gagnon, S. Sauvé, Environ Health Perspect, 117 (2009).

[11] J.M. Conley, S.J. Symes, S.A. Kindelberger, S.M. Richards, Journal of Chromatography A, 1185 (2008) 206-215.

[12] E. Gracia-Lor, J.V. Sancho, F. Hernández, Journal of Chromatography A, 1217 (2010) 622-632.

[13] E. Van Hoeck, F. Canale, C. Cordero, S. Compernolle, C. Bicchi, P. Sandra, Analytical and Bioanalytical Chemistry, 393 (2009) 907-919.

[14] B. Kasprzyk-Hordern, R.M. Dinsdale, A.J. Guwy, Journal of Chromatography A, 1161 (2007) 132-145.

[15] E. Pérez-Carrera, M. Hansen, V. León, E. Björklund, K. Krogh, B. Halling-Sørensen, E. González-Mazo, Analytical and Bioanalytical Chemistry, 398 (2010) 1173-1184.

3.2.1.1 SUBMITTED ARTICLE

Pollution pathways of pharmaceutical residues in the aquatic environment on the island of Mallorca, Spain

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Keywords: LC-MS/MS, Pharmaceuticals, wastewater, leachate, pollution pathways, environment.

Abstract

This work determines the principal environmental pollution pathways of pharmaceutical on the Island of Mallorca (Spain). The evaluation was made on the basis of the quantification of pharmaceuticals residues by liquid chromatography – tandem mass spectrometry in several environmental water samples, including waste water treatment plant (WWTPs) effluents, municipal solid waste (MSW) landfill leachates, ground water and marine water. An overall set of 19 pharmaceuticals has been identified in the environment of the 27 human pharmaceuticals investigated in this study. WWTPs effluents are the main source of the pharmaceuticals into the aquatic environment. The data indicate that re-use of treated domestic waste water for irrigation (which supplies some 30% of the total water demand in Mallorca) contributes to contamination of groundwater. In addition, leaching from landfills is identified as another possible source of introduction of pharmaceuticals to ground water aquifers. Finally WWTP effluents ending in the Mediterranean sea causes pharmaceutical resdues to occur in marine water bodies, primarily highly urbanized areas.

1. Introduction

Human and veterinary pharmaceuticals as well as personal care products (PPCPs) have been of great concern the last decade, since they have been considered emerging contaminants (ECs) and their ecotoxicological effect towards non-targeted organisms are largely unknown (Farré et al., 2008; Richardson and Ternes, 2011). During this time period, the number of studies presenting data on environmental occurrence of PPCPs has increased, (Gómez et al., 2006; Gómez et al., 2007; Kuster et al., 2008; González Alonso et al., 2010; Gracia-Lor et al., 2010; Huerta-Fontela et al., 2010; Pérez-Carrera et al., 2010), as has the number of reviews (Farré et al., 2008; Giger, 2009; Verlicchi et al., 2010). Richardson and Ternes recently reviewed a very comprehensive collection of published works, covering reviews, legislations, occurrence, fate and risk assessment for ECs (Richardson and Ternes, 2011). This has aided in better understanding their environmental behaviour, such as pollutant burden as well as direct and indirect sources by which they are released into the environment. Several pathways have been described of how organic compounds, and by extension PPCPs, can be released into the aquatic environment and aquifer systems (Halling-Sørensen et al., 1998; Díaz-Cruz and Barceló, 2008; Farré et al., 2008). Most of the published articles concerning pharmaceuticals for human use deal with aquatic systems, where wastewater commonly are considered the principal emission source to the environment via excretion of the pharmaceutical either in the prescribed form or as metabolites.

In general, wastewater treatment plants (WWTPs) are not well-designed to completely remove pharmaceuticals (Zhou et al., 2009; Murray et al., 2010; Jelić et al., 2012), thus allowing pharmaceuticals to reach the environment by two different routes: (1) water effluents into the aquatic environment, and (2) sewage sludge residues into the soil environment (Nieto et al., 2010; Runnqvist et al., 2010). Pharmaceuticals for veterinary use are commonly released into the environment by animal's excretion, either through urine and dung from grassing animals or via manure application in agriculture (Thiele-Bruhn, 2003; Oppel et al., 2004; Hansen et al., 2011).

Even though, many environmental occurrence studies have been published, there still lack knowledge on critical issues, such as transformation processes, bioaccumulation, toxicity and pathways which all strongly influences risk assessment and management. Some studies have described different degradation processes, including photolysis (Halling-Sørensen et al., 2002; Lam et al., 2003; Yamamoto et al., 2009), and hydrolysis (Białk-Bielińska et al., 2012) as well as biodegradation by microorganisms (Benotti and Brownawell, 2009; Kagle et al., 2009; Musson et al., 2010). These processes do not necessarily remove contaminants, but may transform them into new compounds with preserved biological activity, which might possess different chemical properties, hence decreasing or increasing the effects of pollution on the environment (Halling-Sørensen et al., 2000; Celiz et al., 2009). Concerning bioaccumulation, the uptake of pharmaceuticals has been reported in both earthworms in the terrestrial environment (Kinney et al., 2008) as well as in fish in the aquatic

environment (Schultz et al., 2011) but much remains to be explored. The large number of pharmaceuticals prescribed combined with an unknown number of degradation products exposed to very differing types of environmental matrices, generates a multitude of interactions. Consequently, pollution pathways might be hard to predict and can only by revealed by determining a multitude of pollutants in a large variety of environmental compartments which are likely to be connected to one another.

Discharge of PPCPs into the environment represents a threat for water resources, since all fresh water sources in industrialized countries are potentially polluted by numerous contaminants (World Health Organization: Drinking-water Quality Committee, 2011). It might be especially severe in locations where natural fresh water sources are scarce or insufficient and reclaimed water is needed to meet the water demands of population, agriculture and industry.

The island of Mallorca (Spain) is the largest of the four Balearic Islands, rather remotely situated in the Western Mediterranean Sea, with a population of around one million people. Overall, from a contamination point of view, the Balearic Islands are most likely rather uncontaminated mainly due to lack of heavy industries and much of the islands are still comparatively pristine. The few studies conducted reveal a relatively low contamination burden of VOCs, PAHs and chlorinated organic compounds in air, sediment and marine invertebrates (Simó et al., 1991; Baumard et al., 1998; Deudero et al., 2007; Rodríguez-Navas et al., 2012; Rodriguez-Navas et al., 2012). These results indicated that the islands are far from major contamination sources, and that the air and waters of the Balearic Islands are comparatively pristine. Despite this, there is growing concern for these islands mainly due to a heavy tourism. Since the 1960ies, the islands have experienced considerable urbanization and a tourist boom, and today the number of tourists are more than 14 million per year (Balearic Islands Government. Ministry of Tourism and Sports, 2010). Consequently, there is a rising environmental pressure in terms of, water shortages which are additionally accentuated by the climate changes (Essex et al., 2004). Especially, in the summer period when water consumption increases these shortages become substantial. In order to reduce these constraints on water demand, local authorities have made substantial efforts since the 1970ies to develop efficient water treatment processes, which enable a suitable reuse of water, according to new and more restrictive regulations about reclaimed water quality. Consequently in 2010, 91% of all domestic and industrial wastewater on Mallorca was treated. Thereby this island was the Spanish location with the highest percentage of treated water, out of which 40% was reused. The three major sources of water are natural surface water reservoirs, treated waste water and specific water aquifers corresponding to 35, 35 and 30 %, respectively. Regarding the treated waste water, this water is only used for irrigation purposes, including agriculture, city areas and golf courts. Consequently, the aim of the present study was to: (1) determine the presence of human pharmaceuticals in the aquatic environment on the Island of Mallorca, (2) identify pathways followed by the pharmaceuticals and (3) evaluate the advisability of new directives for periodical monitoring to assess the suitability of the water quality. . For this

purpose, water samples from several different locations were collected in April 2011. Locations studied included WWTP effluents, municipal solid waste (MSW) landfill leachate pools, ground water, water from marine areas for nature preservation and seawater affected by urban areas.

2. Materials and methods

2.1 Chemicals and standards.

Diclofenac, allopurinol, verapamil, carbamazepine, spironolactone, salbutamol, omeprazole, atenolol, bendroflumethiazide, diltiazem, furosemide, prednisolone, erythromycin, metoprolol, citalopram, cimetidine, and diazepam were obtained from Sigma-Aldrich (Steinheim, Germany). Zopliclone and oxazepam were obtained from Bie and Berntsen (Rodovre, Denmark). Amoxycillin was obtained from Duchefa (Haarlem, The Netherlands), ramipiril from Sequoia Research Products (Pangbourne, UK). Terbutalin and penicillin G were purchased from AstraZeneca (Draco, Sweden), and morphine from Nordisk Droge and Kemikalier (Copenhagen, Denmark). Gestodene was obtained from Chemos (Regenstauf, Germany). Losartan potassium, amlodipine, and simvastatin were obtained from Toronto Research Chemicals (Ontario, Canada). Stock solutions of the individual pharmaceuticals in methanol were prepared at a concentration of 10 mg L^{-1} and stored at −18°C. Deuterated internal standards (IS), d10-carbamazepine and d7-atenolol were obtained from CDN Isotopes (Quebec, Canada).The purity of all analytical standards was above 95%, and deuterated purity above 98%. Abbreviations, therapeutic use, and most relevant physicochemical properties of the pharmaceuticals are listed in Table 1. Ammonium acetate (98%) was obtained from KMF (St Augustin, Germany) and acetic acid (99–100%), aqueous ammonia solution, heptane, ethyl acetate, methanol and acetone were purchased from Merck (Darmstadt, Germany). Ethylenediaminetriacetic acid (EDTA) was obtained from Sigma-Aldrich. Ammonium formate, formic acid, acetonitrile, and water were purchased from Merck. Solid-phase extraction (SPE) was performed with HLB cartridges (hydrophilic-lipophilic balance, poly(divinylbenzene-co-N-pyrrolidone), 200 mg sorbent, 6 mL cartridge) and MAX-cartridges (anion exchanger, N-vinylpyrrolidoneand divinylbenzene polymer, 150 mg, 6 mL), purchased from Waters Oasis (Massachusetts, USA). The Vacmastermanifold for the SPE cartridges was obtained from IST (Glamorgan, UK).

2.2 Sampling campaign.

To better evaluate pharmaceutical transport processes in the aquatic environment, some issues are prerequisite to know prior to the selection of sampling locations. The different usage of pharmaceuticals and disposal practices of these, combined with Mallorca's particular hydrogeological features, are presumed to be the most determinant factors. A critical issue is that Mallorca's hydrogeological context provides the ability to produce large amounts of ground water reservoirs owing the porous soil characteristics (Mateos-Ruiz and Lopez-Garcia, 2003). Furthermore, since no

rivers (but torrents) are present in Mallorca, reclaimed water from WWTPs effluents is used for irrigation of farmlands. Finally, there has historically been a tradition of dumping garbage in landfills, to handle the large amount of waste produced during the touristic season. Based on this information, it can be hypothesized that pharmaceuticals in Mallorca may be released into groundwater aquifers through three different pathways: (1) use of reclaimed water for irrigation, (2) application of sewage sludge as fertilizer (after a 14 days compost storage process) and (3) leaching waste from landfills. In this context it should be noted that treated waste water from WWTP, which is not for irrigation purposes, is discharged directly into the sea and may there cause contamination of marine water bodies.

Several different locations (**Figure 1** and **Table 2**) were sampled from 3-6 April 2011. The first locations were effluents from the two principal WWTPs in Mallorca (named as Palma I and Palma II), treating waste water from Palma main city and surrounding areas corresponding to a total of 400,000 inhabitants (Area 1). Two sample aliquots (named *a* and *b*) were collected the same day at different times from each one of the two WWTPs.. The pH range of these four samples was between 7.9 and 8.1. Leachate reservoirs from three municipal solid waste (MSW) landfills were also analysed. One sample was collected from leachate I (Area 1) while two replicates were collected from leachates II and III, Area 1 and 2 respectively. The pH range for these five samples was from 8.7 to 9.0. One aquifer known to be located under the MSW landfill II (and not declared for drinking water) was sampled to corroborate the possible leach of pharmaceuticals through the soil to the ground water. Two aliquots named GW*a* and GW*b* (Area 2) were taken, both with a pH of 7.2. Eight marine water samples were also collected (pH ranged from 7.5 to 8.1). At the Palma de Mallorca bay, two different locations were sampled as close as possible to two different WWTPs effluents discharge tubes (Area 1). Alcudia Bay, the northern area of the Island with the heaviest tourist impact was also sampled (Area 2). The last marine samples were representative of two natural parks. At Albufera Natural Park (Area 2), two different locations were sampled: the main water canal and a secondary canal, while at Mondragó Park (Area 3), two samples were collected at the beach. Finally, two additional tap water samples (used as quality control samples (QC)) were spiked with a mixed standard solution and an IS solution, to yield a sample concentration of 1000 ng L^{-1} of standards and 500 ng L^{-1} of IS. All, water samples were collected in glass bottles thoroughly cleaned with soap, water and ethanol, and dried at 150ºC prior to sampling. Collected volumes varied from 1-3 liters.

2.3 Chemical analysis

Chemical analysis was carried out following a previously validated SPE-LC-ESI-MS/MS method (Pérez-Carrera et al., 2010). Once in the laboratory and prior to the SPE procedure, the samples were filtered using Empore™ 0.45 μm porous glass fibre disks, conditioned with 500 mg EDTA per litre of sample and pH adjusted to 7.0 with acetic acid. Hereafter, the samples were fortified with 500 ng of each of the internal standards. Samples not immediately extracted were stored in darkness at 4°C for a

maximum of 12 hours prior to SPE.

2.3.1 SPE

Clean-up and pre-concentration were performed using a combination of MAX and HLB cartridges. Briefly, both cartridges were pre-conditioned with 5 mL heptane, 5 mL ethyl acetate, 5 mL methanol, and 2×5 mL tap water (pH 7.0 adjusted). A MAX cartridge was then placed on top of the HLB cartridge with a PTFE adaptor and placed in the SPE manifold vacuum system. The samples were passed through both cartridges at an approximate flow rate of 5 mL min^{-1}. Subsequently the HLB and MAX cartridges were dis-assembled and air-dried for 30 min. Both SPE cartridges were washed with 5 mL heptane. Finally, the MAX cartridge was eluted with 1 mL ethyl acetate, 2 mL methanol, 2 mL methanol containing 2 % acetic acid, and 2 mL methanol; the HLB cartridge was eluted with 3 mL ethyl acetate and 4 mL methanol. These two aliquots from MAX and HLB were combined, divided in two and evaporated to dryness at 60°C and under a gentle stream of nitrogen. Each of the combined eluates was reconstituted in 200 µL mobile phases A and B from HPLC methods I and II, respectively, and transferred into two HPLC vials with 300 µL glass inserts. Each sample extraction was analysed in triplicate.

2.3.2 LC-MS/MS

Analysis of the resulting extracts required two slightly different LC-ESI-MS-MS methods (method I and method II). HPLC separations in methods I and II were achieved by use of a reversed-phase column (XTerra MS-C18, 2.1×100 mm, 3.5 µm) and a normal-phase column (Atlantis HILIC, 2.1×100 mm, 2 µm), respectively, from Waters, (Milford, MA, USA) following Pérez-Carrera et al. procedures (Pérez-Carrera et al., 2010). For both quantification methods, the analytical system consisted of an Agilent 1100 series HPLC system (Agilent Technologies, Palo Alto, CA, USA), equipped with a degasser, a cooled autosampler (4°C), and a cooled column oven (13°C). Detection was performed with a Sciex API 3000 triple-quadrupole mass spectrometer (Applied Biosystems, Foster City, CA, USA) equipped with an ESI source (Turbo Ion spray). For MS detection, the instrument was operated in multiple switching modes and by comparing retention times and substance-specific mass spectra positive identifications were achieved. Precursor ions and product ions for MS detection in methods I and II are, likewise, listed in the work by Pérez-Carrera et al. (Pérez-Carrera et al., 2010).Collection and treatment of data were performed using Analyst 1.4 software (Applied Biosystems) in a Windows XP platform-based data-processing system.

2.4 Quality control and quality assurance

The LC-ESI-MS/MS responses for each of the pharmaceuticals were evaluated for linearity by means of an internal standard (IS) calibration procedure, as the ratio of the target compound output area divided by the internal standard output area. Standard solutions of the target pharmaceuticals in

the appropriate mobile phases (depending on method I or II) were evaluated in the range 1–1000 ng L^{-1}. Internal standard concentrations were set at 500 ng L^{-1} (same as the samples). Linear fit for all 27 standards (n= 3) was within $0.938 < r^2 < 0.993$, except for omeprazole (OP, Method I) showing a poor linear fit of 0.886.

Detection limits of the method (LOD, ng L^{-1}) for all 27 compounds were estimated on the basis of the mean background signal plus three times the standard deviation (LOD = mean blank + 3SD). The blanks consisted of 1L tap water run at the same specified conditions. LOD values for all the compounds were within the range 0.8 – 29.4 ng L^{-1}.

Owing to the high heterogeneity and complexity of the sample matrices, especially in the case of leachates and marine samples, and in order to evaluate SPE extraction procedure, two water samples were spiked with 1000 ng L^{-1} standard mix solution (with IS): Quality control 1 (QC1), consisting of tap water; and Quality Control 2 (QC2), consisting of sea water from the Mondragó Natural Park (Area 3). General recoveries were in the range 25-204 % for all compounds, however, some poor recoveries were obtained for sea water samples (QC2) by both methods I and II, due to ionic matrix interferences with the SPE sorbents. Standards showing recovery levels below 25% or above 225% were discarded for the environmental analysis. Final concentrations of the identified pharmaceuticals in samples were corrected according to each specific recovery rate. Atenolol and carbamazepine the pharmaceuticals with deuterated internal standards (d_{10}-CB and d_7-AT), achieved absolute recovery rates within the range 75-124%.

To assess the reliability of the quantification and the SPE procedure, signal output of atenolol (integrated on the basis of its deuterated standard d_7-AT ratio) was analysed by both LC-MS/MS methods (I and II).Variance between Methods I and II for all sampled locations, estimated as relative standard deviation (RSD), was within the range 2-8 %.

3. Results and discussion

3.1 Pollution sources and occurrence

Measured concentrations are different for each pharmaceutical due to their varying physicochemical properties, such as acidity, polarity and water solubility (Farré et al., 2008; Richardson and Ternes, 2011), combined with the differing nature and complexity of environmental matrices and the various processes acting upon the compounds such as degradation and sorption (Luthy et al., 1997). Therefore pharmaceutical behaviour in the aquatic environment might be difficult to generalize (2011). Yet some overall trends are outlined below.

Fresh and ground water

The concentrations obtained for each compound in the analysed fresh water samples (ng L^{-1}) are presented in Table 3. The results from the WWTPs effluents (Palma I and Palma II, Area 1) revealed a

positive identification of 19 pharmaceuticals. Small variations in concentrations were observed for WWTPs effluents collected at the same day at the same site (samples a and b). A total of 12 different pharmaceuticals were identified in the three different landfill leachates (Leach I-III); 10 pharmaceuticals in leachates I and II (Area 1), and 6 in leachate III (Area 2). Finally, 7 pharmaceuticals were identified in the ground water samples (GW, Area 2).

As expected the highest levels for most pharmaceuticals were found in the WWTP effluents. Total concentrations were estimated as the sum of all identified pharmaceuticals concentrations per sample. On average, Palma I WWTP showed a total mass concentration of ~37000 ng L^{-1} which is 6 times higher than Palma II WWTP of ~6500 ng L^{-1}. It should be stressed though that the major part of this difference is caused by the high concentration observed for omeprazol. This difference between the two WWTPs might also be explained by the fact that WWTP II has an extra depuration step than WWTP I, but also due to the different origin of incoming municipal wastewater to each WWTP.

In Palma I effluent, omeprazole was the most prominent pharmaceutical, accounting for up to 83% of the total mass of monitored pharmaceuticals, followed by atenolol, oxazepam, erythromycin, morphine, diclofenac, amoxicillin, furosemide, salbutamol and carbamazepine. In Palma II effluent, a fairly similar pattern was observed with oxazepam showing the highest concentration corresponding to 79% of the total measured pharmaceutical burden. Thereafter, in order of descending concentrations, carbamazepine, atenolol, amoxicillin, salbutamol, gestodene, diclofenac, erythromycin, diazepam and diltiazem were determined. Individual and total levels are in fairly good agreement with WWTPs effluent data previously reported (Murray et al., 2010).

Relatively high concentration levels were also found in leachates, ranging from c.2500 ng L^{-1} in leachate II and III and up to around 27000 ng L^{-1} in leachate I. In leachate I, omeprazole corresponded to over 90% of the total concentration followed by amoxicillin, gestodene, morphine, carbamazepine and terbutalin. For leachate II and leachate III b, omeprazole was the most and the second most abundant contaminants. The overall contamination patterns were also quite similar to leachate I. Leachate III b deviated to some extent, since a high concentration of furosemide was identified in this sample along with a low level of penicillin G. The reason for this observation is not obvious, but could not be neglected since the compounds were positively identified also after repeated injections. All together the leachate data indicates that pharmaceuticals most likely are dumped into MSW landfills from where they might be transported to the environment. It should be pointed out that these data are among the first analyses performed directly on landfill leachate pools, and to the best of our knowledge we could not identify other studies (determining the same compounds) to compare with. Only the most persistent carbamazepine was recently reported over 10 ng L^{-1} (Eggen et al., 2010). Four compounds could be quantified in both ground water samples (gestodene, omeprazole, cimetidine and carbamazepine) giving a total concentration of around 350 ng L^{-1}. This demonstrates that pharmaceuticals may reach ground water aquifers on Mallorca.

Marine water

Trace levels of pharmaceuticals were found in nearly all marine samples (Table 4). The Palma Bay I harbour sample showed the highest number of identified compounds probably because of its closeness (~50 meters) to the Palma I WWTP effluent discharge position (Area 1). These included for example atenolol, gestodene, allopurinol, cimetidine and diltiazem. The Palma Bay II beach sample, on the other hand, did not contain quantifiable amounts of pharmaceuticals despite being sampled close to the expected outlet of WWTP Palma II (Area 1). The Alcudia Bay sample taken in this massive touristic area of Alcudia only allowed for the quantification of allopurinol (Area 2). Interestingly the Albufera Natural Park (Area 2) also contained trace levels of a few pharmaceuticals (gestoden, furosemid and allopurinol) might be explained by the re-use of reclaimed water for irrigation migrating via run-off to this wet-land area. Only the samples collected in Mondragó Natural Park (Area 3) showed no traces of pharmaceutical contamination. This is probably caused by Mondragó being far from densely populated areas, including both inhabitants and touristic locations in contrast to the Albufera Natural Park, Figure 1. Unfortunately, SPE procedure provided bad recoveries for omeprazole; therefore it could not be measured in marine water.

3.2 Pollution pathways

Based on the occurrence of pharmaceutical in the aquatic environment of Mallorca, available bibliography on pharmaceuticals reported during the last years and the starting premises stated in section 3.1, some general conclusions on pollution pathways can be drawn.

From WWTPs to sea

The occurrence of pollutants in the marine water is most likely caused by WWTPs effluents discharge in the sea (Area 1), since the two biggest WWTPs discharge the non-used reclaimed water into the Palma Bay. That explains the slightly higher concentrations found in Palma Bay than in marine waters on the rest of the Island (Area 2 and 3). A majority of the pharmaceuticals eluting from the WWTPs could not be detected in the marine water. This could be caused by several mechanisms such as degradation and dilution once entering the sea. In all, five pharmaceuticals could be quantified in both Palma I WWTP effluent as well as in the Palma Bay I harbour water. The decreases in concentration of these compounds are shown in Figure 2. On average a 50-fold reduction is seen 50 m from the outlet source of Palma I WWTP meaning. It should however be stressed that little is known about effects on marine organisms after long-term exposure to minute levels of pharmaceuticals, constantly entering the sea. The low levels observed in the Alcudia Bay sample are very welcome from a touristic point of view since this indicates clean water in Area 2. Still there is a chance that the low levels were found because the samples were taken outside the major touristic season (April) or too far away from emission sources, as we could not identify where waste water effluents entered the sea. Concerning the occurrence of pharmaceuticals in the Natural Park of Albufera, there are no clear

evidences on the emission source of PPCPs. It may be speculated that they enter via reclaimed water used for irrigation or intrusion of polluted marine water.

From leachate and irrigation to ground water

The presence of pharmaceutical residues in the ground water reservoir might be connected to downward transport to the aquifer from MSV landfill Leachate III (Area 3), which is situated right above the sampled ground water. As seen in Figure 3, gestodene, omeprazole and amoxycilin were present in 4-17 times higher concentrations in Leachate III than groundwater. However, the re-use of reclaimed water might also be a potential source. Looking at the concentrations of gestodene in Palma I and II WWTP effluents, the concentrations are a factor 10 lower though, meaning that irrigation possibly is less important for this compound. For omeprazole the situation is quite different since the omeprazole concentration varied greatly in Palma I and II WWTP effluents ranging from 360-38000 ng/L. Consequently, agricultural activities might have contributed to the occurrence of this compound in ground water. Finally, amoxycilin is also present in relatively high concentrations in WWTP effluent water (39-283 ng/L) and might therefore also cause leaking to groundwater during irrigation with treated water. Three compounds identified in the leachate III (penicillin G, furosemide and salbutamol), however were not detected in the groundwater. From Table 3 and 4 it is also clear that these compounds are present in WWTP effluents, yet are not detected in marine samples at the discharge point indicating a poor transport or survival to both ground water and sea. The situation is somewhat different for cimetidine and carbamazepine which both were detected in groundwater, while not in leachate (Figure 3). A plausible explanation to this situation is transport via irrigation of re-claimed waste water. Both compounds were found in WWTP effluent water as well as in detectable amounts at the discharge points in the sea. Carbamazepine belongs to a group of compounds that have been reported as very persistent (Murray et al., 2010; Richardson and Ternes, 2011; Jelić et al., 2012) and could possibly leach. Overall the results from WWTP effluents and leachate open up for various pollution pathways in Mallorca including both the re-use of reclaimed water for irrigation and leaching from MSW landfill sites.

3.3 Implications for the island of Mallorca

Detection of pharmaceutical residues in the ground water is especially worrying since this indicates that other aquifers also might be polluted. Unfortunately there are no clear evidences on whether these levels represent a risk for human health or not, according to risk assessment studies made the last few years (Murray et al., 2010). The World Health Organisation (WHO) published a comprehensive report regarding drinking water risk assessment in 2011 (World Health Organization: Drinking-water Quality Committee, 2011). In the report, it was concluded that trace quantities of pharmaceuticals in drinking-water are very unlikely to pose risks for human health; notwithstanding, the conclusions are made on the basis of estimated acceptable daily intakes (ADI) and minimum therapeutic doses (MTD) to

broadly assess and screen risks. These estimations may depend on many factors such as limited occurrence data available for pharmaceuticals in drinking water, the diverse range of pharmaceuticals in use, the wide variation in the use of individual pharmaceuticals between countries, the limited number of data in the public domain and technical limitations relating to assessing risks from chronic exposure to low-dose of pharmaceutical compounds.

Concerning the MSW landfill leachates, to the best of our knowledge this is one of the first analyses made on occurrence of pharmaceuticals directly in an open pool of collected leachate water. Landfill disposal represents a threat for the environment, since many pollutants may leach towards the soil or ground aquifers. The presented data provides new evidences regarding the risk that entails the disposal of pharmaceuticals into landfills, and by extension many other pollutants, which might leach towards groundwater aquifers on Mallorca. Landfill leaching plumes have been reported during the last decade as important emission sources of all kind of organic environmental contaminants (Holm et al., 1995; Schwarzbauer et al., 2002; Barnes et al., 2004; Heim et al., 2004; Buszka et al., 2009), with the identification of more than one hundred organics. Therefore efficient landfills must be constructed in order to prevent and reduce environmental leaching. In Europe, landfills must be constructed according to current European regulation 1999/31/EC on the landfill of waste (European Environmental Agency, 1999). This regulation establishes the way in which leachate drainage must be diverted towards secure and not permeable reservoirs. Landfills in Mallorca are constructed according to this legislation, yet may not be completely sufficient to remove all pollutants as demonstrated by our measurements.

The situation on Mallorca is quite delicate since it is demonstrated that the water environment on Mallorca contains several pharmaceutical residues at the ppb levels, through the re-use of WWTPs effluents and landfill's leach. At the same time, due to insufficient natural fresh water reservoirs combined with heavy water restrictions owing to tourism, it is unconditionally necessary to re-use water to completely supply overall demand. In this context it should be noted that in a study by Adrover et al. (Adrover et al., 2012) analysing soils irrigated with reclaimed water it could be concluded that such practices did not significantly alter 20 chemical properties of Mallorca's soils.

Still re-using water may potentially become hazardous in the future, as the population slowly is polluting its own drinkable water aquifers. Extra stress is also put on water resources by heavy tourism, yet tourism is one of the main incomes for this island meaning that new sustainable solution to water management must be provided. Environmental impact and human risk evaluations concerning pharmaceuticals are currently scarce and far from conclusive. It seems mandatory to develop appropriate measures to prevent contamination by means of efficient waste treatment and disposal processes for all emerging contaminants processes in order to avoid the pollution of available drinkable aquifers and the aquatic environment. Future activities should also include a monitoring

programme of water bodies on the island of Mallorca.

4. Conclusions

Pharmaceutical residues have for the first time been determined in environmental samples on the island of Mallorca to evaluate their environmental impact. Effluent from waste water treatment plants showed the highest total concentration levels, up to 46,180 ng L^{-1}, including 19 identified compounds. This study is one of the first quantifying pharmaceuticals in landfill leaching water, revealing total concentrations between 5,000-25,000 ng L^{-1}. A total of 12 compounds were identified in the leachates. Some pharmaceuticals have been identified also in a ground water aquifer, with a total concentration of 300-400 ng L^{-1} levels. Additionally, some persistent pharmaceuticals were also identified in the sea samples, at very low levels. This study gives new knowledge concerning the pollution pathways followed by pharmaceuticals on the Island of Mallorca. Since treated domestic waste water represents one of the principal water supplies, there is a risk on water self-contamination owing to a reintroduction of pollutants in the water aquifers and agriculture. More comprehensive evaluations are needed in order to meliorate disposal processes mainly through more efficient wastewater treatments, until we better understand the behaviour of pharmaceuticals and other ECs once they reach the environment. We believe the appropriate goal of ECs evaluations should be to demonstrate the necessity to reinforce local regulations in order to stop releasing ECs and improve waste management systems.

Acknowledgements

The authors want to acknowledge the economic support from the Spanish Ministry of Science and Innovation by the pre-doctoral grant BES-2008-003354 and by the Project CTQ 2010-15541, as well as the economic support from the Balearic Islands Government.

The kind collaboration of all personnel at the Waste Management Companies involved in this work is sincerely acknowledged.

Table 1. Details of the pharmaceuticals investigated showing their abbreviation code, therapeutic use, basic physicochemical properties and the LC-MS/MS method used for quantification.

Compound	Code	Therapeutic use	log Kow[1]	pKa[1]	LC-MS/MS
Acids					
Penicilin G[B]	PCG	Antibiotic	1.7	2.5	I
Diazepam[A]	DA	Tranquilizer	2.7	3.4	I
Furosemid[B]	FS	Diuretic	2	3.9	I
Diclofenac[B]	DC	Anti-inflammatory	4.5	4	I
Zopiclon[A]	ZP	Anxiolytic	1.5	6.7	II
Cimetidine[B]	CT	Anti-acidreflux	6.8		I
Neutrals					
Prednisolon[A]	PN	Corticosteroid	1.1		I
Carbamazepin[B]	CB	Antiepilectic	2.5		I
Spironolacton[B]	SL	Diuretic	2.7		I
Simvastatin[B]	SV	Anti-hyperlipidaemic	4.7		I
Gestoden[A]	GS	Contraceptive	1.3		I
Zwitterionics					
Amoxycilin[A]	AC	Antibiotic	0.9	2.8/7.2	II
Ramipril[A]	RM	Cardiac drug	1.1	3.1/5.5	II
Bases					
Omeprazol[A]	OP	Proton pump inhibitor	2.3	7.1	II
Erythromycin[A]	ET	Antibiotic	2.5	8.2	II
Morphine[A]	MF	Analgesic	0.8	7.9	II
Bendroflumethiazid[B]	BF	Diuretic	0.7	8.5	I
Diltiazem[A]	DT	Anti-hypertensive	2.7	8.9	II
Amlodipin[B]	AD	Anti-hypertensive	1.3	9	I
Verapamil[A]	VP	Anti-hypertensive	3.9	9.1	II
Atenolol[A]	AT	β-blocker	0.2	9.2	I/II
Oxazepam	OX	Tranquilizer	2.8	9.2	I
Salbutamol[A]	SB	β-agonist	1.3	9.3	II
Allopurinol[A]	AP	Rheumatic	2.9	9.3	II
Citalopram[A]	CP	Tranquilizer	3.7	9.6	II
Metoprolol[A]	MP	β-blocker	1.9	9.7	II
Terbutalin[A]	TB	Anti-asthmatic	0.9	10.1	II

[A] d_7-Atenolol used as Internal Standard
[B] d_{10}-Carbamazepine used as Internal Standard
[1] From ref. (Pennsylvania Department of Environmental Protection, 2005)

Table 2. Description of sample type, sampling area and pH. Detailed information of sampling areas is given in Figure 1.

Sample	Origin	Sampling area	pH
Fresh water			
Blank	Tap water, University	1	6.6
QC1	Tap water, University	1	6.6
Palma I a	WWTP effluent	1	7.9
Palma I b	WWTP effluent	1	7.9
Palma II a	WWTP effluent	1	8.0
Palma II b	WWTP effluent	1	8.1
Leachate I	MSW landfill leachate	1	9.0
Leachate II a	MSW landfill leachate	1	8.7
Leachate II b	MSW landfill leachate	1	8.7
Leachate III a	MSW landfill leachate	2	8.9
Leachate III b	MSW landfill leachate	2	8.8
Groundwater a	Non potable aquifer	2	7.2
Groundwater b	Non potable aquifer	2	7.2
Marine water			
QC2	Mondragó beach	3	8.1
Palma Bay I	Harbour	1	7.5
Palma Bay II	Beach	1	8.0
Alcudia Bay	Beach	2	8.1
Albufera Park I	Main canal	2	8.0
Albufera Park II	Secondary canal	2	8.1
Mondragó a	Beach	3	8.0
Mondragó b	Beach	3	7.9

Table 3. Average pharmaceuticals concentrations, in ng L^{-1} for each compound in water. Waste water treatment plants I and II (Palma I and Palma II), municipal solid waste landfill leachates I, II and III (Leach I, Leach II and Leach III), and ground water (GW). Total concentration is estimated as the sum of all identified pharmaceuticals in the same sample. Compounds not identified are indicated by a dash line. Identified compounds with concentrations below the limit of quantification are described by <LOQ.

Compound	Palma I a	Palma I b	Palma II a	Palma II b	Leach I	Leach II a	Leach II b	Leach III a	Leach III b	GW a	GW b
Atenolol	2048	2030	224	225	-	-	-	-	-	-	-
Cimetidine	55	115	7	9	-	-	-	-	-	44	64
Penicillin G	<LOQ	<LOQ	-	-	-	-	-	160	-	-	-
Furosemide	266	220	-	-	-	-	-	3840	-	-	-
Prednisolone	-	-	-	-	-	-	-	-	-	-	-
Carbamazepine	185	180	249	247	52	123	122	-	-	19	21
Amlodipine	-	-	-	-	-	-	-	-	-	-	-
Oxazepam	1365	858	3817	5617	-	-	-	-	-	-	-
Bendroflumethiazide	-	-	-	-	-	-	-	-	-	-	-
Gestodene	32	37	82	54	490	1020	1037	581	871	180	169
Diazepam	<LOQ	<LOQ	19	18	-	-	-	-	-	-	-
Diclofenac	271	298	79	52	-	22	40	-	-	-	-
Spironolactone	-	-	-	-	-	-	-	-	-	-	-
Simvastatine	12	19	-	-	-	-	-	-	-	-	-
Omeprazole	38514	19398	515	360	25126	998	2597	479	1403	65	138
Ramipril	-	-	-	-	-	-	-	-	-	<LOQ	<LOQ
Diltiazem	164	115	14	18	-	-	-	-	-	-	-
Metoprolol	-	-	-	-	-	-	-	-	-	-	-
Terbutaline	63	39	-	4	49	<LOQ	-	-	-	-	-
Zopiclone	<LOQ	<LOQ	<LOQ	-	13	-	-	-	-	<LOQ	-
Salbutamol	234	152	93	58	<LOQ	25	38	-	91	-	-
Erytromicin	57	1202	-	49	-	-	-	-	-	-	-
Atenolol	2157	2269	240	219	-	234	237	-	-	-	-
Morphine	522	418	4	4	70	-	-	<LOQ	-	-	-
Amoxyciline	237	283	39	147	1519	<LOQ	92	<LOQ	89	<LOQ	5
TOTAL	46180	27631	5381	7082	27319	2422	4162	5060	2455	307	397

Table 4. Average pharmaceuticals concentrations, in ng L^{-1} for each compound in marine water. Compounds not identified are indicated by a dash line. Identified compounds with concentrations below the limit of quantification are described by <LOQ.

Compound	Palma Bay I	Palma Bay II	Alcudia Bay	Albufera I	Albufera II	Mondragó a	Mondragó b
Atenolol	38	-	-	-	-	-	-
Cimetidine	15	<LOQ	<LOQ	-	-	-	-
Penicillin G	-	-	-	-	-	-	-
Furosemid	-	-	-	-	47	-	-
Prednisolon	2	-	-	-	-	-	-
Carbamazepine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	-	-
Amlodipin	-	-	-	-	-	-	-
Oxazepam	-	-	-	-	-	-	-
Bendroflumethiazid	-	-	-	-	-	-	-
Gestoden	19	-	-	56	-	-	-
Diazepam	<LOQ	-	-	-	-	-	-
Diclofenac	-	-	-	-	-	<LOQ	-
Spironolacton	-	-	-	-	-	-	-
Simvastatin	-	-	-	-	-	-	-
Omeprazol	16	-	15	18	<LOQ	17	14
Ramipril	3	-	<LOQ	-	-	<LOQ	<LOQ
Diltiazem	11	-	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Metoprolol	8	-	<LOQ	-	-	-	<LOQ
Terbutalin	-	-	-	-	-	-	-
TOTAL	111	0	15	75	47	17	14

List of Captions:

Figure 1. Geophysical map of the island of Mallorca Island, Spain, Western Mediterranean Sea. Sampled areas are shown in the map inside dashed circles.

Figure 2. Concentration of pharmaceuticals measured both in the Palma I WWTP effluent samples and the Palma Bay I harbour samples located 50 m from the effluent discharge point in the harbour (Area 1).

Figure 3. Concentration of pharmaceuticals measured in the Leachate III and the Groundwater (Area 3).

Figure 1.

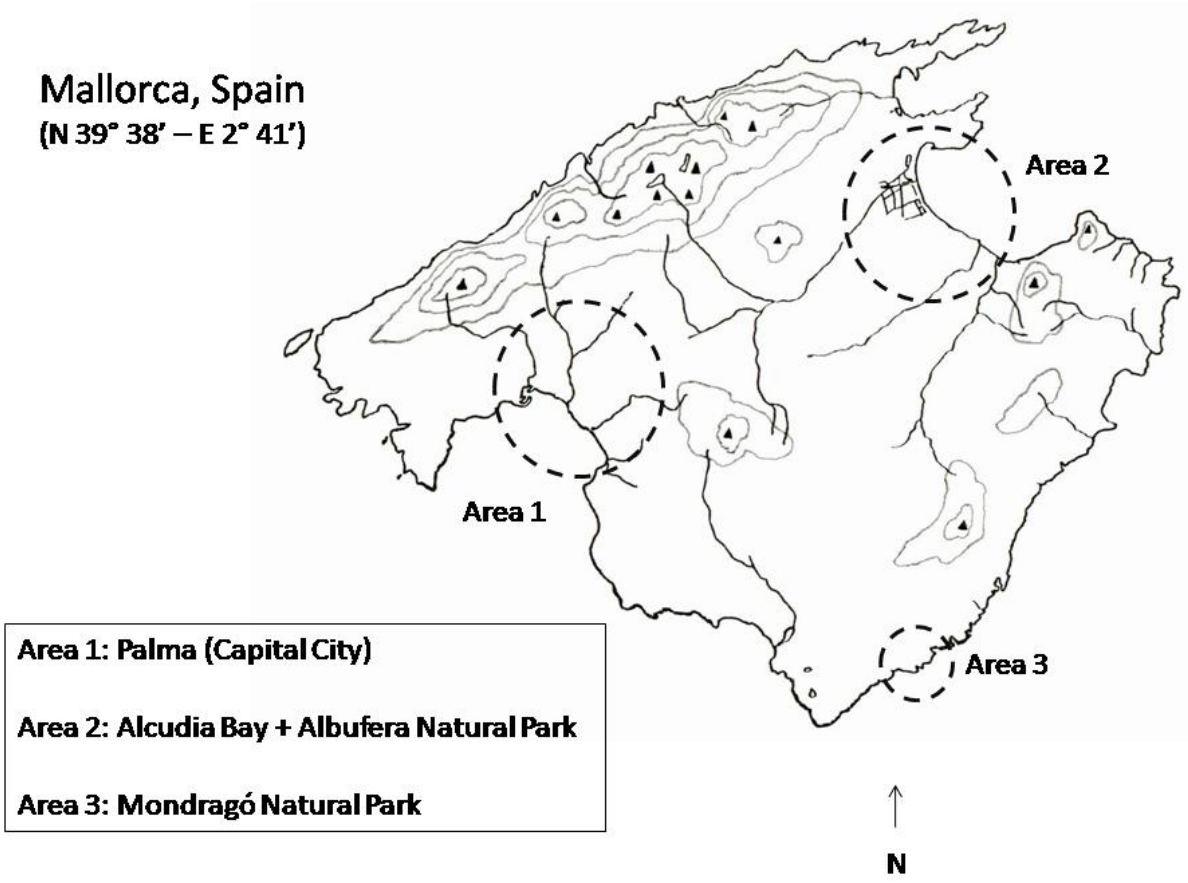

Mallorca, Spain
(N 39° 38' – E 2° 41')
Area 2
Area 1
Area 3
Area 1: Palma (Capital City)
Area 2: Alcudia Bay + Albufera Natural Park
Area 3: Mondragó Natural Park
N

Figure 2.

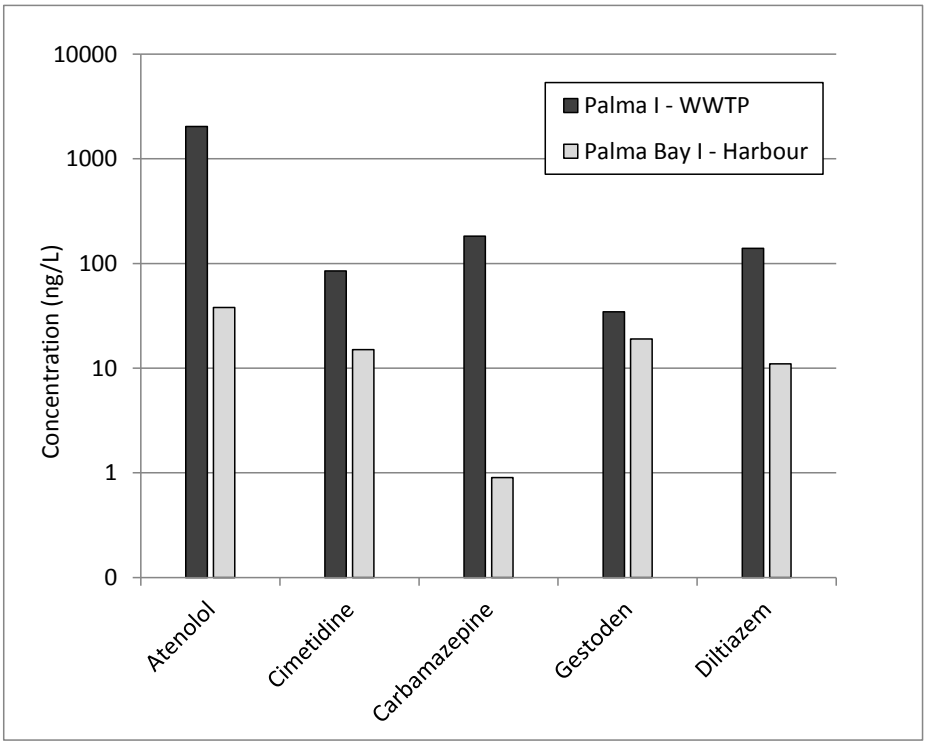
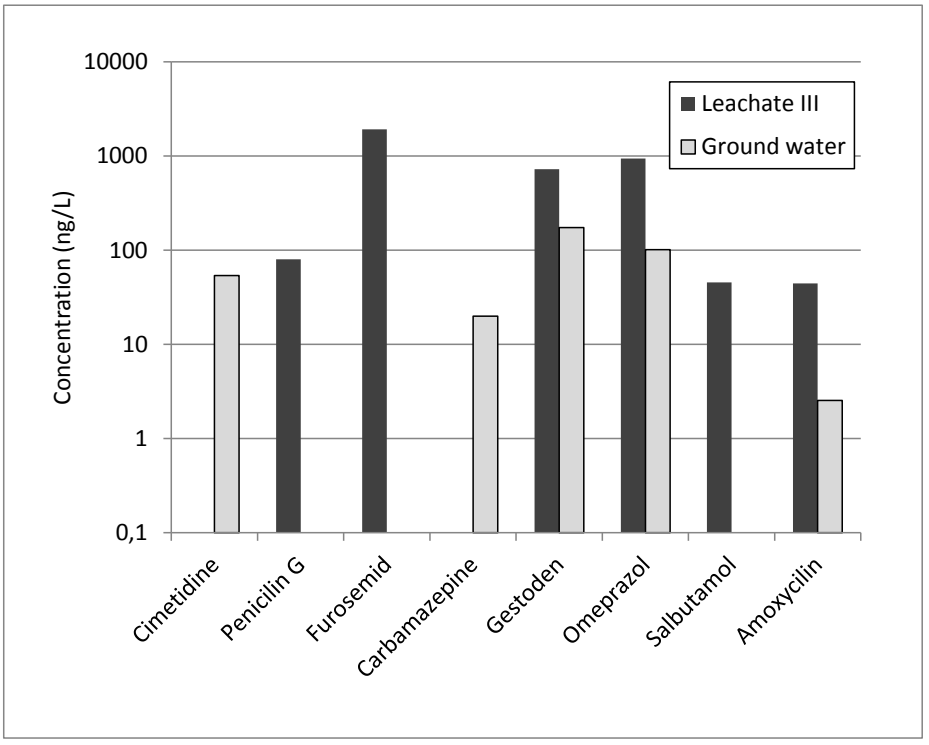


Figure 3.



REFERENCES

Adrover, M., Farrús, E., Moyà, G., Vadell, J., (2012). Chemical properties and biological activity in soils of Mallorca following twenty years of treated wastewater irrigation. Journal of Environmental Management 95, Supplement, S188-S192.

Balearic Islands Government. Ministry of Tourism and Sports, 2010. Tourism in the Balearic Islands. Annual Report.

Barnes, K.K., Christenson, S.C., Kolpin, D.W., Focazio, M.J., Furlong, E.T., Zaugg, S.D., Meyer, M.T., Barber, L.B., (2004). Pharmaceuticals and Other Organic Waste Water Contaminants Within a Leachate Plume Downgradient of a Municipal Landfill. Ground Water Monitoring & Remediation 24, 119-126.

Baumard, P., Budzinski, H., Garrigues, P., (1998). Polycyclic aromatic hydrocarbons in sediments and mussels of the western Mediterranean sea. Environmental Toxicology and Chemistry 17, 765-776.

Benotti, M.J., Brownawell, B.J., (2009). Microbial degradation of pharmaceuticals in estuarine and coastal seawater. Environmental Pollution 157, 994-1002.

Białk-Bielińska, A., Stolte, S., Matzke, M., Fabiańska, A., Maszkowska, J., Kołodziejska, M., Liberek, B., Stepnowski, P., Kumirska, J., (2012). Hydrolysis of sulphonamides in aqueous solutions. Journal of Hazardous Materials 221–222, 264-274.

Buszka, P., Yeskis, D., Kolpin, D., Furlong, E., Zaugg, S., Meyer, M., (2009). Waste-Indicator and Pharmaceutical Compounds in Landfill-Leachate-Affected Ground Water near Elkhart, Indiana, 2000–2002. Bulletin of Environmental Contamination and Toxicology 82, 653-659.

Celiz, M.D., Tso, J., Aga, D.S., (2009). Pharmaceutical metabolites in the environment: Analytical challenges and ecological risks. Environmental Toxicology and Chemistry 28, 2473-2484.

Deudero, S., Box, A., March, D., Valencia, J.M., Grau, A.M., Tintore, J., Calvo, M., Caixach, J., (2007). Organic compounds temporal trends at some invertebrate species from the Balearics, Western Mediterranean. Chemosphere 68, 1650-1659.

Díaz-Cruz, M.S., Barceló, D., (2008). Trace organic chemicals contamination in ground water recharge. Chemosphere 72, 333-342.

Eggen, T., Moeder, M., Arukwe, A., (2010). Municipal landfill leachates: A significant source for new and emerging pollutants. Science of The Total Environment 408, 5147-5157.

Essex, S., Kent, M., Newnham, R., (2004). Tourism Development in Mallorca: Is Water Supply a Constraint? Journal of Sustainable Tourism 12, 4-28.

European Environmental Agency, 1999. Council Directive 1999/31/EC of 26 April 1999 on the landfill of waste.

Farré, M.l., Pérez, S., Kantiani, L., Barceló, D., (2008). Fate and toxicity of emerging pollutants, their metabolites and transformation products in the aquatic environment. Trends in Analytical Chemistry 27, 991-1007.

Giger, W., (2009). Hydrophilic and amphiphilic water pollutants: using advanced analytical methods for classic and emerging contaminants. Analytical and Bioanalytical Chemistry 393, 37-44.

Gómez, M.J., Martínez Bueno, M.J., Lacorte, S., Fernández-Alba, A.R., Agüera, A., (2007). Pilot survey monitoring pharmaceuticals and related compounds in a sewage treatment plant located on the Mediterranean coast. Chemosphere 66, 993-1002.

Gómez, M.J., Petrović, M., Fernández-Alba, A.R., Barceló, D., (2006). Determination of pharmaceuticals of various therapeutic classes by solid-phase extraction and liquid chromatography–tandem mass spectrometry analysis in hospital effluent wastewaters. Journal of Chromatography A 1114, 224-233.

González Alonso, S., Catalá, M., Maroto, R.R., Gil, J.L.R., de Miguel, Á.G., Valcárcel, Y., (2010). Pollution by psychoactive pharmaceuticals in the Rivers of Madrid metropolitan area (Spain). Environment International 36, 195-201.

Gracia-Lor, E., Sancho, J.V., Hernández, F., (2010). Simultaneous determination of acidic, neutral and basic pharmaceuticals in urban wastewater by ultra high-pressure liquid chromatography-tandem mass spectrometry. Journal of Chromatography A 1217, 622-632.

Halling-Sørensen, B., Lützhøft, H.-C.H., Andersen, H.R., Ingerslev, F., (2000). Environmental risk assessment of antibiotics: comparison of mecillinam, trimethoprim and ciprofloxacin. Journal of Antimicrobial Chemotherapy 46, 53-58.

Halling-Sørensen, B., Nors Nielsen, S., Lanzky, P.F., Ingerslev, F., Holten Lützhøft, H.C., Jørgensen, S.E., (1998). Occurrence, fate and effects of pharmaceutical substances in the environment- A review. Chemosphere 36, 357-393.

Halling-Sørensen, B., Sengeløv, G., Tjørnelund, J., (2002). Toxicity of Tetracyclines and Tetracycline Degradation Products to Environmentally Relevant Bacteria, Including Selected Tetracycline-Resistant Bacteria. Archives of Environmental Contamination and Toxicology 42, 263-271.

Hansen, M., Krogh, K.A., Halling-Sorensen, B., Bjorklund, E., (2011). Determination of ten steroid hormones in animal waste manure and agricultural soil using inverse and integrated clean-up pressurized liquid extraction and gas chromatography-tandem mass spectrometry. Analytical Methods 3, 1087-1095.

Heim, S., Schwarzbauer, J., Littke, R., (2004). Monitoring of waste deposit derived groundwater contamination with organic tracers. Environmental Chemistry Letters 2, 21-25.

Holm, J.V., Ruegge, K., Bjerg, P.L., Christensen, T.H., (1995). Occurrence and Distribution of Pharmaceutical Organic Compounds in the Groundwater Downgradient of a Landfill (Grindsted, Denmark). Environmental Science & Technology 29, 1415-1420.

Huerta-Fontela, M., Galceran, M.T., Ventura, F., (2010). Fast liquid chromatography–quadrupole-linear ion trap mass spectrometry for the analysis of pharmaceuticals and hormones in water resources. Journal of Chromatography A 1217, 4212-4222.

Jelić, A., Petrović, M., Barceló, D., 2012. Pharmaceuticals in Drinking Water Springer Berlin / Heidelberg, pp. 1-24.

Kagle, J., Porter, A.W., Murdoch, R.W., Rivera-Cancel, G., Hay, A.G., 2009. Biodegradation of Pharmaceutical and Personal Care Products. in: Laskin, A.I. (Ed.). Advances in Applied Mircobiology, Vol 67. Elsevier Academic Press Inc, San Diego, pp. 65-108.

Kinney, C.A., Furlong, E.T., Kolpin, D.W., Burkhardt, M.R., Zaugg, S.D., Werner, S.L., Bossio, J.P., Benotti, M.J., (2008). Bioaccumulation of Pharmaceuticals and Other Anthropogenic Waste Indicators in Earthworms from Agricultural Soil Amended With Biosolid or Swine Manure. Environmental Science & Technology 42, 1863-1870.

Kuster, M., López de Alda, M.J., Hernando, M.D., Petrovic, M., Martín-Alonso, J., Barceló, D., (2008). Analysis and occurrence of pharmaceuticals, estrogens, progestogens and polar pesticides in sewage treatment plant effluents, river water and drinking water in the Llobregat river basin (Barcelona, Spain). Journal of Hydrology 358, 112-123.

Lam, M.W., Tantuco, K., Mabury, S.A., (2003). PhotoFate: A New Approach in Accounting for the Contribution of Indirect Photolysis of Pesticides and Pharmaceuticals in Surface Waters. Environmental Science & Technology 37, 899-907.

Luthy, R.G., Aiken, G.R., Brusseau, M.L., Cunningham, S.D., Gschwend, P.M., Pignatello, J.J., Reinhard, M., Traina, S.J., Weber, W.J., Westall, J.C., (1997). Sequestration of Hydrophobic Organic Contaminants by Geosorbents. Environmental Science & Technology 31, 3341-3347.

Mateos-Ruiz, R.M., Lopez-Garcia, J.M., (2003). Retroceso de la intrusión marina debido a la substitución de aguas subterráneas por aguas residuales tratadas para el regadío de una zona agrícola. El Pla de Sant Jordi. Tecnología de la intrusión de agua de mar en los acuíferos costeros: Países mediterráneos, IGME, Madrid.

Murray, K.E., Thomas, S.M., Bodour, A.A., (2010). Prioritizing research for trace pollutants and emerging contaminants in the freshwater environment. Environmental Pollution 158, 3462-3471.

Musson, S.E., Campo, P., Tolaymat, T., Suidan, M., Townsend, T.G., (2010). Assessment of the anaerobic degradation of six active pharmaceutical ingredients. Science of The Total Environment 408, 2068-2074.

Nieto, A., Borrull, F., Pocurull, E., Marcé, R.M., (2010). Pressurized liquid extraction: A useful technique to extract pharmaceuticals and personal-care products from sewage sludge. TrAC Trends in Analytical Chemistry 29, 752-764.

Oppel, J., Broll, G., Löffler, D., Meller, M., Römbke, J., Ternes, T., (2004). Leaching behaviour of pharmaceuticals in soil-testing-systems: a part of an environmental risk assessment for groundwater protection. Science of The Total Environment 328, 265-273.

Pennsylvania Department of Environmental Protection, 2005. Environmental Science DatabaseSRC (2005) PhysProp. Organic regulated substances physical and toxicological properties.

Pérez-Carrera, E., Hansen, M., León, V., Björklund, E., Krogh, K., Halling-Sørensen, B., González-Mazo, E., (2010). Multiresidue method for the determination of 32 human and veterinary pharmaceuticals in soil and sediment by pressurized-liquid extraction and LC-MS/MS. Analytical and Bioanalytical Chemistry 398, 1173-1184.

Richardson, S.D., Ternes, T.A., (2011). Water Analysis: Emerging Contaminants and Current Issues. Analytical Chemistry 83, 4614-4648.

Rodríguez-Navas, C., Björklund, E., Forteza, R., Cerdà, V., (2012). Volatile organic compounds in landfill odorant emissions on the island of Mallorca. International Journal of Environmental Analytical Chemistry 92, 1-16.

Rodriguez-Navas, C., Forteza, R., Cerdà, V., (2012). Use of thermal desorption – gas chromatography – mass spectrometry (TD-GC-MS) on identification of odorant emission focus by volatile organic compounds characterisation. Chemosphere (*In press*).

Runnqvist, H., Bak, S.A., Hansen, M., Styrishave, B., Halling-Sørensen, B., Björklund, E., (2010). Determination of pharmaceuticals in environmental and biological matrices using pressurised liquid extraction—Are we developing sound extraction methods? Journal of Chromatography A 1217, 2447-2470.

Schultz, M.M., Painter, M.M., Bartell, S.E., Logue, A., Furlong, E.T., Werner, S.L., Schoenfuss, H.L., (2011). Selective uptake and biological consequences of environmentally relevant antidepressant pharmaceutical exposures on male fathead minnows. Aquatic Toxicology 104, 38-47.

Schwarzbauer, J., Heim, S., Brinker, S., Littke, R., (2002). Occurrence and alteration of organic contaminants in seepage and leakage water from a waste deposit landfill. Water Research 36, 2275-2287.

Simó, R., Colom-Altés, M., Grimalt, J.O., Albaigés, J., (1991). Background levels of atmospheric hydrocarbons, sulphate and nitrate over the western Mediterranean. Atmospheric Environment. Part A. General Topics 25, 1463-1471.

Thiele-Bruhn, S., (2003). Pharmaceutical antibiotic compounds in soils – a review. Journal of Plant Nutrition and Soil Science 166, 145-167.

Verlicchi, P., Galletti, A., Petrovic, M., Barceló, D., (2010). Hospital effluents as a source of emerging pollutants: An overview of micropollutants and sustainable treatment options. Journal of Hydrology 389, 416-428.

World Health Organization: Drinking-water Quality Committee, 2011. Pharmaceuticals in drinking water.

Yamamoto, H., Nakamura, Y., Moriguchi, S., Nakamura, Y., Honda, Y., Tamura, I., Hirata, Y., Hayashi, A., Sekizawa, J., (2009). Persistence and partitioning of eight selected pharmaceuticals in the aquatic environment: Laboratory photolysis, biodegradation, and sorption experiments. Water Research 43, 351-362.

Zhou, J.L., Zhang, Z.L., Banks, E., Grover, D., Jiang, J.Q., (2009). Pharmaceutical residues in wastewater treatment works effluents and their impact on receiving river water. Journal of Hazardous Materials 166, 655-661.

CHAPTER 4

SUMMARY OF RESULTS AND CONCLUSIONS

SUMMARY OF RESULTS AND CONCLUSIONS

In this dissertation, two different analytical methodologies have been developed, optimized and applied for the determination of different groups of organic pollutants with limited regulations if any: pharmaceutical residues and volatile organic compounds, in the aquatic and atmospheric environments of the Island of Mallorca (Spain, Mediterranean Sea). Analytical methods based on solid phase extraction and clean-up approaches, chromatographic separation techniques and selective mass spectrometry detection are presented and applied as suitable methodologies for the periodical environmental monitoring of organic compounds. Its immediate implementation within specific environmental regulations is assumed as urgent to control and amend current environmental pollution levels.

Besides every study described in Chapter 3 include its own individual conclusions, the most significant highlights and merits of the research compiled in this Doctoral Thesis are summarized below:

1. The use of SPE-LC-(ESI)-MS^2 and SPE-TD-GC-MS, for the environmental monitoring of pharmaceutical's residues and volatile organic compounds, by means of a solid phase extraction and clean-up steps ascertain excellent analytical features for environmental monitoring purposes, including low limits of detection and quantification, good extraction recoveries, linear fits, robustness over time, reproducibility and sample frequency.

2. To achieve the aimed analytical characteristics for the determination of volatile organic compounds by the use of commercially available solid sorbents Tenax® TA and Carboxen® 1000 followed by TD-GC-MS, a high-temperature loading strategy has been developed and optimized for the injection of liquid standards. This procedure guarantees high reproducibility and robustness over time, providing a high response factor and enabling the quantification by means of external standard calibration. Two comprehensive environmental occurrence studies to determine VOCs have been performed by means of the proposed high-temperature loading strategy, assuring the suitability of the system.

3. Commercially available solid sorbents Tenax® TA and Carboxen® 1000 were found useful for the extraction of a wide number of volatile organic compounds (up to 93 different compounds) with different physicochemical characteristics such as polarity,

vapour pressure and molecular weight. However the methodology was not suitable for the determination of other polar compounds like organic aliphatic acids, or gases such as H_2S or NH_3, thus commercially available colorimetric tubes (Dräger®) were applied for in-situ determination of the NH_3 and H_2S.

4. Commercial sorbents Oasis® HLB and Oasis® MAX were found to be useful techniques for the extraction of different organic pharmaceuticals from complicated environmental aquatic matrices, including landfill's leachates and marine waters. However it showed some limitations regarding extraction and clean-up of some polar organic chemicals in marine waters, owing the salinity of the matrix.

5. Medicinal pharmaceuticals and volatile organic compounds have been detected, for the first time, as critical environment pollutants in Mallorca. It ascertains the necessity of restrictive regulations, with the goal to (i) reduce current emissions and (ii) continuously monitor environmental occurrence levels by periodic assessment analyses. Municipal solid waste landfills are found massive emitters of VOCs to specific atmospheric environments, which pose a constant risk for surrounding population, as well as flora and fauna, through e.g. photochemical smog generation. Assuming that waste processes produce over 1-2% of the total emissions of VOCs in Europe, there is still much work to do to reach the desired clean environments.

6. Pollution pathways described from the pharmaceutical's residues released by wastewater treatment plants and landfills have shown the problematic of the aquatic contamination of Natural Areas and groundwater, which might pose unknown severe risks. Current knowledge over pharmaceutical's risk assessment is still short to clearly understand the real impact of organic pollutants. Since wastewater treatments technologies are not efficiently removing organic pharmaceuticals (and by extension many other emerging contaminants), the re-use of reclaimed water for whatever purposes can be considered a pollution source for the rest of the aquatic environment in Mallorca, therefore, emissions must be immediately reduced as much as possible.

7. A novel methodology has been developed and applied for the identification of odorant emission focuses, based on the characterisation of volatile organic compounds in the air. A pattern recognition technique on the basis of a Principal Components Analysis (PCA) enables the correlation of a specific ambient air with the emission source. This procedure offers an alternative tool to the local Governments in order to spread over sanctions to emitting facilities/industries/processes. Collaboration between local

Governments, research centres and industrial companies (VOC emitters) has shown a necessary requirement and the most productive way to reach the proposed objectives.

8. No positive correlation was found between odour units, measured by dynamic olfactometry, with the concentration of 42 different VOCs. These evaluations involve multiple factors generating big bias: (1) landfills are extremely heterogeneous samples with different microorganisms' processes beneath the sampled surface, thus VOCs composition might be completely different even at similar spots; (2) odorant measurements involve subjective determination by human panellists which may produce bias on the reliability of the measurements; (3) the nearly unaffordable number of VOCs presented in landfill matrices makes extremely difficult to find a suitable methodology capable to quantify all of them; (4) the correlation probably do not fit a linear interaction owing to possible interactions between odorant compounds, e.g. causing synergic effects.

Future work along the lines of research conducted in the framework of this Doctoral Thesis is devoted to:

- Development and application of a suitable TD-GC-MS methodology for the environmental analysis of polycyclic aromatic hydrocarbons (PAHs) in air and determination of the partition coefficient between air – solids in suspension (particulate matter, PM_x)
- Development of an on-line dispersive liquid-liquid microextraction (DLLME) procedure for the analysis of PAHs in water by exploiting multisyringe flow injection analysis (MSFIA) techniques hyphenated to GC-MS detection.

ANNEX I

List of publications obtained in this doctoral thesis, included in the introduction and the experimental part, which are published or submitted for publication in different scientific journals.

I. *Volatile organic compounds in landfill odorant emissions on the island of Mallorca.*
Authors: Carlos Rodríguez-Navas, Erland Björklund, Rafel Forteza, Víctor Cerdà.
Journal: International Journal of Environmental Analytical Chemistry.
Year: 2012. **Volume:** 92. **Pages:** 1-16

II. *Use of thermal desorption–gas chromatography–mass spectrometry (TD–GC–MS) on identification of odorant emission focus by volatile organic compounds characterization.*
Authors: Carlos Rodríguez-Navas, Rafel Forteza, Víctor Cerdà.
Journal: Chemosphere. **Year:** 2012. (*In press*).

III. *Implementation and optimization of a high-temperature loading strategy of liquid standards in the quantification of volatile organic compounds using solid sorbents.*
Authors: Carlos Rodríguez-Navas, Rafel Forteza, Víctor Cerdà.
Journal: Journal of Separation Sciences. *(Submitted)*

IV. *Pollution pathways of pharmaceutical residues in the aquatic environment on the island of Mallorca, Spain.*
Authors: Carlos Rodríguez-Navas, Erland Björklund, Søren A Bak, Martin Hanse, Kristine A. Krogh, Fernando Maya, Rafel Forteza, Víctor Cerdà.
Journal: Archives of Environmental Contamination and Toxicology. *(Submitted)*

List of conference contributions obtained in this doctoral thesis.

I. Optimization of thermal-desorption experimental conditions in GC-MS analysis of environmental samples.
Authors: Carlos Rodríguez-Navas, Gabriel Vivó-Truyols, Rafel Forteza, Víctor Cerdà.
Conference: 5th EuroAnalysis.
Year: 2009. **Location:** Innsbruck, Austria. **Type of communication:** Poster

II. Characterization of odorant emissions from environmental technologic center by TD-GC-MS.
Authors: Carlos Rodríguez-Navas.
Conference: Les Doctoriales Transfrontalieres.
Year: 2009. **Location:** Pollensa, Spain. **Type of communication:** Poster

III. Study of the volatile organic compounds (VOCs) emission from an urban solid waste landfill in Mallorca (Spain) by TD-GC-MS.
Authors: Carlos Rodríguez-Navas, Rafel Forteza, Víctor Cerdà.
Conference: 28th International Symposium on Chromatography.
Year: 2010. **Location:** Valencia, Spain. **Type of communication:** Poster

IV. Occurrence of PPCPs in the environment on a Mediterranean Sea Island.
Authors: Carlos Rodríguez-navas, Martin Hansen, Fernando Maya, Søren Bak, Rafel Forteza, Victor Cerdà, Kristine A. Krogh, Erland Björklund.
Conference: 3rd International Conference on Occurrence, Fate, Effects and Analysis of Emerging Contaminants in the Environment (EMCON).
Year: 2011. **Location:** Copenhagen, Denmark. **Type of communication:** Lecture

V. Study of VOCs in the Ambient Air of a Waste Treatment and Disposal Zone in Mallorca (Spain) by TD-GC/MS.
Authors: Carlos Rodríguez-navas, Rafel Forteza, Victor Cerdà.
Conference: 13as Jornadas de Análisis Instrumental
Year: 2011. **Location:** Barcelona, Spain. **Type of communication:** Lecture

VI. Study of the volatile organic compounds (VOCs) in the ambient air of a waste treatment technologies zone in South-East Mediterranean Island (Mallorca, Spain) by TD-GC-MS.
Authors: Carlos Rodríguez-Navas, Rafel Forteza, Víctor Cerdà.
Conference: IUPAC International Congress on Analytical Sciences (ICAS).
Year: 2011. **Location:** Kyoto, Japan. **Type of communication:** Poster

Other contributions on conferences not included in this Thesis:

VII. Multisyringe flow injection technique allows fast and sensitive ion chromatographic separations based on the use of surfactant coated short monolithic columns and post-column chemiluminiscence detection.
Authors: Fernando Maya, Carlos Rodríguez-Navas, José Manuel Estela, Víctor Cerdà.
Conference: 5th EuroAnalysis .
Year: 2009. **Location:** Innsbruck, Austria. **Type of communication:** Poster

VIII. A study of the use of optical fibers with MSFIA to spectrophotometrycal determination of sulfides in environmental samples..
Authors: Carlos Rodríguez-Navas, Rafel Forteza, Víctor Cerdà.
Conference: 16th International Conference on Flow Injection Analysis (ICFIA).
Year: 2010. **Location:** Pattaya, Thailand. **Type of communication:** Poster

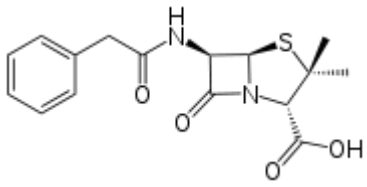
IX. **Conference:** Flow Analysis XI
Year: 2009. **Location:** Pollensa, Spain. **Type of communication:** Attendee/Staff

X. **Conference:** 1st International Conference on Analytical Proteomics (ICAP)
Year: 2009. **Location:** Lisbon, Portugal. **Type of communication:** Attendee/Staff

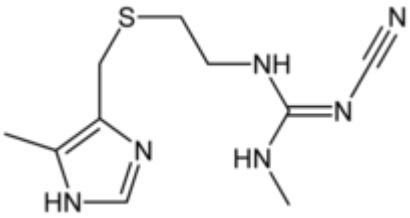
XI. **Conference:** II International Workshop on Analytical Miniaturisation (“lab on a chip”)
Year: 2010. **Location:** Oviedo, Spain. **Type of communication:** Attendee

ANNEX II

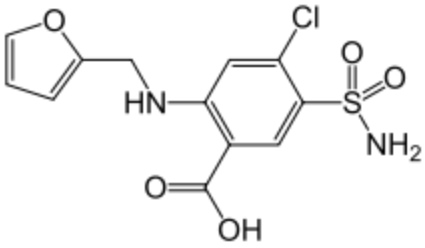
Structure of the pharmaceutically active compounds (PhACs) determined in this Doctoral Thesis (Section 3.1):



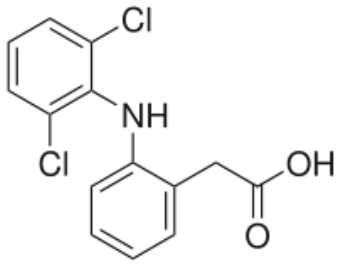
Penicilin G (Antibiotic)



Cimetidine (Anti-acid reflux)



Furosemide (Diuretic)



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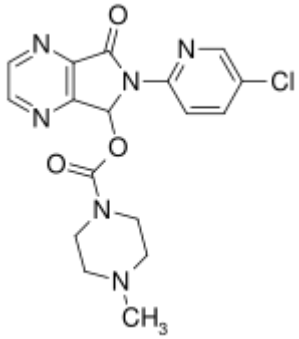
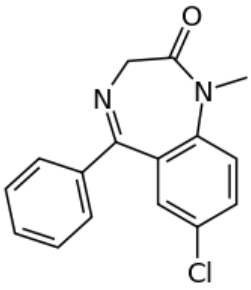
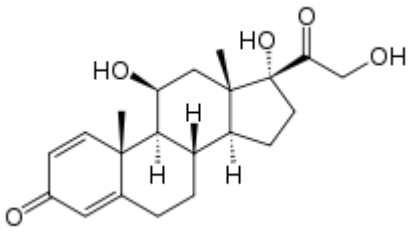


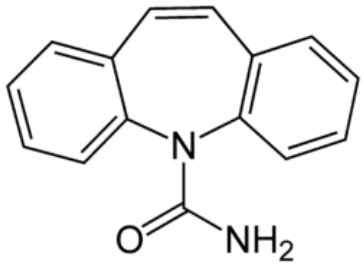
Zopiclone (Anxiolytic)



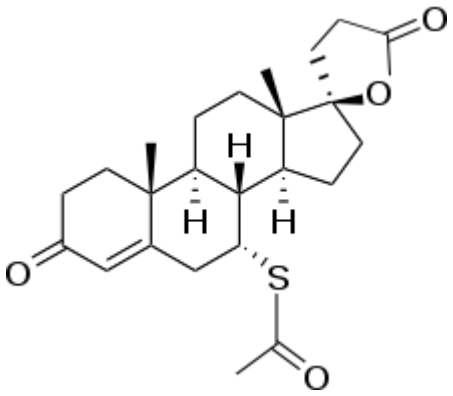
Diazepam (Tranquilizer)



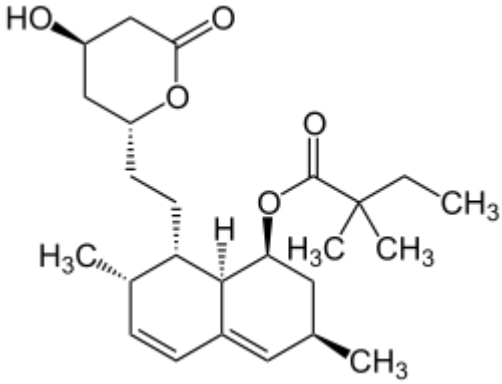
Prednisolone (Corticosteroid)



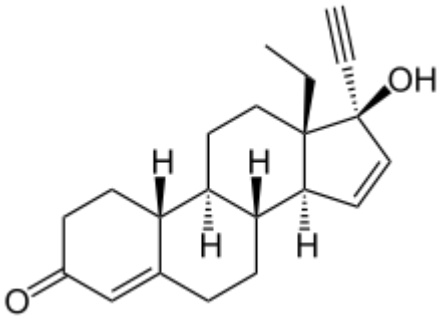
Carbamazepine (Antiepileptic)



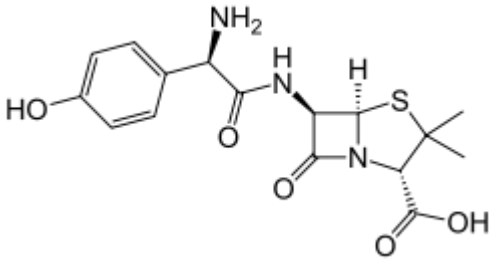
Spironolactone (Diuretic)



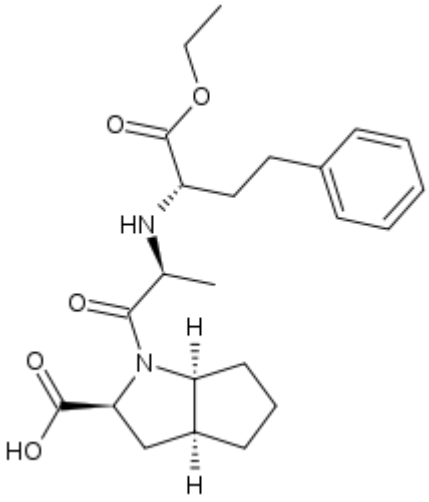
Simvastatin (Anti-hyperlipidaemic)



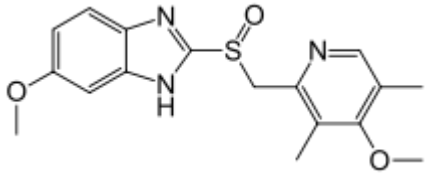
Gestodene (Contraceptive)



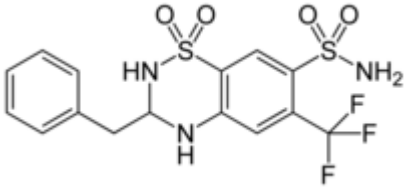
Amoxicillin (Antibiotic)



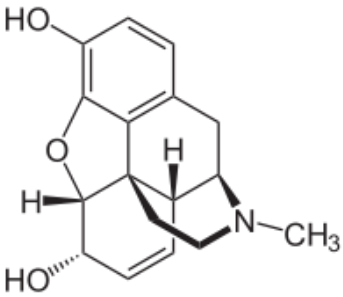
Ramipril (Cardiac Drug)



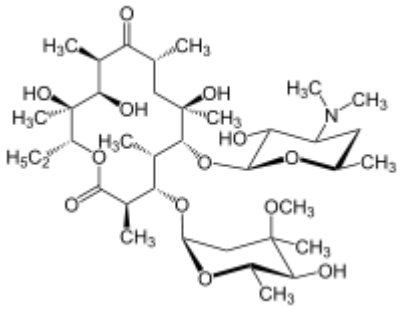
Omeprazole (Proton pump inhibitor)



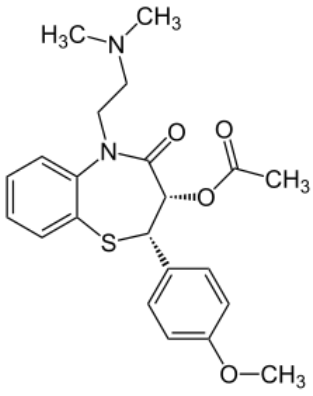
Bendroflumethiazide (Diuretic)



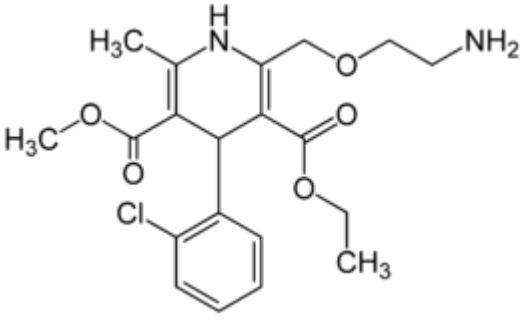
Morphine (Analgesic)



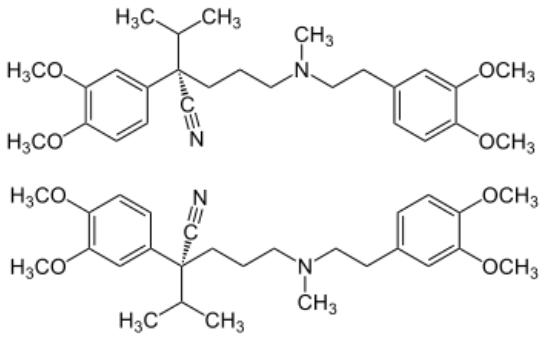
Erythromycin (Antibiotic)



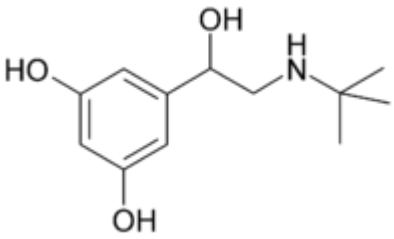
Diltiazem (Anti-hypertensive)



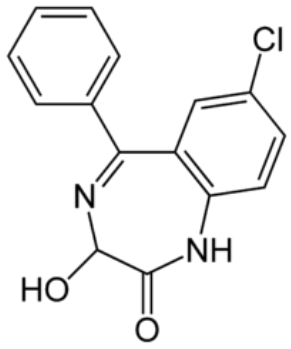
Amlodipine (Anti-hypertensive)



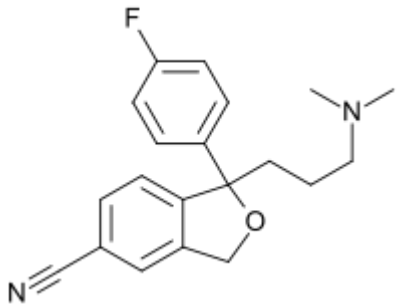
Verapamil (Anti-hypertensive)



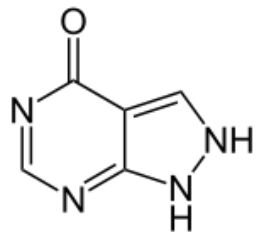
Terbutaline (Anti-asthmatic)



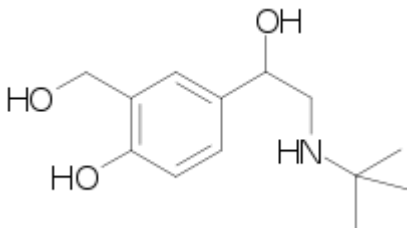
Oxazepam (Tranquilizer)



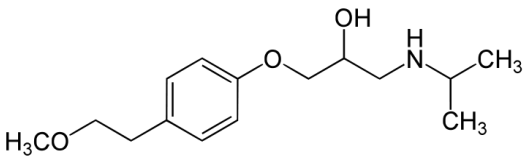
Citalopram (Tranquilizer)



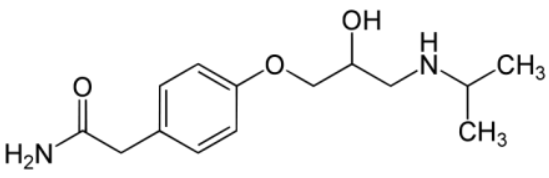
Allopurinol (Rheumatic)



Salbutamol (β-Agonist)



Metoprolol (β-Blocker)



Atenolol (β-Blocker)

ANNEX III

List of Abbreviations

AnVOC	Anthropogenic Volatile Organic Compound
AOP	Advanced Oxidation Processes
APCI	Atmospheric-Pressure Chemical Ionisation
API	Atmospheric Pressure Interface
APPI	Atmospheric-Pressure Photoionization
ASPDE	Accelerated Solid Phase Dynamic Extraction
ASTM	American Society for Testing Materials
BAT	Best Available Techniques
BSTFA	N,O-Bis(trimethylsilyl)trifluoroacetamide
BTEX	Benzene, Toluene, Ethylbenzene and Xylenes
BVOC	Biogenic Volatile Organic Compound
CAFE	Clean Air for Europe
CAS	Chemical Abstract Service
CCL	Candidate Contaminant List
CE	Capillary Electrophoresis
CEN	European Committee for Standardization
CFC	Chlorofluorocarbon
CIT	Cold Ion Trap
CLTRAP	Convention on Long-Range Transboundary Air Pollution
DAD	Diode Array Detector
DBP	Disinfection By-products
DIMS	Direct Injection Mass Spectrometry
DLLME	Dispersive Liquid-Liquid Microextraction
DOAS	Differential Optical Absorption Spectrometry
DS-MS	Direct air-sampling Mass Spectrometry
DVE	Dispersive Vapour Extraction
EAP	Environmental Action Programmes
EC	Emerging Contaminant
EC (in laws)	European Council
ECD	Electron Capture Detector
EDC	Endocrine Disrupting Compounds

EEA	European Environmental Agency
EI	Electronic Ionisation
EIONET	European Environmental Information and Observation Network
ELV	Emission Limit Values
EME	Electro membrane
EMEP	European Monitoring Evaluation Programme
EN	European Standard
EPA	Environmental Protection Agency
E-PRTR	European Pollutant Release and Transfer Register
ESI	Electrospray Interface
EU	European Union
FIA	Flow Injection Analysis
FID	Flame Ionisation Detector
FTIR	Fourier Transform Infrared Spectrometry
GC	Gas Chromatography
HEAL	Health and Environmental Alliance
HF	Hollow Fibre
HILIC	Hydrophilic Interaction Chromatography
HPLC	High Performance Liquid Chromatography
HSSE	Headspace Sorptive Extraction
hυ	Radiation
i.d.	Inner Diameter
IPPC (Directive)	Integrated Pollution Prevention and Control (European Directive)
IR	Infrared
IRIS	Integrated Risk and Information System
ISO	International Standardization Organisation
IT	Ion Trap Analyser
IUPAC	International Union of Pure and Applied Chemistry
LC	Liquid Chromatography
LCP (Directive)	Large combustion Plants (European Directive)
LOD	Limit of Detection
LOQ	Limit of Quantification
LPCI	Low-Pressure Chemical Ionisation
LPME	Liquid Phase Microextraction
MEPS	Microextraction Packed Syringe
MESI	Membrane Extraction with a Sorbent Interface

MIMS	Membrane Introduction Mass Spectrometry
MIP	Molecular Imprinted Polymer
MS	Mass spectrometry
MS^2 or MS/MS	Tandem Mass Spectrometry
MSD	Mass spectrometry Detection
MSFIA	Multisyringe Flow Injection Analysis
MSW	Municipal Solid Waste
MTBSTFA	N-(tert-butyldimethylsilyl)-N-methyltrifluoroacetamide
NCI	Negative Chemical Ionisation
NEC Directive	National Emission Ceiling Directive
NIOSH	US National Institute for Occupational Safety and Health
NMR	Nuclear Magnetic Resonance
NMVOC	Non-Methane Volatile Organic Compound
o.d.	Outer Diameter
OTV	Odour Threshold Value
OU_E	European Odour Units
PA	Proton Activity Coefficient
PAH	Polycyclic Aromatic Hydrocarbon
PAN	Peroxiacetyl Nitrates
PC	Principal Component
PCA	Principal Components Analysis
PCB	Polychlorinated Biphenil
PCDD	Polychlorinated Dibenzo-Dioxin
PCDF	Polychlorinated Dibenzo-Furane
PCP	Personal and Care Products
PDMS	Polydimethylsiloxane
PFBBr	Pentafluorobenzoyl Bromide
PFBOCl	Pentafluorobenzoyl Chloride
PFC	Polyfluorinated Compounds
PhAC	Pharmaceutically active compound
PID	Photochemical Ionisation Detector
PLE	Pressurized Liquid Extraction
PM_x	Respirable Particulate Matter
PNME	Fibre-Packed Needle Microextraction
POCP	Photochemical Ozone Creation Potential
POP	Persistent Organic Pollutants

ppb	Parts per Billion
PPCP	Pharmaceuticals and Personal Care Products
ppm	Parts per Million
PTR	Proton Transfer Reaction
PTV	Programmable Temperature Valve
Q	Quadrupole Analyser
QqLIT	Quadrupole-Quadrupole-Linear Ion Trap Analyser
QqQ	Triple Quadrupole Analyser
Q-TOF	Quadrupole-Time of Flight Analyser
SBSE	Stir Bar Sorptive Extraction
SD	Solvent Desorption
SIA	Sequential Injection Analysis
SIFDT	Selected Ion-flow Drift-Tube
SIFT	Selected Ion-Flow-Tube
SLM	Supported Liquid Membrane
SOC or SVOC	Semi Volatile Organic Compound
SPDE	Solid Phase Dynamic Extraction
SPE	Solid Phase Extraction
SPME	Solid Phase Microextraction
STP	Sewage Treatment Plant
TD	Thermal Desorption
TFEI	Task Force Emission Inventory
TFME	Thin Film Microextraction
TMAH	Trimethylaniline Hydroxide
TMS	Trimethylsilyl
TMSH	Trimethylsulfonium Hydroxide
TMS-Oxime	Trimethylsilyl-Oxime
TOF	Time of Flight Analyser
TP	Transformation products
TPD	Temperature Programmable Desorption
TSP	Total Suspended Particles
WWTP	Wastewater Treatment Plant